ANNALS OF THE
AMERICAN CONFERENCE
OF GOVERNMENTAL
INDUSTRIAL HYGIENISTS

VOLUME 9

THRESHOLD LIMIT VALUES — DISCUSSION AND THIRTY-FIVE YEAR INDEX WITH RECOMMENDATIONS

Edited by
MARSHALL E. LaNIER

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The American Conference of Governmental Industrial Hygienists

The ACGIH, as it invariably is called, is a professional society whose members primarily are industrial hygienists employed by Federal, State, and local governments and universities. Eligible for associate membership are those working for governmental bodies in related activities such as safety. Technical and student memberships also are available.

The principal work of ACGIH is carried out by committees. The best known of these are the Committee on Industrial Ventilation and the Committees on Threshold Limit Values for Chemical Substances and Physical Agents.

The Committee on Industrial Ventilation publishes *Industrial Ventilation — A Manual of Recommended Practice*, which is revised biennially.

The Commmittees on Threshold Limit Values develop the annual list of TLVs®, with a separate publication documenting these values.

The Committee on Air Sampling Instruments publishes and periodically revises their publication, *Air Sampling Instruments.*

The sale of publications from these committees supports their activities and also the activities of the many other ACGIH committees, covering virtually every aspect of occupational health.

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American Conference
of Governmental
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Threshold Limit Values — Discussion and Thirty-five Year Index with Recommendations

Edited by:

Marshall E. LaNier

AMERICAN CONFERENCE OF GOVERNMENTAL INDUSTRIAL HYGIENISTS

CINCINNATI, OHIO
1984

The Annals series will present the latest state-of-the-art information on research and practical applications of science in the field of occupational health. Each issue will be the proceedings of an important symposium, conference, or meeting sponsored by the American Conference of Governmental Industrial Hygienists or other leading professional organizations in, or allied with, the occupational health field. Contents will deal with subjects of current interest. The Annals series will become a valued addition to the international scientific literature.

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CONTENTS

Growth of TLVs and toxic data 1950-1960

TLVs of the 1960s

TLVs and occupational standards 1970 through 1981

Herbert E. Stokinger Lectures

Thirty-five year index with recommendations

1946

1947

Appendices

The American Conference of Governmental Industrial Hygienists (ACGIH) believes it has a responsibility to provide an open forum for discussion of scientific questions. The positions taken by the participants in the reported portions of this text are their own and not those of ACGIH. ACGIH has no intent to influence legislation by providing such forums.

Preface

This publication gathers into one volume the first thirty-five years of recommended threshold limit values developed by and for the American Conference of Governmental Industrial Hygienists. This volume also contains the values used by the various states at the time when the first Threshold Limit Values (TLV) Committee was developing its initial list; the list used by the Defense Department during World War II; the first major comparison of values developed by a number of states with the U.S. Public Health Service values and the American Standards Association Z-37 Committee recommendations; and a group of selected articles from the literature.

The articles selected to appear in the text are considered representative of literature available during the early days of the TLV Committee. Many articles were reviewed and considered for inclusion. A list of some references that were reviewed and not selected also appears in the Appendices section. The articles which were selected for this text are reproduced in their entirety. It can be seen from this literature that some of the scientific thinking has changed since the TLV Committee was conceived, while by the same literature we see that some present day opinions are reinforced.

History reveals that it was known since before the bible was written that certain contaminants in the work environment could affect worker health. At that time some effort was made to provide protective equipment. However, even after the passing of thousands of years the magnitude of the problem still is not completely known.

The mechanism of injury which follows a hazardous exposure at the work site has not always been completely understood. However, with the refinement of analytical tools more can be predicted with certainty about how a given contaminant reacts in the body. Thus, the science associated with industrial hygiene is growing. Yet, when one observes the length of time it has been known that occupational health problems should be controlled, it would seem that more research would have been devoted to this field and the knowledge gained more widely disseminated. Such a goal has not been achieved. In fact, that was probably part of the stimulus for the beginning of ACGIH.

The American Conference of Governmental Industrial Hygienists (ACGIH) has had worker health as its major concern since it was organized in the late 1930s. In the middle '30s state and federal industrial hygienists would meet to discuss items of mutual interest. Since there were no official exposure standards required by Federal law, each situation encountered was treated as a special study. Some of the more common chemical hazards were evaluated and, in more than one state, similar values were developed and used as control guides. Thus, uniformity started as a result of these meetings.

As has been mentioned, some states were establishing their own values. Pennsylvania was one of these states. That state's Department of Health not only set its own exposure limits, but created the United States' first short-term exposure limits (STLs). These values served as background for the TLV Committee's STELs.

It must not be construed that ACGIH was the only organization developing "safe limits." Each group developing American industrial air limits for workplace air contaminants had its own criteria or method for interpretation. None stressed the fact more than ACGIH that their limits were guides to be used in arriving at a qualified control decision and not to be a part of rules and regulations. It should be noted that, although ACGIH continually recommended not to incorporate the actual number into law, many

local, state, national, and even foreign governments did. In adopting the value as law the situation most often omitted was a method of updating the number when new information became available. This probably stems from the fact that people may fail to read and use the preface to the TLV booklet.

Another misuse of the TLVs is their application as community air pollution guides. As early as 1954, the ACGIH emphasized in the preamble that such use was unwarranted since the population exposed and the circumstances surrounding the exposure were not like the average work setting.

The TLV Committee for Physical Agents came about as a separate group in the late 1960s and continues to the present time. This volume also contains those physical agent TLVs recommended through 1981. Although the articles in the text were not specifically selected with the physical agents in mind, they do cover them. The TLVs for physical agents are developed to protect most workers, just as the TLVs for chemical substances are developed to protect most workers. No single value above zero will protect everyone. With that caveat in mind, both the chemical substances and physical agents are covered by the literature selected.

The Thirty-five Year Index portion of this volume lists the first ACGIH recommended MAC values and traces their development into the TLVs. The years 1946 through 1981 are listed individually in this section and contain such entries as the Committee report for that year, a list of the values changed from the previous year, and/or the complete list of recommended values. In addition, the 1961, 1968, 1971, 1976, and the 1981 TLV booklets have been reproduced in their entirety, as well as the first Physical Agents TLV booklet from 1969.

It is hoped that this volume will stimulate constructive dialogue so that future efforts in developing and using occupational exposure recommendations (e.g., TLVs) will result in increased real worker health protection.

—Marshall E. LaNier

Cincinnati, Ohio
June 1984

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INTRODUCTION

The introduction has been narrowed to three articles. The first is not about TLVs but more about how the American Conference of Governmental Industrial Hygienists was created. It begins to set the stage for all to see how and why there was a need that could be satisfied through organized effort. There was no single official governmental worker exposure standard setting unit for most workers. A number of people perceived a need to have conformity of action among the states. The second article was written and presented by the first TLV committee chairman. It provides a background for the development of the first list. It also documents the sincere desire to develop and maintain scientific integrity which has been continued to the present. The third article (the fourth Herbert E. Stokinger Lecture) discusses most adequately the past, the present, and develops a plan with a look to a possible bright future.

What the ACGIH has done for industrial hygiene*

JOHN J. BLOOMFIELD
Regional Consultant in Industrial Hygiene, The Institute of Inter-American Affairs

Some of the old-timers among us can probably remember that ACGIH meeting in 1948, which was held in Boston. At the last minute someone got the idea that it would be a good thing to have a banquet, and as I recall, we did have one at the Old Oyster House of the famous seafood. Of course, no banquet is complete without some formal entertainment, but since our treasury, as usual in those days, was very low, I was persuaded to furnish the entertainment in the form of an account of my adventures in South America, where I had spent nearly all of the previous year as a consultant for the Institute of Inter-American Affairs. As I recall that event, our treasury was so low that I even had to pay for my own dinner. Little did anyone think at the time that we were actually ten years of age.

With the exception of a few of the old guard who are here tonight, I don't suppose that very many people remember how the ACGIH got started, and how it grew to its present stature, and, believe me, it does have stature. I shall assume the prerogative of an anniversary speaker and turn the pages back for a few minutes to give you a little history of our organization and why it was created in the first place.

The ACGIH was really born of necessity. Prior to 1936, industrial hygiene activities in the United States were confined to research work, both in the laboratory and in the field, by the U.S. Public Health Service, the United States Bureau of Mines and one or two universities. Very little application of these findings was in practice in the States, because at that time there were only five States and one city engaged in official industrial hygiene work. In all probability, this limited work in industrial hygiene also accounted for the paucity of instruction in that branch of public health.

Now, as most of you know, the actual responsibility for safeguarding the health of our labor force rests chiefly upon State and local governments. In 1936, when funds were made available by the Social Security Act for the development and extension of all phases of public health work, the U.S. Public Health Service, in cooperation with the Conference of State and Provincial Health Authorities of North America, inaugurated a program designed to establish active industrial hygiene work in State and local health departments.

One of the most pressing problems presenting itself at that time in the development of industrial hygiene services in State and local governments was the lack of trained personnel to evaluate and control the then inevitable hazards associated with industrial work. The burden fell primarily upon the Public Health Service, because of its long experience in industrial hygiene work and its administration of social security funds for this purpose.

Realizing the urgency of the problem, and believing that some standard method of procedure should be set up for the guidance of industrial hygiene workers, the Public Health Service decided to give a short course of instruction to personnel selected by the various State health deparmtents for work in this field. Accordingly, a four-week seminar was held during the summer of 1936, which consisted of lectures on industrial hygiene administration, health hazards, control methods, and similar subjects, as well as laboratory demonstrations of instruments used for investigative and control work. In the summer of 1937, a second seminar was held, since the number of persons engaged in industrial hygiene had increased from approximately forty to more than a hundred. Since these seminars could do no more than introduce the public health worker to industrial hygiene, additional training facilities were furnished by the Public Health Service. This training took the form of cooperative field investigations in various States. For example, studies were conducted in West Virginia, with the industrial hygiene personnel of

* Presented at the banquet of the ACGIH on the occasion of the 20th Anniversary meeting of this organization at Atlantic City, NJ, April 20-22, 1958. Published in the *Am. Ind. Hyg. Assoc. J.* 19:338-344 (1958). Reprinted by permission of the American Industrial Hygiene Association.

that State, on the health of workers in the ceramic industry. Abestosis was studied in North Carolina and South Carolina. The hazards in the hatters' fur carroting and felt hat industry were investigated in Connecticut, and, in 1939, three studies were conducted in cooperation with the Utah State Board of Health, on the problems in the metal and coal-mining industries, and in metal smelting and refining. Such studies served a dual purpose. The United States Public Health Service was fulfilling its function of conducting basic research, since these studies yielded information which could be applied on a national scale, and, at the same time, the State personnel had an opportunity to receive training in the practice of industrial hygiene and to make a good start in the evaluation and control of health hazards in the industries of the State in question.

During the last week of the second seminar in 1937, we came to the conclusion that we should continue these annual seminars but perhaps hold them under the auspices of a non-official organization, similar to the annual Conference of State Sanitary Engineers, which meets yearly with the Division of Sanitary Engineering of the United States Public Health Service. As a matter of fact, in writing the constitution for the ACGIH, we used the constitution of the Conference of State Sanitary Engineers as a guide. An organization of this sort can very often accomplish things which an organization of more official character is unable to do, because of certain limitations imposed upon official organizations. Two organizations which illustrate this point are the Conference of State & Territorial Health Officers, which is an official organization meeting with the Surgeon General of the Public Health Service every year by an act of Congress as in contrast to the non-official State and Provincial Health Authorities of North America. The latter very often makes statements and takes action on matters which the former would not dare to do, even though the same people are talking.

The first annual meeting of our Conference was held in Washington June 27-29, 1938. By that time, believe it or not, we had been able to organize twenty-eight industrial hygiene units throughout the various States and at the first meeting these units were represented by forty-three members, one associate, and six guests. The Executive Committee held its first meeting in my home, and that year the custom began of making the Executive Committee meeting, a dinner meeting, except that in this first year the dinner was held after the meeting at a well known suburban restaurant know as "Mrs. Kay's Toll House Tavern." We had several drinks at my home following the meeting and those must have stimulated all of us to go "all out" on what we ordered, which as I remember, consisted mostly of what all good Americans like; beefsteak, baked potatoes, apple pie, and so on, washed down with sparkling Burgundy. When the bill appeared, it was passed on to me, since I had done all the arranging and was the secretary-treasurer. Much to my consternation, the bill was more than I could pay and then and there I instituted the custom, which I see still holds, of making the Conference pay for the dinner of the Executive Committee. In this particular instance, in order to pay the bill, I began collecting dues from the Executive Committee members and was just barely able to make out with what I collected and with the money I personally had in my pocket book. In those early days our treasury was always bare. As a matter of fact, even two years later, in 1940, the balance at the end of the year was only $19.05, and so it went along for a good many years, until our Industrial Ventilation Committee put us in the "black." In reviewing the 1957 Transactions, I noted that the membership last year reached an all-time high of 374; (today it is more than 400) and that the Conference had a fat balance of six thousand three hundred and eight-two dollars and seventy cents. Of course, the dollar is not worth today what it was twenty years ago, but even so, six thousand and some dollars is not "just hay."

With this much of a background on the early beginnings of our Conference, we might very well ask ourselves whether we, as an organization, have followed the road carved out for us by the founding fathers and what we have done with the heritage left us by the organizers of our association. The objectives of the Conference as set forth in the Constitution in 1938 and reaffirmed in the revised Constitution in 1951, tell us to go forth and,

> *"promote industrial hygiene in all its aspects and phases; to coordinate industrial hygiene activities . . . by official federal, State, local and territorial industrial hygiene agencies; to encourage the interchange of experience among industrial hygiene personnel in such official organzations; to collect and make*

accessible to all governmental industrial hygienists such information and data as may be of assistance to them in the proper fulfillment of their duties . . ."

Now, just how did the Conference proceed to achieve the above objectives? And how well have we succeeded?

At the time the Conference was created twenty years ago, there had already been amassed a considerable backlog of valuable information concerning the health hazards associated with exposure to some of the classical occupational hazards and the means of controlling them. The spectacular radium dial painting cases had already been studied and regulations drawn up for the safe use of radium paint in industry. The classic studies of Leonard Greenburg on benzol poisoning in industry focussed our attention on this extremely useful but very dangerous solvent. Then, too, by that time we had behind us the investigations of the Division of Industrial Hygiene of the United States Public Health Service concerning the dusty trades and the Silicosis Conference which did so much to publicize the notoriously bad working conditions on some of our industries where silica and its compounds were encountered. The first reports on the result of the National Health Inventory were being issued about that time and these included the Occupational Morbidity and Mortality studies which the Industrial Hygiene Division of the Public Health Service had worked on.

The Conference had no more than begun to learn how to walk when, in 1940, it was obliged to concern itself with the trememdous problems brought about by the defense effort which our country was making at that time. World War II taxed the energies of every organization and of every able bodied man and woman. Even before the "Day of Infamy," those of us in public health activities related to defense measures realized that the military had priority on manpower and for that reason it was up to the Public Health Service to jump into the breach with lease-lend equipment and personnel. At the height of the war, we had as many as seventy professional individuals on loan to the various States to help them carry on industrial hygiene work in the war effort.

The old maxim "It is an ill wind that does not blow some good" perhaps holds more truth for industrial hygiene than for many other activities. It seems almost axiomatic that national crises involving social and individual hardships and sacrifices often result in progress which would not have occurred otherwise, or at least would have been delayed. Industrial hygiene got its real beginnings in this country at the time of World War I and got off to a good start at the time of the depression which began in 1929 and which resulted in many social security benefits, including those for industrial hygiene and public health. World War II gave us the opportunity to demonstrate that our profession is here to stay. The obvious need for healthy manpower, and safe and healthy working conditions was our cup of tea, as they say in literary circles.

In looking back over the past two decades of the activities of our organization, we can really be proud of many of our accomplishments. Starting with practically no trained professional personnel we were able in a relatively brief period to muster several hundred persons who with a limited amount of training and experience could cope with the many problems inherent to our war effort. The war also gave us an opportunity to organize and develop industrial hygiene units where they had never before existed, so that by the end of the war we had in this country a network of such units established throughout the Union, in nearly every State, in large industrial cities and in several countries.

Now, I feel that we were able to accomplish all these things because from our very beginning we realized that our real strength as official agencies lay not in large numbers but in our ability to work uniformly and as a team, that we had to operate among forty-eight States. Each perhaps with different legal requirements as to industrial hygiene practices.

From the very beginning of our organization we realized that one of the major functions of our group was the development of standard practices among the various units. For that reason, even during the first year we organized various standing committees to deal with problems of administration, such as those concerning professional qualifications of industrial hygiene personnel, which were very useful in giving our people status within the Merit Systems which were then being developed in the States. It was in those days too that the

Committee on Threshold Limits began to function and, as all of you know today, this very important work has resulted in the annual review and publication of limits of several hundred toxic substances with which the industrial hygienist has to deal in his daily work. The work of this committee has been recognized by the publication of its finding annually and their use throughout the world. The general industrial hygiene code developed by the Committee on Uniform Codes as well as those covering special exposures, or industrial processes, have also achieved national status. Other accomplishments of this character deal with such subjects as standard methods of analysis, instumentation, the uniform reporting of industrial hygiene activities and the uniform collection of occupational disease reports. Perhaps the most outstanding accomplishment of the Conference resulted from its Committee on Industrial Ventilation, which won the first award of the Conference for its outstanding work. To say nothing of the fact that the fruits of the committee's work — the *Manual of Industrial Ventilation* — has put our group on a sound financial basis. Other accomplishments of the Conference have resulted in the development of standard labelling procedures and uniform administrative practices, such as the promotion of small plant health services, uniform records and reports in industry and workers' health information. Today our standing committees are concerned with such additional problems as agricultural health, air pollution, the epidemiology of occupational diseases, and ionizing radiation.

In this manner, I think we did a pretty good job of achieving the objectives of the Conference with respect to the coordination of industrial hygiene activities, with the collection and dissemination of information, and through our annual meetings we were able to encourage the interchange of our experiences. Our various committees and the results of their work filled a vacuum, since the ACGIH was the first to gather the mass of data needed.

I also believe that our Conference, made up as it is of a variety of public health workers, has demonstrated that industrial hygiene is not the exclusive monopoly of any one profession but requires, for its successful appplication, the collaboration of various public health specialists, such as physicians, engineers, chemists, nurses, physicists, and others. Each of these has a specialized function to perform, but essentially they work as a team, each contributing his skill to the study of the hazard and its eventual control. This team approach has been one of the major contributions of the United States to the advancement of industrial hygiene as we know it today.

So much for the credit side. If I were to list anything at all on the debit side, it would be perhaps to mention that the State and local industrial hygiene units do not appear to be as strong and as vigorous as they were at the end of the war. Undoubtedly, this is due to two facts: we have lost many persons from the States to industry, and the various branches of the Defense Department, such as the Army, the Navy and the Air Force, have now developed their own industrial hygiene services. Many of the industrial hygienists among the latter originally came from the civilian agencies. The Atomic Energy commission also has drawn heavily upon Conference members. The emphasis on air pollution control with the creation of special commissions or authorities to handle this problem has also been a drain on the State and local industrial hygiene units. This is all to the good for the industrial hygiene movement, but has considerably weakened the State and local hygiene work. I think this Conference with the cooperation of the United States Public Health Service should accept the responsibility for strengthening the various State and local units in industrial hygiene and should develop a program so that we can once again have strong and dynamic agencies giving services to industry.

I also seem to sense a trend to deviate a bit from the original charter laid down for us by the founding fathers in the nature of our annual programs. Quite early in the life of our association, we realized that in order to keep the Conference meetings from becoming just another reunion of a professional society and also to keep it within the organizational objectives of an official organization meeting to discuss mutual problems with the United States Public Health Service, it was necessary to set aside time for a conference with the staff of the Division of Industrial Hygiene of the Public Health Service. In this manner the Sunday pre-conference program developed, which consists in concurrent sessions of physicians, nurses, chemists, and engineers who meet to discuss technical problems in their respective

fields, and then the night session at which administrative discussions are held to iron out problems of legislation, salaries, relationship with other governmental agencies, and so on. In this way we could sort of let our hair down (those of us who had hair) or, to put it in another way, we could wash our dirty linen in private. I am very pleased to see that these pre-conference sessions on Sunday are still a useful and highly successful item on our annual agenda.

However, there is still the tendency to devote anywhere from one to one-and-a-half days of our limited annual meeting time to the presentation of strictly scientific papers, which I think would be better received at the AIHA or Industrial Physicians' sessions, thus giving our Conference more time for the discussion of solutions to some pressing administrative problems.

From this brief review of the history, early struggles and accomplishments of the Conference over the past two decades, it is evident that we, as an association, although small in numbers by comparison with other organizations of this type, have made an important impact on the industrial hygiene of our country. We may very well ask ourselves at this point what should be our role today and in the immediate future in these rapidly changing times? And they are changing, particularly in attitudes and concepts on the part of our clientele, that is management and labor.

Twenty years is such a short time, that it is easy for me to recall the attitude of management toward industrial hygiene and toward us as protagonists of this discipline. I can very well remember that as a member of the United States Public Health Service and without legal authority to enter industrial plants, I had a hard time convincing industrialists to cooperate in our investigations of health hazards. I still remember a very amusing incident that happened to me during the time when we were studying the hazards associated with sandblasting. I called on one factory in Connecticut and tried to persuade the owner to let me come there and study certain sandblast operations which I was anxious to add to the data we were collecting. He was very dubious about letting me come in and take some samples of air, saying that he was suspicious of any scientific studies and of so-called scientists. Finally, after a considerable sales talk on my part, he said:

> *"Well, all right, young man. You can come here and do these studies; but, you must come yourself. I don't want any of these college boys coming around here!"*

The same difficulties but from a different viewpoint were experienced with labor. Organized labor had had its troubles with management in that from time to time a worker was fired, or not hired, on supposedly health grounds, when sometimes it was due to the fact that a particular worker was considered undesirable because of his union activities. Obviously, with management taking such an attitude, labor fought the physical examination, since it felt that at times it was not used for the purpose intended, that is to assess a man's physical condition and to place him in the job he was physically and mentally qualified to perform.

I can recall the time when labor contracts specifically stated that the physical examination would not be pre-requisite to employment. As result of such a labor attitude, management was at times forced to employ disabled persons who could not be properly placed because of a lack of information on their health status. There were cases of epileptics working on ship construction in places where they were a danger to their fellow workers and to themselves. Many of our early investigations were made difficult for us because of the time wasted in trying to convince labor to submit voluntarily to a physical examination, which we needed in our studies of the relationship between health and working conditions.

I should like to relate one little incident to illustrate the suspicious feeling which prevailed between management and labor in these early times. One day I was inspecting a metal mine in the Far West in connection with one of our silicosis investigations. My guide, the superintendent of the mine, and myself had stopped in one of the levels in the mine to rest a bit and to smoke a cigaret. The level below us was very near; so close that we could hear a couple of miners talking. As near as I recall the conversation between the two miners, it went something like this:

> "Say, Bill, what do you think of this notice the company put up, that every man that has worked for a year will receive ten silver dollars as a bonus for Christmas?"

> The second miner replied, "Well, I'll tell you, Fred. I'm a bit suspicious of all this. I just can't picture the company giving anything away for nothing. And you mark my words, we are going to pay for this one way or another!"

Well, those times have changed for the better and we as a group certainly played a part in bringing about the changes. To understand the new viewpoint of management, one only has to pick up the annual Transactions of the Industrial Hygiene Foundation. In 1935, twenty companies met for the first time to organize an association to combat silicosis. Today, this organization of industrialists can count over four hundred in its memberships, and its annual meetings are a bright star in the industrial hygiene constellation. Although this organization still continues to give services to members on some of the older problems in our field, such as the classic occupational diseases, in late years it also has concerned itself with such important problems as noise, atmospheric pollution, radiant energy, sickness insurance, mental health, social security, the older worker in industry, the impact of automation on health, and the general field of labor and management relationships. Management realizes only too well that if it does not show as much concern for the men who operate machines as it does for those very machines, it will not realize the full potential of the new technology.

Labor also, has come of age and is showing a greater concern for social security for its workers and now considers this as but an extension of its traditional preoccupation with wages and hours and working conditions. That is why we find today many health and welfare programs written into collective bargaining contracts. Recent studies made by the United States Public Health Service show that practically every major union in the country had negotiated to some extent pensions, or health and welfare provisions, for their members. Labor too, has now endorsed the physical examination as a prerequisite to employment and job placement, recognizing that in the long run it is a benefit to the worker and not something to be feared.

In view of these changing concepts in occupational health on the part of both management and labor, we might very well ask ourselves whether or not our role as government officials has changed in any way. To begin with, I think we should bear in mind that although management has assumed greater responsibility than ever before in occupational health, and although labor now realizes that it has much to gain in cooperating more fully in occupational health programs, the role of the government industrial hygienists has far from lessened but has actually increased, and will continue to grow.

It is true that many of the large industries have developed their own industrial hygiene programs, but we still have with us the smaller plants where the bulk of the labor force is employed. These smaller plants — and some of them are not so small — still look to us for guidance in the solution of their health problems. And even the larger industries need our help in assuming their newer responsibilities, such as in the fields of total coverage medical care plans, retirement provisions, the problem of the older worker and rehabilitation. Also, some of the older occupational disease problems are still with us and to these we may add the new ones, such as air pollution and the insecticides. Then there are the problems posed by the ever increasing use of radioactive substances in industry.

In order to make use of the available resources to the utmost, we should begin to consider seriously a plan to integrate administratively the means at our disposal which exist within our local health departments, the small plants, and certain governmental agencies with a stake in the industrial hygiene claim. Instead of just striving for a peaceful co-existance with local health departments and our sister governmental agencies, we should study ways and means to integrate our work in such a manner that we can present a united front and in this way render better and more adequate services, and perhaps really begin to make a dent in the perennial problem of the small plant. I am confident that with the right approach you will receive a real welcome and a will to work in a cooperative manner on the part of these groups.

It should be quite obvious from this brief look at the future that our Conference has a tremendous job ahead of it and we must prepare ourselves to meet the demands which industry will be making for our services. I suppose too, that we must be prepared to continue losing some of our best

personnel to industry unless we make an earnest drive to make government jobs really attractive, and I do not mean just form the view point of take-home pay alone. I know that many of the State jobs pay very poorly and, to make things even worse, have very inadequate retirement plans. One of the reasons that United States Public Health Service has been able to hold on to many of its officers has been the provision of a career service with fairly adequate salaries and excellent social security benefits, including retirement pay and medical care for dependents. I am all for having the Conference appoint a standing committee with some dynamic individuals on it who will develop a plan of action to solve this problem of a career service for our State and local industrial hygiene personnel.

As you know, I have come some four thousand miles to be with you all and to take a backward look at our Conference to see what we have accomplished and what the future holds for us. It is not all so backward either, since we were only striplings when World War II sneaked up on us and put us to the test. You are just now growing a good beard and have acquired the responsibilities which go with that adornment. Your influence has gone beyond the United States, since, as you know, several of your colleagues are now working in Latin America. We now have about twelve countries south of the Rio Grande which boast of modern industrial hygiene programs, comparable to any of those in our own country. There is much to be accomplished in those countries, since they are only now beginning to industrialize and to experience the problems which faced us some twenty years ago when this Conference got its start. Perhaps that is one of the reasons why I find my work in Latin America so satisfying, for I can truly say, "This is where I came in."

John J. Bloomfield, more familiarly known to industrial hygienists as "Jack," was a pioneer in the development of industrial hygiene in the United States, and has been a leader and "sparkplug" in the field since those early days. He has transferred his pioneering and "sparkplugging" to South America, but continues to be a leader even here. This year, "Jack" was the recipient of the Cummings Memorial Award at the A.I.H.A. annual dinner. On the preceding evening, he was the honored guest and speaker at the Twentieth Anniversary Banquet of the American Conference of Governmental Industrial Hygienists.

The birth of the ACGIH Threshold Limit Values Committee and its influence on the development of industrial hygiene*

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At the third annual meeting in Bethesda, Maryland, in 1940, the ACGIH had no TLV Committee. After first hearing a report of the Committee on Codes and then the Committee on Technical Standards, the proceedings show that the writer said the following: "May I inquire what committee, if any, in this organization is responsible for the establishment of safe limits or threshold limits and concentrations?" After some discussion, it was decided that this activity should be a part of the function of the Technical Standard Committee rather than the Committee on Codes. The Executive Committee was directed to take some constructive action before the next meeting.

The *Transactions of the 4th Annual Meeting* in 1941 show Dr. Leonard Greenburg to be Chairman of the Committee on Technical Standards which had now been divided into a subcommittee on technical standards and one on threshold limits. The TLV group consisted of Manfred Bowditch, Phil Drinker, Lawrence Fairhall, Al Dooley and myself as Chairman. The charge to the subcommittee was to gather information on limits and to report the results to the fifth annual meeting in 1942. A survey of values used by the different state and local agencies for a number of common exposures was presented to the annual meetng. As Chairman, I issued the following comment to the committee:

> *"I feel that our subcommittee should assume an active position in the establishment of working limits and should issue a list annually, to be revised each year to conform with newer information and the values suggested by such bodies as the U.S. Public Health Service and the American Standards Association. A plan of action which this committee might follow to advantage would be similar to that of the International Committee on Atomic Weights, which makes annual revisions, incorporating or considering new information which has appeared during the year.*
>
> *"It is not my intent to disregard or belittle the work of existing limit proposing groups, but their machinery at best grinds out its grist finely and slowly. All of us doing field work know that if samples are taken for any contaminant in a plant, we must produce a limit, right or wrong, for the consideration of the management. Otherwise, they feel quite rightly that we were wasting our time and theirs taking the samples in the first place.*
>
> *"I feel that a committee like ours, representing nearly all the government enforcing agencies could, with justification, establish arbitrary limits which appear reasonable, for different classes of material which as yet have been inadequately or not at all investigated from the standpoint of the industrial toxicologist. The fact that some folks will disagree with such values should do much to stimulate the needed research and investigation. For example, all esters and hydrocarbons not elsewhere and specifically mentioned in the list might be set at 500 ppm; chlorinated compounds at 100 ppm; metals such as Co, Ni, W, V, Ta, and U to which definite exposures are now appearing in Detroit, at say 1 mg/10 mg^3. Then as medical or toxicological literature appears which clearly indicates the need for revision, this can be done with ease in the annual report. Likewise, the list can be adjusted to accept the usually very carefully considered values issued by the American Standards Association."*

No standing committee reports were given at the sixth meeting in 1943 nor at the seventh annual meeting in 1944 because of World War II disruptions but in 1944 the TLV Committee be-

* Published in the *Transactions of the Thirtieth Annual Meeting of ACGIH*, May 12-14, 1968, St. Louis, Missouri, pp. 40-43 (1968).

came an independent standing committee retaining the same membership. Manfred Bowditch presented a discussion of the problems of setting threshold limits, in which he stated:

> *"The two questions that all of this generated in my mind are: First, is a single figure adequate in dealing with certain of these materials? It seems to me that those of us who are working as preventive agents have to consider, first, the question of actual systemic poisoning; and, second, this question of temporary indisposition which, after all, is definite illness even though temporary.*
>
> *"But apart from any actual ill health, in the case where we have certain evil smelling materials which perhaps are more evil smelling than toxic — naturally, I am not talking about carbon tetrachloride — we may have to consider the question of just such unpleasant industrial conditions, conditions under which it isn't fair to expect any human being to work for any length of time. So much for the question of whether we should have one figure or several.*
>
> *"But that also brings up the question of whether the ASA method — for which I assure you I have the highest respect, as I have for the ASA itself, and for Mr. Ainsworth — is as applicable to this type of standardization as it is to the mechanical and other forms of standardization with which they have dealt so largely and so successfully in the past, and for which I assume that the ASA was originally set up.*
>
> *"We are dealing here with standards which cannot be arrived at in the same way that we would arrive at the number of threads per inch that should be used on a machine screw of a given size in order to enable everybody to use screws interchangeably. We are dealing with conditions in factories, as to which those of us who are entrusted with the preventive functions have got to use our very best judgement. If a national body like the ASA decides that 100 parts per million is the proper one for safety and our agency in Massachusetts is convinced that that is too high and that safety demands a figure, we will say, of 50, I feel that we would be absolutely false to our trust, false to the citizens of Massachusetts who are employing us, if we did not throw the higher figure out the window and stick to the one which we believe is required for safety."*[1]

No meeting was held in 1945 due to the war but in 1946 the meeting was held in Chicago and the writer felt constrained to get the TLV Committee back into action. On March 29 a draft of a report and a list of some 150 TLVs was sent to the Committee for its consideration. The report stated that the list would be valid for use only in 1946. It also proposed that there be established in due time a list with two sets of values, one physiological and the other optimal. The other Committee members voted for a single set of values to be of all things to all people and so it remains today.

The Committee on Industrial Hygiene Codes made the first report of the session. To the TLV Committee's deep chagrin, the essential content of this report was a list of MAC values arrived at independently. The conference voted the report to be tabled until after the TLV Committee report was heard. The TLV Committee report, which the Chairman presented was:

> *"Considerable difficulty attends the fixing of satisfactory values for Maximal Allowable Concentrations (MAC) of chemicals in respirable atmospheres because of the lack of sufficient toxicological data and the lack of a uniform definition of the maximal allowable concentration concept. One concept is that the MAC value should represent as accurately as possible that concentration at which a worker exposed for a sufficient period of time will just escape physiological or organic injury and occupational disease. A second concept is that the MAC should represent some fraction of that concentration which will injure the worker in order to allow a margin of safety in the design of protective equipment and guard against possible synergistic effects in the case of multiple exposures. A third concept is that the MAC should perform the functions of the former concepts and in addition provide a work environment free of objectionable but non-injurious concentrations of smokes, dusts, irritants, and odors. Obviously all of these concepts cannot be fulfilled with the establishment of a single value. MAC values in use*

at the present time represent examples of all of these concepts.

"The Committee feels that the establishment of dual lists or a single definition of the MAC is not possible at the present time.

"An extensive list of MAC values is presented to the Conference for use during 1946, with the definite understanding that it be subject to annual revision. Values have been compiled from the list reported by this subcommittee at the 5th annual meeting of the NCGIH in 1942, from the list published by Warren Cook in Industrial Medicine, *Vol. 14, p. 936, 1945, and from published values of the Z-37 Committee of the American Standards Association.*

"It will be noted that many of these values have been in general use by members of the Conference for several years."

The Chairman moved that the report be adopted, a prearranged second was immediately forthcoming, the motion was put to a vote and carried without discussion or dissent.

The matter of TLV values in the Code Committee report was now taken from the table for discussion. The Conference fairly clearly resolved to separate TLV values from codes but to this day they appear in many state codes under the faulty precept that industrial hygiene can be practiced by the numbers.

The philosophy of the TLV, as established by ACGIH in those early days of our profession, has remained substantially unchanged and despite carping, criticism, misunderstandings and abuse, today its values, for better or worse, are accepted on an international basis as the best available guides for providing healthful occupational environments for the workers of the world.

TLVs have made it possible for the industrial hygiene method to prevent chronic degenerative health failure caused by stresses in the workplace through the basic technique of recognition, evaluation, and control.

Although the perfect TLV, like the will-o'-the-wisp or the pot of gold at the end of the rainbow, cannot ever be realized, it remains the backbone of successful industrial hygiene practice. Eventually we will know enough to refine the value, to take into account the susceptibilities of numerically important genotypes, the effects of synergism and the adverse influence of concurrent environmental stress, but I doubt if we can ever eliminate the need for the experienced judgement of the Industrial Hygienist for its most effective application.

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The early days of industrial hygiene — their contribution to current problems*

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I am highly honored to be invited to give the fourth Herbert E. Stokinger Lecture not only because of the stature of this American Conference of Governmental Industrial Hygienists (ACGIH) lectureship but also because of my admiration for Dr. Stokinger. Although Herb's greatest contribution to industrial hygiene was through his chairmanship of the TLV committee, it should be noted that he was one of the first to emphasize the value of biological standards and the need to appreciate genetic factors in setting standards. I am also greatly pleased to be classed with the three preceding speakers in this lectureship. They and Dr. Stokinger have one trait in common which has been an important factor in the development of industrial hygiene, that is, their willingness to share their knowledge at any time to anyone who seeks it. I have been on the receiving end of this assistance and am grateful to all of them.

Many of the persons attending this 1980 Industrial Hygiene Conference entered this field of work since the passage of the OSH Act in 1970. In fact, based on the number of members in the American Industrial Hygiene Association (AIHA) today as compared with that in 1970, I would estimate that more than 60% of this audience knows very little if anything about the pre-1970 industrial hygiene concepts and activities. Some insights into certain phases of past activities have been presented in this ACGIH series of lectures honoring Herbert Stokinger, in the AIHA Cummings lectures, and in the proceedings of the 40th celebration of ACGIH in 1978, but I believe that you who are relatively new in this field have much to gain from knowledge of the activities and the philosophy which formed the background of this discipline in its early days.

Industrial hygienists have two major responsibilities, 1) to determine the conditions of work which will allow people to function in their occupation without harmful effects on their health, and 2) to apply these standards to the working population. In this lecture I want to review for you the outstanding contributions in each of these two areas which the members of ACGIH made to this profession in the earliest years of its existence. The first is, of course, the concept of Threshold Limit Values and the continuing revision of these standards at the same level of excellence throughout the past 40 years. For this we are indebted to Herb Stokinger who served as Chairman of the TLV committee for 26 years.[A] The other contribution of the early industrial hygienists is less well known but equally important in my opinion. The members of ACGIH set a pattern of high quality industrial hygiene services in state and local units to provide the first nationwide effort to improve working conditions in industry.

Part I
Development of industrial hygiene standards

Early in this century when Dr. Alice Hamilton began her distinguished career in occupational diseases, no air samples and no standards were available to her, nor indeed were they necessary. Simple observation of the working conditions and the illness and deaths of the workers readily proved that harmful exposures existed. Soon however, the need for determining standards for safe exposures became obvious.

The first list of standards for chemical exposures in industry, called Maximum Allowable Concentrations (MAC), was prepared in 1939 and 1940 and represented a concensus of opinion by the American Standard Association and a number of industrial hygienists who had formed the ACGIH in

* The 1980 Herbert E. Stokinger Lecture presented at the American Industrial Hygiene Conference, May 18-23, 1980, Houston, TX. Published in *Trans. of the Forty-second Annual Meeting* of ACGIH, pp. 10-17 (1981).

[A] *Editors note:* Dr. Stokinger became a member of the committee in 1953, its Chairman in 1962, and served through 1978.

dustrially employed population was considered a responsibility of state and local government. This function was located usually in the Departments of Labor. A number of states had laws chiefly regulating factory and mine safety, hours of work for females and child labor. In some states factory inspection was included but industrial hygiene, as we know it today, was not included until 1913. In that year the New York Department of Labor established the first special Division of Industrial Hygiene to expand the work of the medical and technical inspectors of factories.

Responsibility for the health of federal employees was vested in the Office of Industrial Hygiene and Sanitation which was established in the United States Public Health Service in 1914. The first state to recognize occupational health as a function of the health department appears to have been Ohio which, in 1886, established a commission on Hygiene of Occupations and Railroads. In 1905, the Massachusetts Health Department appointed health inspectors to investigate dangers of occupation but this program was soon transferred to the Department of Labor where it has remained.

The Connecticut Health Department created a Bureau of Occupational Diseases in 1928 and immediately issued a list of 87 hazardous substances, processes and conditions for consideration. By 1935, Mississippi, Maryland, and Rhode Island also had some type of industrial hygiene units in their Health Departments. The entire budget for these five state health units at that time was $30,877.[5] Although for many years the State and Provincial Health Authorities had a committee on industrial hygiene, funds to support any programs in this area were not available.

The occupational health programs in state Health Departments changed dramatically with the passage of the Social Security Act in 1936 when, for the first time, federal financial support for such programs became available to the states. The Public Health Service loaned some of their physicians and other personnel to the states including Mr. John (Jack) Bloomfield, a sanitary engineer who was charged with coordinating the activities of the various state Health Departments as they developed their industrial health programs. In 1936 Dr. R.R. Sayers, Senior Surgeon in the Public Health Service, with Mr. Bloomfield presented the following reasons for supporting industrial hygiene in state and local Health Departments.

> *"In recent years large industrial establishments have contributed much toward the protection of the health of their workers. However, as nearly 90 percent of the plants in the United States employ less than 100 persons, many establishments are not prepared to handle effectively the problem of industrial hygiene alone. It would seem, therefore, that the protection of the health of our workers is indeed an important health function and one which can be handled best through a governmental agency, such as a state or local department of health cooperating with the employers and workers."*[5]

As soon as the Social Security money became available, the states started to develop their programs rapidly. By October 1936, 17 state Health Departments were conducting industrial hygiene activities with a total budget of approximately $350,000. Even this sum represented only an average of $0.014 per gainfully employed worker. By May 1941, 32 states and 4 cities and by 1953, 42 states, 2 territories and 11 cities had industrial hygiene units located in various divisions of their Health Departments. Two states, Massachusetts and New York, continued to maintain their activities in their Labor Departments and Illinois divided its program between the Health and Labor Departments.

Within two years after Social Security funds became available, the American Conference of Governmental Industrial Hygienists was organized by hygienists who were employed in the federal and state programs. Persons engaged in teaching and research in industrial health in universities became associate members. The objective of the conference was for the *"exchange of ideas, and experiences and for the promotion of standards and techniques in industrial health."*

This rapid development of industrial hygiene presented a serious problem to the states similar to that which OSHA faced in 1970, i.e., the lack of trained personnel. The attack on this problem in 1970 and 1930 was very similar — short courses, encouragement of industrial hygiene programs in universities, and field training by federal industrial hygienists. The Industrial Hygiene Committee of the State and Provincial Health Authorities of

North America published in 1936 a list of the duties and qualifications for physicians and engineers in industrial hygiene, which are similar to those recommended today. It is of interest to note that in additon to the professional requirements this list included certain desirable personally characteristics: *"ability to establish contact with plant executives and to enlist the cooperation of executives, foremen, and laborers; initiative; tact; good jugement; and good address."* The salaries recommended in 1936 were $7500 for physicians, $5800 for engineers, $4000 for chemists, and $2000 for nurses.[5]

The industrial hygiene divisions in the state units during the '30s and '40s were responsible for the initiation of programs for all of the industrially employed workers in the states. Their objective was to educate the industries concerning the hazardous exposures and advise them how to prevent harmful effects to their workers. The state industrial health divisions did not have the right to enforce their recommendations. However, most states had some general health laws which allowed entry into a plant if it was known to have a health problem but, on the whole, these measures were rarely, if ever, used for occupational health problems. Thus, the approach to industrial hygiene was different from that required by the OSH Act which is based on the legal power of enforcement with citations, fines, etc. The industrial hygienists who have entered the field since the passage of OSHA cannot understand how industrial health programs can function without the power of a penalty system but indeed they were very successful.

The usual procedure was first to make a general survey throughout the state to determine the types and number of industries in the state, secondly to investigate those believed to have harmful conditions. It was estimated that about 70% of the total staff time was spent in field investigations of occupational hazards, 15% in laboratory services and developmental research, and 15% in teaching health education. The field services included plant surveys, technical studies of occupational health hazards, methods of prevention of harmful effects, services pertaining to promotion of in-plant health programs including nursing and medical service, and follow-up visits on the status of their recommendations. The state Health Department programs did not specifically include safety since this was considered a function of the Labor Departments. Although the majority of the services were initiated by the industrial hygiene units, many requests for service came from industry and labor. The programs were well accepted by industry. Dust diseases, especially silicosis and asbestosis, ionizing radiation, and solvents and gases were the most important problem diseases requiring industrial hygiene.[6,7] As private industry began to employ their own industrial hygienists, the state programs focused on the small plants. The progress which the health units made was truly phenomenal in many states. Studies such as that of the granite industry in Vermont and of the dust diseases in Connecticut were outstanding.

Unfortunately, after the war, the Public Health Service withdrew much of its personnel and financial support from the state programs. Because of the very low salary scale paid by the states, they could not retain their staff and lost many of their industrial hygienists to the larger industries and insurance companies which had become aware of their importance.

I have described in detail these early state industrial hygiene programs because I believe they have a very real application to one of the major problems facing OSHA today, i.e., protection of workers in small industries. Although OSHA has made a number of proposals to deal with this problem, they have not been successful. OSHA has not had the manpower necessary to inspect small plants, to educate the owners, managers or workers, and to assist them to understand their problems. The owners and workers know little or nothing about the complex problems of chemical exposures and are not likely to call upon most of the consulting agencies listed by OSHA, because of OSHA's right of citation and penalty. Although it would be easy for small plants to do self inspection to comply with safety standards, as proposed by OSHA, they do not have the knowledge necessary to evaluate their occupational health problems.

In view of the difficulty which OSHA has had in meeting this problem, it seems to me that a far better way to protect the health of workers in small businesses (those with less than 100 workers) would be to remove small businesses from the jurisdiction of OSHA and to establish industrial hygiene programs in the state and local Health Departments similar to those which were so successful in the '30s and '40s. For this purpose

Congress would have to enact adequate legislation and provide federal funds to the Public Health Service which, in turn, would give grants to the state and local Health Department to establish occupational health and safety programs for small businesses. These programs should be placed as entirely separate units in the state or local Health Departments as free as possible from state politics and pressures of any groups. The programs should be based on the philosophy of education, assistance and service.

Some people will claim that, although programs without penalties were successful in the early part of the century when bad working conditions were very obvious, they will not be effective at this time when the harmful effects are more subtle. My experience is that the harmful conditions in the small plant are still very visible today. Certainly, this approach will not be equally successful in all cases, but I believe it will be of far more value to the workers than exists under present conditions.

The program suggested here might well have a second advantage in areas of the country where NIOSH Educational Resource Centers are located. The doctors, industrial hygienists, and safety engineers-in-training could participate in these state activities and thus have an excellent opportunity for field experience. Where occupational disease clinics have been established by these university centers, the state Health Departments could refer workers for diagnosis and treatment of occupational diseases. If salaries were adequate, some of these trainees might be attracted to accept positions in state health units.

Programs of the type suggested here would allow industrial hygienists to use the current TLVs in the manner for which they are intended and would give them the opportunity for initiative, experimentation and judgment in their profession. In addition, their observations would provide the TLV committee with valuable data.

Thus, I believe strongly that the plan suggested in this paper offers by far the best approach for the protection of the health of workers in small plants. I hope that Congress will give consideration to this proposal.

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Anna M. Baetjer received her B.A degree from Wellesley College in 1920 and her Sc.D. degree from The Johns Hopkins School of Hygiene and Public Health in 1924. She has spent her entire career at The Hopkins rising from the rank of Associate to Professor and since 1970, Emeritus Professor in the Department of Environmental Health Sciences. Throughout her research and teaching career she has been concerned with the effects of the environment and work on man with emphasis on industrial hygiene and environmental toxicology. Dr. Baetjer's research has dealt chiefly with the role of industrial dusts in respiratory diseases, the influence of extremes of temperature and humidity on reactions to toxic chemicals and more recently on the effects of dehydration and food restriction on susceptibility to toxic and infectous agents. Her best known research dealt with the role of chromium in bronchogenic carcinoma.

Dr. Baetjer served as President of AIHA in 1951. She has been honored with the AIHA Cummings Memorial Award; the ACGIH Stokinger Lectureship, the American Academy of Occupational Medicine Robert Kehoe Award of Merit; the Industrial Hygiene Foundation Weidlein Lectureship and others. She has received several honorary degrees, the most recent being a Doctor of Humane Letters from The John Hopkins University in 1979. She is a member of a number of national and international scientific organizations.

In addition to her work at Hopkins, Dr. Baetjer has served on a number of governmental committees and as a consultant to various agencies including the WHO. She has published a number of scientific research papers and contributed to various scientific books. In 1946 she published the first book on *Women in Industry*.

OCCUPATIONAL DISEASE AND TOXIC LIMITS PRE-1950

Prevention of occupational diseases other than those that are caused by toxic dust*

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The use of volatile chemicals has increased greatly during the past few years. They have become indispensable in the manufacture of paints, in dry-cleaning processes, and as solvents in various industrial processes, to mention but a few of their common uses. In fact, so great has been the demand for volatile solvents both by industry and the general public, that new applications for them are constantly being developed and commercialized. The volatile solvents perform a large and important part of industrial expansion into new fields as new uses for them are discovered.

Partly as the result of the increased use of new chemicals in industry, it is now well recognized that the hazards of certain occupations are important factors in the causation of sickness and even death. Dublin[1] has evaluated the effect of the industrial environment on the well being of a large number of workers in a mortality study among more than three million white, male wage earners. The study covered a three-year period from 1922 to 1924, inclusive, and is compared with a similar study made over a similar period from 1911 to 1913. The groups studied constituted a fairly representative social and economic class and were considered as an urban earning population. Dublin has shown by an analysis of the data obtained, that adult males engaged in industrial pursuits had a higher mortality and shorter longevity than those in other types of work such as professional, clerical, etc. In the more recent study, it was further shown that the mortality rates for the industrial workers were more than double the rates for the non-hazardous occupations. In terms of life expectancy, the picture presented was impressive. The industrial worker at the age of 20 had an expectancy of 42 years as compared with the normal of 49 years. In other words, the life of the industrial worker in 1924 was shortened by approximately seven years, while the data for 1911 to 1913 showed the decrease in longevity to be even greater. Considering the characteristics of the groups studied, Dublin was led to the conclusion that in the industrial environment, exposure to abnormal conditions such as toxic dusts, vapors, fumes and gases, radiant heat, etc., explains the difference in longevity between industrial and non-industrial workers. Since, furthermore, there are some 900 separate occupations with exposure to occupational-disease hazards,[2] the magnitude of the preventive problem should merit considerable attention.

Several methods are at present available for the prevention of occupational diseases due to exposure to substances which are injurious to health. Some of these methods have already been extensively discussed in the literature of industrial hygiene with reference to dust hazards, and, in general, the ideas there formulated have a very general application in other related fields. Briefly, these methods of prevention include: *a)* sanitary and occupational survery; *b)* mechanical and personal methods of controlling a hazard at the point of origin; and *c)* periodic medical examinations and surveys. Each of these methods is discussed in the paragraphs which follow.

Sanitary and occupational surveys

Sanitary surveys

No estimate of a hazard can be made until the conditions of the worker's environment have been evaluated. In studies made by the Public Health Service[3] it has been customary, as a first step in its field investigations, to make detailed sanitary surveys. These surveys include a study of the various items with which the worker comes in daily contact. The sanitary survey is, in other words, an "inventory" of all the hygienic items which enter into the

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* Contributed by the Safety Committee and presented at the Annual Meeting of the American Society of Mechanical Engineers, December 3-7, 1934, New York, NY. Published in *Mech. Engrs.*, pp. 13-17 (April 1935). Reprinted by permission of the American Society of Mechanical Engineers.

worker's environment, the manner in which he conducts his work, and the length of time he spends at each task. As a rule, such a study is carried out for each room and for the various occupations in a given plant. This procedure, when completed, gives at once pertinent information as to the types of hazards which are likely to exist and the number of workers which may possibly be affected.

The items which enter into a sanitary survey should include the following:

1. Physical characteristics of building and room in which the survey is made: construction of building; location and size of room; number of workers; type of illumination; type of ventilation.
2. Sanitary facilities for workers: refuse cans, cuspidor and sweeping service; washing facilities; type of toilets; drinking-water facilities; eating facilities; type of care and maintenance given to sanitary facilities.
3. Hazards: safety hazards; dust, vapors, fumes, or gases present; exposure of workers to any sources of radiation or to abnormal temperatures.
4. Analyses of types of employment: list of various operations and number of workers employed in each; materials handled; absenteeism and labor turnover.
5. Preventive methods in use: isolation methods; local exhaust and general ventilation; personal respiratory-protection apparatus.
6. Medical services: type of medical service provided and records kept; periodic medical examinations.

It may be seen from the foregoing list of items that a fairly complete picture of the conditions existing in a plant is recorded. A record of the existence or non-existence of any item at once helps the investigator to form a general conception of the line of study which must be adopted. It further makes available to him a detailed amount of information which is extremely useful. Such a survey may indicate whether or not there is compliance with various state factory or other industrial codes. For example, on the basis of the number of employees found in a given room, it may be determined whether there is ample per capita space, or whether sufficient toilets have been provided.

Occupational analysis

Following the sanitary inspection of a plant, it is then necessary to study the various occupations. The occupational analysis includes an extensive study of the workers' immediate environment wherever a hazard is found to exist. It also entails a correlative study of the health of the workers. One is supplementary to the other and the omission of either cannot be expected to yield results which can be considered satisfactory. The Public Health Service in all its field investigations has attempted by such a procedure to establish what may be considered the safe conditions under which workers may be exposed indefinitely without injury to health. Two examples of the methods used will aptly illustrate the technique employed in making occupations surveys.

In a study of chromium-plating hazards, Bloomfield and Blum[4] examined 23 men, four of whom were not chromium platers and were selected as controls. Five other workers were not actually engaged in chromium plating, but were engaged at various duties at a distance of about ten feet from the plating tanks. The length of service of the workers was carefully determined from the individual occupational histories and varied from zero to seven years.

Since some of the workers were affected by acid mist, it was important to obtain data on the severity of the exposure. Accordingly, determinations of the amount of chromium mist present in the atmosphere were made. The amounts found varied from less than 1 mg to about 56 mg of chromic-acid mist per 10 cu m of air. The tabulated results showing the period of employment, the degree of exposure, and the findings on physical examination of the workers are given in Table I. From an analysis of this table, it may be seen that 3 of the 19 persons employed in the plating rooms had perforated septa, 21 percent had ulcerated septa, 47 percent had marked inflammation of the mucosa and more than half were subject to frequent nose bleeds. From these data it is possible to discover those occupations which require immediate attention. Together with the occupational analysis, the table further shows that the safe limit of concentration of chromic-acid mist in the air is probably under 1 mg per 10 cu m of air. The

TABLE I
Occupational History and Clinical Findings Or Workers in Chromium-Plating Plants

Case No.	Occupation	Months employed in chromium-platingroom	Hours per day over tank	Approximate CrO_2 exposure in milligrams per 10 cubic meters	Perforated septum[1]	Ulcerated septum[1]	Inflamed mucosa[1]	Nose bleed	Chrome holes
1	Chromium plater	6½	4	15.0	+	-	++	+	+
2	Chromium plater	20	4	28.0	++	-	+	+	+
3	Foreman plater	7	2	25.0	-	++	++	+	-
4	Foreman plater	8½	3	25.0	-	++	++	+	-
5	Chromium plater	3½	4	56.0	-	++	++	+	+
6	Chromium plater	¾	7	1.2	-	-	++	+	+
7	Chromium plater	¼	7	1.2	-	-	++	+	-
8	Chromium plater	7	7	1.2	-	-	++	+	-
9	Chromium plater	3	7	1.2	-	-	++	-	+
10	Chromium plater	36	4	2.0	-	-	++	-	-
11	Chromium plater	5	6	1.2	-	-	+	+	+
12	Chromium plater	¾	6	1.2	-	-	+	-	-
13[3]	Chromium plater	12	4	28.0	-	-	-	-	-
14	Chromium plater	⅜	2	28.0	-	-	-	-	-
15[4]	Nickel plater	1½	0	([2])	..	+	+	+	-
16	Racker	8	0	([2])	+	-	+	+	-
17	Racker	¾	0	([2]	-	-	+	-	-
18	Racker	¾	0	([2])	-	-	+	-	-
19	Wiper	1¼	0	([2])	-	-	+	-	-
20[5]	Foreman	0	0	0	-	-	+	-	-
21[5]	Foreman	0	0	0	-	-	+	-	-
22[5]	Clerk	0	0	0	-	-	-	-	-
23[5]	Inspector	0	0	0	-	-	+	-	-

[1] ++ marked; + slight; - negative; [2]Unknown; [3]Used vaseline in nose; [4]Cyanide burns; [5]Work in other departments of factory.

occupational analysis thus often establishes the permissible limit of a contaminant for prolonged exposure.

Frequently, it is not possible to correlate engineering and medical data in an occupational analysis. Thus, in a study of the lead hazard in a storage-battery plant,[5] the Public Health Service adopted a special method of determining the permissible limit of lead dust. The investigation included a sanitary survey as outlined above and an occupational analysis which included a determination of the lead dust and fumes present in the air, a record of employment and of disabling sickness (mostly compensation cases of plumbism), physical examinations, and blood and urine analysis. The medical examinations, because of the nature of lead poisoning, were necessarily extensive. With each worker, subjective symptoms such as colic, weakness, loss of appetite, constipation, nervousness, etc., were noted. Similarly, the important objective symptoms were recorded, including pallor, jaundice, tremor, reflex and pathological changes in the blood and urine. However, although a large number of engineering and medical data were available, it was found to be inconclusive due to the large labor turnover which the plant had experienced during the course of the study. This had already been indicated by the sanitary survey, and as a result a careful record had been kept of the workers who had reported to the plant clinic for various complaints, characteristic of lead poisoning. From the knowledge of the lead concentration to which these workers had been exposed, it was then possible to estimate approximately that concentration of lead for which a minimum number of workers had found it necessary to visit the clinic. Hence, except for prolonged exposure, it was shown in this manner that the safe limit of exposure of lead dust and fumes was less than 1.5 mg per 10 cu m of air.

The foregoing examples show the importance of a carefully conducted occupational analysis. Not all conditions found in practice can be similarly treated, but a few facts stand out and are generally common in most surveys of occupational-disease hazards; these are: *a)* a detailed list of occupations and the number of workers exposed; *b)* a careful occupational history of each worker. This is most important as has already been pointed out with regard to dust hazards,[6] but it is equally applicable to all types of hazards. The occupational history which is a list of all the previous occupations of the worker and his time spent in each is frequently of great assistance in diagnosing ailments which may not be entirely attributed to his present work; *c)* physical examinations of all workers with particular emphasis on the characteristic symptoms of the contaminant to which they are exposed. Careful present and past medical histories must also be taken; *d)* quantitative determinations of the contaminant present in the air; and *e)* a correlative analysis of the medical and engineering findings with a view to establishing threshold or safe limits of exposure.

Threshold limits

Thus far the steps necessary to evaluate a given hazard have been outlined. It is clear that the

TABLE II
Physical and Toxic Properties of Common Vapors and Gases*

Substance	Formula	Ordinary state	Boiling (1) point (deg C)	Spec. gr. of gas or vapor (air = 1)	Inflammable limits (percent)	Physiological action	Least amount detectable by odor (ppm)	Physiological response to various concentrations (ppm) — Kills in very short time	Dangerous for ½-1 hr exposure	Maximum concentration for exposure of ½-1 hr	Amounts causing slight symptoms after several hours' exposure	Maximum allowable concentration for prolonged exposure
Chlorine	Cl_2	Gas	−34.6	2.486 (1)	Non-flamm.	Strong irritant	3-5 (2)	900 (3)	14-21 (3)	3.5 (3)	0.35 (3)	< 0.35 (3)
Bromine	Br_2	Liquid	58.8	5.5[a]	Non-flamm.	Strong irritant	No data	at 550 (3)	at 6-9 (3)	at 3-5 (3)	0 3-0 45 (3)	0 15-0.3 (3)
Ozone	O_3	Gas	−112	1.62 (3)	Non-inflamm.	Strong irritant	0.5-1.0 (3)	No data	5 (3)[b]	No data	0.8-1.8 (3)	< 0.8
Hydrocyanic acid	HCN	Liquid	25.2	0.93[a]	Non-inflamm.	Irritant Asphyxiant	No data	270 (3)	110-135 (3)	45-54 (3)	18-36 (3)	< 18 (3)
Hydrogen chloride	HCl	Gas	−85	1.2678 (1)	Non-inflamm.	Strong irritant	No data	1250-1750	1000-1350 (3)	40-90 (3)	No data	< 10 (3)
Hydrogen fluoride	HF	Liq. or gas	19.4	0.69[a]	Non-inflamm.	Strong irritant	No data	660 (3)[b]	50-250 (4)	10 (4)	10 (3)[b]	3 (4)
Sulphur dioxide	SO_2	Gas	−10	2.2638 (1)	Non-inflamm.	Strong irritant	3-5 (5)	535-650 (3)	150-190 (3)	50-100 (3)	25-40 (3)	10 (3)
Nitrogen tetraoxide	NO_2 or N_2O_4	Gas	−21.3	1.6-3.2[a]	Non-inflamm.	Strong irritant	No data	320-530 (3)[c]	117-154 (6)[c]	105-210 (3)[c]	50 (3)[b,c]	39 (6)[c]
Ammonia	NH_3	Gas	−33.4	0.5963 (1)	16-27 (7)	Strong irritant	53 (2)	5000-10,000 (8)	2500-4500 (9)	300-500 (9)	146 (3)	85 (3)
Carbon dioxide	CO_2	Gas	−78.5	1.5290 (1)	Non-inflamm.	Resp. stim.	No data	50,000-67,000 (3)	33,500-44,500 (3)	33,500-39,000 (3)	11,000-16,700 (3)	5550 (3)
Carbon monoxide	CO	Gas	−19.2	0.9671 (1)	12.5-74.0 (7)	Asphyxiant	No data	> 4000 (8)	1500-2000 (8)	600-700 (8)	500 (10)	100 (8)
Hydrogen sulphide	H_2S	Gas	−59.6	1.190 (1)	4.3-46.0 (7)	Asphyxiant	0.75 (11)	420-600 (3)	360-500 (3)	200-300 (8)	100-150 (8)	85-130 (3)
Arsine	AsH_3	Gas	−55	2.69 (1)	Inflammable	Asphyxiant	No data	250 (3)	15.5 (3)	6.25 (3)	3.1 (3)	< 3.1
Phosphene	PH_3	Gas	−85	1.182 (1)	Inflammable	Asphyxiant	1.4-2.8	400-600 (3)	290-430 (3)	100-190 (3)	7 (3)	< 7
Phosphorus trichloride	PCl_3	Liquid	79.95 Decomp.	4.7[a]	Non-inflamm.	Strong irritant		652 (12)	50-90 (12)	2-4 (12)	0.7 (3)[b]	0.7 (12)
Phosphorus pentachloride	PCl_5	Solid	160-165	Sublimes	Non-inflamm.	Strong irritant		Analogous to phosphorus trichloride (3), (8)				
Arsenious chloride	$AsCl_3$	Liquid	122	6.3[a]	Non-inflamm.	Strong irritant		Analogous to phosphorus trichloride (3), (8)				
Benzene	C_6H_6	Liquid	80.36	2.73 (13)	1.4-7.0 (7)	Asphyxiant		19,000 (14)	3000 (15)	3130-4700 (14)	1570-3130 (14)	100 (16)
Toluene	C_6H_5-CH_3	Liquid	111	3 20 (13)	1.4-7.0 (7)	Asphyxiant		Analogous to benzene (3), (8)				
Xylene (?-zylene)	C_6H_4-$(CH_3)_2$	Liquid	136-141	3 68 (13)	Inflammable	Aphyxiant		Analogous to benzene (3), (8)				
Methanol	CH_3OH	Liquid	66	1.1[a]	7.45-26.5 (17)	Anesthetic		290,000 (3)[b]	No data	No data		
Ethanol	C_2H_5OH	Liquid	78.4	1.6[a]	4-19 (7)	Anesthetic		No data	No data	1380-5000 (19)	No data	No data
Acetone	CH_3CO-CH_3	Liquid	56.5	2.0[a]	3-11 (7)	Anesthetic		46,000 (3)[b]	75,000 (3)[b]	No data	3370-4220 (3)[b]	No data
Formaldehyde	H-CHO	Gas	−21	1.0[a]	Non-inflamm.	Irritant		> 6500 (20)[b]	No data	No data	200 (20)[b]	No data
Methyl chloride	CH_3Cl	Gas	−23.7	1.784 (1)	8-19 (7)	Anesthetic	No data	150,000-300,000 (21)[b]	20,000-40,000 (21)[b]	7000 (21)[b]	500 (21)[b]	< 500
Ethyl chloride	C_2H_5Cl	Gas or liq.	12 2	2.2[a]	4-15 (7)	Anesthetic		150,000-300,000 (21)[b]	60,000-100,000 (21)[b]	40,000 (21)[b]	20,000 (21)[b]	< 20,000
Carbon tetrachloride	CCl_4	Liquid	76	5 3[a]	Non-inflamm.	Anesthetic		10,000 (15)	317 (22)	< 1000 (22)	No data	< 100 (22)
Trichloroethylene	$CHCl$-CCl_2	Liquid	87.1	4.5[a]	Non-inflamm.	Anesthetic		7800 (3)[b]	No data	3700 (3)[b]	No data	No data
Carbon disulphide	CS_2	Liquid	46.2	2.6[a]	1.50 (7)	Anesthetic		4800 (3)	3200-3850 (3)	960-1600 (3)	320-390 (3)	No data
α-Amyl acetate	CH_3COO-C_5H_{11}	Liquid	148	4.5[a]	Inflammable	Anesthetic		No data	900 (23)	No data	No data	No data
α-Butyl acetate	CH_3COO-C_4H_9	Liquid	125	4.0[a]	1.7 (7)	Anesthetic		No data	19,000 (3)[b]	No data	5000 (3)[b]	No data
Nitrobenzene	C_6H_5-NO_2	Liquid	210	4.2[a]	Inflammable	Narcotic		No data	No data	1.0 (8)	0.2-0.4 (8)	< 0.2
Aniline	C_6H_5-NH_2	Liquid	184.4	3.3[a]	Inflammable	Narcotic		> 420 (24)	No data	105-160 (8)	7-26 (8)	< 7
α-Toluidine	CH_3-C_6H_4-NH_2	Liquid	2031	3.7[a]	Inflammable	Narcotic		No data	No data	91-140 (8)	6-23 (8)	< 6
Turpentine	$C_{10}H_{16}$	Liquid	200	4.7[a]	Inflammable	Irritant		2900 (25)[b]	540-720 (25)[b]	No data	720-1100 (25)	No data
Phosgene	$COCl_2$	Gas	8 2	3.4[a]	Non-inflamm.	Strong irritant	5.6 (2)	90 (3)	12.5 (3)	No data	1 (2)	< 1
Gasoline	C_nH_{2n+2}	Liquid	50-144	—	1.4-6.0 (7)	Anesthetic	No data	30-40 mg/l (3)	25-30 mg/l (3)	10-20 mg/l (3)	5-10 mg/l (3)	10 mg/l (3)

* Reproduced as accurate as possible due to poor quality of copy provided.
[a] Calculated.
[b] Based on animal tests.
[c] Computed as NO_2.

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starting point of a preventive program hinges upon the safe limit of air contamination which the worker may breathe continuously without injury to his health. Unfortunately, extensive field studies of the type discussed above have been few and there are still many practical data wanting. However, both in this country and abroad, laboratory experiments have been carried out on animals and humans, and it has been possible to determine approximately the safe limit of exposure to various substances. Such data have, therefore, been tabulated and are presented in Table II. In this table are given the principal physical characteristics of various gases and vapors and the physiological response on exposure to them. The last column in the table represents the concentration of gas or vapor which is considered safe (according to information at present available) and which should not be exceeded. Hence, given the problem of exposure to any of the substances given in the table, it devolves upon the engineer to determine methods which will keep the concentration below the given safe limit, that is, the value in the last column of the table.

Engineering methods of prevention

Until recently, the methods of controlling occupational disease hazards met with little attention. Since, however, the use of substances injurious to health has been associated with a subsequent rise in the number of persons affected by continuous exposure to them, the preventive aspects of the problem have seriously engaged the attention of industrial physicians and engineers. The methods which have been developed differ widely due to the varying ways in which processes and operations are conducted. Detailed information, therefore, cannot be given with respect to the design of control apparatus. In general, the control of a hazard by engineering methods can be achieved in several ways, namely: *a)* by isolation of the hazardous process; *b)* by exhaust ventilation; *c)* by means of personal-protection devices, such as respirators and canister-type masks.

Isolation methods

The object of this method of prevention is to segregate a particular hazard so that a minimum number of workers are exposed. Frequently, a hazardous occupation may affect workers who are not connected with it, but who work close by. An example of such a condition has been given in connection with the five workers in the foregoing chromium study who had ulcerated septa, but who were not engaged in plating operations. Isolation methods have been successfully used in plants where dust hazards exist, such as the modern sand-blast room and the hydraulic shake-out in foundries, which not only tend to localize the hazard within a definite closed area, but also expose few workers who are adequately protected by masks or helmets. Similar developments have also taken place in the spray-painting industries. Thus, spray painting and cabinets have been developed which are automatically operated and require only limited attention by the worker. The same is true of paint-drying rooms and tunnels. Isolation methods are often the simplest and most practical approach in eliminating most occupational-disease hazards. A more extensive use of these methods, however, is often limited because of the complex operations found in many plants which require frequent handling of objects and hence necessitate the exposure of a large number of workers.

Exhaust ventilation methods

The use of exhaust methods near the source of a hazard has grown rapidly in recent years. Briefly, the control of any industrial hazard by local exhaust is based on the principle that sufficient air motion must be created by a hood or opening at the source of the hazard to reduce the concentration below the threshold limit. The amount of air motion necessary cannot always be estimated directly but depends upon a careful study of the relation between the amount of air contaminant present and the airflows handled.[7] Bloomfield applied this procedure with regard to the degree of ventilation required to keep chromic-acid mist below the threshold limit established by an occupational analysis previously discussed.[4] The chromium-plating tanks described in the study utilized lateral exhaust. By varying the air flows handled and making determinations of the chromic acid mist in the breathing zone of the worker, it was found that the air movement in the plane of the opening, necessary to produce a safe concentration of mist, was approximately 1500 fpm. Some variations were found when the current density in the plating process was increased, since

turbulence due to gas formation at the electrodes was increased correspondingly. However, the air movement produced a safe concentration for most conditons encountered.

Since in any case the amount of ventilation required depends on the operations performed and on the shape of the hoods used, it is necessary to study each method of control separately. There are, however, some data on the characteristics of most hoods which are not obstructed in the zone of influence which may prove convenient.[8] These characteristics express the conditions of air flow forward of an opening and thus allow some estimate of the performance of a particular hood. For the approximate calculation of the flow at any point along the axis of a hood without any surrounding barrier, the following formula has proved useful:[8]

$$V = 0.1\ Q/(x^2 - 0.1\ A)$$

where *V* is the velocity of the air in fpm at a point along the axis; x is inches from the opening; *Q* is the volume of air handled in cfm; and *A* is the area of the opening in square inches. If overhead hoods are used for lighter-than-air vapors or gases, the air velocity at the edge of the tank or basin from which they issue is given by the formula:[9]

$$V = 0.71\ Q/PD$$

Here *V* and *Q* are as in the former equation, while *D* is the distance from the hood opening to the edge of the tank in feet and *P* is the tank perimeter in the same unit. Thus, if the air movement necessary to control a given hazard at a point is known for one hood, the amount of air necessary to be handled by a hood of different size may be approximately determined.

In the case of hoods used in spray-painting operations where solvent vapors are found, it is customary, from the nature of the work, to place the object to be sprayed within the hood, while the operator stands just outside the opening. In such cases, the air flow necessary to secure safe limits of exposure is expressed in feet per minute at the opening. From studies made of the benzol hazard in various industries, it has been found that air flows of from 100 to 200 fpm are required to keep the concentration of benzol below the safe limit of 100 parts per million.[10] Here again, however, data on the air movements required to control hazards caused by the use of other substances are lacking, and the investigator must devise special studies and apply the data of Table II.

While no attempt is made in this paper to discuss the various designs of hoods in use, it is necessary to point out a few important factors in design which must be considered. First a careful study of the operation to which a hood is to be applied must be made. A hood should be so designed that it offers a minimum amount of hindrance to the operator. Secondly, due consideration must be given to the nature of the substance to be collected. In Table II, the principal properties of a number of gases and vapors are given. The type of hood design used, therefore, must utilize the fact that if a gas or vapor is heavier than air, it is preferable to use downward or lateral exhaust. This point has been aptly illustrated by Gumaer,[11] who has shown that the tendency of a vapor such as benzol is to form into dense layers which sink gradually downward. Lighter-than-air gases or vapors, on the other hand, are best handled with vertical exhaust, taking advantage of their natural tendency to rise. The importance of utilizing the characteristics of a given gas lies not only in the fact that it simplifies the problem of control, but also it prevents any accumulation of gas in such concentrations that they may be accidentally ignited and cause explosions. For this reason there are given in Table II the inflammable limits of various gases and vapors when data pertaining to them have been available. Finally, the third factor to be considered is the frequent testing and care of the ventilation apparatus. Exhaust systems should always be operated at their maximum efficiency and periodic checks should be made to see that the concentration of air contaminant is kept below the threshold limit.

Personal respiratory-protection methods

Personal respiratory-protection apparatus are widely used, especially when isolation and mechanical methods cannot be properly designed or when workers are exposed for very brief periods of time. Such apparatus cannot be worn continuously because of the inconvenience incurred in wearing them. Consequently, they form a method of protecton when other preventive measures are impracticable. Nevertheless, personal respiratory-protection apparatus form an important part in many preventive programs and a proper knowl-

edge of their uses and limitations is extremely important.

The simplest form of respiratory-protection device is the respirator. Respirators consist of a face piece covering the nose and mouth, with a filter medium to restrain dust or mist on inhalation. A special valve is provided to facilitate expiration. Respirators are used for protection against injurious dusts, such as silica, asbestos, lead, and cadmium oxides. Their effectiveness depends upon the type of filter medium used and the manner in which it fits the wearer. A large number of respirators of various types have been developed. Many of these have been tested and reported upon by the Bureau of Mines.[12] This Bureau has recently prepared a schedule of tests for respirators which attempts to standardize the procedure for determining the effectiveness of various respirators.[13] Heretofore, much confusion has resulted with reference to the claims made by the various manufacturers on respirator efficiencies.

For the prevention of hazards due to exposure to gases and vapors, canister masks have been developed. These masks are made of special fabrics and cover the face completely. A flexible hose connection extends from the lower portion of the mask to a small canister containing an absorbing medium. Thus, the inhaled air is made to pass through the canister and insures pure air to the wearer. Universal canisters are supplied with a variety of absorbing materials arranged in layers and can be employed against most of the commoner gases and vapors found in industry. Canister masks, however, cannot be used where the gases or vapors are in high concentration. A range of 2 to 5 percent of a given contaminant appears to be the maximum limit in which a canister-type mask can be used.[14]

It is important to remember that canister-type masks cannot be employed in an atmosphere deficient in oxygen. Furthermore, great care should be taken to refill canisters at regular intervals to insure high absorption efficiencies.

Still another type of mask used to protect the worker is the positive-pressure mask. Such masks are supplied with a continuous flow of compressed air from a clean source. This method of protection is finding increasing use in many industries because of the high efficiencies which can be obtained. A chief fault to be found with such masks, however, is the inconvenience experienced by the wearer who is compelled to carry about with him an air-supply hose.

Medical aspects of prevention

The industrial physician is in a position to estimate the success or failure of a preventive program. He is the first, by virtue of the workers who report to his clinic, to discover the characteristic symptoms of an occupational disease and to call attention to the specific occupation which are dangerous. In this connection, as has been pointed out by the American College of Surgeons,[15] the periodic medical examination of workers is of immense value. Only in this way is it possible to secure and maintain the physical fitness of employees and to help increase their longevity. Workers exposed to the hazards of volatile solvents, such as benzol, carbon disulphide, etc., and to such gases as carbon monoxide and hydrogen sulphide, require medical examinations at frequent intervals to insure them against serious chronic ailments. Workers showing symptoms of poisoning should be given other jobs, and should be re-examined at later dates to determine their improvement.

Summary

This paper points out the decreased longevity of industrial workers in comparison with workers of similar social and economic status. The importance of possible exposure to occupational-disease hazards as a contributing cause in the decreased longevity is stressed, and methods of their prevention with particular reference to substances other than toxic dusts are discussed. These methods include the preliminary plant survey and occupational analysis and engineering and medical methods of prevention. The plant survey consists of listing all of the hygienic facilities for the purpose of determining those occupations in a plant which require further study. This is followed by an occupational analysis, which is intended to show the severity of the exposure of various occupational groups and to correlate the findings with medical examinations. In this way, it is shown to be possible to determine the safe or threshold limits of exposure. Ths toxic limits of common industrial gases and vapors are included in table form. With regard to the engineering methods of prevention,

there is discussed the comparative features of three methods in present use, namely, isolation, local exhaust, and personal respiratory protection. The value of medical supervison and periodic physical examination as a method of increasing the longevity of workers is shown to form an integral and important part in a preventive program.

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Code for safe concentrations of certain common toxic substances used in industry*

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For some time, Massachusetts has made use of the following figures as a guide to manufacturers and others interested in maintaining satisfactory working conditions. Many of us feel that the codes on toxic limits now being prepared for the American Standards Association will be some time in appearing and we believe that it would help industry if this list were used in the interim.

It is not implied that observance of these figures is a guarantee against possible ill health of workers exposed, or that medical control can be neglected. Revision of any such table from time to time will always be necessary.

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TABLE I
Maximum Concentration Suggested by Massachusetts

Gas or Vapor	ppm	Gas or Vapor	ppm
Ammonia	100	Hydrogen fluoride	3
Amyl acetate	400	Hydrogen sulfide	20
Aniline	5	Lead	0.15*
Arsine	1	Mercury	0.1*
Butyl acetate	400	Methanol	200
Carbon bisulfide	15	Monochlorbenzene	75
Carbon monoxide	100	Nitrobenzene	5
Carbon tetrachloride	100	Nitrogen oxides	10
Chlorine	1	Ozone	1
Chlorodiphenyls	1*	Phosgene	1
Chloronaphthalene	1 to 5*	Phosphine	2
Chromic acid	0.1*	Sulfur dioxide	10
Dichlorbenzene	75	Tetrachlorethane	10
Dichlorethyl ether	15	Tetrachlorethylene	200
Ether	400	Toluene	200
Ethylene dichloride	100	Trichlorethylene	200
Formaldehyde	20	Turpentine	200
Gasoline	1000	Xylene, coal tar naphtha	200
Hydrochloric acid	10	Zinc oxide fume	15*
Hydrogen cyanide	20		

* Milligrams/cu meter.

Toxic logic*

EDITORIAL
Industrial Hygiene Section, Industrial Medicine

"Toss the dust counters into a closet, lock the door and lose the key." "Dust is present, therefore a hazard exists." "This man has worked here the last 40 years without a sick day in his life: the place must be safe." "Carbon tetrachloride is less toxic than gasoline." "Gasoline is less toxic than carbon tetrachloride." "Air analyses don't mean a thing — the conditions change every day." "Toxic limits are valueless — they are all based on animals."

These and many another loose statement have been made and repeated on every side. The closer to the truth the statement is — without actually hitting the bull's eye — the more misleading the impression is apt to be. A general assertion about a scientific fact can often appear logical, even though it is essentially erroneous, by presenting only a portion of the whole situation. By the application of sound common sense to the use of toxic limits for the interpretation of air analyses, the industrial hygienist can utilize a valuable tool for the more effective and more economic control of occupational disease exposures.

A well-rounded presentation of the value of toxic limits, their practical purpose and the limitations of their use has been prepared for this issue by one of the world's most eminent industrial hygienists. His views are based on a wealth of experience in the field and an extensive knowledge of the literature. He is in excellent positon to evaluate the reliability of toxic limits which have so far been published, as most of the actual experimental work has been done on them during the period of his active participation in industrial hygiene. Where the toxic limits of a number of organic solvents were determined on the basis of several hours' experiment on a small number of guinea pigs during the first decade of the century, he visualizes the results, not as figures on a published table to be blindly accepted, but as a group of experiments, the findings of which were published in detail as current literature earlier in his career.

The fallacy of the statement that "carbon tetrachloride is more toxic than gasoline" is that this does not apply to prolonged exposure but was based on brief animal experiment. To be sure, the literature states that only 2.2% of gasoline vapor in air will cause death whereas 4.8% of carbon tetrachloride is required to produce this result, but these findings are based on the concentration which kills a cat in 30 minutes. Where there is prolonged exposure, such as is contemplated in industrial occupation, it has been shown that carbon tetrachloride concentrations should be kept appreciably below those considered safe for gasoline vapor.

Dr. Teleky's observations[A] are the results of his own experiences and may not represent exactly the views of all our readers whose contact with the occupational disease situation may be from a different angle. The point of view of those who approach industrial hygiene in its various phases will be welcomed in connection with the conclusions expressed in Dr. Teleky's paper.

A real endeavor should be made to utilize this tool further. The difficulty of not having data on exposures over long periods of a worker's employment, referred to by Dr. Teleky, should be provided for ahead of time by keeping on record average and representative exposures at potentially hazardous occupations from month to month or year to year depending on the nature of the operation.

An increasing number of industrial concerns and those engaged in mining are obtaining and collating just such data. Not only are these data of value in checking exposure, but they will also afford more exact and reliable information on which to base toxic limits.

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[A] Dr. Teleky's paper appears in its entirety immediately following this article.

The development of methods for the quick and easy determination of injurious materials in air is a long step in the right direction. The caution referred to by Dr. Teleky is to be observed, but it is only by use of methods which short-cut laborious laboratory procedures that we can hope for the mass of data required for positive conclusions.

Appreciate the value of toxic limits but, in making use of them, do not fail to observe their limitatons.

We commend Dr. Teleky's paper to your critical attention with the thought that for the full utilization of the toxic limit, one must apply the logic of practical common sense.

Toxic limits*

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The foundation of modern science and modern technique is the process of weighing, measuring and counting. The step from the empirical state to modern science, from skilled handiwork to mechanical performance was possible only after methods for specific weighing and measuring had been found. Exact examinations of air and its contaminants in factories were great rarities even 20 and 15 years ago; indeed determinations of dust concentrations were the only such measurements made to any appreciable extent and these were done in English speaking countries alone. No other instruments were available for investigations in factories except those for determining the dust contents. (In the United States, the sugar-tube, Palmer apparatus, Greenburg-Smith impinger; in England, Owens dust counter; in South Africa, Kotze konimeter.) The methods and instruments used in laboratories have also been used in factories, instruments difficult to handle and transport, often not accurate. All this is different today.

We now have various instruments suitable for use in factories, although the truly exact instrument and the precise method is still lacking for certain purposes. On the contrary we even suffer from too many offers of instruments made by firms and scientists. Their only small deviation from already existing instruments makes it more difficult to compare the results, since the new instruments often do not guarantee any greater accuracy.

R.R. Sayers[1] published in 1927 data about the most important poisons, briefly summarizing them. As far as I know, Zangger[2] in 1928 was the first author to compile a table "about the effect of irritant and poisonous gases and vapors." For many gases he specified the exact concentration in milligrams per liter which would kill immediately or be fatal after 0.5 to 1.0 hour. He defined which concentration may be borne with large, small or no damaging effect for a period of time. The compilation is supported for the largest part by animal experiments, made by K.B. Lehmann and his collaborators, Zangger, U.S. Bureau of Mines, Haldane, Henderson and Haggard. Experiments on human beings (experiments on the author himself) are rarely reffered to. An extension and completion of this table may be found in the book, *Noxious Gases*, by Flury and Zernik.[3]

The table, "Maximum Allowable Concentrations," compiled by Bowditch[4,5] was especially meritorious as it included tabulation of regulations of other governmental authorities in addition to those suggested for Massachusetts. These had been referred for criticism to more than a score of the leading authorities in this country and abroad prior to their promulgation. This table has been revised and extended by himself, C.K. Drinker, P. Drinker, H.H. Haggard and A. Hamilton.[6] By formulating the problem into *"allowable concentrations"* it has been taken out of the field of theoretical research and *transferred to the practical industrial hygiene.* But the ready availability of apparatus easy to handle and of tables of toxic limits established by well known scientists to which the results can be referred for interpretation may lead to the undesirable situation that men not well trained in industrial hygiene will underestimate the difficulties of obtaining truly representative results. In addition there is the danger that they will employ these results beyond their limits of usefulness and so draw unjustifiable conclusions.

Therefore the *value of the limits,* the *practical purpose* and the *limitations* of their use may be discussed in the following lines.

A sharp distinction must be drawn between acute and chronic action which must be applied especially to those materials which produce acute and chronic occupational poisoning (benzol, toluene, xylene, carbon disulfide, trichloroethylene, aniline, ozone, etc.). The "allowable concentration" is much higher where there is danger of acute poisoning than under conditions where there is

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continuous inhalation for a long time. It is evident that it would be out of place to demand the same limiting value of contamination where the workers are only occasionally exposed to the danger of acute poisoning (transferring benzol, trichloroethylene, carbon bisulfide, etc., or similar intermittent work performed at extended intervals) as in places where there is danger of continuous inhalation for a period of weeks or months.

The Massachusetts publication quoted above seems to give the "allowable concentrations" for those actions which are most important in industrial hygigne: the chronic influence of benzol and its homologues, the acute poisoning by CO. Although the expert knows or is able to find out for which situation the given value is applicable, it would be expedient *to specify in the table the limits for acute and those for chronic poisonings.* If that is not possible or not necessary for some substances, it should be stated clearly whether the quoted value refers to acute or chronic action.

Of course, the conceptions of "acute" and "chronic" are not sharply differentiated. But generally we may call poisonings and damages acute when they can take place within a working day; and we may call them chronic when they need a longer time to develop — usually weeks or even years.

A specification of the concentration fatal in a half hour or less, although scientifically interesting, is of little value for practical industrial hygiene as pointed out below.

As examples of the damages which arise after harmful action of years or decades may be mentioned silicosis, bladder cancer of aniline workers, the symptoms of chronic alcoholism, certain damages by X-rays and radium, some serious forms of carbon bisulfide poisonings, mercury shakes, the changes of the vessels and as a rule the pareses as a result of lead poisoning.

But if a man working with lead for many years falls ill with lead colic, i.e., the subacute form of lead poisoning, it is correct to suspect that he has recently absorbed an exceptionally large amount. The same cause — a larger amount of absorbed poison — may also be considered in case a man working with mercury for many years acquires gingivitis and diarrhea; and if serious blood change in a man working many years with benzol is not started by infectious disease, it is possible that it was caused by a larger recent absorption of benzol.

Many animal experiments are at hand concerning concentration and duration of air contaminations which cause temporary or lasting injury — but their application to man is either not feasible or to be done only very cautiously.

There are important differences between the different species of animals. The fatal concentration of carbon monoxide poisoning at 32°C is above 0.12% by volume for the rat; above 0.25%, for the guinea pig and above 0.38% for the rabbit.

Flury and Zernik[3] tell us that cats, mice, rats are very sensitive to phosgene; dogs are less sensitive, rabbit still less. Horses are less sensitive than human beings. When the driver died in gas attacks during the World War, the horses sometimes showed only slight symptoms of poisoning.

Our conclusions therefore on acute poisonings have to be based preferably on the experiences we have had with man. For chronic poisoning and damages the animal experiments fail entirely to be useful for our purpose because it is impossible to determine the comparability of the time required for injury to develop in animal and in man.

A study of conditons which may produce chronic poisonings presents a number of difficulties. The contamination of the air can be determined during the whole working shift very well, but is it impossible to ascertain the circumstances under which the injurious material was absorbed during months and years gone by.

If it is admitted that the conditions affecting industrial health have improved in the course of years — which is true in general, but not in every single case — or that the working time is shortened, then the amount of injurious material absorbed in a working day was larger in former times than it is now. But it may also be that the damaging material is not used such a long time, as the case history may tell us, or that its concentration has been increased recently; such as unnoticed substitution of benzol for benzine or a benzine-benzol mixture, or substituion of lead for color containing little or no lead.

Therefore it must be remembered that all results are approximate values only. But the most important materials, especially in regard to their chronic poisonings (benzol, carbon disulfide, lead) have

been studied with such thoroughness and skill by our best industrial hygienists that the obtained figures are actually practicable as limits.

But the observations about some other substances (cadmium, chlorine (chronic), dichloroethylene and many others) are too limited in number and not clear and reliable enough to make even partly safe conclusions. If figures about such substances are included in the list at all a *mark of interrogation has to be added.*

The limits are approximate, not only on account of the difficulty of most of the observations, but also on account of differences in sensitivity of individual persons and on account of different amounts of the contaminated air absorbed by the worker under different circumstances. For instance, the worker when working hard inhales much more of the contaminated air (up to 50-60 liters per minute) than when doing light work (8-10 liters per minute).

But these lists of toxic limits give the practical industrial hygienist essential data for his work; they save laborious studies of literature and give him the results obtained by those carrying on research and basic investigation. *Therefore we have to be thankful for the compilations of the limits by their authors.*

How are the "limits" to be utilized? For which purposes may they be used? What is their immediate practical advantage and when may they be applied?

First of all: The limits strongly support the industrial hygienist in arriving at an opinion as to whether the exposure is or is not excessive, and, if so, in convincing incredulous employers and engineers (under certain circumstances) that the contaminated air in their rooms is injurious even though the contamination cannot be readily seen or smelled. The data on the exposures, if properly substantiated, act as impartial arbitrators between the man recommending control measures and the man persisting in the present situation.

The limits are useful in construction and testing exhaust systems. Naturally you will try to remove every contamination of the air, because only that gives complete security. If that is not possible, you must insist that the ventilation has at least such an effect as to reduce the exposure to less than the "allowable concentration" in the breathing zone. If that is impossible, you have to try to bring about hygienic conditions by changing the operation or by abandoning the use of the poisonous substance.

I might indicate that exhaust ventilation seems to be considered too much as the principal remedy nowadays, as the respirator was considered some years ago though with much less foundation. Other procedures mentioned above are sometimes forgotten today, although they have attained great success in industrial hygiene.

If the limits are used, it must be definitely ascertained that *the evaluation of the contamination in the air is reliable.*

Because the testing devices are reasonably priced, easy to handle and because the methods of examination in laboratories are frequently simplified, there is (as marked previously) the danger of unqualified men using them. Therefore the following has to be stressed:

Serious acute poisonings, expecially fatal ones, arise through unforeseen accidents — as leaking of vessels, pipe lines, or by unexpected formation of gases in larger amounts or by other abnormal events. Also, by exceptional atmospheric conditions where the removal of gases is not effected by strong mechanically driven exhaust systems.

A locksmith was found dead beside his forge fire where he had been seen working 20 minutes before. As an exhaust pipe has been installed in this place and the man had worked here for many years, the technician thought a CO poisoning impossible — the blood of the dead man however was found to be saturated with CO. Abnormal cold and severe storms had interfered with the natural up-draft existing at other times. I have seen CO poisoning with unconsciousness in some working places of a large plant in presence of such abnormal weather; the workers had worked in these places without disturbance of health for months.

I have seen poisonings by arsine as a result of using too strong an acid so that the solution was not neutralized; as a result of too much zinc powder being added; and as a result of an exhaust pipe being obstructed by the formation of foam.

Such circumstances caused by abnormal accidental events cannot be investigated by air examination because we do not know all contributing factors and therefore we are not able to reproduce these circumstances (to say nothing of

the danger to the investigator). Therefore, as mentioned above, data about the deadly concentration would be of little practical value.

In all other circumstances it is self evident that *only numerous samples* of air give a true picture of the existing conditions, if taken *at different times* and during different working processes and in the exact working place at the *breathing level* of the worker. Samples taken off-hand are without any value.

The investigator has to be certain that the working processes during the time of examination are the same as at other times. The investigator can be misled intentionally or unintentionally. The occurrence of illness should of course induce the improvement of the working conditions. When we investigate we have to know if such changes have taken place or not. It is sometimes difficult to find that out.

Another difficulty which may be overcome only by patience is the fact that all persons concerned — even involuntarily — work more "according to prescription" if observers and supervisors are present.

In addition it must be taken into consideration that little variations — produced intentionally or not — are able to change the whole picture; small changes hardly detectable in the process produce considerabledifferences inth e amount of contamination in the air; season (open or closed windows), and weather also influence the picture.

An electrolytic nickel plating bath delivers more hydrocyanic acid gas, a chrome plating bath more chromic acid mist, when the current is heavier or the treated objects larger. The amount of lead fumes depends, among other factors, on the temperature of the lead bath, the zinc oxide fumes on the temperature of the molten alloy. More vapor escapes in an apparatus for degreasing by trichloroethylene if the trichloroethylene is heated more and if it is not cooled before emptying. The quantity of excaping vapors changes in the usual degreasing apparatus with the temperature of the wate:" used in the cooling coil, with the size of the objects and their number and with the frequency and speed with which they are taken out.

Ball mills pulverizing rock have often been submitted to my inspection and I was shown they were working without escape of dust, — it was soon after loading large rock. But half an hour later, when the material has been reduced to fine powder, much dust was escaping into the breathing zone.

To give some examples of numerical differences: Dust concentrations found in my investigations in grinding shops[7] in the summer by the Owens dust counter have averaged between 600 and 1500 particles per cm^3 in the same room, at the same speed of rotation of the sandstone wheels but grinding different kinds of knives. In winter, when the windows were closed, the figures ran up to 3700 at the breathing level of the worker. In the air of the room in general the dust figures averaged to 560 in summertime, 3300 in winter. Bowditch and Elkins[8] found in the coating room of an artificial leather factory on different days in March 130-200 parts per million of benzol; concentrations of 300-1300 ppm of naphtha vapor were detected during the work done by one worker in a factory using rubber cement. Greenburg and corroborators found in a rotogravure printing plant 50-1060 ppm of benzol in different parts of the press room.

I think it is not necessary to stress that all the difficulties mentioned above have to be regarded especially if there is a compensaton case, or if there is a question of negligence.

Summarizing

A well-trained industrial hygienist only is able to make investigations in industrial hygiene and especially for answering the question, If, when or how often limits are transgressed; and besides he can answer only after a long-lasting and exact examination.

It should never be forgotten, that all our limits have their origin from health examination of workers and that only from comparison between the results of these physical examinations and the content of contamination in the air do the limits result. All the mentioned uncertainties and difficulties can be avoided in many cases if we refer to this origin. If there is a danger of chronic poisoning the thorough investigation and examination of the workers especially for early symptoms give us a sure answer in cases where the time is long enough for acquiring symptoms of chronic poisoning.

We may also see if the contamination is able to produce acute poisoning by examining the workers at the end of the daily working time.

A special consideration must be given to the question if and how far the results of air examinations and their relation to the limits are able to contribute in determing the occurence of an *occupational disease.*

The question of whether there is an occupational disease presents itself as a medical question. A physician only is able to answer it after considering all the clinical symptoms and after a thorough medical examination executed with all necessary aids.

The clinical pictures (and the pathological one in the autopsy) of the more frequent occupatonal diseaseš (chronic poisonings by lead, mercury, benzol, silicosis, to some extent carbon disulfide, and certain acute poisonings as CO) have been studied so carefully and are so well established that the diagnosis can be made with greatest certainty — by a physician experienced in this field as is the case with every other medical diagnosis.

We have mentioned above the difficulties and uncertainties of air examinations. We cannot guarantee that the air contamination during the investigation was the same as in the time before the poisoning occurred. Therefore negative findings in air contaminations or findings below the limits are never able to shake such a positive medical diagnosis though under certain circumstances it is possible that a former occupation may have been responsible for the disease. Positive findings on the other hand are able to support it. Furthermore if we have a clinical picture that according to medical opinion does not correspond with the well known picture of this poisoning nor with signs of its rare varieties and therefore the physician denies an occupational disease, then the findings of air contamination above the limits is no proof of a causal connection between the illness and the contamination; the illness may have originated entirely independently of the contamination because of an internal or another external cause.

But there is another method which gives us an insight into the circumstances under which the ill man worked prior to his disability and which should be practiced in chronic poisonings if it can be done shortly after the beginning of his illness: The physical examination of the fellow-workers (still working, disabled and dismissed). If the symptoms of the same illness are found, it confirms our diagnosis of the case in question. Negative findings are of small value, because the sick man many have been more exposed to the damaging substance or may be more sensitive.

In acute poisonings the examination of the fellow-workers should be made at the end of the shift.

There is however, a long list of less explored substances (most at present rarely used), the clinical pictures of which are not clearly worked out as yet — nor are their toxic limits. We are able to conclude that there is a causal connection if certain substances are found in the air and contemporarily symptoms of illness determined in a worker and if these symptoms agree with those mentioned in the literature as a consequence of this poison or if similar pictures are to be seen among the fellow-workers.

But cases occur when a positive medical diagnosis alone is not sufficient. For compensation cases and for prophylaxis it may be of greatest importance to know through which kind of work the illness is acquired.

If the examination of the air fails to give exact proof, then all chemical and other processes should be subjected to the opinion of experienced experts in technology, chemistry and industrial hygiene. In such cases all the impurities possible present in the substances used are to be considered.

I wrote about "experienced physicians." The universities (medical schools) should give better instructions to students of medicine in industrial hygiene and in occupational diseases. Especially in the latter field, there should be established short courses for physicians also. The legislation, the industrial commissions, the insurance companies, the employers and the employees should take advantage first of all such trained physicians and thus give them occasion to acquire still great experience.

Summary

1. To define toxic limits of the greatest scientific and of the greatest practical value.
2. It should be made evident whether the toxic limit applies to acute or chronic poisoning, if it is well founded or doubtful.
3. The limits are valuable help in showing the

necessity of prophylactic measures in a plant for the construction of new and for testing and existing installations. But the examinations should be made very carefully and by experienced industrial hygienists. In determining the severity of exposures resulting from existing installations, the medical examination of workers often gives a better insight.

4. It is the field of medical diagnosis to ascertain the presence or absence of an occupational disease. This diagnosis made by an expert physician cannot be shaken by a contrary result of air examinaton, but if this result is certainly representative of the worker's exposure, it may point to the desirability of further investigations.

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Determining margins of safety — criteria for defining a "harmful" exposure*

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The control of the occupational environment to prevent harmful absorption of toxic materials is now a generally accepted principle by employers and employees. The practical problem of defining what is "harmful" presents certain difficulties, and it is well to begin with a discussion of the various criteria which have been used to indicate the degrees of injurious effects. Where a clearly defined severe systemic disease results from an exposure to harmful substances, there can be no question as to the need for measures which will decrease the degree of exposure. But as the environmental conditions are improved, a marginal zone is reached in which the injuries sustained are slight and quickly reversible, or amount only to a discomfort — tolerable, but unpleasant. It is in this zone that one finds the greatest controversy concerning the permissible limits of exposure.

It is good operating practice to control the working environment so that even these mild, transient injuries are prevented, and the discomfort is held at a minimum. An occasional slight anesthetic effect from the inhalation of ether or acetone may result in no permanent systemic injury, but workmen so affected are more liable to sustain accidents, and their working efficiency is impaired. A single, mild attack of metal fume fever — as from the inhalation of zinc oxide fume in the welding of galvanized sheet — may not be severe enough to cause a loss of time, but repeated and frequent episodes cannot be regarded as harmless. Certain substances in concentrations below that which will produce serious harmful effects, may cause moderate irritation to the eyes, mucous membranes, or skin. For example, amounts of chromic acid in the mists over chromium plating tanks which are not sufficient to cause systemic injury, may produce repeated irritation of the mucous membranes of the respiratory tract and destruction of a part of the nasal septum. Good operating technique is now directed at maintaining chromic acid levels below the point where these lesser injuries can occur.

The general trend in industrial hygiene control has been to eliminate, where possible, the environmental conditions which cause sufficient discomfort to interfere with the efficiency of the workman. The evaluation of "discomfort" is admittedly difficult, with psychogenic and aesthetic factors playing so important a part, and the individual response so variable. In certain instances, a further control of the environmental factors contributing to the discomfort is impossible, or, at least, extremely impractical, and a solution of the problem may be had by selection of workmen, usually by a trial and error method, who exhibit a high threshold with respect to the particular exposure. An extreme example of this approach is the case of a workman in a cafeteria, one of whose jobs was to carry out the garbage. Each time he performed this job he became nauseated and frequently vomited. He reported to the medical department after a few days, complaining of these symptoms and of loss of appetite, and he had lost a few pounds of weight in the two weeks of employment. A careful examination revealed no other medical cause for his symptoms, and when he was transferred to other work (and incidentally, more strenuous labor) he regained his appetite and weight in a few days. There certainly was no toxic element associated with carrying out and dumping garbage, but the symptoms and loss of weight were no less real. The fact that many other individuals had performed, and subsequently did perform, this work without untoward results made the transfer of this employee a much simpler solution than any attempt to control the odors and visual stimuli connected with the job.

One aspect of the problem of occupatonal disease control which is receiving more attention is

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that of the relation of the industrial exposure to the possible increase in diseases which are not recognized as specifically occupational in origin, but which are common to the population in general. There are very few of the diseases which are definitely recogized as resulting from exposures to industrial toxins which have pathognomic characteristics, that is, signs and symptoms which are so specific and peculiar to the disease process that the diagnosis is made with such certainty that all other pathologic causes are excluded. When the signs and symptoms of an occupational disease are those which occur with considerable frequency in diseases commonly found in the general population, the picture is much more difficult. Impressions concerning such a relation, even by a competent and careful observer, are often very misleading. Adequate records with a proper statistical treatment and an intelligent, critical evaluation offer the greatest promise in an attack on this pertinent and important problem.

A frequently inaccurate guide as to the safety of an exposure is the statement of an "old-timer" on the job that there is no hazard connected with that operation. This criticism does not imply that such testimonials are valueless, but they must be scrutinized with care. A "natural selection" operates so that in certain circumstances, individuals who have been affected by an exposure to potentially harmful materials are eliminated from those jobs (sometimes only after receiving considerable injury) and the remaining personnel consists of the more resistant individuals. The causes which operate in these circumstances may not be recognized, in fact they frequently are not by the person who remain unaffected, who, if they consider the eliminated workers at all, may regard them as "weak links who could not take it."

The medical examination

The human body posesses the ability of absorbing a limited quantity of any substance without a demonstrable harmful effect. It is only when this tolerance — admittedly small for some compounds — is exceeded that injury results. With certain materials the margin between harmless absorption and severe or even fatal injury is a narrow one. With other substances, large amounts can be absorbed with impunity, or a greater latitude may exist between the quantity which first produces minor injury and that required for a fatal effect. Complicating these relationships are many variables, such as the rate of absorption; the rate of elimination; the rate of recovery from injury by a tissue, organ, or system; and the variability among individuals and in the same individual at different times. In spite of such a complexity it is possible and practical to define certain safe conditions of exposure to a great variety of substances which are found in industry.

The medical examination of the workmen exposed is an essential factor in the evaluation of an exposure, since all of the information gained from a study of the environmental factors has significance only in relation to the medical findings. An industrial hygiene control program cannot insure its effectiveness without such a medical examination, since its ultimate value must depend upon securing the health of the workmen. Frequently, when this integrated information has been sufficiently verified, the analysis of the environmental factors may play a very important or even the chief part in the mechanism of control. The advantages and limitations of such environmental studies will be discussed later.

The scope of an adequate medical and industrial hygiene examination will depend upon the nature of the exposure, determined by such factors as the completeness of information from previous studies, the correlation with environmental analyses, and the nature of the pathologic changes revealed by clinical and experimental research. For example, the medical control program for an exposure to silica dust may depend largely upon analyses of the breathing-zone air and of X-ray examinations of the lungs. Many industrial exposures to silica are now satisfactorily controlled chiefly by repeated air analyses, but the physical examination, including the roentgenogram of the chest, must be made at intervals to insure the efficacy of the environmental studies. When, however, a new chemical, the injurious effects of which are unknown, is introduced, a more comprehensive medical examination is indicated. Experimental studies on animals frequently give invaluable suggestions as to the pathological effects, and consequently the type of studies which are likely to indicate the earliest signs of injury, but the occasional marked discrepancy between the effects on various species places a definite limitation on this type of information. The examinaton of in-

dividuals exposed to a new, potentially toxic material, should be frequent and comprehensive until there is reasonable assurance that no harmful effects are occurring. The period of probation for the new substance may necessarily be a long one. Experience with a chemical such as beta-naphthylamine has shown that relatively small amounts — amounts too small to elicit evidence of a general toxic effect — may produce serious injuries (in this case, tumors of the bladder) only after a period of years. While these exceptions are fortunately rare, they must be kept in mind in assessing the toxicity of a compound.

The medical examination which should be employed to detect the earliest signs of injury from an industrial toxin differs in some respects from that which is generally used in medical practice. Unfortunately many of our medical tools are not sufficiently acute to detect the very earliest evidences of functional failure. In addition, there is an overlapping zone between areas of values which are definitely normal and those which are certainly abnormal. Since industrial exposures often involve many individuals, statistical methods are particularly applicable. If a single individual presents a value for a physiologic characteristic which falls in the marginal zone between the normal and abnormal, it may be difficult to evaluate it, but such a statistically significant deviation occurring in a group of individuals may indicate a common influencing agent — perhaps an industrial toxin. The industrial hygiene medical examination may differ, too, in including some special tools, usually laboratory procedures, such as the determination of lead, mercury, selenium, or an organic dye. Their applications to industrial medicine differ in degree, in that they become routine tools for controlling the absorption of potentially toxic subtances, and not measures for the diagnosis of a disease.

The use of statistical methods has required a careful development of norms. It must be emphasized that the values frequently quoted in textbooks of laboratory medicine are unsuitable, and the investigator must verify the ranges of values for each of the characteristics studied in the particular plant population being examined. The norms for the industrial population will not necessarily agree with those frequently given as "normal," since the former should be derived from a typical cross section of the particular industrial population and should include values from individuals who are suffering from the minor diseases found in an ambulatory working group, but should exclude values from individuals with exposures to potentially toxic materials until it has been demonstrated that those individuals as a group fall within the statistical limits of the control group. An extreme example of faulty choice of normal values is contained in an article on benzene poisoning appearing in one of the better journals a few years ago. The author's criteria of a normal erythrocyte count range was from 4,600,000 to 5,400,000; that is, values below and above this range were considered abnormal, and, in individuals exposed to benzene, indicated a toxic effect. The author did not limit his data to a particular population, with the implication that the standards apply generally. The absurdity of such limits is seen when a comparison is made with the values given in Table I. It will be noted that about half of the erythrocyte count values for this control group would be classed as abnormal under the too rigid criteria set in that author's study. These ranges of "normal" are from studies made on a plant population in Rochester, New York, and include males only, between the ages 18 and 65. They are presented here only as an example of the "normal" values obtained by a comprehensive industrial hygiene study, and should not be applied to studies of individuals from other populations without specific verification.

TABLE I
Norms
Males, 18-65 years, Rochester, New York

	Range (M ± 2 S.D)
Hemoglobin	13.8-17.2
Erythrocyte count	4,600,000-6,400,000
Cell volume (Hematocrit)	42.6-53.0
Mean corpuscular hemoglobin	24.3-32.3
Mean corpuscular volume	76.3-98.3
Mean corpuscular hemoglobin concentration	29.2-35.6
Leukocyte count	4,500-11,000
Schilling index:	
Polymorphonuclears	38-74
Lymphocytes	16-50
Monocytes	3-13
Eosinophiles	0-7
Basophiles	0-2
Reticulocyte count	0-1.0
Icteric index	1-7
Sedimentation rate	0-23

Abnormal physical signs are of much greater value in diagnosis than symptoms. The latter are so frequently colored by the opinions of associates, by misinformation from many sources, by the approach of the examiner, and may take on an epidemic form if the suggestive factors are strong enough. They should be elicited and carefully considered, but their notorious unreliability gives them a secondary value. The physical examination may include a variety of special techniques, such as electrocardiograph, the X-ray, etc., as indicated. A recent development by Dr. John Foulger and his associates makes use of the data obtained from repeated examinations of the blood pressure and pulse rates in identifying the early effects of toxic materials. The evidence presented thus far by his studies shows that this may be a useful and easily applied tool in controlling group of individuals in potentially toxic exposures. He properly emphasizes the desirability of having a method which will reveal early reversible functional changes. Further critical study of the method by other competent observers is necessary before it can be generally accepted as having the significance attributed to it by Dr. Foulger, but it certainly merits a broad trial.

Among the control measures which are extremely useful are those procedures for determining the amount of a foreign substance in the blood or excreta, or of an abnormal metabolite or change in the excretion ratios of a metabolite. An excellent example of the former is the determination of lead in the blood or urine of individuals exposed to that substance. Analytical procedures have become so acute that lead is now found in practically every urine specimen, and a certain amount is regarded as normal. As increasing amounts of lead are found in repeated specimens the probability of the individual developing evidence of lead intoxication increases, and the correlation of quantitative analyses with clinical data has made possible the definition of certain excretion levels, below which there is little likelihood of finding intoxication. The application of this procedure in industrial hygiene is primarily preventive — and not, as it usually is in regular medical practice, a diagnostic one. Careless and incorrect application of the procedure had led in some cases to an improper censure of its value, but there are many competent industrial hygiene laboratories which find it of real worth.

An example of the value of this type of procedure, even where the safe levels of excretion are not known, is this instance from our experience. A chemist was synthesizing an organic compound containing selenium, and, more out of curiosity than a real expectation of finding appreciable quantities of selenium, we asked him to submit a urine specimen. Methods for determining selenium in urine had been worked out by several laboratories in connection with the problem of selenium poisoning ("alkali disease") in animals in the great plains area of this country. In the analytical procedure, the selenium is precipitated as a red material, which if present in more than a few micrograms gives a reddish turbidity to the solution. The first urine specimen precipitate gave an appearance of tomato juice, as did several subsequent samples collected with every possible care to prevent accidental contamination. An investigation was started to determine how absorption occurred. The possibility of accidental ingestion was eliminated, and analysis of breathing zone air showed that inhalation could not possibly account for the large amounts excreted. It was finally proved that the major route of absorbtion was through the skin, and in subsequent experimental studies it was shown that from 5% to 10% of a given amount applied to a skin surface was absorbed in a half hour's exposure. Although it was demonstrated in animal studies that selenium tied up in this particular organic compound was less toxic than inorganic selenium compounds such as sodium selenite or sodium selenate, the really considerable amounts which could have been absorbed over a period of time might well have resulted in severe injury. All of the individuals exposed during the synthesis or subsequent handling were required to submit frequent urine samples, and the relationships between absorption and excretion were worked out so satisfactorily that we could tell the individual time within a half hour that an excessive exposure occurred. The results of the analyses were shown to the individuals exposed, and careful attention to technique in handling kept the absorption at a minimum. The collection of data from complete serial medical examinations over a period of years has shown that certain levels of excretion in excess of the normal selemium excretion may not be associated with any evidence of injury, and that it is practical to control the exposures so as not to exceed these arbitrary levels.

The determination of the urinary organic-inorganic sulfate ratio in exposures to benzene is a good example of a control method which utilizes a change in the ratio of excretion of a normal metobolite as an indication of excessive absorption. Normally from 75 to 90% of the total urinary sulfate, is present as inorganic sulfate and the remainder as organic or etherial sulfate. When there is an excess of phenolic compounds in the body, sulfate combines with a portion which is then excreted through the kidney — one of the normal detoxication mechanisms. When benzene is taken into the body, a portion is oxidized to phenol and is subsequently excreted, at least in part, as the phenolic sulfate. Since the amount of sulfate available is limited, and the phenol takes precedence in combination with sulfate over inorganic radicals, the proportion of organic sulfate to that of inorganic in the urine rises, and the percent of inorganic sulfate may drop to 50 or 25, or even approach zero. It has been shown that, in a group of individuals with an exposure to benzene, those having consistent organic sulfate percentages greater than 50 rarely give any evidence of benzene intoxication, and that the lower this percentage falls, the greater the likelihood of encountering cases of poisoning. The relationship between the sampling time and the exposure must be properly considered, and the tests must be performed often enough to indicate the true exposure if reliance is to be placed upon them as an important factor in the control program.

Analysis of environmental factors

In recent years more and more emphasis has been placed upon the analysis of the environmental factors as a means of controlling the hazards to toxic materials. This approach has developed slowly and is the outgrowth of initial studies made to determine the concentration of a material which actually caused an intoxication. The next step was obvious — the determination of concentrations to which individuals were exposed and which were not associated with evidence of injury. Gradually a considerable body of data has been accumulated for a variety of compounds, giving levels of exposure which have not been associated with injurious effects. The values more generally used are those which apply to a continuous exposure. By the term, "maximum allowable concentration" is meant the upper limit of concentration of an atmospheric contaminant which will not cause injury to an individual exposed continuously during his working day and for indefinite periods of time. For a limited number of substances, upper limit concentrations have been suggested for shorter, specified periods. Frequently, these latter values have the purpose of limiting the "peak" concentrations frequently found in industrial operations.

"Maximum Allowable Concentrations" (MAC) are usually defined in one of two ways: 1) parts per million (ppm), and 2) milligrams per cubic meter (mg/meters^3, or mg/cu meter). Occasionally the latter is given as milligrams per 10 cubic meters (mg/10 meters^3) — the volume of air breathed by an average individual in eight hours at a moderate rate of work. The former classification, parts per million, is commonly used for gases and for vapors of solvents; the latter description, milligrams per cubic meter is usually applied to the fumes of metals and sometimes to the fumes and vapors of other solids and heavier liquids. Parts per million denotes the relationship of the gas volume of a substance (i.e., the volume occupied by the substance in a completely volatile state) and must not be confused, as is frequently the case, by taking the *liquid* volume of the solvent to the total gas volume of the containing air. At 0° Centigrade and 760 mm presure, 1 gram-molecule (the molecular weight in grams) of a substance occupies approximately a volume of 22.4 liters. For example, 154 grams of carbon tetrachloride (molecular weight of CCl = 154) would occupy at 0°C and 760 mm a volume of 22.4 liters if completely volatilized, but as a liquid, only a volume of 0.096 liters. Thus if, by error, the MAC for carbon tetrachloride was calculated using a liquid-gas ratio, the resulting "permissible" concentration would be 233 times the present accepted level.

The setting of such threshold values for the working environment which are consistent with the safety of the workmen, offers several real advantages. It permits a control of the environment in such a manner that the likelihood of injury is reduced to a minimum. It allows a more accurate use of engineering methods, by indicating the requirements which must be met by devices for ventilating, inclosing or otherwise controlling the hazardous materials. It facilitates a more accurate governmental inspection and regulation of the exposure.

In setting threshold limits*

MANFRED BOWDITCH
Director, Divison of Occupational Hygiene, Massachusetts Department of Labor and Industries

I feel sure you will not want to leave when I tell you I interpret my assignment as discussion leader as one which does not call for preparation of a paper, and so I have prepared none. I wish merely to present certain viewpoints of my own, which I feel confident will be torn to pieces — and which I hope will be.

We are definitely not here to discuss the pros and cons of certain failures in the present standard of 100 parts per million for carbon tetrachloride in industry. Nevertheless it is the discussion and controversy over this carbon tetrachloride standard which has placed in the forefront of my mind two important questions, and I would like to put those questions before you. In order to do that effectively, I am going to take the liberty of going back into a little history. Some seven years ago in Massachusetts we set up a list of maximum allowable concentrations for about 40 different industrial chemicals, and among those was carbon tetrachloride, which was set at 100 parts per million — at that time, I think, a pretty generally accepted figure.

Those standards of ours were not regulations. We purposely kept them informal because we thought they would need revison from time to time and we wanted to be able to revise them without going to the legislature or through the cumbersome process of changing officially promulgated regulations.

Sure enough, in the course of time, particularly in the last couple of years, we came to the conclusion that several of our figures called for revision, and among them were those for carbon tetrachloride. The original figures had been established with the endorsement of an advisory committee of doctors, engineers, chemists and toxicologists. When it came to the question of revising this carbon tetrachloride figure, we got in touch with as many of that committee as we could under present circumstances. To illustrate that we really made an effort, I will say we got in touch with one member of the committee who was in New Zealand.

We proposed tentatively changing the figure from 100 to 40 parts per million. Every member of our advisory committee with whom we were able to get in touch approved that change. Then one of our committeemen suggested that we communicate with the manufacturers of carbon tetrachloride. More in outward respect for their judgment than for any other reasons, we wrote letters to, I think, eight different manufacturers of carbon tetrachloride. To put it very mildly, they did not concur. We got a barrage of letters, one of which was eight single-spaced pages of grievance, as to why we were all wet. That was followed by a visit from a gentleman from New York who presented me with two business cards, one indicating that he was an official of an advertising agency, and the other that he was an official of an agency devoted to technical research. Of course, it was in his latter capacity that he came to see me. He informed me that he represented several of the carbon tetrachloride producers. I might say that he, also, did not enthusiastically commend our proposed change.

The American Standards Association Committee, which is dealing so ably on the whole with these proposed standards, had this carbon tetrachloride standard before it, and the committee decided to adhere to the standard of 100 parts per million.

Though I was not present at the meeting in question, I have been told that the principal arguments against lowering the standard for carbon tetrachloride were presented by the insurance men on the committee. While I may be mistaken, it seems to me that it is quite obvious why they should object to such a lowering. If I were an insurance man, I think I would feel exactly as they do, and I don't blame them one bit. It would seem to me that if the standard were lowered from 100,

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we will say to 40, it would enable industrial workers who had been shown to be exposed to concentrations above 40 but below 100 to make claims and secure compensation which they would otherwise not be able to secure. Perhaps it is not as simple as that, but that is my interpretation.

Certain individuals who were members of our Massachusetts advisory committee and also of the A.S.A. committtee reversed their belief previously expressed, and voted for 100 parts per million. Again, I am told that one of these individuals did so with the statement that it was done more or less under protest and for the sake of securing unanimity.

Then, after having passed that vote to retain 100 parts per million, in the face of continued objection from some quarters to that figure, a sort of postscript was added to the proposed A.S.A. standard to the effect that, since it was apparent that conditions of a least temporarily low health, such as nausea, might readily be produced in susceptible individuals by concentrations below 100 parts per million, every effort should be made to work toward lower concentrations. This in my personal opinion, is merely begging the question.

So much for the little bit of history. The two questions that all of this generated in my mind are: First, is a single figure adequate in dealing with certain of these materials? It seems to me that those of us who are working as preventive agents have to consider, first, the question of actual systemic poisoning; and second, this question of temporary indispositon which, after all, is definite illness even though temporary.

I might say here, in passing, that in writing Dr. Gardner about this, he wrote back that he really would think perhaps he was being poisoned if he lost his lunch twice a week. I certainly would!

But apart from any actual ill health, in the case where we have certain evil smelling materials which perhaps are more evil smelling than toxic — naturally, I am not talking about carbon tetrachloride — we may have to consider the question of just such unpleasant industrial conditions, conditions under which it isn't fair to expect any human being to work for any length of time. So much for the question of whether we should have one figure or several.

But that also brings up the question of whether the A.S.A. method — for which I assure you I have the highest respect, as I have for the A.S.A. itself, and for Mr. Ainsworth — is as applicable to this type of standardization as it is to the mechanical and other forms of standardization with which they have dealt so largely and so successfully in the past, and for which I assume that the A.S.A. was originally set up.

We are dealing here with standards which cannot be arrived at in the same way that we would arrive at the number of threads per inch that should be used on a machine screw of a given size in order to enable everybody to use screws interchangeably. We are dealing with conditions in factories, as to which those of us who are entrusted with the preventive functions have got to use our very best judgment. If a national body like the A.S.A decides that 100 parts per million is the proper one for safety and our agency in Massachusetts is convinced that that is too high and that safety demands a figure, we will say, of 50, I feel that we would be absolutely false to our trust, false to the citizens of Massachusetts who are employing us, if we did not throw the higher figure out the window and stick to the one which we believe is required for safety.

It happened quite coincidentally, that only two or three days ago I received from Dr. McDonald, Director of the Bureauo f Occupational Diseases in Baltimore, a letter, of which I brought a copy along. This is dated May 2, 1944, and he says, quite casually, *"You will be interested to know that we have changed some of our regulations with respect to permisslble concentrations, the standard for carbon tetrachlorlde now belng set at 50 parts per milllon."*

I sent a copy of that to Mr. Ainsworth, with whom I had an extremely satisfactory discussion of this whole question. And I said to him substantially what I am saying now: That it seemed to me that if his organizaton set up a figure which any substantial number of states failed to concur in — and I have been told since coming to St. Louis that several of the states are thinking along the same lines that we are and that Dr. McDonald is — the effect would, instead of standardization, be one of producing a high degree of chaos.

I hope we will have some comments on these perhaps radical opinions of mine.

Discussion

DR. HARVEY: I would like to clear up one thing. The A.S.A. has not set up a standard at 100 or 200 or what not. It is in process of setting a standard. I wanted to make that very clear because it has been before them for two years.

MR. BOWDITCH: I didn't mean to imply that they had to set a standard. I merely meant that in the deliberations of the A.S.A. committee they had, to date, voted to retain 100 ppm, but that, of course, has to go to the codes correlating committee before it can be adopted. Mr. Ainsworth told me, just the other day, that he questioned whether there would be any adoption of that or any other figure in the near future.

WILLIAM G. FREDRICK (Detroit): It seems that in the actual enforcement of industrial hygiene or the application of it in the factory, one has to consider not only the toxicity of the material when affixing a limit, but certainly the nuisance value of the material. This is particularly true with respect to the fumes and smoke and dust that are not toxic in character.

After all, our job is to protect the health of the worker and also make him feel reasonably satisfied with his environment. It is a mighty difficult thing to persuade a worker that his environment is satisfactory if his face is filled with fume and smoke and visibility poor, even though the concentration of material in the air is well below that which we believe will cause physiological damage.

Then, in regard to exposure to solvent vapor, we know that many solvents will produce simple inebriation or drunkenness probably a levels well below those which will produce injury, real permanent damage, to the worker, but certainly the worker who is inebriated on the job is not a very good safety risk. We don't like to have him on the job half drunk from alcohol, and I think it makes little difference whether he is half intoxicated from alcohol or tetrachlorethylene or petroleum solvent vapors. This is quite aside from the point of whether he is receiving physiological damage.

Accordingly, if we establish limits which do not take into consideration certain comfort features and the elimination of certain nuisance features in the environment, we have a hard time persuading the workers as individuals or as an organized group that the work conditions and environment are satisfactory. We just can't do it.

DR. A.S. ROBINSON (Akron, Ohio): Goodyear has had a problem with carbon tetrachloride in excessive exposure on a Navy contract. The Navy wouldn't consider any substitute, in spite of the research department providing one. So we have the hazard regardless of any state regulations.

In order to determine the cause of the acute intoxications, nausea and vomiting, a group that has maximum exposure is examined periodically. In addition I am running the alveolar air before they start work and at the end of a shift, and getting the cencentration of the carbon tetrachloride in their working area. In any recording of acute intoxication or nausea I immediately obtain a specimen of the alveolar air. I haven't had a sufficiently large series to draw any conclusions yet.

DR. FRANK S. LOW: I have listened to all of the remarks both this morning and this afternoon with a great deal of interest. I feel that I represent an organization or group, perhaps, that is in the unfortunate position of getting hell from both sides.

There is just one thing I want to leave with you gentlemen to help you understand our position. We are quite as anxious as any of you to see a standard set that will prevent any injury to any workman and, in so far as possible, any discomfort. It is obviously necessary, I think, that such a standard be set up. For example, we ship a carload of carbon tetrachloride in drums to our Chicago warehouse. We don't know where those drums are going. They will be divided up between five or six states. If those five or six states have different standards, it puts us in an impossible condition. We will have to plaster those drums with instructions and warnings to comply in each of the states in order that these instruction and warnings might accomplish their desired purpose.

Several years ago the manufacturers of carbon tetrachloride — there are five of them, by the way — decided that there wasn't enough accurate knowledge regarding the toxicity of that material. They established a so-called technical committee consisting of one member from each one of the

producing organizations, and we made a very careful survey of the literature and agreed that there was no adequate knowledge. So we went back to our respective organizatons and raised a sum of money sufficient to finance a piece of work to determine the safe limits. That fund was turned over to Dr. Henry Field Smyth, of the University of Pennsylvania, and he did what, I think was a very fine piece of research work. It is largely as a result of that work that the present standard in so many states has been accepted as 100 parts per million.

So far as I know, and I have followed the literature as thoroughly and completely as possible, there isn't one authentic case of actual physiological damage from exposure to concentrations as low as 100 parts per million; and I question some of the evidence that has been published concerning the discomfort that has been alleged. In other words, I don't think that the tests, the analytical determinations of the atmosphere, were synchronized sufficiently well with the cases of discomfort so that it could actually be said that 40 parts per million cause nausea and vomiting.

The only appeal I make is that you, who after all are the authorities, will get together and agree on a standard that is uniform and that we can all accept. Entirely apart from the humanitarian motives, it is obviously poor business for us, every time a case of damage or discomfort from carbon tetrachloride or any of the other various chemcials gets into the literature, that we suffer the result in what you might call negative advertising. It is a bad thing and we don't like it.

I can cite the well-known case in the state of Kentucky where 135 parachute workers were, let us say, seriously discommoded — fortunately there was no serious damage — from carbon tetrachloride. I wrote to the Kentucky Board of Health and inquired specifically if all the containers in which that material was delivered carried the customary warning notice. The Board wrote back promptly that every one of them had carried that notice; and that when the superintendent of the plant was taken out and shown the containers with the warning notice, he threw up his hands in amazement — that was the first he ever heard of it.

I think we ought to have — in fact the Manufacturing Chemists Association is very earnestly working on it right now — is a means of getting the information regarding the do's and don'ts of how to handle these hazardous materials into the hands of the people actually use them. It isn't enough to paste a label on the drum. Nobody sees that. We also stamp in red ink on every invoice a similar warning, but the only man who sees that is in the accounting department. We are vigorously working now on a program to make sure that that information is delivered into the hands of the user.

I might add one other point. In the previous discussion the question came up as to how recalcitrant industries might be forced into line. I want to throw this idea out. If any of you state or Federal authorities run into a case of an industry that refuses to cooperate in proper safe methods, if you will communicate with Manufacturing Chemists Association, I think that they will be of very material assistance. I know several cases where the manufacturers have refused to ship to locations where they knew that the material was being improperly used.

CHAIRMAN BREHM: Some reference was made to insurance carriers, and I see there are some representatives in the audience. I wonder if we might hear from the carrier's viewpoint.

***DR. E.G. MEITER** (Milwaukee): My own personal view on this is that these things really should be bench-marks. They fluctuate up and down, and you don't know at any one time whether you have 100 parts per million or 90 parts per million.*

As to the Manufacturing Chemists Association, I think the statement made that the people who do not cooperate should be reported to them is a good idea. In my own experience, while many times it may not be the policy of the manufacturer, the salesmen do tend to minimize the hazards of these chemicals; they nullify what the industrial hygiene unit or the insurance engineer has tried to do.

In many cases perhaps there is not enough information available. I think the limits established should be used as bench-marks only and not considered as, possibly, a law of nature or something of that effect.

***WARREN COOK** (Chicago): Mr. Bowditch made on crack at the insurance man that really shouldn't go unanswered. It was that, because of the medicolegal implications, the insurance adviser on the A.S.A. wants to put the limit up as high as possible, not caring very much whether the worker*

gets poisoned so long as the claim man in the insurance company can say, "Well, the concentration was lower than the limit and so we should not pay the claim."

Perhaps I carried his thought a little further than he intended, but I wanted to clarify the point. From the insurance point of view, the lower the toxic limit and the more adequately the official agencies require manufacturers and users to keep concentrations within that limit, the less the number of cases of occupational diseases from these materials and the smaller the amount of money to be paid out in compensation claims.

My personal thought regarding the ideas, either those expressed so well by Dr. Melter or those expressed in the committee of the A.S.A., is that the individual, whether he happens to be connected with an insurance company or with an official agency, tends to form his own opinion concerning the point at which the toxic limit should be set on the basis of his interpretation of the literature, and on the basis of his personal experience with specific occupational poisons. If in his experience he has found that determinations showed that in one area a number of workers had become poisoned and the concentration of carbon tetrachloride ran 60 to 80 parts per million, his opinion is going to be that the limit should be reduced below 100 parts. I feel it is the background of personal experience rather than the organizaton with which he is connected that has caused him to arrive at an opinion.

There is one other point I wish to make and that is in regard to somebody's statement that there should perhaps be not one limit but two limits. I am furthering the thought that Don Cummings made a few years ago at an American Industrial Hygiene Association meeting, the thought perhaps best expressed by the term "dual standard": that the concentration to which the man is exposed should not be more than, for example, 3 mgs of lead per cubic foot of air, but every effort should be made to keep it below 1.5 mgs. In other words, we will have a limit which should be maintained, that limit being the threshold where pathological conditions result, but the manufacturer should not be satisfied if he just attains that limit. We should never go above the upper limit, but every effort should be made to keep below another figure which is appreciably less than the concentration known to produce actual toxic results.

I feel that this idea is a step to which many of us would look not only to prevent occupational disease cases but also to avoid discomforting conditions which manufacturers and labor today are making increasing efforts to control.

DR. LEONARD GREENBURG (New York): This is a very interesting and important discussion, and I want to leave one thought with you. If there is any implication that the A.S.A. should give up its efforts at standardization, that would be a step in the wrong direction. I don't think we ought to set up two standards because certainly if we have two standards we are not as well off as if we have one bench-mark, as Dr. Melter said. I think, regarding what Mr. Bowditch said, that his basic data, perhaps, were not convincing enough. He tells us that he saw some good reason in the beginning for setting up a standard of 100 parts per million. He and his group around Boston did that, and they must have had a good reason to do it. Then, later on, he thought there was a good reason to change it to 40 or 50 parts, but unfortunately he couldn't convince some of his own committee, when the issue got really interesting, to go down to that figure because they were willing to go along with the higher value. There must have been some reason why they did that.

I have examined the evidence that Mr. Bowditch had in one of this printed reports, and I must admit that I didn't think it was too convincing. That doesn't mean the standard shouldn't be lower. I think if evidence is accumulated that it should, we ought to go along with the evidence. But if he wants to support a lower figure, it has to be supported by more factual evidence than he had at his disposal at that particular time when the subject came up for discussion.

I agree with his general principles and policies except with reference to the question of compensation. I don't know how it goes in other states, but my bet is that in most states compensation isn't decided on a basis of how much carbon tetrachloride there is in the atmosphere. It is decided on the questions of, first, has the man got evidence of carbon tetrachloride poisoning; and, second, has he been exposed to carbon tetrachloride? At least, that is the way it is done in our state, and I believe, in general, the pattern is

about the same. So, I think, there is need for more explicit evidence on his point, on the human side, not the animal side.

In closing, I want to say a word about labeling. What is an effective procedure? Dr. Low himself pointed out this afternoon that the men in the plant didn't know anything about it in spite of the fact the bills of lading and drums were marked in due fashion according to law. The fact of the matter is this stuff is peddled all the way down the line. We have repeated instances of some small chemical company using it to make cement; using it to make a stain or varnish remover, or something like that; and there is no evidence at all as to whether it is benzol or carbon tetrachloride or something else.

I think if the manufacturers are as interested in this problem as they should be in order to protect their best interests, they ought to put on their thinking cap and show us the evidence of their good intentions by taking real steps in the right direction.

***DR. ALBERT GRAY (Hartford):** May I say a word in defense of A.S.A.? They are accustomed to making standards of great variety, and what they do when they make a standard is to get in experts in that particular line. I think Mr. Bowditch will agree that experts are on that committee, of which I happened to be considered one for reasons which as yet I don't know. But at any rate, they had what they felt were the best experts in that line and they arrived at 100 parts per million.*

***DR. GREENBURG:** If evidence should be submitted that the standard is either too high or too low, the standard could be changed within a month or even less. The standard is not inflexible.*

***DR. GRAY:** The standard isn't static at all.*

MR. BOWDITCH: To Dr. Gray and Dr. Greenburg, I would like to say that I am not running any fight against the A.S.A. I was absolutely sincere in my experience of regard for them and their methods and I always shall be. To my good friend Dr. Greenburg, I would like to suggest that if he will take the trouble to read some of the writings emanating from his own division, he will find in them evidence which, in my opinion, is ample, quite apart from anything that has ever been published in Massachusetts, to warrant serious questioning of the retention of 100 parts per million of carbon tetrachloride, I would like to add that I think it is unfortunate that this has degenerated into a discussion of carbon tetrachloride which I tried to point out in the beginning was not the purpose of the discussion at all.

To my equally good friend, Warren Cook, I would like to say that the question of deciding on what basis individuals, insurance men or others, form their opinions, is after all merely termed a question of opinion and therefore cannot be replied to. I would like to say to him very definitely that the words, as I understood them from him, which he tried to place in my mouth, bore not the slightest resemblance to what I actually said in my original discussion.

Finally, to all of here, I would like to say that in engineering safety practice there is such a thing as a factor of safety.

Interpretations of permissible limits*

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Much has been written and said concerning tables of permissible or maximum allowable concentrations of various toxic substances in air, but not enough attention has been given to their limitations and how to use them intelligently. There is a tendency to place too much reliance on figures, with little or no consideration of their real meaning.

The repeated publication of a figure often adds significance to it far beyond that intended by the original publisher. How are these figures referred to as "maximum allowable concentrations" established? What is their real meaning?

To answer these questions it is necessary first to define maximum allowable concentration. The usual definition is somewhat as follows: *"The average concentration to which an industrial worker can be exposed for eight-hours daily for an indefinite period without injury or occupational disease."* This definition is made up of the following items: 1) average concentration, 2) eight-hour day, 3) indefinite exposure period, and 4) lack of injury or occupational disease. There apparently is some controversy regarding item one, items two and three are usually accepted, and there is definite disagreement regarding the interpretation of item four.

To reach a more satisfactory interpretation of maximum allowable concentration, attention is directed to 1) the development of tables of maximum allowable concentrations, 2) criteria on which limits are based, and 3) methods used to obtain data on which limits are based.

Historical development

One of the early tables and one referred to frequently was published in 1912 by Rudolf Kobert.[1] This table is entitled "The Smallest Amounts of Noxious Industrial Gases which are Toxic and the Amounts Which May Perhaps be Endured." Concentrations are listed under four headings: 1) rapidly fatal to man and animals, 2) dangerous in 0.5 to one hour, 3) 0.5 to one hour without serious disturbances, and 4) only minimal symptoms observed after several hours. It is evident from these headings that the values refer to acute effects and are based on toxicity. The table refers to 20 compounds, and it is interesting to note that the values for hydrochloric acid, hydrogen cyanide, ammonia, chlorine, and bromine as given under the heading "only minimal symptoms after several hours" agree with the values as usually accepted in present-day tables of maximum allowable concentrations for repeated exposures. It is also interesting to note that, with the exception of hydrogen cyanide, all of the gases have an irritating action. One other compound, carbon monoxide, has a value of 200 ppm, which does not greatly exceed the 100 ppm usually accepted today, considering the fact that this value was published as early as 1912. However, the values for organic solvents such as benzol, carbon tetrachloride, chloroform, and carbon disulfide far exceed the values used today.

The next table, and one of the first to originate in this country, was published in Bureau of Mines Technical Paper 248[2] in 1921. This table contains 33 compounds. Much of the information was taken from the table previously referred to, with additional information from various other articles. In this table also most of the figures refer to acute toxic effects, although some information is given on the least detectable odor and least amount required to cause irritation.

In 1927 Sayers[3] published information on 27 compounds.

The data refers to 1) percentage fatal in 30 minutes or less, 2) percentage causing dangerous illness in 0.5 to one hour, 3) percentage without serious effect for 0.5 to one hour, and 4) maximum

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* Presented by permission of the Director, Bureau of Mines, U.S. Department of the Interior, at the 75th Annual Meeting of the American Public Health Association, October 7, 1947, Atlantic City, NJ. Published in *Am. Ind. Hyg. Assoc. Q. 8(3)*:55-60 (September 1947). Reprinted by permission of the American Industrial Hygiene Association.

safe concentration. It is not clear whether this latter classification referred to chronic or to acute poisoning. However, it is believed that it referred to acute poisoning. Also in 1927 Henderson and Haggard[4] published information on some 25 compounds. Some of the values are listed as "maximum concentration allowable for prolonged exposure," and these values agree in most instances with values used today as maximum allowable concentrations. Other values are given for "slight symptoms after several hours exposure," and these values refer to acute exposures. In 1929 Sayers and Yant[5] published a table which lists the physiological response to various concentrations of some common gases and vapors. Seventeen compounds are listed, and the values in general refer to acute effects.

Schaedliche Gase,[6] published in 1931, also contains a table of toxicity values ranging, in six steps, from concentrations immediately fatal to those endured for six hours without real symptoms. Twenty compounds are included in the table. The values definitely refer to acute effects.

In 1935 Sayers and DallaValle[7] published a table containing information on "Physical and toxic properties of common vapors and gases." The table lists 37 compounds and gives information on physiological response to five levels of concentrations. The first four refer to acute effects and range from concentrations that kill in a very short time to amounts causing slight symptoms after several hours exposure. The final column, however, lists values for "maximum allowable concentration for prolonged exposure." Up to the time of the publication of this table the information given in the various tables undoutedly referred to acute effects, even though some of the values, particularly those for several of the irritating gases, were the same as are used today for repeated exposures.

Since about 1935 most of the tables listing maximum allowable concentrations do not give a series of values for acute effects but only a single value which refers to repeated exposure. Such tables were published by Lehmann and Flury,[8] Bowditch *et al,*[9] Gafafer,[10] Cook,[11] the American Conference of Governmental Industrial Hygienists,[12] and many others. The number of compounds has gradually increased and some 140 compounds are now listed.

It is evident from the foregoing that our present tables of maximum allowable concentrations have slowly evolved from earlier tables listing values pertaining primarily to acute effects and which might be considered as toxic limits. It is also evident that our present-day tables bear little resemblance to the earlier ones and contain values not based on toxic or pathological effects. However, the tendency to interpret them as relating to the toxic effects is still evident, as indicated by such statements as the following: "Many of us feel that the codes on toxic limits . . ." Also, in some of the state codes, statements such as the following are noted: ". . . concentrations that equal or exceed the following, which constitute harmful exposures or harmful concentrations . . ." Also, one of the recent tables is headed "Toxic Limits of Various Substances." However, that others put a broader interpretation on the values is evident from the following:

> *"A list of accepted and tentative values is also presented for practical use in the control of occupational disease and for the provision of both healthful and comfortable working conditions where toxic or obnoxious materials may be present,"* and *"Considerable difficulty attends fixing . . . maximum allowable concentrations . . . because of . . . lack of uniform definition of the maximum allowable concentration concept. One concept is that the MAC value should represent . . . that concentration at which a worker exposed for sufficient period of time will just escape physiological or organic injury and occupational disease . . . A third concept is that the MAC should perform the functions of the former concepts and in addition provide a working environment free of objectionable but noninjurious concentrations of smokes, dusts, irritants, and odors."*

Therefore, in the evolution of tables of maximum allowable concentrations, values which are based on injury and occupational disease as well as values based on physiological effects and discomfort have been included. It might be well at this point to review briefly some of the criteria which are used in establishing permissible limits as well as the experimental procedures used to obtain the data on which the limits are based.

Criteria used in establishing permissible limits

At least three criteria have been used in establishing the maximum allowable concentrations now in use. These criteria are 1) pathological effects, 2) slight physiological effects which apparently have no discernible untoward effects on health but cause impairment of coordination and reaction time and tend to make workers more prone to accidents, and 3) discomfort or sensory effects.

In those cases where limits have been established on the basis of pathological effects, it is logical to assume that repeated exposure to concentrations significantly in excess of the allowable concentration probably would produce injury. Where the limit has been established on the basis of a slight physiological effect, it is not logical to assume that exposure to concentrations exceeding the allowable concentrations would necessarily produce injurious effects.

It is quite possible that the margin between a concentration that will produce mild response and the concentration that would produce injury would be large, in which case exposure to a concentration considerably higher than the allowable concentration might not be injurious to health. The same is true for maximum allowable concentrations that have been established on the basis of sensory effects of discomfort. In this case the margin between sensory effects and actual damage to health may be even greater. It is obvious, therefore, that in using a permissible limit one must know the criterion used in establishing the limit. One obviously is not justified in assuming that a hazard to health exists because the concentration exceeds the maximum allowable. However, several of the state codes state that concentrations that "equal or exceed the following shall constitute harmful exposures or harmful concentrations."

Even though maximum allowable concentrations were established with a high degree of accuracy, their interpretation must be based on the criteria used in establishing them. However, in addition to this factor one must consider the limitations that are encountered in establishing maximum allowable concentrations and therefore it is necessary to discuss briefly the procedures used.

Procedures used in establishing maximum allowable concentrations

Maximum allowable concentrations are usually established by one of the following procedures: 1) laboratory tests on animals, 2) laboratory tests using human subjects, 3) field investigations, and 4) a combination of all the above methods.

Laboratory tests on animals

Laboratory experiments with animals is one of the most commonly used procedure for establishing permissible concentrations and offers certain definite advantages. It is possible to control the exposures within rather accurately defined limits and to expose the animals to a wide variety of conditions. Such studies are helpful in demonstrating the nature of the damage likely to be produced, and indicate the type of response to look for in industry. By using a number of different types of animals, additional fundamental information can be obtained. The important disadvantage of the method is that it is not possible to interpret such data in terms of human response with a high degree of accuracy. This method is used particularly in establishing limits which are based on pathological effects. Limits which are established on ths basis of animal experiments must be used with caution and careful observations of exposed persons should be made until experience indicates that the limit is satisfactory or should be revised.

Laboratory tests using human subjects

Laboratory tests using human subjects are usually made in establishing maximum allowable concentrations based on slight physiological effects and discomfort or sensory effects. Such tests are usually conducted after sufficient information has been obtained to indicate that such exposure of human subjects can be made with very little likelihood of injury to the subject, in other words, until evidence has been obtained that there is a definite margin between the mild physiological effect or sensory effect and possible injury. Limits based on this procedure should be fairly accurate but are subject to error, owing to the fact that the subjects usually are not accustomed to occupational exposure and therefore in some cases may tend to respond to lower concentratons than would persons working in industry. However, it is not necessary that these limits be established with

a high degree of accuracy because the possiblity of injury is not great.

Field investigations

Investigations are made in industry in which the concentration of contaminant in the work atmosphere is determined and correlated with clinical and physical examiniations of the workmen. This procedure has been used in establishing initial maximum allowable concentrations for some materials and is employed to check on previously established limits. Data of this nature are being continuously obtained by many organizations that have programs which entail air analyses and medical examination of workers. In one respect this procedure can be considered the most important in establishing maximum allowable concentrations since one is working with actual conditions in industry. There are two difficulties encountered in applying the method: 1) satisfactory sampling in order to obtain the average over-all exposure of the person, and 2) the difficulty of diagnosing injurious effects, particularly when they are of a mild or borderline degree and may be due to other factors, such as poor nutrition and general poor health. It is evident that if samples are not collected to give a good measure of over-all exposure one might set the limit too high if samples are taken at the source of contaminant and the person is not exposed to the higher concentration is most of the time and does not show signs of poisoning. Since a good average of over-all exposure is necessary in establishing the limit, obviously in evaluating exposure one should attempt to obtain a good measure of the over-all exposure.

Combination of laboratory and field investigations

The most accurate maximum allowable concentrations are those based on both comprehensive laboratory investigations and field experience. However, regardless of the amount of information available at the time a permissible limit is established, it is always subject to readjustment if new investigations and experience indicate that the value is in error.

All maximum allowable concentrations are subject to the limitations of measuring accurately pathological or physiological response and also to the limitations of the methods of sampling and analysis of atmospheric contaminants. From a consideration of these factors, it is apparent that it is not possible to establish permissible limits with a high degree of accuracy. However, this need not detract from the use of such limit because the accuracy obtainable is satisfactory when permissible limits are used properly.

Discussion

In applying maximum allowable concentrations to interpretation of the result of air analysis, it is necessary to understand the purpose and limitations of such values as well as the limitations of the sampling and analytical procedures. While their fundamental purpose is the promotion of health and efficiency, their practical use is for guidance in establishing control procedures to prevent harmful or objectionable concentrations from accumulating. Samples may be collected to ascertain the source of contaminants or to check on control procedure. In this case, only a few samples may be taken and the analytical procedure may be relatively crude and still satisfactory results may be obtained. On the other hand, if the purpose of the sampling and analysis is to obtain data for legal purposes or for correlation with codes, careful and thorough sampling should be carried out and accurate analytical procedures should be used. Should the results of such careful sampling and anylysis give results which exceed the established maximum allowable concentrations, what interpretation should be put on them?

If the permissible concentration in question has been established on the basis of slight physiological effect or discomfort, one definitely is not justified in concluding that an occupational disease is likely to occur. The same is true even though the permissible limit is based on pathological effects because one must consider not only the extent to which the values have exceeded the maximum allowable concentration but also the time factor. These factors, for example, are taken into consideration in some of the state codes, which contain statements as follows: "Temporary concentrations in excess of the maximum allowable concentrations listed shall not be permitted if exposure to such concentrations for a period of one hour or less may result in an adverse effect on health . . ." In fact, one is not justified under any

circumstances in using air analysis in conjunction with maximum allowable concentrations as a diagnosis of occupational disease, nor conversely, if values are less than the maximum allowable, as evidence that occupational disease cannot occur. Obviously diagnosis of occupational disease should be based on a consideration of all factors including careful clinical and physical examinations as well as air analyses and the fundamental physiological effects of the materials in question. Maximum allowable concentrations serve as a measure of exposure similar to the determination of lead or methanol in the urine or the determination of inorganic sulfates in the urine on exposure to benzol. When used in this manner it is not necessary to place so much emphasis on the absolute value of the maximum allowable concentrations. Emphasis should be placed on interpretation. This should not be taken as a criticism of existng permissible limits nor as an excuse for not establishing limits with as high degree of accuracy as possible. The values should represent our best judgment on the basis of available information and should be subject to change whenever additional experience indicates they are not satisfactory. Maximum allowable concentrations are an important tool of the industrial hygienist and to obtain the greatest value from them they should be used properly.

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The case for maximum allowable concentrations*

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Since the publication in 1927, in the *International Critical Tables,* of data on physiological response to various concentrations of gases and vapors, including concentrations allowable for prolonged periods, the subject of maximum allowable concentrations (MACs) has received much attention from persons interested in protecting the health of workers. Some of the authorities who have contributed in this field are Sayers, DallaValle, Philip Drinker, Bowditch, Yant, Sterner, Teleky, Lehman-Flury, Fredrick, Fairhall and last but not least Warren Cook.

The organizations interested in MACs have included the U.S. Public Health Service, most of the state and local bureaus of industrial hygiene, the American Standards Association and the American Conference of Governmental Industrial Hygienists. Data have appeared in books on industrial toxicology, industrial hygiene, industrial health engineering, the care of the handicapped worker, and various handbooks. Certainly any proposition with such substantial backing must be sound, and acceptable to all interested in industrial health problems.

Yet there has always been a small minority which has been skeptical of, and even hostile to, the use of MACs in preventing occupational disease. Their criticisms vary all the way from complaints about the term "MAC" to personal criticism of the personalities and groups associated with the promulgation of MAC values. Nor does this group consist entirely of obstructionists and professional objectors. At the last meeting of the New England Section of this Association, three of our most eminent and respected members took occasion, out of a clear sky, to decry one phase or another of MACs.

One speaker, an engineer, stated that there was too much emphasis on MACs, leaving the inference, at least, that more attention should be paid to the engineering aspects of control. Another speaker, a physician, deprecated the use of MACs in place of medical control measures, implying that the latter alone were sufficient. The third speaker, while not condemning MACs in general, warned dramatically against suggesting values based on insufficient data. As he put it, we should not "draw a value out of thin air."

Fundamentals of MAC selection

I should like to consider these criticisms and their implications. First, however, it might be worth while to review a few fundamentals. The incidence of intoxication, with different exposures, is shown by the familiar probability curve (Figure 1). Horizontally the minimum concentration which will cause intoxiciation is given, while vertically we have the number of persons affected. This is merely a graphical method of expressing variations in individual susceptibility.

At very low concentration no one is injured; as we increase the exposure a level is reached where a very few individuals are intoxicated; with a further

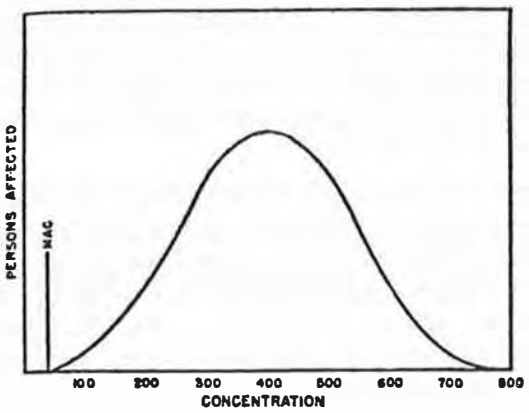

Figure 1 — Probability curve of percentage of persons affected by increasing concentrations of toxic substances. (Percentages not cumulative.)

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increase the number of additional persons affected per increment of increase becomes greater until a concentration is reached where approximately half the population has succumbed. Then each further increase in concentration affects a diminishing number of additional people until all are intoxicated, when further increase is naturally without effect.

At what point on this curve should we select the MAC? The middle of the curve, the LC_{50}, if our criterion of intoxication is death, otherwise the TC_{50} is the value which the experimental toxicologists quote. Even the most backward industrialist, however, would not recommend the TC_{50} as the MAC. If the effects of intoxication are permanent, death or disability, or even serious illness, the MAC should be below the value which produces these effects in even highly susceptible individuals.

On the other hand, if the illness is rather minor and transient, the MAC can be chosen at a level which does affect a minority of workers, but should be below the value which produces these effects in even highly susceptible individuals.

On the other hand, if the illness is rather minor and transient, the MAC can be chosen at a level which does affect a minority of workers, but should be below the value where the average individual suffers.

Some people hold that these minor illnesses should be ignored in establishing MACs. Thus the lachrymation due to formaldehyde, the cough and throat irritation from sulfur dioxide, the runny nose caused by fluorides, the headache resulting from absorption of nitroglycerin, and the fever attributable to zinc fumes, should not be considered as justification for lowering MAC values for these substances to a point where the symptoms noted do not appear.

Now we have heard much recently of the importance of the common cold as an industrial hygiene problem, and ambitious programs to eliminate the common cold from industrial workers have been advocated. To the best of my knowledge these programs, in principle at least, have met with little opposition.

What are the symptoms of a common cold? Your eyes water, your nose runs, you cough, you have a headache and a slight fever — exactly the symptoms produced by so-called non-toxic concentrations of the gases and fumes just mentioned. Yet the same people who are unwilling to ask industry to spend a few dollars to eliminate these symptoms, when they are obviously occupational in origin, are proposing that vastly larger sums be spent in measures of, as yet, unknown efficacy to eliminate the same ill effects when caused by infections not directly attributable to the employment.

What about the criticisms of MACs?

The first one was that MACs are over-emphasized, at the expense of engineering principles. We should spend less time comparing the concentrations of dusts and gases in the work room with the MAC, and more on streamlining exhaust systems and checking air flows. Engineers forget, when they present this argument, that good engineering, when involving toxic dusts and fumes, is a means and not an end. Which is more important to the health of the worker — that the quantity of lead dust, or carbon tetrachloride vapor, be kept at a harmless level, or that the air flow through the exhaust system comes up to the standards of good engineering practice?

From the standpoint of purely engineering considerations benzene vapor is practically identical to the vapor of hexane, methyl bromide and ethyl chloride are almost the same, as are the fumes of zinc oxide and cadmium oxide, and the dusts of calcium carbonate and radium carbonate. If control measures are based solely on engineering factors, either the worker will not be protected, in the case of the toxic material, or else the employer may be penalized, if the substance is non-toxic. If the toxicities of the contaminants are taken into account in specifying control measures, some kind of MAC values must be used.

We have in this state several storage battery plants. The lead hazard inherent in such establishments is familiar to all of you. One of these factories grew, like Topsy, from the owner's basement shop into a building which was formerly a garage, which has since been expanded by adding a little here and a little there. As can be imagined, this plant leaves much to be desired from the standpoint of the engineering perfectionist.

Two of our other plants were planned from scratch by men who knew the business. Each has been characterized by well known engineers as an

ideal plant. But lead dust concentrations were found to be much higher in the ideally engineered plants than in the Topsy-like plant first mentioned. And the incidence of lead poisoning, strangely enough, seems more closely related to the concentration of lead dust in the air than to the degree of streamlining of the exhaust system.

It would appear that in many cases the emphasis is not an MACs at the expense of engineering standards — rather the shoe is on the other foot.

How about the second criticism, that we should rely more on medical controls than on MACs? It seems strange that this opinion should be held today, when the entire philosophy of industrial hygiene is prevention of ill health. It is well recognized that in many cases medical science is unable to detect incipient poisoning until it is so far advanced that permanent injury is probable.

Let us consider just one incident. In a paper by A.R. Smith in 1945, a delayed case of benzene poisoning is discussed. The worker, when first examined, during or just after a period of exposure, had a white blood cell count just below normal. Three months later, with no further exposure, his blood picture was normal. But four years later he died, and the diagnosis was benzene poisoning.

Dr. Smith identified for me the plant in which this man worked. Air analyses showed benzene vapor concentration up to 300 ppm, and averaging 115 ppm — clearly a severe benzene hazard. Yet if we relied solely on the medical examination of a worker so badly poisoned he was to die, we could only say there was a possible hazard, a borderline case.

To abandon MACs and rely solely on medical control measures would be to take a long step toward the dark ages of empiricism in occupation disease control.

Finally, what about MACs taken out of thin air? At first glance it would seem that this is a reprehensible practice, which should be sternly condemned. What, however, are we to do when confronted with the industrial use of a toxic substance for which data on which to base an MAC are lacking? We have several altenatives: 1) no controls, 2) controls based solely on good engineering practices, 3) medical examinations, and 4) fume control based on a tentative MAC.

Let us consider an example: The Massachusetts Fume Code Committee, in 1938, included tetrachloroethane in its list of vapors for which MACs were proposed. There was no information on industrial exposures, and animal data were inadequate to lead to a MAC value. The committee arrived at a figure in a round-about fashion. Certain German authors had stated that tetrachloroethane was 10 times as toxic as carbon tetrachloride. Since the effects of these two vapors were roughly similar, and the MAC for carbon tetrachloride was then considered to be 100 ppm, a value 1/10 as high, 10 ppm was proposed for tetrachloroethane.

Surely this procedure can be classed as "taking a value out of thin air." That was certainly the opinion of the American Standards Association committee and various other authorities, who berated us for proposing such an absurdly low figure.

During the war tetrachloroethane was used in some quantity in a process which need not be described here. I am indebted to Mr. Halpin of the Army Industrial Hygiene Laboratory for information on the experience of the Army with this solvent. I quote from his letter as follows:

> *"Numerous cases of jaundice and toxic hepatitis were reported among worker exposed to tetrachloroethane. Many atmospheric analyses revealed concentrations of less than 10 ppm at the time of sampling, yet clinical and sub-clinical effects continued to be found."*

From this evidence it would seem that 10 ppm is too high for the MAC of tetrachloroethane. If these illnesses were actually due to the use of a MAC "drawn out of thin air," it is indeed a serious indictment against the practice of proposing MAC values based on meager data. However, is there any evidence that the existence of the MAC value contributed to these cases? Would there have been better control if there had been no MAC? I doubt it very much.

The experience of the Army with illness from mustard gas in shell filling plants might be pertinent to this matter. No MAC for mustard gas had been proposed, so engineering and medical control measures were relied upon with no MACs to becloud the issue.

What happened? I will quote from the *Industrial Hygiene News Letter* of January 1948:

> *"About a thousand workers in Huntsville Arsenal . . . show symptoms of excessive exposure to mustard gas. . . . About 300 are under observation or treatment. . . . Most have a true physical disability; a psychoneurotic component is evident in many."*

From these cases one can infer that the use of too high a MAC, as opposed to no MAC at all, does not increase the incidence of occupational illness. However, it does prevent the extreme effects which would result from very heavy exposures, which might otherwise occur. In other words, we can argue that half a loaf is better than none.

There is one clear advantage to use of a tentative MAC drawn out of thin air. We now know that the correct MAC for tetrachloroethane is below 10 ppm — probably study of the Army's data above cited will tell us the proper figure. And where do we stand with mustard gas? So far as available information goes, we are exacly where we were 20 years ago as far as knowing what a safe consideration is.

Establishment of a tentative MAC, from thin air or otherwise, is only a first step in determination of proper and necessary control measures. It encourages measurements of fume concentrations in workrooms, without which the proper value cannot be obtained. In absence of a tentative MAC value such tests all too often are not made.

However, while I believe in the use of tentative MACs, I believe they should be so labelled, so that there will be no excuse for their improper use.

In summary then, MACs are not, in general, too greatly emphasized at the expense of engineering and medical measures. The use of tentative values, based on extrapolation from animal experiments, or even from purely chemical relationships, in absence of other data, is justified. To abandon or sharply curtail this extremely valuable tool of industrial hygiene because it is occasionally misused would be the height of folly.

GROWTH OF TLVs AND TOXIC DATA 1950-1960

Toxicological data — sources of information and future needs*

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The simplest statement about toxicology is that a poison is too much. Any substance is injurious when the intake exceeds some particular amount. Any substance can be tolerated in some particular daily intake, with the possible exception of beryllium, the action of which is not yet fully understood.

It is helpful to have definite quantites to think about. The generally accepted tolerable amounts of some airborne materials can be expressed in terms of the total weight having no effect when inhaled during an eight-hour period every day, by using the rough figure of ten cubic meters as the volume of air inhaled in a working day. A few values will be illustrative.[A] (See Table I.)

TABLE I
Selected TLVs Expressed in mg/10 m^3

Soluble uranium	0.5 mg
Mercury, cadmium, parathion	1.0 mg
Lead	1.5 mg
Arsenic	5.0 mg
Fluoride	25.0 mg
Nitrobenzene	50.0 mg
Carbon disulfide	620.0 mg
Benzene	1100.0 mg
Carbon tetrachloride	1560.0 mg
Acetone	2400.0 mg

One-half hour of breathing 22,000 ppm of carbon tetrachloride will produce deep narcosis with a possible fatal outcome.(1) This datum of concentration and time represents 87 gm. or about two fluid ounces of the solvent in the inhaled air. The 1560 milligrams of carbon tetrachloride which is listed in Table I as tolerable for daily inhalation totals 375 gm. in a year, over a pint. It represents 200,000,000 molecules for every body cell every working day.[B]

One and one-half milligrams of lead a day in the inhaled air can be tolerated, as can 1.5 gm. of carbon tetrachloride. Thus it may be said that lead is 1000 times as toxic as carbon tetrachloride. But it would be misleading to say that lead in an industrial operation is 1000 times as dangerous as carbon tetrachloride. Lead compounds are dense solids and carbon tetrachloride is a volatile fluid. Obviously when the two are handled in the same way, organic vapors in the air will be more likely than lead dust in the air. This crude example emphasizes the fact that knowledge of the toxicity of a material is not sufficient to protect workmen. We must know also the hazards of working methods. For clear thinking about industrial hygiene it is important to distinguish between the toxicity of a material and the hazards of an operation with the material. Hazard involves physical properties as well as such factors as amount handled, surface exposed, temperature and frequency of exposure. In many situations toxicity is a less important contributor to danger than are the working methods.

The industrial hygienist feels insecure when a plant which concerns him is using a chemical until he has an authoritative statement of a value known variously as the hygienic standard of inhalation, the threshold limit and the maximum allowable concentration. When he obtained such a statement his insecurity tends to approach zero. For several reasons this knowledge of the quantitative toxicity of a chemical is only part of the information which is required to use the material safely.

The standard assumes a uniform unvarying concentration throughout the day. Industrial op-

* Presented December 4, 1953 at the Tristate Industrial Health Conference, Newark, NJ. Published in *Am. Ind. Hyg. Assoc. Q.* 15:203-205 (1954). Reprinted by permission of the American Industrial Hygiene Association.

[A] Calculated from values in reference 3.

[B] A.J. Clark,(2) quoting Parker (1930), estimates the number of cells in the body of a 70 kilo man as 26×10^{12}.

erations almost always create widely varying concentrations with peaks well above the average.

With some materials the effect of peaks throughout the day is the same as the effect of the time-weighted average concentration. With others the effect of peaks is greater than the amount they contribute to the day's average. With still others, symptoms of irritation are evident from any briefest concentration above the standard. Tables of standards contain no reference to such differences between the actions of different chemicals, and indeed for many chemicals the behavior in this respect is not understood.

Reliance on a hygienic standard alone for protection of health requires one of three situations, none of which are frequently encountered. Concentrations must not vary from day to day in order that occasional analyses may give assurance that the standard is never exceeded, or recording instruments with alarm or automatic control features must continuously sample all working points, or an industrial hygiene team must be functioning in the area during all working hours.

Furthermore, a standard assumes that workmen are equally sensitive and that their sensitivity does not vary from time to time with changes in their general health. Neither assumption is true. Without some means to detect the particularly susceptible man we must either tolerate his development of serious injury in a concentration which does not affect his fellows, or we must keep concentrations so low that no individual, no matter how sensitive, can possibly be affected. The first alternative is outrageous and the seocnd unduly restricts working methods and would require uncalled for expenditure for protective equipment.

When knowledge of toxicology is sufficient we will have a clear picture of the subjective symptoms and objective signs to be expected from excessive exposure to a chemical long before irrevocable injury is done. When these facts of qualitative toxicology are available we can overcome the deficiencies of quantitative toxicology outlined above. We have assurance that no permanent injury can occur from unanticipated variations in concentration of airborne material, from undetected high sensitivity in a particular individual or from possible error in setting the quantitative hygienic standard.

To be fully effective to the industrial hygiene team, including the responsible physician, toxicological data on a chemical should include answers to the following questions:

1. What uniform concentration is tolerable eight hours a day for a working life time?
2. What correction in the average must be made for brief peak concentrations?
3. What single brief exposure to a high concentration is tolerable each day when there is no exposure the rest of the day?
4. What biological test upon the workman can measure his actual intake of the chemical at his job?
5. What are the earliest symptoms and objective signs of excessive exposure, and how severe can they become before removal from exposure fails to prevent permanent injury?
6. What is the best treatment for the effects of excessive repeated exposure?

The industrial hygienist himself requires information upon the first three points, but it is necessary for his complete functioning that his medical colleague have information upon the last three points. It is probable that the six points listed cannot be completely and satisfactorily answered for any industrial material although fairly complete answers are available for many.

The most dependable American source for opinions upon the long-time intake of familiar airborne chemicals is the annually revised list of threshold limits by the American Conference of Governmental Industrial Hygienists released each April and now published in a Fall issue of the A.M.A. *Archives of Industrial Hygiene and Occupational Medicine*.[3] The values are well-considered and they usually represent the consensus of several years widespread experience with each material. Unfortunately, since the publication of Cook's article in 1945,[4] no one has pointed out the scientific basis for each tabulated value to allow assessment of its relative validity. Some are simply extrapolations from animal experiment which are subject to correction as experience accumulates and others are based on many published reports of human experience. Specifically two values from my own animal work, those for isophorone and

mesityl oxide, have remained unchanged since the first entry, based solely on my 1942 publication.[5] It would be well if some way could be found to indicate the basis and the relative validity of each of the values tabulated.

For newer and less widely used materials there is no one place to look for hygienic standards. One must search the literature, which is best done through Chemical Abstracts, and one must make tentative estimates from any information found, guided somewhat by structural analogies with better known chemicals. Usually the manufacturer of a new chemical will be able to furnish some basis for tentative estimates and hence such direct inquiry is a sound move.

The most valuable current literature and current abstracts are contained in the A.M.A. *Archives of Industrial Hygiene and Occupational Medicine.*

The most convenient source for concentrations tolerable for brief periods is Henderson and Haggard's *Noxious Gases.*[1] Many of the data here go back to animal experiments in Germany during the first quarter of the century but are still sound.

Searches for the qualitative data needed by the physician should be left to those thoroughly familiar with the literature of the medical sciences. The most useful single reference book is Von Oettingen's *Poisoning,*[6] but it leaves something to be desired in its coverage of industrial materials.

Several organizations publish leaflets on single chemcials, each summarizing what is known about the toxicology and safe handling of materials. All are quite limited in number of materials covered and are brief, but some list literature references for more details. Among these organizations are the Manufacturing Chemists' Association[7] and the American Petroleum Institute.[8]

A few groups have attempted to set themselves up as clearing houses for unpublished toxicological results of interest to the industrial hygienist but various factors have prevented useful coverage of the field.

Experimental toxicological study is now the general practice of makers of chemicals. More and more new chemicals are studied by screening methods before any amount is sold. Since 1944[9] the term "rangefinding" is receiving acceptance to describe this preliminary screeening. As it becomes certain that a chemical will be a regular item of commerce more advanced work is performed. The studies of Irish and his group on chlorinated hydrocarbons[10–14] may be considered a pattern for advanced work.

Despite an infinite amount of animal work upon a new chemical the tolerable human intake will remain only tentatively defined until human observations have been made.

A pressing need is for the publication of workroom analyses and clinical examination of the workmen in order to validate more fully or to correct the commonly used hygienic standards for inhalation. At present most detected human injuries are likely to be reported in the literature but instances where no injury results are not published. It is understandable that authors hesitate to write, and editors hesitate to accept, articles which simply reassure. The sensational is more attractive, but we badly need more studies like that of Sterner *et al*[15] on butyl alcohol where air concentrations were followed for 10 years and clinical studies of the workmen involved showed no injuries. We are neglecting our duty if we do not collect and publish such data. Toxicologists properly discharge their duty to use animals to establish profitable safety before human use begins, but after a material is an article of commerce we rely too much on rare accidents to authenticate or to correct the animal predictions. Many files are loaded with pertinent data. How can it be dragged out and published?

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Standards for safeguarding the health of the industrial worker*

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The following is a review of what toxicologists and industrial hygienists are doing to develop threshold limits for concentrations of substances in the air, corresponding biological threshold limits, pretoxicosis tests, and prophylactic and antidotal agents . . . and a discussion of recent developments in the techniques of air sampling and air analysis.

The epitomical statement made some years ago by Dr. James A. Sterner, now medical director of Eastman Kodak Co. and past president of the American Industrial Hygiene Association, announced a change of attitude among industrial hygienists which today is the keynote of enlightened occupational health practice:

> *"No substance is so toxic that it cannot be used if sufficient knowledge of its action has been made available; similarly, no substance is so nontoxic that it should be used without regard to caution."*

Currently, several effective means by which such a concept may be implemented are available: *a)* threshold limits for concentrations of injurious agents in the workroom air, *b)* threshold limits of concentrations of injurious agents or their metabolic products in biological fluids corresponding to the threshold limits for air (biological threshold limits), *c)* tests of pretoxicosis to screen persons for early signs of injury from exposure to hazardous agents, and *d)* prophylactic and antidotal agents.

Occupational hygiene standards in this country have been given various names, the most familiar of which is maximal allowable concentrations. Another designation is threshold limit values, the name used by the American Conference of Governmental Industrial Hygienists. Still another term is industrial hygiene standards, a designation recently adopted by the American Standards Association. All these terms refer essentially to the same concept of permissible contamination of workroom air by dusts, fumes, mists, vapors, or gases, although the bases on which the limits for certain substances are set may differ somewhat in the different lists. The following discussion will be confined chiefly to the list of threshold limit values, with which the author is most familiar. This list is prepared by the American Conference of Governmental Industrial Hygienists' Committee on Threshold Limits, which is composed of persons working in State and local industrial hygiene departments and in Federal industrial hygiene units, and members of the armed services in the United States and Canada.

Only the United States and Russia appear to be currently developing such lists as the threshold limits list, other countries preferring to use those already developed. Partly because of this, but more especially because the abbreviated preface to the list only briefly refers to its application, the following paragraphs discuss in some detail the nature of the list and its purpose, methods by which the values are developed, and interpretation and proper usage of the values.

Nature and purpose of the list

The threshold limits list includes those natural minerals and oils and chemical substances, including economic poisons but excluding radioactive materials in the form of dust, fume, mist, vapor or gas, which are in sufficiently wide use industrially to warrant control of their concentration in the breathing zone of the industrial worker. (Permissible levels of exposure to radioactive materials are independently set by various radiation protection committees throughout the world. Values for many radioactive substances may be found in the National Bureau of Standards Handbook No. 52.) Because of the rapid development and application of certain chemical substances, often a timelag occurs between the industrial use

* Published in *Public Health Reports 70(1)*:1-11 (January 1955).

of a substance and the appearance of the threshold limit value. This interval, however, is becoming shorter as a result of increasing attention of the chemical industries to the development of data on the toxicity and hazards of their products prior to use. Limiting values assigned to each substance in the list represent the maximal atmospheric concentration to which workers may be exposed repeatedly day after day without injury to health.

The purpose of the list is to provide a limiting value of air concentration for injurious substances for use by plant engineers, industrial hygienists, and others concerned with the health and comfort of the workers. The list is intended to be a guide for the control of working atmospheres and to provide management, labor unions, and the worker alike an assurance of healthful conditons on the job.

Development of threshold limits

A value for a toxic substance is assigned on the basis of data accumulated from animal inhalation toxicity studies and on the basis of industrial experience. Together, these represent, of course, ideal requirements not always fulfilled for each substance in the list but approximated as far as possible. Of the two, industrial experience is the test on which the validity of a value must ultimately rest. Because reliable information from industrial experience is frequently difficult to obtain, the Committee on Threshold Limits is often forced to rely on opinion of industrial hygienists, rather than on factual information, or sometimes, merely on animal data. Such opinions, however, are based on specific experience with various substances and come from occupational hygienists throughout the country. The current toxicological literature is also scanned continually for usable information. When the need for the assignment of a value seems urgent, a tentative value is assigned on the basis of the best information available at the time.

Originally, preventing impairment of health was virtually the only consideration in the selection of the proper limiting air concentration of an injurious substance. Now, however, with the increasing emphasis in occupational health on the "total man," more subtle effects on health, such as the effcts of annoying or irritating agents, are also considered. Thus, whereas a threshold limit value of 3 or 4 ppm for chlorine would insure no impairment of workers' health, this value is reduced to 1 ppm in the interest of greater freedom from irritant effects. The levels of other gases and vapors with irritant or other discomforting effects on the workers have been similarly adjusted.

The rapid growth in the number and diversity of industrial substances to which workers are exposed and the increasing attention being given to occupational health in this country have given rise to a very real problem of maintaining the threshold limits list current. To meet this problem, the Committee on Threshold Limits reviews the lists annually, considering carefully each value and any new information pertaining to a change in level. When a value is changed, it is so designated.

In the threshold limits list for 1954, a further accommodation has been made in an attempt to keep pace with the ever-increasing use of new industrial chemcials. This is the additon of a tentative list separated from the list of established values. Henceforth the tentative list will include all substances not previously listed. Because of the lesser certainty sometimes associated with these tentative values, they should provide only general guidance in the control of exposure and should carry no legal weight. The tentative list is looked upon as providing levels under trial and test, to be revised when new information justifies. Substances in the tentative list will not be incorporated in the main list until the values have been proved by experience to be acceptable. It is hoped that the tentative list will stimulate a greater number of yearly additions than in the past, as well as the critical evaluation of these values by greater numbers of industrial hygienists.

Overall maximal upper limits

It is now considered desirable by a majority of the persons concerned with occupational health to assign a maximal upper limit of 1000 ppm for most, although not all, of the gases and vapors that are apparently nontoxic or nonhazardous. Such a limit has been set for certain Freons and other apparently innocuous substances, although it is known that neither health or safety are endangered by exposure to far higher levels under ordinary conditions. In favor of this practice is the argument that it will prevent excessive or wanton exposure to air contaminants. It is recognized that all the facts needed to assure safety are seldom at hand. Physiologically inert substances, such as

certain Freons and sulfur hexafluoride, in unlimited concentration may suddenly become hazardous, in the presence of welding or pumping operations, through decomposition by heat to highly toxic products.

A similar concept is developing with respect to dusts that in the past have been considered essentially nonhazardous or not incapacitating. Numerous reports from various countries make it all too apparent that many dusts formerly considered inert are capable of producing pulmonary changes that are oftentimes disabling.[1-7] It would therefore seem that all insoluble dusts of whatever nature should be held suspect until proved otherwise.[4] Unfortunately, the assignment of a specific level for each mineral dust is impossible at present. Mineral dusts are commonly of complex and inconstant compositon, often varying according to locality, and thus are potentially capable of causing a variety of physiological responses. As a case in point, pulmonary carcinoma is commonly associated with the long-term inhalation of asbestos in England, but not in America.[8] Assignment of specific levels is also difficult because pulmonary changes derived from the inhalation of mineral dusts commonly require years to assess, because sound information relating exposure to response is not, for the most part, available, because exposures are not uniform owing to changes in the industrial process and job changes, and because dusts from operations involving the same materials often differ in size and surface area.

Therefore, it is believed that the validity of the present standards for dust should be reviewed and consideration given to the following suggestions. In the absence of information and in view of the poor prospect of obtaining any in the near future, the conclusion seems inescapable that if protection from dusts is to be guided by hygienic standards, an overall limit value should be selected. Actually, two values appear desirable, one for dusts containing free silica, and another for nonsiliceous dusts.

For silica-bearing dusts, a limit of from 2 to 5 million particles per cubic foot (mppcf) is suggested. It would be applicable to those substances containing free silica of any appreciable percentage (10 percent or more). Such a level appears justifiable on the basis of usage and experience, as shown in Table I, and tacitly assumes no other

TABLE I
Recommended Permissible Limits of Some Silica-Bearing Dusts[a]

Industry or Source	Reported Percent Free SiO_2[b]	Recommended Concentration mppcf
Sydney sandstone	90	6[c]
Silica brick	80	2
Gold mining (Union of South Africa)	80	3[d]
Granite	35	9-20
Pottery	30	4
Gold mining (Ontario, Canada)	25-35	8.5[d]
Pyrophyllite	30-40	10
Anthracite (hard rock)	30	5-10
Nonferrous mines	20-40	5-10
Anthracite (haulageways)	13	10-15
Cement	6	20

[a]From a table prepared by Theodore F. Hatch, professor of industrial hygiene, University of Pittsburgh.
[b]Values are approximate.
[c]Owens Counter.
[d]Konimeter.

mineral is more hazardous than silica and/or any combination of a mineral with silica. Actually, this value represents a rather low level of exposure when expressed in terms of milligrams of substance per cubic meter of air. Depending upon particle size, 5 mppcf silicon dioxide (SiO_2) with a density of 2.2 might range from 0.01 or 0.02 milligram to several milligrams per cubic foot, assuming the general size distribution of industrial dusts thus far recorded by optical methods;[9] with dusts differing in density from SiO_2, corresponding differences in weight concentration, of course, would occur.

The question then arises of how best to express the dustiness of an atmosphere. Although this concerns matters too involved to be entered into here, it would seem that, with an absolute method now available for the measurement of industrial dusts, the limiting concentrations should be expressed in terms of either millions of particles per cubic foot or milligrams per cubic meter, or both, but within a definite size range, this range to be 0-3 μ diameter. Otherwise, dust counts, as well as expressions based on weight per volume of air, become meaningless. Particles of the size 3 μ and below can now be sampled and measured and are believed to be the only ones of hygienic signifi-

cance. Whether the value approximating 5 mppcf will be found to hold when the submicroscopic particles are included is a very important project for future investigation.

A practical threshold limit value for nonsiliceous dusts would appear to be 5 mg/m^3. This value has been in satisfactory use for some years for controlling hematite dust and fume in at least one American plant.[10] It would seem to represent a reasonable level of dustiness for all other presently considered "inert" nonsiliceous inorganic dusts.

More specific designations

With increasing industrial hygiene knowledge and experience, refinements in designating specific substances to which values are assigned will assuredly follow. As yet, however, only a beginning has been made in this respect. For chromium, the designation specifically refers to chromic acid or to chromates. The highly poisonous arsine gas has a threshold limit value of 0.05 ppm, whereas the value for arsenic and its compounds is 0.5 mg/m^3. Differences in toxic action of uranium compounds have been recognized by individualizing the soluble and insoluble compounds.

It would appear that manganese dioxide would be a desirable designation for manganese, because manganese dioxide is the most common industrial hazard of this element. Mercury at 0.1 mg/m^3 should refer to mercury vapor and its inorganic compounds and should not imply inclusion of the more toxic organic mercurials. Similarly, for fluorides the newer organic fluorides which vary widely in toxicity and hazard should be explicitly excluded, and for selenium, the threshold limit should apply only to selenium compounds which are highly toxic, not to elemental selemium dust, which is essentially nontoxic. The value of 0.1 mg/m^3 for cadmium should refer specifically to the cadmuim fume, for use of this limit for most of the insoluble cadmium compounds imposes far too severe a restriction. Different levels for lead and its compounds should be specifically defined according to information accumulated in the lead industries in this country over the past 10 years. Data show that whereas there is no reason to alter the value of 0.15 mg/m^3 for lead fume or for lead dust of submicroscopic size, this value is unrealistically severe when applied to the more insoluble lead salts, and probably to lenient if applied to certain organic lead compounds. These and other desirable refinements in the list will undoubtedly be made in the near future.

Biological threshold limits

One new feature of occupational health standards that appears destined to play a useful role in evaluating personnel exposure in industry is what might be called biological threshold values, for want of a better term. These values refer at the present time to the greatest permissible content of an air contaminant or its metabolic derivatives in the body fluids, usually in blood or urine, although changes in other bodily constituents may in time serve also as measures of exposure. A list of biological threshold values, which correspond to the threshold limits for concentrations of the substances in air, is given in Table II. The values given for some of the substances are tentative, having been derived from limited experience; for others, such as lead and fluorine, the values are well founded. For still others, such as arsenic and mercury, there is considerable disagreement among industrial hygienists as to the usefulness of urinary determinations.

It is probable that the biological threshold limits of only a few selected substances will ultimately find an accepted place in occupational hygiene standards, since all substances are not amenable to accurate analysis in body fluids (complex organic molecules) by reason of wide individual variation in metabolism, interferences from dietary sources (arsenic), or simply the relative absence of constituents in easily obtainable body fluids (chromium, manganese, silver, and probably beryllium). For biological values to be serviceable, repeated determinations must be made on each person exposed, and preexposure control determinations are desirable. When biological threshold limits are used, they should supplement determinations of air concentrations, not replace them. In effect, these biological limits substitute diagnosis for the control or prevention of injury provided by air analysis.

Currently, in the lead industry, considerable enthusiasm is being expressed over the apparently successful use of urinary lead values with or without prior screening by urinary coproporphyrin determinations. The argument in favor of the use of urinary values is that in practice most industrial

exposures are neither uniform nor simple, but are mixed, and, therefore, that the body serves as a better sampling device and indicator of this type of exposure than do air samples. Biological determinations also offer a guide in the diagnosis of illness not provided by air analysis. Whether it is a wise decision to allow the individual to serve as his own indicator of exposure is debatable: derangement of metabolic function or excretion for various causes is not uncommon among working populations, especially in older age groups, and concomitant exposure to other substances or other stresses may deflect normal metabolic pathways. It would appear reasonable, for the present at least, that biological values should be accompanied by one other independent method of evaluating the working environment.

Interpretation and use

After the threshold limits have been accepted, it is most important that they be properly interpreted and used. Because there is some lack of agreement among industrial hygienists as to the use of the values, it might be worthwhile to consider what is meant by threshold limit or maximal allowable concentration. Confusion appears to center on the precise meaning of the term "threshold" or what constitutes "maximal allowable." These are brief terms used to express a rather complex and abstract concept which may be explained philosophically and operationally.

Philosophically, the threshold limit represents a level to which a normal healthy worker may be exposed for 8 hours each workday without harm to his physical or mental well-being. Because, in practice, most situations involve intermittent or varying exposures, the concept of the limit is that the summation of physiological effects of such exposures shall not be greater than the effect of exposure to a constant concentration at the level of the limit.

TABLE II
Biological Threshold Limits[a]

Substance	Blood (mg/100 ml)	Urine (mg/L)
Inorganic Constituents		
Arsenic	—	1.0[b] (0.5 for arsine or lewisite)
Beryllium	—	0.002
Cadmium	—	0.1
Copper	0.1	—
Chromium	—	Any detectable amount
Lead	0.08	0.2
Mercury	—	0.25[c]
Manganese[d]	—	0.001
Thorium	—	Not eliminated in chemically measurable amounts
Vanadium	—	0.05[e]
Uranium	—	0.01[e]
Fluoride	—	4.0
Selenium	—	0.07
Tellurium	—	0.01

TABLE II (Continued)
Biological Threshold Limits[a]

Substance	Blood (mg/100 ml)	Urine (mg/L)
Organic Constituents		
Benzene	—	15% below normal sulfate ratio of inorganic to total sulfate
Bromide	100	—
Carbon disfulide	—	0.15
Dinitro-o-cresol	—	5.0
Methyl alcohol	—	5.0-7.0
Methyl acetate	—	Analyzed as methyl alcohol
Toluene (as hippuric acid)	—	3000
Trichloroethylene (as trichloracetic acid)	—	75.0

[a] Many of the values given here are found in or have been revised from *Chemistry of Industrial Toxicology* by H.B. Elkins, Wiley, New York (1950, and in "Analyses of Biological Materials as Indices of Exposure to Organic Solvents," by H.B. Elkins, *AMA Arch. Ind. Hyg & Occup. Med.* 9:212-222 (March 1954).

[b] H.H. Schrenk, in "New Information on Arsenic Trioxide." *Ind. Eng. Chem.* 45:11A (1953), states that urinary arsenic values of 4-5 mg/L are commonly not associated with signs of arsenic poisoning. Use of urinary values is considered of doubtful worth because of great variation in normal values. Dietary arsenic, such as that obtained from seafoods, would greatly alter the urinary arsenic picture; moreover, arsenic is excreted chiefly in the feces.

[c] Urinary values may not always be reliable in long-term exposures owing to possibility of development of lower nephron nephrosis and for other reasons.

[d] Inasmuch as manganese is eliminated chiefly via the intestine, urinary determination is not a particularly valuable indicator of exposure.

[e] Tentative value.

Operationally, the word limit refers to the highest permitted averaged values of an agent in the workroom air that have been obtained in a complete cycle of operations during the day. Proper averaging of concentrations should take into consideration the duration of exposure at each concentration; this is referred to as a "weighted average." Concentrations far above the limit for periods of 30 minutes or more and prevailing sporadically throughout the day, although possibly equaling the threshold limit, are not within the intended meaning of the term. Such levels come under the classification of acute, high exposures, and suitable measures should be taken to bring such levels in line with the accepted limit. Threshold limit values are not based on high, acute levels superimposed on a persistent lower level irrespective of what value their average is.

Threshold limit values should be used as guides in the control of health hazards and should not be regarded as fined lines between safe and dangerous concentrations, that is, a point above which injury is bound to occur and below which complete safety may be expected for all exposed persons. Competent judgment is required here as in the interpretation of any standard.

Misuse of limits

The threshold limit values should be used only for control of exposure atmospheres for repeated 8-hour working days. They should not be used in the following ways:

1. For brief acute exposures. (The threshold limit values have been set on the basis of chronic exposures, not on the basis of brief acute exposures.)
2. For mixtures of substances. (There is no assurance that mixtures may not have potentiated and enhanced effects greater than the summated effects of each component.)
3. As levels for community air pollution or for levels to be derived therefrom by simple extrapolation. (The threshold limits have been set on the basis of an 8-hour exposure day with the assumption that a subsequent 16-hour period of nonexposure will aid distribution and elimination of the toxic agent from the body; therefore, they cannot apply to 24-hour continuous exposures common in air pollution conditions.)
4. As levels of permissible concentrations in community water supplies or for substances in solution. (Appropriate levels have been fixed specifically for several toxic elements in potable waters.)
5. As the basis for selecting dangerous compounds for labeling. (Hazards involved in handling chemicals frequently arise from routes other than inhalation, which is the basis for threshold limits.)
6. As safe limits for flight personnel in aviation. (Higher standards of safety and performance are required, and degree and duration of exposure at flight altitude differ from the degree and duration at sea level.)

Pretoxicosis tests

Closely related to the biological threshold values are tests of pretoxicosis, the detection of subtle metabolic changes in the body before injury of serious proportions has developed. The idea is not new, the first reported test of this sort having been applied to the hematologic reactions of presaturnism by Heim de Balsac in 1908.[11] Although the determination of pretoxic reaction is unquestionably one of the highly desirable goals of the industrial toxicologist, few such tests have been developed mainly because the mechanism of action of most toxic agents on which such tests are based is not generally known.

A pretoxicosis test for carbon disulfide has been reported by Bourguignon.[12] This test is based on the change in chronaxie, which, in turn, depends upon the knowledge of the vascular and neurologic changes caused by carbon disulfide during the early stages of injury. Chronaxie, by definition, is the minimal time that an electric current of standard strength is required for the excitation of the tissue. Bourguignon's report indicates that after men had been exposed to carbon disulfide for only 2 months and before any clinical signs of disease were manifest, their chronaxie changed. Accordingly, this test permitted early detection of intoxication by carbon disulfide.

Another test of pretoxicosis that is promising although it is still in the developmental stage is the

lowered cystine content of fingernails of individuals exposed to vanadium. The lowered content occurs in the absence of any objective or subjective signs or symptoms in the workers, and it has been experimentally demonstrated in the hair of animals ingesting vanadium compounds in amounts that caused no demonstrable signs of toxicity.[13] When used in combination with urinary vanadium determinations, the test appears to be highly suggestive of early metabolic changes resulting from exposure to vanadium.

The well-known urinary coproporphyrin III screening test for lead poisoning might well be classed as pretoxicosis test. Used in combination with urinary lead values, it is now considered a reliable guide to incipient damage by lead.[14] At potentially harmful body levels, lead is believed[15] to convert more of the normally occurring colorless precursor to the chromogen while increasing the total coproporphyrin of the urine.

The relative paucity of such procedures attests to the extreme difficulty of their development. Investigators should be encouraged to develop this aspect of preventive medicine, however, because its value obviously transcends that of diagnostic tests of established disease.

Prophylactic and antidotal agents

As the realization of the importance of toxicology in the development and safe use of industrial chemicals has widened, more diversified groups of scientists have become attracted to its problems. Such attraction has resulted in the development of a metal complexing agent, the calcium salt of ethylene diamine tetraacetic acid (CaEDTA), for the treatment of lead poisoning.[16] This chelating agent has been given good evidence of effectiveness in numerous clinical trials,[17,18] and it gives promise of considerable versatility. It has been found, for example, to be a satisfactory antidote in experimental vanadium poisoning[19] and to give promise in the treatment of essential hypertension.[20] Further use of CaEDTA for the more rapid elimination of other toxic metals having the capacity to complex firmly with this chelating agent at body pH conditions will undoubtedly be made. Since the advent of BAL (2,3-dimercaptopropanol) for combating arsenic poisoning, no other organic complexing agent has proved of such value, although others, such as aurin tricarboxylic acid for the elimination of beryllium,[21] have been suggested from time to time.

An ingenious and novel use of a complexing agent for combating cyanide poisoning has been recently reported.[22] Cyanideless vitamin B_{12} (vitamin $B_{12}{}^{a}$, hydroxo-cobalamin) is capable of tightly coordinating with the cyanide ion in experimentally poisoned animals and thus preventing toxic symptoms and death.

Well-known reducing agents, such as ascorbic acid, have been reported experimentally at least to be effectvie prophylactically against a variety of toxic agents. For example, vitamin C was shown to function as effectively as CaEDTA against vanadium poisoning in animals,[19] and this vitamin is reported[23] to reduce substantially fatal pulmonary edema and hemorrhage in animals inhaling ozone or nitrogen dioxide. Essentially complete protection against fatal ozone exposures in animals was afforded by a mixture of such reducing substances as glycuronate, cystine, and other similar substances that include vitamin C.

Two-carbon fragments administered as ethanol, acetate, and propanol have been reported to be capable of combating the highly toxic fluoracetate (1080) in animals,[24] and they give promise of successful therapy for this poison. Cystine, methionine, and other sulfur-containing amino acids have been suggested as more general aids to the detoxifying capacity of the liver for protecting animals against the toxicity of 1,2-dichloroethane[25] and methylchloride.[26]

Within the last few years, atropine has proved an effective antidote for parathion and other closely related organic phosphorous insecticides.

Air sampling and analysis

The development of valid threshold limit values goes hand in hand with the development of accurate procedures for sampling and analysis of the industrial atmospheric contaminants.

The Millipore filter

Unquestionably, the greatest boon in recent years to such a development has been the introduction into the field of industrial hygiene of the Millipore filter,[27,28] known also as the membrane filter or molecular filter. This filter has an efficiency of sampling airborne particulates approaching

100 percent for all particle sizes of hygienic significance. The 150 μ thick paper of cellulose acetates and nitrates with 80 to 85 percent voids possesses a high dielectric constant and effectively attracts even noncharged particles of infinitely small size to its surface despite a mean pore size of 0.8 μ. Thus, the paper possesses a collection efficiency independent of the particle size of the aerosol. A limitation of the paper is that oils and tars clog the filter in a very short period of time, making it useless as a sampling medium for these materials.

Valuable use may be made of the property of the membrane to become transparent upon the addition of a limited amount of solvent (acetone, acetates, alcohols). This transparency permits the collected air samples to be directly counted under the optical microscope over a circumscribed, known area of the filter, thus providing a permanent dust mount that may be quantitatively analyzed.

Further advantage has been taken of the solubility characteristics of the Millipore filter by Fraser,[29] who combined the high sampling efficiency of the paper and its solubility properties with electron microscopy to develop for the first time an absolute method of sampling and analyzing solid airborne particulates. In outline, the procedure consists of *a)* collecting a sample of airborne particultes on the Millipore filter, *b)* effecting transfer of the particles to a prepared electron microscope specimen screen after solution of the paper, *c)* photographing the particles, and *d)* determining the size distribution of the particles by visual measurement from their projection on a screen.

It is strongly urged that industrial hygienists take advantage of this powerful technique to explore the heretofore unsampled and unseen particles of industrial atmospheres and use such information to aid in the determination of their industrial health significance. The results of such a study could well revise some of our concepts of the effective number of particles required to produce pneumoconiosis.

In the light of this and other recent developments, the Engineering Section of the Occupational Health Field Headquarters, Public Health Service, has undertaken an extensive reinvestigation of the entire field of dust sampling and measurement with the objective of developing improved generally acceptable methods that incorporate the advantages of these advances. Already the investigation has led to a promising use of the transparent properties of the Millipore filter, referred to above, as a dry, permanently fixed, dust sample for on-the-site use in plant or factory.

An automatic instrument which continuously records the mass concentration of dust in the atmosphere has recently been introduced.[30] This instrument is based on the photoelectric measurement of forward-scattered light from solid or liquid aerosols and has a range from 10^{-3} to 10^{+2} μg/L in terms of dioctyl phthalate as 0.3 μ diameter droplets. A further modification of this device is being undertaken by David Sinclair of the Johns-Manville Research Center in the development of an instrument which will indicate the size of the particulates as well as their concentration by electronically computing the ratio of backward and forward scattered light from the particles.

Another development in dust analysis techniques is the use of the electron microscope as an electron diffracting instrument. This techinque is capable of exploring the surface of particles to the depth of approximately 0.05 μ in respect to their crystallinity or lack of it. In conjunctin with X-ray diffraction techniques which determine similar properties within the core of the particle, it may provide much useful information concerning the relation between the physical structure of dust and its physiological effects. At the Occupational Health Field Headquarters, such work is being done on the various forms of diatomaceous earths, and in Scotland, on various types of silica.[31] Efforts along this line are expected to go far in helping elucidate the etiology of various types of pneumoconiosis.

Vapors and gases

Developments in sampling and analysis in the highly individualized field of vapors and gases during recent years have yielded no new principle or device, but rather they have found application for many of the methods long used in other fields. The study of air pollution has given a sudden impetus in this direction. Among the recent innovations used in the air pollution field are the portable Venturi scrubber,[32] which has proved satisfactory for sampling ammonia, nitrogen ox-

ides, aldehydes and sulfur dioxide, freeze-out trains, large-capacity plastic bags, silica gel, and other solid absorbents.[33]

For the analysis of organic pollutants, the infrared analyzer and the mass spectrometer are being explored rather widely. Chromatographic procedures have also aided in the confirmation of many often closely related organic substances present in the air.

Automation appears to be the only really new basic development in this field in recent years. This principle has been more successfully applied to the measurement of sulfur dioxide in the form of the Thomas Autometer.[34] This instrument is especially useful in situations where round-the-clock measurements are needed, or with further attachments for signaling added, it may be used successfully for control of gaseous concentrations. Automatic analyzers have also been developed for halogen anaylsis, for carbon monoxide,[35] and for other substances. It should be emphasized that such automatic recorders in their present state of development require careful standardization and repeated attention and maintenance to assure faithful recording of actual concentrations. Commercially available recorders vary widely in this respect. If original design has been good and the instrument carefully standardized and maintained, the saving to industry over the years far outweighs the relatively high initial cost. Increasing automation is foreseen for the coming years in this and related fields of analysis and control of air concentrations of contaminants.

It may seem unfortunate that many of the recent developments in the industrial hygiene field often involve the use of equipment that is expensive and nonportable. Immobility, but not expense, is fast being overcome when the need demands. A mobile infrared analyzer has been designed[36] and a portable mass spectrometer as well.[37] High cost, a factor necessarily associated with increased complexity and sensitivity, will be slower to be overcome.

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The following is only the introduction by Dr. Sterner to the panel discussion on threshold limits. The full text appears in the *Am. Ind. Hyg. Assoc. Q. 16*:27-39 (March 1955).

Threshold limits — a panel discussion*

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The concept of the "threshold limit" is the most important single factor influencing present day industrial hygiene practice. The past few decades have witnessed a transition from a mere postulate that an exposure to an industrial toxin could be controlled by limiting the concentrations to a specific "safe" level to the present wide acceptance and application of maximum allowable concentration values for an ever increasing number of commonly encountered hazardous industrial agents.

As experience has demonstrated the utility and reliability of threshold limits in the hygienic control of the industrial environment, there has been a greater emphasis on the routine industrial hygiene activities. The earlier fears expressed by some physicians that an increasing reliance on non-medical control methods would have unfortunate results, have not been realized. This does not mean that the role of the physician in defining threshold limits has diminished. On the contrary, a greater participation by the physician, from the development of the initial medical data to the final testing of a postulated maximum allowable concentration value by prolonged clinical evaluation of workers exposed in actual work conditions, is essential if the limits are to have the reliability and authority which will permit the safe application of environmental controls. It cannot be emphasized too strongly, that the final proof of the effectiveness of the program based on threshold limits, must rest upon a repeated, comprehensive, and thorough medical examination.

Early in the evolution of the threshold limit concept, and still repeated on occasion, an objection was raised that the factor of individual susceptibility would seriously limit, if not actually negate, the application of the principle. If the limits were based on human lethal dose curves — and even though some point far down on the toe of the typical cumulative fatal dose curve were selected, the objection might be valid. What is not clearly recognized is that for a particular substance, the maximum allowable concentration figure is related to a less serious response than lethality, and that usually this selected function is sufficiently lower than the lethal dose curve that there is no practical overlap.

Such a curve may define the relationship to a symptom such as nausea, or upper respiratory tract irritation, or some other factor which should be easily reversible and not closely followed by a serious reaction.

Even here, the 50 percentile point should not be selected, but some significantly lower figure which will insure that all but the exceptional industrial worker can work safely and with reasonable comfort. We know, of course, that we are still a long way from this ideal, but the defect is not in the principle, but in our lack of knowledge and ability to define the limits with sufficient accuracy. The concept of "allergy" has been interjected in many instances where there is not the slightest evidence to support such an action, qualitatively or quantitatively. Not infrequently the "individual susceptibility" objection is based on confused or sloppy thinking, or is interposed in a specific case which is otherwise untenable.

A legimate criticism, and one which as yet has not been answered adequately, is the relative inequality of threshold limit values. The factor of safety between the limit and the level which may cause a serious effect may be relatively narrow for one agent, such as carbon tetrachloride, or have a

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wide margin for another agent, as in the case of acetone.

Similarly, the single threshold limit does little to define the relative hazard of substances with respect to acute or chronic effects — with benzene and carbon tetrachloride as references. Still another factor is the disparity of the information upon which limits are based. In a few instances there is reliable clinical information, developed on a relatively large group of exposed persons and over many years. This contrasts with the values predicated chiefly on animal experimentation, with little opportunity for prolonged and thorough clinical test. These factors are well appreciated by the skilled industrial hygienist, but they may not be immediately apparent to the less experienced person who has reason to consult a table of threshold limits.

In spite of these defects, the value and importance of threshold limits will increase materially. There is no other mechanism which will so effectively permit us to transfer the experience gained in one situation with an industrial toxin to another. We must admit the limitations of our present values, but in doing this we emphasize the paucity of our present information, not the failure of the principle.

All of us recognize that there are no obvious or easy answers to the criticisms which have been raised as to the limitations in applying threshold limits. From my personal experience in guiding a diversified industrial hygiene program, I am most grateful for the threshold limits which others have contributed, and I am certain that the benefit of their experience has enabled us to give our workmen a safer, more healthful, and happier life.

Methods of establishing threshold limits*

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Threshold limits are based upon information derived from many and diverse sources. For each evaluation, data developed by many different methods may need to be considered and weighed; and from this sometimes complicated, often contradictory, and rarely adequate complex of information, a significant value must be developed.

It is customary to append, as reference material, the important published studies from which the conclusions were made. In these studies, particularly if the author felt that his contribution permitted such a judgment, there is often a proposed threshold limit value. Not infrequently, of course, the values suggested by different investigators may disagree. The group which is charged with the responsibility for establishing threshold limits must consider, in addition to the character of the study, such qualities as accuracy, reliability, completeness, and purpose — and, a not insignificant factor, the reputation of the investigator.

The subject, "Methods of Establishing Threshold Limits," has a connotation beyond that of the procedures and techniques reported in the industrial hygiene literature. This has to do with the actual mechanism by which a group or a committee is designated to act as a body for establishing threshold limits, and the principles and practices which actually govern the operation of the committee. In all present evolutionary stage of industrial hygiene, the internal activities of this committee must weigh heavily in any consideration of "methods."

Threshold criteria

It would be worthwhile, if it were possible, to record all of the elements of a deliberation in arriving at a standard. Often, there is considerable material, undocumented, which plays an important role in the evaluation, in additon to the published studies. This may be limited and fragmentary data from industrial or governmental industrial hygiene surveys; or it may be incomplete data from animal experiments; or reports of cases of alleged intoxication from Workmen's Compensation courses.

A still less tangible factor, related to the experience, training, and critical judgement of the individuals performing the evaluation, is the ability to make a variety of extrapolations. In one instance this may involve the estimation of the probable effect in man from data developed in one or more species of lower animals. The experimental toxicology data may be limited to acute or subacute experiments; but even if chronic, long-term studies have been done, the translation from a few years exposure, even though a lifetime for the animal, to the long span of a working lifetime in man is a difficult step. In other cases, the extrapolation may be from experimental or clinical data developed with one chemical to the probable effect of an homologous compound or a material with similar chemical structure.

The behavior of a substance in other fields — as a therapeutic agent, an insecticide, or even as a beverage (as in the case of ethyl alcohol) may contribute important information. The background of the individuals making the judgment, with respect to personal experience ranging from animal experimentation through long-term clinical observation of exposed workmen, with respect to a practical and critical appreciation of the value and limitations of methods for making environmental measurements, determines the ultimate value with which all of these factors, concrete and abstract, are blended to form a valid, practical, and acceptable threshold limit. The more substantial the documented information, the broader the sources of pertinent data, the less the demand for

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these intangible factors to fill the gaps which are inherent in this kind of procedure.

The absolute test of a threshold limit has not been, and probably will not be achieved if the measure of validity is strictly construed in terms of a completely "safe and healthful" environment for the occupational lifetime of an individual. Practically, criteria much less complete are accepted, although the trend is to the constant improvement of our methods for evaluating long-term and more subtle effects. These more remote parameters of injury are seen in the extreme in the study of radiation effects, where consideration is given to such factors as shortening of the total life span, and of genetic effects involving future generations. With the great majority of physical and chemical agents, we must be content with threshold limits predicated upon less extensive and less subtle end-points.

If threshold limits, even with their present imperfections, are accepted as useful and desirable, they must continue to be fabricated from information which is sometimes inaccurate, frequently controversial, and always incomplete. In this discussion, no attempt will be made to define a pattern of acceptability for the various elements of evidence which may be considered in establishing threshold limits (this might be paraphrased as "threshold criteria" for threshold limits). This will vary with the purpose for which the limits are intended, the character of the group making the judgment, and the need for such standards. At this point, it might be suggested that the various bodies which are responsible for establishing standards, attempt to define in general the purposes, criteria for acceptability, and limitations of their function — and perhaps, specifically indicate the basis for their judgment in individual instances where important factors other than the appended reports played a significant part. The publication of this information would not, of course, still all criticism, but it would obviate much of the criticism which is based upon unfamiliarity with the manner in which a decision is made. It is paradoxical, that the greater the need for a threshold limit (in terms of the numbers of individuals actually being exposed, and the severity of exposure) the greater the justificaiton for accepting a tentative standard on inadequate and incomplete information. This practice is defensibile, of course, only if this initial guiding limit is continuously and critically tested by a competent clinical study of the exposed people.

Sources of information

The two general sources from which significant information is developed are the experimental laboratory where the exposure is deliberate, and the actual plant operation, where the exposure is incidental (sometimes accidental). The establishing of threshold limits depends increasingly upon a balance of information developed from both these areas. The more complete the laboratory investigation, the greater the security of the tentative standard for plant exposures. The inherent uncertainty of extrapolation from the experimental data necessarily places the final judgment upon the clinical evaluation of the exposed workmen.

Industrial hygiene laboratory methods run a gamut from the simple, preliminary "screening" procedure using a few small animals to a relatively involved, deliberately exposed to a toxic agent. The studies with lower species should define a range from minimal or no effect through severe injury and lethality, and should indicate the various physiological and pathological mechanisms of injury. The exposure levels for the human subjects usually attempt to define levels associated with "discomfort," "minimal," and earliest "reversible" effects.

There is no formula at present by which it is possible to estimate the pattern or amount of laboratory experimentation which will be required of this component in establishing a threshold limit. In general, the more novel the physicochemical properties of the agent, the more distantly related to other materials which have had industrial hygiene evaluation, the greater the amount and variety of toxicological procedures which must be employed. The direction and extent of further studies must be determined as the pattern of toxicological investigation unfolds. The importance of the various routes of absorption, the relationship of divided dose administration to the single effective dose, the relative primary irritation and sensitization potencies, the behavior in relation to such factors as species of test animal, age, sex, concurrent disease, are only a few of the important items which must be considered in deciding the importance of the role which a particular animal study may play.

Some of the experimental toxicological findings which suggest caution in evaluating a study may be noted. A lethal dose curve whose slope is gradual may overlap the curve of the physiological function upon which the threshold is to be based. A scattered configuration of delayed deaths suggests multiple effects or secondary pathology which may be difficult to evaluate. A substance which is a sensitizer or allergen, even though indicated solely by skin sensitization relation can be established, as contrasted with the more difficulty controlled experience in the plant. More of these studies on a long-term basis are needed, but the cost in effort and in dollars imposes distinct limitations.

This type of experimental approach is of value in determining the earliest (and still reversible) changes in certain physiologic functions, such as vascular instabililty as measured by blood pressure changes, or metabolite excretion, as in the urine sulfate partition with benzol absorption. The objective, of course, is to recognize a reversible, functional change which, if unchecked, may lead to permanent injury. A practical difficulty may develop as the acuity of test procedures increases, since the changes frequently are not specific for the toxin but may occur with many other factors which affect the body — as for example, an excess of alcohol. On the other hand, special application of statistical methods to group exposures may make these techniques one of the most acute methods of signaling injury.

Value of data on worker exposures

The concept that a careful and comprehensive study of the exposed workmen is the most significant factor in establishing a threshold limit, merits repetition. In practice, however, the number of substances for which such complete studies have been reported are few. A number of factors operate against such long-term, comprehensive investigations. The cost of an adequate clinical program, carried on over many years and with continuing negative results, requires the support of an unusually intelligent and understanding management. The development of environmental measurements so as to be effective for correlation with the clinical findings requires a high degree of cooperation and planning between clinical and industrial hygiene activities. And, finally, the job of organizing the extensive data, of deciding that the results are significant, particularly if they are negative in the sense that no injury is found, and of preparing for publication (since there is no Journal of Negative Data), demands of an investigator courage to the point of being foolhardy.

Of the various types of information which can be obtained from actual industrial exposures, the unsupported testimony of workmen and supervisors, even though accompanied by accurate measurements of environmental factors, is generally so unreliable as to merit little weight in establishing a threshold limit. Individuals who are unable to tolerate the work conditions, or those who have actually become ill and left the job, may have been eliminated so gradually that recognition of the cause and effect relationship may not have developed in the remaining personnel. Furthermore, human nature is such that under these circumstances the men remaining on the job are apt to dismiss the others who left as being "too weak to take it."

As in the case of planning a program of experimental laboratory methods for evaluating a toxic agent, the in-plant clinical survey and environmental analysis must develop in relation to the specific hazard. To the basic elements in the medical examination may be added a variety of special test procedures selected to detect the earliest changes in physiologic function. If little is known about the kind of toxic reaction which may develop, a "shot-gun" approach may be justified with the hope that one or more of the battery of tests will signal a harmful effect. As knowledge of the earliest reactions to specific agents increases, the selection of the most sensitive test procedures becomes more practical, and more reassuring.

The recognition of an occupational disease is frequently much simpler than the proof that a particular exposure is free from any injurious effect. As exposures to toxic materials are decreased from levels which can injure in a relatively short time, a point is reached where the signs and symptoms may develop only after a very long exposure time, and the disease so mild as to challenge the best diagnostic program. We can note again the studies with radiation, where minimal shortening of the life span with relatively low exposures can be demonstrated in experimental

animals but would be impossible to detect, with our present techniques, in the human subject.

Clinical observations

The broader the base of the clinical investigation which is associated with a finding of no injury or no significant injury at a particular exposure level, the greater the reliability of the conclusion. To the critical investigator, however, the job is never complete, never without some area in the study which could not have been strengthened or improved. The period of the study can extend into many years, and yet the end point can remain uncertain.

As other techniques are added to the evaluation program — such as studies of morbidity and absenteeism, reasons for dispensary visits, and analysis of cause of death — the problem of interpretation becomes increasingly complicated. An example may be cited in which two young women employees in the same small department developed leukemia within a few months of each other. This occurrence was readily accepted as a chance finding because both girls had clerical positions with no possible exposure to an industrial toxin. Had this occurred following a common exposure, however brief or minor, to a new chemical with a long and unfamiliar name, it is quite likely that medical testimony would have been developed, in a Workmen's Compensation hearing, attributing the disease to the exposure. The effect of the incident might well have extended beyond the cost of compensation and into the area of threshold limits by the publication of a case report. A fine discretion is required in recognizing the first or isolated instances of injury to a new chemcial and yet avoiding the inclusion of cases solely on legal or social motivation.

In a study of the long-term effects of a solvent, records were kept of the causes for dispensary visits. A slightly higher incidence of gastrointestinal complaints was found in the exposed group, and since this had been reported previously by others, it seemed significant. However, the incidence of respiratory complaints was as much lower for the exposed individuals. In an interpretation, it would have been equally proper to assume that the solvent vapors "protected" the individuals against respiratory disease, and that this beneficial effect might offset the gastrointestinal difficulties. As might be suspected, when these relations were put to the test of statistical significance, both could have been due easily to change alone.

A final word is in order concerning the methods for developing data by which the environment is described — the conditions of exposure. As much variability can be, and is, encountered with this function as with the methods for laboratory experimentation and in-plant clinical examinations. The accuracy and reliability of the analytical techniques, the relation of the time and site of sampling to the true exposure, the presence of other agents which might modify the single action of the toxin under study are some of the many factors which must be critically examined in the light of their usefulness for correlation with a given set of experimental or clinical findings.

It is obvious that there is no single method or pattern of methods which can satisfy the varied requirements for establishing threshold limits. It is equally obvious that even though rigid standards were described which would satisfy a discriminating jury of scientists, the available data for establishing threshold limits for all but a very few substances would fail to satisfy such limits. The real use for threshold limits, as a guide for industry in the control of exposures and as a measure for action by governmental agencies, demands a continuing improvement in the quality and quantity of the methods by which truly valid criteria may be achieved.

Prepared discussion†

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Dr. Sterner has discussed the great difficulties attendant on developing adequate data for thres-

† Dr. Stokinger's discussion of the establishment of threshold limits appeared immediately following Dr. Steiner's paper on the same subject in *Am. Ind. Hyg. Assoc. Q.* 17:284-286 (1956). To keep the continuity of the subject it was decided to break from tradition in this volume and begin this discussion in the same manner as the *AIHAQ.*

hold limits, the many imponderables in their interpretation, and their unsatisfactory and necessarily always incomplete nature. All these considerations should certainly be thoughtfully considered and strongly stressed, because errors in judgment cannot be afforded. But lest these many considerations seem so formidable to many potential investigators as to prevent their needed contributions (which was far from Dr. Sterner's intention) or depress the more experienced contributors, it should be immediately pointed out that there are at least two practical and very helpful means of overcoming certain deficiencies inherent in the basic data. One is the safety factor, the other, the periodic re-evaluation of the threshold limit values. The safety factor has been built into most of the values in the threshold limits list.[A] The factors 2, 5, 10 or even greater have been applied to some values. There are, of course, some notable exceptions, such as the present value for trichloroethylene, for which the threshold limit is the absolute ceiling, but generally such instances are rare. In general, the greater the uncertainty in the data's applicability to human industrial exposure, the larger the factor applied. This lowering of the limit value by an arbitrary safety factor may at times provoke some controversy, because now the value becomes one of opinion, not fact. Be that as it may, the safety factor incorporated in the air standards gives increased assurance of safety to many doubtful values.

The re-examination of the listed values by the committee provides annually for readjustment of all values, whatever their sanctity, upon submission to the committee of new and experimentally supported findings. Repeated scrutiny and reappraisal of this sort can lead finally only to assignment of safe values on which complete reliance can be placed. The committee welcomes all such information.[B]

Need for more data

In this connection another point implied in Dr. Sterner's discussion should be strengthened — namely, the need for more data substantiating the choice of safe exposure levels based on industrial experience. Much useful information is undoubtedly in the files of many plants. Indication of this was the fine evidence on six industrial substances derived from many years of plant experience that came to light last year at these meetings from the presentation of Herbert J. Weber.[1] Others should have similar material that should be brought to the attention of the Threshold Limits Committee. Like Weber's material, all of it need not be novel or presented to show need for changing existing limits; equally valuable are data confirming existing limits. As never before, interest in the value of the control of industrial environments is being shared by management generally. Greater numbers of industrial hygienists than ever before are being engaged by industry. Is it too much to hope that meetings such as these will orient the thinking of properly placed industrial hygienists to secure much needed plant information to aid in the choice of safe limits of human exposure?

The type of information needed may be listed as follows:

1. Air concentrations should be determined for the substances under study through a complete cycle of plant operations and with reasonable regularity in order to obtain a true picture of the range and fluctuations of exposure.
2. The data should have good accuracy.
3. The observations should be carried out over a reasonable period of time — a minimum of five years.
4. The air concentration data should be correlated with a good medical program. A pattern for such work is that of Dr. Sterner's 10-year study of workers exposure to butyl alcohol.[2]

There is a real need for more data based on industrial experience. The often-heard statement

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[A]The incorporated safety factor in the threshold limit values, although added at times because of uncertainty in the value as related to human exposure, often actually provides an appreciable margin of safety. For this reason the correctness of the term "threshold limit" may be questioned. It might more properly be replaced with "air hygiene standard."

[B]At the time this paper was written, the point of contact was Allan Coleman, Chairman Threshold Limits Committee, ACGIH, Connecticut State Department of Health, Hartford 1, Connecticut; *Currently* the address is: Committee on Threshold Limit Values for Chemial Substances, c/o ACGIH, 6500 Glenway Ave., Bldg. D-5, Cincinnati, OH 45211.

"the threshold limits are nothing but educated guesses" unquestionably reflects the wish at least that more data be firmly based on industrial experience to substantiate the choice of limits. As a member of the Threshold Limits Committee, I was concerned over the statement and took the trouble to review each substance in the threshold limit list for 1955 as to the basis for choice of the level. The results are shown in Table I. It is possible that everyone would not arrive at precisely the same figures, but I believe that their magnitude would not be much altered. Although the table shows that the educated guesses account for a relatively small number, it does confirm the often expressed feeling of the need for more solidly based levels. Table I shows a number of other interesting facts: 1) that most of the values have some sort of scientific basis; 2) that each level has been documented either by Warren A. Cook,[3] or by the Committee on Threshold Limits; 3) that the values based on animal experiments account for the largest number, 42%; but 4) that values having some industrial basis account for one-third of the total.

The values ascribed to the "man" category arise from two sources — that of Nelson *et al*,[4] and those more recent publications of the Dow Chemical workers, Irish, Rowe, Spencer, Adams *et al.*

The "educated guess"

A few words should be said in defense of the "educated guess." A review of the values described as guesses indicates in the instances in which sound information has later become available that the "guess" was remarkably good. Two prominent examples only suffice — hydrogen fluoride and uranium. A safe exposure level for hydrogen fluoride was set at 3 ppm on the very limited evidence supplied by a study in animals by Ronzani in 1909.[5] Last year a report[6] culminating many years of study of fluoride exposure in the aluminum industry, involving thousands of air and urine analysis for fluoride and studies of roentgenographic changes in bone, showed without question that air levels double the accepted limit gave rise to perceptible changes in bone in only a few individuals, and only after many years of exposure, thus validating the wisdom of this "educated guess."

TABLE I
Basis for Choice of Threshold Limit Values*

Study Type	No. of Listings	Percent Total Listings [223]
Animal	94	42
Industry	51	23
Animal & industry	23	10
Man	25	11
"Educated guess"	21	9
Animal & man	9	4
Source uncertain	3	1

* Based in part on Cook, W.A., *Ind. Med.* 14:936 (1945), and from documented material of Threshold Limits Committee, ACGIH 1953-1955.

In the case of uranium, an engineering benchmark had to be "guessed" at early in the days of the Manhattan Project. After a review of the quite limited animal data on uranium then avaible, Dr. Stafford Warren suggested that the "safe" exposure level for uranium be the same as that for lead, 0.15 mg/cu.m. After $500,000 and many years had been spent in research, the safe levels of exposure to uranium compounds were found to bracket this value very closely.

Levels for cancerigens

There is still one group of substances for which some method should be devised for establishing safe air standards — the industrial cancerigens. How shall we establish the limits for this type of substance? Thus far the question has been sidestepped completely. As a result, with one exception, nickel carbonyl, limits taking into consideration potential cancerigenicity have not been assigned. Several industrial substances are known or suspected cancerigens; many more are suspect on the basis of animal experiments. As a suggested method of approach, the following is offered: to the level judged safe for other types of systemic injury add a safety factor for carcinogenicity. The magnitude of the safety factor is suggested to be from 100 to 500. This provides at least a second power of 10, which, from the well-known dosage-response hypothesis, provides at least a fourfold longer interval before effects may be expected to occur, or conversely at least a response with one-fourth the intensity. This manner of approach has been used for nickel carbonyl. A tentatively safe level for systemic effects from repeated daily exposure has been set at 0.1 ppm; one-hundredth

this level, or 0.001 ppm was set for nickel carbonyl on the basis that nickel poisoning gives rise to a substantial increase in the incidence of lung cancer. It is realized that unfortunately the safe limits for all industrial cancerigens cannot be so readily resolved. This is especially true of dye intermediates, such as benzidine and naphthyl amines whose major route of entry is not commonly via the lungs but through the skin and gastrointestinal tract. These are laundry and protective equipment problems not solvable by air control.

There are undoubtedly substances to which the suggested procedure may not strictly apply, but imperfect as it may be, the suggested method is felt to be a step in the right direction and serves better to curb exposures to industrial carcinogens than considering the problem too difficult to cope with at the present time.

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Improved communication — hygienic standards for daily inhalation*

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Experience convinces us that we humans are unique in the universe. Because of our ability to communicate, we may be well on the way toward emerging into a new level of biological existence. Each individual may eventually share completely all past and present experiences of the species. Each may act in concert with his fellows toward common ideals and goals, still retaining his own individuality. Real progress in this direction has been made during the past ten thousand years through developments of recording, duplicating and retrieval techniques. Despite brief back-sliding, there has furthermore been real spiritual progress, and an increase in the proportion of men of good will. The next ten thousand years should bring substantial achievements in communication upon higher levels, perhaps even through inarticulate contact of mind with mind. There are hints that what some have called the world mind may come into being before the present human species evolves physically into whatever new species its body is tending toward.

However, until the world mind develops, we are forced to depend upon more prosaic means of communication. Not so many generations ago, a natural philosopher like Roger Bacon, whom today we call a scientist, could live a full life investigating the secrets of nature, feeling no need and finding no opportunity to communicate his discoveries and his conclusions to a living soul. He could bury his achievements in code, making them difficult for posterity to unravel. We do not have such people and such situations today. Each one of us benefits from current division of labor, of experience, and of knowledge. Each one of us is a unique specialist, depending upon a multitude of other unique specialists for the achievement of our aims, for our very existence. If nothing else motivates us, simple self-interest should dictate that each one of us ought to make public all that he has learned, in order that his fellow specialists may use it to help us all.

Communication

A year ago Sterner[1] expressed the situation in more concrete terms. We comprise persons separately trained in highly specialized fields, led after training to cooperate in the common aim of providing means by which technological developments in occupation may be utilized in a manner compatible with complete health. He said,

> *"We must provide a fluid and effective means of communication between the chemist, the engineer, the physicist, the toxicologist, the physician, and the other specialists brought into industrial hygiene. There must result from this interchange of ideas not only an appreciation of each team member's contribution, but an ability actually to bridge the gap between the disciplines, to synthesize, from the offerings of each of the fields, the solutions to the ever more complicated problems. Each member specialist must not only contribute the information he is most qualified to give, but also must encourage sympathetic, intelligent, and mutual understanding."*

In this matter of mutual understanding, we are very much like the inhabitants of Looking Glass Land. You remember that the White Queen told Alice, "Now *here*, you see, it takes all the running you can do, to keep in the same place. If you want to get somewhere else, you must run at least twice as fast as that." With the entry of new people into our profession and the recognition of new constituent specialties such as health physics and atmospheric pollution control, each with a tendency to keep to itself, are we running fast enough

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even to stay in the same place? We all feel there are too many conferences and too many committees to leave us time to do our daily work. On the other hand, if we are to do our work as well as it can be done, we must be in constant communication with related specialists, because each one of us fully knows only one facet of his own problems.

Communication is not a simple process. It requires an informed speaker or writer who can express himself at the level of comprehension of his audience. It requires an audience which wishes to receive communication. It must be carried on with words, those abstract symbols for reality, each of which has a different meaning to each individual, shaded by his entire past experience. Only a newly coined word is free from ambiguity, and it remains new for only a brief interval. Most important of all, successful communication requires what is today known as feed-back. By this, the speaker hears his audiences' impressions. He can correct and amplify his words until he thinks his audience truly perceives his meaning. A leisurely conversation can be effective communication through feed-back; an article in a journal is likely to be poor communication because feed-back is inadequate.

The relatively new specialty of industrial toxicology has already contributed to the equally new profession of industrial hygiene by means of communication. The toxicologists are doing an acceptable job for those people who recognize their need for toxicological information and opinion. The job could be done better, but it is at least acceptable. Success is by no means as great in helping those people who do not recognize their need for help. Once more communication cannot succeed unless the audience desires to receive communication.

Acceptable concentrations

The most important communication within industrial hygiene, and between our profession and others, may be the collection of judgments upon acceptable concentrations of contaminants in working atmospheres. During what may be called the age of chaos, every experienced industrial hygienist had a few values uniquely his own, drawn from his own experience. For less familiar substances, he borrowed more or less judiciously from the values cherished by his professional colleagues. Some degree of unanimity was brought about when the United States Public Health Service values, based on its long-time collective experience in industrial hygiene, were published in a manual.[2] Further unanimity followed publication of the values collected and extended by Cook.[3] In 1947 the American Conference of Governmental Industrial Hygienists published its first list in the *Industrial Hygiene Newsletter*.[4] In the next two years revised lists were privately circulated to the members of the Association.[5,6] Then publication took place in a scientific journal,[7] and each year thereafter a revised list of threshold limit values has appeared in the scientific literature, and has been generally accepted.[8-12]

The contributions of Cook[3] in unifying opinion, and in weighing threshold limit values then in use, judging new data and proposing a list of 129 values, are worthy of high regard. Among the 238 values for substances other than mineral dusts in the current list[13] of established and tentative threshold limit values are 54 of those which were first proposed in Cook's list, some as definitely established, others to be used cautiously until verified by actual experience.

Not since Cook has anyone published a summary of the data which serve as bases for the selection of specific threshold limits. The privately circulated documents[14-16] which give some of these data cannot be considered to be publication, although they are freely available to any person.

Threshold limits are, and must continue to be the products of judgment, important if true. Some few truly represent their definition and are approximations of the maximum concentrations which can be inhaled continuously and repeatedly without injury to health. These may possibly be fit parameters for incorporation into codes and regulations. Many of the threshold limits are well below concentrations which can injure health. They represent current judgment as to concentrations to which, good practice dictates, men may be expected to subject themselves. These do not seem fit parameters for regulations. In a particular operation, if possible, it is desirable to maintain concentrations below the bench-mark by reasonable ventilation and precaution. It is always best to reduce exposure to chemicals to the lowest practical level.

Previous suggestions for improvement

During the Ninth Annual Congress on Industrial Health, the writer was chairman of the Committee on Chemical Agents. The report of the 16-man committee[17] devoted considerable attention to praising the development of threshold limits, and to suggesting ways in which their presentation could be made more useful. Since that report, two developments have taken place along lines desired by the Committee. The annual table of the Threshold Limits Committee of the American Conference of Governmental Industrial Hygienists is now published in the *Archives of Industrial Health,* removing the earlier implication of quasi-legal status arising from its appearance in the *Industrial Hygiene Newsletter* of the Division of Industrial Hygiene, U.S. Public Health Service. In 1954, the Committee on Threshold Limits of that Association began to supplement its table of accepted values with a list of tentative values.

Three other suggestions of the Committee on Chemical Agents deserve reiteration and discussion. It was urged that the bases for the selection of each value should be published, that the name should be changed to *hygienic standard,* and that the particular concept of permissible human response behind each value should be clearly indicated.

There is such a multitude of factors involved in the protection of health in our complex civilization that no one person or group of persons is competent to weigh them all with assurance. No oracular or *ex cathedra* statement on health deserves serious attention. Only when the facts upon which a decision are based are furnished for general scrutiny and evaluation can the decision be considered even tentatively sound, and only after there has been adequate opportunity for criticism and modification can it be considered established. All toxicological facts should be published, and all decisions upon the facts should be accompanied by a summary of the reasoning under which they were derived, before anyone should be expected to act upon the decisions. Any publication of standards for maintenance of health ought to include reference to the underlying data.

The second suggestion referred to the name by which the values are known. Semantics is more than a sport for the idle. No matter how thoroughly a concept is originally presented, it always becomes known and referred to by a brief name, a catch-word. Most persons who learn of the concept hear the catch-word name, and do not go back to the original presentation. The meaning they attach to the name comes from their previous experience with the particular words. It may be, but is usually not, exactly what the originator of the idea intended. The more carefully one chooses the name he assigns to a concept, the more likely are others to interpret the concept as he himself does.

The values now known as threshold limits are usually identified by phrases containing the words *allowable* or *permissible.* These two words have connotations of legal regulations. Such connotations cannot properly attach to the judgment of a voluntary professional association. The identifying phrases may also contain the words *maximum, threshold* and *limit.* These words all imply that below the concentration specified, human response is negligible, above the concentration it is dangerous. Actually, it is more than an implication. It is definitely stated. In the introduction to its 1956 list the Committee on Threshold Limits says, *"Values are given . . . for the maximum average atmospheric concentrations of contaminants to which workers may be exposed for an eight-hour working day without injury to health."*[13] Careful study of the data which support the currently accepted values suggests that no such description can be truthfully attached to most of them. Industrial hygienists recognize this. They are accustomed to emphasize that the values should be regarded simply as bench-marks, guides to good practice. Indeed, the Threshold Limits Committee itself confusingly warns *"Threshold limits . . . should not be regarded as fine lines between safe and dangerous concentrations."*[13]

The term *maximum acceptable concentration* being used in revisions of standards by the American Standards Association Z-37 Committee is objectionable only because it will be abbreviated M.A.C. Many will interpret this abbreviation as *maximum allowable concentration,* and nothing will have been gained by the change from *allowable* to *acceptable.*

I conclude that the names *maximum allowable concentration* and *threshold limit* are misleading. They convey a wrong impression to those who are not already familiar with the concepts behind the values. The name suggested in 1949, *hygienic*

standard, is not misleading. Standards of good practice are familiar to all of us in many fields. Looking toward the future provision of a variety of hygienic standards, a series of values should be selected, to be known as *hygienic standards for daily inhalation.*

The third suggestion is more far-reaching. The Committee on Chemical Agents pointed out that there has been no simple or uniform relation between the effects of a substance and the numerical value chosen for tabulation.[17] The Committee concluded that concentrations have been selected on the basis of one of four concepts of the level best suited to hygienic control of inhalation, the choice having been governed by the nature of the toxic response and by the degree of organoleptic response. The Committee's four concepts follow:

a. *Plus or minus:* The maximal time-weighted average concentration which produces only minor injury, and that in a very small proportion of exposed workmen.

b. *Safe:* The maximal time-weighted average concentration which sound evidence leads one to believe will cause no demonstrable illness or other symptom of toxic effect in any workman during a lifetime of industrial exposure.

c. *Bench-mark:* A concentration based on the belief that any unnecessary exposure is undesirable — a concentration lower than that of a or *b,* one as low as is consistent with practical engineering control.

d. *Comfort:* A concentration lower than a or *b,* representing the maximum which in a short time is not objectionable to 9 out of 10 of a group of persons not accustomed to inhalation of the substance.

Note well that these four concepts were judged to be those already used for the selection of hygienic standards for daily inhalation. All four were judged consistent with the goals of industrial hygiene.

Hygienic standards for daily inhalation

The subject of hygienic standards for daily inhalation should be re-examined, the concepts represented by the values should be restated in more realistic toxicological terms, and more consistent and more informative standards should be prepared. Such a step will not undo any of the accomplishments of the profession of industrial hygiene or of any organization. Rather, it will supply informative standards to supplement the accumulation of naked numbers now accepted, some of which have not been critically re-examined for a decade.

It is certainly imperative that the inhalation of substances during the working day shall not be allowed to result in any injury to the physical well-being of workmen. It is furthermore imperative that inhalation shall not increase the probability of accidents through the mental distress occasioned by objectionable eye, nose or throat irritation, transient though it may often be, nor through the impaired judgment and delayed reaction time of light narcosis. It is desirable that inhalation shall result in no degree of discomfort whatsoever. On the other hand, when it is impractical to avoid all discomfort, then such inhalation is certainly justified, provided there results no injury to workmen and no increase in the probability of accidents.

Tables of hygienic standards do not now carry indications of the nature and of the magnitude of the effects to be expected from inhalation of greater concentrations. It is only by a rather thorough study of the available data that one can decide whether or not a particular substance can safelyb e inhaled at a greater concentration. With most substances, it is quite practical to set two standards, one an inoffensive level, another a concentration which cannot safely be exceeded under any pressure of practicality.

Administrative expediency may be served by a table of numbers which constitute a part of official regulations. Regulations need not be defended, they need not cite justifications. However, it is a minority of the profession of industrial hygiene who have regulatory responsibilities. Most of our colleagues act through obtaining voluntary cooperation with their judgments. They would be aided by a greater degree of explanation in a tabulation of standards. They could then show that their recommendations are quite defensible, that they are not arbitrary decisions having no regard for the realities of competitive industrial existence.

A hygienic standard for daily inhalation should specify two concentrations, together with a description of the human response to be expected from

inhalation of each. One concentration should be low enough so that no injurious effect can be expected in any workman, but it may cause a detectable odor, it may cause a detectable eye, nose or throat irritation. The second concentration should produce somewhat more severe, but still reversible and non-progressive effects. From these two concentrations, one can at once see how strictly the standard should be observed, the steepness of the dosage-response curve, the breadth of the plateau of non-injurious concentrations. Despite the wide range in individual susceptibilities of workmen, such values can be selected for most, if not all, substances.

Adequate data for preparing this sort of standard consist of appropriate human experience, or repeated medical examinations of workmen in atmospheres whose concentration has been frequently estimated. Sterner[1] discussed this point in detail. Experiments upon animals, verified by biochemical and physiological studies in humans, may demonstrate conclusively that a substance has an effect during one period of inhalation which does not progress during oft-repeated inhalation. For such a substance, satisfactory data can be obtained from objective study and secretly recorded subjective effects of a group of humans inhaling known concentrations for substantially eight hours. Any lesser body of data should result in a hygienic standard being designated as tentative.

Categories of objectionable action

Judgments should be made to determine which hygienic standards for daily inhalation must be carefully observed, and which may be exceeded when it is impractical to observe them. These judgments will be most consistent if we first decide for each substance what objectionable action we are guarding against by the standard. Every toxicologist will realize that the action at a low concentration which it is most important to guard against, may not be the same as the menace to life to be expected at a high concentration. In a tentative fashion, the writer has made these decisions for the 238 substances, exclusive of the mineral dusts, included in the 1956 tables of proposed accepted and tentative standards.[13] The decisions can be divided into the following nine categories on the basis on the nature of human response.

Chronic toxicity

The most dangerous effect of some substances is a progressive systemic injury, increasing in severity with continuing inhalation. Benzene, carbon disulfide, carbon tetrachloride and lead are the most familiar examples. The lower standard for these substances should be a concentration believed not to produce any effect in any workman, and no considerations of practicality are sufficient to justify inhalation in excess of the standard. Close medical supervision is required for safe use of these toxic substances. The standard for chronically toxic substances should refer to the time-weighted average concentration throughout a working day. Brief peaks of a few times the standard have no significance, save as they increase the average.

Acute toxicity

Some substances do not produce an injury progressing with repeated inhalation. Such systemic injury as they may cause takes place as the result of one excessive inhalation, or not at all. Familiar examples are carbon monoxide and hygrogen cyanide. The standards for acutely toxic substances should be interpreted in the same light as those for chronically toxic substances.

Narcosis

The most dangerous effect of some substances is narcosis, which becomes anesthesia in its extreme state. At a rather low concentration they induce accidents by impairing judgment and delaying reaction time. Familiar examples are ethyl alcohol, ethyl ether and gasoline. The lower standard for a narcotic substance should be a concentration which produces no detectable effect upon judgment and reaction time after eight hours inhalation. It should refer to the average concentration existing during some appreciable period of time, the length of which can be estimated from absorption and elimination data. No considerations of practicality can justify exceeding the standard for a narcotic substance.

Irritation

The most dangerous effect of some substances is irritation. Eye, nose and throat are irritated at a low concentration, the bronchi at a higher concentration, and fatal lung edema may be the result of inhaling an extreme concentration. The aldehydes,

halogens and acids are familiar examples. Highly odorous substances may also be considered in this catagory. The lower standard for an irritant substance should be a concentration which is detectable, but is not objectionably irritating to the majority of unhardened subjects who are exposed for a substantial part of a working day. The higher standard should be set at a concentration which is well under one injuring bronchi or lungs, and which is justifiable when it is impractical to keep concentrations at the lower standard. Standards for irritating substances should refer to concentrations existing for even a brief period during a work day.

Asphyxiation

Some substances are inert in the body and can injure only by asphyxia at extremely high concentrations, excluding the oxygen of the atmosphere. Familiar examples are the fluorochloro refrigerants. The lower standard for these asphyxiants should be a nominal bench-mark of good engineering practice, such as the 1000 ppm concentration now quoted. The inert nuisance dusts like iron oxide might well be placed in this same catagory, and the currently used bench-mark of 15 mg./cu.m. seems an appropriate level. The standard should refer to the concentration existing during any brief period, but it should be recognized that higher concentrations are justified when it is impractical to keep below the standard.

Fume fever

The most important effect of some substances is a transient influenza-like condition known as fume fever. A familiar example is zinc oxide fume. The lower standard for a fume fever producer should be a concentration which will not produce that distressing but not menacing condition in any workman, and it should apply to an appreciable period, such as half an hour. No considerations of practicality can justify exceeding the standard for fume fever producing substances.

Eye pigmentation

The most important effect of two substances, quinone and hydroquinone, appears to be a slowly developing pigmentation of the sclera, which may reduce visual acuity, or even lead to blindness. The lower standard for these substances should be a concentration which produces no pigmentation after years of exposure, and it should refer to the time-weighted average concentration throughout the day. For a few days at a time, conditions of practicality should justify exceeding the standard.

Cancer

One substance is reasonably well established as a cause of respiratory tract cancer. This is nickel carbonyl. It appears probable that the minimum cancerigenic exposure will never be defined. At this time it is prudent to set the standard for a cancerigenic substance substantially at zero, as has already been done for nickel carbonyl, and no considerations can justify allowing the inhalation of any concentration which is avoidable.

Allergy

Some substances are known to sensitize an appreciable proportion of exposed workmen. They may produce distressing and menacing asthma-like attacks when a sensitized person inhales a low concentration. Examples are ethylene diamine and the diisocyanates. At this time there is no rational experimental basis for defining a concentration which will not sensitize a susceptible workman, or one to which no previously sensitized workman will respond. Control of exposure to allergenic substances must rely heavily upon industrial medicine. After experience has allowed withdrawal of workmen susceptible to sensitization, the remaining resistant individuals can be protected by a hygienic standard for daily inhalation based upon irritation or systemic injury. Until it has been demonstrated that a particular group includes no susceptible workmen, no considerations can justify allowing inhalation of any concentration which is avoidable.

(Editor's note: The table which lists the 238 values as well as the discussion that followed this portion of Dr. Smyth's paper is not reproduced in this publication due to space limitations. The interested reader may find the table along with the discussions and references cited on pp. 136-185 of the *Am. Ind. Hyg. Assoc. Q.*, Vol. 17. The 1956 recommended threshold limit values appear in this volume. The *Documentation of the Threshold Limit Values*, 4th ed., provides more up to date information regarding the predicted effects of a given substance. This publication is available from ACGIH, Publications Office, 6500 Glenway Ave., Bldg. D-5, Cincinnati, OH 45211.)

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TLVs OF THE 1960s

A toxicologist's view of threshold limits*

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Conformance with a threshold limit may lead to more absorption of vapor than does conformance with a numerically identical maximal acceptable concentration, because the former is a time-weighted average concentration, while the latter is a limit below which all measurements should fall. The adverse effects which threshold limits are expected to guard against may not include cortical reflexes. Whether or not such reflex effects are of any importance to the well-being of the industrial worker is not completely clear.

I am on record[1] as concluding that experimental study of the effects of repeated inhalation by animals has been as sound a basis for setting threshold limits as any other basis which has been used for the values of the American Conference of Governmental Industrial Hygienists (ACGIH). A considerable proportion of the values set on any basis has been modified later as experience has accumulated, and the proportion has been no greater for those based on experimental toxicology than for other bases. It is the collection of experience through industrial hygienists and industrial physicians, with annual reconsideraton of values, which has made the threshold limits lists dependable.

However, some details are suggested by toxicological considerations. All that I have to say is related to the paragraph which has been used for several years as part of the foreword to the annual tables of threshold limits issued by the American Conference of Governmental Industrial Hygienists.[2] I quote:

> *"Threshold limits should be used as guides in the control of health hazards and should not be regarded as fine lines between safe and dangerous concentrations. They represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day, without adverse effect. The values listed refer to time-weighted average concentrations for a normal workday. The amount by which these figures may be exceeded for short periods without injury to health depends upon a number of factors, such as the nature of the contaminant, whether very high concentrations even for short periods produce acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such periods. All must be taken into consideration in arriving at a decision as to whether a hazardous situation exists. Special consideration should be given to the applicaton of these values in the evaluation of the health hazards which may be associated with exposure to combinations of two or more substances."*

I shall discuss points suggested by three phrases from the quoted paragraph: "The time-weighted average concentration," "The amount by which these figures may be exceeded," and "Without adverse effect," and follow with a brief summary of our own exploration of the conditioned reflex, which leads out of my discussion of the third phase.

"Time-weighted average concentrations"

The Maximal Acceptable Concentrations (MACs) of the American Standards Association Z-37 Committee, are authoritative opinions, which are not widely referred to.

In the mid-1950s the Z-37 Committee undertook to review and to revise earlier standards which it had issued, and to extend the rather brief list to include additional industrial materials. This large Committee, operating under the awkward rule of consensus, with some members unable to vote until official action of their societies has instructed them, has made less than moderate progress. Since 1957 four standards have been

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issued, carbon tetrachloride,[3] benzene,[4] toluene[5] and xylene.[6] The numerical values of these MACs are identical with the 1960 Threshold Limits Values of the ACGIH, namely 25, 25, 200, and 200 parts per million by volume (ppm), respectively.[2]

The agreement is much less than one would think from the correspondence of the numerical values. This is an illustration of the weakness of quoting numbers divorced from their context. The threshold limit values refer to time-weighted average concentration for a normal work day, as explained in the paragraph I quoted.

On the other hand, the maximal acceptable concentrations of the Z-37 Committee refer to that concentration which should not be exceeded at any time during a normal work day. MACs are peak concentrations, not averages. The Carbon Tetrachloride standard reads 25 ppm, "with the understanding that variations should fluctuate around 10 ppm."[3] If this standard is followed literally, the time-weighted average will be in the neighborhood of 10 ppm, only 40% of the threshold limit. The Xylene standard reads 200 ppm, "with the understanding that variations in concentration should fluctuate below this level."[5] Here again, a person working in the MAC conceivably could absorb about half as much as if he were working in the threshold limit concentration.

Thus the numerical identity of the standards of MAC and TL for four vapors, actually mean that the Z-37 Committee concludes that the exposures of workmen should be considerably less than those which the ACGIH Committee concludes are unlikely to cause adverse effect.

The question of which concept is sound, average, or maximun, requires some considerations of the type of injuries against which the standards guard, and of the toxicological mechanisms which cause these injuries. I made a special study of this subject in 1956,[7] and concluded that the injuries guarded against varied widely. I urged that some clue to the type of injury be included in tabulations of standards. Injuries are explicitly described in ASA Standards and in American Industrial Hygiene Association Hygienic Guides, but not in any tabulations I have seen published. Indeed, ASA has set the precedent of naming two standards for inhalation of one substance, to guard against two kinds of injury. In effect, the Xylene Standard[5] says, "To guard against discomfort to workmen, keep concentrations below 50 ppm, and to guard against narcosis and anemia, keep concentrations below 200 ppm."

My 1956 paper[7] concluded that the 238 ACGIH threshold limits and tentative threshold limits then extant guarded against nine different adverse effects.

1. Twelve per cent guarded against acute systemic toxicity. With these, the total amount absorbed in one day usually determines whether injury results, and the time-weighted average concentration is an appropriate guide to safe working conditions. Among the exceptions may be the cyanides, whose detoxicaton in the body is so rapid that the average during a briefer period, or even the instaneous peak, is more important.

2. Thirty-three per cent guarded against chronic toxicity. With these, the total amount absorbed during several days or even weeks determines whether injury results, and the time-weighted average concentration is an appropriate guide to safety.

3. Twenty-three per cent guarded against narcosis. The degree of narcosis in a subject varies with the concentration in the fluid bathing certain cells in the central nervous system, and this is quickly responsive to the concentration being inhaled. The time-weighted average concentration is useless to judge safety. The concentration being breathed should never exceed some particular value, regardless of the days's average.

4. Twenty-six per cent guarded against uncomfortable but not harmful irritation of the eye, nose, or throat. Clearly, for these, the instantaneous concentration is useful for guarding comfort; the daily average is not useful; and neither has much bearing on safety.

5. Six standards are for asphyxiants, but these threshold limits are standards of good practice, so far below a truly injurious concentrations that there is no need to debate which form of standard is the more sound.

6. Three standards guarded against fume fever. The total amount in the lung at any one time is the significant quantity. Lung clearance seems to proceed so quickly that the average concentration in an hour is more significant than that in a day, and a standard based on a maximum in the air seems a sounder index of safety.
7. Two standards guarded against eye pigmentation, more a cosmetic defect than an interference with vision. This condition develops slowly over a very long period, and the time-weighted average seems a sound control.
8. Two standards guarded against allergic sensitization. With these it is possible that no cencentration can be set to which some previously sensitized person will not react. Hence, the standards could well be a form of zero, the smallest amount which can be analytically estimated. The nature of the most sensitive practical analytical method should determine which form of standard is the better.
9. One standard guarded against cancer. We know so little about the causation of cancer by most substances that it may be prudent to limit the concentration to a form of zero, the smallest amount which can be analytically estimated. The nature of the most sensitive practical analytical method should determine which form of standard is better.

For fifty per cent of the substances listed in 1956, I found that the ASA Maximal Acceptable Concentraton concept of an instantaneous or peak concentration was the sounder protection against adverse effect, while the ACGIH Threshold Limit concept of a maximum time-weighted-average concentration over one working day was adequate protection in forty-six per cent of the standards. Since an excessive time-weighted average is impossible if a well-chosen maximum instantaneous concentration is never exceeded, I see no need for the concept of an average to protect health. However, I recognize that the requirements of many sampling and analytical methods make it more practical to determine conformance with an average over an appreciable period than to determine conformance with a maximum. Developments in analytical instrumentation are reducing the relative convenience of a standard for average concentrations, and in some instances make the average very cumbersome to determine.

In summary, when Z-37 and ACGIH standards for inhalation are numerically identical, conformance with the Z-37 standards results in absorption of less toxicant than does conformance with the ACGIH standard. For about half the substances listed the ACGIH concept is physiologically wrong. The Z-37 concept, while likewise physiologically wrong for half the substances in the ACGIH list, errs on the side of safety. Health would be more consistently protected if all standards were written in terms of maximum peak concentration during a working day, rather than in terms of the time-weighted average throughout the day.

"The amount by which these figures may be exceeded"

The ACGIH Committee contemplates that some operations will be conducted in concentrations above the threshold limit for brief periods, for they devote an entire sentence to suggesting the pertinent factors to be considered. Many industrial hygienists are qualified to interpret these pertinent factors for specific substances. Many others, including even lawyers, may blindly rely upon the threshold limits as averages of exposures to unlimited peak concentrations, and this reliance may result in harm to those exposed. How can the Threshold Limits Committee better guard against such misinterpretation?

It seems to be practically impossible to conduct some industrial operations without exposing workmen to concentations above the threshold limit. When the particular substance has a threshold limit which guards against acute toxicity, such as that for arsine, workmen may be seriously injured by relatively brief peak exposures. The operation should be fully automated, or if a workman must be present, adequate personal protection must be provided, maintained, and consistently used. When the substance has a threshold limit which guards against eye, nose, and throat irritation and is far below an injurious concentration, such as acetaldehyde, exposures well above the threshold limit can have no effect except to produce complaints from workmen, and some workmen will perceive no discomfort.

It ought to be possible to agree upon the penalty to health which may be exacted if a threshold limit is exceeded, even continually, and to indicate this in tabulations, as a guide to the solution of problems where operations under the limit are impractical. It is very difficult to find this information in the literature, partly because the bases for threshold limit values have not been explicitly stated by the ACGIH Committee until very recently.

"Without adverse effect"

The threshold limits values are stated to be guides to conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effects, and they are not fine lines between safe and dangerous conditions. Hence most industrial hygienists do not lose faith in the soundness of the values when they learn that every year a few are changed, usually downwards, as a result of industrial experience which comes to the attention of the Committee. However, serious uncertainty was evoked several years ago when it was rumored that values enforced in Russia are in some instances one-tenth or less of the ACGIH values. It was obvious that such a difference could be due only to a difference in concept of what the values should accomplish, because it is thoroughly demonstrated in American industry that guidance by the ACGIH values results in safe working conditions. Nevertheless, lack of information fostered doubts.

In this country the Russian values for concentrations of contaminants in the working environment first became generally known and debated following the XII International Congress on Occupational Health in Helsinki in 1957. The paper by Smeljansky[8] was particularly noteworthy, stating that the concentrations considered safe, and enforced in Russian industry, are lower than in the United States for a number of vapors. The basis for the values was stated to be experimental studies using the Pavlov conditioned reflex technique.

Elkins[9] has recently compared the values used in Russia and in the United States, grouping the substances by nature of action, chemical structure, or physical form. In some categories he finds agreement to be good, in others the Russian values are slightly lower than ours, in still others they are one-tenth or less of ours. He states that where agreement is least, the Russian values are said to be based on conditioned reflex studies with animals.

It is now possible to scrutinize the details of the bases for some of the Russian values, and to infer something of the philosophy under which they have been set, through the translations by B.S. Levine, made available by a Public Health Service Research Grant.[10-16]

The experimental methods which form the bases for the few values I shall discuss, are described in Book 3, pages 102-128, which is the third (1957) report of the U.S.S.R. Committee on the Determination of Limits of Allowable Concentations of Atmospheric Pollutants.[12] This Committee deals with atmospheres outside of work places, but the methods it describes seem to be the same as those relied upon for industrial exposures.

Apparently only six experimental methods are employed. Odor and mucous membrane (eyelid) irritation is a considerably refined method for an estimate of the aggressive characteristics of substances. Less accurate estimates of these characteristics have been much relied upon for setting ACGIH threshold limits.[7] The Russian method uses ten human subjects, analytically verified concentrations, and several days working time for each substance. The Russians are not satisfied with the subjective evaluation of the "objectionable" characteristics of a concentration, as is done in this country. The lowest concentration which can be distinguished from pure air by any one of the ten subjects is used for setting a standard.

The other five methods depend on the thesis that substances have an initial effect on the sympathetic nervous system, producing in the cerebral cortex reflex processes whose actions can be most sensitively detected by phenomena not part of the direct action of the substance.

The pneumographic method depends on the thesis that the body tends to defend itself against objectionable substances, even when they are not consciously perceived. Sympathetic reflexes mediated by the cerbral cortex respond to odor and nasal irritation by causing changes in respiratory rate, volume, and rhythm. By means of a rubber cuff over the thorax, the respiration of a few human subjects is followed during a few minutes inhalation of a concentration of a substance, then of pure air. The lowest concentration which produces a difference in respiration is the threshold of effect

to be considered in setting standards, whether or not the subject is conscious that the substance is being inhaled.

The plethysmographic method depends on the same thesis of a defense reflex. The reflex here is a change in blood vessel constriction, detected by changes in the volume of a finger.

The optical chronaxy method depends on the thesis that irritation of the olfactory centers, even when not consciously perceived, cause a sympathetic irritation in optic centers lying nearby in the cerebral cortex. The elapsed time is measured, in thousandths of a second, between electrical stimulation of human eyelid, and perception of an illusion of luminosity. Irritation from inhaled material reduces this time. Several days are required for training three human subjects, and for tests of chronaxy resulting from five-minute periods of inhalation of various concentrations, to determine the least effective concentration.

The adaptometric test depends on the same thesis of irritation of the optic center, sympathetic to irritation of the olfactory center. It measures the sensitivity to light of trained human subjects, when breathing vapors for fifteen-minute periods after an hour of adaptation of the eye to darkness. The eye is more sensitive when a vapor is being inhaled, whether or not the subject is aware of the inhalation.

The sixth test is the conditioned reflex determination in rats. It is the only one which is designed to produce chronic toxic effects. It seems to depend on the thesis that activation of any sympathetic reflex decreases the ability of the cerebral cortex to carry out conditioned reflex actions. It requires several weeks for training. Rats are trained to reach for food as a reflex response to a bell and to a colored light, but to avoid reaching when a buzzer sounds. By a complex scheduling of these events, one classifies the central nervous activity of the trained rats as to strong and weak, balanced and unbalanced, and uses some of each type in each experimental group. The trained rats are subjected to six months of daily inhalations of a substance. Every day their reflexes are tested, recording the time lapse between the signal and the learned response. At the end of six months one can judge which of the concentrations tested resulted in no change in reflexes, and which produced minimum changes. Some rats are sacrificed at once for tissue study, others are kept for thirty days to judge recovery of their reflex behavior, then tissues are studied. The entire study on one substance requires almost a year.

By relying upon the results of these six tests, the Russians indicate their belief that people should not be subjected to inhalation of a substance at a concentrations which results in any detectable physiological response. They may feel that if there is such a response, a lifetime of exposure may result in injury, impairment of function, disability. I have seen no evidence that experience in industry plays any part in setting their standards. Our feeling has been that people should not be subjected to inhalation which they find consciously objectionable, or which is likely to lead to disability or suffering. Since the concepts of what the standards are expected to guard against are so widely different, it should not be surprising that values for specific substances may be widely different. Experience under standards based upon our concept, during almost twenty years, gives us confidence that we are protecting health.

A review of some of the few available publications of Russian experimental work may be informative. In 1956 Novikov published the experimental work on benzene, upon which the Russian standard seems to be based (Reference 14, p. 185). He considers that the blood-cell changes we see from benzene may be secondary effects of sympathetic disturbances in that part of the central nervous system which regulates the hemopoietic system. He appears to believe that disturbances in the central nervous system which he detects by behavioral changes in conditioned rats, parallel the disturbances which affect the hemopoietic system, and that the only way to prevent blood-cell changes is to keep concentrations too low to affect behavior. At 20 ppm benzene he finds changes in conditioned reflex behavior, most marked in rats of weak, and of unbalanced strong, higher nervous activity. At 4 ppm he finds no effect. Those who have utilized his results seem to feel that there is no difference between human and rat sensitivity to this central nervous system effect, for Elkins[9] reports that the Russian MAC for benzene is 6 ppm. This is to be compared with the ACGIH figure of 25 ppm,[2] based on long industrial experience.[7]

In 1957 Borisova published experimental work on dichloroethane, upon which the Russian standard seems to be based (Reference 15, p. 1100). Using humans, he found that the threshold for increased sensitivity to light, respiratory changes, and constriction of capillaries was 1.5 ppm, below the odor threshold, while 1.0 ppm had none of these effects. Elkins[9] reports that the Russian MAC for dichloroethane is 2.5 ppm. This is to be compared with the ACGIH figure of 100 ppm,[2] based on animal experiment, human experience, and analogy with carbon tetrachloride, but not revised to allow for more recent views about the latter substance.[7]

In 1958 Melekhina published the experimental work on formaldehyde, upon which the Russian standard seems to be based (Reference 15, p. 135). Using humans, the time to perceive a sensation of light as a result of electrical stimulation of the eyelid, was reduced by 0.07 ppm formaldehyde, and not affected by 0.03 ppm, while the threshold of odor was 0.06 ppm. Elkins[9] reports that the Russian MAC for formaldehyde is 0.08 ppm. This is to be compared with the ACGIH figure of 5 ppm,[2] based on complaints of workmen in industry.[7]

Our exploration of conditioned reflex

About eighteen months ago, my group set out to explore the utility of the conditioned reflex technique, with much less knowledge of the Russian methods than we now have. A manuscript describing our first results is in press[17] and a research grant for further work in methodology has been authorized by the National Institutes of Health (OH-16).

There are American reports of one middle-aged woman[18] and two young adult males[19] who worked for several weeks in noticeably high, but unmeasured concentrations of mixed vapors containing the monomethyl ether of ethylene glycol (methyl cellosolve solvent). The three were incapacitied, with headache, drowsiness, forgetfulness, and disorientation, diagnosed as "toxic encephalopathy," and attributed to inhalation of methyl cellosolve. The workers returned to normal after a few weeks of rest in a hospital, without other therapy. A survey of one establishment using the same mixed solvent in the same way, found eight of nineteen workers with non-disabling symptoms suggesting the same injury.[20] Because of these observations, several attempts were made to produce such symptoms in animals.[21-23] The symptoms were not found, but no specialized behavioral techniques were used at that time.

This recorded experience suggested methyl cellosolve a useful substance for exploratory studies of the utility of the conditioned reflex technique. We asked ourselves if such symptoms in overexposed humans would have been predicted had behavioral studies been understood and applied before methyl cellosolve was first used industrially, and if the threshold limit would be lower than it now is.

With no knowledge of the Russian methods, we trained rats in a conditioned avoidance response. At the sound of a buzzer, they climbed a pole, because originally they had received an electric shock while standing on the floor when the buzzer sounded.

Inhalation of methyl cellosolve for four hours daily for several days reduced the number of rats which climbed the pole when they heard the buzzer, but up to a lethal concentration all rats were able to climb when given the electric shock. Inhalation of the vapors reduced the effect of conditioning, but left them able to climb to escape pain. The number of rats affected increased with the days of inhalation, but seemed to reach a maximum by fourteen days. The effect seemed minimal at 125 ppm, five times the ACGIH threshold limit.[2] Some rats, allowed to rest for fourteen days without inhalation, returned to the conditioned behavior without retraining.

Contrasted with the behavior of methyl cellosolve, ethyl alcohol produced no such behavioral change short of a concentration which caused frank depression and ataxia.

This exploratory work, by conditioned reflex methods possibly less sensitive than the Russian methods, does not show an effective concentration lower than the current ACGIH threshold limit, with a vapor to which has been attributed transient human disability arising in the central nervous system.

Summary

Experience in this country with threshold limits based upon toxicological experiment with animals has been good.

Despite the fact that the limits are used only as guides, and are not sharp lines separating safe from injurious atmospheres, more consideration should be given to the condition the numbers are meant to represent. In particular the time-weighted average concentration is physiologically wrong for about half of the limits, and can result in injurious exposures. If the threshold limits referred to a maximum concentration existing at any time during the working day, the substances for which this is physiologically wrong, would be controlled by a conservative standard.

Tables of threshold limits would be more useful if they indicated the injury which could result from a small excess, in order to guide the management of exposures where full conformance is impossible.

The philosophy of the Russian maximum allowable concentrations seems to be that workmen should not be exposed to any concentration which produces a detectable physiological response, with no consideration as to whether such a response is harmful.

An exploratory study of the conditioned reflex behavioral technique indicates that the method may detect effects which other toxicological methods do not suggest.

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Threshold limits and maximal acceptable concentrations: definition and interpretation, 1961*

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Periodically it is necessary to review and restate the principles that guide the American Conference of Governmental Industrial Hygienists' Committee in recommending Threshold Limits.[A] This is not only because of the relatively large number of newcomers entering the field of industrial hygiene, but chiefly because there has been a gradual change in the principles themselves, or a redirection of application, indicating a need for review and reinterpretation.

Two events of widely different character on the desirability of such a review were brought to the Committee's attention. The recent downward revision of the threshold limits of trichloro- and perchloroethylene have precipitated a volume of questions about this action that demonstrated to the Committee that many industrial hygienists are not cognizant of certain basic differences that now prevail in the Threshold Limits of the ACGIH (American Conference of Governmental Industrial Hygienists) and the Maximal Acceptable Concentrations of the ASA (American Standards Associations) Z-37 Committee. Equally cogent in this respect is the fact that the most recent Safety and Health Standards for Federal Supply Contracts[(1)] promulgated by the Department of Labor under provision of the Walsh-Healey Public Contracts Act include threshold limit values and make compliance with them mandatory.

This makes imperative correct understanding of the definition, precise interpretation, and application of these limits.

In 1955, a discussion of the standards then in use for safeguarding the health of the workers was published.[(2)] This discussion reviewed not only what was being done to develop threshold limits for concentrations of substances in the air of work places, but also indicated trends toward changes in philosophy of setting limits. At that time, definitions of the 2 standards, the threshold limits (TL values) of the ACGIH and the maximal acceptable concentrations (MAC) of the American Standards Association Z-37 Committee, however, were identical. Since that time the maximal acceptable concentration, but not the threshold limit, has been redefined.

The maximal acceptable concentration of the American Standards Association was redefined in 1957 by the Z-37 Committee to represent a limiting concentration, or ceiling, below which all values should fluctuate. This was stated in the preface accompanying each standard. Unfortunately, since this change in definition, few standards have been published by the ASA.[B]

The threshold limit of the ACGIH, as defined in the preface to the list, is the average of the time-weighted concentrations throughout the 8-hour daily operations. This is based on the sound toxicologic principle that toxic response follows the absorption of a dose. An inhalation dose is the product of concentration and the time the concentration was experienced. Thus in contrast to the maximal acceptable concentration, the values averaged in the threshold limit may fluctuate a reasonable amount above the recommended limit, providing an equivalent fluctuation below the limit occurs. Because it is an average with permissible excursions, it does not easily lend itself to rigid statutory application and requires considerable judgment in application. What constitutes a "reasonable" excursion depends on the substance's physiologic effect at increasing concentrations beyond the limit. For substances whose threshold limit is based wholly on chronic effects,[C] the

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[A] Published in the October 1961, issue of the *Archives of Environmental Health*.

[B] The definition of maximal acceptable concentration may be found in publications of the American Standards Assocation, A-37.4, Z-37.10, and Z-37.12, 1960.

[C] See section "Justifications of the threshold limits."

average concentration during the entire 8-hour period can often be employed, with only reasonable regard for the momentary concentration in excess of the limit. On the other hand, for substances whose acute effects determine the threshold limit, the latter should not be exceeded for other than relatively brief periods. For many irritant substances, the average concentration during a 5- or 10-minute period should not exceed the threshold limit. With typical narcotic vapors, somewhat longer periods in excess of the limit might be acceptable. For substances that do not cause acute intoxication or discomfort, as indicated above, concentrations of about 8 times the limit may be permitted for an hour provided the exposure for the remainder of the day is nil.

Relative significance of TL versus maximal acceptable concentration values

Compliance with the newly defined maximal acceptable concentration automatically results in a lower average concentration than was permissible under the old definition. This seems to have escaped the attention of most industrial hygienists. Thus, for example, the maximal acceptable concentration of 200 ppm for trichloro- and perchloroethylene, with all values fluctuating below this concentration, is in practice about the same as the TL of 100 ppm which permits reasonable fluctuation above the limit for short periods. In other instances in which the TL is the same value as the maximal acceptable concentration for a substance, the maximal acceptable concentration obviously provides the greater safety factor.

Skin notation

The 1961 list contains for the first time the notation "Skin" after the name of certain substances. This notation is to be interpreted simply as an indicator that skin absorption may contribute to the over-all intake from exposure in addition to that from inhalation. It refers mainly to absorption by liquid contamination. It is left to the industrial hygienist to determine in each particular case the degree of skin absorption that enters into the total body absorption of the toxic agent. If the industrial hygienist believes skin absorption represents a significant intake, protective clothing should be resorted to. Only if skin absorption cannot be made negligible should commensurate reduction in the threshold limit be considered.

Justifications of the threshold limits

Because of the increasing significance that is being attached to hygienic standards for the air of work places by the U.S. Department of Labor through application of the Walsh-Healey Act, and the more definitive studies that are being made today in the laboratory and in the field on new substances, documented justifications for the selection of the threshold limit values are being brought up to date and should be forthcoming in published form shortly.

Such documentations are not new. In 1945 Cook[3] provided excellent statements for the time on all of the 141 substances listed that have since provided a foundation for subsequent documentation of many of them. Later, Smyth[4] provided documentation for a greatly expanded list of substances (about 240). Smith made several constructive criticisms of the Hygienic Standards as they then (1955) existed. Notable among these criticisms was the suggestion that the Threshold Limits be made more informative to describe the type of response expected. Smyth suggested also the addition of another concentration "to permit ready evaluation of how strictly the limit should be observed." Smyth, himself,[4] supplied tabular material for each of the substances listed illustrating the type of condensed information that should accompany each list. The Threshold Limits Committee, however, felt that because of its necessary brevity, Smyth's tabular form fell short of accomplishing the purpose on many, if not most, substances. Moreover, it was the Committee's opinion that in a list of this sort there is great value in simplicity — a substance, a number; memory for the important item is obscured by detail.

The other major criticism of the standards by Smyth and others, that each value should be documented as far as possible with literature references, has now been met. As indicated above, the Committee has prepared, and is now about to publish, justifications for each of the recommended limits. Many of these justifications are satisfactorily complete; others are sketchy because of the lack of published information. A number are based in part on personal experience of the Committee members or on written communications to the Committee members by other

industrial hygienists. Some are based on the former justifications of Cook[3] and Smyth.[4] The published justifications of the Threshold Limits Committee will be revised from time to time as new information appears.

For this reason the Committee welcomes such information on suggested new substances for consideration for addition to the list, as well as information reflecting on the basis for the recommended limit. It is obvious that the Committee prefers to act only on well-documented information for either additions to or changes in the list, but less well-documented recommendations from a number of reliable sources will be given consideration.

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The significance and application of threshold limit data*

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I was asked to talk to you today about the significance and application of industrial hygiene standards such as threshold limit values and maximal allowable, acceptable or permissilbe concentrations, commonly referred to as MAC values.

Since accepting this assignment, I had the privilege of spending a month as a member of a team of six that visited the Soviet Union under the auspices of the U.S. Public Health Service. Our purpose was to study Soviet methods used in industrial toxicology and to learn how they applied the results in their industrial work. I think that this experience will enable me to give you a better discussion of some of the problems associated with the interpretation of threshold limit and MAC values as we see them and as they are viewed by the Soviet scientists.

In the first place, what are these figures commonly referred to as threshold limit values and MAC values? In general, I interpret these values as guides to be used in controlling the degree of exposure to certain airborne contaminants in the environment of workmen exposed seven to eight hours per day, five days per week for an indefinite period of time. They definitely do not represent a fine line between safe and hazardous concentrations.

Even though some persons consider threshold limit values and MAC values to be the same, I do not. This is a difference in philosophy which I believe to be fundamental.

The threshold limit values as published by the American Conference of Governmental Industrial Hygienists, in essence, refer to values obtained by time-weighting the exposure over a seven- to eight-hour day. Maximum acceptable, allowable, or permissible values are in my thinking, just what the name implies — maximum values below which normal fluctuation should occur.

Excursions above the maximum should be limited. The degree to which such excursions are permissible is contingent upon the normal baseline of average exposure intensity and upon the consequences of exceeding the maximum.

It is noteworthy that the ACGIH Threshold Limit Committee is now cautioning in their directions for using the threshold limit values, that care must be taken to avoid exceeding certain of the values because of the possibility of acute effects. This approach is to be commended and it is my hope that the trend will continue, even to the extent that the ACGIH tabulation or some other tabulation eventually will include not only levels acceptable on a time-weighted basis but also will include maximal values and other information pertinent to the intelligent use of such figures.

Back in the late '40s and early '50s the laboratory with which I am associated did a great deal of toxicological work on several of the common chlorinated solvents. This work convinced us that the toxicological properties of these materials were vastly different and that we could not express in a single figure the essential information we felt the industrial hygienist needed to properly assess the hazards of a given situation.

In an attempt to improve communication, we proposed a two-value hygienic standard consisting of a maximum figure and a time-weighted average figure. The maximum was defined as the concentration below which there was little likelihood of any significant acute or chronic effect. The maximum figure was fairly easy to determine from the results of animal experiments and observations on human subjects but the time-weighted average figure was more difficult because in reality, it was an expression of opinion as to how much below the maximum the average should be.

This opinion must be based on several factors. First, such an average concentration should be

* Presented at National Safety Congress, 1963. Published in *Nat. Safety Cong. 12*:33-36 (1963). Reprinted by permission of the National Safety Council.

one which in all probability will not cause significant adverse effects even though exposure be for a prolonged period of time. Secondly, it should include some appropriate margin of safety and this should be based on the consequences of overexposure. A material which causes injury to the central nervous system, the eyes, bone marrow, gonads, or other vital organs should be accorded a wider margin than one which causes slight inebriation or reversible functional changes in the central nervous system or other organs.

It should be noted that there are a number of values in the table of threshold limit values which are based, not upon toxicity, but upon objectionable odor or simple reversible eye or upper respiratory irritation. To me, a value based upon such consequences of overexposure must be used in a manner quite different than one which is based on frank toxic injury. I have no objection to establishing permissible levels in the workroom on the basis of objectionable odor or irritation, but I do believe that when such is done, it should be so designated.

I feel, from practical experience, that there are times when a little unpleasantness can be tolerated, and even permitted, if it is known that no hazard to health is involved in such exposure. True hazard to health cannot be compromised or negotiated, whereas discomfort is, in my opinion, a negotiable item.

Furthermore, it should be remembered that hygienic standards are being used by design engineeers and safety engineers in designing plants. The degree to which the engineer must make certain that normal operation can be carried on within generally recognized hygienic standards will depend upon the severity of the consequences of overexposure. Over designing is expensive and unnecessary.

It is for these reasons that I am basically opposed to a one-value system of hygienic standards. I believe that whenever possible, values should be given indicating: 1) concentrations dangerous to life when exposures are for short periods (perhaps up to 30 minutes); 2) values (MAC values) which cannot be exceeded for more than short periods without causing an adverse effect; and 3) time-weighted average (TLV) values which should not be exceeded for seven to eight-hour day.

In addition, the tabulation should give the approximate odor threshold, the consequences of overexposure from both acute and chronic exposure, not in detail, but in simple language so that the practicing industrial hygienist or industrial physician will know what to expect.

I know this is a departure from our present day concept of such control standards, but we need this information badly now, and we will need it more in the future. I do not go along with those who say that we must keep these tables of industrial hygiene standards one-value tables for the sake of simplicity.

I say the one-value tables are far too complicated. The ordinary person doing safety work looks at such figures as law. He cannot be expected to know the basis upon which they were derived. Therefore he cannot be expected to make judgments, nor should he.

Even some of us who are practicing industrial toxicology and hygiene every day cannot keep up on all the values or the reasons for them. They need so much interpretation that opinions formed one week may be changed next week when new information becomes available. This is the avowed responsibility of the industrial toxicologist and industrial hygienist.

There are those who say that the data to make multiple entry tables are not available and hence there would be a preponderance of empty spaces. That simply means that there is more work to be done. It is no reason why the information available should not be given. Furthermore, I see no reason for not making educated guesses, calling them just that, and then revise the tables each year, adding, changing, deleting as new information becomes available — as the American Conference of Governmental Industrial Hygienists is now doing with their tabulation of threshold limit values.

It must be recognized in industrial hygiene work, however, that a limit or standard is not a sacred value, but is a guide to good operating conditions. Every practicing industrial hygienists knows that the concentration of atmospheric contaminants fluctuates as a process cycles, as leaks develop, as misoperation occurs, thus giving rise to "peak" concentration. If these "peaks" go above the accepted maximum, it is important to know how high they go and how frequently they can be expected to occur.

Once this information is available, it is the job of the toxicologist and/or the hygienist to evaluate the significance to the overall conditions and act accordingly. This is by no means a simple assignment. It is quite possible for a single "peak" exposure to occur during a shift and last for but a few minutes and yet provide a total intensity of exposure in excess of what can be tolerated for the entire shift. If this sort of situation occurs very infrequently, it may not be too serious, but if it happens regularly, then it may present a condition which needs correcting.

If "peaks" are superimposed upon an exposure level which is already crowding the safe level, then they become very significant and may be expected to have an adverse effect. If they are superimposed upon a base level which is well below the accepted limit, then they may have little significance.

It is not uncommon among industrial hygienists to average or to time-weight the values they obtain in a plant survey and to draw conclusions as to the safety of such conditions from the resultant figure. This is not a valid procedure.

Time-weighting assumes that concentration-time (CT) values are constant and this is true only if the slope of the response curve is one; it assumes that CT = K for all ranges of concentration and this is not true because of variations and/or differences in factors such as rates of absorption and elimination and the nature of effects produced.

It also does not take into consideration the chronological order in which these peaks may occur. The response from two or three peaks occurring within a short time can be expected to be much more serious than if these peaks occur at widely separated intervals.

I think it is most important to emphasize the importance of sampling procedures. Spot sampling is a poor way to assess total exposure; it is too easy to miss "peak" exposures, and in the hands of the untrained investigator, it may be too easy to sample only obvious "peak" exposures. Samples taken over a long period of time may be adequate for estimating total exposure, but they only give the average concentration over the sampling period and this may be inadequate. Only when one employs continuous sampling procedures which record the concentration at successive short intervals of time over a prolonged period of time, can one get a true picture of the actual exposure.

Now perhaps I should say a few words about what we saw in the Soviet Union. As many of you know, the maximum allowable concentrations in the U.S.S.R. are almost all considerably below ours and lower than those employed by most other countries.

The reason is that they attach a great deal of significance to *any* change, whether functional, biochemical, or pathological that can be detected in exposed animals or human beings. By this I mean that if they can detect any change they consider this to be detrimental effect even if the change is readily reversible or if acclimation readily occurs.

We saw electroencephalograms taken from animals which showed changes for a few days after the start of a repeated exposure and then the charts were entirely normal even though exposure continued. Even such changes were considered adverse and the limits promulgated were below those causing such effects. I have considerable difficulty justifying such low levels on the basis of such observations.

In another instance, we saw curves representing the effect upon certain conditioned reflexes which indicated quite conclusively that prolonged daily exposure caused a progressive change which could only be considered adverse. This was at a stated concentration below that considered to be without effect in the U.S.A. If this change was actually caused by the stated concentration, then they are right and we are wrong. The only question in my mind in this case is whether their analytical method is reliable and this I have no way of knowing.

There is no doubt that the criteria they are using to measure neurological change are more sensitive than those which have been routinely employed in this country in industrial toxicology. On the other hand, I saw very little analytical equipment which was comparable to ours. They are doing little, if any, continuous analysis of their industrial environments or of their experimental environments or of their experimental inhalation chambers. They are using spot sampling but even here, I was not impressed by the reliability of their sampling or methods of analysis.

I also have the impression that in many instances where they believe they have observed adverse effects in human beings as a result of exposure at levels similar to our standards, they really don't know what the exposure has been — because of inadequate sampling and analytical procedures.

Insofar as industrial hygiene practice in industry is concerned, I can only say that those plants which we were permitted to see were clean insofar as environmental exposure is concerned. They have used various methods of achieving these goals. We saw plants in which every pump was ventilated — and ventilated well. They have employed methods of fabricating which avoid use of solvents, or other materials which might create a toxic hazard. How widely the excellent practices which I saw are actually in use can be surmised.

In spite of their avowed objective of preventing all exposure to hazardous chemicals, they seem to pay little attention to safety. The steps in their factories are broken, there are low overhead pipes and beams, there is unguarded fast moving equipment, there are few barriers at ditches, and rarely did I see safety glasses or eye protection. This apparent lack of attention to such mechanical hazards is indeed hard to rationalize.

In closing I should like to return to my object — the significance and application of industrial hygiene standards.

The values, regardless of what they are called, are not fine demarcations between safe and unsafe exposures, they cannot be used to compare the toxicity of one material with another, they are not toxicity ratings nor are they hazard ratings, and they should not be made a part of laws where interpretation is not possible.

They are figures which represent an over simplification of an attempt to interpret a very complex collection of information. To use them properly, one must know not only the facts upon which they are based, but also the details of the conditions under which they are to be used. The knowledge which enables one to do this, comes only from years of training and experience in the field of industrial hygiene.

Industrial toxicology in the soviet union — theoretical and applied*

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United States Industrial Toxicology Delegation to the U.S.S.R.

Theoretical, laboratory, and field aspects of industrial toxicology in the Soviet Union were observed by the authors during a one-month visit to the U.S.S.R. under the U.S.-U.S.S.R. exchange agreement. The apparent discrepancies between U.S. and U.S.S.R. maximum allowable concentrations derive not only from theoretical differences but differences in industrial hygiene practices as well.

The authors of this report constituted the United States Industrial Toxicology Delegation which visited the Soviet Union from September 16 through October 11, 1963, under the provisions of the U.S.-U.S.S.R. Exchange Agreement for 1962-63. The visit was proposed by the United States in order to clarify reasons for the apparent disparity between Soviet and American threshold limit values for some industrial exposures. Because of the many variables that enter into the setting and application of such values, resolution of the questions that have been raised could not rest with comparisons of the relevant scientific literature. The delegation sought to examine the techniques of Soviet toxicologic testing, their methods of establishing threshold limit values, and insofar as possible, to observe the compliance with these values.

Twenty-eight research institutes, sanitary stations, and industries in five different cities were visited. The delegations suggested a number of the institutes it would like to visit but the final itinerary (Figure 1) resulted from negotiations with the Ministry of Health after we arrived in Moscow. We recognize that we saw a highly selected sample of institutions and had but a brief glimpse of a small portion of a vast country. While it would be misleading to extrapolate from our limited observations to a statement of universal Soviet practices, our experiences do provide a better informed opinion of Soviet toxicology in theory and in practice.

The monolithic structure of the Soviet Union permits a degree of formal planning difficult to achieve under our economy and system of government. The Soviet Ministry of Health is responsible for all facets in the setting and enforcement of threshold limit values ranging from the toxicologic investigations in the laboratory to the supervision of exposures within industry. In the discussions that follow, the reader should not equate the activities of the Soviet government with that of our governments but should compare their governmental contributions with the total of activities carried on by our governments (federal, state, and local), industries, labor groups, insurance carriers, research institutes, universities, professional and trade associations. Such comparisons are not made easily but are needed to emphasize that American toxicologic knowledge and practice are the resultants of diverse resources and viewpoints.

The leader of occupational medicine in the Soviet Union and the Chairman of the Committee setting Soviet maximal allowable concentrations for industrial exposures is Professor A.A. Letavet. The Institute of Industrial Hygiene and Occupational Diseases in Moscow, which Professor Letavet heads, is the principal institute which, in addition to carrying on its own research program, coordinates the work of the thirteen other occupational health institutes within the Soviet Union. Much of this coordination is achieved through conferences on specific subjects arranged either by the Moscow or the satellite institutes. Annual reports are reviewed in Moscow. All of these institutes report to the Ministry of Health. Several of the institutes specialize in problems of particular industries. Thus, the Institute at Kiev, under Professor L.I. Medved, concentrates on agricultural hygiene and

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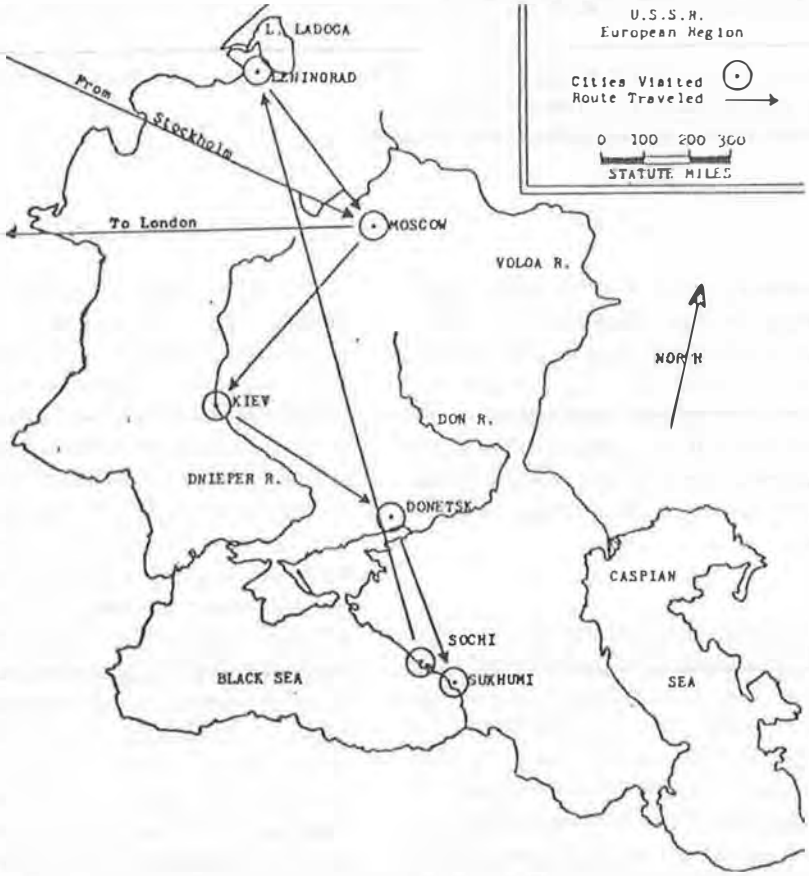

Figure 1 — Itinerary of U.S. Industrial Toxicology Delegation's tour in U.S.S.R.

the toxicology of pesticides. The Institute at Gorki has responsibility for chemical problems; the Krivorog institute for silicosis; and the Sverdlosk institute for metal problems. Letavet's Institute assumes the primary responsibility in metallurgy, the chemical, and machine building industries, and also for light industries.

Professor Letavet, in his discussions with the delegation, tended to deemphasize the differences between the Soviet and American MAC values. He noted that in neither case were the values precise and that it was quite unreasonable to expect identical values with experts operating on opposite sides of the ocean. Noting that the principal differences were in the aromatic hydrocarbons and the chlorinated hydrocarbons, Professor Letavet attributed these to methods of testing, with toxicologists in the Soviet Union placing greater emphasis on the results of changes in the conditioned reflex. He also felt that Soviet scientists made greater use of chronic experiments and of detailed clinical studies than the American scientists. The delegation does not agree with this latter evaluation. Professor Letavet emphasized that data from all sources —laboratory, clinic, and epidemiologic — were considered in establishing Soviet limits.

Philosophical basis of soviet air quality standards

The basic tenets are as follows:

1. The maximal allowable concentration is defined as the concentration of gases, vapors, or other substances encountered in the working environments such that daily working in these environments will not result in any deviation in the normal state of the organism as well as not result in disease.
2. The setting of such concentrations should be based entirely on presence or absence

of biologic effects without regard to whether it is feasible to reach these concentrations in practice.

3. The values set should represent maximum concentrations rather than time-weighted average values.
4. Regardless of the value set, the optimum value and goal to be sought is zero concentration.

The implications of these tenets are not to be passed over lightly. For example, what is meant by "any deviation from normal?" Is physiologic response to any type of stress to be equated with injury produced in response to stress? In our discussions with many scientists, it became clear that any change in response to stimulus was considered a "deviation from normal." This philosophy of zero concentration was reaffirmed by Professor Ryazanov, who occupies the Chair of Community Hygiene at the Central Institute of Advanced Training for Doctors, at Moscow. Professor Ryazanov is Chairman of the Soviet Committee for the Development of Community Air Pollution Standards. The concept implies that any concentration, however small, places an undesirable toxic or nuisance stress on the population. It resembles the approach of the National Committee on Radiation Protection of the United States which admits of no threshold for effects from ionizing radiation. American standards for chemical exposures, be they set by the Threshold Limits Committee of the American Conference of Governmental Industrial Hygienists, the American Standards Association, or some of the state governments are based on the premise that although all chemical substances are toxic at some concentration experienced for a period of time, a concentration exists for all substances from which no injurious effect will result, no matter how long the exposure. A similar premise is applied to substances whose effects are limited to irritation, discomfort, and nuisance.

Although Soviet air standards by definition are maximal values, discussion with scientists coupled with observations in the field confirmed the belief that these are not in fact rigid ceiling values and that excursions above these values "within reasonable limits" are permitted. We, therefore, suggested to Professor Letavet that perhaps the Soviet maximal allowable concentrations could be described as their aspirations based upon medical grounds rather than values which could not be exceeded. This Professor Letavet denied. We then suggested that some of their MAC values seemed to be of more importance than others and we inquired whether there was some sort of priority in attempts to attain these values. We learned that there are such priorities which are set by the Ministry of Health based on the results of periodic examination of workers and on the cases of reported occupational disease occuring among them.

Steps employed in setting of standards

Regulations require the following steps before any new chemical is put into use in the U.S.S.R. First, the chemical and physical characteristics must be defined, which includes the description of vapor pressure, solubility, flammability, methods of detection, etc. Second, the acute toxicity for experimental animals is determined. For substances which present an inhalation hazard, the toxicity is usually determined by static exposures usually lasting for two hours when mice are used, or for four hours when rats are used. Oral and percutaneous administration may be employed. The animals are observed for three weeks post exposure. The experiments are used not only to define the lethal concentration but also to determine the clinical picture of the poisoning.

Acute exposures are also used for the study of changes in the conditioned reflexes as well as changes in the direct reflexes. The reason for this is particularly interesting. The delegation was told that many of the animals would show changes in the conditioned reflex on acute exposures but when exposures were repeated, as in subacute or chronic experiments, these changes disappear. Because of this, the Soviet scientists do not consider subacute and chronic exposures suitable for their studies and changes in the conditioned reflex and tend to limit such studies to acute exposures.

The third step is the study of the effects resulting from subacute exposures. These involve, in the case of inhalation experiments, exposures lasting four hours per day, six days per week for one to two months. The fourth step is the determination of the results of chronic exposures which are defined as exposures carried on for five to six months, four hours per day, six days per week. Following the

chronic exposures, the animals are observed for one month, sacrificed, and the tissues examined for gross and microscopic pathologic changes. Five or six organs, usually the brain, heart, liver, spleen, kidney or lung are examined, but they are not weighed routinely. In certain instances, biochemical tests may be performed such as urinary hippuric acid for liver function, serum electrophoresis for measurement of protein abnormality, or specific enzyme studies, e.g., cholinesterase, when such effects have been identified as in the case of organic phosphate pesticides. We were told that such testing was not confined to mice and rats, but that all appropriate species were employed. We saw experiments on rabbits and on cats, and although we saw a variety of pharmacologic experiments being conducted on dogs and monkeys, we did not see any actual exposure work being conducted on the latter two species.

Accumulation is the next parameter considered. This was emphasized particularly by Professor Medved, Director of the Research Institute for Labor Hygiene and Occupational Medicine at Kiev. His institute has principal responsibility for the study of pesticides. Professor Medved stated that accumulation was measured by giving 1/10 of the LD_{50} each day to the point at which 50% mortality is obtained. If the dose producing 50% mortality by this method equals the dose producing 50% mortality on acute exposure, the coefficient of accumulation is defined as one. For example, the acute oral LD_{50} of DDT was found to be 300 mg/kg. The LD_{50} when 30 mg/kg was given daily was 180 mg/kg. Thus, the coefficient of accumulation for DDT is 180/300 = 0.6. Such a procedure would seem to have considerable merit.

Prior to setting MACs, certain ratios are calculated which are not employed in the United States. First is the zone of acute action which is defined as:

Zone Acute Action = LC_{50}/Limiting Concentration Acute Dose

The limiting concentration of the acute dose is defined as that dose which will just produce an effect measurable by any means, e.g., by conditioned reflexes, by biochemical changes, or by any other method. In a number of the laboratories visited, great emphasis was placed upon the development of more sensitive indicators of the slightest change.

The Zone of Chronic Action somewhat resembles the Zone of Acute Action in that the limiting concentration acute is divided by a limiting concentration chronic. The latter will usually be determined by an effect other than a change in the conditioned reflex since, as we noted above, conditioned reflex testing generally is not done in these chronic exposures.

While we gained the impression that a rigid formula is not adhered to in setting MACs, the following represents the theoretical basis:

$$MAC = LIM_{CH}/K$$

where: K = a safety factor

derived as follows:

$$K = a \frac{\frac{LIM_{AC}}{LIM_{CH}} \times \frac{C_{20^\circ}}{LC_{50}}}{\frac{LC_{50}}{LIM_{AC}}}$$

$$= a \frac{(LIM_{AC})^2 \times C_{20^\circ}}{(LC_{50})^2 \times LIM_{CH}}$$

where:

LIM_{AC} = lowest single dose giving an effect

LIM_{CH} = lowest repeated dose giving an effect

C_{20° = vapor concentration at 20°C

(LC_{50}) = 2 hr LC_{50}

a = 1 for vapors ? for non-volatile materials

LIM_{AC}/LIM_{CH} = zone of chronic action

$C_{20^\circ}/(LC_{50})$ = coefficient of possible inhalation exposure

$(LC_{50})/LIM_{AC}$ = zone of acute action

As an example, for gasoline prepared from shale oil, they found the zone chronic action to be 6, zone of acute action to be 3 and a to be 5. This reduces to a safety factor of 10. In this instance, the MAC was then defined as the limit of the chronic dose divided by the safety factor 10. We were told that if *K* was less than or equal to 1, a value of 1 is used.

We believe that this safety factor is of significance in explaining some of the differences between U.S. and Soviet MAC values, particularly as they relate

to the aromatic hydrocarbons and to the chlorinated hydrocarbons, most of which have a fairly high volatility. The use of vapor pressure in the calculation of MACs is completely foreign to us and, we believe, not appropriate. We conceive of an MAC as a measure of atmospheric concentration. Whether that concentration results from a chemical of low volatility or of high volatility should make no difference in the MAC. The volatility of the chemical will make a difference, of course, in the hazards presented and in the types of control that must be maintained in order to meet the maximum allowable concentration; it should be considered as a factor in the selection of solvents; but we believe it has no relation to the maximal allowable concentration itself.

These laboratory studies serve as the basis for tentative estimates of maximal allowable concentrations and help determine whether preliminary field tests may be made. Professor Medved emphasized the field tests which are employed in the study of pesticides. Following the laboratory studies, carefully controlled working tests were made at collective farms where the inhalation zone concentrations were carefully measured and where the health of the exposed workers was carefully followed. In the case of pesticides, such studies were supplemented by determination of the effects on foods and on community hygiene. These involve the participation of food specialists and community hygiene specialists who are responsible for control of chemicals in soil, water and air pollution. The evaluation of pesticide exposures seemed to be the only area in which great attention was paid to time-weighted average exposures and their correlation with individual health effects.

Based on all available data, recommendations for MAC values are made by a central committee consisting of 35 members. Professor Letavet serves as Chairman of this committee with the membership drawn from the various institutes throughout the Soviet Union. Normally, this committee meets three to four times each year. From our discussions with Professors Letavet and Medved, we believe that there is no single formula or equation that is used to relate all of these experimental values to the maximal allowable concentration. An attempt is made to use each of the parameters we have described as measures of the absolute toxicity of the chemical as well as a measure of the range between the quantity causing the first detectable effects and effects which are truly toxic. In any case, this central committee makes its recommendations to the Soviet Ministry of Health. If the recommendations are accepted by the Ministry, the proposed MAC values have the effect of law.

Somewhat different procedures are followed in the case of carcinogenic substances. The principal work in this area is conducted at the Institute of Experimental Oncology under the direction of Professor Shabad. For routine testing of new chemicals, skin painting, subcutaneous injection, and peroral administration are used. If the chemical is to be used in the food industry, such as food dyes, *per os* testing is conducted first. If the exposures are primarily industrial, skin painting is the first technique employed. The subcutaneous route is of value where very minute quantities of chemical are available, but Professor Shabad felt that the obtaining of positive results by subcutaneous injection was doubtful significance in view of the work of Oppenheimer.[1] Studies are made on mice and rats, with exposures being continued for an 8-month period, which, Professor Shabad feels, is roughly equivalent to the average latent period observed for occupational cancers in man, when the relative life span is considered. Where experimental and epidemiologic studies have demonstrated a carcinogenic hazard, the results are considered by a special committee for carcinogenic substances appointed by the Ministry of Health. This committee recommends to the Ministry whether or not a drug or product should be prohibited from manufacture or use, and the Ministry issues the order.

Plans provide that no chemical be introduced into Soviet industry unless it has been toxicologically tested. This applies to amounts of chemical in excess of 1 to 2 kilograms handled by more than one or two people. Preliminary testing is done in a rapid "screening" test conducted at a sanitation laboratory. The exact nature of this screening was not determined. The full range of toxicologic testing described above is undertaken after it has been determined that the product is commercially useful.

Techniques of toxicological testing

The exposure chambers most frequently observed were miniature models of the so-called

Rochester (New York) design having a capacity of 100 liters. Such chambers were designed to provide data on acute toxicity. Their relatively small capacity, 6 to 10 rats or guinea pigs, 20 to 40 mice, or 1 to 2 rabbits, limits their usefulness for long-term studies in which large numbers of animals are required for the results to have statistical validity. In only two instances did the delegation see larger chambers. One was a head exposure chamber for 40 rats or guinea pigs, the other a full body exposure chamber with a slightly larger capacity. We saw no chambers of the size commonly employed in the United States.

In the operation of the 100 liter chambers, static rather than dynamic exposures appeared to be the rule when acute toxicity was being studied. Since these chambers were designed for dynamic exposures, a number of technical problems arise with static exposures. The temperature cannot be controlled adequately. Because of the relationship between toxicity and temperature, this is a potential source of error. Toxic products eliminated by the exposed animals are not removed and thus contaminate the environment under test. In addition, static exposures require some method of dispersing the exposure material throughout the chamber. This was done by a large rotating fan. Such rapid air movement in the small chamber interferes with isokinetic sampling within the chamber and, more importantly, tends to impinge the particulate aerosols on surfaces rather than maintaining an even suspension throughout the chamber air.

The methods for dispersing high-boiling or high-melting substances appeared to be unsatisfactory. Off-color or carbonized residues were observed, which leads to the conclusion that the substances were overheated. This would result in the formation of various decomposition products of organic compounds which are notorious lung irritants, thus adding to the apparent toxicity of the substance under test. Such decomposition products complicate the analysis of chamber atmospheres with resultant errors in measuring the dose-response relationships.

The small size of the exposure chambers and the emphasis on changes in conditioned reflexes as indicators of toxic response tend to limit the number of animals employed by the Soviet scientists in the measurement of dose-response effects. The former can be overcome by better engineering design of the exposure chambers. The latter is a more complex problem.

In most of the institutes and laboratories visited by the delegation, great emphasis was placed upon the measurement of nervous system response both to toxic agents and to therapeutic agents under study. Eight and 12 channel recorders for the analysis of brain potentials were seen in laboratories whose other equipment would be considered most modest. Electrodes were implanted by stereotactic methods in a variety of mammals ranging from rodents to primates. Conventional methods of recording electroencephalograms were employed in humans in the study of the effects of common community air pollutants as well as in the investingation of occupational diseases. This emphasis on nervous system response, which testifies to Pavlov's influence on Soviet medical science, is greater than is current in most medical laboratories in the United States and deserves careful examination. Whether the results obtained contribute significantly to the establishment of MAC values is not easily determined. The careful mapping of the precise sites of action of drugs acting on the central nervous system and the feedback of that information to programs synthesizing new drugs is an activity which should have long-range scientific benefit.

As an example of the use of encephalographic changes in humans exposed to common air pollutants, Dr. Goldberg, Chairman of the Division of Air Hygiene, the Institute of Community Hygiene in Moscow, discussed his work on carbon dioxide. Changes in the electroencephalogram were demonstrated in humans stimulated by flicker light and exposed to CO_2 at concentrations of less than one percent.

Conditioned reflex responses are the prime tools of investigators in the toxicology and pharmacology laboratories. Animals under study range from fish to primates. As was noted above, the use of conditioned reflexes in the toxicology laboratories is confined to animals acutely exposed to toxic agents. Because of the time invested in conditioning animals, they are frequently used for years in tests of a variety of agents. Considerable ingenuity was shown in devising equipment for the classical conditioned reflexes of food, defense, and orientation, but in only one instance did we

see automated equipment. The usual procedure was to have a technician manually operate the stimulus and manually record the times of response and their nature. The net effect is to have conclusions based upon the responses of few animals. At no point did we see evidence of a statistical approach to such observations in spite of the Soviet emphasis on the differences between so-called "strong" and "weak" mental types of animals. Because of the emphasis on the minimal response to toxic change, we were left with the uncomfortable feeling that these responses were sometimes based on the results in one cat, or at best, a few cats.

Other nervous system measures observed included measurement in humans of the dark adaptation of the eye, visual acuity, and the speed of classification of objects and words. In animals, the learning rate of rodents is tested in mazes, measurement of chronaxie of flexor and extensor groups, and the threshold of perception of electrical stimuli were frequently employed.

Professor P.P. Dvezhkov, pathologist at the Moscow Institute of Industrial Hygiene and Occupational Disease, stated that whenever changes were demonstrable in the conditioned reflexes, histological changes could be demonstrated in the neurons of the frontal cortex. These are best described as a conglomeration of the small dendritic processes along the neurons, shown by Golgi stains. Similar changes may be detected in the dorsal roots of the spinal cord by Cajal stain.

Little was seen to indicate that much effort was being directed to find early sensitive indicators of response other than the changes in higher nervous activity. Biochemical work appeared to be confined to vitamin assays, and to one or two well-known enzymes. We saw no effort toward exploring new enzyme activities or the detection of unusual or special metabolites as indicators of early change. As a corollary to this, we saw no work relative to mechanisms of action or detoxication. Such work may be going on elsewhere but we have no knowledge of it.

In two separate laboratories, we saw attempts being made to study changes in immunologic processes in response to toxic exposures. One involved the measurement of the capacity of the animal host to develop antibodies against enteric organisms following exposure to an industrial chemical. The other was a study of the changes in plasma cells, one of the sources of antibodies, in response to toxic exposure.

Skin absorption and skin irritation measurements appear to receive far less emphasis than is given to similar studies in the United States. Skin irritation is measured by patch tests on rats and rabbits, absorption is measured by dipping the tails of mice in the chemical under study or by applying the material to very limited areas of the skin of rats or rabbits for given periods of time. The technique employed was essentially that of Etchells and Fabian[2] described in 1935 for study irritation.

Methods for the measurement of oral toxicity were similar to those employed in the United States.

Analytical methods

Relating toxic responses to dose is clearly dependent upon accurate sampling and analytical methods for the chemical under question. In contrast to the elaborate instrumentation we saw for the measurement of the electrical potentials of the nervous system, the instrumentation generally available for chemical analyses was less sophisticated. During our entire visit, we saw but one infrared spectrophotometer and one gas chromatograph. The latter was devoid of the more modern detection devices. In the research laboratories, major reliance seemed to be placed upon wet chemical methods. In the field, direct reading instruments appeared to be employed to a much greater extent.

We have already commented on the problems of getting isokinetic samples under the conditions of the Soviet inhalation experiments. In one demonstration of exposure techniques, samples were taken through a considerable length of rubber tubing between the U tube connecting the absorbent and the chamber. The test material was one known to be absorbed in rubber. Analyses were performed in another section of the laboratory by a technician following the manual of standard procedures set for the analyses of such substances. The analysis might be by chemical means or by ultraviolet spectrophotometry.

Some techniques of sampling in the field also were disturbing to us. In one laboratory, we saw

technicians who had just returned from sampling a plant atmosphere for benzene. The air samples had been drawn into well greased desiccators, the tops of which were stoppered with rubber stoppers and the whole apparatus sealed off with clamped rubber tubing. In view of the affinity of benzene for rubber and grease, we could not help but wonder about the accuracy of the results.

We saw various types of field equipment for the measurement of common noxious gases but were surprised to learn that there are no procedures for the calibration of this equipment as a part of its use. We were told that calibration was unnecessary since the equipment had been calibrated at the point of manufacture.

From the instrumentation that we saw in the laboratories and in the field, it is clear that little, if any, continuous monitoring of the environment is carried out. Reliance is placed entirely upon spot sampling. American experience has shown that this is not a reliable method of obtaining data which will describe adequately environmental conditions.

Standard procedures for the determination of various chemicals are promulgated by the central research institutes. These procedures were being used by technicians who followed directions in a laboratory manual. There was no system for checking the accuracy with which the standard procedures were being followed nor was there any system for comparison of analyses on standard samples sent from a single reference source.

Compliance with threshold limit values

The delegation did not, of course, carry any industrial hygiene equipment with it. Our conclusions regarding Soviet compliance with their own standards must rest on certain indirect, but not necessarily inadequate, evidence.

With the state controlling all aspects of the economy, it is possible to bar absolutely the manufacture or the use of certain types of chemicals that are considered too toxic. In the Soviet Union, the use of the following pesticides is prohibited: systox, dieldrin, isidrin and endrin. Use of parathion is prohibited except in greenhouses. Aldrin may be used only on the soil. In 1961, the use of DDT was prohibited near hay and other forage crops used by the dairy industry. Spraying of forests has stopped, except in Siberia where it has continued because of the need to control encephalitis. The use of other highly toxic economic poisons is limited to trained operators connected with the collective farms. If an individual farmer wishes to have his crops treated, he must make arrangements with these trained crews to have the work done. Such arrangements are encouraged in order to lessen the risk of cross infestation from the private plots to the collective farms.

Manufacture of the following chemicals is prohibited because of their carcinogenic hazard: 3-3′-dichlorobenzene, 3-3′-oxybenzidine, dicyclohexylamine, NO_2 derivative of dicyclohexylamine, dianisidine, and beta-naphthylamine.

Our observations on industrial hygiene controls are based on the six different industrial establishments we were permitted to visit which were: a textile mill (2200 employees), a rubber reclaiming and plastics plant (2500 employees), a coke and chemical plant (3000 employees), a coal mine (3500 employees), a drug plant (1200 employees), and a machine cutting tools plant (6000 employees). As was noted above, all of these were selected for us by the Soviet government. None were "small plants" as we use the term. In each of these enterprises, the ventilation equipment we saw was appropriate, was operating in a satisfactory manner, and was as good or better than the ventilation in equivalent operations in the United States. The chemical operations in the chemical and coking plant were completely hermetized with a dual stand-by line available in case of breakdown. The areas around the valves and pumps were carefully vented.

In several areas, noise was considerable. In the spinning rooms of the textile plant, several members of the delegation estimated the noise at 100-105 db, although the noise meter carried by the hygienist from the local sanitary epidemiologic station showed a reading of only 90 db on the "C" band. We were not permitted to shift the instrument to other weightings. Ninety db represents the upper limit permitted by the government. The plant manager stated that a high priority has been assigned to the design of less noisy textile machinery and assured us that if we were to return to the plant five years hence we would not recognize the place.

The substitution of non-toxic chemicals for toxic products appeared to be a common practice. We were interested in the chlorinated hydrocarbons because of the low MACs adopted by the Soviet Union for these compounds. In spite of trying for a month, we never did see a degreasing operation employing such solvents. In the plant of machine cutting tools, the metals were cleaned in caustic and in acid. The only solvent we saw in use was kerosene.

In contrast to these sound industrial hygiene measures, plant safety measures were generally inadequate. Unguarded, or poorly guarded, cutting tools, moving belts, and moving machinery were common. Steps and walkways were in poor repair. Lighting was inadequate by our standards.

Personal protective measures

The provision of protective clothing and the laundering of this clothing, the provision of protective gloves and ointments where necessary seemed to be common practice in the plants that were visited. Eye protective equipment in the form of safety glasses or face masks was conspicuous by its absence in several situations where it would be considered essential in the United States.

A common practice, one required by law in the chemical industry, is the provision of milk supplements to the workers exposed to chemicals. Five hundred ml of milk is supplied daily. This is based on the belief that such food supplementation provides an extra measure of protection against the harmful effect of chemicals. We were in no position to judge the adequacy of the diet generally available to the Soviet worker and have no quantitative information on the merits of this procedure.

In some cases, shortened work weeks or rotation of employees are used to reduce the duration of toxic exposures. We were told that workers may not handle pesticides for more than twenty years, that coal miners retired at the age of 50.

In several of the plants, new employees are required to take formal course work to learn recommended safe working procedures. In some instances, this is supplemented by refresher courses. The chemical and coking plant had class rooms and museums designed specifically for this purpose. The interest of the plant managers in, and their knowledge of, the industrial hygiene problems in their operations was exceptionally high. The knowledge shown was not a quickly acquired veneer in anticipation of foreign visitors.

Training of scientific personnel

Before considering the organization of industrial medicine and industrial hygiene and toxicology within the Soviet Union, a brief review of the training of these scientific workers is required since their training differs in many important respects from that provided in the United States.

All of the Institutes training workers in the health fields are under the administrative direction of the Ministry of Health. The student enters the Medical Institute directly from secondary school. The secondary school concludes some 10 to 11 years of schooling and is roughly equivalent to finishing our high schools. Usually the student is 17 years of age by this time. Entrance is by competitive examination. If the student fails, he has the option of working in a hospital, or some similar enterprise, for two years and then may try again. Once entered in school, some 97-98% finish the curriculum. The successful applicant enters into one of several medical curricula. These are: therapeutic medicine (six years); stomatology (five years); pediatrics (six years); hygiene (six years); pharmacy (five years). In each of these fields, the first three years of the curriculum is identical and includes such subjects as chemistry, physics, social sciences including philosophy and Marxist-Leninism, foreign language, histology, microbiology, and biology. After the basic three years, the curricula diverge into the specialty areas listed above. Students who are to become toxicologists or industrial hygienists follow the hygiene curriculum. The future industrial physician would follow the therapeutic medicine route.

While it is not possible to list the curricula in detail, the students in the hygienist group receive training in the following aspects of industrial hygiene: labor physiology, toxicology, sanitary equipment (including lighting and industrial safety), labor hygiene (including chemistry, agriculture, and machine building). The students in the hygiene option also receive training in individual therapy, gynecology, pediatrics, and infectious diseases.

After graduation from the medical institute, the student takes the state examination for license as

a medical specialist (vratch) in his particular field. We obtained the estimate that approximately 10% of the practitioners in the country are licensed as hygienists. This group serves not only as toxicologists and industrial hygienists, but as food hygienists, community hygienists, air pollution and water pollution specialists, and as health department administrators.

The degree of Doctor of Medicine is the highest academic degree, comparable in many ways to our Doctor of Philosophy. The degree is a prerequisite to becoming chairman of a department in, or head of, a medical institute. The doctorate is obtained only after three to five years of postgraduate work beyond the basic professional training obtained at the medical institute together with research work leading to an acceptable thesis.

Separate technical institutes in engineering are responsible for the training of safety engineers.

A group of health workers unique to the Soviet Union are the feldshers. These are trained at special feldsher schools for approximately three years. Some feldshers are trained primarily in sanitary-epidemiology, others in clinical work, including minor surgery. The trained feldsher is expected to diagnose emergencies with sufficient accuracy to assure proper disposition, to give simple treatment, and to carry out immunization programs. In manning the first-aid stations, he may be expected to suture minor wounds. While we do not have the exact equivalent of the feldsher in the United States civilian practice, the medical corpsman of the armed forces shares some of the same characteristics.

Organization of industrial medical and industrial hygiene services

The Soviet government has placed a high priority on medical services for workers. Because the entire economy is managed by the government and there is no private enterprise as we know it either in industry or the practice of medicine, occupational medicine is integrated with the general curative medical services and industrial hygiene with the general hygienic or public health services. Under the Soviet system, the plant physician gives medical care to the worker regardless of the etiology of the disease.

The administrative norms require the establishment of a medical sanitary center for all enterprises employing more than 4000 workers except in the coal, oil refining, and chemical industries where such centers are required if there are more than 2000 employees. Workers who are not served by such full-time centers receive services through polyclinics on a priority basis.

In addition to the medical centers, physician stations are required at the rate of 1:2000 workers in most industries and 1:1000 workers in the coal, oil refining, and chemical industries.

In the absence of medical-sanitary centers because of the smaller plant size, regulations call for the establishment of physician's stations at all general plants having 800 or more workers; chemical, oil-extracting or refining, mines, and nonferrous metal works with 500 or more workers; and iron and steel works with more than 600 workers.

The above facilities which are manned by physicians are supplemented by feldsher stations, which represent the initial diagnosis and treatment facilities in the plants. In the small plants where there are no physician stations, the feldsher stations represent the only in-plant medical facility.

The medical sanitary centers may be open or closed. The open centers care for the workers' families as well as the workers and may in some areas care for the community as well. The closed centers are available only to workers and managers at the plant or group of plants. Since these facilities are responsible for the total medical care of the worker, there are a number of interesting opportunities for life-time epidemiological studies. The worker's medical record follows him wherever he goes, but the in-plant medical records that we saw were in a form such that any long range studies would be infinitely laborious, if not impossible. Periodic medical examinations are required in a number of industries, but if the patient has been seen by the physician for some other reason since his last periodic examination, it was assumed that the patient had had a second examination and that it was unnecessary to bring him back for an additional check-up.

In a visit as brief as ours and with a relatively superficial contact with the medical departments in the plants visited, it is impossible to draw any firm conclusions regarding the quality of the med-

ical care. In general, the equipment available at these plant medical centers was old and minimal. In one plant which appeared to have considerable noise we asked about audiometric screening. We were first told that this was done routinely on an annual basis but further questioning led to the conclusions that audiometric tests were performed only when the physician suspected some hearing defect. In another plant where there was limited dust exposure to an estimated 40 exployees, we learned that these employees were given prophylactic inhalations of oils, streptomycin, and penicillin.

If a worker's illness is attributable to occupational disease or injury, the worker receives a higher rate of sick leave pay than if his illness is nonoccupational. If there is a dispute between the worker and the plant physician as to whether occupational factors are responsible, the employee has the right of appeal either to his union or to a polyclinic. The ultimate body of appeal in occupational disease cases is Professor Letavet's clinic in Moscow. This clinic, having 110 in-patient beds and outpatient clinic, sees some 1500 to 2000 in-patients per year and conducts some 70,000 ouptatient visits. Of the in-patients, it is estimated that 10-20% do not have occupational diseases. The others represent patients who are brought in for investigation of presumed occupational diseases. Professor Letavet's clinic serves the Moscow oblast which has a population of about eight million. Eighty to 90% of the patients come from the Moscow oblast, the remainder from outlying districts. Similar occupational disease clinics exist in other areas. In Kiev, there are two. One sees 10-20 cases of occupational disease per month, the other about 50. Cases of occupational trauma are referred to separate trauma institutes. These figures are of some interest since it is most difficult to get accurate estimates of the incidence of occupational disease. According to Professor Letavet, the occupational disease seen at his clinic are grouped in descending order of frequency as: 1) dust diseases, e.g. silicosis; 2) neurologic diseases, e.g. from vibration; 3) diseases arising from adverse physical factors; and 4) specific intoxications, e.g., lead, benzene, and mercury. Since this clinic sees only the difficult cases, this distribution is biased. Dermatitis is estimated by Professor Letavet to represent the most frequent occupational disease.

The central medical institutes, such as this one, were well equipped and were staffed by specialists whose clinical competence was readily apparent.

The occupational or industrial hygiene services are integrated with the general sanitary hygiene services of the community. Frequent inspections of the plant operations are carried on by hygienists from the local sanitary-epidemiologic station (health department). Where plant conditions warrant, there may be an industrial hygienist at the plant on a full-time basis and paid by the enterprise. In the coal mine that we visited, the two trained mine inspectors were augmented by 80 worker volunteers who serve as inspectors. One such worker works with each mining team and is expected to report any breach in mine safety rules. These workers are relieved of their regular duties two days a month in order that they may attend seminars on mine safety.

Industrial hygiene services are intimately involved in the planning of any new construction, remodeling or expansion of plants, or in the introduction of new machinery or new substances or processes. Representatives of the sanitary station sit on the architectural and planning boards which must give approval to construction. Consideration has to be given not only to the healthfulness of the building environment but to the effect of the proposal on the environment surrounding the plant. Sanitary protective zones are established around the plants extending for a radius of from 50 to 1000 meters depending on the nature of the industry and the probability of release of air pollutants. These activities have been able to enforce a significant degree of community planning in the development of new industrial establishments.

Role of the trade union

Time limitations prevented our becoming familiar with the role of the trade unions in occupational health in the Soviet Union. We did learn that the trade unions operate the numerous rest homes or sanitaria that are available to the workers for vacations and for convalescent care. At present, there are 1089 such "prophylactoria" having a total of 22,600 beds. The All-Union Council of Trade Unions operates six institutes of labor protection which are primarily engineering institutions whose functions are to advise the trade unions on

legislation, advising management on plant design, and keeping up to date the technical factory inspectorate of the All-Union Council of Trade Unions. This inspectorate is independent of the sanitary stations which are under the Ministry of Health. The union inspectorate may enter any shop or factory, may close the factory if necessary, fine the management, and if necessary bring criminal charges in the courts.

Thus, there exists in the Soviet Union three types of factory inspection. The first is the inspectorate from the sanitary-epidemiologic stations of the Ministry of Health. These inspectors are vratchs who have had the medical training outlined above. The second are the inspectors from the all-union councils. These are primarily engineers by training. Last are the public or volunteer inspectors, elected by the trade union committees and responsible to the plant commission for the protection of labor.

Evaluation

There is an old saying that the only experts on the Soviet Union are those visitors who have been there for less than three weeks or more than twenty years. Our four-week visit was long enough to disqualify us as experts, and this is not said facetiously. The vastness of the country, the language and cultural barriers, even in the scientific field, make one cautious in drawing firm conclusions. Impressions we can give.

We believe that the chief explanation for the differences in threshold limit values between the United States and the Soviet Union lies in the philosophic approach to those limits and not in a difference in the sensitivity of methods used to establish those limits. Were the Soviet limits rigidly enforced, the economic costs involved would probably result in a re-evaluation of the validity of the concepts underlying their limits.

We believe that at least some of the cases of occupational disease reported in the Soviet Union as occurring from exposures at the American threshold limit values represent differences in the analytical techniques employed for the measurement of environmental concentrations of those chemicals. Our experience made us extremely skeptical of the validity of many of these environmental measurements.

The early specialization of their professional workers and the somewhat rigid compartmentalization of research in the several institutes may contribute to the somewhat inflexible research methodology and the failure to draw on the potential contributions from allied biological and physical sciences. Preoccupation with the nervous system may have limited the exploration of the biochemical and immunological approach to some of the problems of experimental toxicology.

We assume that the Soviet industry we visited represented the better industries. The industrial hygiene controls demonstrated were better, except for safety practices, than found in many of our industries, but were not better than that found in most of our industries of equivalent size.

Much that we saw was commendable. Serious attention is given to the reduction of environmental hazards through the absolute prohibition of the manufacture and use of certain highly toxic or carcinogenic chemicals, and through attention to industrial hygiene considerations in plant construction, plant modification, and in community planning. The close relationship of public health and clinical medical services in the industrial setting permits an integration of preventive and curative measures. Worker and management training in the importance of good industrial hygiene was emphasized and a knowledge of these practices was clearly evident.

In the research laboratories, the quality and quantity of work on the effects of drugs and chemicals on the central nervous system was exceptionally high. Such studies may be expected to have important long range results in pharmacology, neurology, and psychiatry.

If one recalls the span of development since the October revolution and the set backs imposed by the destruction of World War II, Soviet progress in industrial toxicology and occupational medicine is remarkable. The delegation was grateful for the opportunity to observe it.

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Modus operandi of threshold limits committee of ACGIH*

HERBERT E. STOKINGER, Ph.D., Chairman
Threshold Limits Committee of the American Conference of Govermental Industrial Hygienists

Certain changes are described in the operations of the Threshold Limits Committee that have occured in the recent past as a result of increased interest in its actions. Although the basic tenets on which it operated a decade ago still hold, some new findings in environmental medicine are resulting in new concepts of the relation of inhaled irritants to health. A new procedure of notification of the Committee's intentions with solicitation of data is described that is hoped will make for a greater annual number of limits in which industry has a voice. Two types of limits, and their basis for selection and application are clearly defined for the first time.

The Threshold Limits Committee is becoming increasingly aware that its activities are being more closely scrutinized as a result of impending changes in the Walsh-Healey Act that may make the Committee's actions more binding on industry. In this light, three main trouble spots appear to be developing:

1. Real concern has been expressed over the Committee's business with limits based on reasons other than health.
2. Fear has been expressed that the Committee may not be cognizant of all the industrial experience available.
3. Suspicion is voiced that the Committee may on occasion be arbitrary and capricious.

Because there tends to be fear and suspicion when there is no enlightenment, the theme, the modus operandi of the Threshold Limits Committee, was chosen. By showing how the Committee takes its actions and the guiding philosophy on which these actions are based, I hope I may be able to dispel some of the misgivings about the Committee's formal actions.

Committee composition

Before going futher, I should call your attention to certain changes that have been made in the physical operation of the Committee, changes that considerably improve its functioning and speed its operation. For the past two years we have functioned as an expanded 14-man committee. This represents an increase of six members. This expansion was made to increase the Committee's coverage of industrial hygiene problems. Its members are actively engaged in control programs in occupational health in ten states and one province of Canada. It should be particularly noted that most of the states from which members come are highly industrialized; annual plant visits number in the thousands in some of the represented states. All disciplines related to the Committee's objectives are represented; these are toxicology, engineering, industrial hygiene, analytic chemistry and medicine. Moreover, members with outstanding competence and experience in specialty areas serve as chairmen of its three subcommittees, Economic Poisons, Organic Solvents, and Mineral Dusts. The Committee is particularly pleased to count among its members leading authorities in these fields.

Committee publications

The primary publicaton of the Committee is the annual printing of the Threshold Limit Values (TLV) which in 1964 lists 341 substances. Substances are listed alphabetically in three main categories; Recommended Values, Mineral Dusts, and Tentative Values. Limiting concentrations of gases and vapors are expressed in parts per million by volume (ppm); liquids and solids, as milligrams per cubic meter of air (mg/m^3); and mineral dusts, as millions of particles per cubic

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foot (mppcf) as determined by light-field count techniques. In addition to the list itself, there is an explanatory preface that defines in general terms the meaning of the limits, special notations set forth in a general way the bases for the choice of the limits or how the limits should be used. In 1962 an appendix was added to provide a place for carcinogens and other substances whose limits could not be described with a single value. In 1963, two other appendices were added, one describing procedures for determining the threshold value for mixtures, the other defining the method the Committee uses to decide whether a substance should rate a "C" or ceiling listing.

The Threshold Limit List may be reprinted with permission obtained from the Secretary of the ACGIH and with the understanding that it be reprinted in its entirety.

Documentation of limits

Recognizing the shortcomings of a single number for use as a guide for reasonable control of the working environment, the *Documentation of Threshold Limit Values* was published in 1962. Its purpose is to supply in brief, referenced form the technical evidence that substantiates the choice of each limit. Each documentation is kept up-to-date by continual revision as new information appears. Supplements will be published every two or three years as warranted. They will be available from the Secretary of the ACGIH.

Ancillary publications

From time to time as occasion demands, the Committee, through its members, publishes reports in the literature or documents relating to its activities. "Standards for Safeguarding the Health of the Industrial Worker,"[1] appearing in 1955, set forth the basis for the American air standards for industry and prescribed their proper use. "Maximum Acceptable Concentrations"[2] drew a comparison between Soviet and U.S. industrial air standards. "Threshold Limits and Maximal Acceptable Concentrations"[3] called attention to the difference in definition of these two sets of limits that was then (1961) producing an ambiguous situation for those substances with a common limit. This report led to a rectification of the situation in 1963 with the adoption of a ceiling limit for certain substances while retaining a time-weighted average for the others. "International Threshold Limit Values — 1963"[4] reported the activities of the Second International Symposium on Permissible Limits of the Air of Workplaces. The TLV Committee of ACGIH has prepared a document, "Principles and Procedures for Developing Experimental Animal Data for Threshold Limit Values for Air." It is believed that this information will satisfy a demonstrated need on procedural requirements to those originating data for such limits. Availability and prices of the document will be announced at a later date.

Committee actions

With the years, the Committee has striven constantly to improve its mode of operating. In addition to making documentation of each revision and addition to the list, two 2-day formal meetings of the plenary committee is also a requirement. Between meetings and throughout the year, communication among subcommittees and members is continuous. A very considerable volume of extra-committee correspondence with both industrial hygienists in the U.S.A. and abroad is maintained by the Chairman.

Notice of intent

Responding to the suggestions of industrial representatives, and in an effort to increase the interchange of toxicologic information developed by industry, a "Notice of Intent" was initiated in 1964 as a step toward informing industry of the intended actions of the Committee prior to taking any final action on threshold limit changes. A list is made available in early January following the first meeting of the Committee with the request for comments on the listed substances, and a solicitation for new substances for listing. Although the first trial could be considered "very encouraging," the responses indicated the need in many instances for industry to develop more than impressions or opinions on industrial experience with toxic chemicals.

Tentative listing

Following the development of the annual list and its acceptance by the American Conference of Governmental Industrial Hygienists at its annual meeting, all new additions and revisions of former values are placed in the Tentative List. Here they remain for at least two years or until such time as it

becomes evident that no further immediate changes is a likelihood. Additions to the Tentative List for the year are so designated as are changes in Recommended Values, for ready identification.

Philosophy of air limits

Threshold Limits for industrial atmospheres are based on the premise that, although all chemical substances are toxic at some concentration experienced for a period of time, a concentration exists for all substances from which no injurious effect will result no matter how often the exposure is repeated. A similar premise applies to substances whose effects are limited to irritation, narcosis, nuisance or other forms of stress. This philosophy thus differs from that applied to substances possessing ionizing radiation for which on current concepts there is no threshold; all exposures, however small, have some associated risk to health. Strictly speaking, the basic premise applying to chemical substances does not admit those chemicals with strong radiomimetic potential, chemical free radicals or free-radical formers. In this sense a threshold limit for substances like ozone, possibly certain epoxy compounds presently assigned a threshold limit is erroneous in the sense that the degree of risk associated with the limit is not stated.

With this admitted error, which is not great because of the limited number of substances with high radiomimetic potential currently in the list, we believe no user can quarrel with the reasonableness of the Committee's basic premises. Compare for example, the greater stringency of the Soviet limits based on a philosophy that "regardless of the value set, the optimal value and goal (the norm) to be sought is zero concentration."[5] Under present Soviet philosohpy, air quality standards are based on the premise that Soviet workers could not be subjected to the additional stress of chemical toxicity and irritation above and beyond the normal stresses of everyday living.

Ceiling and time-weighted average limits

Until 1963, the threshold limit value was defined as a time-weighted concentration averaged over the course of the workday operations. An intolerable situation arose, however, when the maximal acceptable concentration was explicitly defined by the Z-37 Committee of the American Standards Association as a limiting concentraton of "ceiling" below which all concentrations should fluctuate, but with the same assigned limiting value — practically an impossible situation under which to operate. The limiting value for trichlorethylene, for example, cannot at the same time represent a ceiling and also a value with permissible excursions above the limit. To resolve this to a more desirable situation, the Committee had the alternative of adopting a "ceiling concept" for its limits, or suitably lowering the limit and retain the time-weighted average (TWA) concept. Because the TWA concept had, in practical application, much to recommend it, but at the same time possessed a defect for certain fast-acting substances, the Committee adopted both concepts. This procedure has the advantage of bringing into line the limits developed by both committees, but more important, takes recognition of a dichotomy that exists in the toxicologic action of industrial chemicals.

If substances in the threshold list are examined individually from the viewpoint of their toxicologic action, it becomes apparent that substances fall into one of two groups, one, a fast-acting group, the other, a group in which responses are slower. This in itself is insufficient to qualify for a "C" listing. If further, however, the limit of the fast-acting substances has an insufficient factor or safety to permit a designated excursion above the limit, the limit will bear a "C" notation. Judgment must be exercised for certain few substances whose actions are neither predominately in one group or the other. A "C" listing indicates that the stated limit should not be exceeded; a time-weighted average concentration applies to all other listed values. Strictly speaking, a "C" listing implies that a no time should the limit be exceeded, an improbable, practical condition, and one not legally desirable, hence the word *should* is used in preference to *must*.

Basis for assigning "C" listings

In general the bases for assigning or not assigning a "C" value rest on whether excursions of concentrations for periods up to 15 minutes may result in a*)* intolerable irritation; *b)* chronic or irreversible tissue change; or *c)* narcosis of sufficient degree to increase accident proneness, impair self-rescue or materially reduce work efficiency.

In order for the Committee to decide whether a substance is a candidate for a "C" listing, some guidelines must be formulated on the permissive fluctuation above the limit in terms of the seriousness of the response in the categories *a), b)* and *c).* For this the factors given in Table I have been used by the Committee. For both technical and practical reasons, the factors have been pegged to the concentration in an inverse manner. It will be noted that as the magnitude of the TLV increases, a correspondingly decreased range of fluctuation is permitted; not to decrease the factor for TLV's of increasing magnitude would permit exposures to large absolute quantities, an undesirable condition, and a condition that is minimized at low TLVs. Moreover, larger factors at the lower TLVs are consistent with the difficulties in analyzing and controlling trace quantities.

TABLE I
Basis for Assigning a "C" Listing

TLV Range*	Test TLV Factor	Examples
0 to 1	3	Toluene diisocyanate TLV, 0.02 ppm, if permitted to rise above 0.06 ppm may result in sensitization in a single subsequent exposure. "C" listing recommended on category (b).
1+ to 10	2	Manganese TLV, 5 mg/m^3 contains little or no safety factor. All values should fluctuate below 5 mg/m^3. "C" listing recommended on category (b).
10+ to 100	1.5	Methyl styrene, TLV 100, if encountered at levels of 150 ppm will prove intensely irritating. "C" listing recommended on category (a).
100 + to 1000	1.25	Methyl chloroform, TLV 350 ppm, at 438 ppm for periods not exceeding 15 minutes is not expected to result in untoward effects relating to category (c). No "C" listing recommended.

* Expressed as ppm or mg/m^3, whichever unit is applicable.

Application of factors to TWA listings

These same factors used to test the appropriateness of a "C" listing may also be used as a guide for the degree of excursion permitted for a time-weighted average. To date no quantitative statement has been given on the magnitude of the permissive excursions other than that the excursions above the limit should be compensated by an equivalent excursion below the limit.[3] The factors given in Table I are an attempt to provide a reasonable magnitude to these excursions.

Irritants

So much for the basic premises on which the Committee operates. Now for a toxicologic tenet of utmost importance for the understanding of the significance to be attached to physical irritation in recommending threshold limits.

As stated in the introduction, one of the concerns reaching the Committee from various quarters is the question, "Is the recommendations of a limit based primarily on irritation the proper business of the Committee?" Is not health protection its real and only concern? Are nuisance complaints from irritation solely a labor relations matter? In this the Committee holds the view that physical irritation is as proper a basis for limit as are reasons of health, that irritation and health effects are inseparably twined, and thus neither can be a pure labor relations matter.

There is growing recognition not only in the field of occupational health, but in other areas of environmental health as well, air and water pollution and radiation, that although physical irritation *per se* may be no more than a nuisance, yet in combination with other environmental agents an irritant may predispose the individual to heightened or accelerated response and thus may promote a disease that would not otherwise exist or worsen a conditon that does exist. Here is the evidence; it is both epidemiologic and animal experimental.

"The hand writing on the wall"

On the epidemiologic side, Gorham[6] has revealed an association between death rates from pneumonia in the United Kingdom and deposits of atmospheric sulfates (sulfur dioxide), suggesting that air pollutants, quite probably of the irritant type, may affect the incidence or severity, or both, of pneumonia in man. Irritants have been shown by Dalhamn[7] and others to be cilia-static agents, to disturb the normal physiology and histology of the respiratory tract, leaving it more suceptible not only to bacterial invasion but to chemical attack as well. Pemberton and Goldberg[8] had similarly demonstrated previously a significant correlation between the death rate in men over 45 years from

chronic bronchitis and SO_2 levels in the atmosphere, to mention just one more of many such reported correlations.

On the animal experimental side, Purvis, Miller and Ehrlich[9a] have shown that a single exposure of mice to trace quanitites (a few ppm) of the respiratory irritant ozone, increased the death rate of mice previously or subsequently injected with *K. pneumoniae*. Nitrogen dioxide similarly synergized the effect of the microorganism at levels as low as 0.5 ppm but only after nearly continuous exposures for more than three months.[9b] This finding has been confirmed by Coffin *et al*[10] and extended to lower concentrations of ozone; 0.3 ppm increased the mortality of mice exposed a single time for three hours and then challenged with a streptococcal organism. How significant and general this finding is, however, may be questioned; Wagner *et al*[14] observed no difference in response in control animals with mild natural respiratory infection and in their conterparts exposed to NO_2.

Kotin[15] has made good use of this procedure, however; true squamous cancers in the lungs of mice, similar to those found in man, were produced by exposing the animals first to infection then to ozonized gasoline. A virus-type influenza was the infection produced. In the animals exposed to ozonized gasoline alone, there were no significant changes. In those with infection alone, approximately 8% showed squamous changes in the bronchi consistent with the healing process after infection, with only an occasional metaplastic change; however, a striking 30% of the animals exposed to the combination showed squamous carcinoma.

The synergized effect of SO_2 and other acid irritants with NaCl on altering the flow of air through the respiratory passages shown by Amdur,[11] is so well known as not to need repeating.

The toxicologic interaction of irritants with microorganisms or chemicals is not confined to the respiratory tract; the skin is also a site where pronounced interaction of irritants has been demonstrated. Horton *et al*[12] have shown that a single application of a number of hydrocarbons from petroleum was all that was needed to accelerate skin tumorigenesis in mice from small doses of benzpyrene or methylcholanthrene. The property these tumor accelerators had in common was one of irritation. Others (Wynder *et al*[13]) have shown the irritants, phenols and terpenes, to reduce the cancerigenic dose requirement to minute amounts when used as a promotor on mouse skin. And more recently, it has begun to appear that experimental pulmonary carcinogenesis in animals may now be possible through preliminary treatment of the respiratory tract with irritants!

Although it is realized that none of the above-quoted evidence constitutes "proof" that irritants produce potentiated or synergized effects in industrial workers, yet like the evidence linking pulmonary carcinoma to cigaret smoking, it is overwhelmingly suggestive, and the Committee considers it the "handwriting on the wall."

Coverage of information

The Committee has recognized for some time that the increasingly rapid introduction of new substances into industry, new uses for old substances, and the increasing accumulation of unpublished information are making it increasingly difficult to be on top of each new hazardous situation. To cope with these situations, two changes have been made in the Committee's operations. First the Committee has increased the numbers of its members as mentioned previously. This increase has been made on a very selective basis. Because members have been selected from those occupational health units whose activities involve investigation of from hundreds to thousands of plants per year, the Committee feels that there are few hazardous industrial situations of which it is not aware or on which it does not have recent first-hand experience and information. Other committee members not so oriented supplement the first-hand experience with the more academic aspects of the problem on which toxicologic trends are determined, and long-range views and policy are based. Above and beyond all this, several of the members of the Committee have not only national but international reputations. All of this adds to the prestige of the Committee and its decisions. Second, issuing of a "Notice of Intent" provides all interested individuals an opportunity to express their views on intended changes, offer new information, suggest new limits, and thus have a helpful part in the Committee's activities. It

is hoped that the Notice of Intent will also stimulate industry to develop threshold limit data.

The Committee has sensed an impression in some quarters that some of its decisions are considered arbitrary, unfounded and capricious. To this, let the Committee hasten to say that in all its decisions, the Committee is keenly aware of the gravity of its acts and gains the facts and opinions of informed individuals outside the Committee on all important changes. Issuance of the Notice of Intent formalizes this solicitation. There is also a built-in brake against precipitous or unfounded action. It is the policy of this Committee that a documentation must be made of each substance before a revision is proposed or an addition suggested. This evidence must be referenced and submitted in writing for review by the plenary committee. Acceptance of the change is by substantial agreement among all the members. Following this, it is also the policy to place the substance on the tentative list. There it remains for a period of at least two years open to change upon the appearance of new information. It is transferred to the recommended list only after it appears to the Committee that no further information for a change is a near-term prospect.

This committee welcomes suggestions toward improving its sources of information, but its final decisions must be those of the Committee as it is constituted, unfettered by considerations other than the health and well-being of the industrial worker.

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Industrial contribution to threshold limit values*

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On the premise that the Threshold Limit Values (TLVs) are industry's values, industry should be concerned about taking a predominating role in accumulating firm data that will help in developing TLVs. TLVs are predicated on the principle that, although all substances are injurious at some concentration if experienced for sufficient time, there is also a concentration for each substance below which no injury will occur no matter how long the exposure. A similar principle applies to substances whose effects are limited to irritation, narcosis, nuisance, or other forms of stress. This principle thus differentiates between nonradiating chemical substances and those producing ionizing radiation for which there may be no threshold without some attendant risk to health and well-being. Further definition of the TLV is given in the preface to the Threshold Limit Values for 1964.

A review of the approximately 350 substances listed in the TLVs for 1964 shows that industry or industry-sponsored efforts account for 90, or about 25% of the total. However, the counting of an industrial contribution does not necessarily signify that each contribution provided the total basis for the limit, but may signify evidence of only very limited industrial effort. Nevertheless, it is counted as a contribution if 1) it was basic to the determination of the value when used in conjunction with other information, or 2) it was the sole basis for the limit even though it represented a meager effort.

The 25% figure may give the misleading impression that industrial contributions are made commonly throughout the chemical industry. They are not. With one or two very recent exceptions, they are confined to seven chemical companies. Of these, only two made the majority of the contributions; one company made what might be termed a significant but modest contribution, and four made only minor contributions. The size of the company bore no relation to the magnitude of the effort although all are considered to be among the chemical "giants."

Within the last two years a surge of interest in TLV development occurred in certain segments of the chemical industry; for the first time in 13 years, industrial representatives have either appeared in person or written for information to the TLV Committee on how they should proceed to acquire the requisite data for setting a TLV on their products. In response to this interest, a document *Principles and Procedures for Developing Experimental Animal Data for Threshold Limit Values for Air* was prepared,[1] which attempts to outline minimal essentials for accumulating TLV data and principles underlying these procedures, much the same as principles and procedures for determining the toxic effects of food additives of the Food Protection Committee,[2] or the principles and procedures for evaluating the toxicity of threshold substances by the National Research Council.[3]

In addition to the TLVs which are intended for health protection through the working lifetime, limits for brief periods or emergency exposure limits (EELs) may also be objectives. The latter are not the responsibility of the threshold limits committee but represent an activity of the Committee on Toxicology of the National Research Council,[4] and the Toxicology Committee of the AIHA.[5] They differ in the following important respects:

1. They refer to maximum levels of concentration which may be tolerated only for a specified single, brief period, once or rarely in the life of an individual. Such exposure is not to be repeated until and unless the return of the individual to normal condition has been demonstrated by appropirate medical or physiological means.
2. Such conditions may result in acute discomfort, or other evidence of irritation or intoxication.

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3. They contain no known or planned "safety factor."
4. They involve increments of concentration superimposed on concentrations normally prevailing below the TLV.
5. They assume that medical surveillance is at hand.

Although there are three basic ways by which industry can accumulate appropriate data for TLVs or EELs, either by animal or human experimentation or through in-plant studies, animal studies often offer the opportunity of providing the most satisfactory data for the TLV of a new product. Certain substances, the primary effects of which are irritation or narcosis, or manifestations of other forms of stress that are best estimated subjectively may require human experimentation as the only source of data. Obviously also, human exposure is the only method for acquiring valid data on such substances for the development of EEL.

The toxicologic literature has many examples of the use, by industry, of animal experiments leading to the recommendation of a TLV. A few are to be found in references six through nine; fewer studies are to be found of human sensory responses leading to air limits.[10-12] To perform such human studies so that the results are interpretable to working conditions, and hence to TLVs, the studies should be so conducted as to "acclimate" the volunteers to the test substance in a manner simulating work conditions before thresholds of irritation narcosis, etc., are determined. Past studies,[11,12] ignoring this precaution, have produced results at variance with threshold values determined later and more accurately under normal working conditions.[13]

Industry can contribute its most valuable information for TLVs by studying workmen on the job in association with proper measurements of environmental factors. Although this type of study seems to provide ideal information for the purpose, such data can be far from ideal unless the group of workmen under investigation is carefully selected as to the size, and exposure is restricted to a single test substance. In addition, careful measurement of the environmental air contaminant should be made at breathing-zone levels and adequate medical information should be obtained about the workmen through application of appropriate clinical and physiological studies. The greatest deficiency of such investigations is the lack of precise appraisal of the exposure of the workmen and the difficulty in finding tests indicative of early signs of response to that exposure. An example, where all these conditions were ideally met, is the ten-year in-plant study of workmen exposed to vapors of butyl alcohol which led directly to setting of the TLV.[13]

It is obvious that data required for setting EELs can be obtained by a combination of animal experiments and human observations with the limitations and advantages outlined above for TLVs.

A still further contribution may be made by industry in the area of surveillance of TLVs and EELs. TLVs are subject to continual revision as refinements are introduced into the measurements if environmental conditions and responses of workmen confirm or refute recommended TLVs or EELs.

This comprises several ways in which industry can direct the efforts of medical and industrial hygiene departments for the development and improvement of industrial air standards. The matter of how to perform such investigations is beyond the scope of this presentation but careful study of references provided herewith will provide such information.

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Report of an investigation of threshold limit values and their usage*

COMMITTEE ON INDUSTRIAL HYGIENE and CLINICAL TOXICOLOGY
Industrial Medical Association

At the request of the Board of Directors of the Industrial Medical Association, its Committee on Industrial Hygiene and Clinical Toxicology has reviewed the formulation and application of Threshold Limit Values and their implication to industry and makes the following report.

Promulgation of TLVs

For many years the Committee on Threshold Limits of the American Conference of Governmental Industrial Hygienists has published annually a list of TLVs. Each year, prior to publication, previously listed values are reviewed. If no change is indicated, these are carried forward under the heading "Recommended Values."

A second section of the booklet is titled "Tentative Values." This contains compounds previously listed for which changes in TLV are proposed, and new substances for which initial TLVs are proposed. When a previously listed compound is assigned a tentative value, it is removed from the list "Recommended Values." Substances assigned to the "Tentative List" remain there for at least 2 years. This 2-year tentative listing presumably was established to put interested persons on notice and to allow time for the presentation of dissenting data and opinions. After the 2-year period has passed, if no further revision is indicated, the substance is transferred to the "Recommended List" — where it assumes the status of a Recommended Value.

In 1954 the TLV Committee distributed for the first time a "Notice of Intent." This was a list of proposed new and revised TLVs that were on the Committee's agenda for action. It was not published in any scientific journal. The notice did not include the documentation for the new and revised values. Its purpose was to solicit comments and data. Unfortunately, the deadline for replies was less than 60 days from the date of the notice. This was scarcely sufficient time to get the notice into the hands of interested parties, or to have it published, let alone to permit them to marshal whatever data they might have had in their files.

Each year the booklet includes the following statement: *"Threshold limits should be used as guides in the control of health hazards and should not be regarded as fine lines between safe and dangerous concentrations."* Most persons skilled and experienced in the field of occupational health have used TLVs in this manner and have found them to be valuable tools in the management of health hazards of the industrial environment. Differences of opinion occasionally arise about the justification for specific values but, since the TLVs are intended merely as guides, such differences have not caused any great concern or inconvenience until recently.

Misuse of TLVs

In the last few years there has been an increasing tendency to use TLVs in ways and for purposes for which they were never intended. These misuses included the following:

1. At least one attempt has been made to incorporate the entire list of TLVs in Federal legislation as standards of performance.
2. Many state and local health, labor, and safety departments give both the "Recommended" and the "Tentative" Values quasi or even de facto regulatory status.
3. TLVs are being cited increasingly in litigation and workmen's compensation actions as an official standard of performance, with the result that levels which exceed the TLVs are regarded as evidence of negligence.

These trends have apparently caused concern in the Committee on Threshold Limits for, in their

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publication *Threshold Limit Values for 1964*, the following statement of policy was made for the first time:

> *"Legislative Action. The Conference does not consider Threshold Limit Values appropriate matter for adoption in legislative codes and regulations and recommends against such use."*

Despite this demurrer and the short interval since it was published, the 1964 list has already been incorporated into some state legislative codes.

It must be recognized that the existence of TLVs invites misuse, irrespective of what organization promulgates them. The improper use of these values, whether or not sanctioned by ACGIH, can profoundly affect industry in at least 4 ways:

1. By creation of unwarranted problems in labor relations.
2. By stimulation of unjustifiable claims in workmen's compensation actions.
3. By use of the values as evidence of negligence in legal actions.
4. By forcing industry to institute unnecessary and costly changes in process and equipment, as well as in monitoring systems.

Therefore, industry has a legitimate concern about the ways in which TLVs are determined and used.

It is recognized that ACGIH cannot control the way in which TLVs are used, but it is the only group that is potentially able to exert influence to encourage their proper use and to discourage their misuse. Therefore, when it accepts the responsibility for setting such values, it must also accept the responsibility for doing everything within reason to see that they are properly used.

Moreover, it must also accept the responsibility of assuring that the TLVs are based on factual data obtained in a systematic and scientific manner. Such data should be subjected to critical review and either be verified by or acceptable to qualified physicians and industrial hygienists who are experienced with and knowledgeable of the materials in question.

Attitudes in industry

In order to obtain a better definition of the problem to industry and to determine the attitudes and experiences of people in full-time occupational health work, the subject of TLVs was discussed informally with physicians and industrial hygienists. It was also discussed in meetings of various groups and industry associations.

The most significant thing that came out of these discussions was the remarkable amount of agreement on experiences, viewpoints, and attitudes. The majority of those interviewed thought that the Threshold Limits Committee is sincerely motivated, that it is genuinely solicitous of any evidence that might have a bearing on its deliberations, that it has shown some willingness to delay or even reverse its decision when reliable dissenting data were placed before it, and that it has done a good job in discharging a difficult responsibility. Most agreed that the Committee is objective in its approach and few thought that it has acted in an arbitrary or capricious manner.

The expressions of dissatisfaction for the most part seemed to be prompted by proposed downward revisions of the levels for carbon monoxide, acetone, and other substances. It was felt that the evidence upon which the changes were proposed was meager and controversial, and it was assumed (probably correctly) that the proposed tentative values would be adopted as standards by local and state judicial and regulatory bodies.

Many people felt that the TLV Committee does not give sufficient consideration to the impact that new, and especially revised, TLVs may have on industry. The TLV Committee appropriately takes the position that its mandate is to guard the health and well-being of industrial workers. This position is above reproach if the TLVs are used as guides. A serious complicating factor in the usefulness of TLVs is industry's legitimate interest in the cost — sometimes very great — that may be required in needless redesign of equipment and processes to meet a downward revision of a TLV.

It is significant that most felt that the Threshold Limits Committee could act only on the basis of factual data obtained in a systematic and scientific manner, and that it could not be expected to be influenced by empirical statements of experience unsupported by correlated and documented clinical and environmental data.

No one seriously questions that factual data derived from human experience are by far the most reliable basis for TLVs. The only significant

source of such data is industry. Unfortunately, data of this kind are rarely available to ACHIH — either because industry has not taken advantage of its unique opportunity to develop them or because they remain hidden in industry's files for any one of several reasons.

It is in this area that industry has the greatest opportunity to make a significant contribution to the establishment of realistic TLVs and it is in this area that industry has contributed little. This is an important way in which industry can have a voice in the setting of TLVs and certainly a sustained effort along these lines is long overdue.

As evidence of the desire of the Committee on Threshold Limits to be objective and fair, the "Notice of Intent" is an important document. As a practical solution to a problem, it has not accomplished a great deal. For one thing, it does not seem to accomplish much more than has the list of Tentative Values in the booklet issued annually. Moreover, the limited distribution and the unrealistic time for comment defeat the ostensible purpose.

There was substantial agreement that, to be meaningful, TLVs must be established by some group that is not only technically qualified but is also sufficiently interested to devote the considerable time and effort that are required and that, above all, can maintain a completely objective attitude. The ACGIH Committee meets these qualifications.

The suggestion has been made that industry should be represented on the Committee. We do not agree with this, because of the possible inference of bias, although we do feel that it is important that the Committee maintain an awareness of industry's viewpoint and problems. Ways in which this could be achieved should be explored.

TLVs are intended only as guides and are based on considerations of the health and well-being of the industrial worker. Industry takes no exception to this. Nevertheless, TLVs are becoming increasingly more important in legal actions and they are being misused to industry's disadvantage. Under such circumstances, industry's problems must not be ignored.

As currently constituted, the Committee has 12 members.[A] Four of them are physicians. With but one exception, members of the Committee have had limited experience in industry.

An important criticism of the Committee is the fact that so few of its members are physicians. The Committee exists to preserve the health and prevent disease of human subjects. To do this adequately, it must sift and evaluate evidence, much of which is of a clinical medical nature. It must interpret this evidence against a background of accumulated medical experience and consider it in the light of the predictable responses of human subjects. To a large extent the job requires clinical experience. Greater representation by physicians, especially those more experienced in occupational medicine, would be more realistic.

In our opinion it is undesirable that far-reaching decisions on questions that are basically medical in nature are made by a committee two-thirds of whose members are not medically trained. Obviously, many technical skills are needed on the Committee, but we think that physician representation should be at least 50%.

Conclusions and recommendations

1. The Committee on Threshold Limits of the American Conference of Governmental Industrial Hygienists has generally done an excellent job in discharging a difficult responsibility. Industry should give its encouragement and support to the Committee and should cooperate with it to the maximum feasible extent.
2. Threshold Limit Values are being used increasingly in ways and for purposes for which they are not intended.
3. ACGIH should be urged to make a greater effort to promote the concept that TLVs should be used only as guides, and to direct a major campaign toward members of the Conference to ensure that this concept is recognized, accepted, publicized, and practiced.
4. TLVs should be based upon substantial medical and environmental evidence that

[A] In addition, there are 2 consultants, one of whom is a physician. The consultants are considered nonvoting members of the Committee.

is acceptable to physicians and industrial hygienists qualified to render judgments concerning the materials in question.

5. With regard to "Tentative Values," the TLV Committee should be asked to consider carefully the following suggestions.
   a. Remove the table of "Tentative Values" from the annual booklet of TLVs and publish it separately under the heading of "Notice of Intent." This would diminish the tendency to equate Tentative and Recommended Values, which leads to the use of Tentative Values as standards.
   b. Publish the new "Notice of Intent" widely in scientific journals oriented to industrial health, along with documentation for the proposed new values.
   c. Not assign TLVs until 2 years after publication of the "Notice of Intent."
6. ACGIH should be urged to modify the composition of the Committee to provide for greater physician representation.
7. The Committee on Threshold Limits should be urged to give greater consideration to the effects of its actions upon industry, for even under the most ideal circumstances TLVs are bound to be accorded regulatory status in certain quarters and evidential weight in legal actions.
8. We do not believe that industry should be represented directly on the Committee, but we do believe that an advisory committee of industrial physicians should be established.
9. It is of the utmost importance that industry make a concerted and sustained effort to gather correlated clinical and environmental data that will contribute constructively to the establishment of realistic TLVs. Such data should be made known to the TLV Committee and preferably published. A certain amount of such information probably already exists in industry's files. However, industry must recognize that to have an effective voice in setting TLVs it must be willing to share its relevant data with the Committee.
10. A study should be made of the feasibility of establishing an independent or industry-supported clearinghouse for collecting toxicological, clinical, and exposure data. If properly organized, this could assure scientific accuracy, freedom from suspicion of bias, and anonymity of source.

Committee on Industrial Hygiene and Clinical Toxicology

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Excretory and biologic threshold limits*

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"The Industrial Hygienist today recognizes that the peril incurred by the inhalation of harmful dust is a function of two variable factors — the degree of harmful exposure and the specific susceptibility of the exposed individual to . . . injury."(1)

The preceding statement was made by Don Cummings in a paper published some 29 years ago. The following year he repeated a suggestion he had discussed previously.

> *". . . I would suggest that for each hazardous industrial dust two limiting concentrations should be established. The first, to be designated as the* primary threshold, *should express that concentration of dust in which a healthy man may be employed for a working lifetime without incurring a disabling injury. The second, to be designated as the* secondary threshold, *should express that concentration of dust in which a healthy man will inevitably contract silicosis if regularly employed for many years."*

Cummings went on to suggest 5 million particles per cubic foot of air as the primary threshold for quartz, and 100 million or less as the secondary threshold.(2)

Practically all industrial hygienists presently pay lip service to the principle stated in the first of these quotations. The suggestion in the second quotation has been only half adopted. Threshold limits, so-called, or under a different name, have been prepared for over 400 industrial hazards by various organizations in this country and abroad. There seems to be some confusion outside, if not within, the profession, however, over whether these values correspond to the primary or secondary limits proposed by Don Cummings. Certainly, when the observation that one or two workers can endure concentrations well above the TLV for a few months, without obvious ill effects, leads to the conclusion that the threshold limit is too low, it would seem that the observer has the secondary threshold in mind, rather than the primary one.

Now I can see how it is difficult to accept for many industrial hazards the 20-fold spread between the primary and secondary thresholds tentatively proposed by Don Cummings for silica dust. Very likely the spread is much less for a number of substances. If we examine some of the animal experiment reports of toxicologists, we find that frequently the "100% effect" concentration or dose exceeds the "no effect" level by a factor of four or five. And these experiments involve relatively brief exposures of animals of the same species, frequently of a single strain, of the same age and size, fed the same diet and kept in the same cage. Certainly the variation in susceptibility in a typical worker population of all ages and sizes, various eating and living habits, and different hereditary factors, must be much greater than for a uniform lot of small animals. In addition, many workers have been subjected to stress or injury from infectious or other diseases, and consume various drugs and alcohol, and use tobacco, in varying amounts.

Even if there were a sharp limit demarcating the difference between harmless and harmful levels of exposure, in other words, if the primary and secondary thresholds of Cummings coincided, meaning that there were no differences in susceptibility among individuals, we would not find identical responses by different workers to the same concentrations.

Variations in the rate and depth of breathing due in part to differences in degree of physical exertion, would cause different workers to absorb substantially different amounts of dust or fume.

With many dusts, differences in particle size or solubility (frequently dependent on subtle variations in chemical composition) which are practically impossible to measure accurately, deter-

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* 1967 Cummings Memorial Lecture presented at the American Industrial Hygiene Conference, May 1-2, 1967, Chicago, IL. Published in *Am. Ind. Hyg. Assoc. J.* 28:305-314 (1967). Reprinted by permission of the American Industrial Hygiene Association.

mine the fraction of inhaled impurity which is retained or absorbed.

A certain concentration in the air of parathion, or lead dust, may or may not be associated with intoxication, depending on whether or not there is opportunity for significant skin absorption, on the one hand, or ingestion on the other.

A number of papers have been published which are highly critical of the TLV for uranium, as being much too low. As evidence the results of numerous air tests in the uranium refining industry have been given, showing values well above the TLV, without evidence of illness among the employees. One such paper contains a number of pictures of the operations being studied; in nearly every one the workers involved were wearing respirators.[3]

A process where respirators are worn may be considered a special case in the general situation where analysis of the air being inhaled is impractical. Other cases exist where the worker is located in a place which is inaccessible to the investigator for any of several reasons.

These are examples of situations where air analyses, in combination with the atmospheric TLV, are not adequate to precisely evaluate the peril of the hazard, since the amount absorbed cannot be predicted from the data obtained by such determinations. In such situations it is highly desirable to have other means of estimating exposure. With many substances this can be done by analyzing suitable biologic specimens or excretion products for the toxic agent or a metabolite derived therefrom.

The only biologic fluid finding much application for such exposure tests is blood; limited use has been made of biopsy specimens of lung, skin and fat, but these are not very practical for periodic sampling. The excretory products most frequently analyzed are urine and breath; sweat, the other major excretion product, is not well adapted for exposure tests.

If we are to use analysis of blood, breath or urine as a replacement for air analysis, to determine if workers are in danger of injury or intoxication, it is necessary that we have some reference point, analogous to the atmospheric threshold limit, to use in interpretation of the analytical results. Ideally such biologic or excretory threshold limits should correspond to the average levels found when workers are exposed to the atmospheric TLV.

As a general rule, and other things being equal, the higher the atmospheric limit, the more likely it is that a biologic or excretory TLV is practicable. A nonspecific test for alcohols, whether in blood, breath or urine, is more likely to be applicable to ethyl alcohol (TLV 1000 ppm) than to butyl alcohol (100 ppm) to say nothing of allyl alcohol (2 ppm). If the analytical procedure is incapable of detecting the compound (or metabolite) in concentrations resulting from exposure to the threshold limit in air, there is little point in establishing a biologic or excretory TLV. In this respect these values differ from atmospheric TLVs which are not infrequently set at levels difficult to measure by available analytical techniques. For, in spite of pious protestations to the contrary, TLVs are often used to indicate relative toxicity, as well as for their intended purpose. This requirement eliminates a great many substances from inclusion in our biologic-excretory TLV list.

Of the 395 substances in the 1966 tables of threshold limits, some 90-odd may be considered inorganic. Nearly a third of these inorganic substances are highly reactive compounds of relatively common elements, such as chlorine, oxygen, and nitrogen (Table I). Typical members of this group are ozone, chlorine, sulfur dioxide and phosphine. They will not exist long when dissolved in body fluids, and in fact most of them are probably neutralized as soon as they come in contact with the respiratory passages. The increase in the chlo-

TABLE I
Reactive Compounds of Common Elements

Bromine	Oxygen difluoride
Calcium oxide	Ozone
Chlorine	Phosgene
Chlorine dioxide	Phosphine
Chlorine trifluoride	Phosphoric acid
Fluorine	Phosphorus
Hydrazine	Phosphorus pentachloride
Hydrogen chloride	Phosphorus pentasulfide
Hydrogen peroxide	Phosphorus trichloride
Hydrogen sulfide	Sodium hydroxide
Iodine	Sulfur chloride
Lithium hydride	Sulfur dioxide
Nitric acid	Sulfur pentafluoride
Nitrogen dioxide	Sulfuric acid

Useful biologic or excretory TLVs unlikely

TABLE II
Mineral and Insoluble Dusts

Amorphus silica	Portland cement
Asbestos	Quartz
Carbon black	Soapstone
Fibrous glass	Titanium dioxide
Graphite	Tremolite
Iron oxide	Inert dusts
Mica	

Useful blood or urine TLVs dubious

ride or nitrogen content of the blood or urine caused by inhalation of these gases at threshold limit concentrations would be negligible, and it is safe to say that biologic or excretory TLVs for most of these substances are not practicable.

Another 13 inorganic substances comprise the insoluble dusts, which are largely retained in the lungs, and whose effects are mainly confined to that organ (Table II). They include silica, asbestos, mica and other minerals. While some solution occurs, and urinary silica studies have been made of silica-exposed workers,[4] these substances on the whole do not appear good candidates for biologic or excretory TLVs, except perhaps if analysis of lung tissue is considered.

A third group of four inorganic substances consists of metals and metallic compounds which exert primarily local effects on the lungs or upper respiratory passages, and which are poorly excreted in the urine (Table III). In this group we may put beryllium, chromium and vanadium.

A fourth group of 12 substances includes compounds which also have largely local effects, but which contain components that are freely excreted (Table IV). In this group are included many arsenic compounds, nickel, hydrogen bromide, and a number of inorganic fluorides. Whether the latter belong in this group or in the first-named depends largely on the air TLV. HF, at 3 ppm or 2 mg/m^3, represents a quantity of fluoride readily measurable in urine. On the other hand, a concentration of 0.1 ppm, the TLV for fluorine, is probably too low to be definitely reflected in an increased fluoride excretion, especially if the worker consumes fluoridated water.

Group number five consists of four substances, representing three heavy metals, which are classed as systemic poisons that are poorly excreted (Table V). Some would consider lead as rather readily excreted; the fact that levels of lead in excess of 1 mg per liter of urine are seldom found prompts its inclusion in the "poorly excreted" group.

On the other hand, a blood lead TLV is in wide use, and blood manganese has been suggested as a good technique for evaluation of exposure to this metal.

In a sixth group are listed some 15 substances that can be classed as systemic poisons which are freely excreted (Table VI). These include other arsenic compounds, fluoride, mercury, uranium and cyanide. Concentrations of many of these of several mg per liter of urine have been reported numerous times in the literature. It seems logical to presume that, of all the inorganic substances, these are the ones best suited to a list of urinary TLVs. On the other hand, it is probable that blood analysis is not as applicable as to the preceding group.

A seventh group contains three stable gases which are probably eliminated through the lungs and breath, and possibly blood, TLVs may well be

TABLE III
Substances with Local Effects, Poorly Excreted

Beryllium	Ferrovanadium
Chromium	Vanadium

Urinary TLVs of questionable value

TABLE IV
Substances with Local Effects, Freely Excreted

Arsenic	Nitrogen trifluoride
Boron trifluoride	Selenium hexafluoride
Hydrogen bromide	Sulfuryl fluoride
Hydrogen fluoride	Tellurium hexafluoride
Nickel	Zinc chloride
Nickel carbonyl	Zinc oxide

Urinary TLVs should be useful

TABLE V
Substances with Systemic Effects, Poorly Excreted

Cadmium dust	Lead
Cadmium fume	Manganese

Blood TLVs more applicable than excretory limits

practicable; certainly they are for carbon monoxide, by far the most important member of this group (Table VII).

There remains an eighth group, containing some 17 substances, for which inadequate data are available to the writer to permit even an estimate as to whether or not blood or excretory TLVs would be practical (Table VIII). Included are such metals as cobalt, and silver, and compounds such as ammonia and diborane.

I will not attempt a similar classification of the 300-odd organic compounds which comprise the remainder of the TLV list. A few groups, however, may be mentioned.

Many of the aliphatic hydrocarbons and chlorohydrocarbons are little metabolized and relatively insoluble in blood. Breath analysis is the most promising method of evaluation, and breath TLVs could probably be established for some of these.

Some of the volatile alcohols and ketones are also excreted to a high degree in the breath. Since these compounds are water soluble, they are also found in relatively high concentrations in the blood, and may appear in the urine in detectable amounts. According to available data, TLVs for methanol in blood, breath and urine, and possibly also for formate in urine and blood as a methanol metabolite, might be useful.[5]

Many organic compounds contain distinctive elements: examples include heavy metal alkyls, and aliphatic bromides and iodides. Blood bromide determination is a recognized method of evaluating methyl bromide, for example.

The benzene ring appears quite resistant to metabolism, and benzene and many of its derivatives are largely excreted as phenols or other identifiable compounds. Urinary TLVs based on phenols would seem to be feasible for benzene, several chlorinated benzenes, aniline, nitrobenzene and parathion and some other organic phosphate insecticides, to name only a few.

Reliability of urinalysis

A great deal has been written about the erratic results obtained in the analysis of urine for industrial poisons. A favorite target is the spot urine sample. An extreme, but characteristic, comment on the variability of the excretion of lead over short periods is the following, from a recent paper:

TABLE VI
Substances with Systemic Effects, Freely Excreted

Antimony	Mercury
Arsine	Molybdenum
Calcium arsenate	Selenium
Cyanide	Stibine
Fluoride	Tellurium
Hydrogen cyanide	Thallium
Hydrogen selenide	Uranium
Lead arsenate	

Urinary TLVs should be most useful

TABLE VII
Stable Gases, Eliminated in Breath (?)

Carbon monoxide
Nitric oxide
Sulfur hexafluoride

Blood and/or breath TLVs should be applicable

TABLE VIII
Miscellaneous Substances

Ammonia	Osmium tetroxide
Barium	Pentaborane
Boron	Platinum
Cobalt	Silver
Copper dust	Tantalum
Copper fume	Tin
Decarborane	Yttrium
Diborane	Zirconium
Hafnium	

Inadequate information to predict usefulness of biologic or excretory TLVs.

> *"It is apparent that the results of a single voiding of urine are in themselves meaningless, regardless of whether or not, the specimen is collected at some specified time, expressed as rate of excretion or adjusted to either a constant specific gravity or creatinine concentration."*[6]

Now it is granted that the analysis of a spot urine sample may give quite a different result than 24-hour sample or a series of short samples. A similar comment might well be made about air samples.

During the past 20 years we have analyzed for lead on the average, in excess of 1000 urine samples a year. I, personally, have carried out several hundred such determinations; have supervised the analysis of a few thousand more, and

have scrutinized the results and passed on their interpretation for most of the remainder.

On the basis of this experience I do not hesitate to challenge the validity of the statement just quoted. In my opinion, a urinalysis which showed 0.2 mg or more of lead per liter can have only one of four meanings:

1. Significant absorption — not necessarily enough to cause intoxication, but considerably more than is the lot of the average citizen.
2. Contamination — which can occur during collection, storage or analysis of the sample.
3. Incompetence — of laboratory or analyst.
4. Chelation — through administration of EDTA or a similar agent.

On the other hand, a result within the normal range (less than 0.08 mg/liter) can occur (rarely in our experience) in a spot sample from a worker with substantial exposure.

Thus in our opinion a high urinary lead value is never "meaningless" and a low result merits that characterization only occasionally.

The group of substances that I have indicated as the best candidates for urinary TLVs does not contain lead, but does include some arsenic compounds, fluoride, mercury and uranium. Recent industrial hygiene literature is silent on the reliability of urinary arsenic determination except for the observation that high values may result from ingestion of certain sea food.[7] Most papers on fluoride absorption and intoxication seem to take it for granted that urinary fluoride is a good index of exposure; the only disagreement is as to what limit of fluoride in urine is safe for prolonged periods.

With mercury and uranium, however, a number of investigators hold that correlation of urinary excretion with exposure or intoxication is so poor that urinalysis for these elements is, at best, of limited value, and at worst almost useless, for either preventive or diagnostic purposes. The following quotations, from a number of sources, reveal this point of view insofar as mercury is concerned.

"Individual findings, or the findings on small numbers, cannot be used to determine intensity of exposure nor the presence of mercurialism."[8]

". . . one invites great possible error in attempting to correlate exposure and content of urinary mercury on only one occasion."[9]

"Studies of human excretion have led to the conclusion that a high value is of diagnostic significance only when symptoms and signs of poisoning can be demonstrated."[10]

"Levels of mercury in the urine show little or no correlation with manifestations of poisoning. There appears to be no level . . . below which symptoms cannot occur."[11]

"Those investigators who have studied the subject are in almost unanimous agreement that there is poor correlation between the urinary excretion of mercury and the occurrence of demonstrable evidence of poisoning. This . . . means, inter alia, *that studies of mercury in urine are of limited value in preventive programs."*[12]

"Indeed the evidence seems to be growing that possibly the majority of clinical cases have a lower level of excretion than found in nonaffected workers."[13]

These quotations do, indeed, paint a dismal picture of the value of urinalysis for mercury, and the possibility of establishing a useful excretory TLV for this metal. It is not so much the statements themselves — certainly the claim that a test is of "limited value" can hardly be denied — but the mere fact that all these investigators deemed it necessary to include such comments in their reports is the discouraging aspect.

If the situation is as described, however, and there is, as is claimed, virtually unanimous agreement to that effect, one may be permitted to wonder why it was necessary to rediscover, in 1967, a fact that had already been established, in 1950.

Our own experience does not, in my opinion, bear out these pessimistic warnings. In Figure 1 the urinary mercury levels of three workers in a plant in Massachusetts over a period of nearly five years are charted. These men have consistently shown the highest values of any of the employees

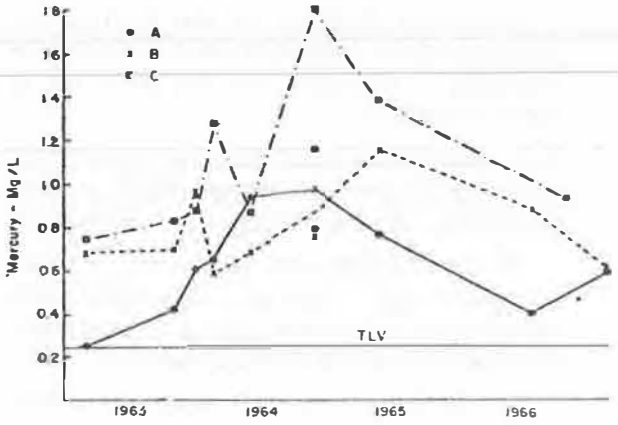

Figure 1 — Urinary mercury levels for three workers.

of the company. And, contrary to what you might believe from the quotations just read, both observation of their jobs and repeated air tests have confirmed the fact that their mercury exposures exceed those of all their co-workers; and the exposure of worker C exceeded that of B and A.

While there is considerable variation among the points, there are no values below 0.25 mg/liter, which we have used as the threshold limit, and only a few less than twice this level. In other words, every result indicates a substantial mercury exposure, and in most instances, an excessive one, by our standards. Not that there are no inconsistencies. The samples marked "V," were taken in July 1963 after a two-week vacation; one value decreased significantly, one increased markedly, and one is unchanged, in comparison with the results obtained six weeks previously.

Now it is true that I have cheated a little in preparing the curves; I did leave out a few values. In Figure 2, the uncensored curve for worker B is shown, with all analyses included. This is more like the picture you would expect from the literature I have cited, since in addition to the high values, there are three results showing negligible to little exposure, all well below 0.2 mg/liter. Let us take a close look at these low results.

The first one, marked with a "K," represents an aliquot of one of the samples we analyzed, that was sent by the employer to a clinical laboratory, which found only a trace of mercury. Examination of the laboratory's report revealed that they knew little (and possibly cared less) about the microdetermination of mercury.

The employer was still unconvinced, however, and checked up on us again, this time sending aliquots to Morris Jacobs. His results too were lower than ours, as the point marked "J1" shows. Inquiry at the company, however, disclosed the fact that the samples had stood around some time at room temperature before being shipped to Dr. Jacobs. While there is some controversy over the effect of urine decomposition on mercury recovery, the consensus is that there is likely to be considerable loss, possibly through volatilization of some organic mercury compound.[14]

When the next samples were collected, we ourselves sent aliquots, with suitable precautions, to Dr. Jacobs, and this time his results checked well with ours (J2).

Finally the third low result "V" was obtained after the subject had been away from work for nearly four weeks.

Thus these three low values (and five others from the other men) were due, not to the capriciousness of the human kidney, but to faulty analysis, incorrect handling of the sample, and improper timing, respectively.

What about the "almost unanimous" conclusion that there is little or no correlation between levels of mercury in urine and mercurialism? Table IX lists the data from some 12 post World War II reports which describe or list a total of 112 cases of mercurialism, including urinary mercury results.

It is reasonable to assume that if all mercury workers are considered, low urinary mercury levels will exceed high ones by a fair margin. Of over 1100 urine samples analyzed by our laboratory,

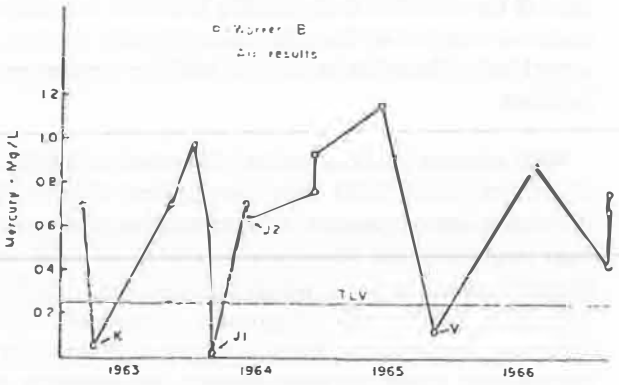

Figure 2 — All urinary mercury values for one worker.

TABLE IX
Mercurialism and Mercury Excretion

Reference	Urinary Mercury – mg/liter or mg/24 hours			
	< 0.2	0.2-1.5	0.5-1.0	> 1.0
	Number of Cases			
Buckell (1946)[15]	2	8	13	16
Bidstrup (1951)[16]	6	7	4	9
Friberg (1953)[9]	—	1	1	—
Bell (1955)[17]	1	—	—	—
Woodcock (1958)[18]	—	1	—	—
Benning (1958)[19]	2	1		1
Kazantzis (1962, 1965)[20,21]	—	—	1	6
Mastromatteo (1965)[22]	3	1	2	1
Parameshvara (1967)[23]	—	—	2	—
Bistrup (1964)[24]	1	6	6	7
Massachusetts (1940 to 1961)	—	—	1	2
TOTAL	15	25	30	42

over 57% contained less than 0.2 mg/liter, while in only 3% was the mercury content above 1 mg/liter. If these figures are representative, the data in Table IX would tend to indicate a high degree of correlation between concentrations of mercury in urine and signs and symptoms of mercurialism. However, there are a number of cases with levels below the suggested threshold limit of 0.25 mg/liter. Careful examination of the reports suggests that at least five of these values should be rejected, two because of unreliable analysis[19] and three because of the interval between exposure and sample collection.[22]

With most of the remaining ten instances, information is lacking to permit a definite judgment of the reliability of the findings. Certainly in many cases which come to medical treatment there is a considerable interval without exposure, before diagnostic procedures are initiated. Faulty handling of the sample as well as errors in analysis can occur; moreover, and I apologize to any physician in the audience, there is such a thing as wrong diagnosis.

It is possible that those who despair of relating urinary mercury to intoxication are subconsciously compairing this determination with a test for a pathogenic organism, whose presence is, by definition, evidence of disease? Or perhaps some may confuse it with measurements of properties such as loss of cholinesterase activity, which is an index of the *effect* of a toxic agent, and can be expected to correlate rather closely with signs and symptoms of intoxication.

Suppose we try out Don Cummings' suggestions of both primary and secondary thresholds, in the cases of lead and mercury in urine. For the sake of simplicity we can set the primary threshold for each at 0.2 mg/liter without being too far off. For lead the secondary threshold would be about 0.8 mg/liter,[25] while for mercury it could be something like 4 mg/liter. Remember that the secondary threshold represents a level which will inevitably lead to poisoning, if the exposure is continued over a period of years, and which will rapidly produce symptoms in a large proportion of cases.

The incidence of intoxication, assuming a symmetric distribution relative to the logarithm of the urinary concentration, and the assumed values of the primary and secondary threshold of these metals is shown in Figure 3. A much greater increase in mercury excretion is necessary to cause a given rise in the probability of intoxication, than is the case with lead. The concentrations resulting in a 50% probability of poisoning, according to these curves, are 0.4 mg/liter for lead, and about 0.8 mg/liter for mercury, in spite of the fact that the primary thresholds are the same.

The result is that the concentration of lead in urine will appear to correlate more closely with

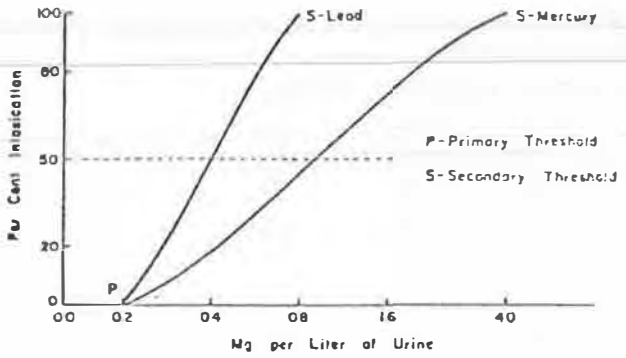

Figure 3 — Intoxication probabilities for lead and mercury.

intoxication than is the case with mercury. Does this mean that the former is superior as a diagnostic and exposure test? This point of view can be argued. On the other hand, the allowable margin of error is much greater in the case of mercury. An inaccurate analysis, or an abnormal result due to the vagaries of the excretion process, is more likely to lead to serious misinterpretation of a lead result, than of one for mercury.

It has already been indicated that the value of urinalysis for uranium has been questioned, even more vigorously than that for mercury.[26]

It is of interest to note that both uranium and mercury, especially the former, are kidney poisons. It has been suggested that prolonged exposure to either impairs the ability to excrete these metals, but the data on human exposure substantiating this theory are not very convincing.[13,27]

If biological and excretory threshold limits are established, it will not be enough to merely give values representing concentrations in the medium in question, as is done with atmospheric limits. The time factor is of major importance, and varies for different substances. In some cases (e.g., benzene) elimination from the system is virtually complete within a few hours; in others (such as lead) many weeks of exposure are needed to build up equilibrium concentrations. It is interesting to note that blood and urine levels do not necessarily show similar relationships to time of exposure with some substances, such as lead and probably mercury.

Another complication relates to the method of expressing results. Urinary excretion may be given in several ways, none of them completely satisfactory. In my opinion some adjustment must be made for very dilute samples, especially if spot samples are taken. If such an adjustment is made, the results of different samples may be the same or vary by as much as a two-fold difference, depending on whether specific gravity, creatinine or the 24-hour excretion method is used. If unadjusted values are included, variations as great as six-fold will not be uncommon.

While I have little experience with breath analysis, it seems likely that similar complications may arise when that technique is employed.

To the question — "Are excretory and biologic threshold limits feasible?" — I would not only answer "yes" but would say that they are inevitable for many industrial hazards.

The fact is, of course, that in effect biologic and excretory threshold limits are in use today. They are the levels selected by each investigator, however, based on his own experience or derived from a tedious search of the literature, and not the recommendations of a committee. There are both advantages and drawbacks to promulgation of threshold limits by committees, as has traditionally been done for atmospheric TLVs. At their best, such values represent the consensus of a group of knowledgable and unprejudiced experts; at their worst, they may result from the biased and uninformed opinion of a single member (or even an outsider) with the other members of the committee tacitly agreeing, due to lack of either interest or knowledge.

Recommendations from a committee usually carry more weight with the layman than do those of a single authority, no matter how eminent. Moreover, they have the advantage, in theory, at least, that the same criteria are used for all substances. No one individual is a real expert on all hazards, and different authorities may use quite different standards in arriving at their recommendations.

It may well be that, as new analytical techniques are developed, blood TLVs may become relatively more important in comparison with those for urine and breath. In the present state-of-the-art, however, the latter are more practicable for most substances.

Further studies are needed, however, of the relationship between blood and urine, and possibly blood and breath, concentrations. The fact that with some of the heavy metals blood and

urine levels seem to bear little relationship to one another is quite discomforting to those of us who feel that these measurements are useful indices of exposure. If we have a high air concentration but a low urine value, we can postulate that the air level does not constitute the true exposure. If we have a high urine value but no symptoms of intoxication in the worker, we can say, "wait a while" if the substance is a chronic poison, or point to the variations in susceptibility among workers. If the blood value is high and the urine level low, or vice versa, we have no very good alibi.

The relationships between time of exposure and length of exposure and results require further study in many instances. Standardization of methods of expressing the findings is desirable. Development of secondary thresholds which will inevitably lead to intoxication, would be of great value whenever possible. But the main task is the establishment of the primary limit, which, to paraphrase the words of Don Cummings, expresses the concentration which a man can tolerate for a working lifetime without incurring a disabling injury.

Acknowledgment

The urinalyses charted in Figures 1 and 2 and referred to in the text were performed under the supervision of John P. Fahy.

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Hervey B. Elkins is widely recognized and honored for his numerous significant contributions to industrial hygiene

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Dr. Elkins received the American Conference of Governmental Industrial Hygienists' Meritorious Achievement Award in 1961. He was made a Corresponding Member of the Czechoslovak Medical Society in 1965, and in 1966 he received the first Leslie Silverman Award of Scientific Achievement presented by the Massachusetts Local Section of AIHA. He was again honored by ACGIH in 1982 when he received the Herbert E. Stokinger Award.

He has been very active in the committee work of both AIHA and ACGIH over the years. Hervey served as the Chairman of the Chemical Substance TLV Committee from 1977 through April 30, 1980. He has over 50 technical publications to his credit and the book *Chemistry of Industrial Toxicology*. Best known for his work on analytical methods and on the setting of acceptable or permissible exposure levels, he also has demonstrated a breadth of interest and knowledge extending into all aspects of industrial hygiene.

Criteria and procedures for assessing the toxic responses to industrial chemicals*

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This working paper for the first ILO-WHO meeting on international limits for air of workplaces 1) sets forth the criteria and procedures that have been used for the past 25 years by the Committee on Threshold Limit Values (TLVs) of the American Conference of Governmental Industrial Hygienists (ACGIH) for the development of TLVs; 2) presents the *modus operandi* of this Committee; 3) reviews and evaluates the experience of the suitability of these limits in American industry; 4) calls attention to the existence and usefulness of other American air limits; and 5) takes brief note of criteria and procedures used elsewhere.

Historical

The TLV Committee of the ACGIH was established in 1941 and was composed of 6 nationally recognized industrial hygienists and toxicologists not associated with private industry. The first list comprising 144 substances with their maximal allowable concentrations (MAC) was promulgated in 1946 as recommendations to industry.[1] A prior list of 45 substances had been published by the Division of Industrial Hygiene of the U.S. Public Health Service in 1943. Although the term MAC was employed, it referred to a time-weighted average concentration, not a maximal ceiling value. Also, just prior to the appearance of the ACGIH list, background information on the limits of all substances was published in 1945.[2]

The ACGIH Committee met annually to revise and add to the list of recommended values. The values so recommended represented the concensus of the opinions of individuals with long experience and continuing practice in industrial hygiene. No formal documentation of these values was begun until 1955. The early documentations were for Committee use only as an aid in revision. A published documentation by the Committee appeared in 1962[3] and comprised 267 substances. A second revised edition appeared in 1966 and included somewhat under 400 substances. Supplements now appear annually as new substances are added or as revisions in the list are made. These are available to subscribers of the Documentations from the Secretary of the ACGIH at 1014 Broadway, Cincinnati, Ohio 45202.[A]

The Committee as it is now constituted, consists of 15 members, that includes a chairman and a secretary. Its members are actively engaged in control programs in the 10 most highly industrialized states and cities of the USA and in one province of Canada. All disciplines related to the Committee's objectives are represented — toxicology, engineering, industrial hygiene, analytic chemistry and medicine. Members of eminence in specialty areas serve as chairman for its 5 subcommittees, Insoluble Dusts, Economic Poisons, Hydrocarbons and Halogenated Compounds, Oxygenated Organic Substances, Miscellaneous Organic Compounds, and Inorganic Compounds.

The criteria and procedures, as well as other actions of the American TLV Committee are governed by the following philosophy: Threshold Limits for industrial atmospheres are based on the premise that, although all chemical substances are toxic at some concentration experienced for a period of time, a concentration exists for all substances from which no injurious effect will result no matter how often the exposure is repeated. A similar premise applies to substances whose effects are limited to irritation, narcosis, nuisance or other forms of stress. This philosophy thus differs from that applied to substances possessing ionizing radiation for which on current concepts there is no threshold; all exposures, however small, have some associated risk to health. Accordingly, the basic premise applying to chemical

* Presented at the first ILO/WHO meeting on international limits, June 1968.

[A] Currently from the Publications Office, ACGIH, 6500 Glenway Ave., Bldg. D-5, Cincinnati, OH 45211.

substances strictly speaking does not admit those chemicals with strong radiomimetic potential, chemical free radicals or substances with free-radical potential, substances like ozone, peroxy and certain epoxy compounds. This philosophy is to be compared with that of the USSR which is "regardless of the value set, the optimal value and goal (the norm) to be sought is zero concentration".[4] *The criteria and procedures to be in accord with these two differing philosophies must obviously differ.*

Other American industrial air limits

In addition to the TLVs recommended by the ACGIH, there are other groups engaged in developing air limits for American industry. The so-called Z-37 Committee of the U.S. of American Standards Institute, composed of about 30 members, many of whom are directly associated with industry but have liaison with governmental agencies and universities, is currently promulgating multiple limits for industrial work places. Included are acceptable concentrations for repeated daily, 8-hour, time-weighted exposures, acceptable ceiling concentrations, short-term exposure limits, and minimal levels of sensory detection and avoidance of discomfort. Physical, chemical, and toxic properties and analytic sampling procedures are given for each substance which is published as a separate.

The State of Pennsylvania, Department of Health, has published regulations regarding permissive limits for short-term (5-, 15- and 30-minute) exposures in industry.[5] Documentation of the approximately 100 substances is available.

Emergency exposure limits are recommended to the military from time to time on a 'need' basis by a committee of the National Research Council. The criteria for these limits differ from all other industrial air limits in that the limit has no incorporated factor of safety and may result in a response provided that this response is reversible and does not prevent self-rescue. These limits are designed for accidental exposure, an event rare in the life of an individual.

Definition of criteria and standards

Criteria, as used here, refer to those measures that are used to define the response from exposure to adverse constituents in industrial air and which may serve as a basis for standards for the air of work places. Inasmuch as criteria vary in sensitivity from highly sensitive changes in enzyme activity and higher nervous functions to grosser changes such as body weight and food consumption, so do standards on which they are based.

Classification of criteria

Examination of the more than 400 substances in the 1968 threshold limits list reveals (Table I) that rather simple and unsophisticated criteria were used for the most part to develop ACGIH TLVs. For convenience they may be classified into four groups: morphologic, functional, biochemical

TABLE I
Classification of Criteria for ACGIH TLVs
Applicable to Man and Animals

Applied Criteria
Morphologic
Systems or organs affected: Lung, liver, kidney, blood, skin, eye, bone, CNS, endocrines, exocrines
Carcinogensis
Roentgenographic changes
Functional
Changes in organ function: Lung, liver, kidney, etc.
Irritation: Mucous membranes; epithelial linings; eye; skin; narcosis; odor
Biochemical
Changes in amounts: Biochemical constituents including hematologic.
Changes in enzyme activity.
Immunochemical allergic sensitization.
Miscellaneous
Nuisance: Visibility; Cosmetic; Comfort; Esthetic; (Analogy)
Potentially Useful Criteria
Teratogenesis
Mutagenesis
Altered reproduction
Body-weight changes
Organ/body weight changes
Food consumption
Behavioral changes
Higher nervous functions
Conditioned & unconditioned reflexes — learning
Audible and visual responses
Endocrine glands
Exocrine glands
Changes in isoenzyme patterns.
Radiomimetic effects.

TABLE II
Distribution of Criteria Used to Develop ACGIH TLVs through 1968 for 414 Substances Exclusive of "Inert" Particulates and Vapors

Criteria	Number	%*
Organ or organ system affected	201	49
Irritation	165	40
Narcosis	21	5
Odor	9	2
Organ function changes	8	2
Allergic sensitivity	6	1.5
Cancer	6	1.5
Biochemical changes	8	2
Fever	2	0.5
Visual changes (Halo)	2	0.5
Visibility	2	0.5
Taste	1	0.25
Roentgenographic changes	1	0.25
Cosmetic effect	1	0.25

* Number of times a criterion was used of total number of substances examined × 100, rounded to nearest 0.25%. Total percentages exceed 100 because more than 1 criterion formed the basis of the TLV of some substances.

and miscellaneous. (Reasons for the practical utility and satisfactory performance of these simple criteria will be given beyond.) Included also in Table I are some criteria that may be found useful in special cases (teratogenesis, mutagenesis, reproductiveness) or valuable, if added effort is subsequently expended in determining their toxicologic (physiologic) significance (changes in endocrine and exocrine gland function, behavioral changes).

Distribution of criteria used for TLVs

Table II shows nearly half of the TLVs recommended to date to have been based upon changes in some organ or organ system. Irritation formed the next largest number, 40%, and narcosis, 5%. All other 11 categories together involved about 10% of the listed values.

Procedures used in developing TLVs

Table III shows that of the five categories of procedures employed to date (1968), 38% made use of the responses of the industrial worker, and that chronic animal inhalation studies were employed about half as frequently (20%). It is interesting to note that the development of TLVs by analogy accounted for about one-quarter of procedures used. Human volunteer studies were responsible for about 1 in 10 of the limits, and the remaining animal procedures other than chronic inhalation accounted for but about 1 in 14 limits. Stated in another way, about half of the limits have been based on procedures involving man himself.

Evaluation of criteria and procedures by TLV Committee — modus operandi

Proper evaluation of the data obtained from the various procedures is recognized to play a highly important part in the development of the TLVs. Prime consideration is given to data obtained through industrial experience when both the environment and the worker have been well monitored; related information from animal studies is used as substantiating evidence. For those substances for which sensory (organoleptic) effects, particularly irritation of the mucous membranes, are the dominant response, human data only are acceptable; animals are useless for recording such effects; only for those substances with strong irritant or corrosive properties are animals suited. Following receipt of such data they are referred to the attention of the appropriate subcommittee for review, evaluation, and combination with whatever relevant information is available in the literature or *is known through the personal experience of the Committee member.* A tentative justification for the selection of the limit is written and submitted to the plenary Committee for study, modification, and adoption. It has now become customary for the Chairman, prior to the meeting of the plenary Committee to discuss the basis for

TABLE III
Distribution of Procedures Used to Develop ACGIH TLVs through 1968 for 414 Substances Exclusive of "Inert" Particulates and Vapors

Procedure	Number	% Total
Industrial (human) experience	157	38
Human volunteer experiments	45	11
Animal, inhalation-chronic	83	20
Animal, inhalation-acute	8	2
Animal, oral-chronic	18	4.5
Animal, oral-acute	2	0.5
Analogy	101	24

changes or new additions to the TLV list before a meeting of interested industrial representatives and to receive comments and suggestions with supportive data from such sources. A "Notice of Intended Changes" is promulgated nationwide to interested agencies and associations for their review at least one month prior to the meeting. If the change is accepted, the substance with its limiting value is placed in a special list, "Notice of Intended Changes," in the TLV annual booklet, where it remains as a tentative value for a period of at least 2 years. During this time, interested parties may submit additional information to the Committee for its consideration.

Procedures suited to animals

The procedures, as well as the principles underlying them, are set forth in an ACGIH publication.[6] The basic animal procedure is the large-scale, long-term inhalation toxicity study. The large scale permits daily exposures (40 hours per week) of statistically significant numbers of animals of multiple species; the long-term aspect permits periodic sampling of the animals for the various routinely used criteria as well as those 'tailored' to the particular toxicologic character of the substance under test. Long-term studies customarily have a duration of at least 1 year, but may extend as long as 2.5 years, essentially the toxicologically useful lifetime of the smaller laboratory species. The long-term inhalation study is considered essential for the development of data appropriate for those TLVs that are based on chronic, slowly developing disease; acute or short-term studies can supply data only for those substances such as sulfur dioxide, cyanide, carbon monoxide, whose sole determinant for the TLV is the fast-acting response. Inasmuch as it cannot usually be predetermined whether a new substance is devoid of chronic effects, the long-term study is essential.

A standard operating procedure allowed by the large-scale inhalation chambers is the use of tumor-susceptible strains of known tumor incidence. Such strains permit the determination of the tumor-accelerating or inhibiting potential or substances by the most sensitive method known because being already susceptible, the animal is responsive to the slightest tumorigenic stimulus.

Large-scale chambers also permit the exposure of additional groups of small species for the evaluation of the effect of simultaneous stresses; groups imbibing alcohol, groups in an exercise cage, or groups for other special purposes. Such additional information furnishes valuable guides for estimating the safety factor to be incorporated in the TLVs based on animal studies.

Good procedure also calls for the use of multiple species on the principle that animal data are after all merely a substitute for data preferably obtained from man. Because of recognized, often wide differences in species response, the use of several species is resorted to on the basis of increasing the probability of finding a species that mimics the human response. The use of monkeys, especially Old World monkeys, an increasingly common practice, is an important step in this direction. The annoying problem of 'translating' animal data to man can be readily resolved, however, if the level at which a single critical response occurs in animals is determined in man; thus the species difference factor may be obtained.

Multi-level exposures are standard operating procedure. A minimum of two levels should be studied; three exposure levels are preferable, however. One of these studies should be made at an exposure level at which frank effects develop, so that the chronic animal response can be precisely delineated. A second level should be tested in which either no response from the chronically inhaled test substances becomes manifest or only minimal, borderline or questionable changes occur in a small percentage of the animals exposed. A third study could be advantageously performed at a level at which no responses become manifest — a "no-effect" level. The spacing of the exposure concentrations to meet these level requirements varies according to the toxicologic characteristic of the test compound. It is not uncommon to find that the "no-effect" level is one-fifth to one-tenth, or less that at which minimal effects occur. The magnitude of the spread between the two levels depends upon the rate of change in exposure level (dosage) or the slope of the response curve. Some estimate of the slope may be gained from the observed spread between the level giving frank effect and that giving minimal change. Extrapolation of the slope should permit in most cases a fairly good estimate of the level to select for test of the "no-effect" level. Error will occur in the estimate if the log dose-response relation departs significantly from linearity, as it is apt to do at the extremes. This is the reason the TLV Committee

prefers data from a study actually performed at the expected "no-effect" level rather than rely on an estimate from the frank-effect and borderline-effect levels, which may be imprecise.

"No-effect level"

There is a growing tendency among experimental toxicologists to refer to a level of an administered dose of the substance that produces no demonstrable effect as a "no-effect" level. This designation, however, is intimately tied to the criteria used for its determination. Clearly, a "no-effect" level based solely on no changes in body weight or organ weight to body weight ratios or in tissue morphology, might prove to be an "effect level," had more subtle and incisive variables such as changes in enzyme activity and intermediary metabolites, respiratory function and hematologic variables been studied in detail. Inasmuch as the prime objective of experimental studies directed toward threshold limit evaluation is to reveal the subtle as well as the gross changes following administration, it is readily seen that the "no-effect" level is a relative term. In view of the present-day standards for safeguarding worker health, investigators should not be content to use the more crude evaluation procedures of the past for determining "no-effect" level, but should employ the more delicate procedures of present-day clinical chemistry. Preferably, these procedures should be so chosen as to be applicable ultimately to industrial workers. For example, the use of serum ornithine carbamoyl transferase is a superior test of liver dysfunction.

The foregoing assumes that the usual basic procedures of animal toxicology are used in obtaining data on body weight, lung to body weight ratios, hematology, histology, etc., as indicated in Tables I, II. Supplemental studies and procedures should be considered if indicated by chemical structure or by previously observed unusual toxic response. In such cases resort should be had to pertinent procedures related to the "Potentially Useful Criteria" given in Table I for elucidation and characterization of the response.

There are a number of more sophisticated, highly sensitive biochemical tests, which have been described in some detail.[7] Since this presentation was given (1963), several sophisticated biochemical indicators of toxic response have not only appeared, but have been confirmed as such, eliminating doubt of their toxicologic significance. Some examples follow. Glucose-6-phosphate dehydrogenase (G-6-PD) of the red blood cell is useful in determining the degree of response to lead.[8] This assay procedure may also be used for detecting early fibrotic changes in the lung as a replacement for the more difficult test for collagen[9] in newly formed connective tissue. A parallelism has been found between the activity of G-6-PD and newly laid down collagen. Thus G-6-PD activity may be used to detect the earliest tissue changes in the pneumoconioses and other situations where fibrosis arises.

Similarly the urinary biochemical constituent, delta aminolevulinic acid (dALA), has now been confirmed in several countries as the most sensitive and reliable guide yet found for estimating the effects of lead on porphyrin synthesis.[10] dALA may also be used for detecting early effects of other substances that affect porphyrin synthesis at the levulinic acid stage. The procedure has now been modified so as to permit large numbers of determinations to be made daily.

Changes in the isozyme patterns of lactic acid dehydrogenase in the serum have shown good correlation with clinical signs of early injury in mercury workers;[11] fraction 5 shows unmistakable increases (5- to 9-fold) only in those workers with clinically evident or preclinical mercury poisoning.

It cannot be too strongly emphasized, however, that, if such highly sentitive tests as changes in enzyme and isozyme patterns or in behavioral response are used, follow-up studies must be made on a long-term basis to establish the *toxicologic* significance of such changes for the host; otherwise intelligent interpretation for TLV development is impossible. An example may suffice: If a certain test substance is found to reduce catalase activity, it must be *further* shown that this reduction is deleterious for the total body economy. This enzyme, as well as numerous others, exists in excess beyond usual stress demands so that inhibited activity, even of moderate degree, may be without toxicologic (health) significance, and hence cannot serve as a TLV criterion.

Procedures adaptable to man

Man, human volunteers and industrial workers, constitute the only reliable source of information

for TLV Committee use in determining thresholds of sensory response for "fast-acting" substances and substances that produce irritation, nausea, narcosis, allergic sensitization, effects on vision, odor, skin or hair color changes (Table I). If such information stems from human volunteers, test procedures should be so designed as to ascertain whether acclimatization (inurement) or sensitization are factors in the response. Failure to make repetitive exposures for these substances has resulted in erroneous judgments of response thresholds, and thus misleading, often overconservative, TLVs. Table III shows that 11% of the TLVs through 1968 were based on human volunteer studies.

Planned human experimentation can be used to establish a relationship between animal and human responses for those substances to which the chief response is nonsensory. Hospitalized volunteers with terminal disease not involving those organs and tissues known to be affected by the test substances may be exposed at or around the level at which the most sensitive response test in animals was positive. Such a procedure was used prior to the development of the air limit for uranium. It was found that man responded at a level 10-fold higher than that of the most sensitve species (the rabbit) as judged by the most sensitive test of uranium toxicity (urinary catalase). Thus a *known* minimal safety factor can be established. Interestingly enough, the uranium limits that were recommended in 1948 were based on conservative rabbit data, paid no heed to human data. Twenty-five years experience in the uranium industry, however, showed that the early limits were far too conservative and resulted in raising the limits in 1967 about 4-fold.

Industrial workers, if properly monitored both medically and environmentally, can constitute another important source of TLV information on both short- and long-term effects provided that exposure conditions are assessable. Table III shows that 38% of all TLVs through 1968 were obtained from observations made on industrial workers.

It should need no mentioning that human exposures are not to be permitted until animal studies have thoroughly characterized the nature of the response(s) and 'borderline' or 'no-effect' levels have been determined.

Why such a relatively large proportion of the TLVs has been derived from industrial experience becomes apparent if one considers the industrial hygiene practices of chemical manuafacturers in the U.S.A. It is customary procedure to initiate a hazard evaluation as soon as a new chemical begins to show promise of getting into pilot plant production. Hazard evaluations consist in determining the acute effects of the new compound by the various routes of industrial exposure, skin, eye, lung and mouth, in single or short-term administrations in small laboratory animals, usually rats and rabbits. If these toxicity tests indicate an acceptable hazard rating, and the compound shows promise for industrial production, more extensive, long-term tests in animals are performed. At the conclusion of these tests, human volunteer studies may be made if indicated. In the meantime, plant industrial physicians and engineers are making observations on the workers and their work place environment. Some TLVs so derived have been based on a decade or two of industrial experience, (acetone, butanol and several other alcohols, many halogenated hydrocarbon solvents, several hydrocarbon solvents, lead, mercury, etc). Clearly, *such procedures can yield indisputable data on which realistic TLVs can be derived,* unsurrounded by that uncertainty and doubt which requires incorporation of large safety factors, leading to wasteful overengineering of plant processes.

"Proof of the pudding is in the eating"

To the author's knowledge of more than a decade and one-half of close association with the TLV Committee, no significant injury to health has occurred where exposures have been kept within the limits recommended by the Committee. Seeming exceptions may have occurred in those who by reason of predisposition, genetic or otherwise, were unusually susceptible. This is in light of the fact that one-million individuals in the United States have been directly involved with the production and handling of chemicals, annually, untold numbers directly and indirectly involved in the use of chemicals. This record is mute testimony to the suitability of the selected values. The values that have been revised downward over the years have been those (e.g. phosgene, benzene, carbon tetrachloride) for which the Committee has had indications that the factor of safety was not sufficiently

large for the seriousness of the potential hazard. On the other hand, there have been other (e.g. arsenic, phosphine, uranium) whose limits have been revised upwards, when after long years of usage, surveillance has indicated the lack of need to impose such strict control.

Validation of TLVs

In recent years the Committee has entered into a second phase of activity — inquiry into the validity of the limits. The inquiry has taken the form of 'hearings' with the industrial representatives of various industries to learn firsthand the reaction of industrial physicians, industrial hygienists, and engineers to the practical, everyday working of the limits. Such hearings have been held with Committee members and representatives of the chromate, vanadium, uranium, and dynamite explosives industries among others, and the limits of safety have been documented from plant exposure and medical records. In some instances (the isocyanate industry) cooperative investigations with industry are leading to the identification of the complex problem of hypersensitivity and toxicity and in their proper relation to the TLV. It is the constant reevaluation of the limits, which zeros-in on the appropriate value that gives confidence in the validity of the TLVs. It should be noted also that these limits provide safety without overprotecting the worker or overengineering plant processes, practices which private enterprise can afford only at the expense of the consumer public which pays the increased cost of their product.

Tests for the detection of the hypersusceptible worker

In an effort to make the protection afforded by the TLVs all inclusive, clinical tests are being recommended that can be used in the preplacement job examination to screen out those individuals who by virtue of some genetic fault in metabolism hyper-react to certain industrial chemicals. ("Preface to TLV Booklet 1967".)

These tests are capable of detecting hypersusceptible workers who may not be protected by the Threshold Limit Values set by the ACGIH which are among the most widely used standards for safe levels of exposure to pollutants in the work environment. The tests are simple to perform, and their practical application in job preplacement examinations will screen out the hypersusceptible workers before onset of illness.

Predictive test for hypersusceptibility to hemolytic chemicals

This is a relatively simple blood test which determines a genetic fault in the red blood cells. The defect results in hypersusceptiblity to concentrations of hemolytic (red-blood-cell-destroying) chemicals in the factory atmosphere, including sulfonamides, aniline, naphthalene, and lead. Exposure to these and many other chemicals by hypersusceptible individuals can cause hemolytic anemia. Industries where this test would prove most beneficial include pharmaceutical factories, textile-dyeing plants, munition plants, rubber tire factories and those chemical industries manufacturing the basic chemicals for these plants.

A pretoxicosis test for carbon disulfide poisoning

This test involves an analysis that predicts abnormal responses to breathing carbon disulfide vapors. Hypersusceptible workers exposed to these vapors can develop polyneuritis, an inflammation of the nervous system. The test is particularly useful in the viscose-rayon industry.

The "serum antitrysin" test

This is a simple test for detecting a blood serum deficiency. The test establishes the extent to which the deficiency is related to an inherited tendency toward pulmonary emphysema. This test is useful in virtually any industry where irritant pollutants exist.

Tests under development

A fourth test, still under development, predicts hypersensitivity to isocyanates, which are chemicals used in the manufacture of foam rubber and other plastic products. Inhalation of these mists and vapors by hypersensitive individuals can cause a respiratory ailment with symptoms similar to asthma.

Criteria for international limits

It is apparent that the criteria just discussed for the TLVs of the ACGIH satisfy the underlying philosophic concepts of one geographic area only. These concepts may not and perhaps should not be acceptable elsewhere. More stringent criteria are naturally required by those countries whose philosophy has as its goal essentially a zero ex-

posure (e.g., USSR). Less stringest criteria may be satisfactory in those areas of the world with emerging industry.

Methods suggested by other countries for TLV development

Horvath and Frantik[12] (Czechoslovakia) have recommended in the interest of international standardization of animal procedures, a method of intercompound comparison whereby the degree of chemical difference is expressed as a partial coefficient of relative toxicity. Partial coefficients are the ratios of equally effective concentrations (or doses) of the test and standard reference substances. In final assessment the weight assigned to the individual partial estimate depends on how characteristic the response was of the substances under test as defined by the reference substance.

The authors recommend various technics for measuring changes in acute and chronic reflex and autonomic behavior in order to attain the necessary standardization and hence universal interpretation of results.

Although much can be said for standardization, the multiple comparison procedures offered by Horvath and Frantik seem unnecessarily involved and time-consuming. Moreover, it would seem that the selection of appropriate reference substances for comparison would pose real problems in many instances. Then too, all too readily, standardization yields to complacency on the part of the investigator and lack of interest to search further to ascertain and define those characteristics that typify the unique toxicologic properties of certain substances.

A short-cut method of arriving at approximate MACs has been proposed by a group of Leningrad toxicologists[13] faced with the problem of the annual introduction of mounting numbers of new industrial chemicals on the market. A number of equations are offered for each category of *a)* organic vapors and gases, *b)* organic substances of high boiling point (aerosols), and *c)* inorganic gases and vapors when toxicity data are available. When such data are not available, equations based on physicochemical data are offered. Required toxicity data for the equations consist of 2-hour LC_{50} values by inhalation, LD_{50} values by gavage, and changes in unconditioned reflexes after 40 minutes of exposure. By the ingenious use of logarithms and selection of arbitrary constants, the calculated MACs are remarkably close to those currently recommended in many instances. The difficulty lies in not knowing whether the item of concern is the one that the equation predicts correctly or does not.

Summary and conclusions

A review of the procedures and activities of the Threshold Limits Committee of the American Conference of Governmental Industrial Hygienists for the past 25 years reveals first and foremost that the TLVs have served their purpose well; with the possible exception of an occasional instance due to hyper-reactors, no reports of significant injury to health of industrial workers have come to the attention of the Committee, if worker exposure had been within the stipulated limits. This favorable history is attributed to three factors.

1. The paramount importance given to information derived from human exposure experience.
2. The continual re-evaluation of the limits in the light of continuing industrial experience and new informaiton, and revision, if safety factors appear of insufficient magnitude.
3. The personal knowledge and mature experience of the Committee members in industrial medicine, toxicology, hygiene, engineering and analytic chemistry in providing the necessary combination of talent to develop practical, protective limits for assurance of human health and reasonable comfort during a working lifetime.

The criteria forming the basis of the ultimate judgments are for the most part relatively simple and unsophisticated, but their particular merit is that they are tailored to the toxicologic requirements of the chemical substances. Thus standardization of criteria and procedures at best represents but the initial step in the toxicologic assessment of noxious substances for industrial air standards.

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Problems of setting occupational exposure standards — background*

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Setting occupational exposure standards involves many a knotty problem as is presented in the succeeding paper, but problems were also encountered prior to the general availability of such standards.

Dramatically described by Madeleine P. Grant[1] in her recent biography of Alice Hamilton are the criteria required to demonstrate the existence of excessive hazards before exposure standards became generally available. In 1910 Alice Hamilton needed factual evidence to support her belief that the exposure in a white lead carbonate plant was excessive and should be brought under control. At that time there were no occupational exposure standards for lead in this country. The evidence Hamilton required was that of authentic cases of lead poisoning. She did find records of 22 workers with symptoms sufficiently severe to need hospital care. How much better it would have been to have had an occupational exposure standard to serve as a criterion before the cases developed!

Another criterion that pointed to the presence of excessive exposures, before the availability of standards, was high labor turnover. Again referring to Alice Hamilton's experience, in one lead-smelting plant 5% to 50% of the workers were reported to have left the job every biweekly payday, presumably because of the excessive lead hazard.

It is to be recognized that even today injurious environmental conditions are still brought to light through development of cases of occupational disease and otherwise unexplained high labor turnover. But occupational exposure standards and the application of them provide a far more satisfactory criterion, whatever the problems incurred in their establishment.

Information on effects of various concentrations of noxious substances was, of course, known long before 1910. But a major problem in these earlier periods was that no means or services were readily available for analysis of the air for most of the atmospheric contaminants.

First phase of exposure standards — short-term

The first of the occupational exposure standards were based on short-time animal exposure. Only infrequently were these backed up by brief human experimentation. As early as 1883 an extensive investigation on animal exposure to carbon monoxide at the Hygienic Institute at Munich was published by Max Gruber in the first volume of *Archiv fur Hygiene*.[2] On the basis of exposures up to 47 hours, over three days, to twelve rabbits and two hens, Gruber concluded that "*It can be asserted that the boundary of injurious action of carbon monoxide lies at a concentration in all probability of 0.05%, but certainly (not less than) 0.02%.*" In arriving at this conclusion, Gruber had exposed himself to concentrations of 0.021% and 0.024% for three hours on each of two consecutive days without detecting any symptoms or uncomfortable sensations. He limited his observations to this brief period of exposure and was satisfied to draw his conclusions merely from subjective observations of the animal behavior and of his own response.

A remarkable series of short-term animal experimentations, resulting in basic data for occupational exposure standards of a wide variety of toxic substances, was conducted by K.B. Lehmann[3] and others under his direction, also at the Munich Hygienic Institute. This series appeared under the title "Experimental Studies on the Effect of Technically and Hygienically Important Gases and Vapors on the Organism." The first of the reports covered ammonia and hydrogen chloride gas, and was accorded 126 pages of the 1886 volume of *Archiv fur Hygiene*. As an indication of the magnitude of this undertaking over the years by Lehmann

* Read before the 28th Annual AMA Congress on Occupational Health, October 1, 1968, New York. Published in *Arch. Env. Health* 19:272-276 (August 1969). Reprinted by permission of the American Medical Association,

and his associates at Munich, and later at the Wurzburg Hygienic Institute, this series of reports on animal experimentation continued through part 35 in Volume 83, by 1914, with a final comprehensive paper covering 137 pages of Volume 116, in 1936, on the chlorinated hydrocarbons.[4]

A second substantial contribution to information on concentrations of toxic substances that were hazardous over short periods, usually up to eight hours, was published by Sayers, Yant, Schrenk, Patty, and others at the US Bureau of Mines in a series of 13 papers, under the title of "Acute Response of Guinea Pigs to Vapors of Some New Commercial Organic Compounds" in *Public Health Reports* from 1930 through 1938.

In 1926 Sayers assembled the most complete list of occupational exposure standards up to that time in Volume 2 of the prestigious five-volume book *International Critical Tables*. A number of errors were included in this list that were corrected in an errata table in Volume 3.

Up to this date nearly all values were based on short-time exposures. The usual notations in many of the publications over these years were "Slight symptoms after several hours of exposure, maximum concentration that can be inhaled for one hour without serious disturbance, dangerous after 30 minutes to one hour, and rapidly fatal for short exposure."

It was fast becoming increasingly evident that these short-period animal experiments constituted an inadequate basis for setting standards for environments where persons might be occupied 40 hours a week for their entire working lifetime.

Extrapolation of the short-exposure data to extended work periods were unreliable. For example, in the latter twenties it was suggested as a rule of thumb that, where a given concentration was safe for eight hours, the acceptable concentration for weeks or months might be taken as a fourth of the eight-hour value. Carbon tetrachloride was reported to be safe for eight hours at 0.16 vol%. Applying the factor, 0.04 vol% or 400 ppm would accordingly be acceptable for an indefinite period.

The fallacy of such extrapolations was readily apparent. In specific reference to carbon tetrachloride, many a case of serious and even fatal poisoning occurred, as reported by Smyth, Smyth, and Carpenter,[5] who in 1936 recommended that the acceptable concentration should be kept at less than 100 ppm. Just how much below this value the carbon tetrachloride level should be kept was later shown by Adams *et al*[6] on the basis of long-term animal exposure. Their conclusion was that the time-weighted average should not exceed 10 ppm, and excursions should be kept below 25 ppm.

Occupational exposure standards for toxic substances causing chronic injury had to be based on long-term observations if they were to be accepted as valid indices of the long-term effect on the worker.

Second phase of exposure standards — long-term

The first long-term standards were based not on animal experimentation but on actual occupational exposure of workers. In the South African gold mines, prior to 1920, a large number of miners exposed to dust high in crystalline free silica were periodically X-rayed and the dust concentration repeatedly determined. On the basis of this large-scale correlative investigation, the initial dust exposure standard of 8.5 million particles per cubic foot of air was set in 1916 for dust with free silica content of 80% to 90%.[7] Shortly after this date, the level was lowered to 5 million.

In this country the earliest study leading to a recommended exposure level based on extended observations was that of Higgins *et al*[8] at the southwestern Missouri zinc lead mines in 1917. The level they initially suggested was 10 mg/cu m, far in excess of later standards for dust high in free silica. From the 1920s, studies of dust exposures leading to recommended occupational exposure standards have been conducted by the Public Health Service in the granite industry and other dusty industries.

Beginning at about this time, long-term studies of other toxic substances were being undertaken. The first of such studies on commercial solvents was that conducted on benzene under the direction of a committee of the National Safety Council.[9] Increasingly, long-term investigations were conducted correlating information on concentrations of toxic substances with presence or absence of injurious action. These investigations have involved both animal experimentation and studies of groups of exposed workers. Many of the present

occupational-exposure standards are based on such work.

Acceleration in standard preparation and application

Toward the middle of the present century, increasing attention was being accorded occupational exposure standards. Throughout the country personnel and facilities for conduct of industrial-hygiene studies were expanding. State departments had been staffed in most of the industrial states. Many industrial concerns were adding industrial-hygiene personnel. The larger casualty-insurance companies were providing such services. Lists of concentrations of substances under a variety of terms were being published. In 1945 a list of 146 substances was published by Cook[10] together with annotated references to original publications of research on which values were based. Stimulated by this publication, the American Conference of Governmental Industrial Hygienists (ACGIH) greatly expanded their annually revised list of occupational exposure standards, using the term Threshold Limit Values, commonly known as TLVs.

A committee, designated as Z-37, of the US of American Standards Institute (USASI), formally the American Standards Association (ASA), had been publishing exposure standards since 1941, using the term "Maximal Acceptable Concentrations." A separate pamphlet was produced for each substance that included pertinent data concerning it. Later the American Industrial Hygiene Association began publishing a series of "Hygienic Standards" that included somewhat similar material. The Manufacturing Chemists' Association has published a series of "Chemical Safety Data Sheets" that present information on exposure standards and methods of handling the substances as well as their injurious effects.

In the United Kingdom, a list of 124 noxious substances was published in 1955 by Goldblatt of the Imperial Chemical Industries, Ltd.[11] Included in this publication are 1) concentrations causing severe toxic effects in persons exposed for one or for 60 minutes, 2) the concentrations that may lead to symptoms of illness if exposure continues for "more than a short time," and 3) concentrations which, if exceeded, indicate unsatisfactory conditions. An additional 27 dusts, fumes, and metals are listed with concentrations only in the third of the foregoing categories.

Reference to 238 substances from the 1956 ACGIH list of threshold limit values was made by Smyth[12] in a paper including data in addition to the actual threshold concentrations. His table lists for each substance 1) the most important effect of inhalation, 2) the predicted effects of daily eight-hour inhalations at the threshold limit and at twice and ten times this value, 3) the important hazards other than from inhalation, and 4) the nature of the interpretive data. This publication also provides an annotated bibliography, with valuable observations by the author concerning the injurious action of each of the substances listed.

The most recent of the organizations to enter the field of presenting occupational exposure standards is the British Occupational Hygiene Society. The uniqueness of their approach is the exceedingly complete description of the method of air analysis as presented in their first standard, that on asbestos.[13]

The zone method for exposure standards

A criticism of the list of precise values of occupational exposure limits has been directed to the implication that the exposure standards are a sharp boundary between injury and no injury, even though preambles disclaim any such interpretation. In an effort to solve this problem, it was suggested that zones of toxicity be used rather than single values. The maximal acceptable concentration of one group of compounds falls into the range of 100 to 500 ppm, the next into the range of 20 to 100 ppm and so on.

This method had a number of advantages. It seemed more realistic than fixing a given value, in view of the lack of preciseness of physiological response to a given concentration of toxic material. It permitted a more easily remembered impression of the relative toxicities of materials. Hopefully, industrial managements would make an effort to keep exposures toward the lower limit of a given zone but avoid any concentrations in excess of the upper limit of the zone.

The zone concept was presented by Drinker and Cook[14] at the Ninth International Congress on Industrial Medicine in London in 1948 and was received with much enthusiasm by the Z-37 Com-

mittee of the ASA at its subsequent meeting the following year. However, this attempt to solve a problem introduced problems of its own. A zone of 2 to 20 ppm would include both carbon disulfide and carbon tetrachloroethane. This would pose no problem in the case of carbon disulfide with its threshold limit value at 20 ppm, but the tacit permission to allow exposures to tetrachloroethane to reach the upper limit of this zone could readily result in cases of poisoning. After much consideration, the zone method was then abandoned. However, at a conference of international authorities on threshold limit values in Geneva in June 1968, consideration was given to incorporating some modification of this zone idea into the general concept.

Third phase of exposure standards — relating concentration to duration

The application of long-term exposure information to occupational-exposure standards has led to values representing time-weighted averages for many substances. Further development of this approach has taken cognizance of the actual industrial environment that involves fluctuations of toxic substances for various durations and frequencies throughout the day or week.

The need for tying exposure values to duration of exposure has been partially met by the ACGIH in their TLV list by designating excursions above the listed value to certain defined limits, excepting where the nature of the injurious action of the substance would make such increased concentrations ill-advised. In such a case, the value is designated with the letter C meaning that the concentration is to be considered a ceiling value not to be exceeded.

The Z-37 Committee of the USASI is somewhat more specific in relating concentrations to duration of exposures and has set up several levels of acceptable concentrations. A celling value is given under which exposures might fluctuate with the provision that they remain within a designated time-weighted average. As it is a not unusual situation under practical operating conditions to experience appreciably higher concentrations for a brief period once or twice a day, an additional level, designated as a peak value, is listed, with limitations as to its permissible duration and number of instances each day. Also a minimum level of sensory response is included with reference to its significance as a warning. This concept of standards has been discussed by Irish.[15] Since publication of his paper, the emergency exposure limit that he mentions has been discontinued by the USASI as it is, of course, not an "accepted concentration."

International standards

Finally, in the background of occupational exposure standards is the problem of whether additional attention should be accorded the criteria utilized by the authorities of the USSR for setting standards with the basic concept that at the stipulated value there should be no deviation in the normal state of the organism. The philosophy and practice of the USSR in this respect have been presented by Magnuson[16,17] and other members of the US Industrial Toxicology Delegation following their visit to the Soviet Union in 1963.

The ACGIH threshold limit values have been accepted for the most part as sound guides in many other countries, notably Germany, Sweden, Japan, England, Canada, Mexico, and in South America. The question of whether publication of the multiple acceptable concentrations by the USASI would delay international agreement on hygienic guidelines was discussed by Dinman and Cook[18] at the Fifteenth International Congress on Occupational Health in 1966, with the conclusion that the technology for evaluation of the several categories of acceptable concentrations is available and the resulting information should be applied to establishing such values.

Summary

This review of the background of problems involved in setting occupational exposure standards over the years has, hopefully, conveyed the impression that a tremendous amount of investigation, research, and interpretive judgment has been brought to bear on the development of our ideas as held today. Many problems remain to be solved. But with our present occupational exposure standards, the industrial hygienist is possessed of a powerful tool in the control of occupational health hazards. And although the physician must be continually alert to the possibility that an occupational exposure standard may not be sufficiently well

established to be completely dependable, where the health hazards within the plant have been shown to be within the exposure standards, he can have much assurance that his patients, the industrial employees, have the benefit of a healthful working environment.

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Current problems of setting occupational exposure standards*

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This year marks the 25th anniversary of the appearance of the first list Threshold Limit Values (TLVs). It would seem appropriate at this quarter-century mark to evaluate not only what has been accomplished, but to define those problems that still remain, in an effort to overcome the problems and to improve the limits and make them more generally useful and effective.

Committee activities and related problems

The TLV Committee has two major activities: development of TLVs and validation of TLVs. Most, but not all, of the problems stem from these two activities. Other problems arise from the misuse and mishandling of the TLVs by government agencies (military) or by the legal profession, by company representatives (salesmen) and some industrial hygienists who have not yet got the complete message.

Composition of TLV Committee

Because there has been some question in the minds of some physicians on the composition and fitness of the TLV Committee, it is important at the outset to identify the professional standing and activities of its members. Of the 14-man committee: physicians, five (one representing Canada); industrial hygienists, toxicologists, eight could be counted here; industrial hygiene engineers, two; analytic chemists, three; pathologists, one.

Most are individuals of national repute, several have international reputations, but probably more important, many of the committee have a background of long experience in occupational health, and still more important, several are actively engaged daily in evaluating plant situations — and note also, membership is derived from the most highly industrial states. To my mind the accumulated background and experience of this committee provides a perspective in occupational health and animal toxicity data of which it is difficult to find the equal.

The problem of data acquisition

Thus we have the requisite group to handle the data and recommend limits, but why, in the face of several hundred *new* products placed on the market annually, is the TLV Committee able to establish annually only two dozen or so limits for *new* substances? *These relative figures point up the greatest problem facing the Committee: The acquisition of industrial hygiene data of the appropriate type to develop TLVs on new substances.*

The TLVs are industry's values. But industry generally does not develop anywhere near enough of kinds and amounts of data that can be used for establishing a TLV of a new substance. But industry has the sole responsibility to develop data on its own products; government is not in a position to develop enough facilities to handle the problem *in total,* nor should it, when reliable toxicologic consultants are now available.

The record clearly shows this.[1] I made a review of the situation in 1965 and found that in all American chemical industry only seven companies have made significant contributions to basic data for TLVs of new substances. Of these seven, only two made major contributions; one company made what might be considered a significant but modest contribution, and four made only minor contributions. This is a pathetic situation when one realizes the dire need. There is no question that inability to obtain industrial hygiene data is one of the greatest problems facing the committee today.

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TABLE I
Distribution of Procedures Used to Develop or Validate ACGIH TLVs through 1968*

Procedure	No.	% Total
Industrial (human) experience	157	38
Human volunteer experiments	45	11
Animal, inhalation-chronic	83	20
Animal, inhalation-acute	8	2
Animal, oral-chronic	18	4.5
Animal, oral-acute	2	0.5
Analogy	101	24

* For 414 substances exclusive of "inert" particulates and vapors.

Types and kinds of data that industry can supply

Perhaps a glance at the procedures used to date to develop TLVs will be helpful in seeing what kinds of data industry can supply to help solve the problem of data lack.

In Table I, I have determined the distribution of the procedures used for TLVs of 414 substances appearing in the 1968 list. It can be seen that *industrial plant experience* (medical surveillance, epidemiologic studies), led the list with 38%. Here is a place that the industrial plant physician can be of real help in supplying data through good medical records, but only if combined with *simultaneously obtained environmental data.* But note this type of plant data is most advantageous in validating a limit already set — rarely are the work conditions sufficiently stable to furnish data to initiate a limit. (A few notable exceptions are butyl alcohol, acetone, and mercury.) Here the Industrial Hygiene Foundation's Repository of Anonymous Data can be of help; it is questionable whether any TLVs will result from the AMA registry.

Human volunteer exposures (line 2, Table I) are becoming increasingly popular of late. They are invaluable for arriving at an estimate of sensory (organoleptic) responses, irritants and narcosis-producing agents —substances for which animals just can't supply the answer. The procedure has lesser application for long-acting cumulative substances. For the fast acting substances, irritants et alia, exposures may be brief, a matter of a few hours. They should be repeated, however, with sufficient frequency to determine whether tolerance of sensitivity is a feature of the exposure. It has been the experience of the committee that TLVs of irritants et alia, based on *single* human exposures, all too commonly result in far too severe limits.

The third listed procedure, *chronic animal inhalation toxicity,* represents the crucial procedure about which this report is mainly developed. Here is the start in acquiring the basic data from which the TLV for new substances stems. This is the category from which the committee most needs data, and which is in the shortest supply. The data are in short supply because industries either do not develop long-term studies, or if they do, more often than not do not see fit to release the data in the open literature. Various reasons are given for this: legal protection of their products, lack of staff time to put data in publishable form. Whatever the reason, the data are not forthcoming.

Validation of TLVs

Since its inception, the TLV Committee has had the policy of reviewing annually the listed values; if new information coming to the attention of the committee indicated the need for change, such changes were proposed in a separate tentative listing. Here they remain for a period of at least two years before being placed in the recommended list. Since 1963, deeper scrutiny has been made into the suitability of the limits. The list of substances that have been given or are being given special and rather extensive scrutiny is shown in Table II.

Procedures used by the committee take three forms:

1. The chairman and members of the appropriate subcommittee hold a meeting with industry's physicians and industrial hygienists and review their experience. This procedure is used where the data has not been assembled or published. This procedure has been used for the TLVs for the chromate industry and the nitroglycols.
2. Where the data or reports have been published, these are reviewed by the chairman and the committee and the action taken is that mutually agreed upon by industry and American Conference of Governmental Industrial Hygienists by letter correspondence. This procedure has been used for beryllium, quartz, uranium, and vanadium pentoxide.

TABLE II
Substances Validated for TLV or Undergoing Validation Since 1963

Validated*	In Process
Beryllium	Asbestos (all forms)
Carbon monoxide	Benzene
Chromates & chromic acid	Carbon disulfide
Cristobalite	Fibrous glass
Nitroglycols	Isocyanates
Quartz	Tetraethyl lead
Uranium	Tetramethyl lead
?Vanadium pentoxide?	Petroleum distillates

* By committee action.

3. Active cooperative projects with industry and toxicology and pathology section of the occupational health program (OHP) are entered into whereby industry supplies the health records or clinical data for review, or active toxicologic research investigations are made by OHP in conjunction with clinical and environmental data obtained by industry. Such is being done cooperatively with a large producer of isocyanates to determine means of detecting the hypersusceptible worker, a side bonus of which will be the validation of the TLV for the isocyanates. A similar study is being cooperatively made of carbon disulfide.

To give a clearer idea of how these validation procedures work, a most productive day's meeting was held with industrial physicians and hygienists of the chromate industry. The reason for selecting the chromate industry was that no evidence of the suitability of the TLV for choromic acid or chromates had ever been brought forth for the prevention of either nasal perforation or bronchogenic carcinoma. All environmental levels had exceeded the recommended limit of 0.1 mg/cu m when large excesses (29-fold) of lung cancer and nasal perforation were found in 1950, and the health experience had not been reviewed in these terms since the industry had improved its control measures to the recommended limit. In brief, the day's discussion revealed that the limit for chromic acid mist was satisfactory in preventing nasal perforation, and in addition contained a safety factor of three or four; that the limit was probably satisfactory for the prevention of lung cancer, as no new cases have appeared since the reduction in exposure occurred, but that the ten years in which the closer controls were operative are probably too short a time to be certain its validity in this respect.

In a similar meeting with representatives of the dynamite explosives manufacturing industry, a question of an improperly stated TLV for intermittent exposure to ethylene glycol dinitrate and nitroglycerin was resolved to the mutual satisfaction of each of the parties. Statements derived from the long experience of the medical directors of the companies that normally would never get to the attention of the committee were elicited in amicable discussions.

In regard to substances in the process of validation, I can mention three — asbestos, carbon disulfide, and isocyanates — that represent extensive, cooperative efforts by both industry and the PHS Occupational Health Program, and five substances that represent purely unsolicited efforts of industry to develop information on a valid TLV (benzene, fibrous glass, tetraethyl and tetramethyl lead and petroleum distillates).

From these cooperative ventures and the increasing number of voluntary efforts of industry itself to validate some of the more controversial limits, we see an encouraging trend. More and more, industries are developing impressive industrial medical departments. More and more, industries are either establishing their own toxicology laboratories or purchasing toxicologic studies from a rapidly expanding number of commercial toxicity testing laboratories. More than 50 of these are available, exclusive of university sources. Not more than a half-dozen are presently sufficiently well equipped to do first rate long-term inhalation studies.

Industrial associations, the American Petroleum Institute, Lead Industries Association, American Welding Association, Automobile-Manufacturers' Association, among others, now have large research programs directed toward supplying data in support of safe limits of their sponsors' products. In addition, one can discern among industry's medical departments a keener interest in solving industrial hygiene and toxicology problems.

These broadened activities of industry would seem to relieve considerably the problem of data lack mentioned earlier. But closer inspection of the type of data being developed indicates that present efforts are directed to the validation of limits already established; little progress has been made toward a freer access of the committee to information on *newly* introduced industrial chemicals. This problem the committee still has with it.

The problem of misinterpretation of TLVs

Another vexing committee problem arises from the misinterpretation and misuse of the TLVs. Particularly culpable are the factory inspector and the legal profession. Their common fault lies in misinterpreting the TLVs as fine lines between safe and dangerous concentrations "either it is, or it isn't" phenomenon. Such strict interpretation is not within the intent expressed in the preface to the TLVs, and places industry in undue jeopardy. Such misinterpretation fails to take into consideration that with few exceptions, the TLV is a time-weighted average value which *permits* excursions above the limit provided equivalent excursions below the limit occur. Thus, a single, or even several, concentrations monitored above the limit is not ipso facto evidence of injury. The reason this is so is that the TLV has an inherent safety zone between the limiting value and the concentration capable of producing injury.

Despite the fact that such principles have been clearly stated for many years in the annually issued TLV booklet, they have been commonly ignored. Recently, however, the development of short-term limits (Pennsylvania), ceiling values, and the concept of "peak" concentrations (USASI, Z-37 Committee) introduce into the picture the concept of variable permissiveness that is incompatible with the interpretation of a limit below which all values must fluctuate for the prevention of injury.

Misapplication and misuse

Misunderstanding on the relationship between TLVs and short-term exposures has on occasion come to the attention of the committee. In attempting to arrive at a short-term community exposure limit for beryllium, the Air Force suggested a limit of 750 μg-min/cu m for a single exposure. This was presumably derived from Haber's Rule, $C \times t = K$, using the Atomic Energy Commission-recommended *in-plant limit* 25 μg/cu m for periods not to exceed 30 minutes. But the permissible *Ct* value for *community* exposures is about 43 μg-min/cu m. Hence the 750 μg limit is considered dangerously excessive.

In another instance, attempts by the Navy to obtain short-term exposure limits, the suggestion was made to multiply the TLV by 10 "across-the-board." This is not considered good practice because some substances do not follow Haber's rule and high concentrations for brief periods are more toxic than equivalent exposures at low concentrations, i.e., *Ct* is not always constant.

Other misapplications

Misuse of the TLVs as a measure of comparative toxicity — frequently used by industry's salesmen to prove the virtues of their products over a competitor's gives the committee frequent headaches. Use of TLVs for comparative toxicity is permissible only when metabolism of the compared substances is similar. In most cases, however, either the metabolisms differ, or they are unknown. In addition, the bases of TLVs for different substances differ; not all TLVs are based on toxicity. A striking example of the erroneousness of such a comparison is that of hydrogen cyanide (HCN), TLV 20 ppm, with sulfur dioxide (SO_2), TLV, 5 ppm. The TLVs indicate that SO_2 is more toxic than HCN, which is ostensibly ridiculous! The reason is of course that the TLV for SO_2 is based *not* on health effects as is HCN, but on irritation.

Future problems — TLVs vs community air limits

Perhaps one of the problems of greatest concern in the committee's future is how to reconcile to the satisfaction of chemical labor union leaders, unions workers, their wives and families, the often large discrepancies in the TLVs for those substances in industry that are to appear (and are now appearing) as community air limits. How to explain, for example, that when a community has a limit for lead in air of 5 μg/cu m (Pennsylvania) that is all right for their "boys" to breathe 40 times this amount for their working lifetime in industrial plants? It is doubtful that the rational bases for the differences can be made sufficiently convincing to

be generally accepted — any more that the rationale for fluoridation has met with general acceptance.

Legalization of industrial air standards

Although it particularly difficult in these days of federal reorganizations to be a prophet of "the shape of things to come," it might be worthwhile to try to foresee what problems will exist when the Occupational Health and Safety Act (or some similar act) is made into law. As the act is now written, the Department of Labor (USDL) will set standards for industrial air upon the counsel of an advisory committee. The present Occupational Health Program in the National Center for Urban and Industrial Health will establish the criteria on which the standards will be based. Because the standards will be "consensus" standards, it is probable that neither the recommendations of the TLV Committee or those of the USASI, Z-37 Committee will be given "carte blanche" acceptance. Being consensus standards, the dominant philosophy and voice of government may be less clear than in the past (the USASI Committee, dominated by industrial representatives, and whose findings are adopted now by USDL, presently attempts to attain a consensus from the *scientific* community). What the future problems will be, will be determined largely by how broad a consensus will be required, which in turn will determine the breadth of the advisory committee. Whether the presently constitued TLV and Z-37 Committees will continue to function in their present capacity seems to me problematic. The old problem of data acquisition, however, could be made easier if substantial government funds are made available to the Occupational Health Program to develop industrial hygiene data on a broad basis.

Reference

1. **Stokinger, H.E.:** Industrial Contribution to Threshold Limit Values. *Arch. Env. Health 10*:609 (April 1965).

Suggested principles and procedures for developing experimental animal data for threshold limit values for air*

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Introduction

The guidelines set forth in this paper are not to be construed that the Threshold Limit Values Committee is interested only in information that meets the minimal standards outlined here. All new additional types of information relating to TLVs, provided it is well documented, is welcomed.

The Threshold Limit Values (TLVs)[A] for air of occupational environments are, with certain exceptions, time-weighted average concentrations of chemical substances that apply to repeated, 8-hour exposures, 5 days weekly, throughout a worker's lifetime. Exceptions are the substances given in Appendix A and those given a "C" listing. A "C" listing refers to a 'ceiling' value that should not be exceeded, and thus is similar to the MAC. The substances to which a ceiling value applies, the basis for this choice, as well as other matters pertinent to the TLVs are given in the annual list of threshold limits.(1)

The threshold limit list now (1965) comprises more than 400 chemical substances. The bulk of the values have been derived from experimental animal studies. Experience has shown that the values so derived have been validated in most instances by industrial experience. The reasons why limits so derived have this validity are given in this paper.

General principles

Duration — chronic study requirement

Threshold Limit Values are based on documented freedom from injury to health, or from irritation and other forms of undesirable stress following repeated daily (*chronic*) exposures to chemicals. Accordingly, the only satisfactory data for Committee action must be derived from long-term, chronic exposure studies; short-term studies or "short-cut" methods are unsatisfactory for this purpose. There are at least three reasons for this:

1. The chronic response of a large number of substances does not resemble the acute response; hence, results obtained from acute studies may be entirely misleading in respect to chronic toxicity and may never define the problem. Among numerous common examples that could be cited of this lack of similarity in response are chronic beryllium granulomatosis, as distinct from the acute pneumonitis from beryllium; the liver injury that commonly results from chronic exposure to certain chlorinated hydrocarbon solvents as opposed to the acute narcotic effects; the chronic pulmonary fibrosis and emphysema of several lung irritants as opposed to acute pulmonary edema; and the chronic allergic sensitization of the respiratory tract from toluene diisocyanate versus local irritation and inflammation from acute exposures.
2. From the standpoint of setting a TLV, chronic effects may be the predominant or sole response to certain chemical substances (benzene, carbon disulfide) and the acute respose may not be the basis of the limit; an acute or short-term study may thus fail to reveal the true character of the response.
3. Characteristic of many compounds showing chronic response is either accumulation of the *compound* in the body as with

* Unpublished paper.

[A] Not to be confused with presently defined maximal acceptable concentrations (MAC) which refer to a 'ceiling' value not to be exceeded for any period however short (*Arch. Env. Health* 4:115, 1962).

quartz, or accumulations of the *effect* as with benzene, acrylamide or carbon disulfide. Thus a single, short-term acute exposure, or even a subacute study, will not provide the required information.

There are, however, some notable exceptions in the recommended threshold limit list where chronicity of response is *not* the basis of limit. This concerns substances such as hydrogen cyanide, whose limit is based on data derived from acute effects from a single exposure. Such substances typify a group of chemicals whose only known effects are acute responses. From the standpoint of developing toxicologic information on new products, however, chronic studies must still be performed to insure that whatever effects are observed, are acute in nature only.

Animal species requirement

Another principle of procedure derives from the fact that animal data are in essence used as a "substitute" for data preferably derived from the industrial worker. It is a commonly recognized toxicologic fact that such substitution may provide results that differ in one extreme, from the inability of the animal to reproduce the human disease (e.g., the rat's lack of susceptibility to triorthocresyl phosphate paralysis), to the other extreme of essentially complete reproducibility (e.g., vanadium effects on cystine and cholesterol metabolism; small rodents' responses to ozone). All intermediary stages are possible. (These response differences have their counterparts in parasitic diseases; no animal has yet been found, for example, that acquires gonorrhea; murine leprosy is an animal form that mimics, but is not the same as the human disease, and rabbit syphilis is not identical to human syphilis.) These shortcomings in animal response clearly indicate the need for use of more than one animal species. The use of multi-animal species is based on the recognized fact that animal species differ widely in their capacity to react to toxic chemicals, either through anatomic or physiologic constitution. For example, dogs, with long respiratory tracts, are a poor choice of animal with which to delineate the effects of highly reactive respiratory irritants such as ozone. The cat is an animal of choice, however, if nervous effects are to be delineated. Other animal species often offer particular sensitivity of response to test substances. The chick, but not the rat, is the animal of choice for testing substances that may cause demyelinization. It is obvious that in the absence of specific knowledge of the most appropriate animal species, the exposure of several will increase the probability of finding a species that will mimic the human response.

There are several reasons for the seemingly random manner that animals mimic or do not mimic human responses to toxic agents. On the basis that toxicity is the net result of two opposing reactions, the toxic agent acting in the body, and the body acting on the toxic agent, differences in the animal's way of acting on the compounds either by differences in absorption, distribution and elimination are the causes for differences in toxicity among species. Of these, metabolism (detoxication) is the major determinant, providing absorption is equivalent. Metabolism is, in turn, determined by genetic constitution which, in turn, determines the kinds and amounts of metabolizing enzymes. Clearly, animal species differ widely in their genetic make-up, and hence their capacity to metabolize and detoxify chemical substances, hence differences in toxicity from species to species. For example, man and most other species, but not the rabbit, detoxify sulfanilamide by acetylation. In certain instances, simple anatomic differences may be the major determinant. The long respiratory tract of the dog is responsible for its relative resistance to ozone; anatomic differences in the gastro-intestinal tract (herbivora vs. carnivora) leading to nutritional differences, also play a part.

Species differences, however, should not be stressed to the extent that species similarities are lost sight of. Basic enzyme similarities are the rule rather than the exception. As a result, humerous instances of close parallelism of toxic response in animal and man are seen repeatedly.

Multi-level exposure requirement

The shortcomings of experimental animal studies predicate still another requirement for threshold limit use, namely, a multi-level chronic exposure study. A minimum of two levels should be tested; three exposure levels are preferable, however. One of these studies should be made at an exposure level at which frank effect develops, so that the chronic animal response can be precisely delineated. A second level should be tested in which either no response from the chronically

inhaled test substance becomes manifest, or only minimal, borderline or questionable changes occur in a small percentage of the animals exposed. A third study could be advantageously performed at a level at which no responses become manifest — a "no-effect" level. The spacing of the exposure concentrations to meet these level requirements vary according to the toxicologic characteristic of the test compound. It is not uncommon to find that the "no-effect" level is one-fifth to one-tenth or less than that at which minimal effects occur. The magnitude of the spread between the two levels depends upon the rate of change in toxic response with change in exposure level (dosage), or the slope of the response curve. Some estimate of the slope may be gained from the observed spread between the level giving frank effect and that giving minimal change. Extrapolation of the slope should permit in most cases a fairly good estimate of the level to select for test of the "no-effect" level. Error will occur in the estimate if the log dose-response relation departs significantly from linearity, as it is apt to do at the extremes. This is the reason the Threshold Limit Values Committee prefers to have the data from a study actually performed at the expected "no-effect" level, rather than rely on an estimate from the frank-effect and borderline-effect levels that be imprecise.

An example of how such data may be plotted is found in a paper by Torkelson *et al*;[2] the "spread" in terms of concentration between various levels of response in the same species provides an estimate of the safety factor, and the change in slope from plots of the chronic data in relation to the acute data, give evidence of cumulative effects, or lack of them, provided again, the same species are tested.

"No-effect level"

There is a growing tendency among experimental toxicologists to refer to a level of an administered dose of the substance that produces no demonstrable effect as a "no-effect" level. Such a designation, however, is intimately tied to the criteria used for its determination. Clearly, a "no-effect" level based solely on no changes in body weight or organ weight to body weight ratios or in tissue morphology, might prove to be an "effect level" had more subtle and incisive variables such as changes in enzyme activity and intermediary metabolites, respiratory function and hematologic variables been studied in detail. Inasmuch as the prime objective of experimental studies directed toward threshold limit evaluation is to reveal the subtle as well as the gross changes following administration, it is readily seen that the "no-effect" level is a relative term. In view of the present-day standards for safe-guarding worker health, investigators should not be content to use the more crude evaluation procedures of the past for determining "no-effect" level, but should employ the more delicate procedures of present-day clinical chemistry. Preferably, these procedures should be so chosen as to be applicable ultimately to industrial workers. For example, the use of serum ornithine carbamyl transferase is a superior test of liver dysfunction.[3]

Basic pilot studies and procedures

Before chronic inhalation toxicity studies are planned, it is usually advantageous to perform a certain number of acute pilot tests. The purpose of such tests is at least three-fold: 1) to learn as quickly and inexpensively as possible the approximate range of toxicity of the test substance by various routes of administration; 2) the nature of the toxic effect and something of the manner in which the substance acts, its fate in the body; and 3) any unusual or other toxicologic actions that may be appropriate to the circumstance. Such information permits a better "zeroing-in" of the different disciplines of toxicology (biochemistry, pharmacology, physiology, hematology) to make the subsequent chronic inhalation studies as revealing and meaningful as possible. The development of emergency exposure limits (EELs) — brief, peak limits — requires carefully produced acute toxicity data also.

Acute LC_{50} determinations — inhalation

First in importance naturally, is the determination of the acute inhalation LC_{50},[B] usually made on rats or mice. This determination not only establishes the inhalation toxicity of the test substance relative to that of other well-known substances, but provides an opportunity to observe the gross signs of toxicity, the type of response, and most important, establishes the range of exposure

[B] LC_{50} is a concentration that kills 50% of an exposed group of animals in a specified period of experienced exposure time.

levels for the chronic inhalation studies. In general, a factor of from 10 to 100 represents the spread between the acute inhalation LC_{50} level and the level productive of definitive response in the chronically exposed animal.

Short-term limits

Direct use may be made of the acute inhalation toxicity data for development of short-term and "emergency exposure" limits.[C] For such purposes the single dose, acute toxicity study, furnishes particularly useful data on fast-acting substance such as irritants, narcosis-producing, and sensitizing substances.

Oral LD_{50}

Determination of the acute oral LD_{50} of the test substance should also be made (usually on rats) because it not only establishes an important toxicologic guidepost, but also because it shows the toxicity of the substance by the oral route relative to that by inhalation, and hence shows the relative contribution by the oral route to the over-all toxicity from inhalation. This is particularly true of test substances that are solid, insoluble particulates, the greater proportion of which find their way into the gastrointestinal tract following inhalation. Should the oral toxicity of a particulate substance under test be relatively high, a significant contribution to the over-all (observed toxicity would be made by that portion of the inhaled dose reaching the intestinal tract. Conversely, if the oral toxicity is found to be relatively low (one-100th or less) compared with inhalation toxicity, the factor of oral toxicity may be disregarded. The factor of oral toxicity may be particularly large for "mouth-breathers" especially when they are at hard work.

Dermal and percutaneous toxicity

The capacity of the test substance to react with the skin, both as a contact irritant and sensitizer, should be established. Dermal reactions are a common type of response to industrial chemicals (e.g., chlorinated hydrocarbon solvents) and if the substance is percutaneously absorbed to a significant degree (as in the case of nitroglycerine, benzidene, aniline, parathion, for example) consideration of such a contribution to the toxicity must be taken into account in recommending a threshold limit.

Ocular toxicity

Because effects on the eye, and even systemic absorption by this route, can be an important part of the over-all exposure problem, the effect of the test substance in the eye should be detemined. For some substances, such as certain substituted aliphatic imines, amines and diamines, ocular toxicity may be one of the basic determinants in recommending a threshold limit.

Supplemental studies

There are an inceasing number of industrial chemicals that, by virtue of their chemical structure and configuration, might be expected to exhibit special or unusual toxicologic actions. Among such compounds are chelating agents, non-metabolizable substances, free radical or free radical yielding compounds, substances with mutagenic or carcinogenic potential, substances with specific effects on endocrine or blood-forming organs, and on reproduction, and finally, hemolytic agents. Tests of such structures should include the appropriate procedures, as outlined in that section of this publication, in addition the basic procedures discussed above. The type of structures producing these specific responses are now recognized in many instances.

Tailoring research to needs

The general principle that may be derived from the foregoing discussion is that test procedures should be adopted that will delineate the special toxicologic characteristics of the substance under test. The day is past when routine, unimaginative, and short-cut procedures are acceptable as evidence of toxic potential. Too much is at stake to allow a response to go unobserved. Although certain basic general criteria, such as body and organ weights, basic hematologic variables, morphologic changes and mortality must be developed if for no other reason than to rule in or out the type and degree of response according to dosage. The study should not rest there — the fate or metabolism of the test substance may reveal how rapidly and completely the substance is eliminated from the body. If animals are exposed to a volatile solvent, a relatively simple determination of the amount exhaled in the breath may show the rapid-

[C]Useful time limits are 5, 15, 30, and 60 minutes.

ity of elimination, thus indicating the relative hazard. A discussion of the relation of expired air and blood concentrations to exposure and toxicity is given by Stewart *et al.*[4] Similarly, determination of urinary excretion will show the rate at which the systemically-absorbed material is eliminated. More detailed study of urinary metabolites may give important clues as to the ease with which the body can metabolize, convert, detoxify the test substance and at the same time may provide a simple test for gauging degree of exposure, and thus subsequently aid in control of worker exposure. If the substance is nonvolatile, a distribution study of the substance or its chief metabolite will reveal the sites and degree of deposition in the body, which in turn may furnish an indication of the site(s) of toxic action. When the sites of action are determined, incisive biochemical investigations can often be made to pin-point the exact biochemical "lesion" or metabolic alteration caused by the toxic agent. Information of this type often permits a classification of the type of toxic action from which the seriousness of the response may be judged. For example, if the test substance is determined to be an inhibitor of red blood cell cholinesterase, this immediately suggests the type and extent of the toxic hazard to be expected in the event of over-exposure and, in this particular case, the form of therapy because a great deal of toxicologic information exists on anticholinesterase agents and methods for combatting their adverse effects. Similarly, if the test substance is found to be a demyelinating agent the serious toxic potential is directly apparent. Again, if the agent is found to oxidize blood glutathione, the potential of the test substance to affect the red blood cells and consequent normal oxygen transfer to tissues is suspected. Other rewarding finds are demonstration of tissue succinoxidase inhibition because alteration in this sulfhydryl-dependent enzyme indicates the test substance to be an SH-blocking agent, one of the most basic of the body's active groups; and demonstration of alkaline phosphatase inhibition — specific inhibition of this enzyme usually is attended with far-reaching toxic effects because of its widespread distribution in the body.

Testing tumor potential

Under ***Procedures***, the suggestion is made of the use of cancer-susceptible strains, on the principle that it is considered good experimental practice to determine the tumorigenic potential of all new substances unless there are reliable grounds for believing that the chemical structure would have no such potential. The use of a strain of animal of known tumor susceptibility offers three distinct advantages. Such a strain is capable of determining not only the tumor-accelerating, but also the tumor-inhibiting potential of a test substance through comparison of the rate of tumor production with that of the controls. Such a strain, moreover, represents the most sensitive test object because being already susceptible, it is responsive to the slightest of stimuli.

Technical advantages of animal research

The various difficulties in translating the results of animal toxicity studies to man have been so repeatedly emphasized that sight has been all but lost of the real advantages of animal experimentation in estimating the toxic potential of a chemical. By comparison with information obtainable from a study of industrial worker exposure, the following factors decidely favor animal experimentation.

Strict control of exposure concentrations

By comparison, in industry at present, it is rare to obtain continuously monitored concentrations characteristic of worker exposure because of technical and economic reasons. Also, more often than not, the worker experiences a mixed exposure that greatly complicates or precludes interpretation. Moreover, the duration that the worker experiences even a moderately well-monitored concentration is rarely known with the desired certainty. Lack or precise knowledge of the most fundamental factor in the environmental evaluation — the intensity of the exposure — is a serious failing of the human experience approach; no such failing need occur in the experimental animal approach.

Strict control of duration of exposure

In contrast to industrial exposures that are more commonly than not sporadic or intermittent, animal exposures can be controlled to be regular and of almost any duration. The toxic potential of most substances is directly a function of the duration of the exposure; a study of the toxic response from an intermittent or irregular exposure in general will be misleading.

More detailed study permitted

Study of the response to exposure of the industrial worker may be hampered at times by poor cooperation of the worker or management, but more importantly by the sheer inability to perform certain types of examination (X-ray, biopsy, blood tests) with sufficient frequency to be of value, if such desirable examinations are permitted at all. No such limitation is imposed by animal studies; blood tests, biopsies and sacrifices may be made almost without limitation to afford a serial view of the course of the response with exposure intensity.

Limitations of animal experimentation

It is clear from the foregoing that animal experimentation offers several advantages that can rarely if ever be completely met by similar studies made in the industrial environment. There are, however, at least two limitations to animal studies.

1. The obvious fact that animals are not people, and thus may respond in varying degrees differently than man to the same exposure. As previously noted, however, the probability of reproducing the human response in animals increases as the number and judicious selection of animal species increase.
2. Animals, being essentially mute, serve best as test subjects for systemically toxic substances; substances whose primary response is sensory are best tested in man who can describe subtle irritations and discomfitures and relate them to the experienced concentration. Behavioral studies in animals are now being developed to the point where even subjective responses may be measured with a considerable degree of objectivity.

Mixtures

Thus far this discussion has dealt with principles of toxicologic testing of single substances because Threshold Limit Values[D] to date have only been recommended for single substances. The time is probably not too far distant when, owing to technical developments, it will be advisable to recommend limiting concentrations for mixtures. Mixtures may take the form of isomers, homologues, or chemically related compounds resulting from a reaction mixture which, for economic reasons, may be offered for sale without separation. Another type of mixture is the proprietary mixture of chemicals commonly used in fixed proportion to accomplish a specific purpose such as represented by disinfectants.

In developing the necessary data for mixtures, two general principles apply.

1. The principles and procedures recommended for single subtances apply to mixtures, i.e., the over-all toxic hazard of the mixture must be evaluated; it is presently not possible to determine with certainty the toxicity of a mixture from the additive toxicities of the individual components.
2. It is advisable to determine also the toxic hazard of the most toxic component of the mixture. Such information is of advantage in the event that change in manufacturing procedures result in alteration of the percentage composition of the mixture. Such additional information may at times enable a determination as to whether synergistic, antagonistic, or purely additive toxicities characterize the mixture. For strict determination of this, however, the toxicity of each component should be evaluated.

The safety factor

In principle, all Threshold Limit Values should have *a factor of safety incorporated in them.* The reasons are that to use a limit based on the upper limiting concentration producing no effect in animals fails to consider the hypersusceptibly responsive individual, assuming complete congruence of human and animal response. Accordingly, a margin of safety must be included in the recommended limit for this factor, but more especially for possible divergence in animal and human response. The magnitude of the safety factor, although ultimately one of Committee judgement, is determined largely by the seriousness of the toxic potential; the more serious the potential, the larger the factor. In extreme cases where death might be the end-point, the allowed margin between the TLV and the "no-effect" level might result in a safety factor of 10; more commonly it is

[D]That is, in the U.S.A.; Russia has a limited number of values for mixtures.

from 2 to 5. The determination of the safety factor is the responsibility of the Committee of Threshold Limit Values.

It is more desirable, and under certain circumstances possible, to determine the factor for the difference between the animal and human response. This may be done for substances whose chief effects are sensory by the method described under ***Procedures*** (next to last paragraph) and for most other substances (final paragraph).

Procedures

The following outline of tests and procedures, with pertinent literature references, is recommended as a guide for manufacturers of new substances or formulations for which it is desired to develop experimental animal toxicologic data for use in recommending Threshold Limit Values. The outline presents merely the kinds and amounts of information that are needed as a basis for an informed estimate of toxic hazards involved upon daily, repeated, inhalation exposures to a substance. Only minimal requirements are given; it is not the intent, however, that they be construed as limiting the amounts and types of data that may be developed in evidence of the limiting concentrations for safe exposure. The data should be developed in a well-staffed laboratory of toxicology by personnel familiar with the objectives of the work and experienced in the procedures to obtain them. The following outline is obviously not meant to replace the judgement of an experienced toxicologist.

The animal procedures should obviously be supplemented to advantage by performing confirmatory studies on human subjects of those aspects of the toxicity amenable to human testing (metabolic, sensory effects).

I. Chemical Identication of Product

A. *Name* — Chemical name, generic name (and trade name, if any). Substances are listed in the threshold limit list, preferably in the above order.

B. *Physicial and chemical properties*, particulary stability.

C. *Impurities* — The nature and amount of all impurities must be given for the material under test, e.g., volatile inhibitors of solvent decomposition. Under only rare circumstances in which "substantial identity" can be proven, will animal test results obtained on a related product or compound be acceptable evidence. Substantial change in product components that may become an airborne hazard necessitates development of new animal toxicity data.

D. *Mixtures* — Chemical name and percentage amounts of *all* ingredients should be given, both "active" and "inert."

E. *Analysis* — The analytic method(s) used for air and/or tissue concentration determination should be given in sufficient detail to permit the TLV Committee to determine the validity of the conclusions.

II. Acute Toxicity Studies

Purpose: To establish the LC_{50} value by inhalation and LD_{50} values by oral and other routes, to obtain an acute toxicity rating relative to that of other known substances.

A. *Inhalation* — Establishment of a 4-hour LC_{50} value in *rats* (usually) according to methods described for 1-hour exposures[5] in which suggestions are given for apparatus design, technics of exposure and methods of estimating the LC_{50} value. Use of the rat and an exposure period of 4 hours are suggested because most of the recent LC_{50} values for industrial products have been determined in this manner and thus permit ready comparison.

B. *Oral* — Establishment of a single dose, oral LD_{50} value for rats, as described in reference five. In addition to a general discussion of principles and procedures found in reference five, a method for calculating the median effective dose is given by Weil *et al.*[6]

C. *Cutaneous and ocular* — 1) Determination of primary irritation related to cutaneous dosage; 2) determination of sensitizing potential; and 3) determination of LD_{50} — degree of absorption through skin. Rabbits and/or guinea pigs are usually employed.

Principles and procedures for determining the three above forms of cutaneous toxicity are given in reference five. For these tests, the methods of Draize *et al* and Draize and Kelley are acceptable.[7,9]

D. *Other parenteral routes* — Tests of intravenous and intraperitoneal toxicity in rats leading to determination of LD_{50} values may prove helpful in understanding the

mode of action of substances in relation to that by other routes.

III. Subacute Inhalation Toxicity Studies

Purpose: To develop information that bridges the gap between acute and chronic toxicity studies which permits *a)* more detailed delineation of signs of response to exposure, and *b)* nature and rate of accumulation of a substance in the body, or accumulation of its effects. These observations allow a better estimate of the levels to be selected for the chronic exposures, the criteria (types of tests) that may be most informative when applied to chronic exposures, the animal species of greatest value, and the most appropriate intervals for periodic examination of the exposed animals.

Subacute inhalation toxicity studies may be omitted under circumstances where proper design of chronic studies is assured from the results of the acute toxicity studies.

A. *Animal species and number.* Three species. At least one nonrodent such as the dog, plus the rat and rabbit. Other species may be used to advantage, depending upon the mode of action of the test compound — cat, monkey, hamster, guinea pig, mouse. A minimum of two each of larger species, 20 each of smaller, with a corresponding number of controls.

B. *Exposure levels.* One (minimum), at one-fourth or one-fifth LC_{50} which produces frank injury in at least one species to permit characterization of the toxic response by at least one criterion (biochemistry, histology, hematology, or other). This permits an estimation of the cumulative effect of the test substance. Another level, at one-tenth or below LC_{50}, provides an indication of the proper level for the "no-effect" level of chromic study.

C. *Duration.* Thirty to 60 days, 6-hour daily repeated exposures, 5 days per week. Toxic effects of most substances are manifested within 30 days at exposure levels of one-fifth LC_{50}. Effects on the lung occur commonly within the first week; liver, bone marrow, second week; kidney, third week; neutral effects, fourth week or later at exposure levels tolerated for 6 to 8 weeks.

D. *Periodic assay.* Weekly serial sacrifice of two or three of the smaller species (rat) for detailed examination by the various applied criteria enable the course of the injury to be determined.

E. *Evaluation.* Following a critical review of the results of the acute and subacute studies, design of the chronic study can be developed.

IV. Chronic Toxicity Studies

Purpose: These studies provide the basic data central to the entire objective of affording unequivocal information for developing a threshold limit.

For design, construction, operation, and performance of animal inhalation exposure chambers, see reference eight.

A. *Animal species and number.* A minimum of two species, selected on demonstrated responses in subacute studies, should be used. For larger species, a minimum of 6, and a minimum of 20 smaller species should be used as intact groups for duration of study. A suitable number of additional animals should be included for periodic assay of response, no less than three per assay of any one species. The desired group number is 10 for assays of enzyme activity. Animals used should be weanling to young adults.

B. *Exposure levels. Use a minimum of two as discussed in* ***General Principles.*** A discussion of dispersing devices, tests for uniformity of distribution of dispersed substance in exposure chamber, air-sampling, air-flow rate, temperature and humidity control, and related factors is given in reference eight.

C. *Duration.* A minimum of one year (18 months to 2 years preferred) of daily, 6-hour exposures, repeated 5 consecutive days weekly.

D. *Periodic assay of response to exposure.* This test is recognized as one of the most important aspects of the study, it permits determination of the course of the response as reflected by changes in the various applied criteria. Assay periods commonly used are 1, 3, 5, 12, 18 months and 2 years, unless otherwise indicated by the subacute studies.

A minimum of five animals of the smaller species of both exposed and controls is recommended; two or three of the larger species should be assayed at more widely spaced intervals, e.g., 1, 6, 12 months and at 2 years.

E. *Criteria*

1. Body weight changes
2. Food and water intake
3. Mortality
4. Organ to body-weight ratio
5. Hematologic changes
6. Biochemical changes
7. Respiratory function tests
8. Pharmacologic tests
9. Histologic changes

Items 2, 4, 7, and 8 are optional, depending on requirements of test substance.

F. *Supplemental studies.* For substances, that by reason of chemical structure or relation to known substances may reasonably be thought to have the potential of special responses, such as bone marrow depressants, mutagenic, radiomimetic or cancerigenic agents, teratogenic or anti-fertility agents, the following types of supplemental investigations should be considered.

1. Special blood studies, bone marrow studies.
2. Reproduction and fertility studies (rats or mice) through F_2 generation.
3. Cancerigenic studies (animal species according to type of cancer, e.g., dog-bladder cancer). For lung cancer production by inhalation, an irritant as adjuvant (e.g., SO_2) is generally a necessity. Lung tumor accelerating or inhibiting properties may be tested in a lung-tumor susceptible strain of animal (CAF_1 Jax mouse).
4. Metabolism studies. Absorption, distribution, and execretion studies, and identification of excretion product(s).
5. Mechanism of Action — Phamacodynamic studies.
6. Determination of characteristic action on specific and organs or enzyme systems.

The above data should be evaluated by a toxicologist experienced in animal inhalation toxicology and the report written from the standpoint of interpreting the data in the light of their intended use, i.e., as bases for threshold limit recommendation.

G. *Human validation of proposed limit.* In such situations as it is possible (availabiity of volunteers, and medical assistance, substances with appropriate toxicologic properties), human exposures of brief duration should be made at the proposed TLV to gain insight on the response to such factors as 1) irritation, 2) narcosis, 3) effect on vision, 4) odor (thresholds), 5) production of offensive body odors, 6) nausea, 7) skin or hair staining, and other factors. The exposures should be repeated to determine whether reduction or increase in sensitivity occurs. Such exposures should be made under close medical supervision.

Planned human experimentation to furnish a tie-in between animal and human response may also be done on substances whose chief response is nonsensory. Hospitalized volunteers with terminal disease, not involving those organs and tissues known to be affected by the test substance, may be exposed at or around the level at which the most sensitive response test in animals was positive. Such a procedure was used prior to the development of the air limit for uranium in which it was found that man responded at a level 10-fold higher than that of the most sensitive species (the rabbit) as judged by the most sensitive test of uranium toxicity (urinary catalase). Thus, if the TLV is based on rabbit data in this instance, a *known* safety factor of 10 is built into the limit.

Finally, some guidelines regarding the magnitude of the safety factor may be derived from worker experience in handling the test substance during the pilot plant stages of production. In any case, industrial experience should be carefully recorded in order to evaluate the suitability of the choice of level.

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Historical development of the Walsh-Healey Noise Regulation*

HERBERT H. JONES
Chairman, Physical Agents TLV Committee

In March of 1964 the Department of Labor revised its publication Bulletin 334 *Guidelines to the Department of Labor's Occupational Noise Standards.* The publication presented a recommended limit of exposure to industrial noise by the Department of Labor for the first time.

This publication was reviewed by the American Industrial Hygiene Associations's technical committee on noise at the American Industrial Hygiene Conference in Philadelphia in May of 1964. The technical committee was very unhappy with the publication and presented their concerns to the AIHA board. The Board called a meeting late one evening during the conference of members of the board and other interested people. It was decided that a proposal would be presented to the Department of Labor whereby a technical committee, with membership from various interested professional groups, would be formed to review the document and make recommendations for a noise standard in return for a delay in implementation of the guidelines. This was presented to the Department of Labor which, as Botsford testified (page 1022, line 8) the Administrator said, "I will not withdraw it but I will not push it." As I recall the Administrator indicated a postponement of 6 months. (I was a member of the AIHA technical committee and also present at the late evening meeting of the AIHA Board. In my opinion the technical committee and the board were not upset with technical defects as Botsford testified but that numbers were being presented for limiting noise exposure for the first time and this was a method of delaying enforcement.)

The AIHA Board than moved ahead to form the committee with the following membership:

American Conference of Governmental Industrial Hygienist
Floyd A. Van Atta, Ph.D.
Alexander Cohen, Ph.D.

American Academy of Ophthalmology and Otolaryngology
Aram Glorig, M.D.
Meyer S. Fox, M.D.

American Academy of Occupational Medicine
Glen S. Usher, M.D.
E.C. Riley, M.D.

American Industrial Hygiene Association
Paul L. Michael, Ph.D.
James H. Botsford

Industrial Medical Association
Joseph Sataloff, M.D.
William L. Baughn, M.D.

Member at Large
Floyd E. Frazier

Chairman
Herbert T. Walworth

This committee began a series of meetings in 1964, 1965, 1966 and 1967 attempting to prepare a report and make recommendations to the Department of Labor.

In early 1966 there still was no recognized noise limits for industrial noise exposure. I suggested to the ACGIH Board that they establish a Threshold Limits Committee for Physical Agents similar to their committee for Chemical Agents. The ACGIH Board set up an ad hoc committee to evaluate this need and report back to the Board their recommendations. I was appointed chairman of the committee; it was the consensus of this committee that there was need for a TLV Committee for physical agents. The ACGIH Board accepted the committee report but delayed setting up a committee as ACGIH had representation on the Intersociety Committee which was working on limits of noise exposure and felt that it would not be appropriate to set up another committee to do the same thing.

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* Unpublished paper provided by Mr. Jones.

In early 1967 the Intersociety Committee completed its report. It had been agreed that each of the professional societies that were represented on the committee would be given the opportunity to review and accept or reject the report. The report was accepted by ACGIH. AIHA referred the report to their technical committee on noise. The technical committee reviewed the report and recommended its acceptance to the AIHA Board. The AIHA Board then voted not to accept the report and recommended disbanding the committee. When this occurred, the ACGIH Board set up a Physical Agents TLV Committee, appointed me chairman and instructed me to organize the committee, work on a noise TLV and have a report ready for the May 1968 meeting. A report was prepared and accepted by the ACGIH Board in May 1968. This noise TLV was discussed in a paper published in the *American Industrial Hygiene Association Journal*.[1]

On September 20, 1968, the Department of Labor published a proposed noise standard with the usual request for comment.[2]

In December 1968, I submitted the proposed ACGIH Noise TLV as a possible replacement for the proposed DOL Standard (see Appendix I at end of this paper for text of letter.)

On January 17, 1969, the Department of Labor published[3] their standard which had the same numbers for exposure limits as the proposed ACGIH-TLV (revising 41 CFR 50-204) with a 30 day effective date.

On February 17, 1969, the effective date of this standard was postponed until May 17, 1969.[4]

With activity by DOL the AIHA initiated a movement to set up the Intersociety Committee again. This was done with the membership as follows:

American Conference of Governmental Industrial Hygienists
Floyd H. Van Atta, Ph.D.
Herbert H. Jones

American Academy of Ophthalmology and Otolaryngology
Aram Glorig, M.D.
Meyer S. Fox, M.D.

American Academy of Occupational Medicine
Edwin DeJongh, M.D.
Nobert Rosenwinkel, M.D.

American Industrial Hygiene Association
Paul L. Michael, Ph.D.
James H. Botsford

Industrial Medical Association
Joseph Sataloff, M.D.
William L. Baughn, M.D.

Chairman
Jack Radcliffe

The ACGIH Physical Agents Committee was receiving comments on their proposed Noise TLV. The proposed TLV was a stepped function limit of exposure as follows:

92 dBA . . . . 4-8 hours
97 dBA . . . . 2-4 hours
102 dBA . . . . 1-2 hours
107 dBA . . . . less than 1 hour

Many comments were received suggesting a line function rather than a step function. By plotting the points at the midpoint of each step as follows:

92 dBA . . . . 6 hours
97 dBA . . . . 3 hours
102 dBA . . . . 1½ hours
107 dBA . . . . ¾ hour

on semilog paper and drawing a straight line through the points one arrived at the following table:

90 dBA . . . . 8 hours
95 dBA . . . . 4 hours
100 dBA . . . . 2 hours
105 dBA . . . . 1 hour
110 dBA . . . . ½ hour
115 dBA . . . . ¼ hour

It was the consensus of the ACGIH Noise-TLV Committee to recommend this to the ACGIH Board as the ACGIH Noise TLV.

Following the postponement of the effective date of the DOL Noise Standard, the Secretary of Labor set up an ad hoc committee to advise him on standards. Members of this committee discussed with me the proposed Noise TLV of May 1968 as this was the basis of the standard published on January 17, 1969. I informed them that many comments had been received on the proposed Noise-TLV and after reviewing these comments the committee would recommend to the ACGIH Board the revised numbers (that is 90 dBA for 8 hours, etc.). The Secretary's ad hoc committee asked the Intersociety Committee for guidance

and this committee said that if ACGIH officially adopted the revised numbers (90 dBA — 8 hours) they would find this limit acceptable. A member of the Secretary of Labor's ad hoc advisory committee informed me that if the Noise-TLV was officially adopted by ACGIH these numbers would be recommended to the Secretary of Labor. The Noise-TLV was adopted by the Conference on May 13, 1969.

The Secretary of Labor had published in the *Federal Register* on May 20, 1969, a noise standard which contained noise exposure limits which were the same as those in the ACGIH Noise-TLV.[5]

The noise standard contained, in addition to the numbers from the ACGIH Noise-TLV, a figure (6-9) which was developed by Mr. Botsford and recommended by the Intersociety Committee to be a part of the standard to permit the use of octive band measurements in addition to dBA measurements.

It was the intent of the ACGIH Physical Agents Threshold Limit Value Committee that the limits of exposure applied to all acoustical energy to which a sound level meter, meeting the standards of the United States of America Standards Institute and operating on the A-weighing network with slow meter response, would respond. This would include continuous and impact noises. The limit of exposure of 140 dB peak sound pressure level was to apply only to discrete noise pulses such as a drop forge and was totally independent of the measurements made by the sound level meter of total acoustical energy.

On February 27, 1982, I talked to Dr. Floyd H. Van Atta, a member of the Intersociety Committee and retired DOL employee. He said that DOL had prepared the necessary paper work for establishing a noise standard in early May 1969, and he attended the ACGIH business meeting on May 13 and immediately following the adoption of the Noise-TLV he telephoned Washington and the Department proceeded to publish its Noise Standard.

Background information on the use of dBA to determine hazard to hearing of industrial noise

In the late 1950s and early 1960s, it had become standard practice in making noise measurements for determining hazard to hearing to make measurements in octave bands. Attempts were made to establish limits of exposure by setting a limit for each octave band. Generally the acoustical spectrum was divided into 8 bands. Much difficulty was experienced in establishing limits for each band and also this gave 8 numbers to be considered for the evaluation of each exposure. At the time the first Intersociety Committee's report was published, this was based totally on octave bands and dBA measurements were not even mentioned.

In 1966 and 1967, James Botsford began to develop a plan to use dBA rather than octave bands. His proposed method was presented in a paper published in the *American Industrial Hygiene Association Journal*.[6] (This is the same issue of the *AIHA Journal* in which the first Intersociety Report was published.[A]) In this paper he presents a method for determining acceptable limits of exposure in terms of dBA. He uses the recommended limits of exposure developed by the National Research Council Committee on Hearing, Bioacoustics and Biomechanics which were expressed in octave bands and presented nomographs to convert these to dBA.

To evaluate this technique he used data from a paper published by Bonvallet.[7] This paper presented octave band data from about 600 industrial plant measurements which included: pneumatic presses, automatic drop hammers, automatic punch presses, automatic screen machines, punch presses, etc. In this evaluation no attempt was made to separate those he now describes as having both continuous and impact noise components. Botsford states *"It appears that A-weighted sound levels are quite satisfactory for appraising hazards of manufacturing noises."*[8]

It was on the basis of Botsford's work and other information available to the ACGIH-Physical Agents TLV committee that a change was made from the proposed TLV published in 1968 and that adopted as the Noise-TLV in 1969. The proposed TLVs included limits in both dBA and octave bands and at a meeting of the committee in October of 1968 it was decided to eliminate or drop the limits in octave bands as was indicated in my letter to the Department of Labor commenting on the proposed standard published September 20, 1968.

[A] Full text appears in this volume.

The paper of Botsford certainly indicates he would have used dBA measurements to evaluate noise exposure to punch presses in 1967.

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Appendix I

Director
Bureau of Labor Standards
Wage and Labor Standards Administration
U.S. Department of Labor
Washington, D.C. 20212

Gentlemen:

The Committee on Physical Agents of the American Conference of Governmental Industrial Hygienists have reviewed the proposed rules for Safety and Health standards for Federal Supply Contracts and wish to express our views on Section 50-204.10 — Occupational Noise Exposure. It is the Committee's judgment that the proposed limits are unnecessarily restrictive and cannot be substantiated by published data that is available at the present time.

The Physical Agents Committee reviewed the data which was available in early 1968 and made recommendations to the Conference that limits be established for occupational noise exposure as follows:

Average Sound Pressure Levels of Octave Bands Centered at 500, 1000, and 2000 Hz	A-Weighting Network of Sound Level Meter	Duration of Exposure per Day
85 dB	92 dBA	4 - 8 hours
90 dB	97 dBA	2 - 4 hours
95 dB	102 dBA	1 - 2 hours
100 dB	107 dBA	less than on hour

These values apply to total time of exposure per working day regardless of whether this is one continuous exposure or a number of short-term exposures but does not apply to impact or implusive type of noises.

When daily noise exposure is composed of two or more periods of noise exposure of different levels, their combined effect should be considered, rather than the individual effect of each. If the sum of the following fractions:

$$\frac{C_1}{T_1} + \frac{C_2}{T_1} + \ldots \frac{C_n}{T_n} = \frac{C}{T}$$

exceeds unity, then, the mixed exposure should be considered to exceed the threshold limit value, C_1 indicates the total time of exposure at a specified noise level, and T_1 indicates the total time of exposure permitted at that level.

The above limits do not apply to impulsive or impact type of noise. It is recommended that exposure to this type of noise should not exceed 140 dB peak sound pressure level.

The Committee met again on October 15, 1968 and reviewed the available published data and concluded that there was no data available which would justify revising these proposed dBA limits. Octave band limits as defined in the recommendation made in May 1968 were withdrawn as they did not appear to be as reliable of an exposure index as dBA. It is therefore suggested that these limits be considered for possible inclusion in Section 50-204.10 rather than the limits which have been published.

Sincerely yours,

/s/ Herbert H. Jones, Chairman
Physical Agents Committee, ACGIH

Guidelines for noise exposure control*

Preface

Growing interest in industrial loss of hearing has emphasized the need for reliable noise criteria for use in noise control and hearing conservation programs for industrial workers. While many hearing loss studies have been reported in the scientific literature, there, heretofore, has been no single source of data relating degree of hearing loss to noise exposure levels. The following *Guidelines* have been developed with the objective of supplying such a source, along with certain basic information for establishing hearing conservation programs.

In the summer of 1964, a number of individuals closely associated with the industrial noise problem consulted several representative technical organizations relative to the establishment of an intersociety committee to develop noise guidelines. An ad hoc committee, composed of two members from each of five technical groups, was formed and given this responsibility. The Committee members who prepared the *Guidelines* and the organizations they represent are:

American Conference of Governmental Industrial Hygienists
- Floyd A. Van Atta, Ph.D.
- Alexander Cohen, Ph.D.

American Academy of Ophthalmology and Otolaryngology
- Aram Glorig, M.D.
- Meyer S. Fox, M.D.

American Academy of Occupational Medicine
- Glenn S. Usher, M.D.
- E. C. Riley, M.D.

American Industrial Hygiene Association
- Paul L. Michael, Ph.D.
- James H. Botsford

Industrial Medical Association
- Joseph Sataloff, M.D.
- William L. Baughn, M.D.

Member at Large
- Floyd E. Frazier

This is the first attempt to extract and condense pertinent data from various scientific literature sources into a meaningful and authoritative guide. Table I and Figure 1 showing the *"Incidence of hearing impairment in the general population and in selected populations, by age groups and occupational noise exposures"* are the results of this condensation. We believe the *Guidelines* will aid industrial management in recognizing the need for noise control programs and will be useful in establishing such programs.

Herbert T. Walworth, *Chairman*
Intersociety Committee on
Guidelines for Noise Exposure Control

I. Foreward

Noise has long been recognized as one of several causes of deafness. Exposure to high noise levels may cause temporary or permanent changes in hearing threshold level. Permanent hearing loss which impairs communication by speech is a handicap or impairment. Competent medical specialists have defined impairment as average hearing threshold level in excess of 15 db at 500, 1000, and 2000 cps.[1,2] This definition is accepted for this document.

Noise-induced hearing loss increases with both the intensity of the noise and the duration of exposure. Generally, many years of exposure to high noise levels are required to produce significant permanent impairment in the exposed group; however, there will be marked differences in the hearing of individuals and in their response to noise. A portion or all of a hearing impairment may be due to causes other than noise exposure. These *Guidelines* will be directed toward the prevention of that portion of the permanent hearing loss resulting from exposure to steady noise.

II. Objective

To provide practical guidelines for evaluating the hazard from noise exposures and for minimizing the development or aggravation of perma-

* Published in *Am. Ind. Hyg. Assoc. J.* 28:418-424 (1967). Reprinted by permission of the American Industrial Hygiene Association.

TABLE I
Incidence of Hearing Impairment[a] in the General Population and in Selected Populations, by Age Groups, and Occupational Noise Exposures

Noise Level (Decibels)		Percentage of Population Having Impaired Hearing By Age Groups				
A-Scale	Average of Three Octave Bands 300-2400 cps	20-29	30-39	40-49	50-59	Source of Information[b]
	Non-noise	3	5	10	20	13(2282)
	General Population	2	5	14	24	14(20,459)
85	78c	2	8	15	25	17(1100)
92c	85	3	9	15	28	14(9653)
95	88c	8	15	25	38	17(1092)
96c	89	3	10	19	—	13(1834)
97	91	7	22	32	48	15(400)
102	95	10	18	30	45	13(666)
104	97	5	21	35	57	16(174)

[a]Average hearing threshold level in excess of 15 db at 500, 1000 and 2000 cps.[1,2]

[b]Refers to list of references at the end of this article, and the number in parentheses is the number of persons in the study group.

[c]Estimated level.

nent hearing impairment resulting from prolonged exposure.

III. Occupational hearing loss control program

The following procedures are necessary to accomplish the objective.

A. Evaluation of the Noise Hazard

The hazard to hearing produced by a given noise exposure depends on the intensity and frequency distribution of the noise and on the duration of the exposure. Each of these factors must be considered in determining which exposures are hazardous.

1. Noise measurement

Continuous or intermittent steady noise is readily measured by standard instruments; impulsive noise requires special procedures not considered here.[3,4]

a. Instruments

All noise level determinations should be made with sound level meters and octave band analyzers meeting the pertinent specifications of the U.S.A. Standards Institute.[5,6]

b. Survey methods

Surveys should be conducted by compentent persons according to accepted practices.[3,7]

1) *Measurement*: Noise may be measured using either the A-scale of the sound level meter or by octave band analysis. Levels measured by the sound level meter should be designated dbA. Where the octave band analysis is made, the hazard rating may be determined from the simple average of the decibel values for the three octaves 300-600, 600-1200, and 1200-2400 cps (see Table I and Figure 1). If the A-scale reading is well above or well below the selected critical level for noise control, the exposure rating based on this measure may be used without validation. Where A-scale readings lie within 3 or 4 decibels of such a level, the exposure rating should be verified by octave band methods.

Noise levels measured at a wide variety of industrial operations have been published[8] and these may serve temporarily as useful guides in the absence of noise surveys.

2) *Duration and time patterns*: The total time of the noise exposure and the distribution of exposure periods throughout the working day should be determined by estimation or measurement.

2. Hazard rating

a. Continuous exposure

Several criteria for acceptable noise exposure have been proposed. The differences between these criteria result primarily from different defini-

tions for acceptable incidence of hearing impairment. Table I and Figure 1 have been prepared from a number of controlled studies which correlate noise exposure with incidence of hearing impairment. The first two columns of Table I indicate the steady noise levels to which the various groups were exposed in terms of the A-scale reading and the corresponding average level for the octave bands between 300 and 2400 cps. In order to complete these two columns, some adjustment of data to convert it from the available form to the desired form was necessary. For example, noise data from sources 13, 14 and 16 were limited to octave band levels in the 600 to 4800 cps frequency range and a correction of one db was added to convert the average octave band level for the 600-4800 cps range to that for the desired 300-2400 cps range. This correction was determined to be the most probable difference by analyzing octave band data on 580 industrial noises.[8] Also, the average difference of seven decibels between known A-scale and average octave band levels of the last three lines of Table I was used in estimating unknown values where indicated.

The remaining columns of Table I show, for various age groups, the percentage of the groups

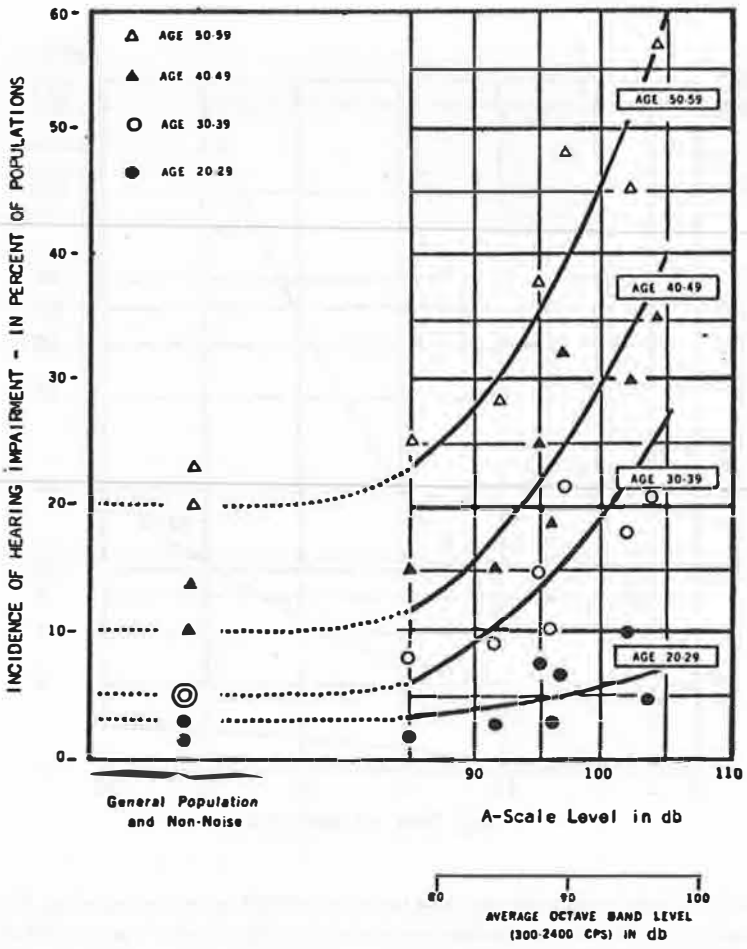

Figure 1 — Incidence of hearing impairment* in the general population and in selected populations by age groups and by occupational noise exposure. (*Average hearing threshold level in excess of 15 db at 500, 1000, and 2000 cps.[1,2]).

having impaired hearing. The first line of the table shows the incidence of hearing impairment in a population having no exposure to injurious noise and no other explanation for observed hearing impairments. It is presumed that at least this minimal incidence of impairment will be found in any population and that the other groups may be regarded as exhibiting injurious effects of noise only if they show significantly higher rates of incidence. The information contained in Table I is presented graphically in Figure 1.

The upper curve in Figure 1 indicates that of 100 persons exposed to 85 dbA (78 db average octave bands 300-2400 cps), about 23 will have impaired hearing when they reach the age group of 50-59. This compares to about 20 persons out of 100 with no occupational noise exposure. This is an increase of three persons per 100 population for the noise exposed group, or three percentage points. Because of the wide scatter of the data, so small a difference between groups cannot be attributed to differences in noise exposure with much certainty and, therefore, is not considered to be real or significant in the statistical sense.

In the population exposed to 92 dbA (85 db average octave bands 300-2400 cps) to age 50-59 the amount of impairment is increased 8 percentage points (eight more persons per 100 exposed) as compared to the population with no occupational exposure. This difference is probably

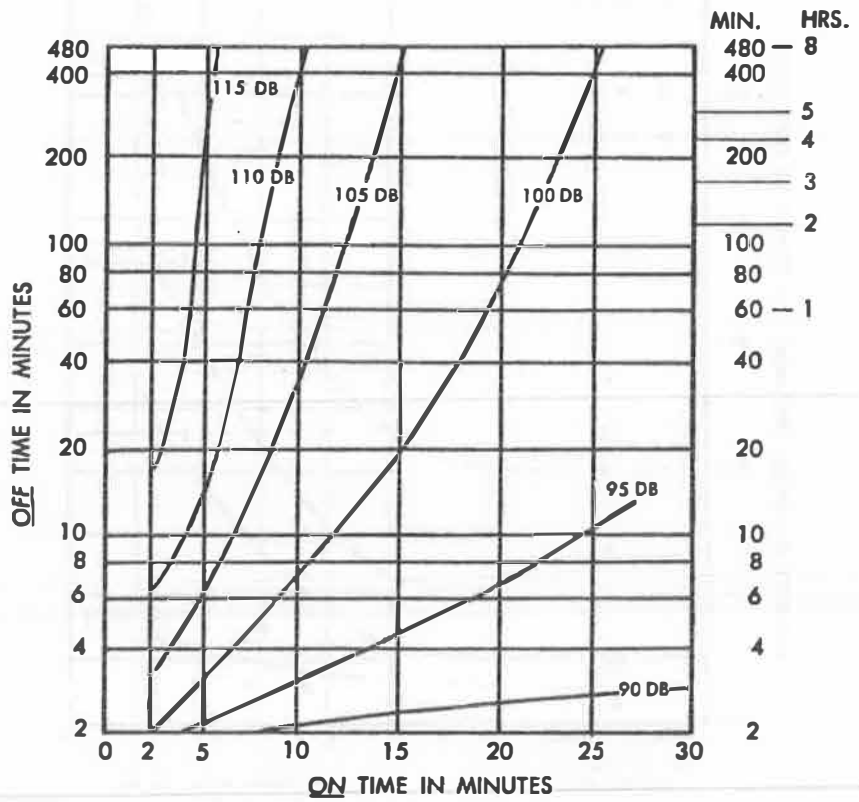

Figure 2 — Guide to allowable exposure times for intermittent noise exposures. The noise exposure curves (from *Guide for Conservations of Hearing in Noise*[9]) are labeled with the average value for the three octave bands between 300 and 2400 cps (or bands whose center-line frequencies are 500, 1000 and 2000 cps). The vertical scale shows the period in harmless noise (off-time in minutes) which must follow noise exposures of the duration shown on the horizontal scale (on-time in minutes) to avoid temporary threshold shifts greater than 12 db at 2000 cps. For example, exposure to 100 db for 15 minutes must be followed by at least 20 minutes in harmless noise.

TABLE II
Permissible Increase in db for Less Than Eight Hours Exposure

Daily Exposure Time (Hours)	Permissible Increase Above Eight-Hour Criterion (Decibels)
8	0
4	5
2	10
1	15
1/2	20
1/4	25

about the same as the limits of precision of the data.

With exposure to 95 dbA (88 db average octave bands 300-2400 cps) until age 50-59 the number of persons with impairment is increased by 16 percentage points (16 more persons per 100 exposed). In other words, after occupational exposure to 95 dbA during their working lives, 64% of persons in the sixth decade will have no hearing impairment and 20% would have some impairment from presbycusis alone, irrespective of occupational noise exposure. Therefore, 84% will probably be little affected by a lifetime occupational exposure to 95 dbA.

b. Intermittent and part-time exposure

The studies on which Table I and Figure 1 are based, dealt with men exposed to noise during a normal workday, of eight hours' duration. There are no long-term studies available of the extent to which the risk of permanent hearing impairment may be reduced by shortening the daily duration of exposure, or by interrupting the exposure periodically. The only possible guidance comes from studies based on temporary threshold shifts (TTS) resulting from various types of noise exposure. Results of TTS studies are summarized in Figure 2 which may be used to estimate the effect of intermittency of noise exposure on risk of hearing impairment. The information in Figure 2 may be approximated by the simple rule that for each halving of daily exposure time, the noise levels may be increased by 5 db up to a maximum of 115 db average of the three octave bands 300-2400 cps (122 dbA) without increasing the hazard of hearing impairment.

The application of this rule is illustrated in Table II.

c. Limitations

The methods of exposure rating proposed in Figure 2 above apply only to groups, not to individuals. They cannot be used to determine whether an individual has or has not suffered a hearing loss resulting from noise exposure; medical evaluation is required for such a determination.

B. Exposure Control Methods

Where noise exposure exceeds the critical level selected for control, measures should be taken to 1) reduce the environmental noise levels, 2) reduce the duration of exposure, or 3) protect the exposed personnel by reducing the noise entering the ear.

1. Noise reduction

The most desirable exposure control method is to reduce noise to noninjurious levels both for the prevention of hearing loss and for other benefits which accrue. Application of known principles of noise control[4] usually can reduce any noise to any desired degree; however, economic considerations and/or operation necessities will often make the application impractical. Where practical methods of reducing noise to safe levels have been developed, they should be adopted.

2. Reduction of exposure time

Reduction of exposure time is seldom a practical method of reducing noise hazards in industry. Where the exposure can be limited and interspersed with recovery periods in noninjurious noise, Figure 2 may be used as a guide.

3. Ear protection

Where it is not feasible to reduce environmental noise to acceptable levels, ear protecters are commercially available which are capable of reducing noise entering the ears to acceptable levels for most noise exposures encountered in industry.[10] Plugs inserted into the ear canal must form an air-tight seal in order to obtain the full noise exclusion of which they are capable. In order to assure satisfactory protection, plugs should be fitted by a competent person. Muffs covering the entire ear are subject to fewer uncertainties of fit and positioning than ear plugs and usually are more dependable.

4. Planning hazard-free operations

Every effort should be made at the planning stage to minimize noise exposure. At this stage, a competent acoustical consultant can provide valuable services.

a. Noise abatement in engineering design

Engineers and architects should consider potentially hazardous noise exposures in the design of buildings and machines, and in the layout of floor plans. They should incorporate architectural and production features such as isolation of noisy operations, sound absorbing materials in construction, spacing of noisy machines and utilize all other available means to minimize noise exposures to personnel.

b. Noise rating considerations in purchasing equipment

Consideration should be given to possible noise exposures when new equipment is ordered or new facilities planned. Where hazardous noise exposures are likely to result from use of the equipment under consideration, noise data should be obtained from suppliers so that realistic estimates of noise exposure can be made. In selecting equipment, noise should be given due consideration.

C. Audiometry

Hearing acuity of persons likely to be exposed to excessive noise should be determined by pure tone audiometry. Audiometry should be conducted under medical supervision according to the conditions and procedures suggested below.

1. Facilities

To insure accurate audiograms, the facility must meet the following minimum standards:

a. Test room

Audiograms should be obtained only in environments which meet the requirements of the U.S.A. Standards Institute for background noise.[11]

b. Audiometer

Audiometers should meet the specifications of the U.S.A. Standards Institute,[12] and should be maintained in calibration in accordance with recognized procedures.

2. Personnel

Persons obtaining audiograms should be trained in air conduction audiometry either by formal course work at accredited educational institutions or by individual instruction provided by an audiologist or otologist. Audiometry should be conducted under medical supervision.

3. Audiograms

Preplacement audiograms should test hearing thresholds for both ears at frequencies of 500, 1000, 2000, 3000, 4000, and 6000 cps. Subsequent audiograms utilizing the same frequencies should be obtained as deemed necessary by the supervising physician. The frequency of follow-up audiograms will generally be related to the type and intensity of the noise exposure.

IV. Review

This document will be reviewed at intervals not exceeding three years and reaffirmed or revised as indicated by the current state of knowledge.

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American Conference of Governmental Industrial Hygienists' proposed threshold limit value for noise*

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The American Conference of Governmental Industrial Hygienists has proposed a Threshold Limit Value for Noise. The limit for broad band noise would be 92 decibels, as measured on the A-scale of a sound level meter (dBA), for exposure of 4 to 8 hours per day; 97 dBA for 2 to 4 hours; 102 dBA for 1 to 2 hours; and 107 dBA for less than 1 hour. The limit for narrow bands of noise or pure tones would be 5 decibels lower than that for broad band noise. A limit of 140 decibels peak sound-pressure level for impulsive or impact noise is recommended.

The American Conference of Governmental Industrial Hygienists has for a number of years recommended limits of exposure to chemical agents in the working environment by the setting of threshold limit values. During the past four years, a number of suggested limits of exposure for physical agents have been proposed by various organizations, but none of these limits have been accepted universally. Due to this lack of uniformity, the American Conference of Governmental Industrial Hygienists (ACGIH) in May 1967 established a Committee on Physical Agents. This Committee was directed to review the existing data on exposure of individuals to various physical agents and from time to time recommend to the Conference safe limits of exposure.

Since the establishment of the Committee, a number of meetings have been held at which data and proposed limits of exposure have been reviewed. At the meeting of the Conference in May 1968, an announcement was made of the intent of establishing a threshold limit value for noise in May 1969. This is in line with the policy established by the Committee on Threshold Limit Values for chemicals, whereby a notice of intent is given several months prior to the establishment of a tentative threshold limit value. This is done in order that interested groups may present evidence in support of the proposed limit or data which indicates that the proposed limit is in error. After all data is evaluated, the Committee will present a tentative threshold limit value to the Conference in May 1969. If this tentative limit is accepted by the Conference, it will remain on the tentative list for two years then be placed on the list of threshold limit values. These limits of exposure are reviewed annually for possible revision.

TABLE I
Percentage Increase in Hearing Impairment with Various Levels of Noise and Length of Exposure

Age, Years	Sound Level, dBA			
	85	90	92	95
20-29	0	1	1	2
30-39	1	4	5	8
40-49	2	6	8	12
50-59	3	8	10	16

The proposed threshold limit value for noise is printed in its entirety as Appendix I. In the development of these limits, much data was considered, and this can best be summarized by considering only one source, *Guidelines for Noise Exposure Control.*[1] Using the data presented in this paper, Table I was developed showing the percentage increase in number of employees with hearing impairment for various levels of noise and lengths of exposure. Hearing impairment is used here as it is defined by the American Academy of Ophthalmology and Otolaryngology[2] and the American Medical Association[3] as an average hearing threshold level in excess of 15 decibels (USASI 224.12-1952) at 500, 1000, and 2000 Hz.

In establishing any limit of exposure, many factors have to considered. Among these are the type of data available, validity of this data, type of control of exposure available, cost of these controls, and, of primary importance, the percentage

* Published in *Am. Ind. Hyg. Assoc. J.* 29:537-539 (Nov./Dec. 1968). Reprinted by permission of the American Industrial Hygiene Association.

of the group which will be protected by the established limit.

After considering the above factors and the data in Table I, the Committee decided that at the present time it appears desirable to establish a limit of 92 dBA for 4 to 8 hours of exposure per day to broad band continuous noise. All sound measurements are to be made with equipment meeting the appropriate standard of the United States of America Standards Institute. Data in Table I indicates that this limit would protect at least 90% of those people exposed to this level for a life-time. As more exposure data becomes available and the cost of engineering control is reduced, it would be desirable to revise the limit, if necessary, to protect a larger percentage of the population.

Laboratory data on temporary threshold shift and a limited amount of field data indicate that, when exposure is for less than a full 8-hour period or is intermittent in nature, the ear can tolerate more acoustical energy per day than for a single exposure to continuous noise.[4-6] Considering these two factors, the limit is increased 5 decibels for each halving of exposure time. The exposure time is the summation of the exposure periods for the work day regardless of whether this is a single exposure or an exposure which is intermittent in nature.

Many work situations are such that the levels of noise vary considerably throughout the work day. There may be a rather continuous background of noise upon which is superimposed various higher levels as equipment is turned on and off. This presents problems in evaluation if different times of exposure are permitted for diffeent levels of noise. The following formula should be used in evaluation of exposure to mixed levels of noise:

$$\frac{C_1}{T_1} + \frac{C_2}{T_1} + \ldots \frac{C_n}{T_n} = \frac{C}{T}$$

where C_1 = the time of exposure at a given level and

T_1 = the allowable time of exposure at this level. As long as the fraction C/T is less than one, it is assumed to represent a safe level of exposure. Exposure to levels of less than 92 dBA would not be included in the formula, as it is assumed that this is a safe level of exposure. The formula would be used as follows for evaluation of exposure:

Example 1

< 92 dBA, 6 hours

92-97 dBA, 1 hour

97-102 dBA, 1 hour

$$\frac{1}{4} + \frac{1}{2} = \frac{3}{4}, \text{ safe}$$

Example 2

< 92 dBA, 4 hours

92-97 dBA, 2 hours

97-107 dBA, 2 hours

$$\frac{2}{4} + \frac{2}{2} = \frac{6}{4}, \text{ unsafe}$$

The limits of exposure for narrow bands of noise or pure tones shall be 5 decibels less than those for broad band noise.[7-9] As the equipment most commonly used for evaluation of industrial noise exposure is the sound-level meter and the octave-band analyzer, narrow bands or pure tones will be assumed to be present if one octave is 5 dB higher than the adjacent octaves.

Very little data is available upon which to base exposure to impact or impulsive noise. It is known that exposure to a small number of 140 dB impulsive noises of short duration will produce a temporary threshold shift.[10-12] Until additional data is available, a limit of 140 dB is being set for impact or impulsive noise.

All data that is available to the Physical Agents Committee will be reviewed prior to the annual meeting of the Conference in May 1969. At this time a tentative Threshold Limit Value will be submitted to the Executive Committee and, if approved, will be submitted to the membership for adoption.

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Appendix I

The American Conference of Governmental Industrial Hygienists announces its intent to establish Threshold Limit Values for Noise, with limits as defined in the attached document at its meeting in May of 1968.

These limits have been proposed by the Physical Agents Committee with membership as follows:

Herbert H. Jones, USPHS, *Chairman*
Lt. Col. Herbert E. Bell, USAF
Irving H. Davis, Michigan Department of Health
Dr. Ernest Mastromatteo, Ontario Department of Health
Fred L. Ottoboni, California Department of Health
William H. Palmisano, U.S. Army
Dr. Charles H. Powell, USPHS
David H. Sliney, U.S. Army
Thomas K. Wilkinson, USPHS

Any comments or questions regarding these limits should be addressed to:

Herbert H. Jones
National Noise Study
Bureau of Occupational Safety and Health
1014 Broadway
Cincinnati, Ohio 45202

Threshold limit values

Noise

These threshold limit values refer to sound pressure levels that represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect on their ability to hear and understand normal speech. The medical profession[1,2] has defined hearing impairment as an average hearing threshold level in excess of 15 decibels (USASI 24.12-1952) at 500, 1000, and 2000 Hz, and the limits which are given have been established to prevent a hearing loss in excess of this value. Because of wide variations in individual susceptibility, exposure of an occasional individual at, or even below, the threshold limit may not prevent annoyance, aggravation of a pre-existing condition, or noise-induced hearing loss.

These values should be used as guides in the control of noise exposure, and due to individual susceptibility, should not be regarded as fine lines between safe and dangerous levels. They are based on the best available information from industrial experience and from experimental human studies. These values will be reviewed annually by the Committee on Physical Agents for revision or additions as further information becomes available.

Recommended values

These values apply to sound energy of noise, which is distributed more or less evenly throughout the eight octave bands with mid-frequencies from 63 to 8000 Hz determined by sound-measuring equipment meeting the standards of the United States of America Standard Institute.

TLVs AND OCCUPATIONAL STANDARDS 1970 THROUGH 1981

Background and interpretation of threshold limit values*

ERNEST MASTROMATTEO, M.D., D.P.H., D.I.H.
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Man in his occupational environment may be exposed to adverse factors and to harmful substances. Mining operations, because of their diversity, present a variety of occupational exposures — to dusts, fumes, gases, vapors, spray mists, noise, vibration, heat, radiation and to other agents. In such occupational exposures, it is necessary to know what levels constitute significant exposure in terms of health effects and alternatively what levels can be accepted without any risk to health.

Industrial hygiene may be defined as the science and art devoted to the recognition, evaluation and control of those enviornmental factors or stresses, arising in or from the work place, which may cause sickness, impaired health and well being, or significant discomfort and inefficiency among the workers. The use of acceptable exposure limits is an important tool for the industrial hygienist.

The concept of a threshold response to environmental agents is not new. Paracelsus in the Middle Ages noted that with poisons the dose was important. This applies equally well to harmful agents encountered at work. Implicit in this threshold concept is the notion that for every substance there is an exposure level at which no harmful effect is produced in the worker. In terms of work exposure, it is necessary to define these threshold levels and where necessary to control the work environment in order that workers will not be adversely affected.

TABLE I
Terms of Abbreviations

MAC	Maximum Allowable Concentration
MPC	Maximum Permissible Concentration
TLV	Threshold Limit Value
STL	Short-Term Limit
EEL	Emergency Exposure Limit
IPC	International Permissible Concentration
MABC	Maximum Acceptable Biological Concentration
BTV	Biological Threshold Value

The terms used to describe exposure limits have undergone gradual evolution and change. Some of the commoner terms and abbreviations used are shown in Table I.

Historical development

1912 — Kobert[1] in Germany published a list of "maximum endurable concentrations." Since this time, hygienic standards for air contaminants have been suggested by many authorities.

1933 — Zhitkova[2] listed allowable concentrations for "14 poisons in the air." These were established as Soviet industrial standards but they were so low that scant attention was paid to them.

1937 — The State of Massachusetts published MAC values.[3]

1940 — The American Standards Association (now American National Standards Institute) began its study of maximum allowable concentrations. These standards were very slow in coming. By 1962, only 18 had been developed.

1943 — The American Conference of Governmental Industrial Hygienists (ACGIH) began drawing up and recommending limits for air contaminants in industrial workplaces.

1947 — ACGIH published its first MAC listing. It contained 159 substances.

1949 — The ACGIH list was incorporated in the Model Code of Regulations of the International Labour Office.

1960 — The ACGIH list was adopted by the U.K. Ministry of Labour under the title of Maximum Permissible Concentrations.

1962 — The ACGIH published its list of Threshold Limit Values (TLVs). The TLV was defined as the time-weighted average concentrations of airborne

* Paper presented to the Mining Section, National Safety Council, October 26, 1971, Chicago, IL. Courtesy of Dr. Mastromatteo.

substances under which it is believed *nearly* all workers may be repeatedly exposed, day after day, for 8 hours a day, 5 days a week for a working lifetime without adverse effect. The documentation for TLVs was also published for the first time.

1963 — "Ceiling" values were shown on TLV list.

1964 — Pennsylvania enacted Short-Term Limits.

1971 — The current TLV lists nearly 500 substances.

Threshold limit values — general comments

The threshold limit values (TLVs) discussed here are those published annually by the ACGIH.[4] These are widely recognized and used around the world. They are intended to provide an effective means of protecting the worker against signficant effects, not only to his health but also to provide comparative freedom from irritation, discomfort and nuisance in his occupation and to improve his general work efficiency.

TLVs are meaningless unless used with the advice given in the introductory remarks in the preface. I believe there has been some tendency for these values to be used improperly by untrained persons. I believe it worthwhile to emphasize some of the comments made by the TLV Committee.

1. TLVs are intended as guides or benchmarks and not as fine lines between safe and dangerous concentrations.
2. Excursions above the TLV are permitted for those substances which do not have a ceiling value ("C" listing). Excursions above the TLV must be compensated by equivalent excursions below the limit during the work day. A guide to the magnitude of the excursions permitted is outlined in the documentation. For substances where the documentation is not explicit in this respect, the following rule of thumb may be used:

TLV (ppm or corresponding mg/m^3)	Excursion Factor
Up to 1	3
< 1-10	2
> 10-100	1.5
> 100-1000	1.25

3. TLVs are intended for use in the field of industrial hygiene and should be interpreted and applied only by persons trained in this field.
4. They are not intented for use, or for modification for use, for comparing the relative toxicity of two substances, for evaluating community air pollution, for estimating the toxic potential of continuous exposures, e.g., airborne contaminants in the home, as proof or disproof of an existing disease or physical condition, and for adoption by other countries with different nutritional status.
5. They are not considered appropriate matter for adoption in legislative codes and regulations. Despite this recommendation, the TLVs have been adopted in many codes.
6. *"Ceiling" limit.* Substances with a "C" prefix are in effect converted from time-weighted concentrations to maximum allowable concentrations or ceiling values. This group includes substances which are predominantly fast-acting and for which the limit is based on this action, e.g. irritant gases.
7. *"Skin" notation.* This notation is designed to draw attention to those substances which can be absorbed through the skin.
8. *Mixtures.* The application of these values to mixtures of two or more substances is covered in the TLV booklet and merits review in assessing mixed exposures.
9. *"Inert" or nuisance particulates.* A TLV of 30 mppcf or 10 mg/m^3 is recommended for nuisance substances for which no specific limit has been set.

All TLVs contain a factor of safety. The magnitude of this safety factor varies from substance to substance depending on:

1. *Seriousness of the toxic response.* If the substance presents a serious hazard, the safety factor is proportionately large — the TLV may be lowered by a tenfold factor from the "no effect" level. Examples: cyanide, carbon tetrachloride and phenol.
2. *Nature of toxic response.* For substances which act primarily as irritants or narcotics,

TABLE II
ACGIH 1971 TLVs Selected Gases and Vapors

		ppm	mg/m³
	*Ammonia	25	18
	Arsine	0.05	0.2
C	Benzene (benzol) — skin	25	80
	Carbon dioxide	5000	9000
	Carbon monoxide	50	55
	Carbon tetrachloride — skin	10	65
	Chlorine	1	3
C	Formaldehyde*	2	3
C	Hydrogen chloride	5	7
	Hydrogen cyanide — skin	10	11
	Hydrogen fluoride	3	2
	Hydrogen sulfide	10	15
	Nickel carbonyl	0.001	0.007
C	Nitrogen dioxide	5	9
	Nitroglycerin — skin	0.2	2
	Ozone	0.1	0.2
	Phosgene	0.1	0.4
	Phosphine	0.3	0.4
	Sulfur dioxide	5	13
C	Toluene-2,4-diisocyanate	0.02	0.14

* Notice of intended change for 1971.

a safety factor of 1.5 to 2 times is considered adequate. Examples: ammonia, trichloroethylene, methyl chloroform.

3. *Supporting data.* A proportionately large safety factor for TLVs is used where the adequacy of the data supporting the limit is in question.

4. *"Grandfather Status."* For some substances with a cumulative effect, the safety margin is rather small, but has been retained through long industrial use and medical experience. Examples: lead, mercury vapor, arsenic.

In summary, TLVs are established for airborne contaminants in occupational exposures on the basis of protecting exposed workers from: 1) discomfort, irritation, or nuisance effects, 2) narcosis, 3) toxic effects, 4) cancer, and 5) allergic effects.

For each TLV there is published data documenting the value selected.[5] Data included in the documentation include: animal experiments, human sensory response, data from exposed workers, accidental over-exposure and epidemiological data.

Stokinger has described the pharmacodynamic, biochemical and toxicologic studies in experimental animals which can be used to derive useful data in establishing threshold effects. He has also described the method of operation of the TLV Committee.

Some TLVs from the 1971 list are shown in Table II for gases and vapors and in Table III for dusts, fumes and mists. These have been selected as those which may be of special interest in mining operations.

The TLVs for mineral dusts are shown on Table IV.

TABLE III
ACGIH 1971 TLVs Selected Dusts, Fumes and Mists

	Substance	mg/m³
	Arsenic & compounds (as As)	0.5
	Beryllium	0.002
	Cadmium (metal dust and soluble salts)	0.2
C	Cadimum oxide fume (as Cd)	0.1
	Chromic acid and chromates (as CrO_3)	0.1
	Cobalt, metal fume and dust	0.1
	Copper, fume dusts and mists	0.1 1.0
	Fibrous glass	10.0
	Fluoride, as F	2.5
	Iron oxide fume	10.0
	Iron, soluble salts, as Fe	1.0
	*Lead, inorganic compounds, fume & dusts	0.15
C	Manganese and compounds, as Mn	5.0
	Mercury (all forms except alkyl)	0.05
	Nickel, metal and soluble compounds, as Ni	1.0
	Oil mist, particulate	5.0
	Platinum, soluble salts	0.002
	Silver, metal and soluble compounds	0.01
	Sulfuric acid	1.0
	Uranium (natural) sol. & insol. compounds	0.2
C	Vanadium, V_2O_5 V_2O_5 fume	0.5 0.1
	Zinc oxide fume	5.0
	Zirconium compounds, as Zr	5.0

* Notice of intended changes for 1971.

TABLE IV
ACGIH 1971 TLVs for Mineral Dusts

Substance	TLV
Asbestos	5 fibers/ml > 5 μ in length.
Coal dust	2 mg/m^3 (respirable dust).
Cristobalite	Use one-half the value calculated from the count or mass formulae for quartz.
Inert or Nuisance Particulates	10 mg/m^3 or 20 mppcf (whichever is the smaller) of total dust < 1% SiO_2.
Quartz	TLV in mppcf: $\frac{300}{\% \text{ quartz} + 10}$
	TLV for respirable dust in mg/m^3: $\frac{10 \text{ mg/m}^3}{\% \text{ resp. quartz} + 2}$
	TLV for "Total dust" respirable and non-respirable: $\frac{30 \text{ mg/m}^3}{\% \text{ quartz} + 3}$
Silica, fused	Use quartz formulae.
Tridymite	Use one-half the value calculated from quartz formulae.

In recent years there has been much discussion about respirable dusts. Many feel that it is more valid to express the TLVs for dust in terms of the amount of respirable dust in the air (in mg/m^3) rather than in terms of dust counts (mppcf). The TLVs listed in Table IV reflect this.

Short-term limits (STLs)

The STLs represent an upper limit of exposure for the specified time. It is assumed that there is sufficient recovery periods between the episodes for recuperation. The daily average exposure to the contaminant, including these episodes, shall be such that the TLV shall not be exceeded.

The need for STLs was felt particularly in smaller industries where short-term exposures existed. In 1964, Pennsylvania adopted 38 STLs for 5, 15 and 30 minute exposure period. In 1965 an additional 50 were approved.

It is important to realize that the STLs have no safety margin. Examples of the STLs are shown on Table V which shows the TLVs for comparison.

Emergency exposure limits (EELs)

The EELs are intended for use in emergency planning by specialists in industrial hygiene. Exposure to airborne contamination at the EELs will result in some discomfort, harm, or illness but of a temprary nature, e.g., mild to moderate irritation of the respiratory tract without residual damage.

These limits have application primarily in military and space programmes or in emergencies with chemical spills. They have no safety margin. These are not to be used for routine operations and they apply only to healthy working populations. The use of these limits assumes that medical surveillance is close at hand. EELs have been drawn up by the Committee on Toxicology of the National Academy of Sciences. Some EELs are shown in Table VI.

USSR permissible standards

No discussion on threshold limit values would be complete without reference to the *Standards of*

TABLE V
Pennsylvania STLs (1966) and ACGIH TLVs (1971)

	STL 1966		Time	TLV 1971	
Substance	ppm	mg/m^3	mins.	ppm	mg/m^3
Ammonia	100	70	30	25	18
Beryllium	—	0.025	5	—	0.002
Carbon monoxide	400	440	15	50	55
Carbon tetrachloride — skin	25	162	30	10	65
Fluoride, as F	—	10	30	—	2.5
C Nitrogen dioxide	25	45	5	5	9
Ozone	1	2	30	0.1	0.2
Sulfur dioxide	20	260	5	5	13

Permissible Level of Toxic Gases, Vapors and Dust in the Air of Industrial Premises published in the USSR. Standards for community air quality are also published in the USSR. The Soviet levels are generally far lower than the ACGIH TLVs. These are maximum concentrations rather than time-weighted averages. These standards are, however, based on different criteria from those in the United States. They are based on physiological not toxicological responses. Thresholds are derived from odour perception threshold, respiratory response threshold, optical chronaxy changes, light sensitivity reflex of the eye, electrocortical conditioned reflexes, and the ability of the cerebral cortex to assimilate imposed stimuli. Even Professor V.A. Ryazanov who is chairman of the equivalent USSR Committee, admits that the standards are not attained in the USSR.[6] They are the "ideal" from the viewpoint of the physiologist and the physician where the goal is as close to zero as possible. Stokinger, the Chairman of the ACGIH TLV Committee remains unconvinced that any of the reflex response procedures have yielded results that could be used for establishing TLVs.[7] In comparing the USSR and U.S. standards, those for dust and fumes are reasonably close, but those for gases and organic vapors are not. Some comparisons are noted in Table VII.

TABLE VII
Comparison of some USSR Permissible Levels (1966) and TLVs (1971)

Substance	(1) USSR mg/m³	(2) TLV mg/m³	Ratio (2:1)
Ammonia	20.0	18.0	1.1
Benzene	100.0	80.0	0.8
Beryllium	0.001	0.002	2.0
Butadiene	99.0	2200.0	22.0
Carbon monoxide	20.0	55.0	2.8
Carbon tetrachloride	2.0	65.0	33.0
Dust, miscellaneous	10.0	10.0	1.0
Fibrous glass	3.0	10.0	3.3
Lead	0.01	0.15	15.0
Manganese	0.3	5.0	16.7
Mercury — metallic	0.01	0.05	5.0
Methylene chloride	5.0	1740.0	348.0
Nitrogen dioxide	5.0	9.0	1.8
Petroleum naphtha	10.0	2000.0	200.0
Phosgene	0.5	0.4	0.8
Silica, 80% free silica	1.0	0.3	0.3
less than 10% Silica	4.0	3.0	1.3
Sulfur dioxide	7.8	13.0	1.7
Toluene	50.0	375.0	7.5
Toluene diisocyanate	0.5	0.14	0.3
Uranium, soluble	0.015	0.2	13.3
insoluble	0.075	0.2	2.7

TABLE VI
EELs Recommended to Military and Space Agencies by Committee on Toxicology N.A.S. - N.R.C. 1966 Compared to 1971 TLVs - ACGIH

Substance	ACGIH TLV ppm	EEL 60 min. (ppm)	EEL 30 min. (ppm)	EEL 10 min. (ppm)
Carbon disulfide	20	50	100	200
Carbon monoxide	50	400	800	1500
Fluorine	1	1	2	3
Hydrogen chloride*	5	10	20	30
Hydrogen fluoride	3	8	10	20
Hydrogen sulfide	10	50	100	200
Monmethylhydrazine*	0.2	3	7	10
Nitrogen dioxide*	5	10	20	30
Oxygen difluoride	0.05	0.1	0.2	0.5
Sulfur dioxide	5	10	20	30

* "C" notation in TLV list.

International permissible limits

At the Second Intenatlonal Symposium on Permissible Limits for Air of Workplaces, held in Paris in 1963, some provisional international values were adopted. They were not unanimous and the ones adopted were for those substances where there were close similarities between the Soviet and the ACGIH lists. It was also agreed to classify the substances into three groups, according to the character and the rate at which the response was evoked. Group I comprised primarily those substances which evoke primarily an acute toxic response; for these, the listed values are considered ceiling values not to be exceeded even for short periods. Group II substances comprised those which evoked primarily cumulative effects; for these time-weighted values are preferable. Group III includes substances that are primarily

TABLE VIII
Provisional International List of Permissible Limits - 1963

Group I		
Gases and Vapours	**ppm**	**mg/m³**
Ammonia	50	35
Arsine	0.05	0.2
n-Butyl alcohol	100	300
Butylamine	5	15
Chlorine	1	3
Hydrogen chloride	5	7
Hydrogen sulfide	10	15
Ozone	0.05	0.1
Sulfur dioxide	4	10
Toluene-2,4-diisocyanate	0.02	0.14
Dusts Fumes and Mists		
Chromic acid and chromate (as CrO_3)		0.1
Sulfuric acid		1
Vanadium, V_2O_5 dust		0.5
V_2O_5 fume		0.1
Zinc oxide, fume		5
Group II		
Beryllium, oxides and salts, as Be		0.002
Cadmium oxide, fume		0.1
Chlorinated naphthalene (more than 5 Cl per mol.)		0.5
Chlorodiphenyl (42% Cl)		1
m-Dinitrobenzene		1
Fluorides		2.5
Parathion		0.1
Trinitrotoluene		1
Group III		
To eliminate from the working environment		
Dimethylnitrosamine and homologues		
Benzidine		
beta-Naphthylamine		
beta-Propiolactone		

carcinogenic or allergenic; for those substances no specific limit is fixed, but contact by any route should not be permitted.[7] The proposed values are shown in Table VIII.

Biological threshold limits

Elkins[8] felt that biological threshold limits were entirely feasible and inevitable for many industrial hazards. in the case of workers exposed to lead, those who had 0.2 mg/L of lead in the urine or less were considered to be at the "primary" threshold, i.e., that excretion threshold which would not result in ill heatlh. Those excreting 0.8 mg/L or more were considered to be at the "secondary" threshold, i.e., that excretion threshold which will inevitably result in lead poisoning. The concept of a biological threshold value is very useful in monitoring groups of workers exposed to toxic chemicals. It is possible to assay urine, blood, faeces, expired breath, sputum, hair, nails and sweat for certain contaminants.

Body burden and air sampling for TLVs

Roach has recommended that for all TLVs the proper sampling time for the substance in air be also shown on the TLVlist. In his view, the sampling period for atmospheric sampling should be proportional to the half-time for the body burden of the particular contaminant, i.e., the time taken by the body to get rid of 50 percent of the absorbed material. Gases and irritants in the main have a short half-time in the body whereas mineral dusts have a long half-time. Roach suggested that the optimum sampling period should be 1/25th of the biologic half-time in body and he has published recommended sampling periods for common air contaminants Table IX. For some air contaminants, continuous monitoring throughout the day is recommended.

Other threshold limit values

Radioactive substances — I have not touched on permissible concentrations for radioactive substances in occupational exposure. There is a complete reference in this field.[9]

Physical agents — The ACGIH have established a Committee on Physical Agents to look into the matter of established threshold limit values for physical agents such as noise, microwaves, lasers, heat, ultrasonics, vibration, pressure and others. There are guidelines for those interested in this field. In 1971 for the first time the TLVs for airborne contaminants and for the physical agents have been published in a separate booklet. TLVs are now published for noise, lasers, microwaves, ultraviolet and heat.

Conclusions

The use of threshold limit values is necessary in the proper evaluation and control of potentially harmful agents encountered in the occupational environment. The TLVs prepared by the ACGIH are extremely useful for those in the industrial hygiene

TABLE IX
Recommended Sampling Periods for Air Contaminants (after Roach)

Substance	1971 TLV ppm	1971 TLV mg/m^3	Biological Half-time	Recommended Sampling Period
Acetone	1000	2400	< 20 mins.	Grab sample
Ammonia	25	18	< 20 mins.	Grab sample
Carbon Monoxide	50		2 hours	1 minute
Chlorine	1	3	< 20 mins.	Grab sample
Ethyl alcohol	1000	1900	10 hours	10 minutes
Hydrogen sulfide	10	15	< 20 mins.	Grab sample
Iron oxide fume	—	10	12 hours	10 minutes
Lead	—	0.15	6 months	8 hours*
Mercury	—	0.05	5 weeks	8 hours*
Nitrogen dioxide	5	9	1 hour	1 minute
Trichloroethylene	100	535	2 hours	1 minute
Mineral dusts	5 - 30 mppcf		> 6 months	8 hours*

* Equivalent to continuous monitoring.

field. Other suggested air contaminant levels have more limited application, e.g., EELs.

TLVs are not magic numbers. They do not mark that fine line between safe and dangerous concentrations. When used, however, by persons experienced in the occupational health field, they become an important tool in evaluating the environment. Their interpretation and application by individuals untrained in their use may lead to difficulties. They should not be regarded as levels to which industry can work up to. The ideal should be to minimize all exposure to chemical agents where possible.

While most industrial hygienists feel that TLVs should not be used in legislative codes, they have been used in such codes. In testing occupational environment for compliance with the TLVs, it must be remember that excesses above the TLV are permissible. These excursions should vary in magnitude with the nature of the substance. In many cases the magnitude of the excusion can be determined by consulting the TLV Documentation or the ANSI limits. If neither has this information, TLV rules of thumb should be applied for excursion.

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Toxicity of airborne chemicals: air quality standards — a national and international view*

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Past reviews in this annual appearing under the broad title "Toxicology" have dealt respectively with selected organic and organometallic substances,[1] selected inorganic substances of both industrial and environmental concern,[2] and Soviet toxicology, including their general principles for establishing tolerance limits for environmental chemicals and their toxicologic methods of handling complex environmental problems.[3] The present review will provide *a)* a critical comparison of the philosophic bases of the American and Soviet air quality standards accounting for the intercountry differences in the limits of certain substances, *b)* a critical discussion of the scientific background (criteria) of the air quality standards of a half-dozen of the those airborne substances of greatest present-day concern for human exposures in both in-plant and urban communities in the USA, and *c)* a presentation of the reasons for differences in the limits of the air quality standards for the two.

Standards for limiting exposures to airborne substances

Control of exposures to airborne chemicals in American industry has been achieved by compliance with Threshold Limit Values (TLVs) recommended largely by the Threshold Limits Committee of the American Conference of Governmental Industrial Hygienists,[4a,4b] for now more than a quarter of a century. Control of similar exposures of urban populations has been attempted by so-called air quality standards, more recently by "emission" standards, an engineering procedure calculated to limit industrial chemical effluents at their source.

The TLVs represent time-weighted average concentrations of airborne substances associated with industrial operations and manufacture, designed to protect the health and well-being of nearly all workers repeatedly exposed during a 7- or 8-hour workday and 40-hour workweek,[4] not only for their working lifetime, but after retirement. Because of the time-weighted averaging of the air concentrations, the TLVs represent guides in the control of health hazards. Hence, the limits should not be considered fine lines between safe and dangerous concentrations. For another reason also, incorporated in the TLVs are "safety factors" of varying magnitudes (depending on the seriousness of the response) that add in most instances a comfortable "cushion" in the form of several-fold decrements from *a)* borderline effects, if the limit is based on human experience, or *b)* "no-effect," if based on animal data. Exceptions to the time-weighted averaging practice are a certain number (ca 6% of the approximately 500, 1971 limits) of substances for which the TLV represents a "ceiling" value, a maximal value that should not be exceeded. Ceiling TLVs are attached to those substances that have the potential of causing *a)* intolerable irritation, *b)* chronic or irreversible change, *c)* narcoses of sufficient degree to increase accident proneness, impair self-resuce, or materially reduce work efficiency.[4] Thus, the basis for limiting exposures to airborne substances in industry is first and foremost for the protection of the health and well-being of the worker. Limits are also established for nonhazardous substances, such as "inert" dusts, mists, and vapors in the interest of good housekeeping and reduction of nuisance. Some TLVs of substances common to both industrial and community atmospheres are given in Table I.

Air quality standards for industry and community

Table I offers a side-by-side comparison of the official (and certain unofficial) air standards in the USA and in the USSR as promulgated by the appropriate agencies of the respective governments. The pollutants in industrial air listed in Table I have been limited to those for which the

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TABLE I
Air Quality Standards for Industry and Community

Air Pollutant	TLV or MPC for Industrial Air mg/m³ USA (4) TLV	USSR (8a) MPC	Int'l[b]	AQS for Community Air mg/m³ USA (6) Primary[a]	USA (6) Secondary[a]	California	USSR (8b)
Acrolein	0.25	0.7	—	0.025		—	0.03
Carbon monoxide	55	20	—	10 (8-hr. max.) (ne) 40 (1-hr. max.) (ne)		10 (12-hr. av.)	1 (24-hr. av.) 3 (max.)
Ethylene	1,100	—	—	—	0.05 rural (8-hr. max.) (5) 0.1 residential 0.15 commercial 0.2 industrial	—	3 (24-hr. av.)
Fluoride, as HF	2	1	1-2	—	0.0035 (24-hr. av.) (5)	—	0.005 (24-hr. av.) 0.2 (max.)
Hydrocarbons	—	—	—	0.16 (3-hr. max.) (ne)		—	—
Hydrogen sulfide	15	10	10-15	—	—	0.05 (1-hr. av.)	0.008 (max. & 24-hr. av.)
Iron oxide	10	—	—	—	0.1 rural (24-hr. max.) (5) 0.15 residential 0.2 commercial 0.25 industrial	—	—
Lead	0.2	0.01	—	—	—	0.0015 (30-day av.)	0.0007 (24-hr. av.)
Nitrogen oxide	C9	5	5-9	0.100 (annual arithmetic mean)		0.45 (1-hr. max.)	0.085 (24-hr. av.)
Particulates	—	—	—	0.075 (annual geometric mean) 0.260 (24-hr. max.) (ne)	0.060 (annual geometric mean) 0.150 (24-hr. max.) (ne)	0.060 (annual geometric mean)	—
Photochemical oxidant (ozone)	0.1	0.1	0.1	0.160 (1-hr. max.) (ne)		0.20 (1-hr. av.)	—
Sulfur dioxide	13	10	10-13	0.080 (annual arithmetic mean) 0.365 (24-hr. max.) (ne)	0.060 (annual arithmetic mean) 0.260 (24-hr. max.) (ne) 1.300 (3-hr. max.) (ne)	—	0.05 (24-hr. max.) 0.5 (max.)

[a]Primary and secondary air quality standards as legally defined in Part 410.2 of (6). Essentially a **primary** standard is based on health effects; a **secondary** standard, on nonhealth effects, such as vegetation damage, soiling, reduction in visibility, etc., i.e. protection of the public welfare as opposed to public health.

(ne) Not to be exceeded more than once per year.

mg/m³ — Milligrams of substances per cubic meter of contaminated air at 25°C and 760 mm Hg pressure.

C — Ceiling or maximal value as opposed to time-weighted average value, corresponding to the USSR, Maximum Permissible Concentration (MPC).

[b]From Joint ILO/WHO Committee on Occupational Health, 6th Report, *Permissible Limits of Occupational Exposures to Airborne Toxic Substances*, Geneva, June 1968. Present international limits are derived only from those substances whose limits differ by no more than a factor of 2 in USA and USSR.

corresponding limits have been set for community air. In the USA six Air Quality Standards (AQS) for community air were promulgated in April 1971,[6] each of which is extensively documented. By comparison, the USSR has standards for 114 substances,[8b] the documentations for which were not available at this time. Without such documentation it is not possible to discover the basis for the differences in the respective air standards of the two countries. For example, on what basis did the Soviet select the low AQS for carbon monoxide of 1 mg/m^3? (Table I).

The standards for industrial air far outnumber those for community air, the USA having somewhat over 500,[4] the USSR somewhat under 500.[8a] Setting of a standard is tantamount to determining compliance with that standard and all that is entailed. Air pollutant control in factories is far more manageable, for each factory has a limited number and furthermore knows what the pollutants are, a situation far from true in respect to community air.

It is evident from Table I that the pollutants of concern are not identical in both countries. For example, the Soviet list for industrial air contains no limit for ethylene or iron oxide, no AQS for community air for hydrocarbons, iron oxide, particulates, or photochemical oxidants. The omission of an AQS for hydrocarbons and photochemical oxidants is understandable, if motor vehicle traffic density and ultraviolet intensity, prime factors for development of these pollutants, are low in the USSR. The USSR limits for hydrogen sulfide and lead may indicate pollutants of present or future concern, or merely a philosophy of "preparedness" in the event of future need, as is readily interpretable from their large list of 114 pollutants. The USA has withheld an official AQS and an emmision standard for lead on the basis that future unleaded gasolines will reduce community air concentrations to levels of no physiologic significance; hydrogen sulfide has been relegated to a low priority.

USA, USSR differences in permissible limits

Comparison of the limiting values for the same pollutants in the USSR and the USA reveals still further international differences (Table I). In general, the USSR standards tend to be lower, both for industrial and community air, than the corresponding standards in the USA. Most notable in this respect is the industrial standard for carbon monoxide (CO), 20 vs 55 mg/m^3, although the standard permits excursions to 50 mg/m^3 for periods not exceeding 1 hour, to 100 mg/m^3 for 30 minutes, and to 200 mg/m^3 for 15 minutes, with the additional stipulation that, when such excursions occur, interruption of exposure should be no less than two hours. The excursion permitted by the State of Pennsylvania, USA, approximates 400 mg/m^3 for 15 minutes, and assumes sufficient recovery periods for recuperation between exposures, with the further requirement that the TLV for the 8-hour workday shall not be exceeded. The USA industrial standard of 55 mg/m^3 has proved, since its issuance in 1965, entirely satisfactory for U.S. workmen, provided there are no significant concomitant exposures to other pollutants (carbon dioxide, motor exhaust, or excessive heat). Hence, it would appear that the Soviet standard contains a very large factor of safety.

A similar conclusion can be reached for the USSR standards for community air, particularly, again, for CO; the 1 mg/m^3 as a 24-hour average concentration is extremely low, when it is realized that man creates for himself a CO environment[14] greater than that exogenously obtained from 1 mg/m^3 in the ambient air. The remainder of the USSR standards are in line with those recommended elsewhere, but with larger safety factors.

A major distinction in the USA standards for community air is the establishment of so-called primary and secondary air standards[6] — the primary standard having its prime concern for the health of man; the secondary standard, for his welfare, the things he sees, feels, and owns, and doesn't like to see degraded, injured, or destroyed. Not all air pollutants have both standards, because many affect health only, and do not affect his senses or possessions. Of the six ambient air pollutants listed in Table I, only two, particulates and sulfur dioxide, have both. The secondary standards, both more stringent than the primary, indicate that lower concentrations are required to protect man's environment than his health. It is not clear why secondary standards were not also set for photochemical oxidants that injure foliage (e.g., tobacco leaves) at far lower levels (0.04 mg/m^3) than those established (0.160 mg/m^3) for health reasons. Similarly, nitrogen dioxide is cor-

rosive to metal surfaces at far lower levels than 0.1 mg/m^3, the standard set for health protection.

Table I also lists the AQS for California as illustrative of the provision that a State may establish its own official standards provided they meet the requirements of the federal standards. California, the first state in the nation to develop AQS (1959), has, on November 19, 1970, officially adopted seven standards. The inclusion of a standard for hydrogen sulfide and lead, not established by the federal government, points up the frequent need for local authorities to establish standards for pollutants special to their particular environment.

There also exist unofficial air standards, "Community Air Quality Guides"[5] developed by an expert committee of the American Industrial Hygiene Association which began issuing the Guides in 1968 and periodically issues additional Guides. Ten Guides are available to 1971: aldehydes, carbon monoxide, ethylene, iron oxide, ozone, particulates, phenols and cresols, sulfur compounds, one on Rationale, and another on Regional Planning. A characteristic feature of some of these Guides is a differential limit according to population density based to some extent on feasibility, i.e., the lower the density, the lower the limit (Table I).

The limited number (about two dozen) of international industrial air standards can be dispensed with by the brief comment appearing in the legend to Table I. No close agreement between the USSR and USA standards could be made at the international meeting in Geneva in 1968 because the documentations providing the bases for the differences were not available from the Soviet Maximum Permissible Concentrations (MPC) Committee, which compares to that of the U.S. TLV Committee.[4b]

Air standards in other countries

The International Labor Organization has assembled (1968) lists of official standards for the air of workplaces (TLVs, MPCs, MAKs, etc.) of 19 countries.[9] Only a few of the highly industrialized nations of the world do not now have official industrial air standards (Italy, France, Czechoslovakia, and the Scandinavian countries — Sweden, Norway, Denmark, and Finland). Whether official or unofficial, the standards adopted by the non-Communist countries have been the threshold limit values of the USA used for the most part as maximal values and with modifications for certain few substances when found by test that a TLV was unsuited for the work conditions of a particular country (e.g., Italy, Japan, and the Federal Republic of Germany). Czechoslovakia, Hungary, Yugoslavia, and Poland have adopted "compromise" standards for those substances for which large differences between the USSR and the USA standards exist. For example, the Czechoslovakian standard for trichloroethylene is 250 mg/m^3, that of the USSR 10 mg/m^3, that of the USA 535 mg/m^3.

A similar list of air standards for community air of ten sponsoring countries has been assembled by the World Health Organization following an interregional symposium held in Geneva, October 1970.[10] Like the industrial standards, the number and type of the community standards of each nation tended to reflect the degree of concern for those pollutants characteristic of the nation. Following USSR with 114, Israel with 44, Czechoslovakia, 18; Italy, 13; West Germany, U.S., and The Netherlands, 6; France and Sweden, 2 and 1, respectively; Japan, oddly one of the most highly airpolluted nations of the world, had but 3.

Documentation of the standards

The bases of all U.S. air standards are fully set forth and documented with references to the scientific literature. For the more than 500 Threshold Limit Values for industrial air the documentations are in a single bound volume now in its third edition.[4b] The far more extensive documentation and background information available on each of the six community air standards include occurrence, properties, background levels, pollutant emission or formation and control, toxicologic effects in animals and man, sampling and measurement, and epidemiologic appraisals. Documentation for each standard is available as a separate document.[11] Documentation for the USSR standards is distributed throughout the Soviet scientific literature. The Czechoslovak committee on MACs (maximal allowable concentrations) published a summary documentation of its MACs for 93 substances most commonly encountered in Czech industry, with a comparison of air standards in other countries.[12]

Distinctions between air quality standards for industry and community

Comparison of the limiting concentrations of the TLVs for industrial air with the AQS for community air reveals, on first glance, outstanding discrepancies in the permissible limits, if the basis, protection of human health, is the same in both cases. Protection of human health, however, is not the sole basis, as the following examination shows.

The bases for AQS for community atmospheres in contrast with those of the TLVs are multifold. Depending upon the type of air pollutant, not only is the protection of human health and well-being considered, but foliage and crop damage, soiling, visibility reduction, corrosion, among other factors, may ultimately be the prime determinants of AQS. Depending upon the specific basis on which the AQS ultimately rests, it may be seen (Table I) that differential factors between AQS and TLVs may range from one-half (ozone) to one-hundredth (nitrogen dioxide, sulfur dioxide, iron oxide) to one-thousandth (lead) or more (hydrogen fluoride). Obviously, such great differentials cannot have as their basis solely the differing susceptibilities of exposed population groups, large though they often are.

Before identifying the basis for differences in AQS and TLVs for each air pollutant in Table I, it is most important to understand why the working population can tolerate higher levels of air pollutant exposure than the population at large. First, the working population is drawn, by and large, from essentially normal, healthy, adult individuals, certainly those who are to be exposed to potentially noxious fumes, dusts, mists, and vapors. This is far from true of the community dweller in the home. The urban dweller is a composite of all ages, with all the ranges in susceptibilities of the very young and the indispositions and debilites of the very old, including in particilar, as far as air pollutants are concerned, diseases of the cardiorespiratory system, chronic obstructive pulmonary disease, chronic bronchitis, emphysema, and other related diseases associated with aging. Such individuals are not in the work force because of age or infirmity. Second, separated out from the work force likely to be exposed to respiratory irritants by virtue of job selection, are the intrinsic and extrinsic asthmatics, for whom the susceptibility factor is estimated to be 5- to 10-fold, depending on the pollutant. Clearly, this and similar job-selective processes make for a worker group with far greater capacity for exposure without response to air pollutants than the population at large. The factors expressing the differential susceptibility between diseased and healthy populations vary widely according to extent of the disease and age of the diseased. The factor for age alone is widely variant, from several-fold positive (increased susceptibility) from infancy and youth, to several-fold negative (increased resistance) in old age, at least for effects of respiratory irritants on the lung, amounting to a factor of 2- or 3-fold.

Basis of AQS-TLV differences

In this section, the scientific basis for the differences in the limiting concentrations of the standards for community and industrial air will be presented for some of the more prominent air pollutants given in Table I. Because the basis for the differences varies markedly from pollutant to pollutant, each will be discussed separately.

Carbon monoxide (CO)

This ubiquitous pollutant of all urban atmospheres, arising as it does from incomplete combustion of fossil fuels and carbonaceous materials, coal, mineral oils, wood, and tobacco particularly, also is a constant endogenous metabolite of man.[1-4] In individuals not otherwise exposed to CO, each molecule of heme destroyed results in one molecule of CO. As there is continuous red cell destruction, a normal adult forms about 0.42 ml CO/hr. Obviously, one who inhales tobacco smoke or is exposed to ambient CO will form additional amounts, as the chief scavenger of either endogenous or inhaled CO is hemoglobin, forming carbon monoxyhemoglobin (COHb). Although the scavenging power of human hemoglobin for CO is about 210 times that for O_2, release of CO through the lungs readily occurs because the differential in partial pressure of CO in the lungs is essentially infinite in a nonCO-containing atmosphere. This excretory mechanism has been partly compromised, however, since the time man first sat by his cooking fire to the present when exogenuous sources such as the unvented oil-burning spaceheater, coal-burning power stations, gasoline-driven vehicles, and tobacco smoke

inhalation have increased the CO partial pressure of his environment. For industrial workers, metal refinery workers, garage mechanics, tunnel and border-crossing attendants, submarine crews, et al, this increase may be of such a degree as to break down completely homeostatic mechanisms requiring exposure limits to prevent unpleasant responses such as sleepiness, headache, and nausea.

Before setting forth the basis of AQS-TLV differences for CO, the importance of the duration of exposure to the response to CO should be emphasized. Because the partition coefficient for CO between alveolar air and pulmonary blood is such as to delay transfer of the CO-laden air to the circulating hemoglobin where it is bound as COHb, it is essential in any estimation of the response to know how long the exposure was experienced as well as the concentration of the exposure. At 100 ppm CO, for example, six to seven hours of inhalation at normal breathing rates are required to attain an essentially steady state value of COHb.[16] Hence, short exposures of a few minutes duration as in a traverse through automotive vehicular tunnels, where CO concentrations may attain 100 or 200 ppm, will have no adverse physiologic effect from CO *per se*, even in individuals with severe cardiorespiratory difficulties.

Those individuals with such difficulties as well as those with the different forms of chronic obstructive respiratory disease, or indeed, anyone who has reduced oxyhemoglobin saturation, will be the ones to respond to, and have to be protected from, levels far below those readily tolerated by the industrial worker, if exposure is of several hours duration, cyclicly repeating, or continuous as is the CO exposure pattern of community air. Recognition of these considerations has been taken in arriving at definitive boundaries for CO exposure for such individuals in the recommendation that community air quality values be set at levels that will not exceed one-half of 5 to 6% COHb prior to tobacco smoke consumption. This provides for susceptibles a time-based margin of safety before reaching the critical 5 to 10% COHb range for such individuals.[5] Recent data indicate that the rate of uptake of CO at levels less than 100 ppm, as well as the rate of formation of COHb, parallels those found for levels greater than 100 ppm as reported by Forbes *et al.*[15] Thus the basis for the AQS-TLV differences rests on the greater ease of attaining critical levels of anoxia in individuals already having reduced oxyhemoglobin saturation. The AQS of 10 mg/m^3 CO as an 8-hour maximum is intended to prevent reaching these critical levels in such individuals.

Support for the validity of the TLV of 55 mg/m^3 CO for healthy adult workers has been reported;[17] no untoward effects were observed in sedentary males exposed at twice the TLV for 8 hours, as determined by lack of impairment in manual dexterity following exposure.

Sulfur dioxide (SO_2)

This air pollutant is unbiquitous wherever fossil fuels, coal, oil-shale, and petroleum are burned. Burning releases SO_2 and SO_3 to the atmosphere in a ratio between 25:1, to 100:1, the latter ratio being more common. Other sources are the roasting and smelting of ores, petroleum refining, and paper-pulp manufacture. These sources produce more localized sulfur oxide pollution.

The chief effect of SO_2 on normal man is upper respiratory tract irritation resulting in reflex bronchoconstriction and increased pulmonary flow resistance. At concentrations in the range of 0.3 to 1 ppm, SO_2 can be detected by the average individual by taste rather than odor. The odor threshold is about 0.5 ppm. Accordingly, neither the annual mean nor the 24-hour maximum primary or secondary U.S. standard permits SO_2 to be detected by odor, and the 3-hour maximum is just at the point of bare detection by some sensitive individuals.

The justification of the industrial TLV of 5 ppm rests on the following considerations. Complaints of discomfort among some uninured workers at 10 ppm, but not at 5 ppm, is a partial basis. Moreover, no chronic, systemic effects were observed in oil refinery workers in Persia exposed for from 1 to 19 years when daily exposures were commonly as high as 25 ppm, and on occasion were as high as 100 ppm.[18] Some basis for these findings may be found in a report showing that virtually all SO_2 gas is absorbed by the nasal mucosa when inhaled by human volunteers at an entering average level of 16 ppm.[19] On the other hand, paper-pulp workers in Norway exposed at SO_2 levels of from 2 to 36 ppm showed an increased frequency of cough, expectoration, and dyspnea on exertion, and lower maximal expiratory

flow rate.[20] Inasmuch as the negative findings were made under conditions of very low humidity (Persian oil fields), whereas positive findings were made at far higher humidities (Norway), one can reasonably conclude that SO_2 at high humidities needs to be controlled to lower levels to be without effect. General confirmation of this observation is seen in the greater frequency of bronchitis associated with SO_2 pollution in highly humid London and Milan than in other SO_2-polluted cities without such humidities. Thus, with adaptation (inurement) of workers repeatedly exposed to SO_2 playing such a large role, coupled with the lack of chronic systemic effects at levels below 10 ppm, the industrial air standard of 5 ppm seems appropriate and has stood the test of time (15 years).

For community air the primary SO_2 standard, like the standard for CO, must take into consideration primarily two groups of individuals, the so-called cardiorespiratory "cripples" (those with chronic obstructive pulmonary disease, COPD, and cardiorespiratory difficulties) and the asthmatics, both groups being unable to sustain any protracted exposures without immediate extreme discomfort (asthmatic attack) or death. Unfortunate for the choice of the primary AQS for SO_2, the laboratory studies on animals are only partly relevant, and those done on man were performed on healthy volunteers.[11] The basis for the primary standard, therefore, had to be derived from epidemiologic data on urban smog episodes (Denora, Pennsylvania; New York City; Chicago; London; Rotterdam; Ruhr). These data were of two kinds; excess mortality or morbidity (increased number of visits to emergency clinics) associated with rise in SO_2-smog levels. The most recent of such studies[21] reported an excess of 10 to 20 deaths per day in New York City on days when SO_2 levels rose from 0.2 ppm (0.57 mg/m^3) to 0.4 ppm (1.14 mg/m^3) or greater. Statistical evidence indicated the mortality was associated with increased levels of SO_2 and was independent of weather conditions. The report did not identify the cause of death, however; the assumption was that they were diseased individuals and not careless motor vehicle drivers and thus died of causes unrelated to air pollution. In another typical study[22] the hospital admissions for respiratory tract "irritation" rose when the SO_2 level rose from 0.11 ppm to 0.19 ppm (0.3 mg/m^3 to 0.5 mg/m^3), some of whom were presumably asthmatics. In such individuals an "attack" can be precipitated at the SO_2 odor detection limit (ca 0.5 ppm; 1.3 mg/m^3).

Using the above-quoted general population response levels of SO_2 ranging from about 0.5 mg/m^3 to greater than 1 mg/m^3, the primary AQS of 0.08 mg/m^3, as an annual mean with a 24-hour maximum of 0.365 mg/m^3, becomes a reasonable standard for preventing exacerbation of COPD and asthmatic attacks. On this basis, the reason for the wide AQS-TLV differences becomes apparent.

For the secondary standards for community air providing protection of the public welfare, the levels of SO_2 that *minimize* its effects on materials and vegetation are the determinants. The levels critical to the development of this standard are the following. On materials, corrosion rate at a mean SO_2 level of 0.12 ppm (0.34 mg/m^3) was about 50% greater than at the least corrosive site (0.03 ppm; 0.08 mg/m^3).[11] Electrical equipment of all kinds is especially susceptible, but building materials — limestone, marble, slate, and mortar, statuary and art works are deteriorated and discolored. Certain textile fibers — cotton, rayon, and nylon are harmed and dyed fabrics fade at annual average SO_2 levels of 0.09 ppm (0.256 mg/m^3). Although vegetation varies widely in susceptibility to acute SO_2 injury, levels of 0.3 ppm (0.85 mg/m^3) as an 8-hour maximum, if not exceeded, will prevent acute damage. (This maximum corresponds to an annual average of between 0.03 and 0.05 ppm). However, these SO_2 concentrations may react synergistically with either ozone or nitrogen dioxide to produce acute injury in some sensitive varieties.

From these criteria, it is clear why the secondary SO_2 air standards are *a)* lower than the primary; and *b)* consequently far more stringent than the corresponding standard for workroom air.

Nitrogen dioxide (NO_2)

This pollutant with a TLV-AQS difference of almost 100-fold has the same value for both primary and secondary ambient air quality standard (Table I). No AQS have been set for other oxides of nitrogen, principally because they react in such a way in air as to produce NO_2. The chief reason for the lack of a secondary standard is that the primary standard for the protection of human health is sufficiently low to protect public welfare also.

The AQS of 100 $\mu g/m^3$ (0.05 ppm) as an annual arithmetic mean was arrived at on the report of greater incidence of adverse health effects (acute bronchitis) in infants and children of school age in areas where the mean 24-hour NO_2 concentration varied from 118 to 156 $\mu g/m^3$ (0.063 to 0.083 ppm). Other reports of increased incidence of acute respiratory disease in family groups have appeared when the mean 24-hour NO_2 concentration was between 117 and 205 $\mu g/m^3$ (0.062 and 0.109 ppm) and the mean level of suspended nitrates was 3.8 $\mu g/m^3$ or greater.[11] Because the NO_2 effects on the generation of oxidant smog, by interaction with "nonmethane" hydrocarbons, the effects on vegetation, and on metal surfaces (corrosion) occur at levels either at or above those producing adverse effects on health, it is clear why both the primary and secondary standards are the same.

The approximately 100-fold higher TLV (a ceiling 0.05 ppm, 8 hours daily, 40 hours per week) is explicable on the basis of long industrial experience in the USA and abroad where measured exposure concentrations five- to seven-fold the TLV resulted in no adverse effects in workers exposed daily for several years.[4b] The TLV is a ceiling or maximum limit as a result of animal experimentation indicating that NO_2 may act as a mild tumor-accelerating agent in lung-tumor susceptible mice.

Hydrocarbons

The designation of this class of air pollutants refers to those organic structures of carbon and hydrogen that exist in the atmosphere in the gas phase. This excludes the polycyclic aromatic hydrocarbons that are scheduled as a separate AQS. Although 26 nonaromatic hydrocarbons have been quantitatively identified in the ambient air of Riverside, California, the unsaturated hydrocarbon, ethylene, proves to be the sole gaseous hydrocarbon of air pollution concern.[11] The concern, however, is not for reasons of public health (although many of the health effects associated with photochemical smog are indirectly related to ambient levels of these hydrocarbons) but for reasons of public welfare; injury to sensitive plants (tobacco, peas, orchids, carnations) has been reported[11] in association with ethylene concentrations of from 1.15 to 575 $\mu g/m^3$ (0.001 to 0.5 ppm) during an exposure of from 8 to 24 hours. The AQS of 160 $\mu g/m^3$ as a 3-hour maximum reflects the need to control hydrocarbons for the protection of sensitive vegetation.

No industrial air standard exists for hydrocarbons as a group; rather, TLVs have been established for individual hydrocarbons. For ethylene, the TLV has been set at 1000 ppm (1100 mg/m^3), the standard for simple asphyxiants and "inert" gases and vapors. Thus, the lack of human health effects makes the huge TLV-AQS disparity of 14,500 fold obvious.

Photochemical oxidant (Ozone)

Discussion of the air standards for this group of pollutants is not concerned with explaining the basis for the difference, for there is little; rather, explanation for the similarity of the industrial and community standards is in order.

Photochemical oxidant represents a group of oxidation products resulting from the interaction of oxygen, nitrogen dioxide, and ultraviolet light on airborne gaseous hydrocarbons discussed in the previous section. Ozone (O_3) is the dominant constituent (up to 90%) of oxidant smog which is defined as a substance that oxidizes a select reagent not oxidizable by oxygen. Within this definition are included besides O_3, free radical oxygen forms, both free and combined with carbon moieties of unmeasured and varying amount, peroxyacyl nitrates (PAN homologues) to the extent of about 0.6% of total oxidant, and certain oxides of nitrogen, NO, and NO_2.

Oxidant at sufficient concentration affects adversely the health of man in brief or protracted exposures, affects vegetation, attacks fabrics, and polymers such as rubber, and fades dyes and coloring materials. Exposure of populations to ambient air containing an oxidant level of about 250 $\mu g/m^3$ (0.13 ppm, maximum daily value) has caused an increase in the number of asthmatic attacks in about 5% of a group of asthmatics,[11] a value associated with a maximum hourly average of 100 to 120 $\mu g/m^3$. By comparison, pure O_3 exposures of nonasthmatic human volunteers at 590 $\mu g/m^3$ resulted in nose and throat irritation after eight consecutive hours, and 980 $\mu g/m^3$ three hours per day gave decreased forced expiratory volume ($FEV_{1.0}$) after eight weeks, but 390 $\mu g/m^3$ (0.2 ppm) was without measurable effect after 12 weeks of 3-hour daily exposures. These

were the data that served as the criteria for the AQS for O_3 of 160 $\mu g/m^3$ for a 1-hour maximum. Although leaf damage to certain sensitive plants (bean, peanut, tobacco, carnation) occurs from exposure to smog, O_3, or PAN at levels somewhat lower than those affecting human health (20-100 $\mu g/m^3$), oddly, no secondary standard was set for photo-oxidants; presumably the economic burden of reducing the primary standard to protect areas where such vegetation is not likely to grow, balanced off the risk to the vegetation.

Particulates

As defined in the official document,[11] atmospheric particulates are either solid or liquid matter suspended in air (hence called aerosols) and obviously, thus comprise a wide variety of substances with one common feature, a submicron size, i.e., less than 1 μm. This characteristic permits their suspension in air for periods of several months, under suitable meteorologic conditions. (The dust cloud from the Krakatoa eruption, estimated to rise 100,000 feet, completely circled the globe 3¼ times before final dissipation, requiring two years before the world's sunset cleared.)

Because of their widely diversified nature, airborne particulates impinge themselves on the polluted environmental scene in eight manners:

1. *Effects on health.* As far as is now known, the effects at current levels of particulates are limited to the respiratory tract by serving as nuclei for carrying toxic gases to the deeper recesses of the respiratory tract that otherwise, because of their solubility, would never reach sensitive sites. Excess mortality and increase in illnesses have been observed in New York City at a smoke-shade index of 5-6 cohs (coefficient of haze) when the SO_2 level was high. The lowest particulate levels associated with health effects showed increased death rates in Buffalo at annual geometric means of 100 $\mu g/m^3$ and above. Further evidence for the role of particulates is the decrease in sputum volume with decrease in smoke pollution.[11]
2. *Effects on visibility.* Airborne particles in smog reduce visibility by scattering and absorbing light. Impingement on public welfare is reflected in restrictions on aircraft operations which occur at particulate loadings of from 75 to 300 $\mu g/m^3$.
3. *Effects on materials.* Particulates may damage surfaces by chemical attack *per se* or by corrosivity of absorbed substances (SO_2, NO_2) or by soiling. Steel samples corroded three times faster at a site where annual particulate concentrations averaged 176 $\mu g/m^3$.
4. *Effects on vegetation.* Although the effects of general particulate pollution are not documented, the effects of specific dusts are known. Cement-kiln dusts, for example, cause moderate damage to bean plants when dusted at the rate of 470 $\mu g/cm^2$/day for two days and then exposed to natural dew. Some dusts (iron oxide) may be beneficial to some plant species.
5. *Particles as odor sources.* If sufficiently volatile and odorous, particles can serve as sources of (generally unpleasant) odors, e.g., motor exhausts, street paving asphalts, trash burning.
6. *Effects on direct sunlight.* At concentrations ranging from 100 to 150 $\mu g/m^3$, where large smoke turbidity factors persist, particulates reduce direct sunlight up to one-third in summer and two-thirds in winter in the middle and high latitudes. The color of sunsets is also changed by particulates.
7. *Effects on public concern.* Public awareness and concern for air pollution increases at levels of particulate concentration up to and above 200 $\mu g/m^3$ particularly in the presence of other pollutants that affect the sensibilities.
8. *Effects on climate near the ground.* The scatter and absorption of sunlight by airborne particulates reduces the amount of sunlight reaching the ground. Total sunlight is reduced 50% for each doubling of the concentration above 100 $\mu g/m^3$. Reduction is most pronounced on ultraviolet radiation.

As a result of these several partial criteria of particulate effects, a primary standard of 75 $\mu g/m^3$ as an annual geometric mean and a secondary standard of 60 $\mu g/m^3$ were officially set (Table I).

No similar TLV was set; industrial air standards relate to specific particulates, such as specific mineral and organic dusts, e.g., metal oxides and oil mists. TLVs range from 2 $\mu g/m^3$ for beryllium dusts to 100 $\mu g/m^3$ for dusts and fumes of cadmium and thallium, to 1000 $\mu g/m^3$ for certain of the metal oxides. TLVs for those organic dusts are readily metabolized to less toxic substances are even higher.

Lead

It may seem odd at first glance (Table I) that no official air quality standard for lead has been set in the USA where the per capita number of motor vehicles far outnumbers that in USSR. Two reasons seem probable. By the time the criteria document was to be prepared, it became apparent that the petroleum industry was working toward the elimination of leaded gasolines. At this time also, the philosophy of control of air pollution changes; control at the source replaced control in the air, i.e., engineering procedures replaced the biologic and medical. California, however, saw fit to set an official standard of 1.5 $\mu g/m^3$, about double that in the USSR.

Summary

Official air quality standards for industry and community have been tabulated, and compared on a national and international basis. In these comparisons, it was felt important to identify clearly the bases for the often large differences between the standards for community air and those for industry, lest the side-by-side comparison of the limiting values prove inexplicable and, in turn, result in widespread, uninformed condemnation of the industrial air limits.

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OSHA — interpretation for the industrial hygienist*

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This is a critical analysis of some of the industrial hygiene aspects of the Occupational Safety and Health Act of 1970, with special emphasis on scientific interpretation. The ability of the Act to achieve its intended purpose of protecting the health of workers is entirely dependent on the prudence with which the administrating federal agency, the Department of Labor, employs the discretion granted to it by Congress.

The primary objective of OSHA is to ensure healthful working conditions for virtually every working man and woman in the United States.[1] Congress derives its power to promulgate OSHA from the commerce clause of the Constitution which empowers it to regulate commerce among the several States and with foreign nations and to provide for the general welfare.[2] Under Section 2(b)(3) of the Act, it appears that Congress intended the broadest application of this power, since the Act applies to all businesses *affecting* interstate commerce rather than requiring that the employer be engaged *in* interstate commerce. This interpretation suggests that 57 million workers in 4 million establishments will be protected by OSHA.[3] The only businesses not regulated by the Act are those over which a federal agency, other than the Labor Department, and state agencies regulating atomic workers are exercising statutory authority to prescribe or enforce job safety standards. Thus, OSHA does not apply to coal mines, metal and nonmetallic mines, railroads, and atomic energy installations.

The general duty clause

Section 5 of OSHA contains a general duty clause that applies to both employers and employees. With respect to employers, they must provide a place of employment free from "recognized" hazards that are causing or are likely to cause death or serious physical harm, and they must comply with all standards promulgated under this Act. There was much debate over this clause as first proposed because it was considered to be vague and would have forced employers to supply every conceivable safety and health need to their employees. In fact, Congressman William A. Steiger referred to this clause as "a *vague mandate to do good and avoid evil.*"[4] Justification for the general duty clause as enacted is based on the fact that industrial environments vary widely in form, and precise standards will not always exist to protect all employees.[5] Therefore, a general duty clause is included to ensure that employers are *always under a duty,* even in the absence of a specific federal standard, to provide their employees with a safe place to work. However, employers should recognize that the following phrase in the general duty clause, "*from any hazards which are* recognized *and are causing or likely to cause death or serious physical harm,*" is a limitation on their general duty requirement. An employer will violate the general duty clause only when he has exposed his employees to recognized hazards, which are the type of hazard that can be detected readily on the basis of the basic human senses. Hazards that require technical or testing devices for detection are not intended to be within the scope of the clause.[6] A "recognized" hazard has has further been defined to be one that is generally known to be hazardous, not one that a particular inspector happens to think is hazardous.[7] During debate in the House, a "recognized" hazard was interpreted to relate to the standard of knowledge in the industry.[7] Thus, a recognized hazard is based on objective criteria and does not depend on whether the particular employer is aware of it.

It is equally important for employers to recognize that there is *no penalty* for violation of the general duty clause. It is only after an employer refuses to correct the unsafe condition that has been called to his attention that a citation can be issued and, following the prescribed statutory period (fifteen days), a penalty imposed.[8]

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There are many instances in which the general duty clause will impose a duty on the employer. The following is an example of one such situation. Section 6 of OSHA requires that *"Any standard prescribed under this subsection shall prescribe the use of labels or other appropriate forms of warning as are necessary to insure that employees are appraised of all hazards to which they are exposed . . ."* With respect to chemical hazards, this section of OSHA would merely force an employer to inform his employees of the hazards associated with their exposure to those toxic chemicals for which standards have been promulgated. At the present time, standards have been promulgated for only a very small number of the chemicals employed in industry.[9] Without the general duty clause, an employer would not have to inform his employees of the potential hazard associated with their exposure to the myriad of other chemicals employed in industry for which standards have not been promulgated. But the existance of the general duty clause will force an employer to also inform his employees of the hazard associated with their exposure to those chemicals designated under Section 20(a)(6) of the Act as toxic substances by the Secretary of Health, Education, and Welfare, as well as all other chemicals generally known (standard of knowledge in the industry — objective criteria) to be hazardous. This carries out the Congressional intent of OSHA to protect workers in the workplace and justifies the interpretation placed on the general duty clause by Congress.

As previously stated, the general duty clause also places a duty on employees, since Section 5(b) states: *"Each employee shall comply with occupational safety and health standards and all rules, regulations and orders issued pursuant to this Act which are applicable to his own actions and conduct."* To determine the Congressional intent of this section of OSHA, reference must be made to the Senate Labor and Public Welfare Committee Report,[10] since the Conference Report[11] summarizing the reconciliation of the Senate and House bills reveals that the House bill contained no provision on employee's duties. The Senate Committee report states that commitment of workers to the health and safety efforts of their employers will be achieved through training and research studies of employee motivation, both of which are authorized by Section 18 of OSHA. Additionally the report states:

> *"It has been made clear to the committee that the most successful plant safety programs are those which emphasize employee participation in their formulation and administration; every effort should therefore be made to maximize such participation throughout industry.*
>
> *"The committee does not intend the employee-duty provided in Section 5(b) to diminish in any way the employer's compliance responsibilities or his responsibility to assure compliance by his own employees. Final responsibility for compliance with the requirements of this act remains with the employer."*

Such an interpretation of the general duty clause in effect places *no duty* on employees when compared to the criminal and civil sanctions which can ultimately be imposed on an employer for a violation of the general duty clause. By effectively placing all the duty on the employer for compliance with OSHA, it appears that Congress has disregarded human nature, as well as the historically documented inability of labor and management to live in peaceful coexistance.

The impractical nature of this imbalance of general duties can be exemplified by the following industrial problem. It is well documented that occupational exposure to excessive noise levels can cause permanent hearing damage.[12] The first government standards to limit the exposure of workers to excessive noise were established in 1965 when the Service Contract Act was passed.[13] When employess were exposed to noise in excess of these standards, feasible administrative or engineering controls were to be employed, but if these failed, personal protective equipment (ear muffs, ear plugs, etc.) was to be provided and used to reduce the sound levels.[14] The common complaint of all employers was that, even though they expended the necesary funds to purchase and fit such personal protective equipment, and even though they promulgated company rules that required all exposed employees to wear the protective equipment, they consistently were in violation of the law because employees would not conscientiously follow the regulations promulgated by the employer. Part of the employee neg-

ligence was due to the fact that all personal protective equipment (ear plugs, face masks, etc.) is to some degree irritating especially when the worker is doing heavy labor and perspiring profusely. However, a finite proportion of this negligence must also be accredited to chronic personal carelessness and the ageless disrespect for authority that has existed not only in employer-employee relations, but in many other areas of society where subjugation to any authority figure of the establishment is required.

There are many other situations in the industrial setting in which an employer's failure to comply with OSHA could be due to employee negligence or a specific labor attempt to sabotage management safety programs. Consequently, it is not equitable that all the duty for compliance with OSHA be the responsibility of the employer.

To amend this inequity, and to effectively place some duty on the employee to ensure compliance with OSHA, the Secretary of Labor should consider employee sabotage or chronic negligence as one basis for mitigating all penalties.

This recommendation does not conflict with the Congressional intent as expressed in the Conference Report which stated: "*Both bills permitted mitigation, compromise of settlement of penalties* (by the Secretary of Labor.)"[15]

The Senate Report specifically stated that

> "... *In the assessment of penalties consideration shall be given to the size of the business involved, the gravity of the violation, the history of the previous violations, and the* good faith *of the employer. The Secretary may compromise, mitigate, or settle any claim for such penalties*" (emphasis added).[16]

OSHA incorporated this Congressional intent into Section 6(e) of the Act which permits the Secretary to compromise, mitigate, or settle any penalty under the Act, but justification for this action must be published in the *Federal Register*.

This appears to be the most equitable solution to the general duty problem, since it might not acquit an employer, a mitigated penalty might still be imposed, and the final responsibility for compliance with the Act would still remain with the employer. This solution might prove more productive in gaining the fullest cooperation of affected employees, since methods of employee training and motivation, which were recommended by the Senate,[17] have been unsuccessful in the past.

Section 12(a) of the Act established The Occupational Safety and Health Review Commission to conduct hearings whenever an employer wishes to contest either a citation or a penalty proposed by the Secretary of Labor under Section 10(c). Since the Commission possesses the discretaion to mitigate *all civil* penalties imposed by the Secretary of Labor under Section 17(j) of the Act, it could apply this remedy to the general duty problem whenever the Secretary of Labor refused or failed to take employee negligence into consideration when imposing a civil penalty.

Section 17(a) of the Act empowers the Secretary of Labor to assess a civil penalty of up to $1000.00 for each repeated violation of a standard as a result of chronic negligence or sabotage by an employee. If the employer were to discharge the employee on the grounds of chronic violation of an OSHA standard, the union may defend the employee and dispute the discharge. If this issue were to come before the National Labor Relations Board (NLRB), there is no assurance that this justification of the discharge would be a complete defense for the employer. Until this issue is presented to the NLRB, it would be prudent for all employers to establish employment contract provisions designating chronic employee negligence or sabotage, resulting in repeated violations of OSHA standards, as justification for employee dismissal.

The use of TLVs as legal standards

The use of TLVs as legal standards has been opposed by the ACGIH. Despite this opposition, the TLVs were first promulgated as federal health standards in the 1960 Walsh-Healey Public Contracts Act.[18] The TLV Committee made every effort to avoid the use of TLVs as legal standards that would be rigidly applied without professional judgment. The fallacy in such an application of TLVs lies in the fact that they will be employed as fine lines between safe and dangerous concentrations. Such strict interpretation is not within the intent expressed in the preface to the TLVs, and places industry in undue jeopardy. In addition, it may be placing an undue burden on society by establishing and enforcing overly stringent standards with-

out sufficent scientific justification. In fact, such misinterpretation fails to take into consideration that fact that, with few exceptions, the TLV is a time-weighted average value which permits excursions above the limit, provided equivalent excursions occur below the limit. Thus, a single, or even several, concentrations monitored above the limit is not ipso facto evidence of injury. This is because the TLV has an inherent safety zone between the limiting value and the concentration capable of producing injury.[19] Determining what may constitute a "reasonable" excursion above the recommended limit depends on professional evaluation of factors such as the nature of the contaminant, whether very high concentrations even for short periods produce an acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such periods.[20]

Now that the TLVs have been adopted under OSHA as legally enforceable standards, every attempt should be made to ensure that the concepts contained in the Preface of the TLVs are employed by the Secretary of Labor. If these values are interpreted or enforced in a manner different from that recommended by the ACGIH-TLV Committee, such action should be immediately contested to protect the interests of both labor and management. A valid basis exists for this contestation, since the Secretary of Labor is only statutorily empowered to adopt and enforce national concensus standards or established federal standards. Enforcement of a national concensus standard in a manner not intended by the standard-setting organizaiton is, in essence, a failure to enforce the consensus standards and a violation of the Act. Such a situation apparently existed when the Secretary of Labor published in the *Federal Register* 3a statement that exposure to concentratons *above* the TLVs should be avoided.[21] As previously stated, this is contrary to the intent of the ACGIH, since they have historically defined TLVs to be time-weighted concentrations for a 7- or 8-hour work day and 40-hour work week. A subsequent publication by the Secretary of Labor corrected this discrepancy.[22]

Innovative research by HEW to formulate standards

Section 20(a)(1) of OSHA empowers the Secretary of Health, Education, and Welfare (HEW) to conduct research to assist the Secretary of Labor to formulate safety and health standards which will then be promulgated in compliance with Section 20(a)(2). The Secretary of HEW is directed to conduct research which includes psychological factors and employs innovative methods and techniques. With respect to industrial standards of airborne contaminants, the Soviets have routinely based their acceptable concentrations on the conditioned reflex type of experiment developed by I.P. Pavlov.[23] This technique has consistently given rise to TLVs that are many magnitudes lower than those developed in the United States.[24] American researchers maintain that the Soviet values are set without regard to the feasibility of being met and thus represent goals rather than realizable limits. There is justification to believe that, if the Soviets were to attempt to rigidly enforce their standards, the economic costs involved would probably result in a re-evaluation of the validity of the underlying concepts.[25]

The Secretary of HEW should avoid using the Pavlovian conditioned reflex experiment when generating criteria upon which the Secretary of Labor can formulate health standards, because the scientific community would immediately contest such standards. In addition, a standard promulgated on such experimental data would be in violation of the Congressional intent, since it would attempt to ensure that *no one* would be subjected to a hazard.[26] Congress intended standards to be based on data which adequately assure, to the extent feasible, that employees chronically exposed to atmospheric contaminants will not suffer material impairment of health, but these standards are not to ensure that *every employee* would be protected from *all hazards*.

Section 6(b)(7) of OSHA also requires that any standard promulgated shall prescribe the use of appropriate forms (that is, labels or material safety data sheets) that appraise employees of all hazards to which they are exposed. If such forms describe the relevant symptoms, and appropriate emergency treatment, this may be sufficient stimulus to cause some employees to develop psychosomatic illnesses. The potential for this to occur is much greater in chemical industries, which handle large numbers and varieties of toxic chemicals, than in the heavy industries. This type of illness can be very expensive for industry when considered from

the standpoint of time lost from work and ultimate treatment.

Standards based on scientific data disclosed by industry

OSHA does not require chemical manufacturers to supply the Department of Labor (DOL) with any of the toxicology and industrial hygiene data which they may have in their possession. However, other federal laws require manufacturers of a limited number of chemicals to submit large quantities of this type of data to one or more federal agencies before the chemical can be marketed in interstate commerce. The Food, Drug and Cosmetic Act with its subsequent amendments,[27] and the Federal Insecticide, Fungicide, and Rodenticide Act[28] with its associated amendments, are the primary statutes requiring manufacturers to submit this type of information. The chemicals that fall within the jurisdiction of these laws constitute only a small segment of the total number of chemicals manufactured each year to which workers are exposed. If OSHA required all data of this nature that may be in the possession of chemical manufacturers to be submitted to the DOL, it would greatly facilitate the establishment of standards (TLVs) and would identify those chemicals that present the greastest potentiality of toxic hazard to workers.

One of the chronic complaints of researchers in the field of occupational health has been that industry has, in the majority of cases, been reluctant to discuss its own health hazards with outsiders.[19] Consequently, the documentation of TLVs[29] which have been adopted as national concensus standards, are based on "*. . . the best available information from industrial experience, from experimental human and animal studies, and, when possible, from a combination of the three*" (emphasis added).[30] However, additional data may exist within corporations which were inaccessible to the committee formulating these values.

In an attempt to stimulate industry to publish this type of data, the American Medical Association's Council on Occupational Health established the Committee on Occupational Toxicology in 1964. This Committee created a Registry on Adverse Reactions to stimulate industrial hygienists, corporate medical directors, toxicologists, and industrial physicians and nurses, as well as physicians at large, to report information both on hitherto unrecognized reactions to well-known agents and on health hazards associated with new materials.[31] This registry is only one facet of the Committee's larger goal of attempting to protect employees from occupational health hazards, familiarize physicians with potential hazards, and help physicians to evaluate the effects of occupational exposure to toxic substances, hazardous materials, and energy sources.

Although this Registry has made contributions to the field of occupational health, response by physicians in industry and private practice was totally discretionary, and significant hazards remained unreported. One government official in NIOSH believes that the Registry is totally ineffective.[32]

There is one possible exception to the statement that OSHA does not require chemical manufacturer to supply the DOL with toxicology and industrial hygiene data which they might possess on their products. This exception is defined by Section 13(a) of the Act to exist when conditions or practices in any place of employment are such that a danger is present which could *reasonably* be expected to cause death or serious physical harm immediately, or before the imminence of such danger can be eliminated through the enforcement procedures provided by the Act. OSHA grants broad discretion to the Secretary of Labor to avoid, correct or remove such an imminent danger, even to the point of cessation of plant operations through injunctive relief. If management of a corporation were faced with such a situation and had in their possession toxicology or industrial hygiene data which would negate the imminent danger charge, they would probably voluntarily divulge this information. Even through the DOL could not force industry to divulge this information, under the foregoing conditions DOL would ultimately gain access to the data.

As Senator Richard Schweiker pointed out in Senate debate, the number of instances in which the imminent danger proviso may be applicable should be very rare.[33]

It is also important for management to realize that the number of instances in which an entire plant would be closed down under this proviso would be extremely rare, since, in the majority of

instances, only the particular machine or area of the plant in question would be closed down.[34]

Another section of OSHA can be interpreted as an attempt to encourage industry to voluntarily divulge this type of data to HEW. Section 20(c) authorizes the Secretary of DOL to enter into contracts with private organizations to conduct studies relating to his responsibilities under the Act. If a chemical possessed toxicological characteristics of a nature that indicated the DOL would ultimately attempt to develop an occupational health standard, it would be advantageous for the manufacturer holding the patent to the chemical to apply for a contract with the DOL to perform the research required to establish the occupational health standard. Such action would generate four benefits for the contracting manufacturer:

1. Ensure reliability and completeness of the biological data upon which the occupational health standard would be based.
2. Present an opportunity for the corporation manufacturing the chemical to suggest an occupational health standard to the DOL and thus be regulated by a self-established standard.
3. Provide an additional source of profit to the company in the form of a government contract.
4. Possibly prevent losses of qualified research laboratory personnel during periods of decreased corporate research activity.

The last method by which the DOL can obtain this type of data is through regulations by the Secretary of HEW, requiring employers to measure, record, and make reports on the exposure of employees to substances or physical agents that may endanger the health and safety of employees as prescribed by Section 20(a)(5) of the Act. The employer can request the Secretary of HEW to defray any additional expense incurred, or to supply any other assistance required. Under these regulations, NIOSH believes that they are empowered to implement the National Surveillance Network for Occupational Health.[35] This network will yield a large amount of epidemiological data concerning the incidence of exposure to toxic substances in industry, but it will not yield basic industrial hygiene data such as workroom air monitoring measurements, or the results of toxicological studies. Therefore, these data will be very ueful to the DOL in establishing priorities for standard setting and inspections, but they will be of little assistance in selecting a finite value for a new standard.

Establishing standards for alleged carcinogenic chemicals

It is of interest that OSHA treats all chemical hazards in an identical manner, regardless of the type of disease entity which will result from excessive exposure. For example, OSHA does not require that human exposure to all chemicals capable of causing cancer in animals or man be zero, or that a standard (TLV) shall not be established for such chemicals. In this regard, OSHA is unique when compared to other federal laws that attempt to protect humans from exposure to nonpharmaceutical chemicals. For example, both the Food, Drug and Cosmetic Act (FDCA) and the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) contain specific provisions to protect man from exposure to alleged carcinogenic chemicals, but OSHA does not. OSHA does not contain a proviso, mandatory or discretionary, setting forth the Secretary of Labor's authority to establish a TLV of zero for alleged carcinogenic chemicals. In fact, the Secretary of Labor has complete discretion concerning the establishment of any standard for a carcinogenic chemical regardless of the information submitted or available to him, the opinions of an advisory committee, or the evidence presented at a public hearing.

This apparent oversight by Congress, of failing to specifically define the authority of the Secretary of Labor when establishing TLVs for alleged carcinogenic chemicals, was beneficial to both labor and industry. A mandatory provision would remove all discretion from the federal regulatory agency, and no consideration could be given to the amount and quality of countervailing experimental evidence if a single, poorly designed research study resulted in cancer in the experimental animals. A mandatory proviso would not permit the federal agency to consider numerous critical experimental variables such as the size of the dose, the route of administration, the species, age, sex, diet, and strain of the experimental animal, and the biotransformation mechanisms involved in the spe-

cies under study. Many responsible scientists believe that the mandatory proviso in the FDCA, the Delaney Amendment, is substantially without scientific basis and is subject to question.[36]

Although carcinogenicity is only one of the many manifestations of toxicity, it has somehow assumed a role of considerable and possibly magnified importance. It is the only manifestation of chemical intoxication that is dealt with by special legislation. There is no counterpart to the Delaney Amendment that is concerned with any other specific pathological condition or form of toxicity.

A recent committee of the National Research Council stated:

> *"Revision of that Clause [Delaney] to provide for exercise of sound, informed scientific judgement with respect to the possibility of carcinogenic risk to man seems to us a sounder and more practical approach to food safety than does the present rigid prohibition."*[37]

Recommendations for revision of the mandatory Delaney Amendment have recently been made independently by three other highly qualified committees: the Panel on Food Safety,[38] the Panel of Food Quality[39] of the White House Conference on Food, Nutrition, and Health, and the Secretary's Commission on Pesticides and Their Relationship to Environmental Health.[40] All the committees concluded that the Delaney Amendment unduly and unnecessarily restricted the application of reasonable, logical, and sound scientific judgment in relation to the use or presence of cancer-producing chemicals in food.

A mandatory proviso in OSHA directing the Secretary of Labor to establish a standard (TLV) of zero for a chemical substance that has produced cancer in animal experimentation, in complete disregard of the poor quality of experimental design, would be assailed with the same vigor and by the same scientists attacking the validity of the Delaney amendment.

Granting discretion in establishing standards for airborne contaminants to the Secretary of Labor with the assistance and guidance of the Secretary of HEW not only is justifiable scientifically, but also appears to be the philosophy employed by the TLV Committee of the ACGIH in establishing the TLVs which were adopted as national consensus standards. Review of the TLVs established by the 1970 TLV Committee of the ACGIH reveals that they did not feel a mandatory obligation to establish a zero TLV for all airborne contaminants that produced cancer (DDT, selenium compounds, chromates, and asbestos), but only for substances that produced a *high incidence* of cancer. The ACGIH-TLV Committee stated:

> *"Because of the high incidence of cancer, either in man or in animals, no exposure or contact by any route, respiratory, oral or skin should be permitted for the compounds:"* [nine compounds listed].[30]

This committee employed this discretion and established a finite TLV when the only incriminating evidence against a chemical was a low incidence of cancer in experimental animals. This is because it is very difficult, if not impossible, to extrapolate these results to prognosticate the effects on man when occupationally exposed to the same chemical. This committee would assign a TLV of zero if the incidence of cancer in animals was very high when exposed to the chemical, or when cases of cancer in humans could be correlated with occupational exposure to the chemical.[41] It is only reasonable that the Secretary of Labor should be able to employ the same discretion as that exercised by the ACGIH when developing standards which were ultimately adopted as national consensus standards.

The Secretary was granted discretion under Section 6(b)(7) of the Act to single out carcinogenic substances, as well as other highly toxic substances, through the labeling requirements of Section 6. This provision was included in the Act in response to repeated testimony by witnesses at the Congressional hearings as to the continued presence and use of carcinogenic and toxic substances and processes in the workplace.[42]

Granting employees access to their exposure records

Section 8(c)(3) of the Act requires employers to permit employees, or former employees, to have access to records of their exposures to potentially toxic materials or harmful physical agents which are required to be monitored or measured under Section 6(b)(7). Revealing this data to some individuals could potentially give rise to psychosomatic illnesses just from the thought of daily

exposure to a toxic chemical, even though the exposure may continuously be below all established standards for contaminants in air. This problem might be intensified when the worker reviewed the label that appeared on the chemical to which he was exposed, since the precautions to be observed after exposure to even very common chemicals (i.e., acids, alkalis) can be very foreboding. There is also a high probability that workers with this predisposition would be the ones most likely to request access to their exposure records. The opportunity for these psychologically traumatic experiences to occur could have been significantly reduced if the Act had required employers to grant employees access to this data *after* an exposure at concentrations or levels exceeding a health standard. This could have been accomplished while the employer was complying with Section 8(c)(3), which requires an employer to promptly notify any employee who has been exposed to toxic materials at concentrations that exceed prescribed health standards.

This limitation on the access of employees to their exposure records seems in keeping with the primary intent of the Act, since exposure to any chemical at concentrations that do not violate an established standard should not have an adverse effect on health. Yet, revealing this data to some employees could trigger an emotional illness.

Granting employees and past employees access to their exposure records may present the additional problem of frivolous claims by these employees of occupationally linked illnesses. The probability of such a claim would appear greatest in hostile past employees. An additional complication could occur when the exposure data was introduced as evidence before a judicial body (in most states a workman's compensation board). Since the TLV is a time-weighted concentration for a 7- or 8-hour work day and 40-hour work week, a question of fact must be decided as to whether the periodic excursions above the standard limit were sufficient to give rise to the alleged occupational disease. The 1970 TLV Committee of the ACGIH defined general permissible excursions above the TLVs, but they were intended to provide a "rule-of-thumb" and may not provide the most appropriate excursion for a particular substance.[30]

Determination of this question of fact would not place a unique burden on the judical forum, since they have historically been called upon to resolve such issues, but the final resolution has great significance to industry. First, any determination of this nature might have significant precendential value in subsequent cases (depending on individual state workman's compensation law), and second, realization that periodic excursions above a TLV could give rise to a question of fact to be resolved by a judicial forum with the assistance of expert testimony should act as a stimulus for industry to keep all concentrations of airborne substances as low as possible.

The imposition of penalties for OSHA violations

The civil penalties in and of themselves are not sufficiently large to ensure that all major corporations will comply with the law. The basic motivating factors that will stimulate corporations to comply are the threat of a labor dispute, and adverse public image and damage to corporate good will. Labor, both organized and unorganized, is not ignorant of this fact and will probably attempt to have all issuances of citations and penalties highly publicized. Even the threat of such publicity, or the threat of a labor dispute, will cause most corporations to comply with the Act and thereby avoid citations.

With respect to the criminal penalties that permit imprisonment of the offender, the Act does not define, with specificity, which level of management should be incarcerated. The DOL would ensure complete compliance by attempting to incarcerate an individual as high up the corporate hierachy as possible. If a corporate vice-president or even plant manager were incarcerated, compliance by that corporation in the future would be guaranteed.

Other than the potential adverse publicity and labor dispute aspects of a citation, which were previously discussed, the imminent danger proviso is probably the most conducive to stimulate compliance by large corporations, since, under this proviso, individual processes or entire plants may be shutdown until compliance is ensured. Even a short shutdown may constitute a very large financial loss to a corporation, and this sum may be much in excess of all civil penalties that could be imposed. However, it should be recalled that probably very few situations will be capable of being classified an imminent danger.

Conclusion

Comprehensive federal legislation in this field was predictable, and not just from public statements in the past few years by Presidents and Congressmen. Experts in the field of occupational safety and health have recognized the problems and recommended solutions which, although not requiring legislation, were not heeded.[43]

The Occupational Safety and Health Act of 1970 contains provisions which should be effective in achieving the Congressional objective of protecting the health of the workers of this nation. However, the ability of any federal legislation to achieve the purpose intended is entirely dependent on the prudence with which the administrating agency carries out the discretion granted to it by Congress. These Congressional objectives are made somewhat more obtainable by provisions in OSHA which regulate the work environment not only through uniformly applied occupational safety and health standards, but through programs of research, education, and training.

It is unfortunate that federal legislation was required to achieve this objective when many employers in a broad spectrum of industries had demonstrated an exemplary degree of concern for health and safety in the workplace. These efforts were offset, to some extent, by other employers — particularly the smaller ones — who were not so concerned. Those small employers who were concerned found that they could not make the necessary investments in health and safety, and still survive in a competitive marketplace, unless all employers were compelled to act in a similar manner.

In summary, the chemical and physical hazards which characterize modern industry are not the problems of a single employer, or a single industry, but the concern of the entire nation. It is only reasonable that federal legislation be enacted to deal with this problem and that the cost of this effort be transmitted to the consumer who directly benefits from the multitude of technological marvels produced by industry.

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Concepts of thresholds in standards setting: an analysis of the concept and its application to industrial air limits (TLVs)*

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The premises on which the concept of thresholds of toxicologic response rest are presented and discussed in light of recent, seemingly conflicting evidence from nontoxicologic quarters. Review of the metabolic factors governing toxicologic response, particularly homeostasis and adaptation, makes a good case for the existence of thresholds for chemical substances generally. Possible exceptions are certain natural body metabolities and long-wave ionizing radiation. Finally, the procedures that have to be taken to modify thresholds for the development of appropriate industrial air standards are presented.

The term "threshold limits" for industrial air originated more than a quarter century ago with the late Lawrence T. Fairhall, Ph.D., my predecessor and Chief Toxicologist for the US Public Health Service in the Division of Industrial Hygiene. He regarded "threshold limits" as a preferred alternative to "maximal allowable concentrations," which, as a term, was increasingly realized to be inexactly descriptive.

I shall present what I believe formed the basis of the Fairhall threshold limits concept as interpreted in terms of present-day usage, the evidence for the general validity of the concept, and how thresholds are incorporated into industrial air standards.

The discussion that follows is confined to the threshold limits for chemical substances in the air of work places.

The threshold concept

The premise on which the concept of thresholds rests is that, although all chemical substances produce a response (toxicity, irritation, sensitization, narcosis, etc.) at some concentration, if experienced for a sufficient period of time, it is equally true that a concentration exists for all substances from which no response of any kind may be expected no matter how long the exposure, on an eight-hour daily, 40-hour workweek basis. Stated mathematically, the threshold concept is a *nonlinear* relationship between dose and response at the initiation of the response, the lower end of the curve in Figure 1, as opposed to a wholly linear nonthreshold response relationship that passes through the origin. The threshold concept seemed at the time (1948; the first list of air limits was published under the title "1946 M.A.C. Values") entirely reasonable and sound scientifically. But it must be remembered that in the early 1940s no great depth of understanding existed in toxicology, and radiation biology was in its infancy; mechanisms of carcinogenesis consisted of crude hypotheses.

Of late, two factors have done much to throw doubt on the threshold concept; 1) the development of increasingly sensitive indicators of response, and 2) a general concern that highly injurious agents at high dosages may still be injurious at any concentration, however small, either *per se* or as a factor in diseases of multiple causation. Examples of the former are tests of behavioral responses; of the latter, fluoride, a recognized rat poison, cannot be envisaged by many as safe at any level. Respiratory irritants usually considered systemically benign at low concentration may have the potential of accelerating the induction of lung cancer. Similar findings have been noted by S. Laskin (unpublished data). Both of these factors act to move the threshold (for chemical substances) closer toward the origin. For extremely toxic substances with their small dose, large response characteristics, this serves to make the two thresholds difficult to distinguish, and is

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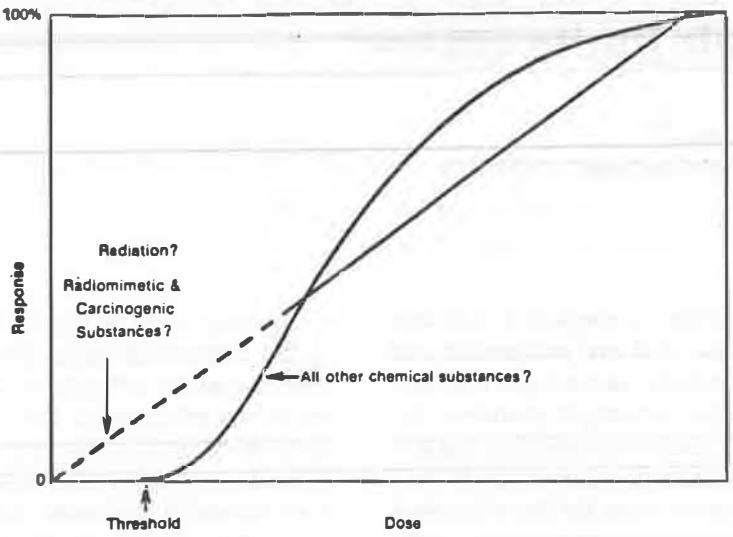

Figure 1 — Thresholds, do they exist?

undoubtedly a major reason for the continuing controversy.

Doubt of the validity of the threshold concept has arisen chiefly from two areas, radiation biology and carcinogenesis. In an effort to provide a better understanding of the nature of thresholds and possibly resolve the question of their existence or nonexistence, a symposium was held in 1970 on the subject, Thresholds — Do They Exist? Despite discussions on many aspects of thresholds, the question of their existence in carinogenesis and radiation biology was unresolved; and moreover, the subject basic to the threshold concept, adaptation, was not discussed.

Homeostasis and adaption

In the thinking of the Threshold Limit Value (TLV) Committee, adaptation represents the most cogent and convincing basis for the existence of thresholds, first through homeostatic mechanisms which commonly find their ultimate expression in tolerance and development against noxious stimuli. Stated in more mechanistic terms, toxicity is the net result of two competing reactions, as diagrammed in Figure 2: Reaction 1, the toxic substance acts on the body, represented by the upward rising arrow at left; and reaction 2, the body reacts to the substance, represented by the downward pointing arrow at right. These reactions are the general basis for the attempt of the body to maintain normality (homeostasis) in the face of noxious stimuli, resulting in the utilization of a certain finite amount (dose) of a toxic agent without production of a toxic effect, hence a threshold.

Evidence for these adaptive mechanisms being operative (and hence, the existence of thresholds) is seen among all types of injurious agents and among all types of injurious responses. Possible exceptions are long-wave ionizing radiation and certain natural body metabolites, such as carbon monoxide and carbon dioxide where no amount above normal, however small, is not attended by some decrement in performance (CO) or cost to body function (CO_2). Certainly there is a recognized threshold for nerve stimulation; the induction of narcosis requires a definite concentration of the narcotizing agents. Thresholds for sensory irritation of the eyes, nose and throat are well-established for many irritants; sensitization even in hypersensitive individuals requires a finite dose well above zero; and inhibition of carcinogenic action is a recognized phenomenon. A striking instance of the body's capacity to adapt to toxic elements has recently been reported.[2]

Tolerance and crosstolerance developed to those elements (arsenic, cadmium, mercury, indium, manganese, lead, silver, and tin) foreign to the mammalian body, whereas, tolerance did not develop to the so-called essential nutrients, copper and selenium. Manganese, an essential nutrient, was the exception.

In short, the entire body physiology is based on stimulating and inhibiting systems. This can only spell one thing, the existence of thresholds, because inhibition is synonymous with dose wastage. Accordingly, with these indisputable facts, the TLV Committee has perpetuated for now more than 25 years the original concept of Dr. Fairhall as a basic premise of the TLVs.

Application of thresholds in setting industrial air standards

In most instances the thresholds cannot be used without modification for establishing the appropriate threshold limit value for the following reasons. First, the thresholds that have been determined for *toxic* injury (more often than not derived from animals) represent an average response value on a genetically more homogeneous species than man; second, the relative sensitivity of the animal species to the toxic agent to that of man is rarely known; third, if the threshold determination has been made on animals, the animals were presumably healthy, generally vigorous young adults, eating a standard diet differing considerably from that of man, and studied under standard conditions of temperature and humidity; all conditions, not met in all industrial situations. It obviously follows, however, that if the threshold determination is made with man as the subject as it is for determination of the thresholds for irritation and odor, then little or no adjustment in the threshold is required. Although here again usually normal, healthy, nondrinking and nonsmoking human volunteers are used as subjects; this indicates the need of an added safety factor. Moreover, it is well recognized that industrial workers differ widely, not only in their nutritional needs and

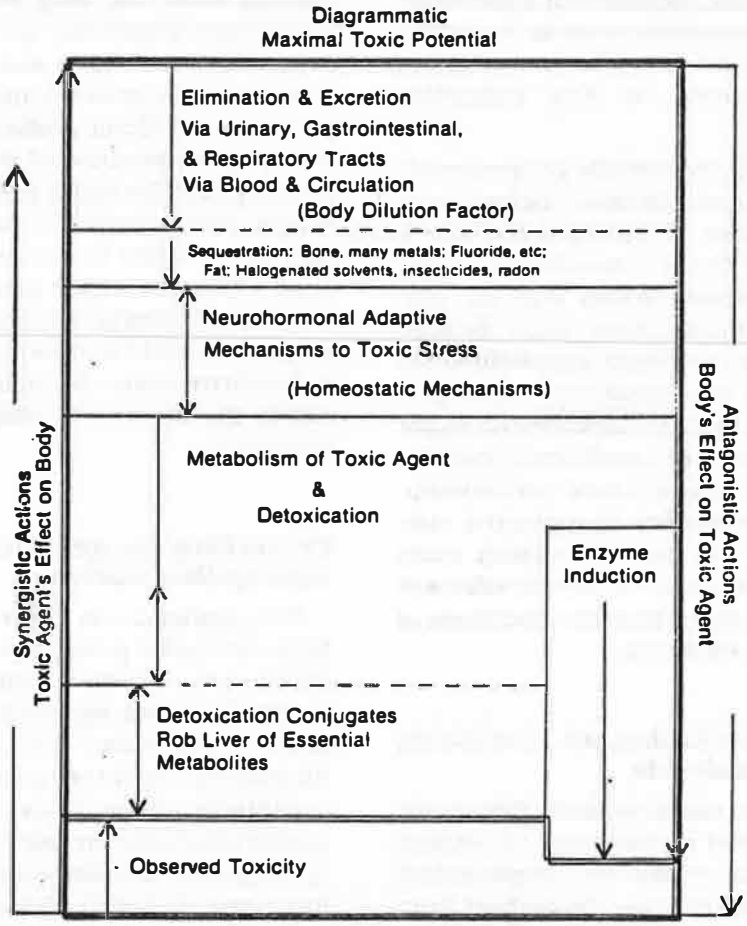

Figure 2 — Concept of toxicity.

habits, from the animals on which the threshold was determined; but also in their personal habits of smoking, drinking, and eating. Among the pneumoconiosis-producing dusts (e.g., asbestos and coal), smoking can cause such a profound shift in the threshold of response as to make the threshold of the particular dust irrelevant. Alcohol drinking causes a similar profound threshold shift in susceptibility to hepatotoxic agents (e.g., halogenated hydrocarbon solvents). Dietary factors are recognized to influence the threshold of response to probably most of those industrial chemicals that are systematically absorbed (e.g., carbon disulfide and vanadium, to name just two on which such evidence exists).[3] Similar findings have been noted by this author (unpublished data).

To the above threshold modifiers must be added preexisting systemic diseases in all their forms and degrees. Tuberculosis has been long known to predispose to silicosis; pneumonia, to beryllliosis; asthma, and other respiratory tract sensitivities, to industrial asthmagens, such as the industrial isocyanates used in foam plastics; preexisting liver and kidney disease, to their respective toxicants.

Clearly, there are a multiplicity of "personal" factors that require consideration before each response threshold can be incorporated into a threshold limit value. Great in number and magnitude as these personal factors may be, procedures, described below, have been devised which make allowance for these threshold shifts before incorporation into standards. These procedures, however, fail to make allowance for major threshold shifts as a result of genetic abnormalities that express themselves as extreme hypersusceptibilities or hypersensitivities to industrial substances. Individuals with such hereditary traits can, however, be protected from adverse effects of exposures by means other than modifications of thresholds as described below.

Procedure for developing air standards with modified thresholds

As indicated above, experimentally thresholds are rarely, if ever, used in the final TLV without adjustment. This is true whether the determination was made in animals or man, or derived from industrial experience. The reason is simply that the human species is genetically diffuse and heterogeneous with widely differing capacities to respond to toxic insult; and its extent is seldom known. Accordingly, a factor of safety is invariably added to the determined threshold to provide a cushion of protection for the more susceptible individuals. The magnitude of the safety factor depends upon the seriousness of the response. For example, the safety factor incorporated in the TLV for cyanide, which has lethal potential, is far larger (by at least tenfold) than that for trichloroethylene, in which the initial reaction is narcosis, or for sulfur dioxide, which produces irritation. The safety factor for narcotizing agents such as trichloroethylene is small for the average worker, but may be nonexistent for the beer drinker. For upper respiratory tract irritants, such as sulfur dioxide, the TLV provides no safety factor for the uninitiated, but for the insured worker the TLV provides a factor of at least five.

The safety factors are all judgmental values derived from the long experience of the TLV Committee members; no value predetermined according to category and degree of action are used. Substances with sensitizing potential pose a particularly difficult problem for the choice of a safety factor because of their varying potencies, ranging from the highly potent industrial, organic isocyanates through the intermediate polyamine-methylene resins to substances of lower potency such as formaldehyde gas. However desirable it might be to incorporate a safety factor sufficiently large to protect the most sensitive individuals, the safety factor cannot be infinitely large but must be within the bounds of analytic and engineering practicality.

Protecting the genetically hypersusceptible worker

This limitation on the magnitude of the safety factor excludes protection by means of the TLVs those workers, who because of inborn errors in metabolism, are hypersusceptible to certain industrial chemicals. Figure 3 illustrates in terms of the plasma content of the indentifying biochemical constituent, phenylalanine, of the hereditary defect phenyl ketonuria, the extreme variation expressed by a genetic deviate, even in the heterozygous form (one allele defective). Greater variation from normal occurs in the homozygous individual in whom both alleles are defective. For these genet-

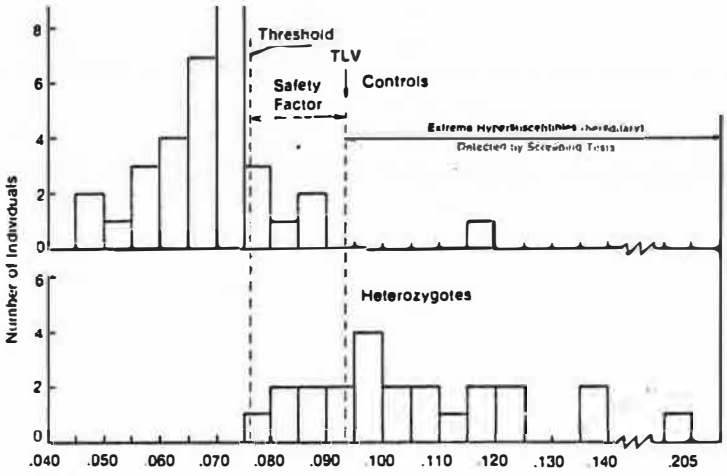

Figure 3 — Distribution of plasma phenylalanine level in 33 controls and 23 heterozygous individuals.

ically defective individuals for whom the TLVs afford little if any protection against certain groups of industrial chemicals, the procedure is to detect such individuals in the preplacement job examination, in much the same way as proper job placement is accomplished in the ordinary medical management programs by detecting prospective workers who may represent an undesirable health risk, if exposed to certain of the company's products during manufacture. Simple tests are now available[4,5] that may be used to detect individuals hypersusceptible to one or another group of industrial chemicals. The serum antitrypsin deficiency test, for example, is available for the detection of those individuals prone to acquire the familial form of pulmonary emphysema from inhaling respiratory irritants; the glucose-6-phosphate dehydrogenase test for those highly susceptible to hemolytic chemicals; immunologic tests for detecting hypersensitivity to the industrial isocyanates and related sensitizing agents. In this way, the individual is kept from unnecessary exposure to substances to which he is peculiarly susceptible and the TLVs are, in effect, made more inclusive.

A similar article by B.D. Dinman, M.D., reaching similar conclusions that thresholds actually exist, has appeared in *Science* (175:495, 1972).

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Industrial air standards — theory and practice*

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The passage of the Occupational Safety and Health Act in the last days of 1970 reaffirmed at a federal level the official nature of the industrial air limits of the Threshold Limit Values (TLVs) of the American Conference of Governmental Industrial Hygienists and the Acceptable Concentrations (ACs) of the American National Standards Institute (ANSI) — limits which up to this time had always been promulgated as unofficial, recommended limits. But being official and legal entails inspection for compliance, and inspection for compliance entails knowledge of the proper use and application of the industrial air standards, as well as a sound statistical procedure of sampling and evaluation of results.

It is our present purpose to point out first, the nature and intent of the North American standards (Canada has representation on the two standard-setting committees) and then to state how these two standard-setting committees would have the factory inspector evaluate compliance with these standards. It is *not* just a simple matter of deciding compliance by comparing the analytic results of a few grab samples with the air standard, as will be shown beyond.

Nature and intent of industrial air standards

The 1972 TLV booklet contains upwards of 550 substances or groups of substances; there are now about 30 ANSI standard documents. Both the Preface to the TLV booklet and the ANSI standards clearly spell out the nature and intended use, as well as the misuse and abuse, of the air standards. To quote:

> *"Threshold limit values refer to time-weighted concentrations for a 7- or 8-hour workday and 40-hour workweek. They should be used as guides in the control of health hazards and should not be used as fine lines between safe and dangerous concentrations. (Exceptions are the substances listed in Appendices A, E, and F, and those substances designated with a "C" or Ceiling value, Appendix D.)"*[1]

The Appendices C, D, E, and F to the TLV booklet provide further guidance on proper bases for judging compliance.

TABLE I
Conditions for Judging Compliance with Industrial Air Standards

1. Guideline-like nature of standards.
2. Excursions above standard value permitted — Ceiling and peak values.
3. Standards contain safety factors.
4. Standards protect vs. well-being and health.
5. Compliance determination by persons trained in industrial hygiene.

Table I lists the conditions that must be appreciated if proper judgment of compliance with the standards is to be made. Item 1 reiterates the point that the air standards do not, in general, demarcate safe from unsafe conditions; that below the limit, workers may suffer no ill effects; and that just above the limit, workers are in trouble. This is for two reasons, as Items 2 and 3 point out: Excursions above the limiting value are permitted in the form of "ceiling" and "peak" values, and in addition, all standards contain safety factors, which means the maximal limit associated with no effect has been further lowered to provide a cushion of safety to health and also well-being (Items 3 and 4). Item 5 states the obvious for intelligent judgments on compliance.

* Presented at the 37th annual meeting of the Industrial Health Foundation, October 10-11, 1972, Pittsburgh. Published in *J. Occup. Med. 15(5)*:429-431 (May 1973). Reprinted by permission of the American Occupational Medical Association.

Acceptable concentrations and permissible excursions

The figure graphically illustrates the relationship between the three types of acceptable concentrations, the time-weighted averages, the ceiling and peak values, and the relation of the acceptable concentrations to zones of health and safety. It is seen that the time-weighted average (TWA) value is not a limiting value, as excursions *above* the stated limit are permissible, provided equivalent excursions occur *below* the limit. These excursions should not, however, exceed a stipulated ceiling value throughout the workday 1) unless a specified peak value has been expressly stated (as in certain ANSI standards), and 2) that the exposure at the stipulated peak value and its frequency does not exceed the concentrations permitted by the TWA and the ceiling value for the workday.

Although the acceptable concentrations of the relatively few ANSI standards specify exact concentrations for all three limits, the permissible excursions recommend for the more numerous TLVs are less exact and are based on a rule-of-thumb as shown in Table II.

TABLE II
Permissible Excursions above TLV

TLV ppm or mg/cu m	Excursion Factor
> 0 to 1	3
> 1 to 10	2
> 10 to 100	1.5
> 100 to 1000	1.25

The magnitude of the excursion factors is pegged to the magnitude of the TLV and the relative precision of the analytic method at the different TLVs. These excursion factors (EFs) serve a dual purpose: they determine the limiting *ceiling* value permitted for each TLV, as well as the TLV for some 32 substances listed as "C" values, or ceiling limits, for which no TWA values are permitted. As these EFs are a rule-of-thumb, there are some substances such as severe respiratory irritants to which the rule does not apply (no EF is permitted). Another example is carbon monoxide; the EF is too low by a several fold factor. The TLVs suggest no peak values.

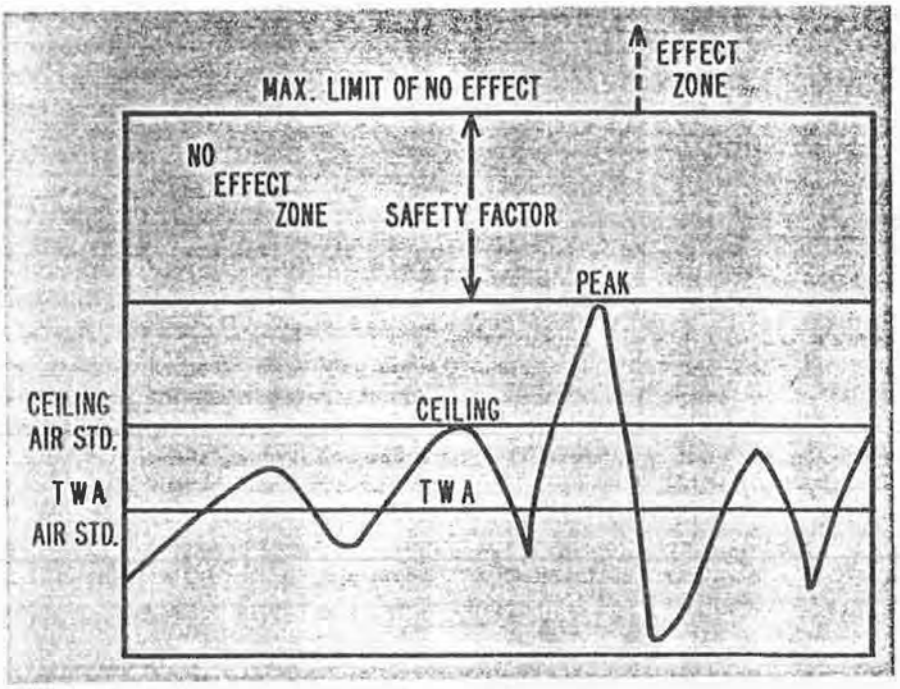

Figure 1 — Acceptable concentrations.

Peak values — Pennsylvania short-term limits

Definite peak values are provided, however, for 142 of the more than 550 TLV-listed substances in the Pennsylvania Short-Term Limits (STLs).[2] These STLs stipulate limiting concentrations for either 5-, 15-, or 30-minute peak exposures, depending on the nature of the toxicologic response. The peak exposures superimposed on time-weighted exposures are such that the TLV shall not be exceeded. The frequency of the peak exposures is limited by the time required for whatever recuperation may be necessary from the peak exposure. As peak exposures are inappropriate for many substances, the 142 peak exposure limits of Pennsylvania represent a very significant coverage of the TLV-listed substances with this conditional exposure.

Documentation of industrial air standards

Further aid to the proper administration of the industrial air standards is familiarity with their documentation. Issued as a separate companion piece to the TLVs, the publication, *Documentation of the TLVs for Substances in Workroom Air*,[3] gives pertinent scientific information and data with references to literature sources on which the TLV was based. As each documentation also contains a statement defining the type of response against which the limit is safeguarding the worker, it provides the administrator of the standards with exact knowledge of the relative seriousness of the hazard, a not inconsiderable aid in judging the consequences of, and levying a fine for, any infraction. For the standards protect against all degrees of hazard ranging from serious hazards to health, including death, to mild irritation and narcosis, to no health effects at all, merely nuisances.

Operational procedures for determining noncompliance

Faced with the conditions set by multiple acceptable concentrations and variable incorporated safety factors in the standards (Table I), how is the factory inspector to test for compliance? And after testing, how to evaluate the results, particularly in light of 1) the limited precision of current air-sampling procedures, 2) the temporal variability of working environmental air concentrations, and 3) having to extrapolate air-sampling data to estimate risk to the worker?

With these conditions, the following are offered as the optimal testing procedures currently used for assuring data suitable for evaluation. First, for those who have the responsibility for sampling the workplace environment: *Obtain representative samples.*

Use personal sampling devices or other means of getting breathing-zone samples. This entails attention to *a)* the time of sampling for assurance that the day of sampling is representative of all other days. For this, and in view of environmental variability in different seasons (closed plant in colder months vs. open-air ventilation in summer), a scheme of sampling at different seasons is necessary (where seasonal temperatures vary significantly). *b)* Attention must be paid to cyclical nature of the operation — whether brief, peak exposures occur, or whether full 8-hour shifts are representative of worker exposure. If exposures are brief, peak exposures, again we repeat: the 5-, 15-, or 30-minute sampling times should conform to these intervals to ascertain peak concentrations. If a full-shift cycle exists, with currently available sampling devices, it is necessary to take a sufficient number of grab samples to be representative of the full shift.

The question now arises, What is a "sufficient number of samples?" NIOSH statisticians have developed a short procedure[4] for determining noncompliance with an 8-hour average standard based on a small number of grab samples. The statistical test shown in Table III determines with 95% confidence if the average of N number of grab samples exceeds the standard. Final judgment is made when the average or mean value of the analyzed samples exceeds the quantity on the left side of the equation, R (the range of the values of the samples), multiplied by ϕ (the statistical factor derived from the number of samples and the estimated errors of sampling and analysis) plus the air standard; there is 95% confidence that the contaminant concentration exceeds the standard and the situation is out of compliance. From the standpoint of practicality, the optimal number of grab samples is six or seven. A slightly modified statistical procedure[4] is used for the determination of noncompliance with ceiling limits, but it is obvious that in sampling for ceiling or peak ex-

TABLE III
Formula for Judging Noncompliance with Air Standard*

$R\phi$ + Air Std. = Air Std. statistically adjusted for errors of sampling and analysis

R = Range of N values ϕ Factor for 95% Confidence

N No. Samples	ϕ	N No. Samples	ϕ
2	3.175	7	0.263
4	0.529	8	0.230
6	0.312	10	0.186

*Modified from Sect. 15-2.2 NBS Handbook 91, Exptl. Statistics

posures, because of the brevity and the recognized variability of short-term exposures, the greater the number of samples, the greater the precision of the measurement and, hence, the estimate of noncompliance. Thus, recognized statistical procedures have shown the optimal amount of sampling, both from practical and theoretic standpoints, required for each of the three acceptable concentrations to obtain satisfactory precision for determining noncompliance. The question still remains, will the 5% uncertainty be regarded by industry as unchallengeable?

Summary and conclusions

Before acceptable, nonchallengeable determinations of noncompliance can be made, air samples statistically appropriate in number and duration to the three acceptable concentrations — time-weighted average, ceiling, and peak values — must be taken. The statistical methods, in turn, must take into consideration the nature and intent of the air standards, namely, 1) their guideline-like nature; 2) that excursions above the standard value are permissible; and 3) that the standards contain safety factors that vary in magnitude according to whether the standards are protecting against health or well-being. When monitoring is performed and evaluated in the suggested statistical manner, the determination of noncompliance is assured at the 95% confidence limit.

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Chemical substances in the work environment: some comparative aspects of USSR and US hygienic standards*

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Maximum permissible concentrations (USSR) and threshold limit values (US) for chemical substances in the work environment are compared and discussed by two Soviet scientists, who work within the field of occupational hygiene.

The major changes which have taken place in the industrial environment have been consequent upon the rapid development and progress of chemistry and chemical technology, which have resulted in the ambient atmosphere of production areas becoming contaminated with noxious substances apt to produce a damaging effect on the health of the operators and their progeny.

Thirty years ago there were no more than a few score of chemical compounds capable of causing occupational poisonings and diseases in the workers.

Today, such industrial poisons are numbered by the hundreds. At the same time, there exist a vast number of toxic substances that, thanks to preventive measures undertaken in the industry, do not cause any poisoning effect, but, nonetheless, are potentially hazardous to health.

Because of an increasing production and synthesis of substances and various materials made thereof, the range of chemical compounds that to varying degrees contaminate the industrial environment is widening year by year.

However, the industrial, as well as the general environment as a whole cannot be allowed to suffer the consequences of unchecked pollution.

In the face of the impossibility of fully protecting the environment against chemical contaminants, it is our duty to know which is the maximum degree of pollution that can be permitted without causing any harmful after-effects on health. Thus, life functions are the basis for the establishing of hygienic standards for chemical contaminants in the human surroundings and, particularly, in the industrial environment, as concentrations of noxious substances therein may be quite considerable.

The establishment of the maximum permissible content harmful substances in the environment is of an immense importance, since it forms a backbone for the environmental protection against pollution. The maximum permissible concentrations (MPCs) enable one to adopt a proper attitude toward and to assess the significance of environmental pollution for health, to forecast its effect on health, and to determine the effectiveness of measures taken for the protection of the environment against contaminants.[1,2]

The development of hygienic standards

In the USSR the first maximum permissible concentrations were set up as far back as in 1922. Initially, they covered sulfurous gas, hydrogen chloride, and nitrogen oxides. In 1924, MPCs were fixed for gasoline. In 1930 the standards embraced 25 industrial poisons and in 1939 the approved State standards for MPCs covered as many as 40 substances. In 1941 the scope of these standards was broadened by the inclusion of the MPCs for "non-toxic dusts."[3]

A gradual increase in the number of the MPC items was paralleled by further theoretical research work in the domain of hygienic standardization. Thanks to works by N.V. Lazarev[4] and N.S. Pravdin[5] the establishment of MPCs within the workroom area proceeded ever more intensively in the subsequent years.

* Published in *AMBIO 4(1)*:30-33 (1975). Reprinted by permission of the Royal Swedish Academy of Sciences, Stockholm.

Since 1956, a special commission headed by Z.B. Smelyansky[6] and Z.I. Izraelson, regularly engaged in determining the MPCs in the air of the workroom area, has been functioning at the Ministry of Public Health of the USSR.

It can be seen from the available literature sources, that the establishment of allowable levels of noxious substances in industry began at a later date in the USA, and it was not until the 1950s and 1960s that there was notable progress in the standardization work.

Present standards

At present the greatest number of standards are available in the USSR and the USA. The nomenclature of the USSR lists over 750 MPC items and that of the USA, over 550.[1,2,7]

The rising commercial production of chemicals requires still more intensive work on the development of standards for chemical substances in the industrial environment. Research in this field has been more active in recent years; this is also the case in a number of other countries.

An analysis of the basic principles used in the establishing of standards bears witness to substantial differences that are most spectacular as regards two countries — the USSR and the USA.

The recommended MPC values in the USSR are lower than in the USA, this being borne out by the relation between the Threshold Limit Values (TLVs) used in the US, and the MPCs applied in the USSR.

TABLE I
Relation Between TLV and MPC Values

TLV/MPC ratio	Number of Substances	Percent of the Total Number
0.20 — 0.49	1	0.6
0.50 — 0.99	11	6.6
1.0	19	11.4
1.01 — 2.00	21	12.6
2.01 — 5.00	32	19.1
5.01 — 10.00	25	14.9
10.01 — 20.00	22	13.2
20.01 — 50.00	18	10.8
50.1 — 100.00	13	7.8
100.01 — 200.00	4	2.4
200	1	0.6

If one considers 167 identical substances figuring in the lists for 1973 of both the USSR and the USA, the relation between the TLVs and the MPCs will be as shown in Table I.

In the USSR the MPC equals 100 percent or more mg/m^3 for only 6 percent of the substances. The respective figure for the USA is 26.5 percent.

A more detailed scrutiny of the MPC and the TLV has demonstrated that 19 substances have the same standard values, 32 compounds differ by a factor of two or less, the standards for 12 substances have a higher standard value in the USSR, while 18 MPC values stand at a level more than 50 times below that of the TLV.

There are extreme differences in the values for propylene oxides (TLV/MPC = a 240-fold difference) and cobalt and its oxides (MPC/TLV = a 5-fold difference).

A detailed consideration of the list of standards revealed differences in individual classes and groups of chemical substances. For a number of irritating poisons the difference between the MPC and TLV levels is insignificant, the only substantial divergences being in the case of acetaldehyde and of formaldehyde (72-fold and 6-fold). In the USSR the standard for acetaldehyde was set up by taking into consideration not only its irritating action, but also an acutely pronounced offensive odor perceptible at very low concentrations. In the USA the standards for acetaldehyde were set up only with the view of protection against an excessive irritation and damage of the respiratory tract in "adapted" workers.

In the USSR the MPC for formaldehyde was revised in 1967 and reduced from 5 down to 0.5 mg/m^3. This change was affected on the basis of numerous occupational health cases of persons employed in hospitals, and experimental material which proved that formaldehyde displays a marked irritating action when present in the atmosphere at a formerly accepted MPC level.

American literature sources carry information on the harmful effect of formaldehyde at the level of 6 mg/m^3, and 5 times below this level. In the TLV documentation for formaldehyde (1966) reference is made to the fact that the 6 mg/m^3 concentration does not provide any safeguards against the irritating action. This, probably, was the reason why the TLV was cut down to 3 mg/m^3 in 1972.

TABLE II
MPC and TLV Values for Some Metals, Metalloids and Their Compounds

Substance	MPC mg/m³	TLV mg/m³	TLV/ MPC
Beryllium and its compounds	0.001	0.002	2
Vanadium and its compounds			
Vanadium pentoxide fumes	0.1	0.05	0.5
Vanadium pentoxide dust	0.5	0.5	—
Ferrovanadium	1	1	—
Cadmium oxide	0.1	0.1	—
Manganese	0.3	5.0	16.6
Molybdenum (soluble compounds)	4	5	1.25
Molybdenum (insoluble compounds)	6	10	1.65
Nickel, metal and soluble compounds (as Ni)	0.5	1.0	2
Metal mercury	0.01	0.05	5
Lead and its inorganic compounds	0.01	0.15	15
Antimony regulus in the form of dust	0.5	0.5	—
Tellurium	0.01	0.1	10
Titanium oxides	10	10	—
Chromic oxide, chormates, bichromates (calculated to the value of CrO_3)	0.01	0.1	10
Zinc oxide	6	5	0.84
Metallic zirconium and its insoluble compounds	6	5	0.84

In addition to the differences with regard to irritants, there are, in a number of instances, significant differences between the MPC and TLV values for aerosols of metals, metalloids and their compounds. In the list of substances in Table II for example, the divergences are significant in the case of such industrial compounds as lead, manganese, chrome and tellurium. Worthy of note is the fact that the American TLVs for manganese and lead are the highest not only by comparison with the Soviet MPCs, but also with those adopted in other countries. Thus, for instance in the ChSSR the mean-shift values for the said compounds are 2 to 2.5 times as low as the TLVs.

Before 1972 the standard for mercury in the USA was ten times higher than in the USSR. However, following the conference in Stockholm in 1969, where an international MPC for mercury equal to 0.05 mg/m³ had been recommended, this value was adopted in the USA as the TLV. It should be mentioned that the international MPC for mercury was based in many years of research work on mercury carried out in the USSR.

The greatest divergences between the MPC and TLV values (up to a 63-fold difference) occur in the series of chlorinated hydrocarbons (Table III).

In some instances figures in the American list for chlorinated hydrocarbons are also much higher than the standards accepted in other countries. The mean-shift value for dichloroethane in Czechoslovakia (ChSSR) and the German Democratic Republic (GDR), for example, is four times as low as in the TLV.[8]

In the solvents group, the discrepancies are somewhat less marked. But here, too, the MPCs for such compounds as benzene and acetone are 16 to 12 times as low as the TLVs. In conformation with experimental and epidemiological findings, the MPC for benzene was reduced in the USSR from 20 down to 5 mg/m³ in 1968. Foreign publications also carry statements pointing to the need

for reducing the MPC for benzene. R. Truhaut,[9] in particular, recommends lowering the TLV for benzene by not less than five times. In this group of compounds the greatest difference (190-fold) is noted in the case of aniline, the MPC for which was reduced from 3 down to 0.1 mg/m^3 in 1971.

The tendency towards reduction of the TLV values that has been prevailing during recent years deserves special attention.

And then, as a rule, the new USA standards approach the Soviet ones and because of this the number coinciding MPC and TLV values increases every year.

Thus, during the last 10 years, 59 of the US standards have been subject to change; and of the substances on this list, the TLV levels of 27 were reduced within the first 6 years, while in the last 4 years the corresponding number was 32. In our opinion this last circumstance forms a basis for establishing uniform international standards.

Differences in definitions

The divergence between the MPC and TLV values should be attributed largely to the fundamental differences in the concept of "maximum permissible concentrations."

TABLE III
MPC and TLV Values for
Some Chlorinated Hydrocarbons

Substance	MPC mg/m^3	TLV mg/m^3	TLV/MPC
Benzyl chloride	0.5	5	10
Vinyl chloride	30	510	17
Dichlorobenzene (ortho)	20	300	15
Ethylene dichloride	50	790	15.8
Dichloroethane (1,2)	10	200	20
Methylene chloride	50	890	17.8
Methyl chloride	5	210	42
Tetrachloroethylene	10	670	67
Trichloroethylene	10	535	53.5
Chlorobenzene	50	350	7
Chloroprene	2	90	45
Carbon tetrachloride	20	65	3.3
Ethyl chloride	50	2600	52

In the Soviet Union the MPC means the concentrations which, with a workday of not more than 8 hours throughout the whole of the service record, do not cause any diseases or have other adverse effects on the health status of the workers that could be detected by the modern methods of investigation, either directly in the course of work or at later dates.[2,6,10-12]

The official preamble to the list of threshold limits,[7,13-15] as well as works of pertinent authors[16-20] contain statements to the effect that the TLVs determine conditions to which workers can be exposed day after day without any adverse effect. However, because of the wide variations in sensitivity of exposure to chemicals at the level of the TLV or below it, a small percentage of workers may feel discomfort, and a still smaller percentage of individuals may demonstrate more serious effects, such as an exacerbation of an already existing pathological condition or the development of an occupational disease.

Hence, the hygienic standards established for chemical compounds in the air of the workplace area in the USA admit the possibility that the health status in some of the operators might be negatively affected.

Furthermore, the Soviet MPCs are, according to the legislation in force, *maximum single-time ones*, whereas most of the American TLVs are weighted mean concentrations and only compounds marked "C" are referred to the category of the maximal ones.

Establishing the standards

The setting of standards for industrial substances in the USSR is effected in three stages.[1]

The first stage — determination of tentative MPC — is timed to the period of laboratory development of new compounds; the second involves substantiation of the MPC in animal experiments, pilot tests and production planning; the third stage includes correction of the experimental MPC through comparisons of work conditions as against the health status of the workers and continues for 3 years from the date of commissioning the industrial plant.

The substantiation of the TLV provides for no such stagewise investigations. At the same time the basic principles and methods of obtaining

data for substantiation of threshold limit values in the air[21] include two sections, namely: 1) principles and methods of animal experiments, and 2) an analysis of information derived from studies on humans.

And while the first section of procedures practiced in the USA includes investigations on animals, the second one is made up of a number of independent items. Thus, for example, it includes experiments with human volunteers aimed at eliciting irritative, narcotic and sensitizing effects. Moreover, it involves hygienic investigations of the operators, and the main program of the investigators calls for classification of workers from the medical standpoint; a technical program of examining the atmospheric environment of industrial plants is also set forth.

A detailed study of a draft for basic principles and methods of obtaining TLV[21] points to the presence of many differences in approaches to the substantiation of the MPC in animal experiemnts. For instance, in the USSR the establishment of the acute action threshold is obligatory, while in the USA it is not.

One should dwell on the research into the chronic action of poisons, in particular. At present, according to methodological directives, the American toxicologists consider it necessary to go on with experimental work for 2 years in order to establish the threshold of chronic effect. Earlier, however, such investigations were not undertaken even in the case of compounds with chronic effects. Thus, for example, H. Stokinger pointed out[18] that only 20 percent of the substances on the TLV list were substantiated on the basis of chronic investigations. The TLV for the supermutagen ethyleneimine, for instance, was established on the basis of its acute and irritative action.

As a result of experiments carried out in the USSR, involving exposure to ethyleneimine at the TLV level existing in the USA prior to 1964, the following were ascertained: a well-marked general toxic, gonado- and embryotropic action and clear-cut mutagenic and carcinogenic effects.

In 1965 the TLV value for ethyleneimine was brought down to 1 mg/m^3. However, further detailed investigations into the general and specific features of the ethyleneimine action showed that this poison displays a pronounced adverse effect at concentrations of 0.7 and 0.4 mg/m^3. Accordingly, the MPC for ethyleneimine in the air of the workplace areas has been set at the level of 0.02 mg/m^3 in the USSR.

Note should be taken of a high level of research work done in the USA in ascertaining the fate or metabolism of industrial poisons in the organism. Tests of this kind form an integral part of investigations into the acute action of the poison. The methodological directives in the USA attach great importance to determination of the substance passed with the expired air and with urine by comparison with its blood content in the case of volatile solutions and also to the distribution in the body and detection of major metabolites of substances of low volatility.

Research workers of a number of countries,[19,20,22-24] including the American ones, pay particular attention to the differences in the sensitivity of methods used in substantiating the MPC and TLV, referring in this connection to the examinations of the nervous system with the aid of the conditioned reflexes method. It should be noted that the frequent application of this method in the USSR is one of the reasons for the divergence between the MPC and TLV.

And, indeed, in a number of American research works use is made of less sensitive methods. In our investigations the application of the conditioned reflex method is, however, not mandatory. In the USSR, the establishing of a standard is effected with reference to a complex set of factors by taking due account of their hygienic significance, the choice of the factors being strictly substantiated by the nature of the action exerted by the substance.

Practical aspects

One of the principal differences in the approach to the establishment of the MPC in the USSR and the USA is the requirement of "technical feasibility." While in the USSR the basic principle in approving the MPC is based on medical indications, in the USA more economic and technical consideration appear to be more important.

Thus, for example, Professor Magnusson[19] is of the opinion that excessive control over the innocuous action produced by highly toxic compounds is a waste of human resources and may hinder proper utilization of chemical substances

and processes that may by themselves be of immense importance for our social, economic and physical health.

We, for our part, believe that the existing extraordinarily broad possibilities of engineering and technology, and their rapid progress, permit them to overcome the difficulties of the past. This point of view is supported by improvements in working conditions and by reduced concentrations of noxious substances at many plants of the chemical and other branches of industry.

In the USSR the purpose of hygienic standardization is the creation of safe working conditons, securing the good health of the operators not only during their employment in a given industry, but also later in their lives.[1,2,10,11]

It may also be that one of the reasons for such substantial discrepancies between the MPC and TLV values is differences in the methods of chemical analysis applied by both parties and differences in the sensitivity of these methods. This question, however, requires special consideration, with the participation of specialists on matters of industrial sanitary chemistry.

The necessity of protecting the industrial environment against chemical contaminants dictates the need for fixing permissible levels of chemicals in the atmosphere of the workroom area in each and every country. It is obvious that even strict observance of these levels cannot ensure optimum environmental quality. These levels may differ somewhat in individual countries, but they should function as safeguards, assuring that the work can be performed in complete safety, with no risk to the health of the workers or their offspring.

The fact that it is not always that all the standards are actually observed in industry does in no way prejudice their vast importance for the whole cause of protecting the environment against all sorts of pollution. It is only the existence of standards that makes it possible to evaluate the environmental contamination from the viewpoint of its hazard to health, and the effectiveness of measures and methods (sometimes very costly and complex) that each country must put into effect to secure the well-being of the people.

In the USSR the health of man is regarded as a priceless treasure, the loss of which cannot be compensated by anything, least of all by material wealth.[2] And this is the reason why as the basis of the establishing of hygienic standards should be the goal of the complete preservation of health, even if considerable expenditures should be involved in maintaining the standards.

Many years of experience with the setting of hygienic standards in the USSR have proved that such standards are highly effective in protecting the workers against the harmful action of occupational hazards. Thanks to this, we have successfully solved the problems of preventing occupational poisonings by metals, organic solvents, and by many synthetic chemical products. We have succeeded in sharply reducing the prevalence of silicosis in the mining and machine-building industries, in the manufacturing of building materials and in other branches of the national economy. The observance of standards in practice is largely dependent not only on government legislation, but also on the intensity with which the engineers and technologists are engaged in the hygienic improvement of technology and of industrial equipment. In the USSR this kind of work is done with the cooperation of qualified scientific bodies, the final goal being realization of hygienic requirements.

Outlook

We believe that the broadening of scientific contacts among countries in the domain of the establishing of hygienic standards will serve the cause of further progress in international cooperation and will lead to the finding of ways for drawing up a list of international hygienic standards. We feel that step by step we move in the direction of creating international standards, if not for all chemicals, then at least for many of those that are being widely used throughout the world. Attempts of this kind have already been made on an international scale. It is possible that these standards will admit a certain range of variations for each substance. But the creation of them should be preceded by the national practice of many countries.

In our belief that the hygienic standard is not the optimum for the environment, that it would be better to do away with dillution altogether. But complete elimination of contaminants of the foreseeable future is unrealistic, since under conditions as they exist in industry we fail to have at our

command an ideal technology, devoid of waste materials.

In the course of modern industrial production there develop, many side, intermediate, and final products that contaminate the air, water, soil and foodstuffs. All these pollutants must be studied from the standpoint of hygiene and toxicology, with the establishment, whenever this is necessary, of hygienic standards, which must serve as the basis of health measures.

The environment surrounding man is the sole source of life and health, the industrial environment being part of it. Much depends on this environment to make labor a factor of health and not a source of diseases, stress conditions and fatigue.

A struggle for the satisfactory condition of this environment is a matter of extreme importance and it demands vast efforts and resources.

We shall be victorious in this struggle only if the problems of protecting the environment are in the center of public attention.

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An international comparison of hygienic standards for chemicals in the work environment*

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In order to control occupational exposure to airborne particulates, gases and vapors, hygienic standards for the work environment are in force in several countries under different names (TLV, MAC, MAK, MPC). The US and Soviet standards comprise about 400 and 500 standards, respectively, but only 169 substances appear in both lists. The following compilation is restricted to those common substances.

Along with the hygienic standards in the USA[1] and the Soviet Union (USSR),[6] are listed the standards of the Federal Republic of Germany (BRD),[2] the German Democratic Republic (DDR),[3] Sweden[4] and Czechoslovakia (CSSR).[5] In other countries, e.g., Argentina, Great Britain, Norway, Peru, the US standards are applied.

It should be noted that the American standards[1] cited in the table are the legal ones, established by Occupational Safety and Health Administration (OSHA) and not the more often quoted values recommended by a committee from the independent organization American Conference of Governmental Industrial Hygienists (ACGIH). Although the values are identical for a majority of the substances, some minor differences exist between the OSHA and the ACGIH lists.

Two different kinds of values are given in the table; 1) 8-hour time-weighted average values, and 2) acceptable ceiling concentrations, marked with (c).

Only the USA, BRD and CSSR have published the underlying documentation on which their standards are based. In the absence of documentation from other countries listed in the table, a comparison of standards must be limited to a comparison of figures.

The table shows that wide discrepancies exist between hygienic standards in different countries. Generally the standards decrease from the left to the right in the table, the USA applying the highest values of the countries cited and the USSR the lowest. For more than a third of the substances the values are at least 10 times higher in the USA than in the USSR. All the Soviet standards are ceiling values, while the majority of the American ones are time-weighted average values, i.e., the Soviet standards are even more rigorous in practice than the figures show.

For primarily irritating substances, e.g., acrolein, along with lung-injuring gases and varpor, e.g., nitrogen dioxide, generally minor variations are seen in the hygienic standards applied by different countries. The same is true for metals and metalloids. With regard to methemoglobin-forming substances, the differences in standards are very small for the aromatic nitro-compounds (e.g., dinitrobenzene, p-nitrochlorobenzene) while they are quite marked for aniline and its derivatives. The Soviet standards for the latter compounds are set at extremely low levels, probably due to the effect of aniline on the central nervous system rather than on methemoglobin-formation. It is well known that Soviet occupational toxicologists, when setting standards, make use of behavioral and neurotoxic effects in animals to a greater extent than do toxicologists elsewhere. Consequently, great differences can be seen between the Soviet and US hygienic standards for substances affecting the central nervous system, e.g., the halogenated hydrocarbons. Standards for alkylating agents such as ethylene imine and ethylene oxide, which generally possess mutagenic effects, also differ considerably.

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TABLE I
Work Environment Hygienic Standards in Different Countries

	USA-OSHA 1974		BRD 1974	DDR 1973	Sweden 1975	CSSR 1969	USSR 1972
	ppm	mg/m^3	mg/m^3	mg/m^3	mg/m^3	mg/m^3	mg/m^3(c)
Acetaldehyde	200	360	360	100	90	—	5
Acetic acid	10	25	25	20	25	—	5
Acetone	1000	2400	2400	1000	1200	800	200
Acetonitrile	40	70	70	—	—	—	10
Acrolein	0.1	0.25	0.25	0.25	0.25	0.5	0.7
Aldrin	—	0.25	0.25	—	—	—	0.01
Allyl alcohol	2	5	5	5	5	3	2
Ammonia	50	35	35	25	18	40	20
Ammonium sulfamate	—	15	15	—	—	—	10
Amyl acetate	100	525	525	200	525	200	100
Aniline	5	19	19	10	19	5	0.1
p-Anisidine	0.1	0.5	0.5	—	—	—	1
Antimony & compounds (as Sb)	—	0.5	0.5	0.5	0.5	—	0.3-2
Arsenic & compounds (as As)	—	0.5	0	0.3	0.05	0.2	0.3
Arsine	0.05	0.2	0.2	0.2	0.05	0.2	0.3
Benzene	12	30	0	50	30	50	5
Benzoyl peroxide	—	5	5	—	—	—	5
Benzyl chloride	1	5	5	5	—	—	0.5
Beryllium	—	0.002	0	0.002	0.002	—	0.001
Boron oxide	—	15	15	—	—	—	10
Boron trifluoride	1(c)	3(c)	3	—	—	—	1
Bromoform	0.5	5	—	—	—	—	5
1,3-Butadiene	1000	2200	2200	500	—	500	100
2-Butanone	200	590	590	300	440	—	200
Butyl acetate	150	710	950	400	710	400	200
Butyl alcohol	100	300	300	200	150	100	10
Butylamine	5	15	15	—	—	—	10
Cadmium (metal dust and soluble salts)	—	0.2	—	0.1(a)	0.05	—	0.1
Cadmium oxide fume (as Cd)	—	0.1	0.1	0.1(a)	0.02	0.1	0.1
Camphor	2	12	2	—	—	—	3
Carbaryl (Sevin)	—	5	5	—	—	—	1
Carbon disulfide	20	60	60	50	30	30	10
Carbon monoxide	50	55	55	55	40	30	20
Carbon tetrachloride	10	65	65	50	65	50	20
Chlorine	1	3	1.5	1	3(c)	3	1
Chlorine dioxide	0.1	0.3	0.3	—	0.3	—	0.1
Chlorobenzene	75	350	230	50	—	200	50
Chlorodiphenyl (42% chlorine)	—	1	1	1	0.5	1	1
Chlorodiphenyl (54% chlorine)	—	0.5	0.5	1	0.5	0.5	1
Chloroprene	25	90	90	10	90	50	2
Chromic acid and chromates (as Cr)	—	0.1(c)	0.1	0.1	0.05	0.05	0.01
Cobalt, metal fume & dust	—	0.1	0.5	0.1	0.1	0.1	0.5
Copper, fume	—	0.1	0.1	0.2(b)	—	—	1
Copper, dusts and mists	—	1	1	—	—	—	1
Crotonaldehyde	2	6	5	—	—	—	0.5
Cumene	50	245	245	50	—	—	50
Cyclohexane	300	1050	1050	—	—	—	80
Cyclohexanone	50	200	200	—	—	—	10
Cyclopentadiene	75	200	200	—	—	—	5
2,4-D	—	10	10	—	—	—	1
DDT	—	1	1	1	—	—	0.1
Dibutylphtalate	—	5	—	—	—	—	0.5
o-Dichlorobenzene	50(c)	300(c)	300	150	—	—	20

TABLE I [Continued]
Work Environment Hygienic Standards in Different Countries

	USA-OSHA 1974		BRD 1974	DDR 1973	Sweden 1975	CSSR 1969	USSR 1972
	ppm	mg/m^3	mg/m^3	mg/m^3	mg/m^3	mg/m^3	mg/m^3(c)
p-Dichlorobenzene	75	450	450	200	—	—	20
Dichlorvos (DDVP)	0.1	1	1	—	—	—	0.2
Dieldrin	—	0.25	0.25	—	—	—	0.01
Diethylamine	25	75	75	50	—	—	30
Diethylamino ethanol	10	50	50	—	—	—	5
Diisopropylamine	5	20	—	10	—	—	5
Dimethylamine	10	18	18	—	—	—	1
Dimethylaniline (N-dimethylaniline)	5	25	25	—	—	—	0.2
Dimethylformamide	10	30	60	30	30	30	10
Dinitrobenzene	0.15	1	1	1	—	1	1
Dinitro-o-cresol	—	0.2	0.2	0.2	—	—	0.05
Dinitrotoluene	—	1.5	1.5	1	—	—	1
Dioxane	100	360	360	200	90	—	10
Epichlorhydrin	5	19	18	5	—	—	1
Ethyl acetate	400	1400	1400	500	1100	400	200
Ethyl alcohol	1000	1900	1900	1000	1900	1000	1000
Ethyl amine	10	18	18	20	—	—	1
Ethyl bromide	200	890	890	500	—	—	5
Ethyl chloride	1000	2600	2600	2000	—	—	50
Ethyl ether	400	1200	1200	500	1200	300	300
Ethyl mercaptan	10(c)	25(c)	1	—	—	—	1
Ethylene chlorohydrin	5	16	16	—	—	—	0.5
Ethylene diamine	10	25	25	—	—	—	2
Ethylene imine	0.5	1	1	1	0	—	0.2
Ethylene oxide	50	90	90	20	36	—	1
Fluoride (as F)	—	2.5	2.5	—	2.5	1	1
Formaldehyde	2	3	1.2	2	3(c)	2	0.5
Furtural	5	20	20	10	—	—	10
Heptachlor	—	0.5	0.5	—	—	—	0.01
Hydrazine	1	1.3	0.13	—	0.13	0.1	0.1
Hydrogen chloride	5(c)	7(c)	7	5	7(c)	8	5
Hydrogen cyanide	10	11	11	5	11	3	0.3
Hydrogen fluoride	3	2	2	1	2(c)	1	0.5
Hydrogen sulfide	20(c)	30(c)	15	15	15	10	10
Iodine	0.1(c)	1(c)	1	—	1(c)	—	1
Isopropylamine	5	12	12	—	—	—	1
Lead, inorganic fumes and dusts	—	0.2	0.2	0.15	0.1	0.05	0.01
Lindane	—	0.5	0.5	0.2	—	—	0.05
Maleic anhydride	0.25	1	0.8	—	1	1	1
Manganese and compounds (as Mn)	—	5(c)	5	5	2.5	2	0.3
Mercury, metal	—	0.1(c)	0.1	0.1	0.05	0.05	0.01
Mercury, alkyl	—	0.01	0.01	0.01	0.01(c)	—	0.005
Methyl acetate	200	610	610	200	—	200	100
Methyl acrylate	10	35	35	20	—	—	20
Methyl alcohol	200	260	260	100	260	100	5
Methyl amine	10	12	12	—	—	—	1
Methyl bromide	20(c)	80(c)	80	50	—	—	1
Methyl chloride	100	210	105	100	—	100	5
Methyl chloroform	350	1900	1080	500	540	500	20
Methyl cyclohexane	500	2000	2000	—	—	—	50
Methyl isocyanate	0.02	0.05	0.05	—	—	—	0.05
α-Methyl styrene	100(c)	480(c)	480	—	—	—	5
Methylene chloride	500	1740	1750	500	350	500	50
Molybdenum, soluble compounds	—	5	5	—	—	—	4
Molybdenum, insoluble compounds	—	15	15	10	—	—	6
Morpholine	20	70	70	—	—	—	0.5
Naphta (coal tar)	100	400	—	—	—	200	100
Naphtalene	10	50	50	20	—	—	20
Nickel carbonyl	0.001	0.007	0.7	—	0.007	—	0.0005
Nickel, metal	—	1	0	0.5	0.01	—	0.5
p-Nitroaniline	1	6	6	—	—	—	0.1
Nitrobenzene	1	5	5	5	5	5	3
p-Nitrochlorobenzene	—	1	1	1	—	1	1

TABLE I [Continued]
Work Environment Hygienic Standards in Different Countries

	USA-OSHA 1974		BRD 1974	DDR 1973	Sweden 1975	CSSR 1969	USSR 1972
	ppm	mg/m³	mg/m³	mg/m³	mg/m³	mg/m³	mg/m³(c)
Nitroethane	100	310	310	—	—	—	30
Nitrogen dioxide	5	9	9	10	9(c)	10	5
Nitromethane	100	250	250	—	—	—	30
1-Nitropropane	25	90	90	50	—	—	30
2-Nitropropane	25	90	90	50	—	—	30
Ozone	0.1	0.2	0.2	0.2	0.2	0.1	0.1
Pentachlorophenol	—	0.5	0.5	0.5	0.5	—	0.1
2-Pentanone	200	700	700	—	—	—	200
Perchloroethylene	100	670	670	300	200	250	10
Phenol	5	19	19	20	19	20	5
Phosgene	0.1	0.4	0.4	0.5	0.2(c)	0.4	0.5
Phosphine	0.3	0.4	0.15	0.1	0.4	0.1	0.1
Phosphorus (yellow)	—	0.1	0.1	—	—	0.03	0.03
Phtalic anhydride	2	12	5	10	12	5	1
Propargyl alcohol	1	2	2	—	—	—	5
n-Propyl acetate	200	840	840	400	—	400	200
Propyl alcohol	200	500	—	—	—	500	10
Propylene dichloride (1,2-Dichloropropane)	75	350	350	50	—	—	10
Propylene oxide	100	240	240	—	—	—	1
Pyridine	5	15	15	10	15	5	5
Quinone	0.1	0.4	0.4	—	—	—	0.05
Selenium compounds	—	0.2	0.1	0.1	0.1	—	0.1
Sodium hydroxide	—	2	2	2	2(c)	—	0.5
Stoddard solvent	500	2950	—	—	600	—	300
Styrene	100	420	420	200	210	200	5
Sulfur dioxide	5	13	13	10	5	10	10
Sulfuric acid	—	1	1	1	1	1	1
Tellurium	—	0.1	0.1	—	—	—	0.01
1, 1, 2, 2-Tetrachloroethane	5	35	7	10	—	—	5
Tetraethyl lead (as Pb)	—	0.075	0.075	0.05	0.075	—	0.005
Tetrahydrofuran	200	590	590	200	—	—	100
Tetranitromethane	1	8	8	—	—	—	0.3
Thallium	—	0.1	0.1	—	—	—	0.01
Thiram (tetramethylthiuramdisulfide)	—	5	5	1	—	—	0.5
Toluene	200	750	750	200	375	200	50
Toluene-2, 4-diisocyanate	0.02(c)	0.14(c)	0.14	0.1	0.07(c)	0.07	0.5
o-Toluidine	5	22	22	10	—	5	3
Trichloroethylene	100	535	260	250	160	250	10
1, 2, 3-Trichloropropane	50	300	300	—	—	—	2
Triethylamine	25	100	100	20	—	—	10
Trinitrotoluene	0.2	1.5	1.5	1.5	—	1	1
Triorthocresylphosphate	—	0.1	—	0.1	—	—	0.1
Turpentine	100	560	560	300	560	—	300
Uranium, soluble compounds (as U)	—	0.05	0.05	—	—	—	0.015
Uranium, insoluble compounds (as U)	—	0.25	0.25	—	—	—	0.075
Vanadium, V_2O_3 dust (as V)	—	0.5(c)	0.5	0.5	0.5	—	0.5
Vanadium, V_2O_3 fume (as V)	—	0.1(c)	0.1	0.1	0.05(c)	—	0.1
Vinyl chloride	1	3	—	500	3	—	30
Vinyl toluene	100	480	480	—	—	—	50
Xylene	100	435	870	200	435	200	50
Xylidine	5	25	25	10	—	5	3
Zinc oxide fume	—	5	5	5	5	5	6
Zirconium compounds (as Zr)	—	5	5	—	—	—	4-6

(a) CdO (b) CuO (c) ceiling value

The case for carcinogen TLVs continues strong*

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The impetus to develop a classification of occupational carcinogens by the TLV Committee of the American Conference of Governmental Industrial Hygienists (ACGIH) arose more than four years ago, when it was felt that the listing of substances as occupational carcinogens was getting out of hand. Substances of purely laboratory curiosity, such as acetylaminofluorene and dimethylaminoazobenzene, which were found to be tumorigenic in animals, were classed along with known human carcinogens of high potency, such as bis-chloromethyl ether.

In short, no distinction was made between an animal tumorigen and a human carcinogen. Each came through to the union leader and the lay worker as equally worrisome.

This, of course, shouldn't be.

The finding of a substance to be tumorigenic, often in a half-dead mouse or rat due to intolerable doses as was the case for chloroform and trichloroethylene, is not *ipso facto* evidence that it will be carcinogenic in man under controlled, working conditions.

Distinction

It is for this reason that the TLV Committee, in the 1972 booklet, made a clear distinction between animal and human carcinogens.

Human carcinogens were listed in two groups: 1) those with an assigned TLV, four in number; and 2) those without an assigned TLV, eight in number. For the latter, *"No exposure or contact by any route, . . . as detected by the most sensitive methods, shall be permitted."*

Substances found tumorigenic in animals were classed as *"Experimental Carcinogens."* The eight substances were listed here under a warning that these substances were capable of eliciting tumors in animals, and that "exposure should be reduced to a minimum."

Classification

Subsequently, a Carcinogen Subcommittee was formed to expand the classification in a way that would be more helpful to the TLV Committee in assigning an appropriate TLV by presenting guidelines on the relative potency of potential occupational carcinogens.

This expanded classification appears under "Notice of Intended Changes" as Appendix A3 of the 1976 edition of the TLV Booklet under the title "Guidelines for the Classification of Experimental Animal Carcinogens."

In essence, the proposed guidelines divided experimental carcinogens into three groups: those of *high, low,* and *intermediate* potency.

To qualify for the different groups, substances must fulfill certain conditions of dosage rates according to the three chief routes of occupational contact: respiratory, dermal and gastrointestinal — which, in the judgment of the Committee, elicit tumors in significant excess above that in negative control animals.

High potency

For example: a substance of *high* cancerigenic potency by the respiratory route must induce malignancy in dosages less than 1 mg/m^3 of inhaled air (or its equivalent in parts per million) in 6- to 7-hour daily repeated exposures throughout the animal's lifetime, or from a single, intratracheally administered dose not exceeding 1 mg of particulate of liquid, per 100 ml or less of animal minute respiratory volume.

Examples: *Bis-chloromethyl ether,* malignant nasal tumors, rats at 0.1 ppm in two years. *Hex-*

* Presented at the ACGIH symposium on Workplace Control of Carcinogens, October 25-26, 1976, Kansasa City, MO. Published in *Workplace Control of Carcinogens, Proceedings of a Topical Symposium,* pp. 54-58 (1977).

amethyl phosphoramide, nasal squamous cell carcinoma, rats at 0.05 ppm in 13 months. *$Be(OH)_2$,* pulmonary adenomas, rats at 40 μg as Be, in one year.

Low potency

By contrast, substances in *low* tumorigenic potency by the respiratory route need only to elicit tumors at dosages greater than 10 mg/m^3 (or equivalent ppm) in daily repeated exposures for 12 months, with holding period for another year, or, from intratracheally administered dosages totaling more than 10 mg of particulate of liquid per 100 ml or more of animal minute respiratory volume.

Examples: *Beryl* (beryllium aluminum silicate), malignant lung tumors, rats at 15 mg/m^3 at 17 months. *Bezidene,* various tumors, rats, 10-20 mg/m^3 at $>$ 13 months.

Obviously, substances of *intermediate* potency have dosage rates intermediate between those of high and low potency. On present evidence, dimethyl sulfate and hydrazine might be considered experimental animal carcinogens of *intermediate* potency.

Dosage limits

Exclusion clause

In order to place in proper perspective the tumorigenic findings in experimental animals in relation to practical occupational concerns for worker protection, specific dosage limits have been set for the three routes of administration for mice and rats above which a substance is *not* to be considered an occupational carcinogen. These limits are defined on Page 40 of the '76 TLV Booklet. Trichloroethylene and dioxane, on this basis, have been excluded from the A2 listing of *"Industrial Substances Suspect of Carcinogenic Potential for Man."*

This list, which presently contains 22 suspect substances, has been developed on the basis of two kinds of information:

1. On limited epidemiologic evidence, exclusive of reports of single cases.
2. Demonstration of carcinogenesis in one or more animal species *by appropriate methods.*

By "appropriate methods," we include only those procedures defined in Appendix A3, "Guidelines for the Classification of Experimental Animal Carcinogens." Animal tumors produced by dosage schedules that result in animal morbidity and altered metabolic patterns are excluded from consideration according to the Exclusion Clause, titled "Exceptions."

Additions

The 22 presently listed chemical substances held suspect carcinogenic potential for the industrial worker do not represent a final number. We may expect the list to change as a result of new knowledge, either by addition or deletion. But irrespective of the size of the list, the most important thing to note is that 14 of the 22 listed substances have an assigned TLV.

What does it mean? It means several things. It means first and foremost that the TLV Committee recognizes practical thresholds for chemical carcinogens in the workplace, and secondly, for those substances with a designated threshold, that the risk of cancer from a worker's occupation is negligible, provided exposure is below the stipulated limit. There is no evidence to date that cancer will develop from exposure during a working lifetime below the limit for any of those substances.

Evidence

Where did the TLV Committee get the idea that thresholds exist for carcinogens? Where's the evidence?

Thresholds for carcinogens is anything but a popular concept, especially since it flies in the face of the biometrician's deeply rooted "one-hit" theory, where all it takes to start the carcinogenic process is to have one molecule of the carcinogen hit the proper site that they now have identified as DNA in the nucleus of the susceptible organ site.

From this it follows as the night the day, there can be no threshold other than zero.

So, you can see if the TLV Committee is to substantiate not only the concept, but come up with numbers for thresholds as well, they had better have some pretty good evidence.

Well, the Committee thinks it has such evidence, and here it is.

It takes three forms:

1. Evidence from epidemiologic studies of industrial plant experience, and from well-designed carcinogenic studies in animals.
2. Indisputable biochemical, pharmacokinetic, and toxicologic evidence demonstrating inherent, built-in anticarcinogens and processes in our bodies.
3. Accumulated biochemical knowledge makes the threshold concept the only plausible concept.

Examples

Start with a confirmed human carcinogen of very high potency, bis-chloromethyl ether. In a dose-response study by inhalation, nasal tumors were elicited in rats after a few months of daily exposures at 0.1 ppm, but not at 0.01 or 0.001 ppm! This indicates a decided threshold for this highly potent carcinogen.[1]

1,4-Dioxane, on the other hand, is an example of tumorigen of low potency. The dose at 0.1% dioxane in the drinking water amounts to 94 mg/kg body weight for male rats, and 148 mg/kg for female rats.

This large dose, although producing variable degrees of kidney and liver degenerative changes, induced no tumors in almost two years of treatment.[2]

Similarily, 111 ppm average daily exposure by inhalation for two years resulted in no tumors, indicating a threshold somewhere between this level and above 1000 ppm.[3]

Again, in some of our own experiments with coal tar pitch volatiles, skin tumors appeared in mice in which it was topically applied at total doses of 6400, 640 and 64 mg but not at doses below 64 mg.[4]

Certainty

Of greater significance and interest are the three and probably four instances of apparent thresholds for man, exhibited by b-naphthylamine, vinyl chloride, dimethyl sulfate, and quite probably, certain insoluble inorganic chromates.

From the information available in late 1975, 22 exposure years have elapsed without bladder tumors appearing in workers exposed to a-naphthylamine containing less than 0.5% b-derivative, whereas tumors occurred in prior exposures to a-naphthylamine containing more than 5% b-derivative.

History

Similarly, 25 years have now elapsed since workers were exposed to vinyl chloride (in addition to small amounts (5 ppm) vinylidene chloride) with occasional exposures to arsenic and other organic chemicals[9] without the appearance of tumors.

Vinyl chloride levels during the '50s although averaging 160 ppm,[8] Table I, rose occasionally at some work operations to more than 1000 ppm. This gives epidemiologic evidence of a threshold somewhere below 50 ppm and above 10 ppm.

In this connection, it is most interesting to note that experimental tests in rats show a few tumors still appearing at the 50 ppm level,[7,23] thus bringing into close agreement biochemical and toxicologic findings.

Suspect

Dimethyl sulfate is another suspect carcinogen for man on the basis chiefly of chronic inhalation studies in the rat. Concentrations as low as 3 ppm (estimated) for one hour daily for 130 days led to carcinoma of the nose and other tumor types in a latent period from 300 to 640 days.[10] Yet an epidemiologic study made in 1972 of three manufacturing plants in the USA showed no excess incidence of cancers of the respiratory tract in workers exposed up to 26 years at levels frequently well above 1 ppm.[11] Similarly, no overt cases of cancer of the lung occurred in a German plant where workers get an annual physical examination.[12]

This indicates two things to the TLV Committee:

1. Predictions of carcinogenesis from animals to man can be misleading in the absence of epidemiologic evidence.
2. Practical thresholds for chemical carcinogens in the workplace can be found that provide no risk to the industrially exposed workers, provided exposure is controlled below the stated limit.

TABLE I
Evidence For Thresholds in Carcinogenesis

Test Substance	Route	Species	Dose Levels Eliciting Tumors	Dose Levels Not Eliciting Tumors	Duration	References
Bis-Chloro methyl ether	Inhin	Rat	100 ppb	10 and 1 ppb	6 mo daily	Leong et al.[1]
1,4-Dioxane	Oral	Rat	1% H_2O	0.1 & 0.01	2 yrs	Torkelson et at.[2]
	Inhin	Rat	> 1000 ppm	111 ppm	2 yrs daily	ibid.[3]
Coal Tar	Topical	Mouse	6400; 640; 64 mg	< 0.64 mg	2x/wk, 64 wks	Bingham[4]
β-Naphthylamine	Inhin & Skin	Man	> 5% β in α-Form	< 0.5% β α-Form	22 yrs	Zapp[5]
Hexamethyl phosphoramide	Inhin	Rat	4000; 400 ppb	50 ppb	8 mo	Zapp[6]
Vinyl chloride	Inhin	Rat	2500; 200; 50 ppm	< 50; > 10 ppm '50-'59, 160 ppm average; 30-170 ppm	7 mo	Keplinger et al.[7] Kramer, Mutchler[8]
(+ Vinylidene chloride	Inhin	Man	> 200 ppm	range '60 < 50 ppm, decreasing to 10 ppm	25 yrs	Ott et al.[9]
Dimethyl sulfate	Inhin	Rat	10; 3 pm (Est'd)	Unknown	> 10 mo	Druckrey et al.[10]
	Inhin	Man	Unknown	< 2-5 ppm	15 yrs	Pell, DuPont[11]

Conflict

Examples of the misleading nature of extrapolating original data on tumorigenesis to man are accumulating almost weekly.

Ethylene dibromide, an industrial chemical, has been shown to elicit squamous cell carcinomas of the stomach in mice and rats at very high incidences (87% and 76%), yet nearly 50 years of industrial experience has revealed no evidence of adverse health effects[14] in the manufacture and handling of ethylene dibromide. This incidence can be multiplied to include trichloroethylene,[15] carbon tetrachlorlde,[16] chloroform,[17] Dioxane,[2] to name a few. Other instances will certainly appear.

Returning to Table I, hexamethyl phosphoramide, an experimental carcinogen of about the same high potency as bis-chloromethyl ether, appears to exhibit a threshold.[6] Whether longer exposures will ultimately reduce the present threshold of less than 400 ppb to above 50 ppb is for future investigation.

Critical

In summary of the information in Table I indicating threshold responses for a number of occupational carcinogens, note especially a number of critical features of these 10 instances that were cited.

First, the carcinogens are of widely differing chemical structures, producing many different tumor types, presumably by different mechanisms.

Note also, thresholds were evident for all three major routes of entry, and irrespective of whether the carcinogens were of very high or low potency.

And, most important of all, thresholds could be distinguished in three instances of human carcinogenesis: b-naphthylamine, dimethyl sulfate, and vinyl chloride.

No discussion of the subject should avoid the role of the cocarcinogen in response thresholds. Implicit in the foregoing statement is the simple reaction of carcinogen with a target site constituent. Cocarcinogens, promoters, accelerators cause a downward shift in the threshold.[17] (This has been shown by Eula Bingham for accelerators of skin tumors.) But they do not eliminate it, for the reason that these adjuvants likewise are governed by the same metabolic patterns and conditions that govern the action of the simple carcinogen.

Biology

Although it has been recognized for almost 100 years that the body has endogenous antagonists that counteract the toxicity of substances foreign to it, it is only within the last two or three years that evidence has been forthcoming on specific body antagonists to potentially carcinogenic molecules. Such evidence, of course, is basic to the threshold concept. For if a significant number of carcinogen molecules can be destroyed by normal metabolic processes before they can exert their action, or conjugated with endogenous metabolites, or immunochemically suppressed, a very strong case for thresholds for chemical carcinogens exists.

Such a case has been made by Dinman[19] and Stokinger.[20] In essence, the argument runs:

> A finite number of molecules are required for measurable functional activity (homeostasis). This was estimated to vary between $> 10^{14}$ to from 10^4 to 10^6. Further, the number of inhibitor molecules *per cell* to produce 13% to 27% inhibition is appreciably finite, varying from 4×10^4 to 2.5×10^5.

Stimulus

When these values are multiplied by the number of cells in the target organ(s), a significantly large threshold value emerges. When the process of enzyme induction, a common property of polycyclic aromatic hydrocarbons at least, is added to the basic metabolic activities, and the additional antigenic stimulus provided by the carcinogenic process through the mediation of the lymphocytes of the thymus and bone marrow, is further considered (adaptation), additional credence must be given to the threshold concept of carcinogenesis.

The salient fact must be grasped that the body metabolized potential carcinogenic, cocarcinogenic, et al, molecules in the same manner as any other foreign toxic molecule, at least in the initial stages.

Experiments

So much for the more or less theoretic aspects of carcinogenic thresholds. What is the experimental evidence to date?

Vinyl chloride

Watanabe *et al*,[21] Dow Chemical Co., have presented what must be accepted as indisputable biochemical evidence for a threshold for vinyl chloride carcinogenesis in rats. Here's how they did it. Using available hepatic nonprotein-SH an indicator of the body's capacity to neutralize vinyl free radicals, a distinct dose-reposne relation was found for six exposure levels from 2000, 1000, 250, 150, 50 and 10 ppm. Exposure at the four highest levels from 150 ppm to 2000 caused a progressive depression of the hepatic non-protein sulfhydryl content, whereas no depression was observed at 10 ppm. And exposure at 50 ppm resulted in inconsistent depression, indicating a threshold for vinyl chloride hemangiomas of the rat liver somewhere above 10 ppm and below 50 ppm.

Compensatory

The same authors have also reported[22] indications of a compensatory synthesis of hepatic nonprotein sulfhydryl groups following exposure to vinyl chloride, further raising the threshold level.

Now, it is known that the predominant nonprotein sulfhydryl compound in the liver is glutathione, which has a half-life of from 1.75 to 4 hours, accounting for the plateauing effect of the sulfhydryl at 150 ppm, even after further exposure to vinyl chloride.

These biochemical findings, indicating an experimental carcinogenic threshold, correlate very well with the reported incidence of hepatic hemangiomas in rats by Maltoni and Lefemine.[23] The incidence of tumors from repeated, daily 4-hour exposures at 6000 and 2500 ppm was 22%. From exposures at 500, 250 and 50 ppm, 12, 7 and 5%, respectively.

Pathway

The isolation and identification of three major urinary metabolites from rats dosed orally with 0.05 to 100 mg/kg ^{14}C-vinyl chloride further confirms the primary metabolic pathway of detoxication of this human carcinogen.[24] Two primary metabolites, accounting for about 70% of the total ^{14}C activity in the urine, have been identified as thio-diglycolic and N-acetyl-S-(2-hydroxyethyl)-cys-

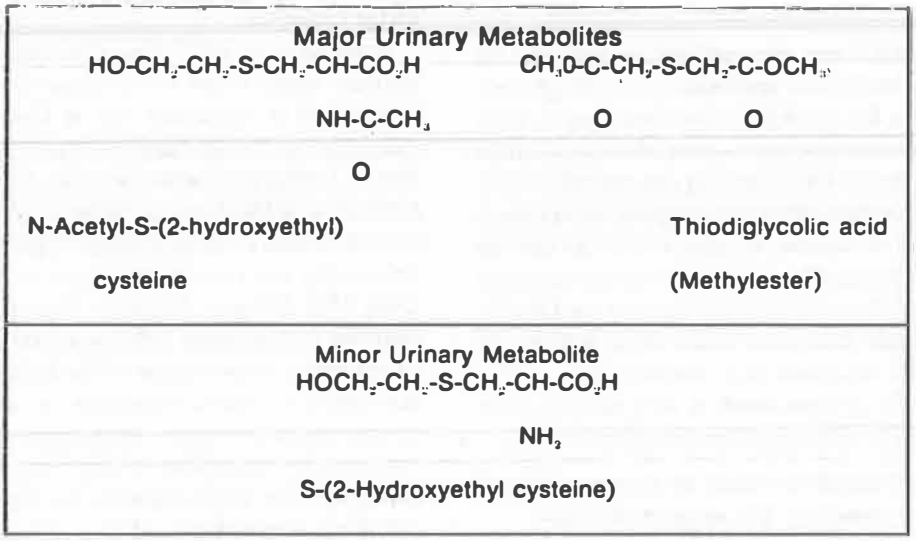

Figure 1 — Vinyl chloride metabolites isolated from rat livers after exposure to vinyl chloride (Dow Chemical Company, August 1975).[A] *Postulate:* free SHs of liver acts as scavengers of vinyl free radicals converting them to inactive metabolites. However when vinyl chloride exceeds available liver SH, vinyl free radicals can initiate cancerigenesis.

teine which suggests that the initial metabolic step in detoxication is glutathione (GSH) (Figure 1).

GSH has similarly been postulated to be involved in antagonized benzo(a)pyrene [B(a)P] carcinogenesis by Lu, Levin and Conney.[23]

Figure 2 shows the GSH complex formed from the epoxide, which upon oxygen ring facture and formation of free radical, is believed to be the true carcinogen; the GSH complex diverts this pathway, converting B(a)P into a non-carcinogenic GSH complex.

Threshold

Thus, a threshold of carcinogenic response can be anticipated from this natural body reserve of GSH alone. Other such antagonists have been discovered, with more to come.

That this is not merely a vain conjecture is shown by the reported inactivation of B(a)P carcinogenesis by cis-aconitic acid, a component of the Krebs cycle, again a natural body metabolite.[26]

Previously, the same investigator had shown that putrescine, produced by bacterial activity by decarboxylation of ornithine, a natural body constituent, can inhibit B(a)P carcinogenesis in mice.[27]

The report of vitamin A's capacity to reduce the appearance of dimethylbenz(a)anthracine papillomas in mouse skin[28] has spurred NCI to re-explore in greater depth the role of lipid-soluble vitamins as natural antagonists of carcinogensis generally.[29] (Reported in *Federation Proceedings* two months ago.)

Anticarcinogens

I don't have time to relate here the capacity of other natural antioxidants such as vitamin E, selenium, as well a synthetic antioxidants to inhibit various forms of carcinogenesis.

Suffice it to say:

> By the end of 1974, 16 other such anticarcinogenic subtances had been reported in the scientific literature.[30] Accordingly, we will conclude in the belief we have adduced sufficient evidence for the existence of both natural dietary sources of anticarcinogens to establish a sound basis for carcinogenesis, and sound

[A] Formal prepublication a part from McGowan, Watanabe, Gehring, November 7, 1975.

support for setting practical limits for chemical carcinogens in the workplace.

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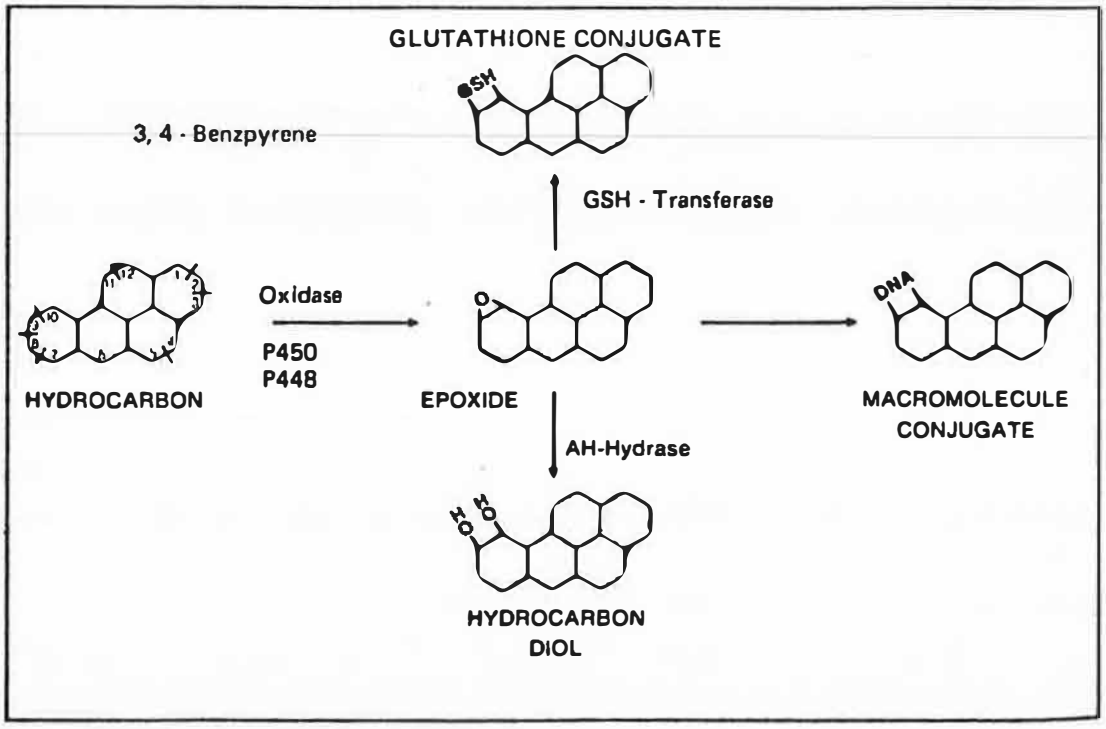

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The problem of thresholds for chemical carcinogens — its importance in industrial hygiene, especially in the field of permissible limits for occupational exposure*

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First of all, I want to express my deep gratitude to the President, Managing Director and Members of the Board of Directors of the American Industrial Hygiene Association for selecting me to receive the 1980 Yant Award. This constitutes for me a very great honor and creates in my heart a profound emotion, because when I entered in the career of toxicologist for teaching and making research, I knew and admired Dr. William P. Yant who was for me an example in these two directions.

The whole world owes him gratitude for his pioneering achievements in the field of industrial hygiene and occupational health.

I devote my lecture to his memory.

The subject I selected is, at the same time, very actual, very controversial and difficult.

It is: "*The problem of thresholds for chemical carcinogens.*" I will treat it in a broad overview, but, taking into account the fact that this Conference is devoted to industrial hygiene, I have the duty to consider the importance of the problem in this special field of toxicology, notably in regard to the establishment of permissible limits for occupational exposure.

The plan of my talk will be the following:

1. Introduction and brief historical background.
2. Arguments in support of the theory that there are no thresholds for carcinogens.
3. Arguments against the theory that there are absolutely no thresholds for carcinogens.
4. Discussion and general considerations — importance of the problem in the field of industrial hygiene and for the protection of the industrial and agricultural workers.

Introduction and brief historical background

The golden rule in toxicological evaluation of environmental pollutants is to establish dose-effect (exposure-effect or dose-response) relationships, in order to set *toxicity thresholds* and, consequently, *permissible limits* of exposure. This approach, which constitutes a fundamental principle of prevention, has been widely applied, particularly to food additives, pesticide residues, food and water contaminants and air pollutants in working areas as well as in urban and industrial environments.

In this regard, it is worthwhile mentioning the setting of acceptable daily intakes (ADIs) for food additives and pesticide residues and of maximum allowable concentrations (MACs) or threshold limit values (TLVs) for airborne substances in occupational environments. These recommended values constitute *guides*, notably for those who have the task of establishing analytical methods for the control of environmental pollutants, which must remain within the limits of such permissible concentrations.

However, in the case of carcinogens, a current view is that it is impossible to establish safe levels, because there are no thresholds for their action. With regard to food additives, for example, at the UICC symposium held in Rome in 1956, it was stated that "any substances proved to be carcinogenic, at any dose, in any species, and by any route," should not be authorized for use in food.[1]

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* Yant Memorial Lecture presented at the American Industrial Hygiene Conference, May 18-23, 1980, Houston, Texas. Published in *Am. Ind. Hyg. Assoc. J.* 41:685-692 (1980). Reprinted by permission of the American Industrial Hygiene Association.

Later, a Joint FAO/WHO Expert Committee on Food Additives[2] supported the view that any attempt to establish a safe dose for carcinogenic substances in the human diet would, at present, be unwise. This philosophy is reflected in the Delaney amendment which is applied in the USA, at least for intentional food additives.

As another example, with regard to airborne pollutants in occupational areas, the Scientific Committee on permissible limits for toxic substances in industry, attached to the International Permanent Commission on Occupational Health, recommended at its second international symposium, held in Paris, April 1963, that carcinogenic substances be excluded from the working environment.

More recently, the report of a group of WHO temporary advisers on occupational cancer, Geneva, October, 1971, stated:

> *"Since a 'no-effect level' cannot at present be determined experimentally for carcinogenic substances, no tolerance levels such as MAC values or TLV can be rationally set at this time."*

However, in the same report appeared the following:

> *"As or where sensitive and reproducible quantitative measures become available, it will be possible to define levels of carcinogens present naturally and irremediably in our environment. From such knowledge, it may then be possible to establish 'socially acceptable levels of risk' for carcinogens in workplaces and in the general environment."*

This concept of *socially acceptable risks* has already been put into action in the case of ionizing radiations.

Arguments in support of the theory that there are no thresholds for carcinogens

The main arguments can be stated briefly:

1. Cancer may result from a mutation in a *somatic cell.*
2. The cancer cell is self-replicating; this may result from a change *in only one molecule* of DNA.
3. The results of quantitative studies conducted on laboratory animals with carcinogens, such as paradimethylaminoazobenzene, paradimethylaminostilbene and dialkylnitrosamines, were interpreted, no-

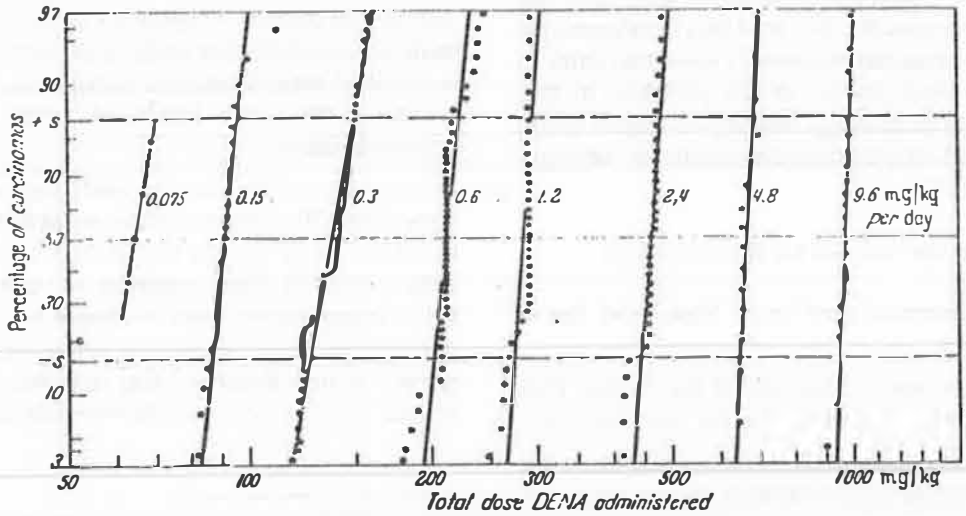

Figure 1 — Dose-response relationships for the carcinogenic action of diethylnitrosamine (DENA) in BD II rats. 8 dosage groups, ranging from 0.075 to 9.6 mg per kg body weight, given in the daily drinking water. Each dot corresponds to an individual rat with carcinomas. Normal distribution over the total dose administered = sum of all daily doses. Abscissa 5-fold elongated.

TABLE I
Induction of Liver Cancer in Rats by Paradimethylaminoazobenzene [PDAB] in the Daily Dose Dependency of Induction Time and Carcinogenic Total Dose Upon Daily Dosage[3]

d Daily Dosage mg/rat	t Induction Time days	D Total Dose mg/rat
30	34	1.020
20	52	1.040
10	95	950
5	190	950
3	350	1.050
1	700	700

tably by Druckrey and his co-workers, as indications that the primary carcinogenic effects of any individual dose, even the smallest, persist and remain irreversible during the entire lifespan of the animals, resulting finally in the manifestation of a tumor. Accordingly, the carcinogenic activity (A) may be considered to be a function (f) of the sum of all consecutive doses (d), even if they are inactivated metabolically in the body and/or rapidly excreted.

$$A = f(d)$$

This corresponds to a summation of totally irreversible effects and can be expressed by the equation:

$$Dt = k$$

where: D = dose, t = time, and k = constant, and even by the equation:

$$Dt^n + k$$

where *n* is greater than 1 and indicates the potency of the carcinogen. The effect increases proportionately with the time over which the partial doses are distributed. (See Table I and Figure 1).

This extreme cumulation of effects prohibits, according to Druckrey,[3,4] the possible establishment of a safe dose for carcinogens, particularly for repeated human exposures, during an entire lifespan, even to minute doses (for example, exposure to chemicals incorporated, whether intentionally or not, into food, or exposure to air pollutants).

4. Evidence from experiments on tumor initiation and promotion in the skin indicates that a lasting change is induced by one tumor-initiating event. The classical investigations are those of Berenblum and Shubik[5-8] with dimethylbenzanthracene and croton oil.
5. Cancer can occur in response to chemicals, even in single doses, long after their disappearance from the body. In this regard, the results obtained in transplacental carcinogenesis with nitrosamines and nitrosamides are demonstrative.

On the basis of all these arguments, it has been widely accepted that those events essential to carcinogenesis are irreversible.

Arguments against the theory that there are absolutely no thresholds for carcinogens

In recent years, the following arguments have been raised against the concept that the effects of carcinogens are *totally* irreversible:

1. With regard to the time necessary for tumor induction, it has been stressed that every living organism has a limited lifespan and that, in this sense, there is, for each individual, a real threshold.
2. Even if one postulates that a single cell which has been transformed from a normal to a cancerous state can survive and proliferate, a carcinogen, in order to act on the sensitive site of the cell, must reach it: the probability of this happening is lowered with tiny doses. In this regard, one should consider the intervention of a number of *modifying factors*, including the existence, for the majority of chemical carcinogens, of metabolic transformations which eventually lead either to activation (→ proximate carcinogen → ultimate carcinogen) or to detoxication, with intrications between the two types of processes.
3. Even if the molecular target, for example DNA, is reached, and the initial causative alteration occurs, one must consider, in

the light of recent findings in molecular biology, the possibility of *repair* of such an alteration. In fact, it is now known that there are cellular mechanisms such as excision and post-replication for the repair of DNA. Most data on the repair of DNA have evolved from investigations in which microbial systems were treated with ionizing radiations or certain chemical carcinogens, such as alkylating agents; however, there are reasons to believe that similar processes occur in mammalian cells.

In biological systems with an efficient DNA repair mechanism, the implication that there is threshold exposure for point mutations and deletions is very strong. However, it has not yet been established whether or not such mechanisms are in fact present in various types of mammalian cells or if these mechanisms function *in vivo*. If cancer results from such mutations in a somatic cell, the above conclusion regarding a threshold may apply to carcinogenesis.

In man, *xeroderma pigmentosum*, a recessive autosomal disease, characterized by an excessive sensitivity to ultraviolet radiations from sunlight which leads to a high frequency of skin cancer, constitutes a spectacular example of a human cancer which is induced by an exogenous agent and in which the absence of enzymes involved in DNA repair by excision of thymine dimers appears to be the causal factor. In normal subjects, the possiblity of repairing DNA lesions is the limiting factor in the production of skin cancer due to ultra-violet solar radiations. This constitutes a practical situation in which, fortunately, there is obviously a threshold for a physical carcinogenic agent.

4. According to Latarjet,[9] one of the main reasoning made to support the theory of no thresholds for carcinogens is false. This reasoning is, as already stated, the following:

> *"Transformation of a normal cell into a malignant cell is by definition a mutation. What is right for mutagenicity is also right for carcinogenicity. In particular, since there is no threshold for radiomutation, there is also no threshold for carcinogenicity of radiation and, by extension, of chemicals."*

In fact, this reasoning entails a confusion between malignant cellular transformation, a mutation which is the first stage of malignancy, and the clonal development of the transformed cell which leads to the emergence of a cancer.

At this point, Latarjet stressed that the presence of the transformed cell is not a cancer, happily, since all of us probably carry large number of cancerous cells and, grossly, only one of five of us will develop cancer.

Cancer occurs only if a transformed cell finds conditions favorable for its development and, in particular, can overcome certain antagonistic reactions of the organism. According to Latarjet, it is at this point that the phenomena which define a threshold dose can intervene.

5. A number of chemically induced tumors possess antigenic properties and are capable of inducing immunological, tumor-associated rejection reactions.[10] Immunological surveillance mechanisms that protect the host against neoplastic cells have been postulated,[11] and this idea is supported by studies on host immunity to autochthonous tumors in man and animals,[12] in which it was found that immuno-deficiency diseases lead to an increased risk of neoplastic diseases. At this point, it must be stressed that many carcinogens are at the same time immunosuppressors. Clearly, further basic studies are needed before a correlation between chemical carcinogenesis and host immunity in man can be established.

6. Epidemiological studies suggest the existence of a threshold in the case of certain exogenous carcinogenic factors; cigarette smoking, for example, is known to cause human lung cancer in a dose-related fashion. The observation that ex-smokers who stopped smoking have a lower risk of

developing lung cancer than those who have continued to smoke suggests that the effects of cigarette smoking are partly reversible, although according to Doll,[13] this is a misinterpretation.

In the same field of epidemiological studies, in the case of radiations, observations point to the existence of practical thresholds. For example, according to Latarjet,[14] the amount of cosmic radiations in the high plateaux of the Andes mountains is about three times that measured in the plain. Nevertheless, statistics have disclosed no difference in frequency of cancer between the populations living in the two regions. It must, however, be noted that the number of people exposed may be too low to confirm whether or not the statistical results are truly significant.

7. Certain experimental findings tend to indicate existence of thresholds for carcinogens.

   a) Results of Roe and his colleagues[15] concerning the initiation and promotion of tumors, in which application of a promoting agent (a phorbol ester) to the skin of mice after initial treatment with DMBA was delayed for longer and longer intervals, suggest that the effect of an initiating agent may disappear with time.

   b) In the USSR, Yanysheva *et al*[16,17] tested increasing doses of several carcinogenic polycyclic aromatic hydrocarbons, notably benzo(a)pyrene by intratracheal instillation, for their ability to induce lung cancer in rats. Thresholds were determined in a number of their experiments. Such results and others, which, in our opinion, should be examined critically, have led the Soviet authorities to adopt the following permissible limits for benzo(a)pyrene: 0.15 $\mu g/m^3$ in the atmosphere of working areas and 0.001 $\mu g/m^3$ in the general environment.

8. The action of the majority of carcinogenic compounds is associated with preliminary changes, such as hyperplasia and cirrhosis, although their role is not always clear. Some chemicals, on the other hand, give rise to neoplasms *only* after inducing particular pathological effects; these types of carcinogens have not been shown to undergo chemical interaction with macromolecules such as DNA and RNA directly (alkylating agents) or after metabolic activation. We have personally proposed that they be designated 'secondary carcinogens.'

   a) Examples are those of chemicals such as the food emulsifier MYRJ 45 (polyoxyethylenemonostearate) and CYASORB (2-hydroxy-4-octoxy-benzophenone) used as an adjuvant in certain food-packaging materials, which, when fed to rats in relatively high doses, induce cancers of the urinary bladder; these are thought to be caused, however, by the bladder calculi that are induced by high doses of the chemicals, rather than by their direct action.

   The same is true for 4-ethylsulfonylnaphthalene-1-sulfonamide (ENS) which, after prolonged dietary administration, produces bladder cancer in the mouse.[18,19]

   The formation of bladder calculi might also explain the production of bladder cancer in certain animal species given relatively high doses of chemicals, such as cyclamates, saccharin, xylitol, etc.

   It might thus be possible to establish a no-effect level for chemicals that produce tumors in this way.

   b) A second example is that of the class of carcinogens which act by producing a hormonal imbalance, e.g., oestrogens and goitrogens, such as thiourea, aminotriazol (amitrol) and related compounds. Carcinogens of this type manifest their activity in two stages: 1) induction of hyperplasia in the hormone-dependent organ or tissue (thyroid, mammary gland, uterus, etc.), and 2) induction of malignant changes in the thus

modified organ. It is obvious that a threshold must exist for the first stage.

In the case of hormones, an evaluation of their carcinogenic effects must take into account their endogenous occurrence and their participation in the regulation of physiological functions. If the intake of hormone does not increase their levels beyond the physiological range, then this probably represents a non-toxic effect level. It is evident that, in the experimentation aimed at toxicological evaluation, the endocrine status of the animal species tested should be as similar as possible to that of man.

c) A third example is that of some naturally occurring trace elements, such as selenium, which, in low doses, is an essential element for cattle, sheep and poultry and, most probably, for man. On the other hand, at least in one experiment, selenium can induce liver cancer in rats that have chronically been fed a diet containing 5-10 ppm. It is obvious that there must be a threshold for its carcinogenic action. The same can be said for arsenic which is present at very low levels in every living organism and, consequently, in natural foods.

d) Most probably, the carcinogenic potential of many other chemicals is the result not of a genotoxic mechanism, but of a two-step process and for which, consequently, a threshold should be envisaged for the first step of action. We have especially in mind, among many others, compounds which have been shown to induce hepatomas *in mice,* such as DDT and other aromatic chlorinated chemicals used as pesticides and also phenobarbital. There is a suspicion that the induction of a microsomal enzymatic systems may play a role in the carcinogenic potential of those products which are often considered to act like promotors.

There is a strong need for research to improve our knowledge in this direction.

Discussion and general considerations — importance of the problem in the field of industrial hygiene and for the protections of the industrial and agricultural workers

Almost all of the arguments described briefly above were examined critically by a WHO Scientific Group at a meeting held in Geneva for assessing the carcinogenicity and mutagenicity of chemicals.[20] The main conclusion, expressed *in very careful terms,* was "that possible existence of a threshold in the effects of both chemical carcinogens and mutagens should be envisaged."

The scientific group stated, in addition, that there are nevertheless great difficulties in determining a threshold *for a population,* and mathematically derived conclusions which show that it is impossible to demonstrate non-toxic-effect levels in experimental investigations of *very low doses* cannot be ignored. For this reason, one of the recommendations of the WHO Scientific Group was the following:

> *"In those situations where carcinogens are unavoidable or where the banning of a substance would impose a hardship or an unrealistic economic burden, the toxicologist must assess the risks associated with different levels of exposure."*

In this regard, approaches, such as those of Mantel and Brian,[21] Albert and Altschuler,[22] Friedman,[23] and Brown,[24] have been proposed for use in assessing human health hazards from chemical carcinogens on the basis of data from animals submitted to several levels of exposure. In such calculations, different levels of statistical assurance are used or different slopes of the dose-response curve are assumed.

This type of mathematical exercise seems to us to be too theoretical. There is generally a large difference between the lower doses used in investigations on laboratory animals and the levels to which humans may be exposed: the latter are generally very much lower. Even if one assumes that the carcinogen behaves in the same way if animals and in man, an assumption which, on the basis of all known facts, is unlikely *to be always true,* there is no proof that the organism handles such widely differing levels of the chemical in the same way. On the contrary, the diverse processes involved in the fate of the chemical, i.e., activation and/or detoxication, rate of elimination and repair

mechanisms after reaction with target sites, may be quite different with very low levels.

In addition to the relationship between the dose and the rate of tumor induction, one must take into account the time of induction, which may greatly exceed the lifespan of the species under consideration.

Thus, the rigid application of mathematical concepts to biological parameters, which are *essentially variable,* should, in our view, be subject to very strong limitations until our knowledge about the mechanisms of malignant proliferation are at a more advanced stage.

As a member of the above-mentioned WHO Scientific Group, we remain in agreement with the conclusions of its report; however, we feel that two points must be emphasized:

1. For the majority of carcinogenic chemicals, there are at present, no adequate quantitative data for the establishment of no effect levels; it is therefore necessary to await these data before any positive recommendation can be made. One must remember that, in comparable test systems, chemical carcinogens can vary in potency by a factor of as much as 10^7.
2. In our opinion, tumor induction should be considered as a manifestation of toxicity that must *be studied as an individual problem in each instance* (not forgetting the impurities which might be present in the technical product, such as tetrachloroparabenzodioxine in the herbicide 2,4,5,T). One must not forget that a carcinogen as such may not always have the same mechanism of action. In some cases, notably that of 'secondary carcinogens,' the available data may reasonably permit the determination of tolerance levels, whereas in others, especially those carcinogens called genotoxic, which react on nucleic macromolecules, such an approach will not be possible on a scientific basis, at least at present.

   Among the parameters to be taken into account in making a toxicological evaluation, in addition to scientific facts, are practical considerations such as the irreduceable environmental background level and the benefit of use for the community, as adequately evaluated by, as much as possible, objective criteria.

The concept that there are no thresholds for carcinogens, along with the idea of 'zero' tolerance, is thus not always applicable, even by those who still strongly defend it at least in the case of genotoxic carcinogens.

The concept is applicable in the case of chemicals that are *intentionally* added to the environment, for example, food additives and cosmetic ingredients. For them, the best mean of prevention is not to grant authorization for their use.

On the contrary, the concept is not applicable to chemicals that are unavoidably present in the general environment, such as polycyclic aromatic hydrocarbons. The only way of dealing with the situation is to make every effort *to reduce their levels to a feasible minimum.* With compounds such as aflatoxins, which may be active in microgram doses, the achievement of this objective may raise a number of difficulties.

There are cases in which the use of a chemical shown to be carcinogenic under certain conditions could be prohibited, but in which such an action would result in unfavorable social conditions or have other adverse consequences for the society. For example, when the use of drugs, for which there is no substitute, is recognized as essential for combatting certain diseases, *'calculated risks'* may reasonably be taken.

In the case of carcinogenic industrial chemicals to which workers are likely to be exposed, those for which there are viable substitutes should be eliminated from the working environment. To this aim, the ideal measure of prevention is to stop their manufacture. About 25 years ago, with our dear friend and colleague, the late Michel Williams, we recommended this type of action to the case of β-naphthylamine which, in our view, could be replaced by Tobias acid in the manufacture of several dyes and, as another example, in the case of paradimethylaminoazobenzene which could be replaced by its isolog paradiethylaminoazobenzene which did not manifest any carcinogenic activity in laboratory animals.

But, very often, the problems are more delicate, because, in practice, prohibition of use of a given chemical poses great practical difficulties. Con-

sequently, various proposed lists of permissible limits for occupational exposure give values, *Indeed as low as possible,* for chemicals which have been shown to be carcinogenic either in laboratory animals (so called 'potential carcinogens'), either in humans (so called 'human carcinogens') or even in both animals and humans.

It would be tedious to elaborate on this point and we wish to stress that the complexity of the situations is reflected by the differences in recommendation made by various groups. For example, in the West German list of MAC values, no values are given for substances which, on the basis of pertinent experience, are recognized to be capable of inducing cancer in man. But, on the other hand, in the comments, it is stressed that if, for technical reasons, utilization of such substances is unavoidable, appropriate protecting and supervisory measures are indispensable so as to eliminate potential hazards *wherever possible.* Finally, the philosophy of this approach is not very different from that adopted by, at first look, more flexible groups.

Most of the present increasing concerns over occupationally related cancer arose from two recent incidents in which it was discovered that workers have developed cancer after long term exposure to certain chemicals. In one case, vinyl chloride monomer caused a rare liver cancer in exposed workers; in another case, the chemical bis-chloromethylether was found to cause lung cancer. During the long period in which these two chemicals were produced, neither has been considered carcinogenic. Substances such as asbestos, β-naphthylamine, benzidine and 2,xenylamine, as well as some mixtures or industrial processes, were known to be cancer hazards on the job, but the number of occupational carcinogens was thought to be limited.

Today, over 20 substances or mixtures inducing occupational cancer hazards are subject to workplace control.

At a period where an increasing number of chemicals are manufactured, it is the duty of the Society to protect the populations and especially the workers against carcinogenic chemicals.

As we stressed in previous articles,[25] it is not possible to prevent toxicity risks, unless they are recognized. Consequently, the major rule of prevention of carcinogenic hazards is to disclose them.

For this purpose, in the framework of general toxicological evaluation of chemicals, it is necessary to apply *adequate methodological approaches.* Without elaborating, in our view, there are three stages for achieving this aim:

A. *Collection of facts,* either in laboratory animals or certain *in vitro* systems by experimental investigation, and either in humans by clinical observations or, overall, by epidemiological studies.

B. *Interpretation of these findings.*

C. *Decisions to be taken.*

The *first stage* should represent a fruitful collaboration between experimental toxicologists, occupational physicians and epidemiologists.

We share the opinion of David Rall[26] and R. Kroes[27] on the predictive value of laboratory animal studies in estimating carcinogenic risks for man.

Diethylstilbestrol, vinyl chloride and bis-chloromethylether are recent demonstrative examples in this regard. But, for *quantitative evaluation* and especially for the *risk assessment* of man's exposure, one must keep in mind the importance of a number of factors and considerations. For this assessment, it is customary, as already stated, to extrapolate from *high doses* at which tumor induction is observed in animals, to low doses in the human environment and, assuming that no threshold exists, to extrapolate even to zero. This hypothesis implies that there will be a certain tumor incidence in the exposed population, *no matter how low the exposure is.* Consequently, cancer incidence at very low doses will be considered to be a linear function of high doses. However, species differences in the metabolic activation and inactivation processes and differences in biological responses as compared to low doses complicate the establishment of the dose effect relationship. Without elaborating, we want to stress that, at present, the quantitative phase of risk assessment in chemical carcinogenesis is, very often, highly speculative and, consequently, uncertain. For this reason, we are reluctant to admit the very rigid approach of OSHA for the assessment of occupational carcinogenic risk.[28] In this regard,

the case of benzene would be worthwhile to discuss.

In our opinion, there is a need for a *value judgment* in the interpretation of the experimental and epidemiological findings, the *second stage* of toxicological evaluation mentioned above.

In the *third stage* (decisions to be taken), *except if* the chemical under consideration is a potent genotoxic carcinogen and has valuable substitutes and, consequently, has to be banned, a reasonable attitude seems to us to take into account the *benefit for the collectivity at large* of the industrial use of the product and to apply the concept of *socially acceptable* risk in establishing permissible limits of occupational exposure *at the feasible minimum*. This pragmatic attitude, in a context of prudence for ensuring the highest safety in use, is indeed comparable to that adopted for ionizing radiations. All of you know that this attitude was adopted for many years by the TLV Committee of the American Conference of Governmental Industrial Hygienists, such as arsenic, trioxide, asbestos, bis-chloromethylether, chromates and vinyl chloride.

Conclusion

At the end of this lecture on a very controversial problem, we hope to have made understandable to all of you the opinion of a man who devoted his scientific career to toxicological research and especially to the study of insidious long term effects including carcinogenic ones.

In the beginning, we were very rigid and even emotional. Along the years, we became somewhat more flexible. This does not mean that we are ready to accept the use of chemicals the exposure to which would induce cancer in workers. We still fight strongly against those who have a tendency to minimize the carcinogenic hazards.

But we are open to an intelligent and reasonable interpretation of the scientific facts, interpretation which, without endangering the health of the workers, would not suppress real benefits for society.

Before thanking you all for your attention and your patience, we want to stress that, maybe more than in other fields of science, specialists in toxicology are men who have selected a certain kind of ignorance, or more rightly, have some gaps in their ignorance.

This means that very large avenues of research are open in industrial hygiene and this constitutes a stimulating promise for improvement in the prevention of occupational diseases and, especially, occupational cancer.

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Threshold limit values*

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PART I

The TLVs stand for Threshold Limit Values which are limits of permissible exposure to potentially hazardous materials and designed to safeguard the health and comfort of industrial workers. The story of the origin of the TLV Committee and the evolution of the actual TLVs from their early beginnings as unofficial, recommended values to their adoption by OSHA as official, legal standards, forms Part I of this two part series. Part II tells of the way the TLV Committee operates, what bases it uses for setting limits, its precedent-setting means of protection for even the hypersusceptible worker, and dealing with occupational carcinogens in a manner that industry can live with.

Birth of the TLV committee

It all began a few years before World War II when Bill Fredrick was Director of the Bureau of Industrial Hygiene, Department of Health of Detroit, instigated the establishment of a subcommittee of American Conference of Governmental Industrial Hygienists (ACGIH) for the development of air contamination working limits, at its 3rd annual meeting in 1940.[1] His proposal was born of a desire to bring some order and uniformity out of the then chaotic situation existing among the various state and local industrial hygiene units with their individual and often conflicting air standards, for the protection of workers. Fredrick's view was shared by a small group of well-known and leading industrial hygienists such as Manfred Bowditch, Phil Drinker, Lawrence T. Fairhall, and Alan Dooley, who formed an ACGIH subcommittee on Threshold Limits with Bill Fredrick, as chairman at the 4th annual meeting of the ACGIH in 1941. The charge to the committee was "to gather information relating to limits and to report this information to the 5th annual meeting in 1942."[1]

The founding principles

The information the subcommittee presented at the 5th meeting was a survey of the industrial air limits used by the 26 state and local (city and county) health units on more than 100 gases and vapors, 27 toxic dusts, fumes and mists, 10 mineral dusts, and 4 radiation standards, with the following recommendation to the ACGIH by Chairman Fredrick.

> *"I feel that our subcommittee should assume an active position in the establishment of working limits and should issue an annual list to be revised each year to conform with newer information and values suggested by such bodies as the U.S. Public Health Service and the American Standards Association."*[1]

Although no subcommittee reports were given at the 6th and 7th annual ACGIH meeting because of World War II disruptions, in 1944 the TLV Committee became and independent standing committee retaining the same membership. Manfred Bowditch, then director of the Department of Industrial Hygiene for the state of Massachusetts, in discussing the problem of setting TLVs, said among other things: "The question of whether the method of the American Standards Association — is as applicable to this type of standardization as it is to the mechanical and other forms of standardization,"[2] thus provided a sound, rational basis for entry of the TLV Committee in the field of setting industrial air limits.

He might have added another reason. The ASA Z-37 Committee charged with setting air limits, was ponderous and slow to arrive at a unanimous decision. With a committee of more than 30, each of whom had to review and comment on each draft, and then each and all to approve of the final draft in writing, required and inordinate and unacceptable length of time to make changes.

No meeting was held until 1946 due to the war. It was then that Chairman Fredrick sent to the Tech-

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nical Committee of ACGIH a list of some 150 single value TLVs for use in 1946, despite previous proposals for a dual listing, one physiologic, the other, optimal. And thus it stands today, almost 40 years later!

So, the founding fathers, like the founding fathers of the 13 Colonies, planned well, for their original plans of action are those still followed. But the TLV Committee has added one essential ingredient more, the experienced judgment from long years of on-the-job observation in the fields of industrial hygiene and toxicology. (Fredrick, Bowditch, Drinker and Dooley) and in industrial analytic chemistry and toxicology (Fairhall).

Early TLVs

The first meeting of the TLV Committee of the ACGIH since World War II, held in 1946, brought forth the first list of threshold limits. It was a typed list of 158 values captioned MACs, mimeographed and available to ACGIH members, and comprised values for 114 gases and vapors, 26 toxic dusts, fumes and mists, 14 mineral dusts, and 4 radiation limits. No explanation was given of the meaning of the values or their sources until 1953, although Cook had published a documentation of these values in 1945.[3] The first published list appeared in 1950 in the *Archives of Industrial Health,* again without any explanatory preface.

When the prefacing statements to the TLVs appeared regularly after 1953, they were defined as "maximum *average* atmospheric concentrations — for an 8-hour day —." This definition of the TLVs is important to note, because it differed from the general understanding of industrial hygienists of the original term, MACs or maximum allowable concentrations, which are essentially ceiling values below which all values must fluctuate. The definition still used for the MAKs of USSR

This MAC definition was so firmly entrenched in the thinking of U.S. industrial hygienists that it persisted for a decade as seen in publications appearing as late as 1956![4] So great was the confusion, that this writer felt compelled to publish an explanatory statement on the definition and interpretation of the threshold limits and MACs.[5] Gradually the definition appearing annually in the preface to the TLVs became firmly established and is now accepted generally.

Documentation of the TLVs

A major step forward in the progress of authenticating the TLVs was the decision to document each value with references to the literature and to unpublished surveys and personal observations of Committee members. The decision was made in 1955 under the chairmanship of Allan L. Coleman, then director of industrial hygiene for the State of Connecticut. This decision was prompted by several factors.

1. A change in the philosophy of setting limits.[6]
2. The desire to avoid any semblance of arbitrariness or capriciousness by Committee members in setting TLVs.
3. The increased significance attached to hygiene standards for the air of workplaces by the U.S. Department of Labor through enforcement of the Walsh-Healey Act.
4. Increasing number of basic toxicology and epidemiologic studies, useful for setting TLVs.
5. Constant prodding by such far-sighted men as Henry Smyth,[7] and Clark Cooper, who later became a member of the TLV Committee and did his share of documentation preparation.

This was indeed how the first TLV documents were prepared; the 300 or so TLVs were farmed out in numbers and subject according to each of the 6 members intimate knowledge and familiarity with the substance. After almost 7 years of unremitting effort, the first edition of the Documentation of the TLVs for chemical substances appeared in 1962, 112 pp. 121 substances.

This published documentation was a landmark in industrial hygiene progress, for up to this time no other nation had such a document.[A] Through its subsequent 3 editions, the last, in 1980, and several revised and updated supplements, it has served to provide an example of good standard-setting practice for other nations.[A]

Provisions in the documentation

"No one using the TLVs should be without it"

The TLV document furnishes several pieces of information for the proper understanding of the reasons for selecting the particular TLV, beyond

that of providing references to the literature. The Document provides first of all a summary of the pertinent data from animal studies or from human experience, points out whether the TLV has its basis because of toxicity, or irritation (providing comfort) or just nuisances (e.g., cement, carbon dust). Also included is whether effects from exposure above the TLV are acute, such as from formaldehyde or sulfur dioxide; or whether effects take a chronic form, as from benzene; or the substances can do both (beryllium, nitrogen dioxide, ozone). And, if data are available, the Document tells how substances are metabolized, their levels of distribution and excretion for safety or injury, with methods of detection (Biologic TLs) such as are found in the Documents for fluoride and lead. Finally, the Document points out the chief site of action of the substance, the system or organ, lung, skin, eye, kidney, liver, etc. which can be expected to be injured from exposures above the TLV.

The TLVs become legal standards

By the passage of the Steiger bill in the last waning days of 1970, NIOSH, the National Institute of Occupational Safety and Health in the Department of Health and Welfare, and OSHA, the Occupational Safety and Health Administration in the Department of Labor were created, NIOSH to be the recommending body, OSHA, the regulatory, enforcing agency. As the chief aim of the bill was to protect the health and safety of workers, and one of the ways to enforce air standards, something the understaffed state and local agencies could only do in part, OSHA turned to the TLVs. The TLVs were adopted as of the 1968 list to become the official, legal standards of the 50 States.(8) To give semblance of consensus standards, the 22 air standards of the American Standards Association were incorporated in the overall list of 440 substances.[B] Unfortunately, as adopted in accordance with the working of the Act, the standard values can be changed only by an act of Congress, which to date has not been done. So, there they stand as values of a bygone day; some 160 revisions both upward and downward in the TLV list of 1980 have been made since 1968.

In an effort to remedy this incongruous situation, NIOSH developed Criteria Documents for a Recommended Standard for some 70 substances, to be acted upon by OSHA to update its 1968-adopted TLV list. The first documents on asbestos and lead appeared in 1972 and 1973, chiefly the work of the NIOSH staff and with reviews by experts in the respective areas.

Because publication by this procedure proved too time-consuming for the urgency of the situation, a procedure of farming out the subsequent documents under contract proved more expeditious (and much more costly $50,000 to $100,000 per document). Unfortunately for the final result and the consternation of industry, the NIOSH-recommended limit proved unrealistically low in many cases for industry to conform to. This was the result of 3 sets of conditions.[C]

1. Document development by individuals unfamiliar with setting industrial air limits and related industrial operations.
2. The review procedure, although including individuals with recognized expertise in the respective fields, was altogether too hurried; a week to 10 days was all that was allotted to review a document often of 100 pages and several hundred references and review stacks of often illegible xeroxed reprints resulting in too superficial reviews.
3. All too often, comments and remonstrances of the reviewers went unheeded.

As a result of all this great effort extending over a period of 7 years, OSHA as of this writing, has not acted on any of NIOSH's recommendations, and has developed on its own, only standards for a

[A] Oddly, little has been done in this direction elsewhere until the West German Republic began documentating their MAKs in 1970. Czechoslovakia published a very abbreviated semblance of a documentation of 93 of their MAKs in 1969. The U.S.S.R., the only other industrialized nation with numbers of MAKs comparable to those of the U.S.A. has refused to assemble the basic documentaries for the selection of their often unrealistically low MAKs despite repeated urgings for more than a decade by this writer since his visit to the Dept. of Health of the U.S.S.R. in 1963.

[B] Oddly, the U.S.A. was, up to this time, the only industrialized nation in the world not to have official, government-enforceable industrial air standards.

[C] The writer served as reviewer in toxicology of many of the NIOSH documents.

pathetic few, asbestos, beryllium, lead and 14 industrial carcinogens. Thus ends the story of 40 years evolution of the TLVs.

PART II

Part I of this series gave an historical account of the TLV Committee from its conception before World War II, to its inception in 1944, and to the adoption of the TLVs by OSHA as official, legal standards of the United States. Part II tells how the TLV Committee operates in the face of ever changing number and differing types of industrial products, all within an atmosphere of greater governmental concern for the health and safety of industrial workers.

We'll begin by asking a few questions. How does the relatively small Committee cope with the hundreds of newly introduced industrial chemicals which annually appear in the market? And, how can these keep pace with the increasingly strict testing requirements of government agencies attempting to insure complete protection of worker health and well-being from undue risks of cancer and from birth defects of children yet unborn of working mothers? All this apart from not overlooking other insidious effects resulting after a working lifetime with a variety of chemicals.

To answer the first question: there aren't "100s of new chemicals reaching the market annually."[D] This is a myth perpetrated by health administrators to justify their existence and support their budgets. Rather, because of the extended time required for product testing, less than a few dozen reach marketability annually. Many 100s may have been synthesized, scores even reached pilot stage, but few survive all the hurdles.

To answer how the Committee manages to develop TLVs for newly marketed industrial products today on which extensive toxicologic investigations are required, any delay comes about prior to the launching of the product by the company. As it is the large chemical companies that generate the bulk of new products and are financially better able to undertake the required extensive testing program, they routinely set in motion, early in the product development stage, the acute and chronic toxicity tests including tests on reproduction and cancer potential. The results of these investigations are either published in the open literature, readily available to the Committee or are in-house reports or product brochures available on request. In some instances, toxicologic investigations include determination of the way the substance is handled by the body — how much can be absorbed before breakdown of the body's natural defenses occur, a biochemically based TLV from a biochemical threshold of response! To speed TLV development, industrial hygienists and toxicologists of some of these companies serve as consultants to the Committee ensuring first-hand information and knowledge.

Data sufficient to make a good TLV have not always been so accessible. As late as 1965, data sources generated by industry were so small that the Chairman of the TLV Committee in a communication to the *Archives of Environmental Health*,[9] felt the need to chide industry for not taking a more active role in supplying the Committee with data useful in setting TLVs. This action was prompted after a review of the 350 TLVs of 1964 showed that industry or industry-sponsored efforts accounted for only 90, or about 25%, of the total. And closer scrutiny of the documentations showed in many cases that industrial contributions provided only a partial basis for the limit, amounting to a very small industrial effort. Moreover, such was the state of industrial apathy in this endeavor that contributions were confined to seven chemical companies, with one or two minor exceptions. Of these, only two made the majority of the contributions; one company made what might be termed a significant but modest contribution, and four made only minor contributions. The size of the company bore no relation to the magnitude of the effort although all are considered to be among the chemical "giants."

Whether because of this exhortatory blast, or in spite of it, a surge of interest in TLV development occurred in certain segments of the chemical industry. For the first time in 13 years, industrial representatives either appeared in person or wrote for information to the TLV Committee on how they

[D]When this statement became the keynote of budget-justifying health agency administrators, and widely quoted by environmentalists, the author took the trouble to compare the number of marketable industrial chemicals in the *Chemical Buyers Directory* for 1973 with that for 1972, and found not the large increase stated, but 50 fewer! This listing refers of course to heavy chemicals available in quantity, not drugs and pharmaceuticals and the large.

should proceed to acquire the requisite data for setting a TLV on their products.

In response to this interest, a document *Principles and Procedures for Developing Experimental Animal Data for Threshold Limit Values for Air* was prepared,[10] which outlined minimal essentials for accumulating TLV data, and set forth principles underlying these procedures, much the same as principles and procedures for determining the toxic effects of food additives of the Food Protection Committee,[11] or the principles and procedures for evaluating the toxicity of threshold substances by the National Research Council.[12]

The TLV committee — membership and activities

The year 1969 marked the 25th anniversary of the appearance of the first published list of TLVs. What better time to pause, reflect, and project on what has been accomplished and what needs to be done to improve the limits and make them more generally useful and effective? The regulatory Occupational Safety and Health Act had not yet been passed, and the Committee felt as a whole that too many industries still did not have the proper regard for the TLVs. Accordingly, a paper was prepared for publication in the *Archives of Environmental Health,* a journal widely read by the industrial profession.[13] To stir up greater interest among industrial medical directors, in the value of the TLVs, it was read before the American Medical Association at its 28th Annual Congress on Occupational Health, New York, October 1, 1968. Much of the material was adapted from an earlier paper on the modus operandi of the TLV Committee.[14]

The presentation attempted, among other things, to allay questions in minds of some physicians on the composition of the Committee and their fitness to establish air limits for their industry, and thus, an account of the professional standing and affiliations of the Committee was made. Five members were physicians (one from the Canadian Health Department); eight could be counted as industrial hygienists and/or toxicologists; two with degrees in chemical engineering, active daily in their respective health departments; three actively practicing industrial analytical chemistry, and one pathologist, long an investigator of respiratory diseases. In addition, Committee members could call upon experts outside their field for consultation on special problems as the need arose. Most were individuals of national repute and well-known to the industrial community; several had international reputations and a long background of experience in occupational health that provided the perspective needed in occupational health matters and for evaluation of animal toxicity data.

Six subcommittees of the parent committee were responsible for the various areas of industrial health interest including economic poisons, with members assigned to the areas of their special expertise who drafted documentation in support of new TLVs.

Apart from the main effort of acquiring and assembling data needed to draft documentation for TLVs, a growing activity of the Committee was the validation of the TLVs. Industrial products selected for special attention were those on which new information was accumulating, but not assembled or published, e.g., the production of chromates in the chrome industry and the nitroglycols. In these instances, the Chairman and members of the appropriate subcommittee would hold a meeting with the industry's physicians and industrial hygienists and review their experiences in relation to the suitability of the respective TLV.

Another precedure for validating TLVs in cases where data and reports had been published, these were reviewed by the Chairman and the subcommittee, and any action that was taken, was that mutually agreed upon by industry and the American Conference of Governmental Industrial Hygienists by letter correspondence. This procedure has been used for beryllium, quartz, uranium, and vanadium pentoxide.

A third procedure involved active, cooperative projects with industry and the toxicology and pathology sections of the U.S. Occupational Health Program (OHP) whereby industry supplied the health records or clinical data for review, or active toxicologic research investigations were made by occupational health programs in conjunction with clinical and environmental data obtained by industry. Such was done cooperatively with a larger producer of isocyanates to determine means of detecting the hypersusceptible worker, a side bonus of which was the validation of the TLV for the isocyanates. A similar study was cooperatively made of carbon disulfide through a PL-480 grant

with the Institute of Occupational and Radiological Health, Belgrade, Yugoslavia, initiated by the TLV Chairman. A similar cooperative PL-480 grant was initiated on cadmium toxicology in Lodz, Poland.

An especially encouraging trend at this time was the unsolicited efforts of industry to develop additional information on such longstanding TLVs as benzene, fibrous glass, tetramethyl and tetraethyl lead and petroleum distillates, which resulted in more firmly based TLVs, and in some cases, TML and TEL, a revision of TLVs as a result of improved analytic procedures.

Adoption of TLVs as legal U.S. standards

The passage of the Occupational Safety and Health Act in the last days of 1970 was followed by the adoption of some 400 TLVs by OSHA, to the great satisfaction of the TLV Committee members, making them finally the official, legal standards of the nation, subject to supervisory and regulatory action to enforce the standards by OSHA. Now, no longer did the Committee feel the sense of frustration that often followed their best efforts to convince industry of the validity of the limits, only to be confronted with general apathy in their application. For long observation had shown that no worker had sustained serious effects on health. Provided exposure was within the stipulated TLVs, every counterclaim when investigated, revealed exposure had exceeded the TLV! This is a claim the Committee can well be proud of.

With the proper interpretations and use of the industrial air standards encouraged by OSHA's factory inspectors, no longer would the Committee be vexed with misinterpretation and misuse of the TLVs by considering them "fine lines between safe and dangerous concentrations," or by attempts to convert a TLV designed for an eight-hour day into one for thirty minutes, and thus, provide a dangerously excessive limit, or find that TLVs controlling industrial air levels were being used for limiting pollutants in urban community air.[15]

Adoption of TLVs by foreign countries

If great satisfaction was felt in the adoption of TLVs as legal U.S. standards, even greater satisfaction was the knowledge that the TLVs were being adopted by industrialized countries throughout the world.[16] At least 17 countries have either adopted the TLVs as legal standards, or as guides to legislative action. Seven other countries, Bulgaria, China, Czechoslovakia, Hungary, Poland, Romania, and Yugoslavia have followed the USSR example of controlling atmosphere concentrations by the use of maximum allowable concentrations (MACs). They are legally binding and absolute standards. China (not included in the ILO compliation [16]), adopted in 1956, the Soviet MACs as temporary standards for some 230 substances during the Communist regime of Mao when there was cosiderable interchange between Mainland China and the USSR.[E] Although official government standards, no punitive measures are taken for infractions, rather, dependence is placed on educating factory managers. Like all countries which adopted foreign standards, China has, since the establishments of a Peking Committee in 1963, undertaken to establish standards of their own.

Of the other iron-curtain countries, Czechoslovakia, which originally attributed the meaning of "ceiling" values to their MACs, adopted a "mean" MAC at an International Symposium in Prague in 1959. Thus, the changed meaning is essentially the time-weighted average (TWA) of the ACGIH. The Czechoslovakia Committee for MACs issued a summary documentation substantiating the values for 77 "most used" substances in 1969; for other substances, the MAC values for USSR are recommended. Yugoslavia has adopted as legal standards, MACs as TWAs and ceiling values where appropriate, and has further followed the ACGIH recommendation of biologic measurements as guides to controlling exposure of the individual worker.

Unfortunately, the ILO compliation is incomplete.[16] In addition to China, no listing appears for Canada, Egypt, France, India, Mexico, New Zealand, Thailand, Union of South Africa, or other African countries, all of which have either adopted the U.S. TLVs in principle or in fact.

Other countries adopting the TLVs include those of Western Europe, the Scandinavian countries and Japan. All have followed a similar pattern.

[E] According to Dr. Liano You-xin, Dept. Ind. Health, Shanghai First Med. College, who visited the author in Cincinnati, Jan 1981 to learn how the TLV Committee operates.

After having adopted the TLVs *in toto* and without change, committees were formed and adaptations of the TLVs were made to conform more closely to work conditions and other factors peculiar to the country. This was particularly true of Japan, where the work shift may run to 60 hour/week, and body build and nutritional factors differ considerably from those in the U.S.A. Similarly, the Federated Republic of Germany; at the beginning, the Commission for Hazardous Industrial Materials endorsed the ACGIH lists with a few modifications, but in 1969, the Commission started the preparation of a list of MAK values with documentations, independently, founding its deliberations on a set of criteria and methods developed from practical experience in that country.

One further accomplishment of the present Committee was the publication in December 1980 of documentations of the 550 listed TLVs, done through the efforts of an enlarged committee of 20, and eight consultants under the direction of Chairman, Hervey Elkins and Executive Secretary of ACGIH, William Kelley.[17]

Although the Committee relished the worldwide acceptance of their TLVs, during the 1960s, there were some large, important issues still confronting the Committee — the problem of the hypersusceptible worker and the question of thresholds for industrial carcinogens. How these were resolved by the Committee is the subject of Part III of this Series.

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Genetic screening of employees: resistance and responsibility*

HERBERT E. STOKINGER, Ph.D.
TLV Committee Chairman, 1962-1977; Liasion Member of American Standard Association Z-37 Committee, 1955-1972

"Whatever it is, or who commenced it, we're against it." **— Anon.**

This quotation, unfortunately an all too pervasive posture of the times, typified the climate in which two of the more creative activities of the TLV (Threshold Limit Value) Committee was launched — the recommendation of the use of tests for detecting the worker who is hypersusceptible to certain industrial chemicals and stresses, and the extension of the TLV concept to include industrial carcinogens. The former has been decried by critics as job discriminatory and needlessly ethnocentric;[1a] the latter, as contrary to all statistical theory and the customary view of cancer experts.[2]

In what follows, we shall examine the nature of the proposed tests and the arguments against their use, and see what approach was taken that made it possible to assign practical and realistic thresholds to industrial carcinogens.

The Author

Almost a score of years have passed since the first suggestions were made to identify those workers with a genetic potential to hyper-react to industrial chemicals.[3] Such tests were recommended as a means of protecting those workers who would not otherwise be protected by the TLVs. One of the innate characteristics of the TLVs is that they protect "nearly all," but not every worker "because of wide variation in susceptibility."[4] These tests then, were envisioned as overcoming this deficiency in the TLVs, while broadening their coverage. When properly performed and results interpreted in terms of substances involved in plant operations, the tests indicate which substances, or groups of substances, the worker should avoid, and thus work at operations where no risk of exposure can occur. Like diagnosis of a hidden ailment, the tests are capable of discovering an in-born error of metabolism of which people are generally unaware, thus offering a real health benefit to the workers and a feeling of real achievement to the Committee.

How the so-called "genetic screening" came about makes an interesting story. Expanding horizons in human genetics during the '60s[5,6] made it highly probable that most, if not all, of the hypersusceptible responses in workers were genetic in origin. By 1970, 92 human disorders had been identified for which genetically determined specific enzyme deficiency had been found.[6] In the meantime, relatively simple tests were becoming available which could be performed by industrial medical departments.[7] What remained now was to select those tests for specific abnormalities for which there was a relatively high prevalence in the U.S. workforce, and which involve substances commonly occurring in industry.

Tests for detecting the hypersusceptible worker

From the host of human disorders just noted above, five have been selected (Table I). Selection has been based firstly on the availability of a relatively simple test; secondly, on the frequency which the disorder occurs among U.S. workers; thirdly, on the tests' coverage of industrial substances to which large numbers of workers are exposed. Three of the tests, Numbers 1, 2, 5, Table I, detect hypersusceptibility to a large array of substances encountered in industry. Number 1, the antitrypsin test, when positive, is an indicator of potential emphysema in these hypersusceptible individuals resulting from exposure to all kinds of respiratory irritants, whether they be gases, vapors or particulates. Emphysema, a disabling, often fatal disease of the lungs, develops at an accelerated rate in these hypersusceptible individ-

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TABLE I
Categories of Genetic Variation in Man

Category	Test Substance
1. Missing or deficiency of essential antibody	α-1-Antitrypsin deficiency
2. Deficiency or absence of enzyme system	Glucose-6-phosphate dehydrogenase
3. Alteration in cellular transport of metabolite	CS_2 sensitivity
4. Abnormal antibody production	Reaginic antibodies to allergenic pollen antigens in "Hayfever" 'spread' to certain industrial chemicals
5. Presence of abnormal protein	Hemoglobin S in sickle-cell anemia

uals because of a deficiency of antitrypsin, which in normal individuals, prevents destruction of the delicate alveolar wall of the lung. Persons with complete (homozygous) deficiency, exposed to respiratory irritants, have died by age 50. In Pi^{ZZ} individuals the emphysematous process may appear before the age of 30.[8] If this test applied in the job preplacement, examination could prevent such a dismal outcome, the TLV Committee was all for it.

The G-6-PD test for deficiency of the enzyme glucose-6-phosphatase (No. 2, Table I) and the test for sickle-cell trait (No. 5) are two other tests for identifying individuals hypersusceptible to hemolytic chemicals that lead to hemolytic crises and anemia. These include a wide group of chemicals (Table II), embracing both inorganic and organic chemicals, many commonly used drugs, and physical stress, such as altered O_2 pressure.

G-6-PD deficiency of an incidence warranting genetic screening occurs among blacks who have their origins in Equatorial Africa, among populations bordering on the Mediterranean, especially Italians, Scilians, and Sardinians, East Indians, some Orientals, Oceaninas, and Filipinos.[9] Blacks represent the largest ethnic group of U.S. workers in most plants, in some, however, Italians outnumber them.[1b] It is the blacks also which form the largest group in industry with sickle-cell trait (red cells with 20%-40% hemoglobin S); but the trait occurs also in some parts of India, the Middle East, and around the Mediterranean.[7] The possibility of G-6-PD deficiency co-existing with sickle-cell abnormalities should not be excluded.

Apart from the numerous industrial substances affecting the hypersusceptible (Table II) many of which are found in the dye industry, common drugs can account for a significant part of industries' absenteeism among this group. The chronic "pill taker" among the G-6-PD deficient develops a protracted response to his drug treatment for such things as headache, the common cold, arthritis.[7] This can show as jaundice resulting from intravascular blood destruction and hemorrhage in these individuals.

Thus, preemployment screening for G-6-PD deficiency serves a dual purpose. It makes such workers aware of a condition outside of employment to which they are uniquely vulnerable. At the same time, it alerts the industrial physician to the possibility of nonjob-related employee illness, and helps him decide between job-connected and self inflicted illness.

Not to be overlooked also is the potentiating effect of physical stress on those G-6-PD deficient and those with sickle trait. Physical stress takes two forms — strenuous physical exertion, and altered ambient oxygen pressure. Sudden death has occurred in poorly conditioned blacks with the sickle-cell trait while undergoing military training at moderate altitudes (4060 ft).[10] In these individuals physical exertion at reduced O_2 pressure, initiated and hastened red blood cell sickling through the development of hypoxia (lowered blood O_2 tension) chemically reducing the S-

TABLE II
Some Hemolytic Industrial Chemicals and Stresses

Acetanilid	Nitric oxide
Amyl nitrite	Nitrites
Aniline	Nitrosamines
Arsine	p-Nitrochlorobenzene
Benzene	p-Phenylenediamine
Benzidine	Phenylhydrazine
Carbon tetrachloride	Phosphorus
Chlorate	Selenium dioxide
Chloronitrobenzenes	Stibine
Chloroprene monomer	Tetrachloroethane
Cresol	Toluidine
Dinitrobenzenes	Toluylenediamine
Dinitrotoluenes	Trinitrotoluene
Guaiacol	
Hydroxylamine	
Lead	Numerous N-containing drugs
Methylcellosolve	Altered oxygen pressure
Naphthalene	

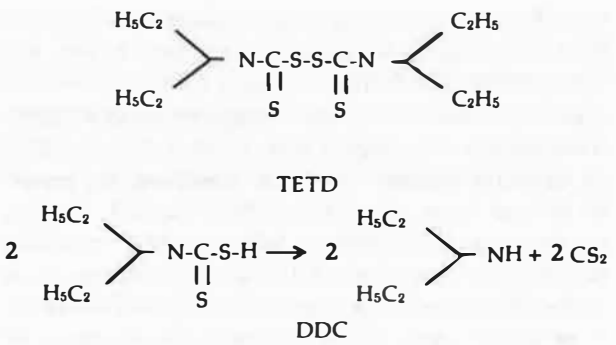

Figure 1 — Tetraethylthiuram disulfide (TETD) and metabolites.

hemoglobin, a necessary condition for sickle-cell formation. Associated factors increasing sickling are acidosis, dehydration and reducing agents, such as lactic acid, all the result of intense muscular activity. The sickle-cell crisis is characterized by massed sickle cells that plug the vessels of the liver, kidney and spleen leading to death.

Incidents such as this has led to the screening for these traits throughout the Armed Forces and the policy of not allowing anyone with the sickle-cell trait to be on a flight crew; and the Air Force[A] has expelled blacks with the trait on the grounds that the rigorous training of new enlistees at the 7000 ft altitude of the Academy could jeopardize the lives of unadapted blacks.[11]

High ambient O_2 levels can likewise lead to serious consequences, and which likewise indicate the need for genetic screening. The writer recalls an episode of pulmonary hemorrhage in a black undergoing astronaut training which in the early days, was at high O_2 cabin pressure. When his blood was screened for G-6-PD deficiency, it was found positive. We, therefore, recommended screening before entrance into the mission, to prevent further serious episodes.

Two additional recommended genetic screening tests, one, for carbon disulfide (CS_2) susceptibility, or for substances which metabolize to CS_2; the other, for hypersensitivity to organic isocyanates[7] (Numbers 3 and 4, Table 1). These tests differ in one respect from the foregoing in that they screen for susceptibility to one or a small group of specific chemical structures, CS_2 or NCO.

Antabuse test for susceptibility to CS_2

As in all recommended genetic screening tests, the Antabuse (tetraethyl thiuram disulfide, TETD) test identifies those individuals (rayon and cellophane workers and others handling CS_2) who, upon repeated exposure to CS_2 hyperreact with clinical signs of CS_2 poisoning in the form of polyneuritis, due to their inability to metabolize CS_2 at a rate comparable to that of CS_2-resistant workers.[12]

Antabuse was selected as the test agent because of its metabolic similarity to CS_2 (Figure 1). Administered in the preemployment medical examination, those with potential hypersusceptibility to CS_2 have a urinary excretion of diethyl dithio carbamate (DDC) (Figure 1) below the threshold of those resistant to CS_2 (50 vs. 90 average μg/g DDC as creatinine). Those undergoing Antabuse treatment for alcoholism but not exposed to CS_2 values of urinary DDC approximate those of unexposed controls (158 vs. 160 μg/g creatinine).[12]

Immunologic screening tests for hypersensivitity to organic isocyanates

An immunologic screening test for hypersensitivity to aliphatic and aromatic isocyanates was developed when it was learned that in addition to the purely toxic response, an allergic type of delayed hypersensitivity developed in some workers following exposure to exquisitely small amounts, well below threshold limits (0.02 ppm), if previously exposed above the limit. As the severity of the hypersensitivity response precluded tests on workers themselves, serum screening tests were developed in animals.[7]

Hapten-specific antigens, made by linking a specific isocyanate with a protein (egg or serum albumen) were used for testing for reaginic antibodies in the serum of workers previously exposed to isocyanates by injecting workers' serum into monkeys and reading the cutaneous response. Of more than 1000 sera tested, 0.5% of clinical cases of delayed hypersensitivity were found by this test, and 1.5% of "wet" allergic hypersensitivity (pollen-like sensitivity) among the U.S. worker population.[7]

It is important to note here as in other industries, steel mills, coke ovens, foundries, metal-produc-

[A] *EDITOR'S NOTE:* In United States the Air Force was the only operator of a major service academy to disqualify any candidate for admission simply because he possessed a gene for sickle trait. This policy was challenged and subsequently dropped.

tion plants, et al, that no amount of control of workplace air can "make the workplace safe for everybody, including the most sensitive members of the population," as disparagers of genetic screening have claimed.[1a,b,d] The Soviet practice of reducing industrial air standards to "as near zero as possible"[B] has failed to protect the hypersusceptible or the hypersensitive worker. The tests do not "deny employment" or "discriminate arbitrarily against minority groups"[1d] but allows for better health protection through appropriate job assignment.

The case for thresholds in occupational carcinogenesis

Answer to the question, why a case has to be made for thresholds for carcinogens in the workplace would seem to be unnecessary, when it is a logical extension of the threshold concept. Unfortunately, it is necessary because of a persistent blind adherence to a statistical theory based on outmoded biologic concepts (the "one-hit" theory, linear extrapolation from high to low doses) and applied to the population at large, and not on industrial workers as a group. What these adherents have failed to recognize, among other things, is that the industrial worker is a group apart from the general population in several respects. First, he is of an age from 18 to 65, the years when immunologic competence is strong. Second, he is comparatively far more healthy because of preemployment and periodic medical examinations, which provides for good health maintenance by proper job placement (see preceding section). Third, his exposure to carcinogens (and cocarcinogens) is not only known but controlled.

A case had to be made for other reasons also. Administrators of health agencies, buoyed by the OSHA act of 1970, were adopting ultraconservative measures for controlling carcinogens in the workplace that in certain cases amounted to outright banning and thus were unacceptable and impractical for industry to comply with, and to the TLV Committee, for being contrary to the threshold concept. Substances were designated carcinogens irrespective of whether true human carcinogens, or whether merely "suspect" carcinogens, as determined from animal experimentation. Control of suspect carcinogens was equally restrictive whether used on a purely laboratory scale as on an industrial scale. (The now famous OSHA list of 14, 5 of which were either suspect carcinogens, or erroneously considered carcinogens (benzidine, naphthylamine), and two were of no industrial importance.) Clearly there was a need to break out the known from the suspected. This was the first action of the TLV Committee in 1972, done for the purpose of making clear this distinction, and hence to provide guidance on the relative degree of concern for their respective health hazards.[13]

More compelling even than the foregoing for the establishment of thresholds for occupational carcinogenesis was the growing amount of evidence both from epidemiologic and experimental investigations that started in the mid-70's (Table III). Here was unmistakable evidence pointing to thresholds for occupational carcinogenesis. Here also was a way to replace statistical guesswork on risk assessment for general populations with solid evidence directed to the more pertinent industrial population.

The theoretic basis

The concept of "no-threshold" for carcinogenesis, fostered in part by unsupported biologic theory (the "one-hit" model) and promoted over the years by unrelenting, specious, statistical gimmicks (linear extrapolation from high to low doses) has become precious to those in the cancer field to support their activities, and used as a solid defense for the extreme actions taken by health regulators. That the threshold concept has a far more sound biologic basis, has been demonstrated by Dinman[14] and Stokinger.[15] The demonstration is based on the knowledge that a finite and not inconsiderable number of molecules, (varying between 10^{14} to 10^4 to 10^6), are required, depending upon the biologic system involved, to effect a measurable functional change. Thus, Dinman points out that the "no threshold" concept has no rational biological basis.

[B]When the writer visited Soviet Union at the request of the U.S. State Department for the purpose of understanding why the Soviet industrial air standards were so low, it was learned that their only approach to protect the hypersusceptible worker was to lower the standards to as near zero as possible, an unequited effort.

TABLE III
Evidence For Thresholds in Carcinogenesis

Test Substance	Route	Species	Dose Levels Eliciting Tumors	Dose Levels Not Eliciting Tumors	Duration	References
Bis-Chloro methyl ether	Inhin	Rat	100 ppb	10 and 1 ppb	6 mo daily	Leong et al.[18]
1,4-Dioxane	Oral Inhin	Rat Rat	1% H_2O > 1000 ppm	0.1 & 0.01 111 ppm	2 yrs 2 yrs daily	Torkelson et at.[19] ibid.[20]
Coal Tar	Topical	Mouse	6400; 640; 64 mg	< 0.64 mg	2x/wk, 64 wks	Bingham[21]
β-Naphthylamine	Inhin & Skin	Man	> 5% β in α-Form	< 0.5% β α-Form	22 yrs	Zapp[22]
Hexamethyl phosphoramide	Inhin	Rat	4000; 400 ppb	50 ppb	8 mo	Zapp[23]
Vinyl chloride	Inhin	Rat	2500; 200; 50 ppm	< 50; > 10 ppm '50-'59, 160 ppm average; 30-170 ppm	7 mo	Keplinger et al.[24] Kramer, Mutchler[25]
(+ Vinylidene chloride	Inhin	Man	> 200 ppm	range '60 < 50 ppm, decreasing to 10 ppm	25 yrs	Ott et al.[26]
Dimethyl sulfate	Inhin Inhin	Rat Man	10; 3 pm (Est'd) Unknown	Unknown < 2-5 ppm	> 10 mo 15 yrs	Druckrey et al.[27] Pell, DuPont[28]
Asbestos	Inhin	Man	> 125 mppcf	< 125 ppm	up to 25 or more years	Enterline[30]

Part of the basis supporting the finite number of molecules for functional response, is the fact recognized for more than 100 years, that the body has "built in" antagonists which counteract the action of substances foreign to it. More recently, the counteracting roles of repair by DNA, the putative receptor site of all carcinogens, and immunosurveillance mechanisms, are functionally strong in the worker age groups exposed to industrial carcinogens.

The theoretic basis for carcinogenic thresholds has been voiced in another way by Kotin,[16] who, as a pathologist, noted that as there are thresholds of response for each of the sequences for the six steps in the carcinogenic process as postulated by Farber, it follows that an overall threshold exists. It may be further pointed out that, in the industrial situation, the presence of cofactors (synergists or promoters) if they are present, their nature and amount are generally known, and not unknown, as it is among the general population. Thus, one factor leading to uncertainties in setting thresholds is eliminated.

Industrial carcinogens have been pretty well defined through intensive investigation during the past decade, and are under constant control through the application of industrial air standards. Uncertainties relating to host factors and disease both genetic and acquired, common factors in the general population, are essentially nonexistent in industry, where preplacement job and periodic medical examinations lead to hiring and maintaining the physically fit.

Beginning in the mid-'70s, reports of animal and epidemiologic studies provided unmistakable evidence of the existence of thresholds for recognized occupational carcinogens found in the workplace, and for which the TLV committee could use as a data base to establish TLVs. Table III presents such evidence for nine industrial carcinogens.[17]

First to be noted in Table III is a considerable variety of chemical structures, ranging from complex carcinogenic mixtures of PAH in coal tars of relatively low carcinogenic potency as judged from the latency period, to the highly potent structures of bis-CME and HEMPA, with short latent periods

even at ppb levels. Response thresholds are not confined to any one route of entry, but are common to all three, irrespective of whether the carcinogen was of very high or low potency. Probably the strongest case for thresholds is their occurrence in three instances of human carcinogenesis: β-naphthylamine, dimethyl sulfate and vinyl chloride.

Space does not permit detailed presentation of the basis for the data in Table III. Suffice it to say that 25 years or more have elapsed since workers were first exposed without the appearance of tumors. In some cases also (vinyl chloride) animal studies have confirmed epidemiologic findings. For further evidence supporting these thresholds, see reference 17.

Concluding with these nine examples of carcinogens with thresholds should not be taken as all that can be mustered, but rather as indications of what measures need to be taken to discover thresholds for carcinogens.

The TLV Committee is not alone in extending the TLVs to industrial carcinogens. Truhaut[31] in his 1980 Yant Award Lecture presented convincing evidence for carcinogenic thresholds along much the same lines as given in the foregoing. Soviet industrial health authorities have also begun to adopt permissible limits for certain carcinogens, and WHO, while not admitting completely their validity, does not rule out the possibility.[31]

The cause for carcinogenic thresholds may actually be taking hold even among those heavily imbued with the statistical approach at the National Cancer Institute, if we interpret some of their latest statements correctly. A report[32] concerning the mouse liver tumor as an endpoint in carcinogenesis tests ended with the statement that

> *"the question whether chemicals causing liver tumors in mice would increase the risk of human cancer, may never be answered because industrial . . . exposure to these chemicals is being reduced. . . ."*

The TLV Committee interpreted this statement to be a tacit admission of carcinogenic thresholds.

Note Added in Press. An indepth review of the U.S. Food and Drug Administration's massive ED_{01} study by an Society of Toxicology task force failed to confirm the FDA conclusion of a lack of threshold effect, definitely pointing out "a tumor-free period as a function of dose with a scope indistinguishable from zero over a considerable region".[33]

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ACGIH TLVs and the sensitive worker*

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The sensitive worker has, through the years, been addressed by the Threshold Limit Values Committee. The Preface of the Airborne Contaminants portion of the 1972 ACGIH TLV booklet states that threshold limit values referred to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variation of individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit. A smaller percentage may be affected more seriously by aggrevation of a pre-existing condition, or by development of an occupational illness.

The Committee advocates that if the worker has become sensitized, then one ought to exclude him from the place of exposure rather than attempt to recommend a threshold limit value that would protect the sensitized worker.

The sensitized worker

One must, when addressing the Threshold Limit Values of the American Conference of Governmental Hygienists (ACGIH) and their relationship to the sensitive worker, define the sensitive worker in context. For purposes of this presentation, the "sensitized" worker is differentiated from the "sensitive" or hypersusceptible worker. A discussion of the sensitized worker ought to have certain preconditions imposed before one makes the judgement that the worker is sensitized. Specifically, there must have been a prior exposure either to the compound in question or a very similar compound, which resulted in an immunologically defined response.

The sensitized worker may display an asthmatic-like reaction, a rash, or a series of different responses based upon the specific chemical hapten, and the nature of the immunological response. The sensitization itself may be incurred due to skin contact, inhalation, ingestion, or mucous membrane contact. The exposure need only be a one time event in order to produce the sensitization phenomena. In the case of toluene diisocyanate, it has been demonstrated that an increase in titer may be noted after only one exposure. The case of the sensitive worker, and the response of the sensitive worker need not entail a biochemical change. Another problem with an immunologically related response is the challenge of developing an acceptable exposure limit for an event that does not appear to either have a threshold or fit the standard dose response relationship. The sigmoid curve does not appear to fit this phenomenon. The phenomenon of desensitization such as may be reflected in a decrease in response due to thickening of skin, necrosis or sensory endings, or tachyphylaxis shall not be addressed.

The idiosyncratic response

Another response that may be confronted in the workplace is the genetically defined idiosyncratic response. Until more specific information is available, one should either address the idiosyncratic responder as a separate class, or as a major subdivision of the hypersusceptible. However, one might be an idiosyncratic responder to one material and be hypersusceptible and/or sensitized to another. An example of an idiosyncratic response is the finding that some individuals are more sensitive to the methemoglobin producing effects of exposure to nitrates. This is due to a recessive gene. I have not been able to find an example of a TLV that takes into consideration the idiosyncratic responder. Given the probable mathematical odds involved, one would not expect to find that an exposure limit had been developed with these types of responders in mind.

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The sensitive worker

The sensitive worker might be exemplified by contact lens wearers in the presence of very low concentrations of formaldehyde. They may be the best organic indicator of the presence of formaldehyde that one could have in a laboratory. However, the ACGIH TLV does not take into account the fact that some technicians wear contact lenses, which mechanically makes them sensitive workers.

Other sensitive workers may be defined as those workers who, due to the medication they are receiving, join the ranks of sensitive workers during the time of their therapeutic regimen (Table I). This may be exemplified by the worker who is receiving antabuse treatment. Another group of workers considered in developing TLVs has been the dependent employee. The worker exemplified by this category would be found in a nitroglycerin plant. There are numerous variations of the stories about workers who took nitroglycerin home during the weekend to avoid the effects of withdrawal from their weekly exposure.

TABLE I
Topical Sensitizers and Immunochemically Related Drugs*

Topical Sensitizers	Immunochemically related drugs
Hydrazine hydrobromide	Isoniazid, Apresoline, Nardil
Para-amino compounds	Para-aminobenzoic acid (PABA) and related local anesthetics (Benzocaine, Procaine)
	Azo dyes in foods and drugs
	Dymelor, Orinase, Diabinese, Sulfonamides
	Diuril, Hydrodiuril, Saluron, Renese
	Para-aminosalicylic acid (PAS)
Neomycin sulfate	Streptomycin, Kanamycin
Resorcin	Hexylresorcinal (Crystoids, Caprokol)
Organic and inorganic mercurials	Mercurial diuretics
Metallic mercury	Calomel
Cobalt	Vitamin B_{12}
Thiamine	Coenzyme B (cocarboxylase)
Ethylenediamine hydrochloride	Aminophylline, Antistine, Phenergan, Pyribenzamine, Synopen, Neohetiamine
Formaldehyde	Urotropin, Maldelamine, Urised
Thiram and disulfiram	Antabuse
Halogentated hydroxyquinolines	Vioform, Diodoquin
Chlorobutanol	Chloral Hydrate
Iodine	Iodides, iodinated organic compounds
Benadryl	Dramamine

* Drill, V.A. and P. Lazer: *Cutaneous Toxicity.*

Philosophy of TLVs

When beginning the development of this presentation, the author was concerned with the question of how the TLV Committee has addressed this problem through the years. He has only been associated with the Threshold Limit Values Committee since 1973, and others had addressed this problem long before he joined the Committee. The attitude that the author has always had as a member of the Committee was that the worker assumed a certain degree of acceptable risk when he came into the workplace, providing that the risks and associated hazards had been explained to him and he understood the explanation. It is presumed that socioeconomic conditions have not forced the worker to accept risks that he really was not willing to accept. The threshold limit values assume complete free will on the part of the worker.

The Preface of the Airborne Contaminants portion of the ACGIH TLV Booklet, in 1972, states that threshold limit values referred to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be exposed repeatedly day after day without adverse effect. Because of wide variation of individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit. A smaller percentage may be affected more seriously by aggravation of a preexisting condition, or by development of an occupational illness.

"Simple tests are now available[1,2] that may be used to detect individuals hypersusceptible to a variety of industrial chemicals (respiratory irritants, hemolytic chemicals, organic isocyanates, carbon disulfide). These tests may be used to screen out by appropriate job placement of the hyperactive worker, and thus improve this 'coverage' of the TLVs."[3]

The sensitive worker has, through the years, been addressed by the Threshold Limit Values Committee. Within recent years, more attention has been directed to the teratogenic effects of chemicals, since the pregnant woman and her fetus are considered special, if not sensitive models. For example, if one reads the TLV documentation for pentachlorophenol,[4] reference is made to a Schwetz and Gehring paper indicating that the rat embryo was shown to be most susceptible to the toxic effects of pentachlorophenol during the early phases of organogenesis.

With regard to sensitized workers, the chemical most often referred to is toluene diisocyanate, but other chemicals have long been known to cause these types of problems. The documentation for p-phenylenediamine indicates that the threshold limit value is believed to be sufficiently low to minimize the numbers of people who become sensitized, but it is recognized that the limit is not low enough to prevent exacerbation of asthma in those already sensitized to p-phenylenediamine.[5]

Teratology and reproductive data, when available, have been used as in the case of 3,5-dinitro-o-toluamide. In the case of this material, no effects were seen on fertility, gestation, viability, or lactation in rats fed either at 6 ppm or 3 ppm per day for three generations. As all of you are aware, unfortunately, these reproductive data are generally not available for most chemicals. Some of the TLVs do not address the potential problem of either mutagenicity or teratogenicity. This is due to the fact that some of the threshold limit values were developed several years ago or data are not available and/or are questionable.

Carcinogenicity/sensitive worker

How does one address the question of carcinogenicity and the sensitive worker? There are threshold limit values that address the toxicology of a particular compound, particularly with respect to a given organ system, and it would appear that if one is able to prevent changes, as measured by certain biochemical indices, that one does not find epidemiological evidence of carcinogenicity. This is irrespective of the studies that have been performed in mice or rats. The case in point is the experience at DuPont and BASF with dimethyl sulfate. It is conceivable that the same may be said of dimethyl carbamyl chloride. Due to the high toxicity of the material, exposure has been well controlled and a survey made in 1976 of about 300 people in the chemical industry indicated no human cases of cancer attributable to dimethyl carbamyl chloride had been reported.

The ACGIH was one of the first standard setting groups to note that cigarette smoking can enhance the incidence of respiratory cancers. In the case of lung cancer, one might consider the smoker to be the hypersusceptible individual. A comment first appeared in the 1975 TLV booklet stating that "cigarette smoking may substantially enhance the incidence of bronchiogenic carcinoma from this and others of these listed substances or processes."[6]

The TLV Committee attempted to address the question of materials known to be human carcinogens versus materials that are alleged to be carcinogens either due to anecdotal information, one case report, or extraordinarily high doses provided to a rodent species. In this instance, the Committee decided that it was necessary to separate the potential for materials to be regarded as carcinogens, based upon the types of data available. Again, the Committee found itself in a more flexible position than a Federal agency would, in that one could approach the data, based upon the information that was available at that time, and provide a leadership role. In this case, the data, rather than the individuals, were hypersusceptible. The hypersusceptibility being the readiness at that time for people to call a material a carcinogen based upon highly suspect rodent data.

Sensitizing chemicals

The majority of the TLVs that deal with chemicals with a high sensitization potential, such as diethylene triamine, are set low enough to avoid a sensitization response. In some instances, the response to exposure to given chemicals, such as carbon disulfide, would appear to vary among workers in different countries. One reason may be nutritional differences, the other may be due to the interrelationships, not clearly understood at this time, between copper and zinc and other materials. It is sufficient to say that trace elements in a diet can exert a profound effect on the response of the effect of carbon disulfide exposure. On the other hand, differences in hereditary susceptibility have not been explored with regard to

this particular compound. As pointed out in the documentation, workers with a reduced capacity to metabolize tetraethylthiuram disulfide are considered hypersusceptible and the frequency of hypersusceptibles may either vary in different countries or this may be an idiosyncratic response.

The threshold limit value for toluene diisocyanate (TDI) is designed to help prevent the development of sensitization. However, the level is not low enough to protect the sensitized worker. One of the problems long recognized by the Threshold Limit Values Committee is that specific data were not available with regard to what level will protect the sensitized worker. In addition, different sensitized workers are more sensitive than other workers, and this too has been recognized by the Committee. Since a great deal of the data are derived from animal work, one must acknowledge that the animal models for sensitization, particularly with regard to inhalation sensitization, until recently have been extremely poor. It is only very recently that a model has been developed which will respond to polyisocyanates. Dr. Karroll's work at the University of Pittsburgh indicates that a very sensitive model is being developed that is transferrable directly to humans.[7] Perhaps by addressing the sensitized population, using appropriate immunotoxicologic techniques, we will be able to develop suitable models and suitable test systems for use in humans to identify these sensitized workers. One of the items of interest from Dr. Karroll's work is that by using her test techniques, she was able to identify that workers exhibited titers after only one exposure to TDI. The implications are that one exposure is probably all that is necessary to produce a sensitized worker.

Through the years, the Threshold Limit Values Committee of the ACGIH has recognized the existence of sensitive or hypersusceptible workers and has attempted to make provision for these workers when data were available. This ranged from the attempt to establish doses that would not cause sensitization, to the recognition of responses like the antabuse effect, to the more recent concern with regard to women of childbearing age. It would appear that due to DBCP that this concern has been transferred to males as well. The Committee has gone one step further, if one wishes to extend the definition, and has acknowledged that TLVs can be established for chemicals that are potential human carcinogens.

In summary, one hesitates to state what the philosophy of the Committee is or has been, since the Committee is composed of a group that changes from time to time, and the leadership of the Committee has changed through the years. One can only invite your attention to the TLV booklet and documentation, and provide the observations with respect to how the Committee has approached the question of the sensitive or hypersusceptible individual. Whenever possible, the Committee has attempted, if the workforce demonstrated that it was more susceptible in one locale than another and that a reason could be found for this difference, to take this geographic difference into consideration. However, the Committee has always advocated that if the worker has become sensitized, then one ought to exclude him from the place of exposure rather than attempt to recommend a threshold limit value that would protect the sensitized worker.

The Committee has documented its opinion that the use of a skin test, or some other approach was useful and did not discriminate arbitrarily against minority groups, or any other group, since the purpose of the threshold limit value is to protect the worker. The Committee may have an advantage over other standard-setting groups that are associated with the Federal government in that it can address what it thinks are the best approaches to producing a valid threshold limit value based upon available data rather than complicated sociological or political relationships.

We believe that our approach to the sensitive worker (in the broad sense) has been one of leadership coupled with caution. And until such time as there are better defined models, the threshold limit value will probably continue to address the sensitive individual as representative of a small portion of the population and take the position that the threshold limit values should be so set as to protect against development of sensitization and through the use of screening tests either prevent the exposure or at least minimize the number of hypersusceptible or sensitive workers who might be exposed during the working experience.

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Occupational exposure limits and the sensitive worker: the dilemma of international standards*

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Occupational exposure limits in the United States, as well as those used by most of the Western European countries, Japan, and Australia, have evolutionized over the decades so that, for the most part, they are fairly well suited to the working populations for which they are meant. As can be expected, there are still problems with a number of the four to five hundred exposure limits which have been established in these countries; there are some groups who would have us believe that the exposure limits published for Western countries are much too lenient, whereas other groups maintain that they should be even more lenient. In contrast are the occupational exposure limits of the Soviet Union and other Eastern Bloc Countries for which the limit values for most substances are considerably lower (or more severe) than for any of the countries of the western world. But, even most of the Soviet limits are understandable if one views them from the standpoint of the philosophy and approaches taken in their development. Consider, however, the plight of the many nations who are beginning to industrialize or those nations who are just beginning to emerge on the industrial scene, many of which are referred to as developing countries. What can these nation's leaders believe when it comes to the development of standards, or more simply the adoption of guidelines, for occupational exposure limits? This is not just a moot question, because it is happening quite often in countries whose work forces and production are such a critical factor of the economy. Few governments today can afford to ignore the health status of their working force, although some who employ a high percentage of non-nationals are not greatly concerned about the health of those individuals. The concept of "sensitive worker," as we know it for the United States and other Western Countries, has a somewhat different meaning when equated with worker populations in countries less developed than our own; the ramifications of this situation point to different needs for exposure limits.

One has only to review a sample of the occupational exposure limits proposed (and sometimes used) by nations around the world. It is then that one begins to appreciate the use of the word "dilemma" in the title of this paper. Table I is a synopsis of a review of selected chemical substances which illustrate exposure limit (EL) values for 18 countries. A few of the values shown may not be the most current for a particular country, but this is not so important since the trends I wish to depict will not be changed significantly. All of the ELs have been converted to, and are shown as, mg/m^3 values for ease of consistent comparison. This table is used only to show general trends. In fact, the substances listed were selected purposely because of the variability of exposure limits between countries, but the reader will recognize that these substances are generally important and the countries are heavily to moderately industrialized. For now, consider the range extremes of exposure limits; for example, the first substance, acetaldehyde has a high EL value of 360 mg/m^3, and a low value of 5 mg/m^3. As can be seen, 360 mg/m^3 represents several countries, while 5 mg/m^3 is the Soviet (USSR) limit. Note that the USA value used by OSHA is 360, but the ACGIH value for this substance is 180 mg/m^3. These are the trends which carry through for the entire Table.

Skipping across to the last four columns, i.e., styrene, trichloroethylene (TCE), toluene, and xylene, for which there are EL values claimed by each of the 18 countries, it is seen that the extreme lows are for Bulgaria and the USSR, with intermediate values between the lows and highs for the remainder of the Eastern Bloc Countries, while highs are seen generally for the USA, Australia, Japan, and the Western European countries.

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TABLE I
Comparison of Selected Chemical Substances and Their Occupational Exposure Limits for 18 Countries

EXPOSURE LIMITS mg/m³

	Acetaldehyde	Aldrin	Carbon disulfide	Dieldrin	Malathion	Methyl bromide	Lead	Styrene	TCE	Toluene	Xylene
Australia	180	.25	60	.25	—	60	.15	420	535	375	435
Belgium	180	.25	60	.25	10	60	.15	420	535	375	435
Bulgaria	—	—	10	.01	.6	—	—	5	10	50	50
Czechoslovakia	200	—	30	—	—	—	.05	200	250	200	200
Finland	180	.25	30	.25	10	60	.15	420	260	750	435
German D.R.	100	—	50	—	—	50	.15	200	250	200	200
Fed. Rep. Ger.	360	.25	30	.25	15	80	.20	420	260	750	870
Hungary	—	.01	20	.01	—	10	.02	50	50	50	50
Italy	100	—	30	—	—	—	.15	300	400	300	400
Japan	—	.25	15	—	—	—	.15	210	268	375	670
Netherlands	180	.25	60	.25	10	60	.15	420	190	375	435
Poland	100	.01	25	.01	15	5	.05	100	50	100	100
Romania	100	.20	30	.20	10	50	.10	250	200	300	300
Sweden	90	—	30	—	—	—	.10	210	160	375	435
Switzerland	180	.25	30	.25	10	60	.15	420	260	380	435
USSR	5	.01	10	.01	.5	1	.01	5	10	50	50
USA, OSHA	360	.25	60	.25	15	80	.20	420	535	375	435
ACGIH	180	.25	30	.25	10	20	.15	215	535	375	435
NIOSH	—	.15	3	.15	15	—	.05	—	535	375	—
Yugoslavia	360	.25	50	.25	.5	80	.15	420	200	200	50

TABLE II
Comparison of the Occupational Exposure Limits and FV Values for 11 Chemical Substances

Substance	EL* Extremes	FV† Values
Acetaldehyde	360/5	36
Aldrin	.25/.01	25
Carbon disulfide	60/3	20
Dieldrin	.25/.01	25
Malathion	15/.5	30
Methyl bromide	80/1	80
Lead	.2/.01	20
Styrene	420/5	84
Trichloroethylene	535/10	54
Toluene	750/50	15
Xylene	870/50	17

* EL values in mg/m^3.
† Factor of variance = high EL/low EL.

When we examine these values more closely it is seen, for example with these last four substances, that the exposure limit range for styrene has a high value of 420 mg/m^3 whereas the low value is 5 mg/m^3. Thus, those countries using a value of 420 mg/m^3, e.g., Austrialia, Belgium, Finland, and the Federal Republic of Germany (West Germany), the Netherlands, Switzerland, and the United States OSHA standard have an exposure limitation placed on styrene which is 84 times less, or more lenient, than the EL value of 5 mg/m^3 claimed by Bulgaria and the USSR. The Factor of Variance, or FV value, therefore, equals 84.

Note that the threshold limit value (TLV) of the American Conference of Governmental Industrial Hyienists (ACGIH) for this particular substance is 215 mg/m^3, which is 1.9 times lower than the ELs of 420; the ACGIH TLV, is, on the other hand, 43 times higher, i.e., 43 times less stringent than the EL valve of 5 mg/m^3 claimed for Bulgaria and the USSR.

For ease of comparison, Table II lists the FVs for the exposure limits of each of the same substances listed in the first table. Column two gives the EL extremes, i.e., the high and low values in mg/m^3, and column three shows the FV for those extremes. Accordingly, it is seen in this table that the FVs range from a low of 15 for toluene up to a high of 84 for styrene.

The author does not wish to give the impression that all exposure limit values have such great variance between countries, but these examples were used to illustrate why agreement in development and establishment of international exposure limits is such a difficult thing to accomplish. As a good estimate, of the 400 to 500 substances that are considered important enough by most countries to give guidelines or standards on exposure concentrations for the work environment, probably no more than 60 to 75 of the substances have an FV value of less than two. That is to say, that the lowest EL and the highest EL used by the various countries for a particular substance differs by a factor of two or less in only 15 to 20% of the cases.

Before proceeding further, it should be pointed out that it cannot be stated catagorically that the Soviet Union or that the Eastern Block Countries consistently have lower (or more stringent) exposure limits. Notice in Table III that there are a few very important substances for which the USA has significantly lower ELs than the Eastern Bloc Countries, Bulgaria, and USSR, as illustrated by ELs for cotton dust, selenium, and silca which have FV values of 30, 10, and 20, respectively, when compared to the U.S. The value for cotton dust in the USSR is probably explained by the fact that most is hand picked and contains less trash than machine-picked cotton, therefore it is less hazardous in production of bysinosis.

TABLE III
Comparison of Some Extreme Values for Occupational Exposure Limits

Substance	EL Extremes[a]	FV Values[b]
Ammonia	Bulg. = 35/USA = 18	1.9
Asbestosc	USSR = .8/USA = .1	8.0
Arsine	USSR = .3/SWD = .05	6.0
Cadmium oxide	USSR = .1/USA = .05	2.0
Cotton dust	USSR = 6/USA = .2	30.0
Selenium	USSR = 2/USA = .2	10.0
Silicad	USSR = 1/USA = 0.5	20.0
Toluene 2,4-diisocynate	USSR = .5/USA = .14	3.5
Vanadium pentoxide	USSR = .1/USA = .05	2.0

[a] In mg/m^3 except where other noted.
[b] Factor of variance
[c] Fibers/m^3.
[d] 100% SiO_2.

TABLE IV
Comparison of Some Occupational Exposure Limits* and FV Values for the United States

Substance	OSHA	ACGIH	NIOSH	FV
Acrilonitrile	20.0	SC	SC	—
Carbon disulfide	60.0	30.0	3.0	20
Carbon tetrachloride	63.0	30.0	13.0	5
Chloroprene	90.0	45.0	SC	2
Ethylene dibromide	20.0	SC	SC	—
Ethylene dichloride	50.0	40.0	5.0	10
Lead	0.2	0.15	0.05	4
2-Nitropropane	175.0	35 + SC	SC	5
Vinly chloride	2.0	10 + C	2 + C	5

* EL values expressed as mg/m^3.
C = Caracinogen.
SC = Suspect carcinogen.

Thus, the picture for international occupational exposure limits is dismal, although this may not be of much concern to most of you. But, having worked for the World Health Organization (WHO), and having worked with representatives and/or health officials of many countries, these discrepancies in numbers became a real concern because I had some responsibility in trying to explain them, or perhaps more appropriately, in trying to explain them away. Believe me, it can be difficult to explain the status quo of exposure limits, particularly when trying to convince someone that principles of good science are the bases for developing and setting standards and/or guidelines.

Still another aspect of confusion, and one closer to home, is brought about by the practice of multiple recommendations in some countries, as exemplified by our own situation. There are several sources and types of standards or guidelines used in the United States. Perhaps the best known of this group is the ACGIH TLV, but there are the ANSI standards, the old Z-37 Committee of course, and the OSHA standards, as well as NIOSH recommended ELs in the form of criteria documents — more specifically known as *Criteria for a Recommended Standard: Occupational Exposure to —*.

In foreign countries the best known of these is the ACGIH TLVs. As a matter of fact, many foreign nationals equate the TLV to the official standards for the U.S. Many also know of the NIOSH Criteria Documents, and they know that they are recommended by a National Institute in the U.S. An attempt to explain the origins and difference of occupational exposure limits to a foreigner not acquainted with our systems usually results in much confusion, but to appreciate the situation it must be viewed from their perspective, as well as from the examples shown in Table IV.

From these few examples, it is seen that we may be confused also; observe the FV valves for the 9 substances, and draw your own conclusions. The first is acrylonitrile which has an EL of 20 mg/m^3, in terms of the OSHA standard. The 1981 ACGIH TLV booklet shows this substance as being a suspect carcinogen and without an EL; the NIOSH recommendation is the same. The second compound listed is carbon disulfide, with an OSHA EL of 60 mg/m^3, with an ACGIH EL of 30 mg/m^3 and a NIOSH recommendation of 3 mg/m^3; note also that the FV between the extremes is 20. Does this, then, mean that our experts in the U.S. vary in their opinions by such a great degree regarding the "safeness" of exposure to carbon disulfide? Most of us know that this is not the case since the high valve of 60, shown as an OSHA standard, is actually a holdover from what the old ACGIH TLV used to be some years back; this, you recall, was when OSHA came into existance (in 1970) and adopted many of the ACGIH TLVs as standards to be used and enforced under the Occupational Safety and Health Act. However, for those not familiar with this history of exposure limits, guidelines, and standards in the U.S., it can only seem that we are rather erratic since some portion of our experts believe that carbon disulfide exposure is permissible up to 60 mg/m^3 for the working life of an individual, whereas another group of experts believe that exposure to this agent should be at or below 3 mg/m^3, day after day, throughout a worker's time on the job. You and I know, however, that we are not really erratic, since the current ACGIH TLV for this substances is 20 mg/m^3 and not 60 as it used to be when OSHA adopted that value. This means, then, that the more appropriate FV, i.e., the variance between the current ACGIH TLV and the NIOSH recommendation, for all intent and purposes, is 10. But, of course, we know that the published records show that the U.S. has three different EL values for carbon disulfide, these being 60, 30, and 3 mg/m^3. It follows, therefore, that it also should be recognized that this presents a difficult, if not impossible, situation for the outsider looking in.

TABLE V
Comparison of Exposure Limits[a] for Some Priority Heavy Metals

Metal	WHO	OSHA	U.S.A. ACGIH	NIOSH	East. Block[b] MAC	FV (Extremes)
Cadmium[c]	0.02	0.1	0.05	0.04	0.1	5
Lead[c]	.03-.06[d]	0.2	0.15	0.05	0.01	20
Manganese	0.3	5.0	5.0	—	0.3	
Mercury	0.05	0.1	0.05	0.05	0.01	10

[a]Expressed as mg/m^3.
[b]For Bulgaria and/or USSR.
[c]Recommended air and biological limits (WHO).
[d]Depending upon average base Pb=B level of control population.

Such is the dilemma, then, of having to make heads or tails of exposure limits from a broad perspective, or from a completely neutral viewpoint, or as seen by the novice in this field. The World Health Organization has tried to ease the dilemma by convening an expert committee, with participation of the International Labour Organization (ILO), and publishing their findings,[1] but little has changed since that report in 1977. A later Report of a WHO Study Group[2] proposed the "two-step" procedure for establishing occupational exposure limits, hopefully to encourage the recognition of "health-based" recommended ELs as a first step to be developed solely on the basis of scientific evidence as judged by experts. The second step is the translation of the health-based limits into operational limits or standards after discussion between the government and representatives of employers and workers. The operational limits would, therefore, equate to the enforceable limit or standard. By this method the WHO hopes to obtain agreement between international experts in development of internationally recommended exposure limits, and it would appear that it has had some degree of success, inasmuch as its first published effort[2] does represent an international agreement among countries.

Unfortunately, these international efforts will be uncommonly slow in bearing fruit. The above mentioned report is the first of the published recommendations for exposure limits, and deals only with four priority heavy metals, while deliberations have begun on small numbers of priority solvents, pesticides, and dusts.

Table V puts into perspective the final recommendations of the WHO Study Group, relative to ELs from other sources for the same heavy metals. As seen, the cadmium values for OSHA and the Eastern Bloc (Bulgaria) are the same ($0.1\ mg/m^3$), but these are five times higher than the WHO recommended level of $0.02\ mg/m^3$. In the case of lead, the OSHA value[A] is 20 times higher than the Eastern Bloc Countries but only 3.5 to 7 times higher than the WHO recommended value of 0.03 to $0.06\ mg/m^3$. For manganese the recommended EL and that of the Eastern Bloc is the same, but these are 16.6 times higher than the OSHA and ACGIH value. And, in the last instance (mercury) the EL values of ACGIH, NIOSH, and WHO are the same, i.e., all are $0.05\ mg/m^3$, this being 5 times lower than the OSHA EL of $0.1\ mg/m^3$ and 5 times higher than the Eastern Bloc.

Accordingly, the discrepancies are still present in these cases, but generally speaking the wide spread of variance is due to comparison of the rather lenient OSHA exposure limits with the usually stringent Eastern Bloc values. It is pointed out that in the example of the heavy metals, with the exception of manganese, the ACGIH, NIOSH, and WHO values are close, and the NIOSH and WHO values are very similiar.

So how does all of this relate to the specific aspects of the topic at hand, other than showing that there is, indeed, a dilemma if one views exposure limits from their many points of origin or from the international viewpoint?

There are two major aspects of emphasis I would like to make in this regard. First, the impression of confusion and near chaos that is

[A]It is noted that this value is now $0.05\ mg/m^3$ and changes this statement of comparison.

gained by those countries who hope to develop and use their own occupational exposure limits. Secondly, and more directly related to the topic of this Conference, i.e., problems of occupational exposure limits as associated with exposure of the sensitive worker, is the fact that many countries have worker populations with high numbers of individuals who must be regarded as though they are sensitive workers. That is, with almost the same connotation of sensitivity as we in western nations view our relatively rare cases. Workers suffering from malnutrition or diseased from parasitism (or other diseases), as well as unhealthy underaged and overaged individuals, are common to the work force of developing and newly industrializing countries. It is my impression from experience that many of these countries would like to make a beginning attempt at occupational exposure limits, but do not know where to begin. Because of the lack of adequate health services these countries, either unknowingly or knowningly, employ high numbers of workers who are unhealthy and unfit for the work they must do. Moreover, the concepts and practices of personal protective equipment in guarding against harmful exposure of workers are woefully lacking; hence, great numbers of individuals are at risk, and that the risks are generally far greater than anything that has been experienced in the U.S. since before World War II. At any rate, these are the countries who need and should have tight, or stringent, exposure limits for workplace agents, yet they are, at the same time, the countries who prefer not to have stringent limits because of economic factors; that is to say, they feel that they cannot afford to penalize their industries by having them control to hard to-attain exposure limits or standards.

This does not, however, completely let them off the hook and they know it. They realize that they should, at the very least, have a contingency plan for occupational exposure limits, this being one which can be measured against a plan of operational exposure limits which are more lenient and to be used with the idea that there would be a continuing improvement toward more exacting limits. These countries require some plan of this type so as to permit systematic phase-in of rigorous standards at a pace commensurate with growth and successful industrialization. It was partly for this reason that WHO recently suggested the aforementioned "two-step" procedure for establishing occupational exposure limits. However, unless something can be done to speed up the snail's pace of the approach taken by WHO, the dilemma will be with us for a long time to come. This is not meant as malicious criticism, since I am fully aware of their problems of financing such programs, and these same drawbacks are faced by the ILO, although this latter Organization does have the capability of a mechanism which could put in place a scheme for two-phase exposure limits appropriate for new industrializing and developing nations. Such a scheme would, of course, require a combined effort from both the ILO and WHO, which essentially means support from all developed nations; most of all it would be requisite that WHO and ILO present a unified front to these countries, rather than their usual image of bickering and petty jealousy.

If these two agencies could work together in harmony, and if two-phase (or multi-phase) exposure limits were established solely for the purpose of giving new industrial nations something to start with, it is very likely that the highly industrialized countries would acquiesce; I say this because it would not be the same as trying to convince them of the merits of a single internationally accepted listing of occupational exposure limits. Rather, it would be a listing of recommended "start-up" exposure limits. In some ways a start-up EL would be a prelude to what is referred to as "operational" by recent WHO terminology; the fundamental difference being that start-up as used herein would recommend limits for first use, these attainable and reasonably safe, but not as fine-tuned as the exposure limits which a country might, and should, ultimately choose as standards. A start-up EL, therefore, could be thought of as an interim standard, but would not reflect the political process of the operational limit proposed by WHO. In brief, then, the start-up EL could be defined simply as a composite of what is already available from countries who have been using experience limits all along, whose value is generally somewhere between the extremes of EL values used by those countries.

I can already hear some of the comments in response to this suggestion: namely, "*. . . it makes second rate citizens out of worker populations in developing countries,*" or "*. . . reasonably safe occupational exposure limits are not good enough,*" and similar, or more caustic, remarks. Consider,

however, the real liklihood (perhaps fact) that without some form of two-phase (or multi-phase) guidelines to choose from, most countries in the throes of beginning industrialization will not make a serious effort to reduce or control occupational exposures. This was one of the rationale of the WHO Study Group[2] which said,

> *"The difference in existing exposure limits have led to uncertainty in the choice of values to be implemented in many developing countries, and may have been instrumental in delaying the protection of workers from harmful agents."*

Moreover, rather than accept "impossible" values, most countries will adopt none, and I have heard it rationalized by saying *". . . the U.S and Western countries went through the growing pains and tribulations of becoming industrialized, so why not let the newly emerging countries do the same?"* In a manner of speaking, this is somewhat analogous to saying that they should be permitted to have their epidemics of diseases since we were permitted to have our own, or never mind the experiences of others, as we want to do our own thing.

Accordingly, the commonality of this paper and this Conference on Sensitive Work populations rests mostly on the contention that occupational exposure limits are in a terrible mess — at least from an international viewpoint, and that many countries have worker populations comprised of sensitive individuals who might stand a better chance for protection from exposure in their place of work if the use of two-phase (or multi-phase) exposure limits were made acceptable to their governments.

This could be accomplished if the ILO would take the initiative, asking for WHO cooperative input, to convene a meeting of international stature for purposes of developing a list of start-up exposure limits. Attendees should be notified that the foremost objective would be to develop such a list of EL values, each of which would be merely a composite, and generally a median, of the ELs currently on the books of the 18 or so countries who have them. It should be made clear that such a meeting would not, therefore, be a battle ground of crusaders for either more severe or more lenient limits, but for the purpose of giving guideline values which are reasonably safe and attainable, to be used by those countries wishing to first begin with start-up and operational limits before going to full-blown, fine-funed, standards.

Such a listing could prove invaluable if published in conjunction with the ILO Publication No. 37, *Occupational Exposure Limits for Airborne Toxic Subtstances*,[3] which is due for updating. Since the aim of Publcation No. 37 is to provide a tabulated form of review of exposure limits, it would serve as the ideal format for additional entries of values designated as start-up ELs. In this way, the publication would offer a resource far more meaningful and useful to individuals and/or representatives of newly emerging industrializing countries, as well as serving in its usual capacity for persons whose nations/states/organizations already represent advanced industrialization.

At least, if this were accomplished it would be another step toward some measure of protection for the truly sensitive worker populations which currently exist in so many countries of this changing world. It seems that they would fare better with start-up limits than if there were not any exposure limits in place or if exquisitely fine-tuned limits were there in name only, but never put to use — as is the case in some of the developing, as well as developed, countries today.

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Development of hygiene guides*

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Background

The American Conference of Governmental Industrial Hygienists (ACGIH) Subcommittee on Threshold Limits, with Bill Fredrick as chairman, was formed in 1941. It originated from a desire to bring some order and unformity to the then existing situation where various state and local industrial hygiene units had their own, and often conflicting, industrial air standards. Although this committee's activities were delayed somewhat by World War II, a list of 148 Maximum Allowable Concentration (MAC) values was submitted in 1946. This was the beginning of an activity which presently provides exposure guidelines for over 650 compounds with methodology was buried by the no threshold dose concept. True scientific interchange of varying points of viewwas overcome by emotional dialogue and accusations. Fortunately, the committee did not over-react to this situation. The carcinogenic hazard has taken its rightful place in the TLV process, but has not become the over-riding issue in establishing exposure guidelines.

The effects of compounds on the unborn fetus as well as on male and female germ cells pose another difficult problem of recent origin in the hazard evaluation process. In reality, this problem has the potential for more emotional interplay then the chemical carcinogenesis problem. Hopefully, the disciplines of industrial hygiene, occupational medicine, and toxicology are scientifically better prepared to handle this problem than we were during the era of the "carcinogen of the week."

Increasingly stringent regulations governing the use of human subjects in experimentation will continue to reduce this source of information for setting chemical exposure limits. Retrospective epidemiology is of use primarily for determining the success or failure of past exposure limits. Therefore, data from animal studies will be increasingly relied upon for establishing new TLVs. Extrapolation of animal toxicity data to the human has been, and continues to be, a subjective and difficult process. This task is made more difficult by the large number of studies which make no effort to provide dose-response information. The former NCI Chemical Carcinogenesis Bioassay is a case in point. These studies, by admission, were designed to determine the potential of a chemical to invoke a carcinogenic response rather than defining the associated carcinogenic hazard. Yet the TLV Committee, as well as other standards setting groups, continue to attempt to use these types of studies in hazard evaluation. A similar situation exists with the use of *in vitro* methodology, especially in the area of genetic toxicology. Unfortunately, the cost of a well-designed, multiple concentration, inhalation study which defines and correlates genetic, carcinogenic, and other toxic responses in a dose related manner will limit such studies to chemicals which are produced in large volume and are widely used.

Future

Addressing the future of this committee or any other group in the hygienic guidelines arena is somewhat hazardous. I am continually reminded by individuals everywhere of the importance and impact of the deliberations and recommendations of this committee. It is often more difficult to maintain excellence once attained than it is to obtain it initially.

We are all aware of the changes that have occurred in the area of occupational health standards during the past decade. This has certainly contributed to the large increase in volume of the literature covering chemical toxicology. Unfortunately, this increase in volume has not been accompanied by a relative increase in the studies which are directly applicable to establishing hygienic guidelines. Selection of those studies, which

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should be included in the TLV supporting documentation, is becoming an increasingly time-consuming task for the committee members.

The committee, throughout the years, has managed to remain an apolitical body. I am aware that at various times in the past, it has been accused of favoring one viewpoint over another. However, this is only natural considering the environment in which we operate. If the committee is to maintain a reputation of making decisions only on the scientific information available, it must cooperate with, and solicit information from, all available sources including industry. Above all, it must be certain that proper consideration is given to solicited information. As a toxicologist, I know of nothing more disgusting than to have an organization encourage research on a compound and subsequently find that the results are considered only if it supports preconceived opinions concerning a recommended exposure level.

The committee must continue to incorporate new technology which will provide an improved scientific basis for the TLV process. A prime example is the use of pharmacokinetics (toxicokinetics) in the animal to human extrapolation process. The use of kinetics to explain the observed species differences in experimental responses to chemical injury should begin replacing the more traditional "most sensitive species" methodology used in the past. Although kinetics has been employed for such purposes in pharmacology and the pharmaceutical industry for years, there seems to be a reluctance among those of us in the chemical hazard assessment area to employ such methodology. This possibly reflects the inability of some of our more traditional toxicologists to deal with a technology with which we are not completely familiar. We certainly must recognize that such technology may very well challenge the premise that the human is always more sensitive than is the animal to chemical injury.

Conclusion

I have tried to provide a short summary of my personal opinions concerning the status and problems facing a committee on industrial hygiene guidelines striving to serve an increasingly needed function and maintain the excellence it has attained. Given the situation in which we find ourselves in the 1980s, how long can a group of twenty-five volunteers continue to function as we have in the past and maintain this excellence? I do feel that an ever increasing commitment of time and effort from the committee members as well as possible additional resources from the ACGIH may be needed or we face the danger of mediocrity resulting from a poorly accomplished task.

Dr. Carter received an MS degree in pharmacology from Ohio State University and a doctorate in veterinary medicine from Auburn University. His career in toxicology was spent primarily in the U.S. Air Force. He was serving with the Toxic Hazards Division, 6570th Aerospace Medical Research Laboratory at Wright-Patterson AFB when he became Chairman of the Chemical Substances TLV Committee in 1980. He is currently Associate Dean of the College of Veterinary Medicine, Ohio State University.

HERBERT E. STOKINGER LECTURES

The Herbert E. Stokinger Lecture and Award was created to give recognition for outstanding contributions to the broad field of industrial toxicology. The award was established in 1976 by the Board of Directors in honor of Dr. Stokinger's many years of service to ACGIH as Chairman of the Chemical Substances TLV Committee, and to the science of toxicology. The first lecture was given in 1977 and is an annual feature of the American Industrial Hygiene Conference.

The first five lectures (1977-1981) are reprinted in this publication. The fourth Stokinger Lecture appears in full as a part of the Introduction. The lectures after 1981 appear in the Annals of American Conference of Governmental Industrial Hygienists.

An acceptable level of exposure*

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Consultant

I consider it a great honor that the American Conference of Governmental Industrial Hygienists selected me to receive the first Herbert E. Stokinger Award and to have the privilege of delivering the first Stokinger Lecture, and I thank you for that honor and privilege. Fortunately, this is not a memorial lecture, and I am doubly pleased that Herb Stokinger is here with us to experience the honor that the ACGIH has bestowed upon *him in his lifetime,* and because I have known Herb as a friend and fellow toxicologist for some thirty years.

Herb Stokinger has made many contributions to the field of toxicology and industrial hygiene in the course of his career, but one of the major contributions must be his work as Chairman of the Threshold Limits Committee of the American Conference of Govermental Industrial Hygienists, and it is for this reason that I decided to discuss today some aspects of the concept of an acceptable level of exposure; for if there is such a thing, Threshold Limit Values have scientific meaning. If, on the other hand, there is no such thing as a no-effect but finite level of exposure, then the TLVs must be considered in terms of that which is socially and politically acceptable, rather than in terms of what is scientifically correct.

Toxicity, the capacity to produce serious bodily injury or death, is an inherent property of every chemical substance. It is manifested when the substance is taken into the body in sufficient amount. Even those substances which we ordinarily think of as nontoxic, such as sugar, salt or water, possess the inherent capacity to produce serious bodily injury or death, but to a slight degree relative to other substances which we ordinarily think of as highly toxic.

Some of these substances which exhibit a high degree of toxicity were known to the ancients. Pliny, Hippocrates and Galen wrote of the toxicity of lead; Pliny and Galen as well as others described the toxic effect of mercury; and Aristotle, Galen and Livy were among those who described the toxicity of fumes from burning charcoal. Socrates, as you will recall, was executed by being required to drink a cup of poison derived from hemlock; and the word toxicity is derived from the Greek "toxikon pharmakon," bow drug, or as we would say arrow poison. A *toxicologist* is an expert in poisons, but a *toxocologist* is an expert in archery.

The early knowledge of poisons was empirical, and recorded information was confined to description of effects caused by relatively ordinary doses or exposures. Moderate or slight toxicity was not recognized, and it is likely that the ancients believed that most substances did not possess the property of toxicity. Hence their understanding of toxicity was largely qualitative. Yet even then there was some understanding of the relation between dose and effect. In Plato's account of the execution of Socrates, he mentions that the jailer brings Socrates the cup of poison. Socrates asks: "What do you say about making a libation out of this cup to any god? May I, or not?" The reply was: "We only prepare, Socrates, just so much as we deem enough." And if we wonder how the jailer knew how much was enough, we can imagine that he was drawing on experience from earlier executions, out of which came a knowledge of how much was needed to obtain the desired effect.

In pursuing the trail of quantitative toxicology a little farther, I should like to mention the contribution of two workers, one from the 15th and one from the 16th century. In the year 1473 a German physician, Ulrich Ellenbog[1] wrote for the benefit of goldsmiths and other metal workers a little treatise on the toxic vapors and fumes associated with metal working. He described the injurious effects of vapors and fumes from silver, mercury and lead, as well as the toxic effects of fumes from burning charcoal, which we now recognize as carbon monoxide, and he also offered advice on how to avoid these effects. The advice was simple. Work in the open if possible. If you must work indoors,

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open the windows. Turn your face away and keep your mouth closed. Protect yourself as much as possible. This litte tract may be the first publication on industrial hygiene.

Then, in the 16th century the physician-alchemist Theophrastus Bombastus von Hohenheim, known as Paracelsus, enunciated a very important and fundamental principle of quantitative toxicology. Paracelsus had some revolutionary ideas about the treatment of disease. He introduced specific remedies for specific diseases, including the use of mercury for the treatment of syphilis which was, at that time, a much more lethal disease than now. Like many innovators his ideas were condemned by the establishment. He was accused of using poisons to treat disease. Paracelsus enjoyed controversy and published a series of defenses in rebuttal. In the Third Defense,[2] written in 1538, he said: *"Was ist das nit glfft ist; alle ding sind glfft und nichts ohn glfft/Alleln die dosis macht das eln ding keln gift ist"* or "What is it that is not poison? All things are poison and none without poison. Only the dose determines that a thing is no poison." The usual quotation attributed to Paracelsus is from a later Latin translation which reads: *"Dosis sola facit venenum"* or, "The dose alone makes a poison."

If you stop to think about it, the work of the industrial hygienist and the efficacy of industrial hygiene measures depends upon the validity of the Paracelsus principle. My own opinion is that Paracelsus was right, or at least right enough for all practical purposes, and I would not anticipate too much disagreement from those who are engaged in the practice of industrial hygiene. But this is parenthetical.

The Industrial Revolution produced among other things an abundance of occupational injuries and intoxications. In 1831, Dr. C.T. Thackrah, a pioneer in British industrial medicine, noted that miners seldom attained the age of 40, that fork grinders who use a dry grindstone die at the age of 28 or 32, and that table knife grinders, on the the other hand, who use a wet stone survive to between 40 and 50. He further stated:

> *"Most persons who reflect on the subject, will be inclined to admit that our employments are to a considerable degree injurious to health . . ."*

and he added:

> *"Evils are suffered to exist, even when the means of correction are known and easily applied. Thoughtlessness or apathy is the only obstacle to success."*

If we ask why easily remedied evils were suffered to exist in 1831, the following brief quotation from the Cambridge Modern History may be enlightening:

> *"The Bolton cotton spinner of 1842 had no need to keep his children in health, or his house healthy; his wife could with absolute impunity let the babies die, the whole household was free, in fact to live practically as it chose, even if it infected and demoralized the neighborhood."*

It is interesting that in this period, less than 150 years ago, social and political concerns over health and safety ran far behind scientific knowledge of the cause and prevention of illness and injury. We know, of course, that all this changed, and the change occurred long before the Occuptional Safety and Health Act of 1970, or the establishment of the Environmental Protection Agency.

It is my impression that the change in attitude toward occupational illness and injury occurred largely because of economics. The Industrial Revolution brought more and more people into work environments which produced ever increasing numbers of disabilities which rendered employees unfit for further work. The employers, quite naturally for that time, simply dropped them from the payroll and they became a charge on society as a whole. It then began to appear reasonable to legislators in various industrialized countries that the industry responsible for occupational disabilities should bear their cost rather than the general public.

Germany led the way in 1883 with the passage of a Workingmen's Insurance Law which set up an insurance fund into which both workmen and employers paid up to 6 percent of the workers' annual earnings. For this, the worker obtained free medical care and treatment, as well as some compensation during periods of disability.

Since insurance premiums depend upon the payout, and since both workers and employers were paying the premiums, each now had an

economic incentive for minimizing the payout, and each group developed an interest in applying available remedies which would reduce disabilities.

In the year 1914, the first American book on occupational disease was published. It was written by W.G. Thompson, M.D., and he showed a rather modern outlook on occupational disease. According to Dr. Thompson:[4]

> *"It is quite true that many processes of manufacture will always involve risks to health, as many trades necessarily involve risk to limb and life. One cannot handle white lead without risk of disease, just as one cannot use dynamite without risk of injury. Yet, in each case the workman has the right of warning against the hazard, the right of such protection as modern scientific knowledge affords, and should have the right of compensation when disabled as a result of the lack of such warning and protection."*

I have no difficulty in endorsing Dr. Thompson's statement as of today. And I think it was accepted by responsible employers well before OSHA and EPA came into being. In fact, it was at about the time of Dr. Thompson's writing that some of the larger industries began hiring full time medical directors and physicians to provide onsite medical services. No law required that they do so.

The organic chemicals industry in the United States was born after World War I. Employers and employees with no previous experience in making and handling organic chemicals began encountering the side effects of unanticipated toxicity. That toxicity was not wanted; it was counterproductive; it was a problem among other problems. Problems had to be managed if the industry was to survive.

To manage a problem it must be anticipated, the causes must be indentified and analyzed quantitatively, and practical means of prevention must be available. To this end we saw the birth of industrial preventive medicine, of experimental toxicology, and of industrial hygiene, sponsored by government and by industry and by a few universities.

By 1938 there were enough government affiliated people engaged in the practice of industrial hygiene to make possible the founding of the American Conference of Governmental Industrial Hygienists. In 1939 the American Industrial Hygiene Association was founded. They sought to bring collective knowledge and skills together in order to achieve a sound basis for all to carry out their responsibilities for recognizing, evaluating and controlling those hazards and stresses of the workplace which cause occupational illness and disability, or even discomfort and reduction in efficiency. Above all, they believed in the possiblity of control of hazards through reduction of exposure to an acceptable level.

The American Conference of Governmental Industrial Hygienists took the lead in publishing and updating annually a list of atmospheric exposure levels deemed to be acceptable, the Threshold Limit Value list. This list has served a very useful and practical purpose. It is known, respected and used all over the world. It reflects great credit on the ACGIH, the TLV Committee, and its long-term Chairman, Herb Stokinger.

This audience knows that the numbers in the TLV list were never meant to be guaranteed safe levels of exposure for all exposed workers under all conditions. They were meant to be guides for the professional industrial hygienist who would take into account such modifying factors as temperature, pressure, hours of work, individual hypersusceptibility and possible aggravation of preexisting conditions. Until a few years ago, the preamble stated that the TLVs were not suitable for use as legal limits of exposure.

With respect to the last point, they were adopted by some state governments and by the Federal government as legal limits anyway. The 1968 TLV list was incorporated into the regulations of the Walsh-Healy Public Contracts Act, and was borrowed from those regulations for incorporation into the regulations of the Occupational Safety and Health Act of 1970.

It may well be that regulatory agencies will, in the future, publish their own competing lists of permissible exposures, and that these, because they will have the force of the law, may lead the ACGIH to abandon its efforts to maintain, revise and update its TLV list. I hope not, because your list will still have the respect of, and utility for, the professional industrial hygienists around the world that it has enjoyed in the past so long as the numbers represent the best judgment of qualified profes-

sionals, unbiassed by political considerations, as they have been in the past.

The industrial hygienist who is able to keep his levels of exposure below the TLV limits is not guaranteed freedom from any problem whatsoever, but if a problem does occur it should be manageable, and that is very important. One can say almost the same kind of thing for speed limits on the highway. An accident can occur while you are operating within a speed limit. It may not occur when you exceed the speed limit. But if an accident does occur while you are operating above the speed limit, it will be more severe and less manageable than if you are operating within the limit.

Today the big topic of discussion about acceptable limits of exposure concerns those chemical substances which might possibly induce cancer. Cancer is the second most important cause of death in the United States. The cure rate is not impressive. The process of dying may be painful, prolonged and expensive. If we had a choice with respect to our mode of death, not many would elect cancer.

You will recall that Percival Pott in 1775 associated soot with scrotal cancer in chimney sweeps. By the close of the 19th century, solar and ionizing radiation, arsenic, coal tar and certain petroleum fractions had also been associated with skin cancer. In 1895, Rehn, in Germany, associated with bladder tumor among workers in the aniline dye industry with exposure to aniline. He was right about the bladder tumors but wrong about the causative agent. But late as 1952, Professor William Salter of Yale, in his *Textbook of Pharmacology*,[5] stated that only three unadulterated agents were known to cause cancer in man, these being 1) radiation, 2) beta-naphthylamine, and 3) arsenic.

We have come a long way since 1952, only twenty-five years ago. Today the National Institute of Occupational Safety and Health lists some 1500 chemical substances as, in some way, associated with the production of neoplasms or cancer according to the published literature.

Faced with the knowledge that many rather than few chemicals possess to some degree the potential to induce cancer, it is natural that the public has gotten the impression that the environment is a sea of man-made carcinogens; that this accounts for the importance of cancer as the second leading cause of death.

This thought could not have been expressed better than it was by Ralph Nader, who spoke at a symposium conducted by the U.S. House of Representatives on January 12, 1976. Mr. Nader's opening statement made three points: 1) experts now believe that 60 percent to 90 percent of all cancer is caused by environmental factors; 2) each year industry introduces thousands of new chemicals into the environment; and 3) we should stop calling it "environmental" cancer and call it "corporate" cancer. If Mr. Nader is right, we industrial toxicologists and industrial hygienists have failed badly in our obligation to both workers and the public. But most of those in this audience could demonstrate quite easily that Mr. Nader's arguments are nonsequitur.

He is right in his first point about the opinion of experts, but the environmental factors of which they speak are not the factors in Mr. Nader's mind. As to the second point it is quite possible that thousands of new compounds are, or may be synthesized each year, but only a few enter the environment in significant amounts. Finally, occupational or environmental exposure to specific carcinogens is responsible for a relatively minor proportion of cancer deaths. In our present state of knowledge, it would be grossly incorrect to speak of "environmental" cancer as "corporate" cancer.

Dr. Irving Selikoff,[6] speaking in Milan in December 1975, described what he called the Paradox of Rehn in the following words:

> *"In 1895, Rehn reported the first three cases of cancer of the bladder among anlline workers. When additional cases of this association were identified in the next 15 years ln Germany and Switzerland, lt was projected that the developing chemical industry, wlth lts increasing number of synthetic chemicals new to the human environment, would brlng wlth lt a host of problems and an unhappy harvest of cancer. This prediciton ln the next decades seemed far from unreasonable when our colleagues demonstrated carcinogenicity ln literally hundreds of chemicals ln animal test programs. Yet, by and large, the prophecy was not seen to be fulfilled ln the first half of the 20th century. Even until recently, human*

chemical cancers have been relatively few and seemingly restricted in type and number, almost as exceptions to the broad spectrum of human cancer, viz. beta-naphthylamine and benzidine bladder cancer, radium neoplasms, coal tar skin cancers, etc.

"Thus, until recent years, we were faced with something of a paradox; Rehn and his contemporaries had shown that human cancer could result from chemical industry exposure, laboratory studies indicated that the agents could be varied and numerous, yet human experience had not demonstrated this to be a major problem.

"In recent years, the question has again been put before us in pressing terms. Do experiences with vinyl chloride, bis-chloromethyl ether, chromates, etc., demonstrate that the prophecies were really correct, merely premature? We do not yet know, but the question is an important one and must now be addressed."

Dr. Selikoff's remarks were made exactly one month to the day, before Mr. Nader's, so the two opinions do not reflect a substantial interim change in the state of knowledge. Perhaps we have not done such a bad job in industrial hygiene after all, for if agents of demonstrated carcinogenic potential have not produced the predicted unhappy harvest of cancer, it seems to me that exposures have been kept below the effect level for the most part.

In making this last statement, I realize that I have expressed a personal bias. I believe that no-effect levels exist for carcinogens, but other scientists believe just as firmly that there is no threshold for carcinogens. I find it hard to explain why, if they are correct, we have this Paradox of Rehn. Indeed, I find it hard to explain why four or five of us do not die of cancer when we are exposed from birth on to small amounts of such naturally occuring carcinogens as ultraviolet radiation, background ionizing radiation, aflatoxins and others.

The ACGIH has established TLVs for certain carcinogens, and this indicates that your belief coincides with mine that, for practical purposes, thresholds for carcinogens exist, and that in some cases, at least, we may be able to recognize acceptable limits of exposure. Nevertheless, we might look briefly at the arguments.

The no-threshold believers point to the fact that cancer involves a DNA mutation. One molecule of carcinogen, or one hit with ionizing radiation can, in the laboratory, react with one molecule of DNA and produce a mutation. That mutated molecule of DNA may, in the body, be self-replicating. If it is, cancer is born, and it is only a matter of time until tumors appear.

On the other hand, there is a long step between a molecole and an organism. The organism has defenses which the molecule does not possess. Carcinogens may be detoxified before they reach a vital target. Genetic damage can be repaired. If a cell does become malignant, it may be dealt with by the body's immunological defenses. We know that they exist, and the present status of our knowledge is reviewed in the May 1977 issue of *Scientific American* by L.J. Old of the Sloan-Kettering Institute. We know that there is a dose: disease effect for carcinogens, as there is a dose: effect relationship for other toxic manifestations. We see it in the laboratory. As the dose of carcinogen is increased, the proportion of animals getting tumors is increased and the proportion which does not get tumors is decreased. As we lower the dose, the proportion of the animals which get tumors is decreased. In the laboratory one can find a dose which does not produce any excess tumors within the lifetime of the animals under test.

This latter point, "within the lifetime," becomes important. As the dose of a carcinogen is increased, the proportion of exposed animals developing tumors is decreased. As the dose of carcinogen is decreased, the proportion of exposed animals developing tumors is not only decreased, but the time to appearance of tumors is increased. Druckerey,[8] in Germany, proposed a mathematical relationship which is very simply expressed:

$$Dt^n = k$$

Here D = total dose of carcinogen, t = time to appearance of tumors, and n is an exponent greater than one which expresses relative potency of the carcinogen. In Druckerey's own experiments with multiple dose levels of a potent carcinogen, he eventually reached a low dose level which did not produce any tumors. He reasoned, by extrapolation, that this dose would have produced tumors if only the animals could live long enough.

A World Health Organizaiton Scientific Group[9] commented on the phenomenon as follows:

> *"The summation effect described by Druckerey and others is not questioned and his equation characterizing carcinogenic potency may be accepted. Nevertheless, every organism has a limited life span and in this sense there is, for each individual a real threshold."*

I think we should let the case rest here, but we are still faced with the dilemma of defining an acceptable level of exposure for carcinogens. Every method of estimation, as is true for all substances on the TLV list, involves extrapolation and extrapolation by definition involves uncertainty. We cannot estimate a safe level of exposure for any individual and guarantee the result. As the late Homer Smith[10] pointed out some 30 years ago, the normal probability curve is a graphical epitome of nature, a cabalistic symbol of her compounded mysteries and we don't know where we, as individuals, fit on that curve.

Nevertheless, we can set a goal which I believe is attainable. That goal would be to keep the incidence of toxic effects, including cancer, within the background noise level. The Paradox of Rehn suggests that we have done this in many cases without knowing it. In many instances the arbitrary safety factors which we have been using to establish presumed safe levels of exposure in the workplace have been validated by experience, and this may explain the Paradox of Rehn. Dichlorobenzidine, for example, has been shown to be carcinogenic for three species of laboratory animal. It produces bladder tumors in the dog. Yet there is no epidemiological evidence that has produced an identifiable excess of tumors in those manufacturing and using it. I interpret this as indicating that the conditions under which dichlorobenzidine has been made and used have resulted in exposure levels which were not discernible effect levels. I see no reason why dichlorobenzidine, given sufficient exposure, would not produce tumors in man.

Where there has been a sufficiently long period of human exposure to a substance, it may well be worthwhile to do retrospective epidemiologic studies to see whether any peaks of disease have emerged above the noise level. If such peaks have emerged, as they did with asbestos, vinyl chloride, bis-chloromethyl ether, and a few others, we know that exposure levels were too high. They must be lowered. We know also that such retrospective epidemiologic studies have been fraught with difficulties of our own making because we didn't keep good records of people under risk or of their levels of exposure. We can make the epidemiologic tool much more serviceable in the future if we recognize that error and keep good records from now on.

When new chemicals are proposed for commercialization, we should characterize their toxicity potential in advance of marketing. Some companies have been doing this for many years, but I will wager that some in this room will receive at this meeting offers of employment from companies which heretofore had not felt the need for toxicologists or industrial hygienists.

We should remember that each toxicity test is designed to answer a specific question and only that question. Acute toxicity tests, for example tell us nothing about chronic toxicity. We must decide what tests are appropriate for evaluation of the toxic potential of a given chemical substance under all reasonably foreseeable conditions of use. And, of course, the testing procedures must be valid and the results must be interpreted properly. With application of appropriate safety factors we may well be able to estimate acceptable levels of exposure, i.e., levels which produce no identifiable incidence of toxic effects. We have succeeded in doing this many times in the past. We have not always succeeded but failures have occurred too often because of ignorance and apathy in the application of existing knowledge.

One thing we can count on. The lower we can hold exposures below the level which we estimate to be safe, the less chance there will be for a problem to arise. Human exposure should be minimized where it is practical to do so. But on the other hand, I do not think it is productive to concentrate on leveling molehills when there are mountains in our path.

In summary, I believe that industrial toxicology and industrial hygiene have accomplished a great deal in this century. We still have a great deal to accomplish. We will not be able to eliminate all risk from our employments. We will not be able to calculate guaranteed safe levels of exposure. But if we can, at this time estimate exposure levels which would keep toxic effects below that point where

they emerge from the background and become identifiable, I would characterize those levels as acceptable levels of exposure for now. If, in time, we can reduce the noise level, we shall be able to detect small peaks and deal with them.

At this point I should like to close by expressing a wish on behalf of myself and all of us to Herb Stokinger. It consists of two lines from Goethe's "Faust" and goes as follows:

> *"Gesundheit dem bewahrten Mann Dass es noch lange helfen kann."*

or, as it appears in one of the translations of Faust:

> *"To him, preserved, good health, good will, and may he live to help us still."*

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Dr. John A. Zapp, Jr., was director of DuPont's Haskell Laboratory for Toxicology and Industrial Medicine for 24 years before his retirement in June 1976, and is now a consultant to DuPont and Mobil Oil Corporation. He received his Ph.D. in physiological chemistry from the University of Pennsylvania in 1938. Before joining DuPont (in 1946), he was a commissioned officer in the U.S. Public Health Service (R) serving with the U.S. Office of Civilian Defense, the National Defense Research Committee, and the Chemical Warfare Service.

Dr. Zapp was born June 22, 1911, at Pittsburgh, PA. He was graduated from Harverford College in 1932 with a Bachelor of Science degree. He then took post-graduate work in biochemistry at the University of Pennsylvania, receiving his Master's degree in 1934 and his Doctor of Philosophy degree in 1938. From 1932 to 1943 he served as an assistant instructor and instructor in physiological chemistry at the university's School of Medicine, and as instructor in research medicine.

Dr. Zapp is a member and past president of both the American Industrial Hygiene Association and the Society of Toxicology. He is a consultant to the Department of Environmental, Public and Occupational Health of the American Medical Association, and is certified in the practice of toxicological aspects of industrial hygiene by the American Board of Industrial Hygiene. He is a fellow of the American Association for the Advancement of Science and the American Institute of Chemists, and serves on the committee on ethics of animal and human experimentation of the Society of Toxicology.

Dr. Zapp is a member of the American Academy of Industrial Hygiene, the Permanent Commission and International Association on Occupational Health, the American Chemical Society, American Physiological Society, American Society for Pharmacology and Experimental Therapeutics, the American Statistical Association, and the Biometrics Society. He is an honorary member of the American Academy of Occupational Medicine, and a member of the University of Delaware Research Foundation. He is the author of over forty publications in the field of toxicology, industrial hygiene and industrial preventive medicine.

Industrial health in 1978: a perspective*

RALPH C. WANDS
Cosmetic Ingredient Review

This discussion, presented at the 1978 Herbert E. Stokinger Award Lecture, focuses the attention of toxicologists and industrial hygienists on some problems of today, predicts some for the future, and suggests how some may be resolved. One of today's primary problems is the prediction of human effects from animal data, including those from in-vitro techniques. More inter-species bridges of comparative data on pharmacology, biochemistry, pharmacokinetics, pathology, and physiology are needed for reliable estimation of human risk. This estimation needs to be confirmed by improved reliability, specificity, and sensitivity of our epidemiology. It is suggested we may soon have our first example of a chemical carcinogenic to animals and non-carcinogenic in humans. A consortium of professional scientific organizations, the National Council for Human Protection, is proposed as a powerful voice for science in the Washington arena.

Introduction

Dr. Craft, officers and members of the American Conference of Governmental Industrial Hygienists, ladies and gentlemen, we pass milestones every day in our lives and seldom notice them. There are some that are counted for us by those who love us, such as our first baby tooth and perhaps the day we die. In between there are a few that each individual treasures. Today is such a one for me. To be given the Herbert E. Stokinger award by my peers is certainly one of the milestones of my life. It ranks along with the day I had the good fortune and sense to marry the infinitely patient Jeanette Morgan, and the subsequent birthdays and commencement days of our children.

By so honoring me today for the skills and services I have contributed to industrial toxicology, and thus to the broad area of occupational health, you also honor my mentors who in large part have made me whatever this Conference found worthy. In addition to the faculties of Kent State and Minnesota who laid the groundwork, let me name a few whom I hold in particular esteem as responsible for me. (That's a horrible thing to blame on anybody!) Dr. Stokinger himself, with his patient and witty guidance; my predecessor in this award, Dr. Zapp; others such as Harry Hays, V.K. Rowe, Arnold J. Lehman, W.F. von Oettingen, Harold Hodge, Horace Gerarde, and Henry Smyth have been the source of much of my toxicology. On the industrial hygiene side of my career which is completely intermingled with the toxicology work—just as it is in our profession, I look to Harold Paulus, the Crawley brothers, Bill Fredrick, Bob Eckardt, Howard Kusnetz, Ken Nelson, Anna Baetjer, Charles Bergthold, and lots of you in the audience.

Discussion

I have chosen as my topic "Industrial Health in 1978: A Perspective" and I will touch on some of the problems we face today, predict some for tomorrow, and suggest how we might resolve some of these.

Fifty to one hundred years ago our society was in the era of industrial laissez-fair in which working conditions and manufacturing methods were almost primitive. Out of that social system we saw two things develop. The first, and strongest, was unionism; the second was industrial hygiene. It is interesting that only recently have the unions employed full-time industrial hygienists even though the basic goals of employee protection are the same. This may indicate a shift of emphasis by the unions from dollars to health and safety. I hope they at least use industrial toxicologists as consultants.

There is a strong trend in our society today that I call the industrial regulatory era. Some of those among us would say that the regulatory officials are acting as though working conditions of the laissez-faire era were still with us. Yet I doubt if any of us would eliminate the regulatory agencies.

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Within today's regulatory system there is a refreshing system called the IRLG, Interagency Regulatory Liaison Group, consisting of the heads of CPSC, EPA, FDA, and OSHA. They and their staffs are workings hard to coordinate and, insofar as possible, consolidate their regulatory requirements for information and testing as well as the standards which they issue. This is a good move one wonders why it wasn't done before.

As most of you know, there are numerous teams of people from each of these agencies working on such things as coordination of literature searching, data collection, and preparation of standard toxicology testing procedures. Let me call your attention to some of the things that are taking place. I learned last Friday that a young man at EPA/TSCA who holds an M.S., as do I, is using Brian McMahon's text to draft a standard protocol for epidemiology. Mr. Jellinek, Associate Administrator of EPA for TSCA, has recently announced[1] that he looks upon his TSCA information-gathering system as a "support service" for the Occupational Safety and Health Administration. That's the kind of cooperation the IRLG is providing. He further said that it was "not out of the question" for EPA in the future to offer "incentives" for companies "to tattle on each other."

Mr. Jellinek[2] also said last December that in calculating risks and benefits to society, "We must ask the following questions in deciding what action, if any, to take on individual chemical substances:

What health hazards does the chemical pose?
Does it cause cancer? Birth defects?
Does it damage growing fetuses?
Are there other health problems?"

These indicate the concerns and levels of toxicology understanding at high levels in EPA.

Public concern for hazards posed by chemicals is not new. Neither is the lack of appreciation for their benefits when properly used. Years ago when I was a graduate student I earned a little extra money by painting and paperhanging. One day I was papering a ceiling for a lady who was berating all those horrible chemicals that were getting in our lives and she said, "Land sakes, it just gives me a headache to think about it! Where did I put my bottle of aspirin?"

Herb Stokinger, among many other things is a dreamer, a dreamer of great dreams. Just a few years ago several of us were invited to attend his "half-way birthday party." Herb was 65 on that occasion and took this means of announcing his intention to take care of himself so he could live to be at least 130. I'm sure we all wish him success. Another dream that Herb has shared with many of us during his 26 years of the TLV Committee, he shared it by insisting that we carry it out, is the two-part dream that (first) all toxicology will be done as good science — not just counting dead rats or how many lumps can dance on a mouse liver. Herb's dream goes on to the second part that the evaluation and application of good toxicology science for society's problems will involve scientists and scientific thinking. I'm sure we all wish success for ourselves in achieving this dream of Herb's.

Professor R.J.L. Allen, of England, spoke on this issue in March 1977 to the industry, which I am proud to be serving, at a meeting of the Society of Cosmetic Chemists.[3] He said, "It is no longer a question of whether industry is going to be closely regulated, but how." Industrial toxicologists are well aware of regulations for occupational safety and health. We also should be well aware that the scientific data we generate, whether of good quality or bad will be applied, not only to occupational health but also, to consumer safety — where my primary responsibility now lies, and to environmental quality as well as to foods and drugs. It therefore behooves us to live fully within Herb Stokinger's dream of doing good science, that is, complete and thorough science. If not, we shall see regulatory action taken, in the face of presumed public pressure, on the basis of poor and incomplete scientific evidence. I need only to point to the banning of spray adhesives on the basis that one pediatrician found ten people with altered chromosomes. Fortunately, this piece of non-science was recognized and corrected quickly. Not quickly enough to prevent nine needless abortions nor 1100 frantic inquires about abortions.[3] You see how the second part of Herb's dream for good scientific regulation is dependent on the first part of having good scientific data.

It is my firm belief that no manufacturer can fulfill his obligations to protect the health of his employees, his customers, and the general public

without extensive animal testing. I am on record in papers presented a few years ago at the Wright-Patterson Toxicology Conferences as calling for more animal carcinogenicity tests because they are predictive of most known human cancer chemicals. After all, that's the basis of all toxicology, that animal effects are predictive of human effects.[4,5] The reliability of these animal experiments is not always as good as we would like. Everyone was excited last November to hear Professor Maltoni's report that he had produced tumors by benzene.[6] I have three questions, how many of you have heard of a zymbal gland before Dr. Maltoni's work on vinyl chloride? How many of you know whether or not man has a zymbal gland? Does a zymbal tumor equate with bone marrow damage? There are some who will say it doesn't matter. A tumor is a tumor and thus there there is a risk to humans, and with this I agree, but how much risk? Recently Arnold Brown, Chairman of NCI's Cancer Clearinghouse, was our guest and he said that it was hard enough to determine from the NCI Bioassay Data whether or not a compound had caused cancer in the experimental animals. He was very glad he did not have to translate that to a regulatory decision involving human risk. It is not easy to do.

We all recognize the increasing expensiveness of animal testing and thus we all look forward to the day when quicker, less expensive tests will be available for toxicology. The *in vitro* methods are showing great promise and are useful even at this stage of their development in establishing priorities for animal studies. No one knows today what the significance might be for humans of a positive mutagenic response in the Ames test. Dr. Ames has said he doesn't, but it is frightening to contemplate what future generations will be like if the Ames procedures are 100% predictive. I have two questions. What is the dose in milligrams per kilogram that causes those individual bacteria to mutate? Can that same dose be delivered to human reproductive cells or even somatic cells?

You all realize the point I'm making is an old one. The prediciton of human effects from animal data is far from being 100% reliable. For example, the animal evidence that hydrazine is a mouse carcinogen is quite good; however, human evidence to the contrary is becoming stronger. Isoniazid, the drug that has brought tuberculosis under control, is metabolized in humans and in some animals to hydrazine. Yet, in 1976, Stott and his co-workers in England[7] reviewed the histories of 3842 adult TB patients, of whom 2696 were treated with isoniazid between 1950 and 1957, an average of 19 years, and found, "There is thus no evidence of any association between total or maximum daily dosage of isoniazid and the risk of death from malignant neoplasms." Similarly, Beard and Noller at Mayo, have found that 767 women receiving metronidazole, another hydrazine derived drug, between 1960 and 1969, "have no susbtantial increase in total cancer incidence over that expected for a normal population."[8] We may soon have the first clear example of animals not being predictive of human effects for cancer.

What does Herb Stokinger's dream call for us to do in the face of such paradoxes? Obviously, to perform good toxicology science and apply the data scientifically. Equally obviously, the exact meaning of that is subject to wide variation among individuals and situations. Social values and acceptable risks change from time to time. That's why each TLV is re-evaluated every year. Some values are raised and some are lowered reflecting both an increased knowledge and a changing level of acceptable risk. The concept of acceptable risk can be a moving target masquerading as an analytical sensitivity! Acceptable risk is generally inversely related to the level of knowledge. All of us prefer to wrestle with a devil or an angel we know. Thus, the more we improve the quality of our toxicology science the better off we will be when regulatory standards are set for the workplace, or any other place.

Recommendations

Let me suggest a few things to improve the scientific quality of industrial toxicology and the entire area of occupational health and safety.

We need to build bridges between our animals and humans. For this we need to do much more in the way of comparative studies in pharmacology, biochemistry, pharmacokinetics, pathology, and physiology. To do so without excessive human experimentation might be accomplished if we had many more reliable human tissue cultures or even whole organ cultures available. We transplant corneas and kidneys from cadavers, why not acquire some livers for experimental studies?

We need to improve the reliability, specificity, and sensitivity of our epidemiology studies. I think we need to place more emphasis on prospective rather than retrospective epidemiology. I am co-author of a paper later this week in which we suggest some of the things to be done and not be done in this area.[9] Again, we will call for good science and that ultimately and fundamentally rests on good data. We need to plan prospective epidemiology studies of our workers and to retain these data, perhaps beyond their lifetimes, not just the mortality data on the workers but the data on their morbidity and equally important on their exposures.

We need to keep our workers informed about the risks associated with their employment. This will increase their cooperation in controlling exposures, in reporting effects, and in calling attention to non-work-related factors that might change the risks at work. Examples would be atherosclerosis, pregnancy, exposure to chemicals in hobbies. Off-the-job exposures must be documented.

Last year in a lecture to Navy Occupational Health personnel, I expressed the opinion that in the workplace all jobs should be equally accessible and performable by men or women.[10] I then went on to emphasize that the only basis for differentiation, not discrimination, was the third party — the unborn fetus. Here I still take the firm position that this exposure is the responsibility of the woman and her physician. No one else can know as well of the possible existence of that third party. The responsibility is clear. The decisions rest finally with them. The employer, through the occupational physician, toxicologist, nurse, industrial hygienist has a prime responsibility to inform the female employee, in advance of her pregnancy, of the risks, whatever they may or may not be, that are associated with her employment. The same may be said of the male employee also, especially in view of recent data on the reversible effects of a halogenated compound on the sperm of exposed males. If corporate management does not feel sufficiently protected by this arrangement they will have to accept the EEO consequences of assigning only sterile women to certain tasks. The alternative of zero exposure is recognized as impossible. At the same time the industrial hygienist must work to keep such exposures to a minimum.

While I am speaking of keeping employees informed let me suggest that you should undertake an employee education program to reduce not only occupational health claims but also to reduce the costs of your general employee medical benefits and retirement programs. Dr. Ernst Wynder at Columbia has shown that only 5-10% of all cancer cases have any relation to occupational exposures.[11] A much larger proportion of cancer is caused by improper diets. If you couple this disease burden with that of cardiovascular disease from improper diet you will readily see the need for nutritional training for employees. I think you will find it will pay off in dollars as well as in morale and humane concerns. Prevention is much better than all the clinical care in the world.

We also need to be flexible in the standards we set. People are different from one to another and from time to time. That is why the TLVs refer to concentrations and conditions "under which it is believed nearly all workers may be repeatedly exposed."[12]

We need to pursue opportunities for cooperation and collaboration among ourselves. This permits the pooling of resources and of data in the conduct of toxicity tests or of epidemiologic studies. It also provides an influential base from which to bring good science into the evaluation and application of the data to developing standards for employee protection. The truly classic example of this is your TLV Committee where data are gathered from all sources and throughly worked over by a variety of scientists of differing backgrounds and views before a TLV is recommended.

I would like to propose to the governing bodies of ACGIH and AIHA that they take the initiative in forming a consortium of professional and scientific organizations to speak out on the regulatory and political scene for good science in government. Such a group, representing a large body of health related societies, would be listened to by people such as Frank Press, Science Advisor to the President, the heads of regulatory agencies, the committees of Congress and the members of Congress such as Kennedy, Steiger, Rogers, and Muskie, to name a few. The unions and the industrial communities have their political action committees. It is time for the health scientists to have theirs. We need a National Council for Health Protection.

Conclusion

Ladies and gentlemen, we have more than enough work to do. Let us proceed to do it in the concept of Herb Stokinger's dreams of doing good scientific work with proper scientific evaluation. Perhaps then we may all move closer to realizing his dream of living to be 130.

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Current confidence in occupational health*

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Little if any real justification is found for current apprehensions about health hazards in the work place. However, communications from some who are responsible for defining and controlling hazards tends to destroy confidence, rather than to build it up, as their knowledge and authority should obligate them to do. I attribute the unfortunate effect of their statements to confusion of association with cause and effect, reliance upon inappropirate experimental talk of conceivable possibilities rather than of realistic probabilities, and haste to announce suspicions before they can be confirmed or denied.

Chairman Trayer, ladies and gentlemen, I am most flattered and gratified to have been invited to deliver the Herbert E. Stokinger Lecture for 1979. I believe that my remarks rather closely relate to Herb's many years of concern with occupational health.

Current state of occupational health

Today many feel that toxicity and hazards were discovered only yesterday, and that no standard concerned with them can be sound if it has been in existence for more than five years. We are running scared of, among other things, the safety of the workplace. Recently Wildavsky, a political scientist, wrote,

> *"The richest, longest-lived, best protected, most resourceful civilization, with the highest degree of insight into its own technology, is on the way to becoming the most frightened. — Chicken Little is alive and well in America. — Is it our environment or ourselves that have changed?"*[1]

I shall examine some of the roots of our feeling of insecurity in respect to occupational health, and suggest remedies.

I believe that our environment *has* changed; it has changed for the better. I am convinced that the workplace has never been so healthful. Those who see an epidemic of occupational diseases should reread the accounts of Ramazzini[2] and of Alice Hamilton[3] to refresh their memories about what working conditions once were. But we ourselves have also changed. We are deluged with speculations and contradictory opinions from experts, many of them viewing with alarm. Our confidence is being destroyed.

During the 1920s and the 1930s I had firsthand familiarity with every industry in the Philadelphia area, either as an industrial hygienist measuring exposures, or as a guest accompanying classes in occupational medicine on tours of local industry. I was familiar with operations with major airborne hazards, such as benzene, white lead, asbestos, silica, aniline and phosgene. Despite attention to control, concentrations of that day had to be seen to be believed. Perhaps my outstanding memory is sampling at the breathing zone by a roll-coating operation, the benzene concentration at which I found to be 1700 ppm. The operator had worked for several years at the same machine. He looked underweight and anemic, but still competent. I have seen an asbestos weaving operation where dusts made a strong nimbus around lights and windows. I have seen workers grinding lead pigments who were yellow from face to feet, due to litharge dust, or red from red lead. Soon after I moved to Pittsburgh in 1937 I was shown a hospitalized worker whose benzene exposures had resulted in petichael hemorrhages over his entire body, so abundant as to be almost confluent. Where today could we find exposures so great?

These memories convince me that working conditions are now better than they were fifty years ago. I cannot accept the claim that there is an epidemic of occupational diseases today, although I recognize that my conviction will not be shared by those who only yesterday became concerned with the protection of occupational health.

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Standards for acceptable exposure

I attribute a major part of the improvement to the promulgation and application of TLVs. Measurement, interpretation and correction of exposure is the only new tool for the protection of occupational health introduced since the 1700s of which Ramazzini wrote.[2] After about 30 years of reliance upon TLVs, we are in the process of shifting to OSHA standards. To the extent that OSHA standards may better protected health, while still allowing practical industrial production, the change cannot be lamenated. To the extent that no gain in occupational health results and industrial production becomes burdensome, the situation parallels the action of Gresham's Law in economics, bad standards driving out good.

Experience with the TLV for benzene exposure deserves attention. It was first set at 100 ppm, following Winslow's extensive survey of industrial use and worker health.[4] By stages the value has been reduced to 10 ppm.[5] To evaluate the reduction properly, we must bear in mind the details of Winslow's conclusions. He said that 100 ppm was the lowest exposure that engineering know-how of this day could maintian. He said that injury developing in those exposed to 100 ppm (and careful study of his tables shows that he found one-third of them responding adversely) would not be irreversible by the time that periodic medical examination could detect it. Since Winslow's day we have found no new information which defines a lower acceptable level of exposure, but our concept of what is acceptable has changed. It is now practical to maintain concentrations below 100 ppm, but adverse reactions in one-third of those exposed is no longer acceptable, no matter how certain we are that it can be detected while in a reversible stage. Is it any wonder that the TLV has been reduced to 10 ppm, with no new knowledge of the exposure/response relationship? The rare occurence of leukemia, which has caused OSHA to brand benzene as a carcinogen, is not newly discovered. More weight is now given to benzene as an inciting cause than to the apparently rare biological condition which results in an exposed worker developing malignancy.

My attitude toward benzene is somewhat irrationally influenced by my own experience. During the spring of 1926 I was engaged in a study of spray-painting hazards.[6] I was spraying moderate quantities of lacquer intentionally doped with benzene, while I measured air currents and benzene concentrations around simulated furniture in a large spray booth. At the end of the study, after some 100 gallons of lacquer and 10 gallons of benzene had been used, it was found that I had a clear, but trivial, response to benzene in my differential white cell count. There was no quantification of my time-weighted-average exposure. At about the same time, a friend worked in a linoleum printing operation, cleaning printing blocks over an open vat of benzene, with no ventilation whatever. Every night he was essentially drunk from inhalation of vapors, and probably also from skin penetration. His exposure must have been a multiple of the 100 ppm standard being set by Winslow[4] at about the same time. My friend did not realize until years later that he should have been severely injured, or doomed. He is alive and well today. Of course I realize that single isolated instances prove nothing except the variability of individual responses.

Animal models for setting standards

I am more concerned with those hygienic standards which are based primarily upon animal experiment, because study of animal models of anticipated human exposure has occupied most of my working time for fifty years. As more and more newly available chemical substances are introduced into industry, it is obvious that we must rely more and more heavily upon extrapolation from animal experiment for defining acceptable working conditions. Because it is now unthinkable to allow any exposure without guidance beyond guesswork, these extrapolations must serve until they can be replaced with documented human experience.

As a matter of fact, it can be maintained that animal models may be a sounder guide. Conclusions from human observation are vulnerable to the biostatistical trap for the unwary, the fallacy that association proves cause. Some 30 years ago a friend illustrated this point in his lectures by showing a slide of the close parallel between the incidence of lung cancer in the country and the number of flush toilets.

The underlying cause of the conditions we lump under the heading of cancer are still not understood, but it seems that at least one molecule of

DNA must be altered before the process can start. Thus it appears that cancer does not begin until our DNA repair mechanisms are attenuated by age, or some other cause. At that time, any of the multitude of agencies with which we are surrounded —radiation, natural substances, body components or industrial materials — may start the process. I am convinced that cancer begins with the weakening of our defense mechanisms, and the associations with epidemiology sometimes reveals are of minor significance to its cause, although they seem to govern the organ or system in which it centers. I find it persuasive that those with weakened DNA repair mechanisms will succumb to their first sufficient contact with any adventitious agent. The biological defect is of more significance than the particular agent. I believe that the part of our present apprehensions which result from the frequent characterization of substances as "cancer causing agents" is due to gross misuse of words. The frequency of this misuse is beginning to backfire by producing a "wolf, wolf" attitude, public mockery of the "cancer of the week."

Is it logical to fear vinyl chloride because almost every case of angiosarcoma of the liver is in those exposed to it, when we know that very few so exposed develop the condition? It is nonsense to say that there will be multitudes of cases among today's workers after a sufficient induction period has elapsed. The monomer has been used in quantity for at least fifty years, and it is certain that the early workers were more heavily exposed than those today. Cancer associated with vinyl chloride exposure did not begin when we first recognized the association two or three years ago. Plenty of time has elapsed for all cancers to develop in those first exposed. Concentrations being lower today, cancers we may attribute to vinyl chloride will decrease, not increase. The situation with benzene is even less menacing. A smaller proportion of benzene workers develop leukemia, and there are more frequent apparent causes than inhalation of benzene.

Pitfalls in animal models

Pitfalls inherent in animal models may be no less a threat to sound conclusions than is the association-versus-cause trap of epidemiology. They lie both in the design of experiments, and in interpretation of their results. I like to sum up avoidance of pitfalls in design by using the word "appropriate," brought to the attention of toxicologists by the much debated Delaney Clause of the Food Additive Amendment of 1958.

Appropriate species

To be appropriate, a model of human exposure must treat a species which responds to the substance being studied in the same way and to about the same extent as does the human. Early attempts to find the substance associated with what was then called aniline bladder cancer were fruitless while they relied upon testing rodents. It was studies on dogs which finally pointed the finger at beta-naphthylamine,[7] and now we know that this was because dogs and man biotransform the amine to 1-hydroxy-2-aminonaphthalene, the proximate carcinogen, while rodents do not.

The mouse and the rat are much used for studying many aspects of the cancer process, but I conclude that they are not appropriate for predicting the incidence of human cancer by extrapolation from experimental incidence to lower dosages. It is persuasive that use of these rodents overestimates human incidence, and underestimates the human dosage which may yield certain low incidences judged to be acceptable. I have already pointed out that the process which leads to cancer does not begin until DNA repair mechanisms are attenuated or broken down. The rate of DNA repair in the mouse and the rat is about one-fifth that in man.[8] Presumptively, these rodents are about five times as likely to develop cancer in a given situation as is the human. An appropriate, but perhaps not very convenient, species from this point of view, appears to be either the cow or the elephant. Their DNA repair rates are very close to that of man.

In consideration of the fact that the albino rat is used more often than any other experimental animal, I feel called upon to quote myself from a 1960 paper.

> *"Never has one species voluntarily done so much for the eventual benefit of another as man has done for the rat. Should the rat survive man, as is not unlikely, he will find in our libraries all that he needs to know to be safe in any degree of technological civilization he cares to adopt."*[9]

Appropriate routes of entry

The route of entry in the model should result in the same sequence of opportunities for biotransformation and injury as will occur in the human whose exposure is being considered. When a substance under study is rapidly transformed to a less or more injurious metabolite, an oral dose is not an appropriate model for human inhalation or skin penetration. From the digestive tract the absorbed substance passes directly to the liver, to be exposed to the vast armementarium of transforming enzymes in that organ. The portion which reaches the target organ or system is appreciably metabolized, and may not have the same quantitative or qualitative effects as did the original substance. On the other hand, inhaled substances or those penetrating the skin reach the liver only after they have passed through all other body systems. The target organ is contacted by the original substance, which has been little if any biotransformed. Thus, feeding substances in the diet is not an appropriate route for studying cancer associated with human inhalation, particularly when metabolic activation is needed to make the proximate carcinogen.

I do not intend the last point to be a criticism of those few TLVs which have been set on the basis of feeding substances in the diet of animals. I recognize that the TLV Committee has an obligation to give what guidance it can when it learns that occupational exposure to a substance is to take place, even when completely satisfactory toxicological data do not exist. The pesticides have been studied in an animal model which is appropriate to the study of food additives, that is to say in two-year feeding studies in rats. Since pesticides as a class are systemically toxic, with respiratory tract irritation a minor effect, doses by mouth can yield reasonable satisfactory standards for acceptable inhalation concentrations.

Appropriate dosage

Much physical and engineering study utilizes accelerated tests, for instance devices which subject painted surfaces to frequent cycles of ultraviolet radiation and of salt water spray, to produce in a few days an approximation to the stress of a year or more of exposure to the weather. Accelerated tests are reasonably predictive of the survival of painted surfaces in actual use. It is often thought that the same sort of accelerated testings will be found in animal studies. However, biological systems have defenses which are not present in non-living systems. Animal response to a large dose does not predict the degree or even perhaps the nature of response to small doses.

My group found that several hours inhalation by rats of a few thousand ppm of acetonitrile is fatal.[10] Astoundingly, the cause of death, delayed several hours after inhalation is ended, is cyanide poisoning. On the other hand, 100 ppm inhaled for several weeks to total about the same CT value, produces no more than trace narcosis and minor kidney irritation. The blood rhodinase is adequate to convert cyanide from enzymatic action to comparatively harmless thiocyanate as rapidly as it forms from a small absorption of acetonitrile, but is inadequate to convert a large absorption. The resulting accumulation of cyanide eventually reaches a fatal level, and the rat dies of delayed cyanide poisoning. The same phenomenon has occurred in humans.[11]

Another example appears in a recent publication on dioxane.[12] In rats, up to about 18 mg/kg/hr is hydrolyzed to 2-hydroxyethoxyacetic acid. Greater rates of intake saturate this biotransforming pathway and the excess is excreted unchanged in the urine and expired air. Study of repeated animal inhalation reveals that the onset of injurious response occurs at concentrations which saturate the pathway, and injury is absent at lower concentrations.

Current knowledge of biotransformation of xenobiotic substance shows that use of doses and concentrations higher than those to which humans will be exposed is not an appropriate model to study. It may expose the experimental animal to substances to which humans will not be exposed. It is likely to result in adverse response totally different from that which humans can manifest in actual use of the substance being studied. I consider it to be unacceptable, irresponsible or possibly intellectually dishonest.

Other ways in which an experimental animal model may not be appropriate appear to have had less impact on extrapolation of results to predict human hazards.

Interpretation of result

In any event, reliable prediction from the results of experimental study requires that the model be appropriate to the anticipated human exposure. In engineering, much study of models has led to the definition of scale factors by which experimental results can often be extrapolated with confidence to predict successfully the behavior of the full-size system. We have barely begun to attain an equal understanding of the relations between biological models and the real world. Indeed, too often we consider that we have finished our job when we have completed our study of the model. We confuse the model with reality. The purpose of experimental toxicology is not to determine animal responses to a substance; it is to estimate the likelihood of human injury from the anticipated manner and quantity of use. Speaking only of the model overemphasized injury, tends to arouse apprehension. We are not finished until we have utilized the fate of the model to predict the fate of the human. Unfortunately there is not yet a completely rational way to replace intuition in this operation.

A tacit acknowledgment of this fact in a non-occupational field is the well-known and often abused factor of safety of 100, which is applied to studies of food additives. In 1955 the Food and Drug Administrtation published the statement that, where there is no human experience with a pesticide, it is logical to assume that humans are 10 times as sensitive as are experimental animals, and that the weakest human is 10 times as sensitive as is the average human; hence, it said, the greatest amount which will be allowed in the human diet is one one-hundredth of the largest amount which does not injure experimental animals.[13] The sound qualifications of this arbitrarily selected number were soon forgotten, even by the FDA, and it has become a "bare naked number," hallowed by a generation of use as a hedge factor to compensate for ignorance. Unhappily, many newcomers to the field use the factor of safety of 100 as a way to pass from any animal results to predict toxic or safe doses for humans. They believe it to have originated from consensus, rather than from an arbitrary administrative decision.

There is no similar factor of safety customarily used to pass from an animal model of inhalation, to an acceptable human exposure. Often one considers that absence of observed animal injury at a given concentration indicates that concentration is acceptable for humans. To the extent that the adverse reaction is surface irritation of some part of the respiratory tract, this may be justified. To the extent that systemic action is involved, with opportunity for species difference in biotransformation, the direct relationship is less justified. To be sure, there is an often overlooked built-in safety factor in the relationship between respiratory volume and body surface. In proportion to body weight, more air enters the lungs of the rat than of the man, for the same degree of activity. Hence the rat's blood reaches equilibrium with vapors in the air more rapidly than does man's. The rat's blood is at peak concentration longer than is man's during an 8-hour exposure period. Thus there is more chemical stress on a rat exposed to a given concentration than to a man exposed to the same concentration. However, this built-in safety factor does not approach the magnitude of the 100 used for food additives.

With today's emphasis on cancer, there seems to be little concern about uncertainties in passing from the animal model to the human worker, in relation to systemic effects, such as liver injury. This is regrettable. Many more workers are likely to respond adversely from systemic toxicity or neurological effects and enzyme inactivations than from cancer. No consensus exists about interpreting the animal model. I emphasize that interpretation is completely undependable unless the model is appropriate in species, dosage and route of entry at the very least. Then these factors are completely appropriate, it is not unsound to consider that a one-to-one relationship may exist between the model and the exposed worker, based upon concentration in the air. This keeps the relationship between body size and respiratory volume as a slight cushion.

Recapitulation of errors

I briefly review what I regard to be the most frequent errors which have led to incorrect conclusions in research into occupational hazards, hence have contributed to insecurity and fear.

Confusion of association with evidence of cause and effect has lead to characterization of substances as occupational cancer risks when they seem to be no more than opportunistic agents

which carry to completion a biological process which has already doomed the individual.

Use of inappropriate animal species has led to attributing injuries or quantitative incidences to exposures which cannot affect humans at all, or cannot produce the incidence foreseen. I feel that it is most frequent in the use of rodents for predicting cancer incidence for humans.

Use of large experimental exposures or dosages for convenience often produces biotransformation products in animals which are not formed from the levels which humans encounter, hence may cause effects in the model which do not occur in humans.

Speaking of the model as if it were reality overemphasizes harm and leads to unjustified apprehensions.

Recommendations

We should all bear in mind that protection of occupational health requires the fostering of confidence, avoidance of sensationalism, as much as it does detection and elimination of true hazards.

I do not find factual justification in the field of occupational health for the public fright which Wildavsky[1] discusses at length. Nevertheless, I do see a multitude of public statements which can arouse unfounded apprehensions. Their prevention in the future requires attention to perspective, semantics and communication, and suggests a redirected emphasis in cancer research. It is fashionable to blame the media for distortion of the meaning of the scientist. However, in this instance I blame the scientist for both the choice of model to study and the terms in which he reports his findings. At times he may accept without protest distortions which his employing agency applies. The media simply repeat his words, albeit with more emphasis and more frequency than the scientist intends or expects.

I recommend that the epidemiologist remember that it is premature to conclude that cause and effect have been revealed by his first recognition of an association. One occupational cancer is most lamentable. However, I am not sure that it represents more harm than the apprehensions of 1000 unaffected workers and their families, created by the publicity accorded the investigator who first reports an association between the case and the job.

Experts should realize their responsibilities. They should speak of their area of special knowledge in terms which the public can properly interpret, without arousing unjustified apprehensions. It is irrational, misleading and dishonest to refer to chemicals which have been found to cause cancer in mice as "cancer causing." Statements which are literally true, become lies if the audience will not understand them in the same sense as does the speaker. The lay public has no knowledge to look below the surface of this phrase, and believes it means that it has been shown that the substances have caused human cancer.

I recommend more emphasis upon search for means to abort the biological process which ends in cancer. This would pay more dividends in confidence and health than will elimination of exposure to each and every opportunistic agent which can be found to complete the process but which, I believe seldom if ever initiates it.

I recommend more consideration of the appropriateness of experimental models. It is unacceptable, essentially a lie, to base predictions of human risk on the study of animal models which are not appropriate, particularly in respect to species and dosage. We can have no confidence that behavior of an inappropriate model mirrors human responses.

I advise less public speculation arising from suggestive but not conclusive results. In the absence of appropriateness, if we should feel compelled to speak, it can be only speculation, in terms of "may be." Communication from the land of "may be" is one of the surest ways to destroy public confidence, to create hysteria. It makes impossible any rational communication between the expert and the lay public. The expert should use restraint. He should keep his speculations and visions of doom to himself until he has proven that the possibility he sees in his model is a probability for the humans he hopes to protect. Part of his protection should be to give them no cause for panic. I give him a final recommendation most difficult to follow: — to keep his mouth shut until he is sure.

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Henry F. Smyth, Jr. has been retired since 1967. He is currently Adjunct Professor of Industrial Toxicology in the Graduate School of Public Health of the University of Pittsburgh, and Advisory Fellow in the Carnegie-Mellon Institute of Research. Prior to retirement, he directed the Chemical Hygiene Fellowship of Mellon Institute, in Pittsburgh, for 30 years, managing experimental toxicological studies for Union Carbide Corporation. Before that, for 9 years he was Instructor in Sanitary Chemistry at the University of Pennsylvania, and concurrently a partner with his father in Smyth Laboratories, offering consulting services in industrial hygiene, occupational medicine and experimental toxicology.

Dr. Smyth received the B.S. degree in Chemical Engineering from the University of Pennsylvania in 1925, and the Ph.D. in Medical Sciences in 1934. He is a Registered Professional (Chemical) Engineer in Pennsylvania.

For eight years Dr. Smyth was Executive Secretary of the American Industrial Hygiene Association, and he has been a Director and its President. He has served on the American Board of Industrial Hygiene since 1960, for the first 6 years as its Secretary-Treasurer. In 1956 he received the Donald E. Cummings Award from AIHA, in 1966 the Merit Award of the Society of Toxicology, and in 1976 the Mellon Institute Award. He has served on the Food Protection Committee of the National Academy of Sciences-National Research Council, and on the Committee on Toxicology of its Advisory Center on Toxicology. He has served as an expert on food additives for the World Health Organization.

Dr. Smyth is author or co-author of some 140 published papers on the toxicology of industrial chemicals and industrial hygiene, as well as three chapters in monographs. He is a member of the American Industrial Hygiene Association, the American Academy of Industrial Hygiene, the Society of Toxicology, and the American Chemical Society.

On the concept of threshold*

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Introduction

I am greatly honored by the American Conference of Governmental Industrial Hygienists in being asked to give the fifth Stokinger Lecture. I have had a long and, for me, stimulating association with both the Conference and Dr. Herbert E. Stokinger. The Conference is to be congratulated for setting up this lecture in honor of Dr. Stokinger while he is still alive and active in the field of occupational health.

I have also had the honor to serve as Chairman of the Conference. This gave me the opportunity to work with occupational health professionals who willingly gave of their time and experience in furthering the objectives of the Conference. The Conference has as its objectives the exchange of ideas and experiences, and the promotion of standards and techniques in the field of occupational health. The Conference has set about to achieve its objective by establishing special committees to develop recommended standards, guidelines, and codes of practice by convening special meetings and conferences on topical issues in the field of occupational health.

Early in its history, the Conference established the Threshold Limit Values Committee which was so ably served by Dr. Stokinger for 26 years. The recommendations of the TLV Committee were orginially intended to provide guidelines for occupational health professionals employed by governmental agencies. Threshold limit values (TLVs) were not intended to be incorporated into legal codes. In fact, the TLV Committee had specifically recommended against this. The TLVs did fill a real need for the practicing industrial hygienist in helping them in the recognition, assessment, and control of health in the workplace. The TLVs have been widely adopted for use in many countries, and this is a widespread reflection of their validity and practicability.

Dr. Stokinger's contributions in the field of occupational toxicology and occupational health are respected, both in the United States and abroad. It is probably his work on the TLV Committee for which he is best known.

In 1968, Dr. Stokinger and I served as governmental representatives at a joint WHO/ILO meeting in Geneva. The meeting was called in the hope of achieving some international agreement on occupational exposure limits. There was then, as there is now, a wide disparity between the Maximum Allowable Concentrations (MACs) of the Soviet Union and the TLVs of the American Conference of Governmental Industrial Hygienists. Dr. Stokinger impressed me with his direct, but scientific approach, his organizational ability, his zeal, his humor, and his Tabasco Sauce. Dr. Stokinger always insisted on having proper scientific documentation to support the recommendations of the TLV Committee. There was little published documentation for the Soviet Maximum Allowable Concentrations. The scientific support, which was available, was based on studies of conditioned reflexes and neurophysiologic changes. In general, such procedures are derived from Pavlov's classical studies and they are of primary interest to Soviet toxicologists. Various neurophysiological testing methods are used, including optical chronaxy, olfactory analyzer activity, and auditory analyzer activity. Dinman[1] has reviewed and commented on some of the toxicity testing techniques used in the Soviet Union. They are not comparable to toxicology assessment in experimental animals in the United States and elsewhere.

Later, when I worked with the ILO, I had the opportunity to visit a number of workplaces in the Soviet Union. It became apparent that the MACs represented ideal objectives. At the actual worksites, more "practical" exposure limits were, in fact, used.

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* The 1981 Herbert E. Stokinger Lecture, presented at the American Industrial Hygiene Conference, May 24-29, 1981, Portland, OR.

I had some difficulty in picking a subject for my Stokinger Lecture presentation. I am by training a physician with a strong interest in industrial hygiene. I have no special expertise in toxicology, epidemiology, air sampling methodology, analytical chemistry, or industrial ventilation. A lecture dealing with some aspects of the development or use of the TLVs would seem to be appropriate in terms of both the Conference and Dr. Stokinger. I am aware that the previous Stokinger lecturers also dealt with particular reference to the Threshold Limit Values. Without the concept of a threshold, there could be no TLVs.

The concept of threshold

As noted in the preface of the TLV booklet:[2]

> *"Threshold Limit Values refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variation in individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit; a smaller percentage may be affected more seriously by aggravation of pre-existing condition or by development of an occupational illness."*

In this important opening statement, the TLV Commitee clearly enunciates a number of principles:

1. Certain airborne concentrations in the workplace may be tolerated for long periods of time without adverse health effects to most workers.
2. The recommendations represent the judgment of the TLV Committee ("conditions under which it is *believed*").
3. Not all workers will be protected even with the proper application of TLVs. Stokinger had noted earlier that TLVs would not protect certain hypersusceptible workers and I will discuss this aspect later.

Zapp,[3] in the first Stokinger Lecture, provided his concept of an acceptable level of exposure. He also gave a very interesting historical overview of the development of toxicological principles. Poisons were known and used by ancient people. The word toxicology is derived from the ancient Greek use of arrow poisons, and the early Greeks were clearly familiar with dose-response differences for acute poisons. The sixteenth century physician-alchemist Philippus Aureolus Theophratus Bombatus von Hohenheim, who took the name Paracelsus, was accused by his colleagues of poisoning his patients by giving them mercury for the treatment of syphilis, In his defense, Paracelsus enunciated a fundamental principle of toxicology:

> *"What is it that is not poison? All things are poison and none without poison. Only the dose determines that a thing is no poison."*

This principle underlies the very basis in the use of threshold limit values. Dr. Zapp noted that he was in agreement with the threshold concept as used by the TLV Committee.

I believe it is now appropriate to review the concept implicit in the term "Threshold Limit Values" as used by the TLV Committee.

The word "threshold" has two chief meanings. It is used to indicate an entrance or the beginning as, for example, the threshold of a new career. It also refers to the lowest limit of perception for a stimulus. The scientfic literature contains reference to many types of thresholds, such as the auditory threshold, the erythemal threshold, the galvanic threshold, the threshold of consciousness, and the threshold of feeling, discomfort, or pain. The characteristics of the signal and the measuring technique should be specified in describing a threshold. In acoustics, for example, the auditory threshold refers to the intensity of a barely perceptible sound vibration. It is expressed customarily in decibels relative to 0.0002 microbar. This was thought to approximate the normal threshold of hearing in young persons at 1000 Hertz. A threshold shift in an audiogram describes hearing loss in terms of a decibel shift from the previous audiogram. In physiology, the rheobase (galvanic threshold) represents the minimal strength of an electrical stimulus that is able to cause excitation of muscle or nerve tissue. In clinical chemistry, a threshold body or threshold substance refers to any material in the blood stream that is excreted in the urine only when it exceeds a certain physiologic value, e.g., glucose, sodium chloride, etc. This mechanism is relevant to biological threshold values.

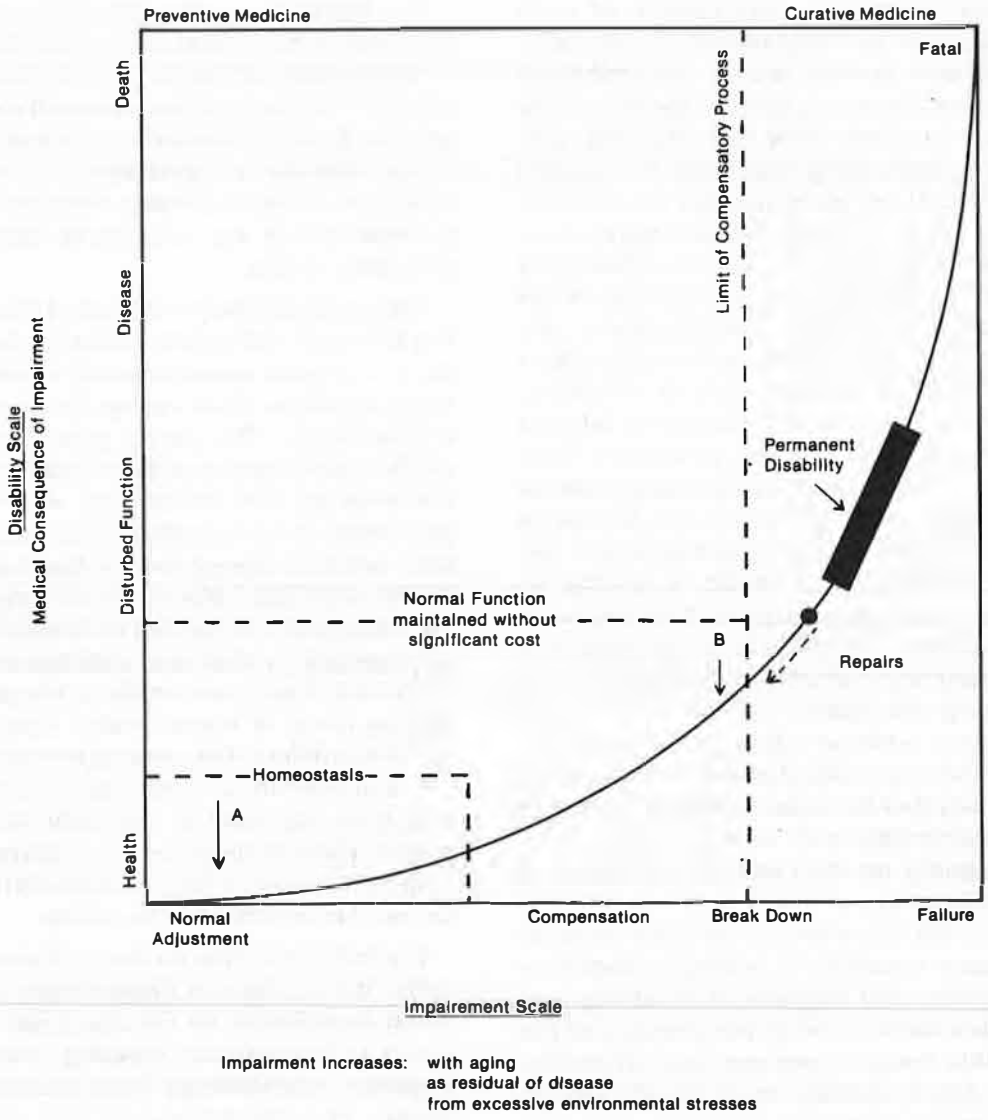

Figure 1 — Suggested relationship between impairment and disability. Considerable movement along the scale of impairment accompanied by relatively little disability.

The words "limit" and "value" refer to specific quantitative determinations.

A threshold limit value for chemical substances in the workroom air thus becomes an airborne concentration which may produce adverse health effects — perceived by the worker and/or his physician, and those concentrations which cause no adverse health effects. While thresholds clearly apply to exposure to irritating, narcotic, and systemic agents, many believe that they do not apply to agents which cause cancer, mutagenic, or teratogenic effects. I will discuss this aspect later.

Figure 1 illustrates an attempt by Hatch[4] to separate the dose-effect continuum into no-effect, normal adjustment, impairment, disability, and death. For this figure he states,

> *"A distinction is made between impairment and disability, the two scales representing, respectively, the underlying disturbance of*

the system and the consequence of such disturbance in terms of identifiable disease. Starting with normal health, the individual progresses, for one reason or another along the scale of impairment and disability, ultimately to death. Early departures from health (impairment) are accompanied by little disability. In the beginning, the normal homeostatic processes insure adequate adjustment to offset stress and for a distance beyond this early zone of change, compensatory processes similarly maintain the overall function of the system without serious disability. Further increments in impairment beyond the limits of compensatory processes, however, are accompanies by rapidly increasing increments in disability and the individual moves into the region of sickness and disability; terminating in death. A healthy individual, functioning at point A on the curve and subjected to a given kind and degree of stress may respond with relatively minor and temporary disturbance and will return to his underlying position when the stress is removed. An individual at point B, on the other hand, may find the same kind and degree of stress intolerable and, in the consequence, move rapidly up the curve to a position of serious disability and even death. In our past concern with occupational diseases, relationships were established between conditions of exposure and degrees of disability and objectives were to bring the stresses of the job within limits to prevent such disability. For the future, concern must be with impairment, rather than with disability, and relationships have to be demonstrated between the stresses of the job and the more subtle disturbances. The degree of impairment must be kept within limits well below the level of disease."

The dose response relationship is still the cornerstone of modern toxicology. As Hatch pointed out, some biological responses are trivial, well within the body's normal homeostatic ability. Some responses require compensatory mechanisms within the body which are compatible with normal biological function. If environmental exposures are increased beyond this compensatory range, impairment and disability will result.

The assessment of health risk revolves about our ability to detect and understand these changes — particularly where biological changes are involved.[5,6] Some changes are easy to detect, others are not. Analytic capabilities are now available to detect changes or responses to chemical agents at very low levels. Some responses are now routinely measured in the microgram, nanogram, and picogram ranges.

But are all measured biological changes indicative *per se* or deleterious effects? I do not believe so. It is a basic requirement of physiology that a living organism must respond to external stress if it is to survive. The use of graded stress on the cardiovascular system with the resultant responses are seen as non deleterious and, indeed, are presumed to be beneficial. Exercise or physical work are thus viewed on one hand as beneficial. On the other hand, biochemical changes or effects are commonly interpreted as deleterious in workers exposed to chemical substances. Could not biochemical responses reflect changes within the normal range of homeostatis? More research is needed to differentiate among homeostatic, adaptive, and deleterious responses in short-term and long-term exposure to chemical substances on the job. There is also a need to determine whether long-term stress on the homeostatis mechanisms can lead to adverse health effects.

The Subcommittee on the Toxicology of Metals under the Permanent Commission and International Association on Occupational Health convened an international meeting to discuss dose-response relationships from exposure to toxic metals. The proceedings of this meeting have been published.[7] The following statement is taken from the Subcommittee proceedings:

> *"The basis for a threshold dose concept lies in the interference of metals with certain biochemical processes and structural components, e.g., membranes, organelles, and the enzyme systems within the bodies of cells. Usually a certain reserve capacity on the enzymatic level allows the cell to absorb certain amounts of metal without undergoing evident functional change."*

This Subcommittee adopted a number of definitions which are of interest in our discussion on the concept of threshold. These definitions are noted below:

Critical Concentration for a Cell was defined as the concentration at which adverse functional changes, reversible or irreversible, occur in the cell.

Lethal Concentration for a Cell was defined as the cellular concentration which was sufficient to cause death of the cell.

Critical Organ Concentration was defined as the mean concentration in the organ at the time any of its cells reaches critical concentration.

Critical Organ was defined as the particular organ which first attains the critical concentration under specified circumstances of exposure and for a given population. This definition of critical organ differs from that given by others including the International Commission of Radiological Protection. Since biological variations of sensitivity occur there may be inter-individual and inter-population differences in critical organ concentration. The organ or tissue of greatest concentration is not necessarily the critical organ, e.g., in lead exposure the highest concentrations may be reached in the bone without any identifiable effects on the bone.

Critical Effect was defined as the point at which a critical concentration is reached in a critical organ. The critical effect may or may not be of immediate importance for the health of the whole organism.

Subcritical Effects were defined as effects which are evident by means of biochemical or other tests at exposures lower than those giving rise to the critical organ concentration of the metal. The concentrations producing such effects are defined as subcritical concentrations and each must be related to a defined effect. The Subcommittee voted that the biological meaning of a subcritical effect is sometimes not known. In some cases it indicates only that an exposure has taken place or it may be a sign of adaptation. In other cases, it may be a precursor of a critical effect. This latter effect is especially useful in applying preventive measures. For example, in lead exposure, an inhibition of the enzyme delta-aminolevulinic acid (ALA) dehydrogenase in the cells of the bone marrow is a subcritical effect which precedes an increased level of ALA in blood and urine, and the occurrence of anemia (critical effect).

Effect was defined as a biological change caused by an exposure.

Dose-Effect Relationship is established from measurements on many individuals over a range from no effect, minimum effect, to maximum effect. This relationship should be expressed in terms of mean values and their standard deviations at various doses.

Response was used to mean that proportion of the population that demonstrates a specific effect, and its correlation with estimates of dose provides the dose-response relationship.

Dose, in the Subcommittee's view, is ideally defined as the amount or concentration of a given chemical at the site of effect. The determination of this amount is often not possible in practice, and therefore dose is often an estimate based on many considerations including administered doses to experimental animals; airborne concentrations at the workplace; general environmental exposures from air, food, water, beverages, and tobacco; and from measurements of index media such as blood, urine, or hair. These dose estimates must consider interactions and biotransformations, as well as the accuracy and precision of the sampling and analytic methods used.

These definitions and concepts of the Subcommittee on the Toxicology of Metals also support the concept of a threshold effect for the metals studied. At some exposure levels no biological effects are evident even though elevated tissue levels and elevated excretion rates occur. At higher exposure levels damage to individual cells and to critical organ systems occur.

Threshold for occupational carcinogens

The TLV booklet contains an appendix listing occupational carcinogens, and the TLV Committee has recommended TLVs for many of those listed.

The available scientific data point to the conclusion that cancer results from inheritable mutations induced in somatic cells. Weisburger and Williams[8] have classified carcinogenic chemicals according to their proposed modes of action, see Table I. The genotoxic category contains agents

TABLE I
Classes of Carcinogenic Chemicals[8]

Type	Mode of Action	Example
A. Genotoxic		
1. Direct-acting or primary carcinogen	Electrophilic, organiccompound, genotoxic, interacts with DNA.	Ethylene imine bis(chloromethyl) ether
2. Procarcinogen or secondary carcinogen	Requires conversion through metabolic activation by hose or **in vitro** to type 1.	Vinyl chloride Benzo(a)pyrene 2-Naphthylamine Dimethylnitrosamine
3. Inorganic carcinogen	Not directly genotoxic, leads to changes in DNA by selective alteration in fidelity of DNA replication.	Nickel Chromium
B. Epigenetic		
4. Solid-state carcinogen	Exact mechanism unknown, usually affects only mesenchymal cells and tissues; physical form vital.	Polymer or metal foils Asbestos
5. Hormone	Usually not genotoxic, mainly alters endocrine system balance and differentiation; often acts as promoter.	Estradiol Diethylstilbestrol
6. Immunosuppressor	Usually not genotoxic; mainly stimulates "virally induced," transformed or metastatic neoplasms.	Azathioprine Antilymphocytic serum
7. Cocarcinogen	Not genotoxic or carcinogenic, but enhances effect of type 1 or type 2 agent when given at the same time. May modify conversion of type 2 to type 1.	Phorbol esters Pyrene Catechol Ethanol n-Dodecane Sulfur dioxide
8. Propoter	Not genotoxic or carcinogenic, but enhances effect of type 1 or type 2 agent when given subsequently.	Phorbol esters Phenol Anthralin Bile acids Tryptophan metabolites Saccarin

that function as electrophilic reactants. Inorganic chemicals have been included in the genotoxic variety, although they seem to exert their effect through the fidelity of DNA polymerases.[9] The epigenetic carcinogens comprise those for which no evidence of direct interaction with the genetic material exists. As noted by Weisburger and Williams, this classification, if ultimately validated, would have implications for extrapolation of experimental data to man, and for recommending exposure levels for workers to carcinogenic substances.

Chemical carcinogens show a dose dependent response in experimental animals. Carcinogens, however, differ from the toxic actions of other chemicals. Carcinogens leave irreversible effects on the receptor cells, which may manifest overt malignancy after a relatively long latent period. Some experimental studies have demonstrated that lower dose levels of known carcinogens can be given to experimental animals without producing cancer.[10] Epidemiological studies in workers and cigarette smokers indicate that the cancer risk is proportional to the length of time in exposure or to the number of cigarette smoked per day. In fact, for cigarette smokers the curve is concave upwards, showing that higher doses are considerably more effective than lower doses. These data are suggestive, but not conclusive of a threshold for carcinogens.

The question of a no-effect level for carcinogens, i.e., the concept of threshold, is a hotly debated subject. I believe there are such thresholds in intact animals and in man, both of which have DNA

repair capability and immunological protective systems.

Much of the assessment concerning human risk factors from exposure to carcinogens is derived from experimental data in animals and from bioassy testing. I am in complete agreement with the view that these data should be evaluated critically in assessing human risk from exposure to carcinogens. I concur with the need to identify an appropriate species, appropriate routes of entry, appropriate dosage, and appropriate interpretation of results from experimental data. Smyth[11] made these points emphatically in the 1979 Stokinger Lecture. I realize the dilemma of having to use either very large numbers of experimental animals or large doses of chemical agents to test for carcinogenesis. Nevertheless, I have some real difficulties in interpreting data in animals given the "maximum tolerated dose" because of differences in metabolism and the pharmacokinetics between the appropriate and the maximum tolerated dose.[12]

Eckardt[13] has commented on the extrapolation of carcinogenesis data from animal experiments to man as follows:

> *"So my answer to the question of whether we can extrapolate carcinogenesis experiments from animals to man is yes, this can be done, providing that we do it with intelligence, with understanding and with intellectual honesty, making sure that we take into account basic species differences which may be operative in any particular circumstance. This, I think, is why it is so important that we spend our time not so much in doing relatively gross experiments in which we administer the maximum tolerated dose for the longest period of time possible, but rather make some attempt to understand the various factors that are operative in a particular carcinogenic situation, such as metabolic pathways, host protective mechanisms, promoting, cocarcinogenic, and perhaps inhibitory reactions with some of the carcinogens."*

I had some other general comments in regard to occupational carcinogenesis. I believe greater attention should be paid to the isolation and speciation of occupational carcinogens, particularly to inorganic agents which are considered to be carcinogens. I also believe that where valid epidemiological experience is available in exposed workers, it should take precedence over experimental data.

Mutagens, teratogens and reproductive hazards

At present there is little direct evidence of the interaction of chemical agents at the workplace with the process of heredity.

Teratogens are substances which cause defects in fetal development. The process of embryogenesis is a precisely programmed sequence of cell proliferation, differentiation, migration, and organogenesis. Various types of adverse effects on the human fetus have been reported for about 200 different chemicals according to Harbison.[14] Human experience and animal experiments have demonstrated that susceptibility to teratogenic agents varies with the development stage at the time of exposure. The most critical period in humans is the first three months of pregnancy. Chemically induced teratogenic effects are dose-related, and there is a threshold below which teratogenic effects do not occur according to Harbison and Becker.[15] There is a marked species difference with many teratogens. For example, the smallest teratogenic dose in humans for thalidomide was 0.5 to 1.0 mg/kg, whereas the largest no effect dose in the rat and mouse was 4000 mg/kg. Teratogens in animal models include organic and inorganic mercury compounds, lead, thallium, selenium, agents causing hypoxia, e.g., carbon monoxide and a number of organic solvents such as benzene, xylene and cyclohexanone. Present information on teratogenic hazards from exposure to chemical agents in the workplace is still sparse. As such information becomes available it should be included in appropriate TLVs.

Toxic effects of drugs and chemicals on the male and female reproductive systems have also been reported. Male workers exposed to 1,2-dibromo-3-chloropropane (DBCP) became sterile. The effects of chemicals on human reproduction and the risks from occupation are difficult to assess because of the complexity of the reproductive process and the length of time required for human maturation.

Hypersusceptible workers

As noted earlier, TLVs represent exposure concentrations under which it is believed that nearly all workers will not suffer an adverse health effect with prolonged exposure. TLVs are not designed nor intended to protect all workers. Some workers are known to be more susceptible than others to the effects of exposure to chemicals for a variety of reasons, including inherited genetic disorders, nutritional deficiencies, parasitic diseases, pre-existing diseases such as bronchial asthma or chronic bronchitis, alcohol and drug consumption, and cigarette smoking.

Some individuals have a deficiency of glucose-6-phosphate dehydrogenase (G-6-PD) in their red cells. Because of this inherited genetic trait they are more likely to develop hemolytic anemia with exposure to certain industrial chemicals. This trait is found more frequently in United States black males, certain groups of Mediterranean origin, and in some other groups. Stokinger and Mountain[16,17] have described the workplace exposures which may present additional risk for this group of workers and tests which may be applied to detect this trait. The preface of the TLV booklet also contains a note concerning hypersusceptible workers.

Serum alpha-antitrypsin deficiency is another example of an inherited genetic condition which has been associated with increased risk of developing chronic respiratory disease.

Emery *et al*[18] found that patients with squamous cell carcinoma of the lung had increased aryl hydrocarbon hydroxylase (AHH) activity over that found among matched controls or among patients with other types of cancer. This suggests that there may be individuals who are predisposed genetically to lung cancer should they smoke cigarettes or be exposed to environmental agents which cause cancer.

It is important to determine whether hypersusceptibility exists in order to protect this group of workers. TLVs are not adequate nor appropriate in cases where workers have a different response threshold. There are, however, difficulties with this concept because screening procedures for hypersusceptible workers are interpreted by some as contrary to the requirements for equal employment opportunity and nondiscrimination, and used against the interests of the workers. I believe that there are two competing social priorities in this case — the protection of health and safety versus equal opportunity employment. In my opinion, prudence would dictate that safety and health concerns take priority.

Biological thresholds

Elkins,[19] who succeeded Stokinger as Chairman of the TLV Committee, felt that biological threshold limit values were entirely feasible and inevitable for many occupational exposures. Elkins distinguished between a primary biological excretion threshold which was not associated with ill health and a secondary threshold which, if exceeded, would inevitably lead to symptoms of poisoning. This viewpoint again confirms the concept of a threshold effect as determined by biological indices.

The preface of the TLV booklet makes mention of Biological Limit Values (BLVs).

> *"These values represent limiting amounts of substances (or their effects) to which the workers may be exposed without hazard to health or well-being as determined in his tissues and fluids or in his exhaled breath."*

BLVs are useful in that they reflect total exposure — dermal, oral, and airborne. They also reflect exposures off the job as well as on the job. BLVs also reflect the worker's individual response to chemical substances.

Measurements may be made of the chemical substance itself, its metabolite(s), or the effects of exposure on some critical enzyme system or physiologic function. Samples of blood, urine, hair, nails, or expired air may be analyzed for this form of health surveillance. It is important to stress that health surveillance, including the use of BLVs is not to be regarded as a substitute for the proper control of the work environment, but rather as a supplement and back-up to these measures.

It is of interest that, at the present time, both the ACGIH TLV Committee and the German MAK Committee are currently considering BLVs for a number of chemical substances.

Conclusions

Thanks to the foresight of the ACGIH and to the professional integrity and skills of individuals

such as Dr. Stokinger, the TLVs have been developed for a large number of chemical substances. I sometimes wonder where we would be today in occupational health if there had not been the TLVs for industrial hygienists, state agencies and others to draw on, and for all of us in the field of occupational health to criticize.

TLVs are of great use to industrial hygienists and others in helping to assess and control workplace exposure to chemical and physical agents. In my opinion, there will continue to be a need for such a committee, comprising knowledgeable and representative groups of experts, who can assess the scientific information, and, in the light of their experience and judgment, recommend appropriate exposure TLVs.

I believe the scientific information supports the concept of dose-effect threshold for most chemical substances. I believe that, even for chemical carcinogens, the prudent extrapolation of data from the human and animal studies will permit the development and use of TLVs for these substances. TLVs can never be used to guarantee absolute safety, but they can be used to control adverse health effects of all types below the point at which they can be distinguished from their background occurrence.

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Dr. Ernest Mastromatteo was born in Toronto in 1923. In 1947 he received his M.D. degree from the University of Toronto. From 1947 to 1948 Dr. Mastromatteo did his Junior Internship at St. Michael's Hospital in Toronto. He received his D.P.H. degree from the same University in 1950, and from 1948 to 1949 he was a Senior Intern of Medicine at Ottawa General Hospital, Ottawa. In 1949 Dr. Mastromatteo became Medical Director of Virden Health Unit in Virden, Manitoba and held this position until 1952. From 1952 to 1974 Dr. Mastramatteo was director of the Occupational Health Protection Branch of the Ontario Ministry of Health. He also received his D.I.H. in 1958 from the University of Toronto. Dr. Mastromatteo was chief from 1974 to 1976 of the Occupational Safety and Health Branch of the International Labour Organization in Geneva, Switzerland. In 1976 Dr. Mastromatteo became the Director of the Occupational Health of INCO Limited, and in 1979 became an Honorary Consultant of Occupational Medicine at St. Michael's Hospital in Toronto.

The following are some of the professional activities of Dr. Mastromatteo: Certified as Specialist in Occupational Medicine, American Board of Preventive Medicine; served on Chemical Substances Threshold Limit Values Committee of ACGIH for many years; Chairman, American Conference of Governmental Industrial Hygienists, 1969-1970; served as consultant on occupational diseases, Ontario Workman's Compensation Board, 1966-1974; lecturer, professor and head (part-time), Department of Environmental Health, School of Hygiene, University of Toronto 1972-1974; Trustee and Board member, American Board of Preventive Medicine, 1969-1978; served as WHO-ILO Consultant on Occupational Health; member, Ontario Medical Association; Chairman, Section on Occupational Health; member, Permanent Commission and Interna-

tional Association on Occupational Health; recipient of the Canada Safety Council's Achievement Award for Occupational Safety and Health in Canada, 1979; about 35 papers on occupational health, including papers on toxicity of vinyl chlorides, mortality in city fire fighters, health hazards in welding, etc. While serving with the ILO, visited many countries to review and assist in their national programs in occupational safety and health; conducted a seminar in Singapore on Health and Safety in Relation to Occupation, and led a study tour to the Soviet Union to revelw occupational safety and health in heavy construction.

THIRTY-FIVE YEAR INDEX WITH RECOMMENDATIONS

1946

Report of the sub-committee on threshold limits*

DR. FREDRICK: Considerable difficulty attends the fixing of satisfactory values for maximal allowable concentrations of chemicals in respirable atmospheres because of the lack of sufficient toxicological data and the lack of a uniform definition of the maximal allowable concentration concept. One concept is that the M.A.C. value should represent as accurately as possible that concentration at which a worker exposed for a sufficient period of time will just escape physiological or organic injury and occupational disease. A second concept is that the M.A.C. should represent some fraction of that concentration which will injure the worker in order to allow a margin of safety in the design of protective equipment and guard against possible synergistic effects in the case of multiple exposures. A third concept is that the M.A.C. should perform the functions of the former concepts and in addition provide a work environment free of objectionable but non-injurious concentrations of smokes, dusts, irritants and odors. Obviously all of these concepts cannot be fulfilled with the establishment of a single value. M.A.C. values in use at the present time represent examples of all of these concepts.

The committee feels that the establishment of dual lists or a single definition of the M.A.C. is not possible at the present time.

An extensive list of M.A.C. values is presented to the conference for use during 1946, with the definite understanding that it be subject to annual revision. Values have been compiled from the list reported by this sub-committee[A] at the 5th annual meeting of the N.C.G.I.H. in 1942, from the list published by Warren Cook[B] in *Industrial Medicine,* Vol. 14, p. 936, 1945, and from published values of the Z-37 Committee of the American Standards Association.[A]

It will be noted that many of these values have been in general use by members of the conference for several years.

Maximum Allowable Concentrations of Air Contaminants for 1946

(These values are subject to annual revision)

Data for these values have been obtained primarily from the report of this Committee in 1942, the compilation by Warren Cook, *Industrial Medicine,* Vol. 14, p. 936, 1945 and the values established by the American Standards Association Committee.

Group I Gases and Vapors

Substance	M.A.C. (ppm)
Acetaldehyde	200
Acetic acid	10
Acetone	500
Acrolein	0.5
Acrylonitrile	20
Ammonia	100
Amyl acetate	200
iso-Amyl alcohol	100
Aniline	5
Arsine	1
Benzene (Benzol)	100
Bromine	1
1,3-Butadiene	5000
n-Butanol	50
2-Butanone	200
n, Butyl acetate	200
Butyl cellosolve	200
Carbon dioxide	5000
Carbon disulfide	20
Carbon monoxide	100
Carbon tetrachloride	50
Cellosolve	200
Cellosolve acetate	100
Chlorine	5
2-Chlorobutadiene	25
Chloroform	100
1-Chloro-1-nitropropane	20
Cyclo hexane	400
Cyclo hexanol	100
Cyclo hexanone	100
Cyclo hexene	400
o-Dichlorobenzene	75
Dichloro difluoro methane	10,000
1,1-Dichloro ethane	100
1,2-Dichloro ethane	100
1,2-Dichloro ethylene	200
Di chloro ethyl ether	15
Di chloro methane	500
Di chloromonofluromethane	5000

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* Published in the *Proceedings of the Eighth Annual Meeting of the American Conference of Governmental Industrial Hygienists,* April 7-13, 1946 Chicago, IL, pp. 54-55.

[A] *See* Appendix A of this volume.

[B] *See* Appendix C of this volume.

Substance	M.A.C. (ppm)
1,1-Dichloro-1-nitro-ethane	10
Dichlorotetrafluoro ethane	10,000
Dimethylaniline	5
Dimethylsulfate	1
Dioxane	500
Ethyl acetate	400
Ethyl alcohol	1000
Ethyl benzene	200
Ethyl bromide	400
Ethyl chloride	5000
Ethylene chlorhydrin	10
Ethylene dichloride — see 1,2-Dichloroethane	
Ethylene oxide	100
Ethyl ether	400
Ethyl formate	200
Ethyl silicate	100
Freon — see dichloro difluro methane	
Formaldehyde	10
Gasoline	500
Heptane	500
Hexane	500
Hydrogen chloride	10
Hydrogen cyanide	20
Hydrogen fluoride	3
Hydrogen selenide	0.1
Hydrogen sulfide	20
Isophorone	25
Mesityl oxide	50
Methanol	200
Methyl acetate	100
Methyl bromide	20
Methyl butanone	200
Methyl cellosolve	100
Methyl cellosolve acetate	100
Methyl chloride	200
Methylcyclohexane	500
Methyl cyclo hexanol	100
Methyl cyclo hexanone	100
Methyl ethyl ketone	200
Methyl formate	400
Methyl iso-butyl ketone	200
Mono chloro benzene	75
Mono fluro trichloro methane	10,000
Mononitro toluene	5
Naphtha (coal tar)	100-200
Naphtha (petroleum)	500
Nitro benzene	5
Nitro ethane	200
Nitrogen oxides (other than nitrous oxide)	25
Nitroglycerin	0.5
Nitromethane	200
Octane	500
Ozone	1
Pentane	5000
Pentanone (methyl propanone)	200
Perchloroethylene — see tetrachloroethylene	
Phosgene	1
Phosphine	1
Phosphorus trichloride	0.5
iso-Propanol	400
Propyl acetate	200
iso-Propyl ether	500
Stibine	10
Stoddard solvent	500
Styrene monomer	400
Sulphur chloride	1
Sulphur dioxide	10
1,1,2,2-Tetra chloroethane	10
Tetra chloro ethylene	200
Toluene	200
Toluidine	5
Trichloroethylene	200
Turpentine	100
Vinyl chloride	500
Xylene	200

Group II Toxic Dusts, Fumes and Mists

Substance	Mg/M^3
Barium peroxide (as Ba)	0.5
Cadmium	0.1
Chloro di phenyl	1.0
Chromic acid and chromates (as Cr_2O_3)	0.1
Dinitro toluene	1.5
Fluorides (as F)	2.5
Iodine	0.1
Iron oxide fume	15
Lead	0.15
Magnesium oxide fume	15
Manganese	6
Mercury	0.1
Pentachloronaphthalene	0.5
Sulfuric acid	0.5
Tellurium	0.01
Tetryl	1.5
Trichloronaphthalene	5
Trinitrotoluene	1.5
Zinc oxide fume	15

Group III Mineral Dusts

Substance	M.P.P.C.F.
Alundum	50
Asbestos	5
Carborundum	50
Portland cement	50
Mica (below 5% free silica)	50
Nuisance (no free silica)	50
Silica — High (above 50% free SiO_2)	5
Silica — Medium (5-50% free SiO_2)	20
Silica — Low (below 5%)	50
Slate — (below 5% free SiO_2)	50
Soapstone (below 5% free SiO_2)	50
Talc	20
Total dust (below 5% free SiO_2)	50

Group IV Radiations

Material or Radiation	Radiant Energy
Radon or thoron gas	10^{-8} Curries/M^3
X or Gamma Radiation	0.1 Roentgen per 8 hr day

CHAIRMAN BREHM: Thank you, Dr. Frederick. Is there any comment? If not, the chair will entertain a motion regarding that report.

... It was moved and seconded that the report be accepted. The motion was put to a vote and carried ...

CHARIMAN BREHM: The motion is carried. Thank you, Dr. Fredrick.

Committee members:

Dr. W. G. Fredrick, *Chairman*
Mr. M. Bowditch
Mr. A. M. Dooley
Dr. P. Drinker
Dr. L. T. Fairhall

1947 M.A.C. Values*

The following maximum allowable concentration values were a part of the report submitted by the Committee on Threshold Limits and accepted by the American Conference of Governmental Industrial Hygienists at the 1947 meeting. These values are revised annually.

Gases and Vapors

Substance	M.A.C. (ppm*)
Acetaldehyde	200
Acetic acid	10
Acetic anhydride	5
Acetone	500
Acrolein	0.5
Acrylonitrile	20
Ammonia	100
Amyl acetate	200
iso-Amyl alcohol	100
Aniline	5
Arsine	0.05
Benzene (benzol)	50
Bromine	1
1,3-Butadiene	1000
n-Butanol	50
2,Butanone	200
n,Butyl acetate	200
Butyl "cellosolve"	200
Carbon dioxide	5000
Carbon disulfide	20
Carbon monoxide	100
Carbon tetrachloride	50
"Cellosolve"	200
"Cellosolve" acetate	100
Chlorine	2
2-Chlorobutadiene	25
Chloroform	100
1-Chloro-1-nitropropane	20
Cyclohexane	400
Cyclohexanol	100
Cyclohexanone	100
Cyclohexene	400
Cyclopropane (propene)	400
o-Dichlorobenzene	50
Dichlorodifluoromethane	1000
1,1-Dichloroethane	100
1,2-Dichloroethane (ethylene dichloride)	75
1,2-Dichloroethylene	200
Dichloroethyl ether	15
Dichloromethane	500
Dichloromonofluormethane	1000
1,1-Dichloro-1-nitroethane	10
Dichlorotetrafluoroethane	1000
Dimethylaniline	5
Dimethylsulfate	1
Dioxane	100
Ethyl acetate	400
Ethyl alcohol	1000
Ethyl benzene	200
Ethyl bromide	200
Ethyl chloride	1000
Ethylene chlorhydrin	5
Ethylene oxide	100
Ethyl ether	400
Ethyl formate	100
Ethyl silicate	100
Formaldehyde	10
Gasoline	500
Heptane	500
Hexane	500
Hydrogen chloride	10
Hydrogen cyanide	20
Hydrogen fluoride	3
Hydrogen selenide	0.1
Hydrogen sulfide	20
Isophorone	25
Mesityl oxide	50

* Published in *Transactions of the Ninth Annual Meeting of the American Conference of Governmental Industrial Hygienists*, April 26-27, 1947 Buffalo, NY, and in the *Industrial Hygiene Newsletter*, p. 15 (August 1947)

Substance	M.A.C. (ppm*)
Methanol	200
Methyl acetate	200
Methyl bromide	20
Methyl butanone	100
Methyl "cellosolve"	25
Methyl "cellosolve" acetate	25
Methyl chloride	100
Methylcyclohexane	500
Methyl cyclohexanol	100
Methyl cyclohexanone	100
Methyl formate	100
Methyl iso-butyl ketone	100
Monochlorobenzene	75
Monofluortrichloromethane	1000
Mononitrotoluene	5
Naphtha (coal tar)	200
Naphtha (petroleum)	500
Nickel carbonyl	1
Nitrobenzene	1
Nitroethane	100
Nitrogen oxides (other than nitrous oxide)	25
Nitroglycerine	0.5
Nitromethane	100
2-Nitropropane	50
Octane	500
Ozone	1
Pentane	1000
Pentanone (methyl propanone)	200
Phosgene	1
Phosphine	0.05
Phosphorus trichloride	0.5
iso-Propanol	400
Propyl acetate	200
iso-Propyl ether	400
Stibine	0.1
Stoddard solvent	500
Styrene monomer	200
Sulfur chloride	1
Sulfur dioxide	10
1,1,2,2-Tetrachloroethane	5
Tetrachloroethylene	100
Toluene	200
Toluidine	5
Trichloroethylene	150
Turpentine	100
Vinyl chloride (chloroethane)	500
Xylene	200

Toxic Dusts, Fumes, and Mists

Substance	mg/m³*
Antimony	0.1
Arsenic	0.1
Barium	0.5
Cadmium	0.1
Chlorodiphenyl	1
Chromic acid and chromates (as CrO_3)	0.1
Cyanide, as CN	5
1,2-Dichloropropane (propylene dichloride (ppm)	75

Substance	mg/m³*
Dinitrotoluene	1.5
Flourides	2.5
Iodine	0.1
Iron oxide fume	15
Lead	0.15
Magnesium oxide fume	15
Manganese	6
Mercury	0.1
Pentachloronaphthalene	0.5
Pentachlorophenol	0.5
Phosphorus (yellow)	0.1
Phosphorus pentachloride	1
Phosphorus pentasulfide	1
Selenium, compounds as selenium	0.1
Sulfuric acid	0.5
Tellurium	0.1
Tetryl	1.5
Trichloronaphthalene	5
Trinitrotoluene	1.5
Zinc oxide fumes	15

Mineral Dusts

Substance	M.P.P.C.F.*
Alundum	50
Asbestos	5

M.A.C. Values

Substance	M.P.P.C.F.*
Carborundum	50
Dust (nuisance, no free silica)	50
Mica (below 5 percent free silica)	50
Portland cement	50
Silica high — (above 50 percent free SiO_2)	5
Silica — medium (5 to 50 percent free SiO_2)	20
Silica — low (below 5 perent free SiO_2)	50
Slate (below 5 percent free SiO_2)	50
Soapstone (below 5 percent free SiO_2)	50
Talc	20
Total dust (below 5 percent free SiO_2)	50

Radiations

Material or Radiation	Radiant Energy
Gamma radiation	0.1 roentgen per day.
Radon	10^{-8} curies per cubic meter.
Thoron	10^{-8} curies per cubic meter.
X-ray	0.1 roentgen per day.

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* ppm = parts per million.
* mg/m³ = milligrams per cubic meter.
* M.P.P.C.F. = million particles per cubic foot of air, standard light field count.

Committee members:
Same as 1946.

1948

Report of the committee on threshold limits*

DR. L.T. FAIRHALL (U.S. Public Health Service): It is obviously difficult, where a large number of substances is involved, to review the maximum allowable concentration values in detail at an annual meeting. For that reason, provision was made early in the organization of the American Conference of Governmental Industrial Hygienists for a Committee on Threshold Limits to study this question and to report to the Conference at its annual meeting. The composition of this Committee is not fixed but is changed by annual appointment and the threshold limit values are similarly maintained in a fluid state by annual revision. For a number of years the Committee has subjected these values to careful scrutiny and attempted to bring them into close conformance with practice.

During the present year, it was felt that the concept of maximum allowable values had now reached a stage where more extensive participation of the members of the Conference in the formulation of these values based upon personal experience in the field would be of decided assistance. This year, therefore, your Committee has for the first time, I believe, made a direct attempt to obtain a statement from each member of the Conference with reference to the annual threshold limit values and the response from the individual members has been most generous and helpful.

In view of the annual revision of threshold limit values, it has been the purpose of the Conference to seek values which, on the one hand protect the individual workman, and on the other would impose no impossible burden on the manufacturer. This balance is difficult to achieve but can be attained by just such a series of adjustments as is provided for in the Constitution of the Conference. There is no industrial poison so potent, so virulent, that it cannot be manufactured safely under carefully controlled conditions. The manufacture and widespread use of such a substance as lead tetraethyl and the preparation of extremely poisonous war gases are good illustrations of this. In fact, the chemical manufacturing industry in general has been able to maintain a high standard of safe industrial practice by the installation of suitable control measures for the protection of its workers. There is no reason why such safe industrial control measures cannot be extended to industry in general wherever industrial poisons occur.

In addition to the comments of the members of the Conference, a few criticisms from other sources have reached us concerning the 1947 values. These may be briefly summarized as follows:

1. Concerning the membership at large, criticism has taken the form that a) values were arrived at by consulting the membership at large, and b) that the members were not consulted.
2. The publication of the values in the *Industrial Hygiene Newsletter* made it appear that the values were those of the U.S. Public Health Service. Whether this was wishful thinking or not, the source of the 1947 values was clearly indicated at the time of publication.
3. Criticism has also taken the form that the values given were not arrived at or based upon scientific evidence. The latter has particularly interested your present Committee. No specific "scientific evidence" has so far been presented for our consideration along with this criticism.

While it will doubtless be very advantageous to have what might be called permanent or standard maximum allowable concentration values, it must be borne in mind that all our values at the present time are fluid and subject to annual revision. They should not be adopted as fixed or legal values, but merely as guides to assist us in defining more or less safe working conditions. It is felt that eventually definite values can be established which will give full and ample protection to the worker.

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* Published in *Transactions of the Tenth Annual Meeting of the American Conference of Governmental Industrial Hygienists*, March 27-30, 1948 Boston, MA, pp. 29-31.

The following changes have been made in the values from those of the 1947 conference:

Benzene has been decreased from 50 to 35 ppm
Chlorine has been decreased from 2 to 1 ppm
Formaldehyde has been decreased from 10 to 5 ppm
Hydrogen chloride has been decreased from 10 to 5 ppm
Hydrogen cyanide has been decreased from 20 to 10 ppm
Hydrogen selenide has been decreased from 0.10 to 0.05 ppm
Trichloroethylene has been decreased from 150 to 100 ppm
Iodine has been changed from 0.1 mg./cu.m. to 1 ppm
2-Butanone has been increased from 200 to 250 ppm
Isopropyl ether has been increased from 400 to 500 ppm
Antimony has been increased from 0.1 mg./cu.m. to 0.5
Arsenic has been increased from 0.1 mg./cu.m. to 0.5
Sulfuric acid has been increased from 0.5 mg./cu.m. to 1.0

It must be borne in mind that these values are not indices of toxicity and are not intended to approach that value. Accordingly, the comparative toxicity of these compounds cannot be established on the basis of their numerical maximum allowable concentration value.

People vary greatly in response to drugs and toxic substances. Therefore, it is a figment of the imagination to think that we can set down a precise limit below which there is complete safety and immediately above which there may be a high percentage of cases of poisoning among those exposed.

With these facts in mind the Committee has set values below which it is fair to expect reasonable protection and above which it is reasonable to expect that we can have occasional cases of poisoning.

Threshold Limit Values

Adopted at the April 1948 meeting of American Conference of Governmental Industrial Hygienists in Boston, Massachusetts.

Gases and Vapors

Substance	P.P.M.
Acetaldehyde	200
Acetic acid	10
Acetic anhydride	5
Acetone	500
Acrolein	0.5
Acrylonitrile	20
Ammonia	100
Amyl acetate	200
iso-Amyl alcohol	100
Aniline	5
Arsine	0.05
Benzene (benzol)	35
Bromine	1
1,3-Butadiene	1000
n-Butanol	50
2-Butanone	250
n-Butyl acetate	200
Butyl cellosolve	200
Carbon dioxide	5000
Carbon disulfide	20
Carbon monoxide	100
Carbon tetrachloride	50
Cellosolve	200
Cellosolve acetate	100
Chlorine	1
2-Chlorobutadiene	25
Chloroform	100
1-Chloro-1-nitropropane	20
Cyclohexane	400
Cyclohexanol	100
Cyclohexanone	100
Cyclohexene	400
Cyclopropane (propene)	400
o-Dichlorobenzene	50
Dichlorodifluoromethane	1000
1,1-Dichloroethane	100
1,2-Dichloroethane (ethylene dichloride)	75
1,2-Dichloroethylene	200
Dichloroethyl ether	15
Dichloromethane	500
Dichloromonofluoromethane	1000
1,1-Dichloro-1-nitroethane	10
1,2-Dichloropropane (propylene dichloride)	75
Dichlorotetrafluorethane	1000
Dimethylaniline	5
Dimethylsulfate	1
Dioxane	100
Ethyl acetate	400
Ethyl alcohol	1000
Ethyl benzene	200
Ethyl bromide	200
Ethyl chloride	1000
Ethylene chlorohydrin	5
Ethylene oxide	100
Ethyl ether	400
Ethyl formate	100
Ethyl silicate	100

Substance	PPM
Formaldehyde	5
Gasoline	500
Heptane	500
Hexane	500
Hydrogen chloride	5
Hydrogen cyanide	10
Hydrogen fluoride	3
Hydrogen selenide	0.05
Hydrogen sulfide	20
Iodine	1
Isophorone	25
Mesityl oxide	50
Methanol	200
Methyl acetate	200
Methyl bromide	20
Methyl butanone	100
Methyl cellosolve	25
Methyl cellosolve acetate	25
Methyl chloride	100
Methylcyclohexane	500
Methylcyclohexanol	100
Methylcyclohexanone	100
Methyl formate	100
Methyl iso-butyl ketone	100
Monochlorobenzene	75
Monofluorotrichloromethane	1000
Mononitrotoluene	5
Naphtha (coal tar)	200
Naphtha (petroleum)	500
Nickel carbonyl	1
Nitrobenzene	1
Nitroethane	100
Nitrogen oxides (other than N_2O)	25
Nitroglycerin	0.5
Nitromethane	100
2-Nitropropane	50
Octane	500
Ozone	1
Pentane	1000
Pentanone (methyl propanone)	200
Phosgene	1
Phosphine	0.05
Phosphorus trichloride	0.5
Iso-Propanol	400
Propyl acetate	200
Iso-Propyl ether	500
Stibine	0.1

Committee members:

Dr. L. T. Fairhall, *Chairman*
Mr. A. N. Setterlind
Dr. W. G. Fredrick
Dr. Leonard Greenburg
Dr. H. Elkins

1949

Report of the committee on threshold limits*

DR. L.T. FAIRHALL (Public Health Service, Bethesda, Maryland): During the present year, your Committee has again been fortunate in receiving suggestions, comments, and data from the individual members of the Conference with reference to the threshold limit values in current use. In addition, a few suggestions have been received from non-members. These have all been of the greatest service to the Committee as they present a practical approach to the question of utilizing these values to best advantage.

The response to the current list of threshold values has, on the whole, been very favorable. In general, some sixteen of the present values are considered to be somewhat too high by members of the Conference. On the other hand, we have received comments from outside the Conference that a few, namely benzene, carbon tetrachloride, and arsine, are too low. The value for arsine, which is well justified if we are to use the present value for arsenic, presents some difficulty and it is a matter of some question as to whether any continuous exposure to arsine should be permitted in industry, however small. The toxicity of arsine is so great and its effects so immediate that the industrial hygienists should be alert to the danger and should anticipate control of this hazard in all possible cases.

Your Committee has reviewed all the cases where changes have been suggested but has made no substantial changes in the present list of values. While data have been presented to us in a number of cases and which would appear to justify such changes, these data were in general insufficient. The current literature presents many cases of industrial poisoning but, in most instances, those cases resulted from accident, and exposure at the time of accident was unknown or if occupational illness resulted from continuous exposure,

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* Published in *Transactions of the Eleventh Annual Meeting of the American Conference of Governmental Industrial Hygienists,* April 2-5, 1949 Detroit, MI, pp. 63-65.

no measurements of such prior exposure had been made. Experience of many industrial hygienists in plants where hazardous substances are in use has been very helpful, however, and it is to be hoped that individual members of the Conference will continue to accumulate data and to correlate these data with occupational illness so that threshold limit values based upon human experience will be arrived at with more precision.

Owing to the insufficiency of the data at present available for further changing the current values, the Committee has adopted a new form of presentation. Briefly this consists of 1) the table of recommended threshold limit values for 1949, which is identical with that of 1948; 2) threshold limit values for new substances suggested by the Committee with threshold limit values based upon review of adequate data; 3) substances for which no present threshold limit value exists; and 4) substances for which somewhat lower values have been suggested by members of the Conference.

These various values are presented in the following tables:

TABLE I
New Threshold Limit Value

Ortho-dinitro-cresol
A value for ortho-dinitro-cresol of 0.2 milligram per cubic meter of air has been suggested on the basis of plant experience with this substance.

TABLE II
Proposed New Substances for which no Threshold Limit Value has been Established

Asphalt fumes and dust	Ketene
Beryllium	Monochloromonobromomethane
DDD	Pentachlorophenol
DDT	Propylene glycol
Ethylene glycol	Triethylene glycol
Diethylene glycol	
Dipropylene glycol	

TABLE III
Substances for which Lower Threshold Limit Values have been Suggested by the Conference Members

Acetic acid	Hydrochloric acid
Acrolein	Naphtha (petroleum)
Alcohol, amyl	Nuisance dust
Alcohol, isoamyl	Ozone
Ammonia	Radiation, gamma
Benzene	Radiation, X-ray
Bromine	Silica
Carbon monoxide	Stoddard solvent
Carbon tetrachloride	Sulfuric acid
Hexavalent chromium	Trichloroethylene

Report of the committee on dust counting

DR. W.G. FREDRICK (Detroit Department of Health): Your Committee has critically reviewed the optical counting methods in general use for evaluating atmospheric dustiness. This is a preliminary report of the Committee.

1. Light field counting methods in general use will, under desirable conditions and in the hands of skilled observers, yield order of magnitude estimates of the extent of atmospheric dustiness, e.g., 1 million, 5 million, 20 million, 50 million, 100 million. Variations of considerable magnitude are expectable among evaluations made by experienced observers using similar procedures on identical samples.
2. Light field optical methods, using 16 mm. objectives, are of little utility for samples containing a significant percentage of particles below one micron in size. Such samples should be examined by auxiliary methods capable of resolving small particles.
3. Standardization of counting cells, media and similar details produces little improvement of accuracy.
4. The accuracy of optical methods of counting cannot be substantially improved.
5. The present light field optical method should be retained until new methods of evaluation based on particle surface area, electronic counting, etc., are developed or devised.

6. Use of the light field optical counting method should be restricted to evaluating mineral dusts for which suitable chemical methods of analysis are not available.
7. More accurate physiological information concerning the effect of concentration, particle size, surface area and solubility is needed to expedite the development of new evaluation procedures.
8. Methods now available for estimating the silica content of airborne dust samples will be inadequate when more precise total dust evaluation methods are developed.
9. Methods used by industrial hygienists for evaluating particle distribution are for the most part obsolete. Techniques developed for use in other fields of study should be applied to this industrial hygiene problem.

Committee members:

Dr. H. H. Schrenk, *Chairman*
Dr. J. Shilen
Mr. L. F. Garber
Mr. C. E. Couchman
Mr. F.R. Ingram

1950

Report of the committee on threshold limits*

DR. L.T. FAIRHALL (U.S. Public Health Service): The Committee on Threshold Limits has this year proposed a few changes in the values from those previously reported and has made a few suggestions which I take pleasure in reporting.

It is suggested that more attempt should be made on the part of those reporting original work to define safe working conditions, that is, permissible concentration values to which workers may be exposed. All too frequently original work on the toxicity of a given substance fails to take into account the possible need for such data and it requires much study to arrive at any conclusion regarding its usefulness for inclusion in a table of threshold limit concentrations.

At the present time there is a great deal of interest in a number of organic insecticides, some of which are very poisonous indeed. It is also a matter of increasing interest to the industrial hygienist and is being brought to his attention by fatal and near-fatal cases in industry as well as in the application of these materials. It is in question how far we feel we should enter into this field and whether we should consider the matter of threshold limits for such insecticides. Also, it is complicated by the fact skin absorption occurs in many cases as well as injury from inhalation.

The changes in the Table which the Committee recommends for the present year are as follows:

1. Gamma radiation should be placed at 0.3 roentgen per week in place of 0.1 roentgen per day.
2. X-ray radiation should be placed at 0.3 roentgen per week in place of 0.1 roentgen per day.
3. o-Dinitro cresol should be added to the table with a value of 0.2 milligram per cubic meter of air.
4. n-Butanol should be changed from 50 parts per million to 100 parts per million.
5. It is also suggested that the hygienic significance of tripoli should be reviewed for future inclusion in the Table.

In connection with its review of the threshold limit values hitherto reported, the Committee has undertaken the special task of bringing the significant information (concerning these substances) together in permanent form. "Documentation," I believe is the term in current parlance. This enormous task could not, of course, be completed in one year. However, twenty-five substances have been reviewed, and the references together with the abstracted material have been compiled. It is to be hoped that future committees will continue this work, as this will eventually constitute a valuable set of reference material for the individual members of the Conference.

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* Published in *Transactions of the Twelfth Annual Meeting of the American Conference of Governmental Industrial Hygienists*, April 22-25, 1950, Chicago, IL, pp. 33-34.

Threshold Limit Values

Adopted at the April 1950 meeting of the American Conference of Governmental Industrial Hygienists in Chicago. Reprinted from the *Archives of Industrial Hygiene and Occupational Medicine* 2:98-100 (July 1950).

Gases and Vapors

Substance	P.P.M.
Acetaldehyde	20
Acetic acid	10
Acetic anhydride	5
Acetone	500
Acrolein	0.5
Acrylonitrile	20
Ammonia	100
Amyl acetate	200
Isoamyl alcohol	100
Aniline	5
Arsine	0.05
Benzine (benzol)	35
Bromine	1
1,3-Butadiene	1000
n-Butanol	100
2-Butanone	250
n-Butyl acetate	200
Butyl cellosolve® (2-Butoxyethanol)	200
Carbon dioxide	5000
Carbon disulfide	20
Carbon monoxide	100
Carbon tetrachloride	50
Cellosolve® (2-Ethoxyethanol)	200
Cellosolve® acetate	100
Chlorine	1
Chlorobenzene	75
2-Chlorobutadiene	25
Chloroform	100
1-Chloro-1-nitropropane	20
Cyclohexane	400
Cyclohexanol	100
Cyclohexanone	100
Cyclohexene	400
Cyclopropane (propene)	400
o-Dichlorobenzene	50
Dichlorodifluoromehtane	1000
1,1-Dichloroethane	100
1,2-Dichloroethane (ethylene dichloride)	75
1,2-Dichloroethylene	200
Dichloroethyl ether	15
Dichloromethane	500
Dichloromonofluoromethane	1000
1,1-Dichloro-1-nitroethane	10
1,2-Dichloropropane (propylene dichloride)	75
Dichlorotetrafluoroethane	1000
Dimethylaniline	5
Dimethylsulfate	1
Dioxane	100
Ethyl acetate	400
Ethyl alcohol	1000
Ethyl benzene	200
Ethyl bromide	200
Ethyl chloride	1000
Ethylene chlorohydrin	5
Ethylene oxide	100
Ethyl ether	400
Ethyl formate	100
Ethyl silicate	100
Fluorotrichloromethane	1000
Formaldehyde	5
Gasoline	500
Heptane	500
Hexane	500
Hydrogen chloride	5
Hydrogen cyanide	10
Hydrogen fluoride	3
Hydrogen selenide	0.05
Hydrogen sulfide	20
Iodine	1
Isophorone	25
Mesityl oxide	50
Methanol	200
Methyl acetate	200
Methyl bromide	20
Methyl butanone	100
Methyl cellosolve® (2-methoxyethanol)	25
Methyl cellosolve® acetate	25
Methyl chloride	100
Methylcyclohexane	500
Methylcyclohexanol	100
Methylcyclohexanone	100
Methyl formate	100
Methyl iso-butyl ketone	100
Naphtha (coal tar)	200
Naphtha (petroleum)	500
Nickel carbonyl	1
Nitrobenzene	1
Nitroethane	100
Nitrogen oxides (other than N_2O)	25
Nitroglycerin	0.5
Nitromethane	100
2-Nitropropane	50
Nitrotoluene	5
Octane	500
Ozone	1
Pentane	1000
Pentanone (methyl propanone)	200
Phosgene	1
Phosphine	0.05
Phosphorus trichloride	0.5
Iso-propyl alcohol	400
Propyl acetate	200
Iso-propyl ether	500
Stibine	0.1
Stoddard solvent	500
Styrene monomer	200
Sulfur chloride	1
Sulfur dioxide	10

Substance	P.P.M.
1,1,2,2-Tetrachloroethane	5
Tetrachloroethylene	100
Toluene	200
Toluidine	5
Trichloroethylene	100
Turpentine	100
Vinyl chloride	500
Xylene	200

Toxic Dusts, Fumes and Mists

Substance	Mg. Per Cu. M.
Antimony	0.5
Arsenic	0.5
Barium	0.5
Cadmium	0.1
Chlorodiphenyl	1
Chromic acid and chromates, as CrO_3	0.1
Cyanide, as CN	5
Dinitrotoluene	1.5
o-Dinitrocresol	0.2
Fluoride	2.5
Iron oxide fume	15
Lead	0.15
Magnesium oxide fume	15
Manganese	6
Mercury	0.1
Pentachloronaphthalene	0.5
Pentachlorophenol	0.5
Phosphorus (yellow)	0.1
Phosphorus pentachloride	1
Phosphorus pentasulfide	1
Selenium, as Se	0.1
Sulfuric acid	1
Tellurium	0.1
Tetryl	1.5
Trichloronaphthalene	5
Trinitrotoluene	1.5
Zinc oxide fume	15

Mineral Dusts

Substance	M.P.P.C.F.
Alundum	50
Asbestos	5
Carborundum	50
Dust (nuisance, no free silica)	50
Mica (below 5% free silica)	50
Portland cement	50
Talc	20
Silica	
high (above 50% free SiO_2)	5
medium (5 to 50% free SiO_2)	20
low (below 5% free SiO_2)	50
Slate (below 5% free SiO_2)	50
Soapstone (below 5% free SiO_2)	20
Total dust (below 5% free SiO_2)	50

Substance	M.P.P.C.F.
Radiations	
Material or Radiation	
Gamma (roentgens per week)	0.3
Radon (curies per cubic meter)	10^{-8}
Thoron (curies per cubic meter)	10^{-8}
Roentgen ray (roentgens per week)	0.3

Committee members:

L.T. Fairhall, *Chairman*
Dr. Joseph Shilen
Mr. L. F. Garber
Mr. C. E. Couchman
Mr. F. R. Ingram

1951

Report of the committee on threshold limits*

DR. W.G. FREDRICK, Chairman (Detroit City Department of Health): Your Committee has received scanty correspondence from the membership this year, indicating, perhaps, reasonable satisfaction with values established to date.

Information available at the present time remains inadequate for establishment of limits for insecticides in air.

A real need has developed for a threshold limit value for noise or sound and it is believed that a value can be established soon. Similarly, it now appears that sufficient data have been accumulated to permit setting up limit values for radioactive isotopes, beryllium and uranium. It is recommended that the chairman of this committee appoint sub-committees of special experience and qualifications to assist in this work.

The changes in the Table which the Committee recommends for the present year are as follows:

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* Published in *Transactions of the Thirteenth Annual Meeting of the American Conference of Governmental Industrial Hygienists*, April 21-25, 1951 Atlantic City, NJ, pp. 27-28.

1. The value for Mica dust shall be 20 M.P.P.C.F.
2. The value for Radium 226 in air shall be 8×10^{-6} micro curies per cubic meter.
3. The value for Polonium 210 in air shall be 1×10^{6} micro curies per cubic meter.

Committee members:

W. G. Fredrick, *Chairman*
K. E. Charron
K. E. Markuson
Arthur Vorwald

1952

changes from 1951

The following new threshold limit values are recommended for addition to the 1951 list (NV).

Cresol	5 ppm
Di-ethyl amine	25 ppm
Ethyl amine	25 ppm
Methylal	1000
Phenol	?

Deletions

Radon (curies per cubic meter)	10^{-8}
Thoron (curies per cubic meter)	10^{-8}
Radium 226 (microcuries per cubic meter)	10^{-6}
Polonium 210 (microcuries per cubic meter)	10^{-6}

Committee members:

Allan L. Coleman, *Chairman*
D. H. Byers
L. T. Fairhall
Kingsley Kay
Arthur J. Vorwald
L. F. Weller

1953

changes from 1952

The following is the first proposed preface for the MAC values.

"Values are given in the following tables for the maximum average atmospheric concentration of contaminants to which workers may be exposed for an eight-hour working day without injury to health.

"These values are based on the best available information from industrial experience, from experimental studies and, when possible, from the combination of both. They are not fixed values, but are reviewed annually by the Committee on Threshold Limits for changes, revisions or additions as further information becomes available. Threshold limits should be used as guides in the control of health hazards and should not be regarded as fine lines between safe and dangerous concentrations. They represent conditions only within which it is felt that workers may be repeatedly exposed, day after day, without adversely affecting their health. It is felt, at the present time, that workers should not be exposed to a working environment containing any of these substances in excess of the value indicated."

New Values

1,2-Dibromoethane (ethylene dibromide) — 25 ppm
Fluorine (gas) — 0.1 ppm/1,1,1-Trichloroethane (methyl chloroform) — 500 ppm
0,0-Diethyl-0-p-nitrophenyl thiophosphate (parathion) — 0.1 ppm
Uranium (soluble compounds) — 0.05 mg/m^3
Uranium (insoluble compounds) — 0.25 mg/m^3

Revised Values

Acetone — 1000 ppm
Carbon tetrachloride — 25 ppm
1,2-Dichloroethane (ethylene dichloride) — 100 ppm
Tetrachloroethylene — 200 ppm
Trichloroethylene — 200 ppm

Committee members:

Allan L. Coleman, *Chairman*
William L. Ball
L. T. Fairhall
Kingsley Kay
H. E. Stokinger
A. J. Vorwald
Louis F. Weller

1954

changes from 1953

Revised Values

Nickel carbonyl — 0.001 ppm
Nitrogen oxides (other than N_2O) — 25 ppm
  Change to: Nitrogen dioxide — 5 ppm
Ozone — 0.1 ppm

Change in listing

n-Butanol — 100 ppm
  TO: n-Butyl alcohol — 100 ppm
Methyl butanone
  TO: Hexanone (methyl butyl ketone) — 100 ppm
Portland cement
  TO: Cement
Selenium, as Se
  TO: Selenium compounds, as Se — 0.1 mg/m^3

Deletions

Dichloromethane — 500 ppm
Radiations and radioactive substances

Excerpt from the 1954 committee report*

In view of several inquiries received during the year, on the subject of air pollution, your Committee considers it desirable to add the following statement to the section introducing the list of threshold limit values published annually.

"These values are not intended for use, or for modification for use, in the evaluation or control of community air pollution or air pollution nuisances."

In addition to the recommended changes mentioned above, your Committee suggests the adoption of a new procedure in the compilation of the table of threshold limit values. The established list would be continued in its present form, but would be supplemented by a second list known as "Tentative Threshold Limit Values" because of the lesser certainty associated with the values assigned. The adoption of this tentative list is suggested for the following reasons:

1. It is felt that a need exists for such a list.
2. Tentative values based on even limited information are felt to provide at least general guidance in the control of exposure.
3. Long intervals often elapse between the development of the first experimental data and its practical industrial experience from which many values have been assigned in the past.
4. The tentative list would serve as a clearing house until such time as the values were more definitely established.

It is suggested that all new values be placed on this tentatvie list before their appearance on the list of values approved by the Conference.

The following is a list of 37 material and tentative values presented by your committee for further study and consideration.

Substance	(ppm)
Allyl alcohol	5
Allyl propyl disulfide	2
Benzyl chloride	1
Diacetone alcohol (4-Hydroxy-4-methyl pentanone-2)	50
Di isobutyl ketone	50
Furfural	5
Mercaptans	
Methyl mercaptan	50
Ethyl mercaptan	250
Butyl mercaptan	10
Perchlormethyl mercaptan	0.1
Methyl isobutyl carbinol (methyl amyl alcohol)	25
p-Nitroaniline	1

Pesticides	(mg/m^3)
Organic Phosphates	
Parathion (O,O-diethyl O-p-nitrophenyl thiophosphate	0.1
TEPP (tetraethyl pyrophosphate)	0.05
TEDP (tetraethyl dithiono pyrophosphate)	0.2
EPN (ethyl-p-nitrophenyl thiono benzene phosphonate	0.5
Malathion (O,O-dimethyl dithio phosphate of dimethyl mercaptosuccinate	15
Chlorinated Hydrocarbons	
Lindane (hexachlorocyclohexane)	0.5
DDT (1,1-dichloro-2,2-bis (p-chlorophenyl) ethylene	1
Chlordane (4,7-methano-3a,4,7,7a-tetrahydro-4,5,6,7,8,8-hexachlorindene)	2
Aldrin (1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-dimethanonaphthalene)	0.25

* Full text published in the *Transactions of Sixteenth Annual Meeting*, April 24-27, 1954, Chicago, IL, pp. 22-24.

Pesticides	(mg/m^3)
Dieldrin (1,2,3,4,10,10-hexachloro-6,7, epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4,5,8-dimethanonaphthalene)	0.25
Methoxychlor (2,2,diparamethoxyphenyl-1,1,1-trichloroethane)	15
Inorganic Compounds	
Calcium arsenate	0.3
Lead arsenate	0.2
Organo mercurials (as mercury)	0.01
Organic Herbicides	
2,4,D (2,4-dichlorophenoxyacetic acid)	10
Ammate (ammonium amidosulfate)	15
Crag Herbicide (sodium-2,4,dichlorophenoxy ethyl sulfate)	15
Phenylhydrazine (ppm)	5
Picric acid (mg/m^3)	10
Pyridine (ppm)	10
Sodium hydroxide (mg/m^3)	2
Sulfur hexafluoride (ppm)	1000
Sulfur pentafluoride (ppm)	0.025
Titanium dioxide (mg/m^3)	15
Vanadium (mg/m^3)	
(V_2O_5 dust)	0.5
(V_2O_5 fume)	0.1
Ferro vanadium dust	1

Reference material has been prepared on each of the above substances and, though in some instances rather meager, is available from the chairman for distribution. The Committee would welcome suggestions of substances to be added and also comments, additional references or experience with these materials.

Committee members:

Same as 1953.

1955

changes from 1954

New Values

None.

Revised Values

None.

Committee members:

Same as 1953.

1956

changes from 1955

Threshold Limit Values adopted at the Eighteenth Annual Meeting of the American Conference of Governmental Industrial Hygienists, April 21-24, 1956, Philadelphia, PA.

New Values

Gases and Vapors	ppm	mg/m^3
Allyl alcohol	5	12
Allyl propyl disulfide	2	12
Benzyl chloride	1	5
Butylamine	5	15
Chlorine Trifluoride	0.1	0.4
Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone)	50	240
Diborane	0.1	0.1
Difluoro dibromomethane	100	860
Diisobutyl ketone	50	290
Ethylenediamine	10	30
Ethylene imine	5	9
Hydrazine	1	1.3
Hydrogen bromide	5	17
Hydrogen peroxide, 90%	1	1.4
Isopropylamine	5	12
Methyl acetylene	1000	1650
Methyl isobutyl carbinol (methyl amyl alcohol)	25.	100
p-Nitroaniline	1	6
Phenylhydrazine	5	22
Propylene imine	25	60
Pyridine	10	30
Sulfur hexafluoride	1000	6000
Sulfur pentafluoride	0.025	0.25
p-Tertiary butyltoluene	10	60
Tetranitromethane	1	8
Trifluoromonobromo methane	1000	6100

Toxic Dusts, Fumes and Mists	mg/m^3
Aldrin (1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-dimethanonaphthalene	0.25
Ammate (ammonium sulfamate)	15
Cadmium oxide fume	0.1
Chlordane (1,2,4,5,6,7,8,8 octachloro-3a,4,7,7a-tetrahydro-4,7-methaniondane	2.0
Chlorinated diphenyl oxide	0.5
Crag herbicide (sodium 2-(2,4-dichloro-phenoxy) ethanol hydrogen sulfate	15
2,4-D(2,4-dichlorophenoxyacetic acid)	10
Dieldrin (1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4,5,8-dimethano-napthalene)	0.25
EPN (o-ethyl o-p-nitrophenyl thionobenzene phosphonate)	0.5
Ferrovandium	1

Toxic Dusts, Fumes and Mists	mg/m³
Hydroquinone	2
Lindane (hexachlorocyclohexane, gamma isomer)	0.5
Malathion (O,O-dimethyl dithiophosphate of dimethylmercapto succinate)	15
Mercury (organic compounds)	0.01
Methoxychlor (2,2-di-p-methoxy-phenyl-1,1,1-trichlorethane	15
Molybdenum (soluble compounds)	5
Picric acid	0.1
Sodium hydroxide	2
TEDP (tetraethyl dithionopyro-phosphate)	0.05
TEPP (tetraethyl pyrophosphate)	0.05
Titanium dioxide	15
Vanadium	
(V_2O_5 dust)	0.5
(V_2O_5 fume)	0.1
Zirconium compounds (as Zr)	5

Revised Values

Iodine changed from 1 ppm to 0.1 ppm

Deletions

Cadimum (0.1 mg/m³)

EDITOR'S NOTE: In 1956 the value "approximate milligram per cubic meter" appeared for the first time.

Committee members:

Allan L. Coleman, *Chairman*
William L. Ball
L. T. Fairhall
H. E. Stokinger
Ralph S. Smith
W. H. Reinhart
S. D. Silver
A. J. Vorwald

1957

changes from 1956

Threshold Limit Values adopted at the Nineteenth Annual Meeting of the American Conference of Governmental Industrial Hygienists, April 20-23, 1957, St. Louis, MO.

New Values

Gases and Vapors	ppm	mg/m³
Allyl chloride	5	15
Chloropicrin	1	7
Decaborane	0.05	0.3
Ethylacrylate	25	100
Furfural	5	20
Methyl acrylate	10	35
Nitric acid	5	25
Tetrahydrofuran	200	590

Toxic Dusts, Fumes, and Mists	mg/m³
ANTU (alpha-naphthyl-thiourea)	0.3
Calcium arsenate	0.1
Chlorinated camphene, 60%	0.5
Chlorodiphenyl (54% chlorine)	0.5
DDT (2,2-bis (p-chlorophenyl)-1,1,1-trichloroethane)	1
Dinitrobenzene	1
Ferban (ferric dimethyl dithlocarbamate)	15
HETP (hexaethyl tetraphosphate)	0.1
Lead arsenate	0.15
Nicotine	0.5
Pyrethrum	2
Rotenone	5
Sodium fluoroacetate (1080)	0.1
Strychnine	0.15
Thiram (tetramethyl thioram disulfide)	5
Warfarin (3-(α-acetonyl benzyl)-4-hydroxycoumarin)	0.5

Revised Values

Substance		ppm	mg/m³
Benzene	from	35	110
	TO	25	80
Butyl cellosolve	from	200	970
	TO	50	240
Ethylene dioxide	from	100	180
	TO	50	90
Lead and inorganic compounds	from	—	0.15
	TO	—	0.2
Styrene monomer (Phenylethylene)	from	200	850
	TO	100	420
Sulfur dioxide	from	10	25
	TO	5	13
Thallium (soluble comps)	from	—	0.15
	TO	—	0.1

Deletions

Acrylonitrile (20 ppm and 45 mg/m³)
Dieldrin (0.25 mg/m³)
Slate (below 5% free SiO_2) (50 mppcf)
Total dust (below 5% free SiO_2) (50 mppcf)

Committee members:

Allan L. Coleman, *Chairman*
William L. Ball
W. Clarke Cooper

L. T. Fairhall
W. H. Reinhart
S. D. Silver
Ralph S. Smith
H. E. Stokinger

1958

changes from 1957

Threshold Limit Values adopted at the Twentieth Annual Meeting of the American Conference of Governmental Industrial Hygienists, April 19-22, 1958, Atlantic City, NJ.

New Values

Gases and Vapors

None.

Revised Values

Substance		ppm	mg/m³
Mesityl oxide	from	50	200
TO		25	100
Nitric acid	from	5	25
TO		10	25

Deletion

HETP (hexaethyl tetraphosphate)

Committee members:

Allan L. Coleman, *Chairman*
William L. Ball
W. Clarke Cooper
Hervey B. Elkins
Keith H. Jacobson
Warren H. Reinhart
Herbert E. Stokinger

1959

changes from 1958

Threshold Limit Values adopted at the Twenty-First Annual Meeting of the American Conference of Governmental Industrial Hygienists, April 18-21, 1959, Chicago, IL.

New Values

Gas and Vapors	ppm	mg/m³
Acetylene tetrabromide	1	14
Beryllium	—	~~20~~ 0.002
Methyl styrene	100	480
Monomethyl aniline	2	9
Paradichlorobenzene	75	450
Propylene oxide	100	240
Tertiary butyl alcohol	100	300
Toluene-2-4-diisocyanate	0.1	0.7
Triethylamine	25	100
Vinyl toluene	100	480
Xylidine	5	25

Revised Values

Substance		ppm	mg/m³
Bromine	from	1	7
TO		0.1	0.7
Chloroform	from	100	490
TO		50	240
Chloropicrin	from	1	7
TO		0.1	0.7

Deletions

Hexone (methyl isobutyl ketone)

Committee members:

Same as 1958.

1960

changes from 1959

Threshold Limit Values adopted at the Twenty-second annual Meeting of the American Conference of Governmental Industrial Hygienists, April 23-26, 1960, Rochester, NY.

New Values

Gases and Vapors	ppm	mg/m³
Boron Trifluoride	1	3
Chlorine dioxide	0.1	0.3
Dimethyl formamide	20	60
1,1-Dimethylhydrazine	0.5	1
Dipropylene glycol methyl ether	100	600
Furfural ~~alcohol~~	5	20
Methyal (dimethoxymethane)	1000	3100
Lithium hydride	—	0.025
Phosphoric acid	—	1.0
Yttrium	—	5.0

Mineral and Non-Metallic Inorganic Dusts	mppcf
Crystabolite (above 5% silica)	5
Amorphous silica	20

Furfuryl alcohol 50 200

Miscellaneous

Aluminum oxide	50
Calcite	50
Dolomite	50
Limestone	50
Marble	50
Silicon carbide	50

Revised Value

Manganese from 6 mg/m^3 to 5 mg/m^3

Deletions

Dust (nuisance, no free silica)
Cyclopropane

Committee members:

Allan L. Coleman, *Chairman*
William L. Ball
W. Clarke Cooper
Hervey B. Elkins
Keith H. Jacobson
William F. Reindollar
Warren H. Reinhart
Herbert E. Stokinger

1961

changes from 1960

Threshold Limit Values adopted at the Twenty-third Annual Meeting of the American Conference of Governmental Industrial Hygienists, April 9-12, 1961, Detroit, MI.

New Values

Gases and Vapors	ppm	mg/m^3
p-Dichlorobenzene	75	450
Dimethyl acetamide — skin	10	35

Mineral and Non-Metallic Inorganic Dusts

Other inert dusts — 50 mppcf

Revised Values

Substance		ppm	mg/m^3
Allyl alcohol	from	5	12
	TO	2	5
2-Butanone (methyl ethyl ketone)	from	250	750
	TO	200	590
Cyclohexanol	from	100	410
	TO	50	200
Cyclohexanone	from	100	400
	TO	50	200
Hydrogen bromide	from	5	17
	TO	3	10
2-Nitropropane	from	50	180
	TO	25	90
Perchloroethylene	from	200	1350
	TO	100	670
Pyridene	from	10	30
	TO	5	15
Toluene-2,4-diisocyanate	from	0.1	0.7
	TO	0.2	0.14
Trichloroethylene	from	200	1050
	TO	100	520

Deletions

Paradichlorobenzene

The skin notation

The word "skin" was first used in the 1961 listing to indicate that the liquid compound can penetrate the unbroken skin to cause systemic effects. The skin notation is an editorial caution rather than a part of the adopted value. Therefore, the skin notation has not been subject to the Notice of Intended Changes provisions of the Committee. This notation was added to the following:

Gases and Vapors

Acrylonitrile
Allyl alcohol
Aniline
Carbon disulfide
Carbon tetrachloride
Cresol (all isomers)
Decaborane
Dimethylaniline (N-dimethylaniline)
1,1-Dimethylhydrazine
Dimethylsulfate
Ethyl acrylate
Ethylene chlorohydrin
Ethylene imine
Hydrazine
Hydrogen cyanide
Methyl acrylate
Methyl bromide
Monomethyl aniline
p-Nitroaniline
Nitrobenzene
Nitrotoluene
Phenol
Phenylhydrazine
Propylene imine
1,1,2,2-Tetrachloroethane
o-Toluidine
Xylidine

Dusts, Fumes and Mists

Aldrin
Chlorodiphenyl (42% chlorine)
Chlorodiphenyl (54% chlorine)
Cyanide (as CN)
Dieldrin (1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4,5,8-dimethanonaphthalene)
Dinitrobenzene
Dinitrotoluene
Dinitro-o-cresol
EPN (o-ethyl o-p-nitrophenyl thionobenzene phosphate)
Malathion (O,O-dimethyl dithiophosphate of diethyl mercaptosuccinate)
Mercury (organic compounds)
Nicotine
Parathion (O,O-diethyl-o-p-nitrophenyl thiophosphate)
Pentachloronaphthalene
Pentachlorophenol
Picric acid
Sodium fluoroacetate (1080)
TEDP (tetraethyl dithionopyrophosphate)
TEPP (tetraethyl pyrophosphate)
Tetryl (2,4,6-trinitrophenylmethylnitramine)
Trichloronaphthalene
Trinitrotoluene

In 1961 the threshold limit values were first published in booklet form. Following is the complete text of the 1961 TLVs.

Threshold Limit Values for 1961

Adopted at the 23rd Annual Meeting of the American Conference of Governmental Industrial Hygienists, Detroit, Michigan, April 9-12, 1961

Threshold limits should be used as guides in the control of health hazards and should not be regarded as fine lines between safe and dangerous concentrations. They represent conditions under which it is believed that nearly all workers may be repeatedly exposed, day after day, without adverse effect. The values listed refer to time-weighted average concentrations for a normal workday. The amount by which these figures may be exceeded for short periods without injury to health depends upon a number of factors such as the nature of the contaminant, whether very high concentrations even for short periods produce acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such periods. All must be taken into consideration in arriving at a decision as to whether a hazardous situation exists. Special consideration should be given to the application of these values in assessing the health hazards which may be associated with exposure to combinations of two or more substances.

Threshold limits are based on the best available information from industrial experience, from experimental studies, and, when possible, from a combination of the two. These values are based on various criteria of toxic effects or on marked discomfort; thus, they should not be used as a common denominator of toxicity, nor should they be considered as the sole criterion in proving or disproving diagnosis of suspected occupational disease.

These limits are intended for use in the field of industrial hygiene and should be employed by persons trained in this field. They are not intended for use, or for modification for use, in the evaluation or control of community air pollution or air pollution nuisances.

These values are reviewed annually by the Committee on Threshold Limits for changes, revisions, or additions as further information becomes available. The Committee welcomes the suggestion of substances to be added to the list and also comments, references or reports of experience with these materials.

RECOMMENDED VALUES

Gases and Vapors

Substance	ppm*	Approx. mg. per Cu. M.†
Acetaldehyde	200	360
Acetic acid	10	25
Acetic anhydride	5	20
Acetone	1000	2400
Acetylene tetrabromide	1	14
Acrolein	0.5	1.2
Acrylonitrile — Skin	20	45
Allyl alcohol — Skin	2	5
Allyl chloride	5	15
Allyl propyl disulfide	2	12
Ammonia	100	70
Amyl acetate	200	1050
Amyl alcohol (isoamyl alcohol)	100	360
Aniline — Skin	5	19
Arsine	0.05	0.2
Benzene (benzol)	25	80
Benzyl chloride	1	5
Boron trifluoride	1	3
Bromide	0.1	0.7

NOTE: The word "skin" following a compound's name indicates that the liquid compound can penetrate the skin to cause systemic effects.

Substance	ppm*	Approx. mg. per Cu.M.†
Butadiene (1,3-butadiene)	1000	2200
2-Butanone (methyl ethyl ketone)	200	590
Butyl acetate (n-butyl acetate)	200	950
Butyl alcohol (n-butanol)	100	300
tert. Butyl alcohol	100	300
Butylamine	5	15
Butyl cellosolve (2-butoxyethanol)	50	240
p-tert. Butyltoluene	10	60
Carbon dioxide	5000	9000
Carbon disulfide — Skin	20	60
Carbon monoxide	100	110
Carbon tetrachloride — Skin	25	160
Cellosolve (2-ethoxyethanol)	200	740
Cellosolve acetate (2-ethoxyethyl acetate)	100	540
Chlorine	1	3
Chlorine dioxide	0.1	0.3
Chlorine trifluoride	0.1	0.4
Chlorobenzene (monochlorobenzene)	75	350
Chloroform (trichloromethane)	50	240
1-Chloro-1-nitropropane	20	100
Chloropicrin	0.1	0.7
Chloroprene (2-chloro-1,3-butadiene)	25	90
Cresol (all isomers) — Skin	5	22
Cyclohexane	400	1400
Cyclohexanol	50	200
Cyclohexanone	50	200
Cyclohexene	400	1350
Decaborane — Skin	0.05	0.3
Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone)	50	240
Diborane	0.1	0.1
o-Dichlorobenzene	50	300
p-Dichlorobenzene	75	450
Dichlorodifluoromethane	1000	4950
1,1-Dichloroethane	100	400
1,2-Dichloroethane (ethylene dichloride)	100	400
1,2-Dichloroethylene	200	790
Dichloroethyl ether	15	90
Dichloromonofluoromethane	1000	4200
1,1-Dichloro-1-nitroethane	10	60
Dichlorotetrafluorethane	1000	7000
Diethylamine	25	75
Difluorodibromomethane	100	860
Diisobutyl ketone	50	290
Dimethylaniline (N-dimethylaniline) — Skin	5	25
Dimethylformamide	20	60
1,1-Dimethylhydrazine — Skin	0.5	1
Dimethylsulfate — Skin	1	5
Dipropylene glycol methyl ether	100	600
Dioxane (diethylene dioxide)	100	360
Ethyl acetate	400	1400
Ethyl acrylate — Skin	25	100
Ethyl alcohol (ethanol)	1000	1900
Ethylamine	25	45
Ethylbenzene	200	870
Ethyl bromide	200	890
Ethyl chloride	1000	2600
Ethyl ether	400	1200
Ethyl formate	100	300
Ethyl silicate	100	850
Ethylene chlorohydrin — Skin	5	16
Ethylenediamine	10	30
Ethylene dibromide (1,2-dibromoethane)	25	190
Ethylene imine — Skin	5	9
Ethylene oxide	50	90
Fluorine	0.1	0.2
Fluorotrichloromethane	1000	5600
Formaldehyde	5	6
Furfural	5	20
Furfuryl alcohol	50	200
Gasoline	500	2000
Heptane (n-heptane)	500	2000
Hexane (n-hexane)	500	1800
Hexanone (methyl butyl ketone)	100	410
Hexone (methyl isobutyl ketone)	100	410
Hydrazine — Skin	1	1.3
Hydrogen bromide	3	10
Hydrogen chloride	5	7
Hydrogen cyanide — Skin	10	11
Hydrogen fluoride	3	2
Hydrogen peroxide, 90%	1	1.4
Hydrogen selenide	0.05	0.2
Hydrogen sulfide	20	30
Iodine	0.1	1
Isophorone	25	140
Isopropylamine	5	12
Mesityl oxide	25	100
Methyl acetate	200	610
Methyl acetylene	1000	1650
Methyl acrylate — Skin	10	35
Methyal (dimethoxymethane)	1000	3100
Methyl alcohol (methanol)	200	260
Methyl bromide — Skin	20	80
Methyl cellosolve (2-methoxyethanol)	25	80
Methyl cellosolve acetate (ethylene glycol monomethyl ether acetate)	25	120
Methyl chloride	100	210
Methyl chloroform (1,1,1-trichloroethane)	500	2700
Methylcyclohexane	500	2000
Methylcyclohexanol	100	470
Methylcyclohexanone	100	460
Methyl formate	100	250
Methyl isobutyl carbinol (methyl amyl alcohol)	25	100
α-Methyl styrene	100	480
Methylene chloride (dichloromethane)	500	1750
Monomethyl aniline — Skin	2	9
Naphtha (coal tar)	200	800

Substance	ppm*	Approx. mg. per Cu.M.†
Naphtha (petroleum)	500	2000
Nickel carbonyl	0.001	0.007
Nitric acid	10	25
p-Nitroaniline — Skin	1	6
Nitrobenzene — Skin	1	5
Nitroethane	100	310
Nitrogen dioxide	5	9
Nitroglycerin	0.5	5
Nitromethane	100	250
2-Nitropropane	25	90
Nitrotoluene — Skin	5	30
Octane	500	2350
Ozone	0.1	0.2
Pentane	1000	2950
Pentanone (methyl propyl ketone)	200	700
Perchloroethylene (tetrachloroethylene)	100	670
Phenol — Skin	5	19
Phenylhydrazine — Skin	5	22
Phosgene (carbonyl chloride)	1	4
Phosphine	0.05	0.07
Phosphorus trichloride	0.5	3
Propyl acetate	200	840
Propyl alcohol (isopropyl alcohol)	400	980
Propyl ether (isopropyl ether)	500	2100
Propylene dichloride (1,2-dichloropropane)	75	350
Propylene imine — Skin	25	60
Propylene oxide	100	240
Pyridine	5	15
Quinone	0.1	0.4
Stibine	0.1	0.5
Stoddard solvent	500	2900
Styrene monomer (phenylethylene)	100	420
Sulfur dioxide	5	13
Sulfur hexafluoride	1000	6000
Sulfur monochloride	1	6
Sulfur pentafluoride	0.025	0.25
1,1,2,2-Tetrachloroethane — Skin	5	35
Tetrahydrofuran	200	590
Tetranitromethane	1	8
Toluene (toluol)	200	750
Toluene-2,4-diisocyanate	0.02§	0.14§
o-Toluidine — Skin	5	22
Trichloroethylene	100	520
Triethylamine	25	100
Trifluoromonobromomethane	1000	6100
Turpentine	100	560
Vinyl chloride (chloroethylene)	500	1300
Vinyl toluene	100	480
Xylene (xylol)	200	870
Xylidine — Skin	5	25

* Parts of vapor per million parts of air by volume at 25°C and 760 mm Hg pressure.

† Approximate milligrams per cubic meter of air.

§ Probably sufficiently low to protect against primary sensitization, but may not protect persons specifically sensitized.

Dusts, Fumes and Mists

Substance	Mg. per* Cu. M.
Aldrin (1,2,3,4,10,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4,5,8-dimethanonaphthalene) — Skin	0.25
Ammate (ammonium sulfamate)	15
Antimony	0.5
ANTU (alpha-naphtyl-thiourea)	0.3
Arsenic	0.5
Barium (soluble compounds)	0.5
Beryllium	0.002
Cadmium oxide fume	0.1
Calcium arsenate	0.1
Chlordane (1,2,4,5,6,7,8,8-octachloro-3a,4,7,7a-tetra-hydro-4,7-methanoindane)	2
Chlorinated camphene, 60%	0.5
Chlorinated diphenyl oxide	0.5
Chlorodiphenyl (42% chlorine) — Skin	1
Chlorodiphenyl (54% chlorine) — Skin	0.5
Chromic acid and chromates (as CrO_3)	0.1
Crag herbicide (sodium 2-(2,4-dichloro-phenoxy) ethanol hydrogen sulfate)	15
Cyanide (as CN) — Skin	5
2,4-D (2,4-dichlorophenoxyacetic acid)	10
DDT (2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane)	1
Dieldrin (1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-1,4,5,8-dimethano-naphthalene) — Skin	0.25
Dinitrobenzine — Skin	1
Dinitrotoluene — Skin	1.5
Dinitro-o-cresol — Skin	0.2
EPN (O-ethyl O-p-nitrophenyl thionobenzene-phosphonate) — Skin	0.5
Ferbam (ferric dimethyl dithiocarbamate)	15
Ferrovanadium dust	1
Fluoride	2.5
Hydroquinone	2
Iron oxide fume	15
Lead	0.2
Lead arsenate	0.15
Lindane (hexachlorocyclohexane, gamma isomer)	0.5
Lithium hydride	0.025
Magnesium oxide fume	15
Malathion (0,0-dimethyl dithiophosphate of diethyl mercaptosuccinate) — Skin	15
Manganese	5
Mercury	0.1
Mercury (organic compounds) — Skin	0.01
Methoxychlor (2,2-di-p-methoxyphenyl-1,1,1-thrichloroethane)	15
Molydenum (soluble compounds)	5
(insoluble compounds)	15
Nicotine — Skin	0.5
Parathion (0,0-diethyl-0-p-nitrophenyl thiosphosphate) — Skin	0.1
Pentachloronaphthalene — Skin	0.5

Substance	Approx. mg. per Cu.M.*
Pentachlorophenol — Skin	0.5
Phosphoric acid	1
Phosphorus (yellow)	0.1
Phosphorus pentachloride	1
Phosphorus pentasulfide	1
Picric acid — Skin	0.1
Pyrethrum	2
Rotenone	5
Selenium compounds (as Se)	0.1
Sodium fluoroacetate (1080) — Skin	0.1
Sodium hydroxide	2
Strychnine	0.15
Sulfuric acid	1
TEDP (tetraethyl dithionopyrophosphate) — Skin	0.2
TEPP (tetraethyl pyrophosphate) — Skin	0.05
Tellurium	0.1
Tetryl (2,4,6-trinitrophenylmethylnitramine) — Skin	1.5
Thallium (soluble compounds)	0.1
Thiram (tetramethyl thiuram disulfide)	5
Titanium dioxide	15
Trichloronaphthalene — Skin	5
Trinitrotoluene — Skin	1.5
Uranium	
(soluble compounds)	0.05
(insoluble compounds)	0.25
Vanadium	
(V_2O_5 dust)	0.5
(V_2O_5 fume)	0.1
Warfarin (3-{α-acetonylbenzyl}-4-hydroxycoumarin)	0.5
Yttrium	5
Zinc oxide fume	15
Zirconium compounds (as Zr)	5

* Milligrams of dust, fume, or mist per cubic meter of air.

Radioactivity: For permissible concentrations of radioisotopes in air, see U.S. Department of Commerce, National Bureau of Standards, Handbook 69, *Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure,* June 5, 1959. Also, see U.S. Department of Commerce, National Bureau of Standards, Handbook 59, *Permissible Dose from External Sources of Ionizing Radiation,* September 24, 1954, and addendum of April 15, 1958.

Mineral and Non-Metallic Inorganic Dusts

Substance	MPPCF*
Silica	
Quartz	
High (above 50% free silica)	5
Medium (5 to 50% free silica)	20
Low (below 5% free silica)	50
Cristobalite (above 5%)	5
Amorphous	20
Silicates	
Asbestos	5
Mica	20
Portland Cement	50
Soapstone	20
Talc	20
Miscellaneous:	
Aluminum oxide	50
Calcite	50
Dolomite	50
Limestone	50
Marble	50
Silicon Carbide	50
Other inert dusts	50

* Millions of particles per cubic foot of air based on impinger samples counted by light-field techniques.

TENTATIVE VALUES

Substance	ppm*	Approx. Mg.† per Cu. M.
Acetonitrile	40	70
Allyl glycidyl ether (AGE)	10	45
Boron oxide	—	15
tert. Butyl chromate (as CrO_3)	—	0.1
n-Butyl glycidyl ether (BGE)	50	270
Butyl mercaptan	10	35
Chloroacetaldehyde	1	3
Chlorobromomethane	200	1050
DDVP (O,O-dimethyl-2,2-dichlorodivinyl phosphate)	—	1
Diglycidyl ether (DGE)	10	55
Dimethyl acetamide	10	35
Endrin (1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octa hydro-1,4-endo, endo-5,8-dimethano-naphthalene)	—	0.25
Ethanol amine	0.5	1
Ethyl mercaptan	250	640
Glycidol	50	150
Heptachlor (1,4,5,6,7,8,8-heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene)	—	0.25
sec-Hexyl acetate	100	590
Isopropyl glycidyl ether (IGE)	50	240
Ketene	0.5	0.9
Methyl mercaptan	50	100
1-Nitropropane	25	90
Pentaborane	0.005	0.01
Perchloromethyl mercaptan	0.1	0.8
Phenyl glycidyl ether (PGE)	50	310
Phosdrin (2-carbomethoxy-1-methyl vinyl dimethyl phosphate)	—	0.1
n-Propyl nitrate	25	110
Systox	—	0.2

Substance	ppm*	Approx. mg. per Cu.M.†
2,4,5T (2,4,5-trichlorophenoxy acetic acid)	—	10
Teflon decomposition products (as F)	—	0.05
1,2,3-Trichloropropane	50	300
1,1,2-Trichloro-1,2,2-trifluoro-ethane	1000	7600
Triorthocresyl phosphate	—	0.1
Triphenyl phosphate	—	3

* Parts of vapor or gas per million parts of air by volume at 25°C and 750 mm Hg pressure.

† Approximate milligrams per cubic meter of air.

Committee members:

Allan L. Coleman, *Chairman*
William L. Ball
W. Clarke Cooper
Hervery B. Elkins
Keith H. Jacobson
William F. Reindollar
Russell G. Scovill
Herbert E. Stokinger

1962

changes from 1961

Threshold Limit Values adopted at the Twenty-Fourth Annual Meeting of the American Conference of Governmental Industrial Hygieniests, May 12-15, 1962, Washington, DC.

EDITOR'S NOTE: This is the first year that gases, vapors and dusts were combined into a single list.

New Values

Substance	ppm	mg/m^3
Acetonitrile — skin	40	70
Boron oxide	—	15
n-Butyl glycidyl ether	50	270
Chloroacetaldehyde	1	3
Ethylene glycol nitrate — skin	0.2	1.2
Ethyl mercaptan	250	640
Glycidol (2,3-epoxy-1-propanol)	50	150
Isopropyl glycidyl ether	50	240
Perchloromethyl mercaptan	0.1	0.8
Phenyl glycidyl ether	50	310
n-Propyl nitrate	25	110
1,1,2-Trichloro 1,2,2-Trifluoroethane	1000	7600
Triorthocresyl phosphate	—	0.1
Triphenyl phosphate	—	3

Revised Values

Substance		ppm	mg/m^3
Calcium arsenate	from	—	0.1
	TO	—	1
Carbon tetrachloride	from	25	160
	TO	10	65
Chlordane (1,2,4,5,6,7,8,8-octachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene	from	—	2
	TO	—	0.5
1,2-Dichloroethane	from	100	400
	TO	50	200
Nitroglycerin — skin	from	0.5	5
	TO	0.2	2
Pyrethrum	from	—	2
	TO	—	5
Sodium fluoroacetate (1080) — skin	from	0.1	5
	TO	—	0.05
Warfarin (3-[α-acetonylbenzyl]-4-hydroxycoumarin)	from	—	0.05
	TO	—	0.5
Zinc oxide fume	from	—	15
	TO	—	5

Mineral Dusts

Silica*
Crystalline
Quartz, threshold limit calculated from the formula:
$$250/(\%\ SiO_2 + 5)$$
Cristobalite same as above

* See 1960 list for previous procedure.

Skin notation added

DDT
Nitroglycerin

EDITOR'S NOTE: 1962 marks the first appearance of any cautionary Appendices. The text is as follows:

Appendix

A[1] Benzidine. Because of high incidence of bladder tumors in man, any exposure, including skin, is extremely hazardous.

A[2] β-Naphthylamine. Because of the extremely high incidence of bladder tumors in workers handling this compound, and the inability to control exposures, β-naphthylamine has been pro-

hibited from manufacture, use and other activities that involve human contact by the State of Pennsylvania.

A[3] N-Nitrosodimethylamine. Because of extremely high toxicity and presumed carcinogenic potential of this compound, contact by all routes should not be permitted.

A[4] Teflon® decomposition products. At least one identified component of Teflon® decomposition products is extremely toxic, but, in the absence of more complete toxicity information and suitable analytical methods, a definite threshold limit value is not recommended at this time.

Committee members:*

Herbert E. Stokinger, *Chairman*
Harry B. Ashe
E. J. Baier
Allan L. Coleman
Hervey B. Elkins
Bernard Grabois
Wayland J. Hayes
Keith Jacobson
Harold N. MacFarland
William F. Reindollar
Russell G. Scovill
Ralph G. Smith
Mitchell R. Zavon

* EDITOR'S NOTE: From the 1962 Transactions: *"The membership of the committee has been enlarged to 14 from its previous number of 8. . . ."*

1963

changes from 1962

Threshold Limit Values adopted at the Twenty-fifth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 6-7, 1963, Cincinnati, OH.

New Values

Substance	ppm	mg/m^3
Benzidine	—	A[1]
Cobalt	—	0.5
Dimethyl acetamide	10	35
Ketene	0.5	0.9
1-Nitropropane	25	90
β-Naphthylamine	—	A[2]
N-Nitrosodimethylamine (dimethylnitrosamine) — skin	—	A[3]
Pentaborane	0.005	0.01
Perchloryl Fluoride	3	13.5
Phosdrin	—	0.1
Platinum (soluble salts)	—	0.002
β-Propiolactone	—	A[5]
2,4,5-T (2,4,5-Trichlorophenoxy-acetic acid)	—	10
Teflon® decomposition products	—	A[4]

Revised Values

Substance		ppm	mg/m^3
Acrolein	from	0.5	1.2
	TO	0.1	0.25
Allyl chloride	from	5	15
	TO	2	5
Allyl glycidyl ether		*add:* C	
Ammonia	from	100	70
	TO	50	35
Amyl acetate	from	200	1050
	TO	100	525
Benzene (benzol) — skin		*add:* C	
Boron trifluoride		*add:* C	
Butylamine		*add:* C	
Chlorine trifluoride		*add:* C	
Chloroacetaldehyde		*add:* C	
Chloroform		*add:* C	
Dichloroethyl ether		*add:* C	
1,1-Dichloro-1-nitro ethane		*add:* C	
Diglycidyl ether	from	10	55
	TO "C"	0.5	2.8
Ethyl benzene		*add:* C	
Ethyl mercaptan	from	250	640
	TO "C"	20	52
Formaldehyde		*add:* C	
sec-Hexyl acetate	from	100	590
	TO	50	295
Hydrazine		*add:* C	
Hydrogen chloride		*add:* C	
Hydrogen sulfide		*add:* C	
Iodine		*add:* C	
Manganese		*add:* C	
Methyl bromide — skin		*add:* C	
Methyl chloride		*add:* C	
Methyl mercaptan	from	50	100
	TO "C"	20	40
Nitrogen dioxide		*add:* C	
Nitroglycerin (combined EGDN plus NG) — skin		*add:* C	

Substance	ppm	mg/m³
Phosphine ..... from	0.05	0.07
TO	0.3	0.4
Toluene (toluol)	*add:* C	
Toluene-2,4-diisocyanate	*add:* C	
Vinyl chloride (chloroethylene) ..	*add:* C	
Xylene (xylol)	*add:* C	

EDITOR's NOTE: 1963 marks the first appearance of the procedure for determining TLVs for mixtures (Appendix B) and the bases for assigning limiting ceiling (C) values (Appendix C). The text of these two appendices is as follows:

Appendix B

Threshold Limit Values for Mixtures

When two or more hazardous substances are present, their combined effect, rather than that of either individually, should be given primary consideration. In the absence of information to the contrary, the effects of the different hazards should be considered as additive. That is, if the sum of the following fractions,

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \ldots \frac{C_n}{T_n}$$

exceeds unity, then the threshold limit of the mixture should be considered as being exceeded. C indicates the observed atmospheric concentration, and T_1 the corresponding threshold limit, (See Example 1A.a.).

Exceptions to the above rule may be made when there is good reason to belive that the chief effects of the different harmful substances are not in fact additive, but independent as when purely local effects on different organs of the body are produced by the various components of the mixture. In such cases the threshold limit ordinarily is exceeded only when at least one member of the series (C_1/T_1 or C_2/T_2, etc.) itself has a value exceeding unity (See Example 1A.b.).

Antagonistic action or potentiation may occur with some combinations of atmospheric contaminants. Such cases at present must be determined individually. Potentiating or antagonistic agents are not necessarily harmful by themselves. Potentiating effects of exposure to such agents by routes other than that of inhalation is also possible, e.g., imbibed alcohol and inhaled narcotic (trichloroethylene). Potentiation is characteristically exhibited at high concentrations, less probably at low.

When a given operation or process characteristically emits a number of harmful dusts, fumes, vapors or gases, it will frequently be only feasible to attempt to evaluate the hazard by measurement of a single substance. In such cases, the threshold limit used for this substance should be reduced by a suitable factor, the magnitude of which will depend on the number, toxicity and relative quantity of the other contaminants ordinarily present.

Examples of processes which are typically associated with two or ore harmful atmospheric contaminants are welding, automobile repair, blasting, painting, lacquering, certain foundry operations, diesel exhausts, etc. (Example 2.)

Examples of Threshold Limit Values for Mixtures

THRESHOLD LIMIT VALUES FOR MIXTURES EXAMPLES

1A. General case, where air is analyzed for each component:

a. *ADDITIVE EFFECTS*

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \frac{C_3}{T_3} + \ldots \frac{C_n}{T_n} = 1$$

Air contains 5 ppm of carbon tetrachloride (TLV, 10) 20 ppm of ethylene dichloride (TLV, 50) and 10 ppm of ethylene dibromide (TLV, 25)

$$\frac{5}{10} + \frac{20}{50} + \frac{10}{25} = \frac{65}{50} = 1.3$$

Threshold limit is exceeded.

b. *INDEPENDENT EFFECTS*

Air contains 0.15 mg/m³ of lead (TLV, 0.2) and 0.7 mg/m³ of sulfuric acid (TLV, 1).

$$\frac{0.15}{0.20} = 0.75; \quad \frac{0.7}{1} = 0.7$$

Threshold limit is not exceeded.

1B. Special case when the source of contaiminant is a mixture and the atmospheric composition is *assumed* to be similar to that of the original material; i.e., vapor pressure of each component is the same at the observed temperature.

a. *ADDITIVE EFFECTS*, approximate solution

1. A mixture of equal parts (1) trichloroethylene (TLV, 100), and (2) methyl chloroform (TLV, 350).

$$\frac{C_1}{100} + \frac{C_2}{350} = \frac{C_m}{T_m}$$ Solution applicable to "spot" solvent mixture usage, where all or nearly all, solvent evaporates.

$$C_1 = C_2 = \frac{1}{2} C_m$$

$$\frac{C_1}{100} + \frac{C_1}{350} = \frac{2C_1}{T_m}$$

$$\frac{7C_1}{700} + \frac{2C_1}{700} = \frac{2C_1}{T_m}$$

$$T_m = 700 \times \frac{2}{9} = 155 \text{ ppm}$$

1B.b. General Exact Solution for Mixtures of N Components With Additive Effects and Different Vapor Pressures.

(1) $$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \ldots + \frac{C_n}{T_n} = 1;$$

(2) $$C_1 + C_2 + \ldots + C_n = T;$$

(2.1) $$\frac{C_1}{T} + \frac{C_2}{T} + \ldots + \frac{C_n}{T} = 1.$$

By the Law of Partial Pressures,

(3) $C_1 = ap_1$.

And by Raoult's Law,

(4) $p_1 = F_1 p_1^\circ$.

Combine (3) and (4) to obtain

(5) $C_1 = aF_1 p_1^\circ$.

Combining (1), (2.1) and (5), we obtain

(6) $$\frac{F_1 p_1^\circ}{T} + \frac{F_2 p_2^\circ}{T} + \ldots + \frac{F_n p_n^\circ}{T} =$$

$$\frac{F_1 p_1^\circ}{T_1} + \frac{F_2 p_2^\circ}{T_2} + \ldots + \frac{F_n p_n^\circ}{T_n} =$$

and solving for T,

(6.1) $$T = \frac{F_1 p_1^\circ + F_2 p_2^\circ + \ldots + F_n p_n^\circ}{\frac{F_1 p_1^\circ}{T_1} + \frac{F_2 p_2^\circ}{T_2} + \ldots + \frac{F_n p_n^\circ}{T_n}}$$

or $$\sum_{i=1}^{i=n} F_1 p_1^\circ$$

(6.2) $$T = \frac{i = 1}{\sum_{i=1}^{i=n} \frac{F_1 p_1^\circ}{T_1}}$$

T = Threshold Limit Value in ppm.
C = Vapor concentration in ppm.
p = Vapor pressure of component in solution.
p° = Vapor pressure of pure component.
F = Mol fraction of component in solution.
a = A constant of proportionality.
Subscripts 1,2, . . . n relate the above quantities to components 1,2, . . . n, respectively. Subscript i refers to an arbitrary component from 1 to n.
Absence of subscript relates the quantity to the mixture.

Solution to be applied when there is a reservoir of the solvent mixture whose composition does not change appreciably by evaporation.

Exact Arithmetic Solution of Specific Mixture

	Mol. wt.	Density	T	p° at 25° C	Mol fraction in half-and-half solution by volume
Trichloroethylene (1)	131.4	1.46g/ml	100	73mm Hg	0.527
Methychloroform (2)	133.42	1.33g/ml	350	125mm Hg	0.473

$F_1 p_1^\circ = (0.527)\ (73) = 38.2$
$F_2 p_2^\circ = (0.473)\ (125) = 59.2$

$$T = \frac{38.2 + 59.2}{\frac{38.2}{100} + \frac{59.2}{350}} = \frac{(97.4)\ (350)}{133.8 + 59.2} = \frac{(97.4\ \ (350)}{193.0} = 177$$

T = 177 ppm (Note difference in T.L.V. when account is taken of vapor pressure and mol fraction in comparison with above example where such account is not taken).

2. A mixture of one part of (1) parathion (TLV, 0.1) and two parts of (2) EPN (TLV, 0.5).

$$\frac{C_1}{0.1} + \frac{C_2}{0.5} = \frac{C_{mi}}{T_m} \quad C_2 = 2C_1$$

$C_m = 3C_1$

$$\frac{C_1}{0.1} + \frac{2C_1}{0.5} = \frac{3C_1}{T_m}$$

$$\frac{7C_1}{0.5} = \frac{3C_1}{T_m}$$

$$T_m = \frac{1.5}{7} = 0.21 \text{ mg/m}^3$$

1C. *INDEPENDENT EFFECTS*

1. From naphtha (TLV, 500) containing 10 mole percent benzene (TLV, 25) the narcotic effects can be considered as approximately the same as that of benzene-free naphtha.

The blood effects can be considered as due to the benzene alone.

For **intermittent exposure,** a TLV of 500 ppm may be used as long as the **average** concentration does not exceed $25 \times \frac{100}{10} = 250$ ppm, the TLV based on the benzene content.

2. Diesel engine exhaust contains several irritants, one of which is nitrogen dioxide. A limit of 2 ppm NO_2 has been found to correlate fairly well with the beginning of subjective (irritation) effects from such gases, although no subjective effects are experienced from NO_2 alone at 5 ppm.

Appendix C
Bases for Assigning Limiting "C" Values*

Appendix C

BASES FOR ASSIGNING LIMITING "C" VALUES*

T.L.V. RANGE ppm* or mg/m³	Permitted Fluctuation Factor of T.L.V. for 10 or 30 min.	Examples
0 to 1	3	Boron trifluoride (1 ppm) at 3 ppm if repeatedly encountered for periods of 5, 10, or 30 minutes, may lead to pneumonitis; a "C" listing recommended.
1+ to 10	2	
10+ to 100	1.5	Ethyl benzene (200 ppm) at 250 ppm if repeatedly encountered for periods of 5 or 10 minutes may prove intolerably irritating to the eyes; a "C" listing recommended.
100+ to 1000	1.25	

Committee members:

Same as 1962.

1964

changes from 1963

Threshold Limit Values adopted at the Twenty-Sixth Annual Meeting of the American Conference of Governmental Industrial Hygienists, April 25-28, 1964, Philadelphia, PA.

New Values

Substance	ppm	mg/m³
C tert-Butyl chromate (as CrO_3)	—	0.1
Camphor	—	2
DDVP (O,O-Dimethyl-2,2-dichlorovinyl phosphate)	—	1
Endrin (1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8aoctahydro-1,4-endo-5,8-dimethanonaphthalene) — skin	—	0.1
Heptachlor(1,4,5,6,7,8,8a-heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindane)	—	0.5
Oil mist (mineral)	—	5

Mineral Dusts

"Inert" or nuisance particulates — 5 mppcf or 15 mg/m³ whichever is the smaller.

Revised Values

Arsenic — *add:* and compounds, as As
Antimony — *add:* and compounds, as Sb
o-Dichlorobenzene — *delete:* "C"
Ethylene glycol dinitrate — *add:* "C"
Hydrazine — *delete:* "C"
α-Methyl styrene — *add:* "C"
Styrene monomer — *add:* "C"
Toluene — *delete:* "C"
Vanadium — *add:* "C"

Placed on Notice of Intended Changes list

Dimethylformamide
Hydrogen sulfide
Methyl mercaptan
Nitric acid
Phosgene
Selenium

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* According to this limitation, the presently listed TLVs will or will not be candidates for a "C" (ceiling) listing. 1963 TLVs not coming within this limitation will bear a "C" before the substance name. Judgement is based on whether the excursions in concentration under the time limits stated may result in *a)* intolerable irritation, *b)* chronic or irreversible tissue change, or *c)* narcosis of sufficient degree to increase accident proneness or materially reduce work efficiency.

1965

changes from 1964

Threshold Limit Values adopted at the Twenty-Seventh Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 2-4, 1965 Houston, TX.

New Values

Substance	ppm	mg/m^3
Copper fume	—	0.1
Demeton (Systox®) — skin	1	—
Epichlorhydrin — skin	5	19
Ethanolamine	3	6
Hafnium	—	0.5
C Methylene bisphenyl isocyanate	0.02	0.2
Polytetrafluoro-ethylene decomposition products*	—	A[A]
β-Propiolactone	—	A[5]
Tantalum	—	5
Tetraethyl lead (as Pb) — skin	—	0.075
Tin (inorganic compounds)	—	2

*Trade Names: Algoflon, Fluon, Halon, Teflon, Tetran. *EDITOR'S NOTE:* In previous years the list had utilized a trade name not the chemical name.

Mineral Dusts

Graphite — 15 mppcf

Revised Values

Substance	ppm	mg/m^3
Ethylenediamine ..... from	10	30
TO	10	25

Placed on Notice of Intended Changes list

Butyl acetate
Carbon monoxide
Chlorine
Cyclohexane
Cyclohexene
1,2-Dibromoethane
Ethylamine
Ethylbenzene
Ethyl mercaptan
Ethylene imine
Iron oxide fume
Propylene imine

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1966

changes from 1965

Threshold Limit Values adopted at the Twenty-Eighth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 16-17, 1966, Pittsburgh, PA.

New Values

Substance	ppm	mg/m^3
Anisidine (o, p-isomers) — skin	—	0.5
Benzoyl peroxide	—	5
Carboryl (Sevin®)	—	5
Cotton dust (raw)	—	1
Cyclopentadiene	75	200
1,3-Dichlorl-5,5-dimethyl hydantoin	—	0.2
Dimethlamine	10	18
Dimethyl 1,2-dibromo-2,2-dichloro ethyl phosphate, (Dibrom®)	—	3
Dimethyl formamide — skin	10	30
Di-sec, octyl phthalate (Di-2-ethyl hexylphthalate)	—	5
Hexachloroethane — skin	1	10
Hydrogen sulfide	10	15
L.P.G. (liquified petroleum gas)	1000	1800
Methyl acetylene-propadiene mixture (MAPP)	1000	1800
C Methyl mercaptan	10	20
Methyl methacrylate	100	410
Morpholine — skin	20	70
Naphthalene	10	50
Nickel, metal and soluble compounds	—	1
Nitric acid	2	5
p-Nitro-benzene — skin	—	1
Nitrogen trifluoride	10	29
Oxygen diflouride	0.05	0.1
p-Phenylene diamine — skin	—	0.1
Phosgene (carbonyl chloride)	0.1	0.4
Phthalic anhydride	2	12
Propane	1000	1800

Substance	ppm	mg/m³
Selenium compounds (as Se)	—	0.2
Silver, metal and soluble compounds	—	0.01
1,1,1,2-Tetrachloro-2,2-diflouroethane	500	4170
Yttrium	—	1

Revised Values

Amyl alcohol changed to Isoamyl alcohol

Cobolt moved to NIC

Demeton (Systox®) — skin from 1 ppm to 0.1 mg/m³

Freons appear on recommended list

Gasoline moved to A⁶

Propyl alcohol changed to Isopropyl alcohol

Propyl ether changed to Isopropyl ether

Trichloroethylene changed from 100 ppm and 520 mg/m³ to 100 ppm and 535 mg/m³

Committee members:

Same as 1965.

1967

changes from 1966

Threshold Limit Values adopted at the Twenty-Ninth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 1-2, 1967, Chicago, IL.

New Values

Substance	ppm	mg/m³
Acrylamide — skin	—	0.3
2-Aminopyridine	0.5	2
sec-Amyl acetate	125	650
Azinphos-methyl — skin	—	0.2
Bromoform — skin	0.5	5
Butyl acetate (n-butyl acetate)	150	710
n-Butyl acetate	150	710
sec-Butyl acetate	200	950
tert-Butyl acetate	200	950
Cadmium (metal dust and soluble salts)	—	0.2
Carbon black	—	3.5
Carbon monoxide	50	55
C Chlorine	1	3
o-Chlorobenzylidene malononitrile (OCBM)	0.05	0.4
Coal tar pitch volatiles (benzene soluble fraction)(anthracene, BaP, phenanthrene, acridene chrysene, pyrene)	—	0.2
Crotonaldehyde	2	6
Cumene — skin	50	245
Cyclohexane	300	1050
Cyclohexene	300	1015
Diazomethane	0.2	0.4
1,2-Dibromomethane (ethylene dibromide) — skin	25	190
Diethylamino ethanol — skin	10	50
Ethylamine	10	18
Ethyl sec-amyl ketone (5-methyl 3-heptanone)	25	30
Ethyl benzene	100	435
Ethyl butyl ketone (3-heptanone)	50	230
Ethyl mercaptan	10	25
Ethylene glycol dinitrate — skin	0.2	1.2
Ethylene imine — skin	0.5	1
n-Ethylmorpholine — skin	20	94
Formic acid	5	9
Iron oxide fume	—	10
Iso amyl acetate	100	525
Iso butyl acetate	150	700
Isopropyl acetate	250	950
Methylamine	10	12
Methyl (n-amyl) ketone (2-heptanone)	100	465
Methyl iodide — skin	5	28
Methyl isocyanate — skin	0.02	0.05
C Monomethyl hydrazine — skin	0.2	0.35
Oxalic acid	—	1
Phenyl ether	1	7
Phenyl ether-Biphenyl mixture (vapor)	1	7
Pival (2-Pivalyl-1,3-indandione)	—	0.1
Propylene imine — skin	2	5
Rhodium, Metal fume and dusts soluble salts	—	0.001
Selenium hexafluoride	0.05	0.4
Tellurium hexafluoride	0.02	0.2
Tetramethyl lead (TML) (as lead) — skin	—	0.075
Tetramethyl succinonitrile — skin	0.5	3
1,1,2-trichloroethane — skin	10	45
Xylene (xylol)	100	435

Respirable Dust Evaluated by Count

New Values

Tremolite — 5mppcf

Revised Value

Substance	ppm	mg/m³
sec-Hexyl acetate	50	295
from TO	50	300
Naptha petroleum	500	200
from TO: Petroleum distillates (naptha)	500	2000

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1968

changes from 1967

Threshold Limit Values adopted at the Thirtieth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 13, 1968, St. Louis, MO.

New Values

Substance	ppm	mg/m^3
sec-Butyl alcohol	150	450
α-Chloroacetophenone (phenacylchloride)	0.05	0.3
Chromium, soluble chromic, chromous salts as Cr	—	0.5
Metal and insoluble salts	—	1
Cobalt, metal fume and dust	—	0.1
Dibutyl phosphate	1	5
Dibutyl phthalate	—	5
Diisopropylamine — skin	5	20
Dimethylphthalate	—	5
Diphenyl	0.2	1
Hexachloronaphthalene — skin	—	0.2
Isobutyl alcohol	100	300
Maleic anhydride	0.25	1
Nitric oxide	25	30
Octachloronapthalene — skin	—	0.1
Paraquat — skin	—	0.5
Propyl alcohol	200	500
Ronnel	—	15
C Terphenyls	1	9
Tetrachloronapthalene	—	2
Tributyl phosphate	—	5
Zinc chloride fume	—	5

Revised Values

Substance	ppm	mg/m^3
1,2-Dibromethane (ethylene dibromide)	*Add:* C	
C Ethylene glycol dinitrate — skin — from	0.2	1.2
To: Ethylene glycol dinitrate and/or Nitroglycerin — skin	0.2[d)]	1
Naptha (coal tar) — from	200	800
TO	100	400
Phyenyl glycedyl ether — from	50	310
TO	10	60

d) An atomospheric concentration of not more than 0.02 ppm, or personal protection may be necessary to avoid headache.

Placed on Notice of Intended Changes list

Butyl mercaptan	Oil mist
Cadmium oxide fume	Pentane
Ethyl mercaptan	Tetraethyl lead
Methyl mercaptan	Tetramethyl lead

Mineral Dust

Silica
- Crystalline
- Cristobalite
- Silicates
- Asbestos

EDITOR'S NOTE: This is the first year that the old TLV remained on the recommended list as it also was being considered on the Notice of Intended Change list. See the full text of the 1968 TLV booklet that follows.

Threshold Limit Values for Airborne Contaminants for 1968

Threshold limit values refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day, without adverse effect. Because of wide variation in individual susceptibility, exposure of an occasional individual at or even below the threshold limit may not prevent discomfort, aggravation of a pre-existing condition, or occupational illness.

Clinical tests are becoming available that permit detection of those individuals who will hyperreact upon exposure to certain industrial substances. Being predictive in character, they may be applied as screening tests in the preplacement job examination. Requests for further details of these tests should be directed to the Chairman of the Committee.

Threshold limits should be used as guides in the control of health hazards and should not be regarded as fine lines between safe and dangerous concentrations. Exceptions are the substances given in Appendix A and certain of the sub-

stances given a "C" listing. The values not given a "C" listing refer to time-weighted average concentrations for a conventional 7 or 8 hour workday.

Time-weighted average concentrations permit excursions above the limit, provided they are compensated by equivalent excursions below the limit during the workday. The degree of permissible excursion is pegged to the threshold limit value of a particular substance as given in table in Appendix C under "Test TLV Factor." Hence, it is not considered appropriate to interpret air concentration values as exceeding time-weighted average limits, if such values lie within the permissible excursions. (See section on Legislative Code.)

The amount by which these concentrations may be exceeded for short periods without injury to health depends upon a number of factors such as the nature of the contaminant, whether very high concentrations even for short periods produce acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such periods. All must be taken into consideration in arriving at a decision as to whether a hazardous situation exists. Enlightened industrial hygiene practice inclines toward controlling exposures below the limit rather than maintenance at the limit.

Threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and when possible, from a combination of the three. The basis on which the values are established may differ from substance to substance; protection against impairment of health may be the guiding factor for some, whereas reasonable freedom from irritation, narcosis, nuisance or other forms of stress may dominate the basis for others. The Committee holds to the opinion that limits based on physical irritation should be considered no less binding than those based on physical impairment; growing bodies of evidence indicate that physical irritation may promote and accelerate physical impairment.

These limits are intended for use in the field of industrial hygiene and should be interpreted and applied only by persons trained in this field. They are not intended for use, or for modification for use, (1) as a relative index of hazard or toxicity, by making a ratio of two limits, (2) in the evaluation or control of community air pollution or air pollution nuisances, (3) in estimating the toxic potential of continuous, uninterrupted exposures, (4) as proof or disproof of an existing disease or physical condition, or (5) for adoption by countries whose working conditions differ from those in the United States of America and where substances and processes differ.

Documentation of Threshold Limit Values. A separate companion piece to the TLVs is issued by ACGIH under this title. This publication gives the pertinent scientific information and data with reference to literature sources that were used to base each limit. Each documentation also contains a statement defining the type of response against which the limit is safeguarding the worker. For a better understanding of the TLVs it is essential that the Documentation be consulted when the TLVs are being used.

Ceiling vs Time-Weighted Average Limits. Although the time-weighted average concentration provides the most satisfactory, practical way of monitoring airborne agents for compliance with the limits, there are certain substances for which it is inappropriate. In the latter group are substances which are predominantly fast acting and whose threshold limit is more appropriately based on this particular response. Substances with this type of response are best controlled by a ceiling "C" limit that should not be exceeded. It is implicit in these definitions that the manner of sampling to determine compliance with the limits for each group must differ; a single brief sample, that is applicable to a "C" limit, is not appropriate to the time-weighted limit; here, a sufficient number of samples are needed to permit a time-weighted average concentration throughout a complete cycle of operations or throughout the work shift.

Whereas the ceiling limit places a definite boundary which concentrations should not be permitted to exceed, the time-weighted average limit requires an explicit limit to the excursions that are permissible above the listed values. The magnitude of these excursions may be pegged to the magnitude of the threshold limit by an appropriate factor shown in Appendix C. It should be noted that the same factors are used by the Committee in making a judgment whether to include or exclude a substance for a "C" listing.

"Skin" Notation. Listed substances followed by the designation "Skin" refer to the potential contribution to the overall exposure by the cutaneous route including mucous membranes and eye, either by airborne, or more particularly, by direct contact with the substance. Vehicles can alter skin absorption. This attention-calling designation is intended to suggest appropriate measures for the prevention of cutaneous absorption so that the threshold limit is not invalidated.

These values are reviewed annually by the Committee on Threshold Limits for revision or additions, as further information becomes available.

Mixtures. Special consideration should be given also to the application of the these values in assessing the health hazards which may be associated with exposure to mixtures of two or more substances. A brief discussion of basic considerations involved in developing threshold limit values for mixtures, and methods for their development, amplified by specific examples are given in Appendix B.

"Inert" or Nuisance Particulates. A number of dusts or particulates that occur in the working environment ordinarily produce no specific effects upon prolonged inhalation. Some insoluble substances are classed as inert (e.g. iron and steel dusts, cement, silicon carbide, titanium dioxide, cellulose); others may be soluble (starch, soluble oils, calcium carbonate) but are of such a low order of activity that in concentrations ordinarily encountered do not cause physiologic impairment; still others may be rapidly eliminated or destroyed by the body (vegetable oils, glycerine, sucrose). In the case of the insoluble substances, there may be some accumulation in the respiratory passages. In the case of the soluble substances, this accumulation will ordinarily be temporary but may interfere to some extent with respiratory processes. Hence, it is desirable to control the concentrations of such particulates in the air breathed by any individual, in keeping with good industrial hygiene practice.

A threshold limit of 15 mg/m^3, or 50 mppcf, whichever is less, is recommended for substances in these categories and for which no specific threshold limits have been assigned. This limit, for a normal work day, does not apply to brief exposures at higher concentrations. Neither does it apply to those substances which may cause physiologic impairment at lower concentrations but for which a threshold limit has not yet been adopted. Some "inert" particulates are given in Appendix D.

Simple Asphyxiants — "Inert" Gases or Vapors. A number of gases and vapors, when present in high concentrations in air, act primarily as simple asphyxiants without other significant physiologic effects. A TLV may not be recommended for each simple asphyxiant because the limiting factor is the available oxygen. The minimal oxygen content should be 18 percent by volume under normal atmospheric pressure (equivalent to a partial pressure, pO_2 of 135 mm Hg). Atmospheres deficient in O_2 do not provide adequate warning and most simple asphyxiants are odorless. Several simple asphyxiants

present an explosion hazard. Account should be taken of this factor in limiting the concentration of the asphyxiant.

Physical Factors. It is recognized that such physical factors as heat, ultraviolet and ionizing radiation, humidity, abnormal pressure and the like may place added stress on the body so that the effects from exposure at a threshold limit may be altered. Most of these stresses act adversely to increase the toxic response of a substance. Although most threshold limits have built-in safety factors to guard against adverse effects to moderate deviations from normal environments, the safety factors of most substances are not of such a magnitude as to take care of gross deviations. For example, continuous work at temperatures above 90° F, or overtime extending the work-week more than 50%, might be considered gross deviations. In such instances judgment must be exercised in the proper adjustments of the threshold limit values.

"Notice of Intent." At the beginning of each year, proposed actions of the Committee for the forthcoming year are issued in the form of a "Notice of Intent." This Notice provides not only an opportunity for comment, but solicits suggestions of substances to be added to the list. The suggestions should be accompanied by substantiating evidence.

As Legislative Code. The Conference does not consider the Threshold Limit Values appropriate matter for adoption in legislative codes and regulations and recommends against such use. If, however, the list is so used, the intent of the concepts contained in the Preface should be maintained and provisions should be made to keep the list current.

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Substance	ppm[a]	mg/m³[b]
Acetaldehyde	200	360
Acetic acid	10	25
Acetic anhydride	5	20
Acetone	1,000	2,400
Acetonitrile	40	70
Acetylene dichloride, see 1, 2-Dichloroethylene		
Acetylene tetrabromide	1	14
Acrolein	0.1	0.25
Acrylamide — Skin	—	0.3
Acrylonitrile — Skin	20	45
Aldrin — Skin	—	0.25
Allyl alcohol — Skin	2	5
Allyl chloride	1	3
C Allyl glycidyl ether (AGE)	10	45
Allyl propyl disulfide	2	12
2-Aminoethanol, see Ethanolamine		
2-Aminopyridine	0.5	2
Ammonia	50	35
Ammonium sulfamate (Ammate)	—	15
n-Amyl acetate	100	525
sec-Amyl acetate	125	650
Aniline — Skin	5	19
Anisidine (o-, p-siomers) — Skin	—	0.5
Antimony & Compounds (as Sb)	—	0.5
ANTU (α-Naphthyl thiourea)	—	0.3

*1968 Addition

Substance	ppm[a]	mg/m³[b]
Arsenic & compounds (as As)	—	0.5
Arsine	0.05	0.2
Azinphos methyl — Skin	—	0.2
Barium (soluble compounds)	—	0.5
C Benzene — Skin	25	80
Benzidine — Skin	—	A[1]
p-Benzoquinone, see Quinone		
Benzoyl peroxide	—	5
Benzyl chloride	1	5
Beryllium	—	0.002
Biphenyl, see Diphenyl		
Boron oxide	—	15
C Boron trifluoride	1	3
Bromine	0.1	0.7
Bromoform — Skin	0.5	5
Butadiene (1, 3-butadiene)	1,000	2,200
Butanethiol, see Butyl mercaptan		
2-Butanone	200	590
2-Butoxy ethanol (Butyl Cellosolve) — Skin	50	240
Butyl acetate (n-Butyl acetate)	150	710
sec-Butyl acetate	200	950
tert-Butyl acetate	200	950
Butyl alcohol	100	300
*sec-Butyl alcohol	150	450
tert-Butyl alcohol	100	300
C Butylamine — Skin	5	15
C tert-Butyl chromate (as CrO_3) — Skin	—	0.1
n-Butyl glycidyl ether (BGE)	50	270
**Butyl mercaptan	10	35
p-tert-Butyltoluene	10	60
*Cadmium, (metal dust & soluble salts)	—	0.2
**Cadmium oxide fume, as	—	0.1
Calcium arsenate	—	1
Calcium oxide	—	5
**Camphor	—	2
Carbaryl (Sevin®)	—	5
Carbon black	—	3.5
Carbon dioxide	5,000	9,000
Carbon disulfide — Skin	20	60
Carbon monoxide	50	55
Carbon tetrachloride — Skin	10	65
Chlordane — Skin	—	0.5
Chlorinated camphene — Skin	—	0.5
Chlorinated diphenyl oxide	—	0.5
**C Chlorine	1	3
Chlorine dioxide	0.1	0.3
C Chlorine trifluoride	0.1	0.4
C Chloroacetaldehyde	1	3
α-Chloroacetophenone (Phenacylchloride)	0.05	0.3
Chlorobenzene (Monochlorobenzene)	75	350
o-Chlorobenzylidene malonoitrile (OCBM)	0.05	0.4
Chlorobromomethane	200	1,050
2-Chloro-1, 3-butadiene, see Chloroprene		
Chlorodiphenyl (42% Chlorine) — Skin	—	1

**See Notice of Intended Changes

Substance	ppm[a]	mg/m³[b]
Chlorodiphenyl (54% Chlorine) — Skin	—	0.5
1-Chloro, 2, 3-epoxypropane, see Epichlorhydrin		
2-Chloroethanol, see Ethylene chlorohydrin		
Chloroethylene, see Vinyl chloride		
C Chloroform (Trichloromethane)	50	240
1-Chloro-1-nitropropane	20	100
Chloropicrin	0.1	0.7
Chloroprene (2-chloro-1, 3-butadiene) — Skin	25	90
Chromic acid and Chromates, (as CrO_3)	—	0.1
*Chromium, Sol. chromic, chromous salts, as Cr	—	0.5
Chromium metal & insol. salts	—	1
Coal tar pitch volatiles (benzene soluble fraction) (anthracene, BaP, phenanthrene, acridine, chrysene, pyrene)	—	0.2
*Cobalt metal fume & dust	—	0.1
Copper fume	—	0.1
Dusts & Mists	—	1
Cotton dust, raw	—	1
Crag® herbicide	—	15
Cresol, all isomers — Skin	5	22
Crotonaldehyde	2	6
Cumene — Skin	50	245
Cyanide, as CN — Skin	—	5
Cyclohexane	300	1,050
Cyclohexanol	50	200
Cyclohexanone	50	200
Cyclohexene	300	1,015
Cyclopentadiene	75	200
2, 4-D	—	10
DDT — Skin	—	1
DDVP — Skin	—	1
Decaborane — Skin	0.05	0.3
Demeton® — Skin	—	0.1
Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone)	50	240
1, 2-Diaminoethane, See Ethylenediamine		
Diazomethane	0.2	0.4
Diborane	0.1	0.1
C 1, 2-Dibromoethane (Ethylene dibromide) — Skin	25	190
Dibrom®	—	3
2-N-Dibutylaminoethanol — Skin	2	14
*Dibutyl phosphate	1	5
*Dibutyl phthalate	—	5
C o-Dichlorobenzene	50	300
p-Dichlorobenzene	75	450
Dichlorodifluoromethane	1,000	4,950
1, 3-Dichloro-5, 5-dimethyl hydantoin	—	0.2
1, 1-Dichloroethane	100	400
1, 2-Dichloroethane	50	200
1, 2-Dichloroethylene	200	790
C Dichloroethyl ether — Skin	15	90
Dichloromethane, see Methylene chloride		
Dichloromonofluoromethane	1,000	4,200
C 1, 1-Dichloro-1-nitroethane	10	60
1, 2-Dichloropropane, see Propylene dichloride		
Dichlorotetrafluoroethane	1,000	7,000
Dieldrin — Skin	—	0.25
Diethylamine	25	75
Diethylaminoethanol — Skin	10	50
Diethyl ether, see Ethyl ether		
Difluorodibromomethane	100	860
C Diglycidyl ether (DGE)	0.5	2.8
Dihydroxybenzene, see Hydroquinone		
Diisobutyl ketone	50	290
*Diisopropylamine — Skin	5	20
Dimethoxymethane, see Methylal		
Dimethyl acetamide — Skin	10	35
Dimethylamine	10	18
Dimethylaminobenzene, see Xylidene		
Dimethylaniline (N-Dimethylaniline) — Skin	5	25
Dimethylbenzene, see Xylene		
Dimethyl-1, 2-dibromo-2, 2-dichloroethyl phosphate (Dibrom®)	—	3
Dimethylformamide — Skin	10	30
2, 6-Dimethylheptanone, see Diisobutyl ketone		
1, 1-Dimethylhydrazine — Skin	0.5	1
*Dimethylphthalate	—	5
Dimethyl sulfate — Skin	1	5
Dinitrobenzene (all isomers) — Skin	—	1
Dinitro-o-cresol — Skin	—	0.2
Dinitrotoluene — Skin	—	1.5
Dioxane (Diethylene dioxide) — Skin	100	360
*Diphenyl	0.2	1
Diphenylmethane diisocyanate, see Methylene bisphenyl isocyanate (MDI)		
Dipropylene glycol methyl ether — Skin	100	600
Di-sec, octyl phthalate (Di-2-ethylhexylphthalate)	—	5
Endrin — Skin	—	0.1
Epichlorhydrin — Skin	5	19
EPN — Skin	—	0.5
1, 2-Epoxypropane, see Propylene oxide		
2, 3-Epoxy-1-propanol, see Glycidol		
Ethanethiol, see Ethyl mercaptan		
Ethanolamine	3	6
2-Ethoxyethanol — Skin	200	740
2-Ethoxyethyl acetate (Cellosolve acetate) — Skin	100	540
Ethyl acetate	400	1,400
Ethyl acrylate — Skin	25	100
Ethyl alcohol (Ethanol)	1,000	1,900
Ethylamine	10	18
Ethyl sec-amyl ketone (5-Methyl-3-heptanone)	25	130

Substance	ppm[a]	mg/m³[b]
Ethyl benzene	100	435
Ethyl bromide	200	890
Ethyl butyl ketone (3-Heptanone)	50	230
Ethyl chloride	1,000	2,600
Ethyl ether	400	1,200
Ethyl formate	100	300
**C Ethyl mercaptan	10	25
Ethyl silicate	100	850
Ethylene chlorohydrin — Skin	5	16
Ethylenediamine	10	25
Ethylene dibromide, see 1, 2-Dibromoethane		
Ethylene dichloride, see 1, 2-Dichloroethane		
C Ethylene glycol dinitrate and/or Nitroglycerin — Skin	0.2[d]	1
Ethylene glycol monomethyl ether acetate, see Methyl cellosolve acetate		
Ethylene oxide	50	90
Ethylidene chloride, see 1, 1-Dichloroethane		
N-Ethylmorpholine — Skin	20	94
Ferbam	—	15
Ferrovanadium dust	—	1
Fluoride (as F)	—	2.5
Fluorine	0.1	0.2
Fluorotrichloromethane	1,000	5,600
C Formaldehyde	5	6
Formamide	20	30
Formic acid	5	9
Furfural — Skin	5	20
Furfuryl alcohol	50	200
Gasoline	—	A[6]
Glycidol (2, 3-Epoxy-1-propanol)	50	150
Glycol monoethyl ether, see 2-Ethoxyethanol		
Guthion®, see Azinphos-methyl		
Hafnium	—	0.5
Heptachlor — Skin	—	0.5
**Heptane (n-Heptane)	500	2,000
*Hexachloroethane — Skin	1	10
*Hexachloronaphthalene — Skin	—	0.2
Hexane (n-hexane)	500	1,000
2-Hexanone	100	410
Hexone	100	410
sec-Hexyl acetate	50	300
Hydrazine — Skin	1	1.3
Hydrogen bromide	3	10
C Hydrogen chloride	5	7
Hydrogen cyanide — Skin	10	11
Hydrogen fluoride	3	2
Hydrogen peroxide, 90%	1	1.4
Hydrogen selenide	0.05	0.2
Hydrogen sulfide	10	15
Hydroquinone	—	2
C Iodine	0.1	1
Iron oxide fume	—	10
Isoamyl acetate	100	525
Isoamyl alcohol	100	360
Isobutyl acetate	150	700
*Isobutyl alcohol	100	300
Isophorone	25	140
Isopropyl acetate	250	950
Isopropyl alcohol — Skin	400	980
Isopropylamine	5	12
Isopropyl ether	500	2,100
Isopropyl glycidyl ether (IGE)	50	240
Ketene	0.5	0.9
Lead	—	0.2
Lead arsenate	—	0.15
Lindane — Skin	—	0.5
Lithium hydride	—	0.025
L.P.G. (Liquified petroleum gas)	1,000	1,800
Magnesium oxide fume	—	15
Malathion — Skin	—	15
*Maleic anhydride	0.25	1
C Manganese	—	5
Mercury — Skin	—	0.1
Mercury (organic compounds) — Skin	—	0.01
Mesityl oxide	25	100
Methanethiol, see Methyl mercaptan		
Methoxychlor	—	15
2-Methoxyethanol, see Methyl cellosolve		
Methyl acetate	200	610
Methyl acetylene (propyne)	1,000	1,650
Methyl acetylene-propadiene mixture (MAPP)	1,000	1,800
Methyl acrylate — Skin	10	35
Methylal (dimethoxymethane)	1,000	3,100
Methyl alcohol (methanol) — Skin	200	260
Methylamine	10	12
Methyl amyl alcohol, see Methyl isobutyl carbinol		
Methyl (n-amyl) ketone (2-Heptanone)	100	465
C Methyl bromide — Skin	20	80
Methyl butyl ketone, see 2-Hexanone		
Methyl cellosolve — Skin	25	80
Methyl cellosolve acetate — Skin	25	120
C Methyl chloride	100	210
Methyl chloroform	350	1,900
Methylcyclohexane	500	2,000
Methylcylohexanol	100	470
o-Methycyclohexanone — Skin	100	460
C Methylene bisphenyl isocyanate (MDI)	0.02	0.2
Methylene chloride (dichloromethane)	500	1,740
Methyl ethyl ketone (MEK), see 2-Butanone		
Methyl formate	100	250
Methyl iodide — Skin	5	28
Methyl isobutyl carbinol — Skin	25	100
Methyl isobutyl ketone, see Hexone		
Methyl isocyanate — Skin	0.02	0.05
**C Methyl mercaptan	10	20
Methyl methacrylate	100	410
Methyl propyl ketone, see 2-Pentanone		
C α-Methyl styrene	100	480
Molybdenum		
Soluble compounds	—	5
Insoluble compounds	—	15
Monomethyl aniline — Skin	2	9

Substance	ppm[a]	mg/m³[b]
C Monomethyl hydrazine — Skin	0.2	0.35
Morpholine — Skin	20	70
*Naphtha (coal tar)	100	400
Naphthalene	10	50
β-Naphthylamine	—	A[2]
Nickel carbonyl	0.001	0.007
Nickel metal	—	1
Nickel, metal and soluble compounds	—	1
Nicotine — Skin	—	0.5
Nitric acid	2	5
*Nitric oxide	25	30
p-Nitroaniline — Skin	1	6
Nitrobenzene — Skin	1	5
p-Nitrochlorobenzene — Skin	—	1
Nitroethane	100	310
C Nitrogen dioxide	5	9
Nitrogen trifluoride	10	29
C Nitroglycerin — Skin	0.2	2
Nitromethane	100	250
1-Nitropropane	25	90
2-Nitropropane	25	90
N-Nitrosodimethylamine (dimethylnitrosoamine) — Skin	—	A[3]
Nitrotoluene — Skin	5	30
Nitrotrichloromethane, see Chloropicrin		
*Octachloronaphthalene — Skin	—	0.1
**Octane	500	2,350
**Oil mist (mineral)	—	5
Osmium tetroxide	—	0.002
Oxalic acid	—	1
Oxygen difluoride	0.05	0.1
Ozone	0.1	0.2
Paraquat — Skin	—	0.5
Parathion — Skin	—	0.1
Pentaborane	0.005	0.01
Pentachloronaphthalene — Skin	—	0.5
Pentachlorophenol — Skin	—	0.5
**Pentane	1,000	2,950
2-Pentanone	200	700
Perchloroethylene	100	670
Perchloromethyl mercaptan	0.1	0.8
Perchloryl fluoride	3	13.5
**Petroleum distillates (naphtha)	500	2,000
Phenol — Skin	5	19
p-Phenylene diamine — Skin	—	0.1
Phenyl ether (vapor)	1	7
Phenyl ether-Biphenyl mixture (vapor)	1	7
Phenylethylene, see Styrene		
*Phenyl glycidyl ether (PGE)	10	60
Phenylhydrazine — Skin	5	22
Phosdrin (Mevinphos®) — Skin	—	0.1
Phosgene (carbonyl chloride)	0.1	0.4
Phosphine	0.3	0.4
Phosphoric acid	—	1
Phosphorus (yellow)	—	0.1
Phosphorus pentachloride	—	1
Phosphorus pentasulfide	—	1
Phosphorus trichloride	0.5	3
Phthalic anhydride	2	12
Picric acid — Skin	—	0.1
Pival® (2-Pivalyl-1, 3-indandione)	—	0.1
Platinum (Soluble salts)	—	0.002
Polytetrafluoroethylene decomposition products	—	A[4]
Propane	1,000	1,800
β-Propiolactone	—	A[5]
n-Propyl acetate	200	840
*Propyl alcohol	200	500
n-Propyl nitrate	25	110
Propylene dichloride	75	350
Propylene imine — Skin	2	5
Propylene oxide	100	240
Propyne, see Methylacetylene		
Pyrethrum	—	5
Pyridine	5	15
Quinone	0.1	0.4
Rhodium, Metal fume and dusts	—	0.1
Soluble salts	—	0.001
*Ronnel	—	15
Rotenone (commercial)	—	5
Selenium compounds (as Se)	—	0.2
Selenium hexafluoride	0.05	0.4
Silver, metal and soluble compounds	—	0.01
Sodium fluoroacetate (1080) — Skin	—	0.05
Sodium hydroxide	—	2
Stibine	0.1	0.5
**Stoddard solvent	500	2,900
Strychnine	—	0.15
**C Styrene, monomer (Phenylethylene)	100	420
Sulfur dioxide	5	13
Sulfur hexafluoride	1,000	6,000
Sulfuric acid	—	1
Sulfur monochloride	1	6
Sulfur pentafluoride	0.025	0.25
Sulfuryl fluoride	5	20
Systox, see Demeton®		
2, 4, 5-T	—	10
Tantalum	—	5
TEDP — Skin	—	0.2
Teflon® decomposition products	—	A[4]
Tellurium	—	0.1
Tellurium hexafluoride	0.02	0.2
TEPP — Skin	—	0.05
*C Terphenyls	1	9
1, 1, 1, 2-Tetrachloro-2, 2-difluoroethane	500	4,170
1, 1, 2, 2-Tetrachloro-1, 2-difluoroethane	500	4,170
1, 1, 2, 2-Tetrachloroethane — Skin	5	35
Tetrachloroethylene, see Perchloroethylene		
Tetrachloromethane, see Carbon tetrachloride		
*Tetrachloronaphthalene — Skin	—	2
**Tetraethyl lead (as Pb) — Skin	—	0.075
Tetrahydrofuran	200	590
**Tetramethyl lead (TML) (as Pb) — Skin	—	0.075
Tetramethyl succinonitrile —		

Substance	ppm[a]	mg/m³[b]
Skin	0.5	3
Tetranitromethane	1	8
Tetryl (2, 4, 6-trinitrophenyl-methylnitramine) — Skin	—	1.5
Thallium (soluble compounds) — Skin	—	0.1
Thiram	—	5
Tin (inorganic compounds, except oxide	—	2
Tin (organic compounds)	—	0.1
Titanium dioxide	—	15
Toluene (toluol)	200	750
C Toluene-2, 4-diisocyanate (TDI)	0.02	0.14
o-Toluidine	5	22
Toxaphene, see Chlorinated camphene		
*Tributyl phosphate	—	5
1, 1, 1-Trichloroethane, see Methyl chloroform		
1, 1, 2-Trichloroethane — Skin	10	45
Trichloroethylene	100	535
Trichloromethane, see Chloroform		
Trichloronaphthalene — Skin	—	5
1, 2, 3-Trichloropropane	50	300
1, 1, 2-Trichloro 1, 2, 2-trifluoroethane	1,000	7,600
Triethylamine	25	100
Trifluoromonobromomethane	1,000	6,100
2, 4, 6-Trinitrophenol, see Picric acid		
2, 4, 6-Trinitrophenylmethylnitramine, see Tetryl		
Trinitrotoluene (TNT) — Skin	—	1.5
Triorthocresyl phosphate	—	0.1
Triphenyl phosphate	—	3
Turpentine	100	560
Uranium soluble compounds	—	0.05
insoluble compounds	—	0.25
C Vanadium (V_2O_5 dust)	—	0.5
(V_2O_5 fume)	—	0.1
Vinyl acetate	10	30
Vinyl benzene, see Styrene		
C Vinyl chloride	500	1,300
Vinyl cyanide, see Acrylonitrile		
Vinyl toluene	100	480
Warfarin	—	0.1
Xylene (xylol)	100	435
Xylidene — Skin	5	25
Yttrium	—	1
*Zinc chloride fume	—	1
Zinc oxide fume	—	5
Zirconium compounds (as Zr)	—	5

a) Parts of vapor or gas per million parts of contaminated air by volume at 25°C and 760 mm. Hg. pressure.
b) Approximate milligrams of particulate per cubic meter of air.
d) An atmosphere concentration of not more than 0.02 ppm, or personal protection may be necessary to avoid headache.

Radioactivity: For permissible concentrations of radioisotopes in air, see U.S. Department of Commerce, National Bureau of Standards Handbook 69, "Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure," June 5, 1969. Also, see U.S. Department of Commerce National Bureau of Standards, Handbook 59, "Permissible Dose from External Sources of Ionizing Radiation," September 24, 1954, and addendum of April 15, 1958.

MINERAL DUSTS

Substance	m.p.p.c.f.[e]
SILICA	
Crystalline	
** Quartz, Threshold Limit calculated from the formula	250[f] / % SiO_2 + 5
** Cristobalite " " "	
Amorphous, including natural diatomaceous earth	20
Tremolite	5
SILICATES (less than 1% crystalline silica)	
** Asbestos	5
Mica	20
Soapstone	20
Talc	20
Portland Cement	50
GRAPHITE (natural	15
"Inert or Nuisance Particulates	50 (or 15 mg/m³ whichever is the smaller)

see Appendix D

Conversion factors:
mppcf × 35.3 = Million particles per cubic meter
= particles per c.c.

e) Millions of particles per cubic foot of air, based on impinger samples counted by light-field technics.
f) The percentage of crystalline silica in the formula is the amount determined from airborne samples, except in those instances in which other methods have been shown to be applicable.

NOTICE OF INTENDED CHANGES

These substances, with their corresponding values, comprise those for which either a limit has been proposed for the first time, or for which a change in the "Recommended" listing has been proposed. In both cases, the proposed limits should be considered trial limits that will remain in this listing for a period of at least two years. During this time, the previously Recommended Limit will remain in effect. If, after two years no evidence comes to light that questions the appropriateness of the values herein, the values will be placed in the "Recommended" list. Documentation is available for each of these substances.

Substance	ppm[a]	mg/m³[b]
Abate	—	15
Boron tribromide	1.0	—
Bromine pentafluoride	0.1	—
+Butyl mercaptan	0.5	—

Substance	ppm[a]	Mg/m[b]
+C Cadmium oxide fume (as Cd)	—	0.1
Camphor	2	—
Chlorine	1	—
Cyanogen	10	—
++C Dichloroacetylene	0.1	—
C Diethylene triamine — Skin	10	—
Diphenyl amine	—	10
++Endosulfan (Thiodan®) — Skin	—	0.1
+Ethyl mercaptan	0.5	—
Fibrous glass	—	5
+Heptane	500	2,000
++Indene	10	—
Indium and compounds, as In	—	0.1
Iron salts, soluble, as Fe	—	1
++Methyl isoamyl ketone	100	475
+Methyl mercaptan	0.5	—
C Methyl silicate	5	—
+Octane	400	1,900
+Oil mist (particulate)	—	5[g]
+Oil vapors	[h] A[6]	—
++Pentaerythritol (tetramethylomethane)	—	15
+Pentane	500	1,500
+Petroleum distillates	[h] A[6]	—
Propargyl alcohol — Skin	1	—
RDX — Skin	—	1.5
+Stoddard Solvent	200	—
Styrene	50	—
+Tetraethyl lead (as Pb) — Skin	—	0.100[i]
+Tetramethyl lead (as Pb) — Skin	—	0.150[i]
++Trimethyl benzene	25	—
Tungsten & compounds, as W		
Soluble	—	1
Insoluble	—	5
Uranium, sol. & insol. compounds as U	—	0.2

Substance	
+Asbestos	12 fibers/ml > 5μ in length[j], or 2 mppcf[k]
+Cristobalite	Use one-half the value calculated from the count or mass formulae for quartz.
+Quartz	(1) TLV for respirable dust in mg/m^3: $\frac{10 \text{ mg/m}^3}{\% \text{ Respirable Quartz} + 2}$ [m] (2) "Total dust" respirable and nonrespirable: $\frac{30 \text{ mg/m}^3}{\% \text{ Quartz} + 2}$
+Tridymite	Use one-half the value calculated from formulae for quartz.

+1968 Revision
++1968 Addition

a) Parts of vapor or gas per million parts of contaminated air by volume at 25° C and 760 mm. Hg pressure.
b) Approximate milligrams of particulate per cubic meter or air.
g) As sampled by method that does not collect vapors.
h) According to analytically determined composition.
i) For control of general room air; biologic monitoring is essential for personnel control.
j) As determined by the membrane filter method at 430× phase contrast magnification.
k) As counted by the standard impinger, light-field count technique.
m) Both concentration and percent quartz for the application of this limit are to be determined from the fraction passing a size-selector with the following characteristics:

Aerodynamic Diameter (μ) (unit density sphere)	% passing selector
≈ 2	90
2.5	75
3.5	50
5.0	25
10	0

APPENDIX A

A[1] *Benzidine.* Because of high incidence of bladder tumors in man, any exposure, including skin, is extremely hazardous.

A[2] *β-Naphthylamine.* Because of the extremely high incidence of bladder tumors in workers handling this compound and the inability to control exposures. β-naphthylaimine has been prohibited by the State of Pennsylvania from manufacture, use and other activities that involve human contact.

A[3] *N-Nitrosodimethylamine.* Because of extremely high toxicity and presumed carcinogenic potential of this compound, contact by any route should not be permitted.

A[4] *Polytetrafluoroethylene* decomposition products.* Thermal decomposition of the fluorocarbon chain in air leads to the formation of oxidized products containing carbon, fluorine and oxygen. Because these products decompose in part by hydrolysis in alkaline solution, they can be quantitatively determined in air as fluoride to provide an index of exposure. No TLV is recommended pending determination of the toxicity of the products, but air concentrations should be minimal.

A[5] *β-Propiolactone.* Because of high acute toxicity and demonstrated skin tumor production in animals, contact by any route should be avoided.

A[6] *Gasoline and/or Petroleum Distillates.* The composition of these materials varies greatly and thus a single TLV for all types of these materials is no longer applicable. In general, the aromatic hydrocarbon content will determine what TLV applies. Consequently the content of benzene, other aromatics and additives should be determined to arrive at the appropriate TLV (Elkins, et al. A.I.H.A.J. *24*:99, 1963).

*Trade Names: Algoflon, Fluon, Halon, Teflon, Tetran

APPENDIX B

B.1 THRESHOLD LIMIT VALUES FOR MIXTURES

When two or more hazardous substances are present, their combined effect, rather than that of either individually, should be given primary consideration. In the absence of information to the contrary, the effects of the different hazards should be considered as additive. That is, if the sum of the following fractions,

$$\frac{C_1}{T_1} + \frac{C_1}{T_2} + \cdots \frac{C_n}{T_n}$$

exceeds unity, then the threshold limit of the mixture should be considered as being exceeded. C_1 indicates the observed atmospheric concentration, and T_1 the corresponding threshold limit (See Example 1A.a.).

Exceptions to the above rule may be made when there is a good reason to believe that the chief effects of the different harmful substances are not in fact additive, but *independent*

as when purely local effects on different organs of the body are produced by the various components of the mixture. In such cases the threshold limit ordinarily is exceeded only when at least one member of the series $\frac{C_1}{T_1}$ + or + $\frac{C_2}{T_2}$ etc. itself has a value exceeding unity (See Example 1A.b.).

Antagonistic action or potentiation may occur with some combinations of atmospheric contaminants. Such cases at present must be determined individually. Potentiating or antagonistic agents are not necessarily harmful by themselves. Potentiating effects of exposure to such agents by routes other than that of inhalation is also possible, e.g. imbibed alcohol and inhaled narcotic (trichloroethylene). Potentiation is characteristically exhibited at high concentrations, less probably at low.

When a given operation or process characteristically emits a number of harmful dusts, fumes, vapors or gases, it will frequently be only feasible to attempt to evaluate the hazard by measurement of a single substance. In such cases, the threshold limit used for this substance should be reduced by a suitable factor, the magnitude of which will depend on the number, toxicity and relative quantity of the other contaminants ordinarily present.

Examples of processes which are typically associated with two or more harmful atmospheric contaminants are welding, automobile repair, blasting, painting, lacquering, certain foundry operations, diesel exhausts, etc. (Example 2.)

THRESHOLD LIMIT VALUES FOR MIXTURES EXAMPLES

1A. General case, where air is analyzed for each component:

a. *ADDITIVE EFFECTS*

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \frac{C_3}{T_3} + \ldots \frac{C_n}{T_n} = 1$$

Air contains 5 ppm of carbon tetrachloride (TLV, 10 ppm) 20 ppm of ethylene dichloride (TLV, 50 ppm) and 10 ppm of ethylene dibromide (TLV, 25 ppm)

$$\frac{5}{10} + \frac{20}{50} + \frac{10}{25} = \frac{65}{50} = 1.3$$

Threshold Limit is exceeded.

1B. Special case when the source of contaiminant is a mixture and the atmospheric composition is *assumed* to be similar to that of the original material; i.e., vapor pressure of each component is the same at the observed temperature.

a. *ADDITIVE EFFECTS,* approximate solution

1. A mixture of equal parts (1) trichloroethylene (TLV, 100), and (2) methylchloroform (TLV, 350).

$$\frac{C_1}{100} + \frac{C_2}{350} = \frac{C_m}{T_m}$$

Solution applicable to "spot" solvent mixture usage, where all or nearly all, solvent evaporates.

$$C_1 = C_2 = \frac{1}{2} C_m$$

$$\frac{C_1}{100} + \frac{C_1}{350} = \frac{2C_1}{T_m}$$

$$\frac{7C_1}{700} + \frac{2C_1}{700} = \frac{2C_1}{T_m}$$

$$T_m = 700 \times \frac{2}{9} = 155 \text{ ppm}$$

1B.b. General Exact Solution for Mixtures of N Components With Additive Effects and Different Vapor Pressures.

(1) $\frac{C_1}{T_1} + \frac{C_2}{T_2} + \ldots + \frac{C_n}{T_n} = 1;$

(2) $C_1 + C_2 + \ldots + C_n = T;$

(2.1) $\frac{C_1}{T} + \frac{C_2}{T} + \ldots + \frac{C_n}{T} = 1.$

By the Law of Partial Pressures,

(3) $C_1 = ap_1.$

And by Raoult's Law,

(4) $p_1 = F_1 p_1^\circ.$

Combine (3) and (4) to obtain

(5) $C_1 = aF_1 p_1^\circ.$

Combining (1), (2,1) and (5), we obtain

(6) $\frac{F_1 p_1^\circ}{T} + \frac{F_2 p_2^\circ}{T} + \ldots + \frac{F_n p_n^\circ}{T} =$

$$\frac{F_1 p_1^\circ}{T_1} + \frac{F_2 p_2^\circ}{T_2} + \ldots + \frac{F_n p_n^\circ}{T_n} =$$

and solving for T,

(6.1) $T = \frac{F_1 p_1^\circ + F_2 p_2^\circ + \ldots + F_n p_n^\circ}{\frac{F_1 p_1^\circ}{T_1} + \frac{F_2 p_2^\circ}{T_2} + \ldots + \frac{F_n p_n^\circ}{T_n}}$

or $\sum_{i=1}^{i=n} F_i p_i^\circ$

(6.2) $T = \frac{\sum_{i=1}^{i=n} F_i p_i^\circ}{\sum_{i=1}^{i=n} \frac{F_i p_i^\circ}{T_i}}$

T = Threshold Limit Value in ppm.
C = Vapor concentration in ppm.
p = Vapor pressure of component in solution.
p° = Vapor pressure of pure component.
F = Mol fraction of component in solution.
a = A constant of proportionality.
Subscripts 1,2, . . . n relate the above quantities to components 1,2, . . . n, respectively. Subscript i refers to an arbitrary component from 1 to n.
Absence of subscript relates the quantity to the mixture.

Solution to be applied when there is a reservoir of the solvent mixture whose composition does not change appreciably by evaporation.

Exact Arithmetic Solution of Specific Mixture

Solvent		Mol. wt.	Density	TLV	p° at 25°	Mol fraction in half-and-half solution by volume
Trichloro-ethylene	(1)	131.4	1.46g/ml	100	73mm Hg	0.527
Methychloro-form	(2)	133.42	1.33g/ml	350	125mm Hg	0.473

$$F_1p_1^\circ = (0.527)\ (73) = 38.2$$
$$F_2p_2^\circ = (0.473)\ (125) = 59.2$$

$$T = \frac{38.2 + 59.2}{\frac{38.2}{100} + \frac{59.2}{350}} = \frac{(97.4)\ (350)}{133.8 + 59.2} = \frac{(97.4)\ (350)}{193.0} = 177$$

T = 177 ppm (Note difference in T.L.V. when account is taken of vapor pressure and not mol fraction in comparison with above example where such account is not taken).

2. A mixture of one part of (1) parathion (TLV, 0.1) and two parts of (2) EPN (TLV, 0.5).

$$\frac{C_1}{0.1} + \frac{C_2}{0.5} = \frac{C_{mi}}{T_m} \quad C_2 = 2C_1$$

$$C_m = 3C_1$$

$$\frac{C_1}{0.1} + \frac{2C_1}{0.5} = \frac{3C_1}{T_m}$$

$$\frac{7C_1}{0.5} = \frac{3C_1}{T_m}$$

$$T_m = \frac{1.5}{7} = 0.21\ mg/m^3$$

1C. T.L.V. for Mixtures of Mineral Dusts.

For mixtures of biologically active mineral dusts the general formula for mixtures may be used. With the exception of asbestos, pure minerals are assigned TLV of 2.5, 20 or 50.

For a mixture containing 80% talc and 20% quartz, the TLV for 100% of the mixture "C" is given by:

$$TLV = \frac{1}{\frac{0.8}{20} + \frac{0.2}{2.5}} = 8.4\ mppcf$$

Essentially the same result will be obtained if the limit of the more (most) toxic component is used provided the effects are additive. In the above example the limit for 20% quartz is 10 mppcf.

For another mixture of 25% quartz 25% amorphous silica and 50% talc:

$$TLV = \frac{1}{\frac{0.25}{20} + \frac{0.25}{2.5} + \frac{0.5}{20}} = 7.3\ mppcf$$

The limit for 25% quartz approximates 8 mppcf.

APPENDIX C
BASES FOR ASSIGNING LIMITING "C" VALUES

By definition in the Preface, a listed value bearing a "C" designation refers to 'ceiling' value that should not be exceeded; all values should fluctuate below the listed value. In general the bases for assigning or not assigning a "C" value rest on whether excursions of concentration above a proposed limit for periods up to 15 minutes may result in a) intolerable irritation, b) chronic, or irreversible tissue change, or c) narcosis of sufficient degree to increase accident proneness, impair self rescue or materially reduce work efficiency.

In order for the Committee to decide whether a substance is a candidate for a "C" listing, some guidelines must be formulated on the permissive fluctuation above the limit in terms of the seriousness of the response in the categories a, b, c, given above. For this the factors given in the table below have been used by the Committee. For both technical and practical reasons, the factors have been pegged to the concentration in an inverse manner. It will be noted that as the magnitude of the T.L.V. increases a correspondingly decreased range of fluctuation is permitted; not to decrease the factor for T.L.V.s of increasing magnitude would permit exposures to large absolute quantities, an undesirable condition, a condition that is minimized at low T.L.V.s. Moreover, larger factors at the lower T.L.V.s are consistent with the difficulties in analyzing and controlling trace quantities.

T.L.V. RANGE ppm* or mg/m³	Test T.L.V. Factor	Examples
0 to 1	3	Toluene diisocyanate-T.L.V., 0.02 ppm, if permitted to rise above 0.06 ppm may result in sensitization in a single subsequent exposure. "C" listing recommended on category b.
1+ to 10	2	Manganese-T.L.V., 5 mg/m³, contains little or no safety factor. All values should fluctuate below 5 mg/m³. "C" listing recommended on category b.
10+ to 100	1.5	Methyl styrene-T.L.V. 100 if encountered at levels of 150 ppm will prove intensely irritating. "C" listing recommended on category a.
100+ to 1000	1.25	Methyl chloroform-T.L.V. 350 ppm, at 438 ppm for periods not exceeding 15 minutes is not expected to result in untoward effects relating to category c. No "C" listing recommended.

*Whichever unit is applicable

PERMISSIBLE EXCURSIONS FOR TIME-WEIGHTED AVERAGE (TWA) LIMITS

As stated in the preface, the same factors may be used as guides for reasonable excursions *above* the limit for substances to which the time-weighted average applies. The time-weighted average implies that each excursion *above* the limit is compensated by a comparable excursion below the limit. Thus, a value of 6 ppm HF is permissible for periods not exceeding 15 minutes, provided an equivalent decrease below the limit of 3 ppm obtains.

APPENDIX D

Some "Inert" or Nuisance Particulates*
TLV, 30 mppcf or 10 mg/m³

Alundum (Al_2O_3)	Limestone
Calcium carbonate	Magnesite
Cellulose	Marble
Portland Cement	Pentaerythritol
Corundum (Al_2O_3)	Plaster of Paris
Emery	Rouge
Glycerin Mist	Silicon Carbide
Graphite (synthetic)	Starch
Gypsum	Sucrose

Vegetable oil mists (except castor, cashew nut, or similar irritant oils)	Tin Oxide
	Titanium Dioxide

* When toxic impurities are not present.

APPENDIX E

Some Simple Asphyxiants — "Inert" Gases and Vapors.

Acetylene	Hydrogen
Argon	Methane
Ethane	Neon
Ethylene	Nitrogen
Helium	Nitrous Oxide
	Propane

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1969

changes from 1968

Threshold Limit Values adopted at the Thirty-First Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 11-13, 1969, Denver, CO.

New Values

Substance	ppm	mg/m^3
Abate	—	15
Boron tribromide	1	—
Bromine pentafluoride	0.1	—
Chlorine	1	—
Cyanogen	10	—
C Diethylene triamine — skin	10	—
Diphenyl amine	—	10
Indium and compounds, as In	—	0.1
Iron salts, soluble, as Fe	—	1
C Methyl silicate	5	—
Propangyl alcohol — skin	1	—
RDX — skin	—	1.5
Tungsten and compounds, as W		
Soluble	—	1
Insoluble	—	5
Uranium (natural)		
Soluble and insoluble compounds, as U	—	0.2
Camphor ... from:	—	2
TO	2	—
Gasoline ... from:	—	A[6]
TO	—	A[3]
β-Naphthylamine ... from:	—	A[2]
TO	—	A[1]
N-Nitrosodimethylamine (dimethylnitrosamine) — skin ... from:	—	A[3]
TO	—	A[1]
Polytetrafluoroethylene decomposition products ... from:	—	A[4]
TO	—	A[2]
β-Propiolactone ... from:	—	A[3]
TO	—	A[1]
Sulfurpentafluoride ... from:	0.025	—
TO	0.25	—

EDITOR'S NOTE: Listing of 1,2-Diaminoethane, see Ethylenediamine Diazonmethene with values of 0.2 ppm and 0.4 mg/m^3, should have been listed as follows: 1,2 Diaminoethane, see Ethylenediamine and a separate listing for Diazomethane at 0.2 ppm and 0.4 mg/m^3.

Appendix A

A1. Because of the high incidence of cancer, either in man or in animals, no exposure or contact by any route, respiratory, oral or skin should be permitted for the compounds:

2-Acetylaminoflourene
4-Aminodiphenyl
Benzidine and its salts
Dichlorobenzidine
4-Dimethylaminoazobenzene
β-Naphthylamine
4-Nitrodiphenyl
N-Nitrodimethylamine
β-Propioactone

Because of the extremely high incidence of bladder tumors in workers handling beta-naphthylamine and the potential carcinogenic activity

of the other compounds, the State of Pennsylvania prohibits the manufacture, use and other activities that involve human exposure without express approval by the Department of Health.

A2. Polytetrafluoroethylene* decomposition products. Thermal decompostion of the fluorocarbon chain in air leads to the formation of oxidized products containing carbon, fluorine and oxygen. Because these products decompose in part by hydrolysis in alkaline solution, they can be quantitatively determined in air as fluoride to provide an index of exposure. No TLV is recommended pending determination of the toxicity of the products, but air concentrations should be minimal.

A3. Gasoline and/or Petroleum Distillates. The composition of these material varies greatly and thus a single TLV for all types of these materials is no longer applicable. In general, the aromatic hydrocarbon content will determine what TLV applies. Consequently the content of benzene, other aromatics and additives should be determined to arrive at the appropriate TLV (Elkins *et al, AIHA J. 24*:99, 1963).

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* Trade Names: Algoflon, Fluon, Halon, Teflon, Tetran.

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Threshold Limit Values of Physical Agents Adopted by ACGIH for 1969

Preface

These threshold limit values refer to levels of physical agents and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variations in individual susceptibility, exposure of an occasional individual, at, or even below, the threshold limit may not prevent annoyance, aggravation of a pre-existing condition, or physiological damage.

Threshold limit values refer to levels of exposure for a 8-hour workday for a 40-hour work week. Exceptions are those limits which are given a ceiling value (C). They should be used as guides in the control of health hazards and should not be used as fine lines between safe and dangerous levels of exposures.

These threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and when possible, from a combination of the three.

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, 1) in the evaluation or control of levels of physical agents in the community, 2) as proof or disproof of an existing physical disability, or 3) for adoption by countries whose conditions differ from those in the United States of America.

These values are reviewed annually by the Committee on Threshold Limits for Physical Agents for revisions or additions, as further information becomes available.

Ceiling Value — There are some physical agents which produce physiological response from short intense exposure and whose threshold limit is more appropriately based on this particular response. Physical agents with this type of response are best controlled by ceiling "C" limit which is a maximum level of exposure which should not be exceeded.

Notice of Intent — At the beginning of each year, proposed actions of the Committee for the forthcoming year are issued in the form of a "Notice of Intent." This notice provides not only an opportunity for comment, but solicits suggestions of physical agents to be added to the list. The suggestions should be accompanied by substantiating evidence.

As Legislative Code — Although the Conference does not consider the Threshold Limit Values appropriate matter for adoption in legislative codes and regulations, it recognizes that the values may be so used. If so used the intent of the concepts contained in the Preface should be maintained and provisions should be made to keep the list current.

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THRESHOLD LIMIT VALUES

Noise

These threshold limit values refer to sound pressure levels that represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect on their ability to hear and understand normal speech. The medical profession[1,2] has defined hearing impairment as an average hearing threshold levels in excess of 15 decibels (USASI Z24.12 — 1959) at 500, 1000, and 2000 Hz, and the limits which are given have been established to prevent a hearing loss in excess of this value. These values should be used as guides in the control of noise exposure and, due to individual susceptibility, should not be regarded as fine lines between safe and dangerous levels.

1. Guides for the Evaluation of Hearing Impairment. *Transactions of the American Academy of Ophthalmology and Otolarygology*, pp. 167-168 (March-April 1959).
2. Guides to the Evaluation of the Permanent Impairment; Ear, Nose, Throat and Related Structures. *J. Am. Med. Assoc. 197*:489 (August 1961).

Continuous and Intermittent

The sound level shall be determined by a sound level meter, meeting the standards of the United States of American Standards Institute and operating on the A-weighting network with slow meter response. Exposure shall not exceed that shown in Table I.

These values apply to total time of exposure per working day regardless of whether this is one continuous exposure or a number of short-term exposures but does not apply to impact or impulsive type of noises.

When the daily noise exposure is composed of two or more periods of noise exposure of different levels, their combined effect should be considered, rather than the individual effect of each. If the sum of the following fractions:

$$\frac{C1}{T1} + \frac{C2}{T2} + \ldots \frac{Cn}{Tn}$$

exceeds unity, then the mixed exposure should be considered to exceed the threshold limit value, C1 indicates the total time of exposure at a specified noise level, and T1 indicates the total exposure permitted at that level. Noise exposures of less than 90 dBA do not enter into the above calculations.

TABLE I
Permissible Noise Exposure

Duration per day Hours	Sound Level dBA[a]
8	90
6	92
4	95
3	97
2	100
1 1/2	102
1	105
3/4	107
1/2	110
1/4	115-C[b]

[a] Sound level in decibels as measured on a standard level meter operating on the A-weighing network with slow meter response.

[b] Ceiling Value

Impulsive or Impact Noise

It is recommended that exposure to impulsive or impact noise should not exceed 140 decibels peak sound pressure level-C.

THRESHOLD LIMIT VALUES

6943Å Lasers

Eye Protection

The threshold limit values for exposure of the eye refer to levels of laser energy at the cornea under conditions to which nearly all workers may be exposed without adverse effects. The threshold limit values should be used as guides in the control of exposures to the eye from Q-Switched, and Non-Q-Switched laser energy at 6943Å, and should not be regarded as fine lines between safe

and dangerous levels. They are based on the best available information from experimental studies.

Adopted Values

The values apply to direct illumination or specular reflected laser energy (6943Å) at the cornea and do not apply to laser energy at any other wave length or operational mode.

Mode	J/cm² [d]
Q-Switched (In sec. - 1μ sec. pulse)	1×10^{-7} C
Non-Q-Switched (1μ sec. - 0.1 sec. pulse)	1×10^{-6} C

b) Ceiling Value

d) Joules per square centimeter — energy density

THRESHOLD LIMIT VALUES

Continuous Wave Lasers

Eye Protection

The threshold limit values for exposure for the eye refer to levels of laser energy at the cornea under conditions to which nearly all workers may be exposed without adverse effects. These threshold limit values should be used as guides in the control of exposures to the eye from Continuous Wave laser energy in the 4000Å to 7500Å region of the spectra, and should not be regarded as fine lines between safe and dangerous levels. They are based on the best available information from experimental studies.

Adopted Values

The values apply to direct illumination of specular reflected continuous wave laser energy (4000Å to 7500Å) at the cornea and do not apply to laser energy at any other wave length or operational mode.

Mode	W/cm² [e]
Continuous Wave (> 0.1 sec.)	1×10^{-5} C [b]

b) Ceiling Value

e) Watts per square centimeter — power density

THRESHOLD LIMIT VALUES

Lasers

Skin Protection

The Threshold limit values for exposure of the skin to levels of laser energy in the visible, near infrared, and infrared portions of the spectra are under conditions which it is believed nearly all workers may be exposed without adverse effects.

These values should be used as guides in the control of exposure to pulsed and continuous wave laser energy, and should not be regarded as fine lines between safe and dangerous levels. These threshold limit values are based on the best available information from experimental studies.

The notation "SKIN PROTECTION" refers to the potential risk of exposure of the skin to laser energy. These limits are not directly related to, or part of, the threshold limit value for eye protection and are intended to suggest that appropriate control measures may be necessary to prevent damage to the skin.

Adopted Values

The values apply to the maximum intensity of laser energy incident on the skin (excluding eyes) in the visible, near infrared and infrared wave lengths.

Mode	J/cm² [d]	W/cm² [e]
Pulsed	0.1 C [b]	
Continuous Wave		0.1 C

b) Ceiling Value

d) Joules per square centimeter — energy density

e) Watts per square centimeter — power density

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1970

changes from 1969

Threshold Limit Values adopted at the Thirty—Second Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 10-12, 1970, Detroit, MI.

New Values

Substance	ppm	mg/m^3
Bromine pentafluoride[T]	0.1	0.7
C Cadmium oxide fume (as Cd)	—	0.1
Chlorine[T]	1	3
C Dichloroacetylene	0.1	0.4
Endosulfan (Thiodan®) — skin	—	0.1
Indene	10	45
Methyl isoamyl ketone	100	475
Oil mist, particulate*	—	5[h]
Oil mist, vapor	[i]	A[3]
Pentane	500	1500
Trimethyl benzene	25	120

Mineral Dust

Talc (fibrous), use asbestos limit.

[T] First listing of this value.
* Oil mist mineral changed to Oil mist particulate.
[h] As sampled by method that does not collect vapor.
[i] According to analytically determined composition.

Appendix E

Appendix E first appeared in 1965 listing — Some Simple Asphyxiants — "inert" gases and vapors. Each substance is given the designation "E" as an adopted value in 1970. Propane was added in 1968.

Acetylene Hydrogen
Argon Methane
Ethane Neon
Ethylene Nitrogen oxide
Helium Propane

EDITOR'S NOTE: Appendix D first appeared in 1965 listing some inert or nuisance paticulates. In 1966 Bentonite was deleted. Pentaerythritol was added in 1968. Kaolin was added in 1970. The footnote "when toxic impurities are not present" was added in 1966. In 1969 "e.g., quartz < 1%" was added.

Appendix D

Some "Inert" or Nuisance Particulates[q]

Alundum (Al_2O_3)
Calcium carbonate
Cellulose (paper fiber)
Portland Cement
Corundum (Al_2O_3)
Emery
Glycerine Mist
Graphite (synthetic)
Gypsum
Kaolin
Limestone
Magnesite
Marble
Pentaerythritol
Plaster of Paris
Rouge
Silicon carbide
Starch
Sucrose
Tin oxide
Titantium dioxide
Vegetable oil mists (except castor, cashew nut, or similar irritant oils)

---

q) When toxic impurities are not present, e.g., quartz < 1%.

Revised Values

Substance		ppm	mg/m^3
Butyl mercaptan	from:	10	35
	TO	0.5	1.5
DDVP	changed to: Dichlorous		
Diethylene triamine — skin			
	NIC from:	10	—
	TO	10	42
Ethyl mercaptan	from:	10	25
	TO	0.5	1
Methyl mercaptan	from:	10	20
	TO	0.5	1
Nitroglycerin — skin		*Delete:* C	
Octane	from:	500	2350
	TO	400	1900
Petroleum distillate (naptha)	from:	500	2000
	TO	[i]A[3]	—
Propane	from:	1000	1800
	TO	E	—
Stoddard solvent	from:	500	2900
	YTO	200	1150
Teflon® decomposition products	from:	—	A[4]
	TO	—	A[2]
Tetraethyl lead (as Pb) — skin	from:	—	0.075
	TO	—	0.1[j]
Tetramethyl lead (as Pb) — skin	from:	—	0.075
	TO	—	0.15[j]

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j) For control of general room air, biologic monitoring is essential for personnel control.

Placed on Notice of Intended Changes list

Allyl glycidyl ether
Asbestos, all types
Cristobalite, Chystalline
Formaldehyde

Methyl chloride
Quartz

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1971

changes from 1970

Threshold Limit Values adopted at the Thirty-Third Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 24-28, 1971, Toronto, Canada.

New Values

Substance	ppm	mg/m³
2-Acetylaminofluorene — skin	—	A[1]
4-Aminodiphenyl — skin	—	A[1]
Asphalt (petroleum) fumes	—	5
Dichlorobenzidine	—	A[1]
4-Dimethylaminoazobenzene	—	A[1]
Ethylene glycol monomethyl ether acetate (methyl cellosolve acetate) — skin	25	120
Glass, fibrous[e] or dust	—	D
2-Methoxyethanol (methyl cellosolve) — skin	25	80
Methyl 2-cyanoacrylate	2	8
Methyl demeton — skin	—	0.5
Methyl parathion — skin	—	0.2
Phenothiazine	—	5
Vinyl acetate	10	30

e) = < 5-7 μ in diameter.

Revised Values

Substance		mg/m³
Abate	from:	15
	TO	10
Ammonium sulfamate (Ammate)	from:	15
	TO	10
Boron oxide	from:	15
	TO	10
Crag® herbicide	from:	15
	TO	10
Ferbam	from:	15
	TO	10
Magnesium oxide fume	from:	15
	TO	10
Malethion — skin	from:	15
	TO	10
Mercury (all forms except alkyl)	from:	0.01
	TO	0.05
Methoxychlor	from:	15
	TO	10
Methyl Cellosolve — skin changed to: 2-Methoxyethanol — skin		
Methyl cellosolve acetate changed to: Ethyleneglycol monomethyl ether acetate		
Molybdenum insoluble compounds	from:	15
	TO	10
Oil mist, particulate:	change footnote from h to f	
Oil mist, vapor:	change footnote from i to g	
Perchloryl fluoride	from:	13.5
	TO	14
Petroleum distillates (naphtha):	change footnote i to g	
Styrene	*Delete:* C	
Tetraethyl lead (as Pb) — skin:	change footnote j to h	
Tetramethyl lead (as Pb) — skin:	change footnote j to h	

Placed on Notice of Intended Changes list

Acetaldehyde
Acetic anhydride
Allyl glycidyl ether
Ammonia
Camphor (synthetic)
Chloroform (trichloromethane)

1,2-Dibromoethane (ethylene dibromide) — skin
1,1-Dichloroethane
Dichloroethyl ether — skin
Diisobuty ketone
2-Ethoxyethanol — skin
Flourine
Furfuryl alcohol
Isophorone
Iso propylether
Lead
Methyl bromide — skin
Methylcyclohaxanol
o-Methylcyclohexanone — skin
Toluene
Vinyl chloride

Deletions

Methylcyclopentadienyl manganese tricarbonyl (as Mn) — skin

EDITOR'S NOTE: This is the first year that the old value does not appear as an adopted value for those substances for which there is an intended change. This is also the first year that the airborne contaminants and physical agent TLVs were combined into one booklet. The text of the 1971 TLV booklet follows in its entirety.

Threshold Limit Values for Airborne Contaminants and Physical Agents with Intended Changes for 1971

PREFACE
AIRBORNE CONTAMINANTS

Threshold limit values refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variation in individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit; a smaller percentage may be affected more seriously by aggravation of a pre-existing condition or by development of an occupational illness.

Simple tests are now available (J. Occup. Med. 9: 537, 1967; Ann. N.Y. Acad. Sci., *151, Art. 2:* 968, 1968) that may be used to detect those individuals hypersusceptible to a variety of industrial chemicals (respiratory irritants, hemolytic chemicals, organic isocyanates, carbon disulfide). These tests may be used to screen out by appropriate job placement the hyperreactive worker and thus in effect improve the "coverage" of the TLVs.

Threshold limit values refer to time-weighted concentrations for a 7 or 8-hour workday and 40-hour workweek. They should be used as guides in the control of health hazards and should not be used as fine lines between safe and dangerous concentrations. (Exceptions are the substances listed in Appendices A and E and those substances designated with a "C" or Ceiling value, Appendix C.)

Time-weighted averages permit excursions above the limit provided they are compensated by equivalent excursions below the limit during the workday. In some instances it may be permissible to calculate the average concentration for a workweek rather than for a workday. The degree of permissible excursion is related to the magnitude of the threshold limit value of a particular substance as given in Appendix C. The relationship between threshold limit and permissible excursion is a rule of thumb and in certain cases may not apply. The amount by which threshold limits may be exceeded for short periods without injury to health depends upon a number of factors such as the nature of the contaminant, whether very high concentrations — even for short periods — produce acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such periods. All factors must be taken into consideration in arriving at a decision as to whether a hazardous condition exists.

Threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and, when possible, from a combination of the three. The basis on which the values are established may differ from substance to substance; protection against impairment of health may be a guiding factor for some, whereas reasonable freedom from irritation, narcosis, nuisance or other forms of stress may form the basis for others.

The committee holds to the opinion that limits based on physical irritation should be considered no less binding than those based on physical impairment. There is increasing evidence that physical irritation may initiate, promote or accelerate physical impairment through interaction with other chemical or biologic agents.

In spite of the fact that serious injury is not believed likely as a result of exposure to the threshold limit concentrations, the best practice is to maintain concentrations of all atmospheric contaminants as low as is practical.

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, (1) as a relative index of hazard or toxicity, (2) in the evaluation or control of community air pollution nuisances, (3) in estimating the toxic potential of continuous, uninterrupted exposures, (4) as proof or disproof of an existing disease or physical condition, or (5) for adoption by countries whose working conditions differ from those in the United States of America and where substances and processes differ.

Ceiling vs Time-Weighted Average Limits. Although the time-weighted average concentration provides the most satisfactory, practical way of monitoring airborne agents for compliance with the limits, there are certain substances for which it is inappropriate. In the latter group are substances which are predominantly fast acting and whose threshold limit is more appropriately based on this particular response. Substances with this type of response are best controlled by a ceiling "C" limit that should not be exceeded. It is implicit in these definitions that the manner of sampling to determine compliance with the limits for each group must differ; a single brief sample, that is applicable to a "C" limit, is not appropriate to the time-weighted limit; here, a sufficient number of samples are needed to permit a time-weighted average concentration throughout a complete cycle of operations or throughout the work shift.

Whereas the ceiling limit places a definite boundary which concentrations should not be permitted to exceed, the time-weighted average limit requires an explicit limit to the excursions that are permissible above the listed values. The magnitude of these excursions may be pegged to the magnitude of the threshold limit by an appropriate factor shown in Appendix C. It should be noted that the same factors are used by the

Committee in making a judgement whether to include or exclude a substance for a "C" listing.

"Skin" Notation. Listed substances followed by the designation "Skin" refer to the potential contribution to the overall exposure by the cutaneous route including mucous membranes and eye, either by airborne, or more particularly, by direct contact with the substance. Vehicles can alter skin absorption. This attention-calling designation is intended to suggest appropriate measures for the prevention of cutaneous absorption so that the threshold limit is not invalidated.

Mixtures. Special consideration should be given also to the application of the TLVs in assessing the health hazards which may be associated with exposure to mixtures of two or more substances. A brief discussion of basic considerations involved in developing threshold limit values for mixtures, and methods for their development, amplified by specific examples are given in Appendix B.

Nuisance Dusts. In contrast to fibrogenic dusts which cause scar tissue to be formed in lungs when inhaled in excessive amounts, so-called "nuisance" dusts have a long history of little adverse effect on lungs and do not produce significant organic disease or toxic effect when exposures are kept under reasonable control. The nuisance dusts have also been called (biologically) "inert" dusts, but the latter term is inappropriate to the extent that there is no dust which does not evoke some cellular response in the lung when inhaled in sufficient amount. However, the lung-tissue reaction caused by inhalation of nuisance dusts has the following characteristics: (1) The architecture of the air spaces remains intact. (2) Collagen (scar tissue) is not formed to a significant extent. (3) The tissue reaction is potentially reversible.

Excessive concentrations of nuisance dusts in the workroom air may seriously reduce visibility (iron oxide), may cause unpleasant deposits in the eyes, ears and nasal passages (Portland Cement dust), or cause injury to the skin or mucous membranes by chemical or mechanical action per se or by the rigorous skin cleansing procedures necessary for their removal.

A threshold limit of 10 mg/m^3, or 30 mppcf, of total dust $< 1\%$ SiO_2, whichever is less, is recommended for substances in these categories and for which no specific threshold limits have been assigned. This limit, for a normal workday, does not apply to brief exposures at higher concentrations. Neither does it apply to those substances which may cause physiologic impairment at lower concentrations but for which a threshold limit has not yet been adopted. Some "inert" particulates are given in Appendix D.

Simple Asphyxiants — "Inert" Gases or Vapors. A number of gases and vapors, when present in high concentrations in air, act primarily as simple asphyxiants without other significant physiologic effects. A TLV may not be recommended for each simple asphyxiant because the limiting factor is the available oxygen. The minimal oxygen content should be 18 percent by volume under normal atmospheric pressure (equivalent to a partial pressure, pO_2 of 135 mm Hg). Atmospheres deficient in O_2 do not provide adequate warning and most simple asphyxiants are odorless. Several simple asphyxiants present an explosion hazard. Account should be taken of this factor in limiting the concentration of the asphyxiant. Specific examples are listed in Appendix E.

Physical Factors. It is recognized that such physical factors as heat, ultraviolet and ionizing radiation, humidity, abnormal pressure (altitude) and the like may place added stress on the body so that the effects from exposure at a threshold limit may be altered. Most of these stresses act adversely to increase the toxic response of a substance. Although most threshold limits have built-in safety factors to guard against adverse effects to moderate deviations from normal environments, the safety factors of most substances are not of such a magnitude as to take care of gross deviations. For example, continuous work at temperatures above 90° F, or overtime extending the workweek more than 25%, might be considered gross deviations. In such instances judgment must be exercised in the proper adjustments of the Threshold Limit Values.

"Notice of Intent." At the beginning of each year, proposed actions of the Committee for the forthcoming year are issued in the form of a "Notice of Intent." This Notice provides not only an opportunity for comment, but solicits suggestions of substances to be added to the list. The suggestions should be accompanied by substantiating evidence. The list of Intended Changes follows the Adopted Values in the TLV booklet.

Legal Status. By publication in the Federal Register (Vol. 36, No. 105, May 29, 1971) the "Threshold Limit Values for 1970" are now official federal standards for industrial air, except for the American National Standards and except for certain values for mineral dusts.

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Substance	ADOPTED VALUES TWA ppm[a]	mg/m^3[b]
Abate	—	10
**Acetaldehyde		
Acetic acid	10	25
**Acetic anhydride		
Acetone	1,000	2,400
Acetonitrile	40	70
*2-Acetylaminofluorene — Skin	—	A[1]
Acetylene	E	—
Acetylene dichloride, see 1, 2-Dichloroethylene	—	—
Acetylene tetrabromide	1	14
Acrolein	0.1	0.25
Acrylamide — Skin	—	0.3
Acrylonitrile — Skin	20	45
Aldrin — Skin	—	0.25
Allyl alcohol — Skin	2	5
Allyl chloride	1	3
**C Allyl glycidyl ether (AGE)		
Allyl propyl disulfide	2	12
Alundum (Al_2O_3)	—	D
*4-Aminodiphenyl — Skin	—	A[1]
2-Aminoethanol, see Ethanolamine	—	—
2-Aminopyridine	0.5	2
**Ammonia	25	18
Ammonium sulfamate (Ammate)	—	10
n-Amyl acetate	100	525
sec-Amyl acetate	125	650
Aniline — Skin	5	19
Anisidine (o-, p-siomers) — Skin	—	0.5
Antimony & Compounds (as Sb)	—	0.5
ANTU (α-Naphthyl thiourea)	—	0.3
Argon	E	—
Arsenic & compounds (as As)	—	0.5
Arsine	0.05	0.2
*Asphalt (petroleum) fumes	—	5
Azinphos methyl — Skin.	—	0.2
Barium (soluble compounds)	—	0.5

*1971 Addition
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	mg/m³[b]
C Benzene (benzol) — Skin	25	80
Benzidine — Skin	—	A[1]
p-Benzoquinone, see Quinone	—	—
Benzoyl peroxide	—	5
Benzyl chloride	1	5
Beryllium	—	0.002
Biphenyl, see Diphenyl	—	—
Boron oxide	—	10
Boron tribromide	1	10
C Boron trifluoride	1	3
Bromine	0.1	0.7
Bromine pentafluoride	0.1	0.7
Bromoform — Skin	0.5	5
Butadiene (1,3-butadiene)	1,000	2,200
Butanethiol, see Butyl mercaptan	—	—
2-Butanone	200	590
2-Butoxy ethanol (Butyl Cellosolve) — Skin	50	240
Butyl acetate (n-butyl acetate)	150	710
sec-Butyl acetate	200	950
tert-Butyl acetate	200	950
n-Butyl alcohol	100	300
sec-Butyl alcohol	150	450
tert-Butyl alcohol	100	300
C Butylamine — Skin	5	15
C tert-Butyl chromate (as CrO_3) — Skin	—	0.1
n-Butyl glycidyl ether (BGE)	50	270
Butyl mercaptan	0.5	1.5
p-tert-Butyltoluene	10	60
Cadmium, (Metal dust and soluble salts)	—	0.2
C Cadmium oxide fume (as Cd)	—	0.1
Calcium carbonate	—	D
Calcium arsenate	—	1
Calcium oxide	—	5
**Camphor, (synthetic)		
Carbaryl (Sevin®)	—	5
Carbon black	—	3.5
Carbon dioxide	5,000	9,000
Carbon disulfide — Skin	20	60
Carbon monoxide	50	55
Carbon tetrachloride — Skin	10	65
Cellulose (paper fiber)	—	D
Chlordane — Skin	—	0.5
Chlorinated camphene — Skin	—	0.5
Chlorinated diphenyl oxide	—	0.5
Chlorine	1	3
Chlorine dioxide	0.1	0.3
C Chlorine trifluoride	0.1	0.4
C Chloroacetaldehyde	1	3
α-Chloroacetophenone (Phenacylchloride)	0.05	0.3
Chlorobenzene (Monochlorobenzene)	75	350
o-Chlorobenzylidene malonoitrile (OCBM)	0.05	0.4
Chlorobromomethane	200	1,050
2-Chloro-1, 3-butadiene, see Chloroprene	—	—
Chlorodiphenyl (42% Chlorine) — Skin	—	1
Chlorodiphenyl (54% Chlorine) — Skin	—	0.5
1-Chloro, 2, 3-epoxy-propane, see Epichlorhydrin	—	—
2-Chloroethanol, see Ethylene chlorohydrin	—	—
Chloroethylene, see Vinyl chloride	—	—
**C Chloroform (Trichloromethane)		
1-Chloro-1-nitro-propane	20	100
Chloropicrin	0.1	0.7
Chloroprene (2-chloro-1,3-butadiene) — Skin	25	90
Chromic acid and Chromates, (as CrO_3)	—	0.1
Chromium, Sol. chromic, chromous salts, as Cr	—	0.5
Coal tar pitch volatiles (benzene soluble fraction) anthracene, BaP, phenanthrene, acridine, chrysene, pyrene	—	0.2
Cobalt metal, dust and fume	—	0.1
Copper fume	—	0.1
Dusts & Mists	—	1
Corundum (Al_2O_3)	—	D
Cotton dust, (raw)	—	1
Crag® herbicide	—	10
Cresol, (all isomers — Skin	5	22
Crotonaldehyde	2	6
Cumene — Skin	50	245
Cyanide, as CN — Skin	—	5
Cyanogen	10	—
Cyclohexane	300	1,050
Cyclohexanol	50	200
Cyclohexanone	50	200
Cyclohexene	300	1,015
Cyclopentadiene	75	200
2, 4-D	—	10
DDT — Skin	—	1
DDVP, See Dichlorvos	—	—
Decaborane — Skin	0.05	0.3
Demeton® — Skin	—	0.1
Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone)	50	240
**1, 2-Diaminoethane, See Ethylenediamine	—	—
Diazomethane	0.2	0.4
Diborane	0.1	0.1
1, 2-Dibromoethane (Ethylene dibromide) — Skin		
Dibrom®	—	3
Dibutyl phosphate	1	5
Dibutylphthalate	—	5
C Dichloracetylene	0.1	0.4
C o-Dichlorobenzene	50	300
p-Dichlorobenzene	75	450
*Dichlorobenzidine — Skin	—	A[1]
Dichlorodifluoromethane	1,000	4,950
1, 3-Dichloro-5, 5-dimethyl hydantoin	—	0.2
**1, 1-Dichloroethane		

Substance	ADOPTED VALUES TWA ppm[a]	mg/m³[b]
1, 2-Dichloroethane	50	200
1, 2-Dichloroethylene	200	790
**Dichloroethyl ether — Skin		
*Dichloromethane, see Methylene chloride	—	—
**Dichloromonofluoromethane	1,000	4,200
C 1, 1-Dichloro-1-nitroethane	10	60
1, 2-Dichloropropane, see Propylene dichloride	—	—
Dichlorotetrafluoroethane	1,000	7,000
Dichlorvos (DDVP) — Skin	—	1
Dieldrin — Skin	—	0.25
Diethylamine	25	75
Diethylaminoethanol — Skin	10	50
**C Diethylene triamine — Skin		
Diethyl ether, see Ethyl ether	—	—
Difluorodibromomethane	100	860
C Diglycidyl ether (DGE)	0.5	2.8
Dihydroxybenzene, see Hydroquinone	—	—
**Diisobutyl ketone		
Diisopropylamine — Skin	5	20
Dimethoxymethane, see Methylal	—	—
Dimethyl acetamide — Skin	10	35
Dimethylamine	10	18
*4-Dimethylaminoazobenzene	—	A[1]
Dimethylaminobenzene, see Xylidene	—	—
Dimethylaniline (N-Dimethylaniline) — Skin	5	25
Dimethylbenzene, see Xylene	—	—
Dimethyl-1,2-dibromo-2-dichloro-ethyl phosphate, see Dibrom	—	—
Dimethylformamide — Skin	10	30
2, 6-Dimethylheptanone, see Diisobutyl ketone	—	—
1, 1-Dimethylhydrazine — Skin	0.5	1
Dimethylphthalate	—	5
Dimethylsulphate — Skin	1	5
Dinitrobenzene (all isomers) — Skin	—	1
Dinitro-o-cresol — Skin	—	0.2
Dinitrotoluene — Skin	—	1.5
Dioxane (Diethylene dioxide) — Skin	100	360
Diphenyl	0.2	1
Diphenylamine	—	10
Diphenylmethane diisocyanate, see Methylene bisphenyl isocyanate (MDI)	—	—
Dipropylene glycol methyl ether — Skin	100	600
Di-sec, octyl phthalate (Di-2-ethylhexyl-phthalate)	—	5
Emery	—	D
Endosulfan (Thiodan®) — Skin	—	0.1
Endrin — Skin	—	0.1
Epichlorhydrin — Skin	5	19
EPN — Skin	—	0.5
1, 2-Epoxypropane, see Propylene oxide	—	—
2, 3-Epoxy-l-propanol see Glycidol	—	—
Ethane	E	—
Ethanethiol, see Ethyl mercaptan	—	—
Ethanolamine	3	6
**2-Ethoxyethanol — Skin		
2-Ethoxyethyl acetate (Cellosolve acetate) — Skin	100	540
Ethyl acetate	400	1,400
Ethyl acrylate — Skin	25	100
Ethyl alcohol (Ethanol)	1,000	1,900
Ethylamine	10	18
Ethyl sec-amyl ketone (5-Methyl-3-heptanone)	25	130
Ethyl benzene	100	435
Ethyl bromide	200	890
Ethylbutyl ketone (3-Heptanone)	50	230
Ethyl chloride	1,000	2,600
Ethyl ether	400	1,200
Ethyl formate	100	300
Ethyl mercaptan	0.5	1
Ethyl silicate	100	850
Ethylene	E	—
Ethylene chlorohydrin — Skin	5	16
Ethylenediamine	10	25
Ethylene dibromide, see 1, 2-Dibromoethane	—	—
Ethylene dichloride, see 1, 2-Dichloroethane	—	—
C Ethylene glycol dinitrate and/or Nitroglycerin — Skin	0.2[d]	—
Ethylene glycol monomethyl ether acetate (Methyl cellosolve acetate) — Skin	25	120
Ethylene imine — Skin	0.5	1
Ethylene oxide	50	90
Ethylidene chloride, see 1, 1-Dichloroethane	—	—
N-Ethylmorpholine — Skin	20	94
Ferbam	—	10
Ferrovanadium dust	—	1
Fluoride (as F)	—	2.5
**Fluorine		
Fluorotrichloromethane	1,000	5,600
**C Formaldehyde	5	6
Formic acid	5	9
Furfural — Skin	5	20
**Furfuryl alcohol — Skin		
Gasoline	—	A[3]
Germanium tetrahydride	0.2	0.6
Glass, fibrous[e] or dust	—	D
Glycerin mist	—	D
Glycidol (2, 3-Epoxy-1-propanol)	50	150
Glycol monoethyl ether, see 2-Ethoxyethanol	—	—
Graphite (Synthetic)	—	D
Guthion®, see Azinphos-methyl	—	—
Gypsum	—	D
Hafnium	—	0.5
Helium	E	—
Heptachlor — Skin	—	0.5
Heptane (n-Heptane)	500	2,000

Substance	ADOPTED VALUES TWA ppm[a]	mg/m³[b]
Hexachloroethane — Skin	1	10
Hexachloronaphthalene — Skin	—	0.2
Hexane (n-hexane)	500	1,800
2-Hexanone	100	410
Hexone (Methyl isobutyl ketone)	100	410
sec-Hexyl acetate	50	300
Hydrazine — Skin	1	1.3
Hydrogen	E	—
Hydrogen bromide	3	10
C Hydrogen chloride	5	7
Hydrogen cyanide — Skin	10	11
Hydrogen fluoride	3	2
Hydrogen peroxide	1	1.4
Hydrogen selenide	0.05	0.2
Hydrogen sulfide	10	15
Hydroquinone	—	2
Indene	10	45
Indium & Compounds, as In	—	0.1
C Iodine	0.1	1
Iron oxide fume	—	10
Iron salts, soluble, as Fe	—	1
Isoamyl acetate	100	525
Isoamyl alcohol	100	360
Isobutyl acetate	150	700
Isobutyl alcohol	100	300
**Isophorone		
Isopropyl acetate	250	950
Isopropyl alcohol	400	980
Isopropylamine	5	12
**Isopropylether		
Isopropyl glycidyl ether (IGE)	50	240
Kaolin	—	D
Ketene	0.5	0.9
**Lead		
Lead arsenate	—	0.15
Limestone	—	D
Lindane — Skin	—	0.5
Lithium hydride	—	0.025
L.P.G. (Liquified petroleum gas)	1,000	1,800
Magnesite	—	D
Magnesium oxide fume	—	10
Malathion — Skin	—	10
Maleic anhydride	0.25	1
C Manganese & Compounds as Mn	—	5
Marble	—	D
Mercury (Alkyl compounds) — Skin	—	0.01
Mercury (All forms except alkyl)	—	0.05
Mesityl oxide	25	100
Methane	E	—
Methanethiol, see Methyl mercaptan	—	—
Methoxychlor	—	10
2-Methoxyethanol — Skin (Methyl cellosolve)	25	80
Methyl acetate	200	610
Methyl acetylene (propyne)	1,000	1,650
Methyl acetylene-propadiene mixture (MAPP)	1,000	1,800
Methyl acrylate — Skin	10	35
Methylal (dimethoxymethane)	1,000	3,100
Methyl alcohol (methanol) — Skin	200	260
Methylamine	10	12

Substance	ADOPTED VALUES TWA ppm[a]	mg/m³[b]
Methyl amyl alcohol, see Methyl isobutyl carbinol	—	—
*Methyl 2-cyanoacrylate	2	8
Methyl isoamyl ketone	100	475
Methyl (n-amyl) ketone (2-Heptanone)	100	465
**Methyl bromide — Skin		
Methyl butyl ketone, see 2-Hexanone	—	—
Methyl cellosolve — Skin see 2-Methoxyethanol	—	—
Methyl cellosolve acetate — Skin, see Ethylene glycol monomethyl ether acetate	—	—
**C Methyl chloride	100	210
Methyl chloroform	350	1,900
Methylcyclohexane	500	2,000
**Methylcylohexanol		
**o-Methycyclohexanone — Skin		
Methylcyclopentadienyl manganese tricarbonyl (as Mn) — Skin	0.1	0.2
*Methyl demeton — Skin	—	0.5
Methyl ethyl ketone (MEK), see 2-Butanone	—	—
Methyl formate	100	250
Methyl iodide — Skin	5	28
Methyl isobutyl carbinol — Skin	25	100
Methyl isobutyl ketone, see Hexone	—	—
Methyl isocyanate — Skin	0.02	0.05
Methyl mercaptan	0.5	1
Methyl methacrylate	100	410
*Methyl parathion — Skin	—	0.2
Methyl propyl ketone, see 2-Pentanone	—	—
C Methyl silicate	5	30
C α-Methyl styrene	100	480
C Methylene bisphenyl isocyanate (MDI)	0.02	0.2
Methylene chloride (dichloromethane)	500	1,740
Molybdenum (Soluble compounds) (Insoluble compounds)	—	5
	—	10
Monomethyl aniline — Skin	2	9
C Monomethyl hydrazine — Skin	0.2	0.35
Morpholine — Skin	20	70
Naphtha (coal tar)	100	400
Naphthalene	10	50
β-Naphthylamine	—	A[1]
Neon	E	—
Nickel carbonyl	0.001	0.007
Nickel, metal and soluble compounds (as Ni)	—	1
Nicotine — Skin	—	0.5
Nitric acid	2	5
Nitric oxide	25	30
p-Nitroaniline — Skin	1	6
Nitrobenzene — Skin	1	5
p-Nitrochlorobenzene — Skin	—	1
Nitroethane	100	310
Nitrogen	E	—
C Nitrogen dioxide	5	9
Nitrogen trifluoride	10	29
Nitroglycerin — Skin	0.2	2

Substance	ADOPTED VALUES TWA ppm[a]	mg/m³[b]
Nitromethane	100	250
1-Nitropropane	25	90
2-Nitropropane	25	90
N-Nitrosodimethylamine (dimethylnitrosoamine) — Skin	—	A[1]
Nitrotoluene — Skin	5	30
Nitrotrichloromethane, see Chloropicrin	—	—
Nitrous oxide	E	—
Octachloronaphthalene — Skin	—	0.1
Octane	400	1,900
Oil mist, particulate	—	5[f]
Oil mist, vapor	[g]A[3]	
Osmium tetroxide		0.002
Oxalic acid	—	1
Oxygen difluoride	0.05	0.1
Ozone	0.1	0.2
Paraquat — Skin	—	0.5
Parathion — Skin	—	0.1
Pentaborane	0.005	0.01
Pentachloronaphthalene — Skin	—	0.5
Pentachlorophenol — Skin	—	0.5
Pentaerythritol	—	D
Pentane	500	1,500
2-Pentanone	200	700
Perchloroethylene	100	670
Perchloromethyl mercaptan	0.1	0.8
Perchloryl fluoride	3	14
Petroleum distillates (naphtha)	[g]A[3]	
Phenol — Skin	5	19
p-Phenylene diamine — Skin	—	0.1
Phenyl ether (vapor)	1	7
Phenyl ether-Diphenyl mixture (vapor)	1	7
Phenylethylene, see Styrene	—	—
Phenyl glycidyl ether (PGE)	10	60
Phenylhydrazine — Skin	5	22
*Phenothiazine — Skin	—	5
Phosdrin (Mevinphos®) — Skin	—	0.1
Phosgene (carbonyl chloride)	0.1	0.4
Phosphine	0.3	0.4
Phosphoric acid	—	1
Phosphorus (yellow)	—	0.1
Phosphorus pentachloride	—	1
Phosphorus pentasulfide	—	1
Phosphorus trichloride	0.5	3
Phthalic anhydride	2	12
Picric acid — Skin	—	0.1
Pival® (2-Pivalyl-1, 3-indandione)	—	0.1
Plaster of Paris	—	D
Platinum (Soluble salts) as Pt	—	0.002
Polytetrafluoroethylene decomposition products	—	A[2]
Propane	E	—
β-Propiolactone	—	A[1]
P. opargyl alcohol — Skin	1	—
n-Propyl acetate	200	840
Propyl alcohol	200	500
n-Propyl nitrate	25	110
Propylene dichloride (1, 2-Dichloropropane)	75	350
Propylene imine — Skin	2	5
Propylene oxide	100	240
Propyne, see Methyl-acetylene	—	—
Pyrethrum	—	5
Pyridine	5	15
Quinone	0.1	0.4
RDX — Skin	—	1.5
Rhodium, Metal fume and dusts (as Rh)	—	0.1
Soluble salts	—	0.001
Ronnel	—	10
Rotenone (commercial)	—	5
Rouge	—	D
Selenium compounds (as Se)	—	0.2
Selenium hexafluoride	0.05	0.4
Silicon carbide	—	D
Silver, metal and soluble compounds	—	0.01
Sodium fluoroacetate (1080) — Skin	—	0.05
C Sodium hydroxide	—	2
Starch	—	D
Stibine	0.1	0.5
Stoddard solvent	200	1,150
Strychnine	—	0.15
*Styrene (Phenylethylene)	100	420
Sucrose	—	D
Sulfur dioxide	5	13
Sulfur hexafluoride	1,000	6,000
Sulfuric acid	—	1
Sulfur monochloride	1	6
Sulfur pentafluoride	0.025	0.25
Sulfuryl fluoride	5	20
Systox, see Demeton®	—	—
2, 4, 5-T	—	10
Tantalum	—	0.2
TEDP — Skin	—	0.2
Teflon® decomposition products	—	A[2]
Tellurium	—	0.1
Tellurium hexafluoride	0.02	0.2
TEPP — Skin	—	0.05
C Terphenyls	1	9
1, 1, 1, 2-Tetrachloro-2, 2-difluoroethane	500	4,170
1, 1, 2, 2-Tetrachloro-1, 2-difluoroethane	500	4,170
1, 1, 2, 2-Tetrachloroethane — Skin	5	35
Tetrachloroethylene, see Perchloroethylene	—	—
Tetrachloromethane, see Carbon tetrachloride	—	—
Tetrachloronaphthalene — Skin	—	2
Tetraethyl lead (as Pb) — Skin	—	0.100[h]
Tetrahydrofuran	200	590
Tetramethyl lead as (Pb) — Skin	—	0.150[h]
Tetramethyl succinoitrile — Skin	0.5	3
Tetranitromethane	1	8
Tetryl (2, 4, 6-trinitro-phenylmethylnitramine) — Skin	—	1.5
Thallium (soluble compounds) — Skin (as Tl)	—	0.1
Thiram	—	5
Tin (inorganic compounds, except SnH_4 and SnO_2) as Sn	—	2
Tin (organic compounds)		

Substance	ADOPTED VALUES TWA ppm[a]	mg/m³[b]
— Skin (as Sn)	—	0.1
Tin oxide	—	D
Titanium dioxide	—	D
**Toluene (toluol) — Skin		
C Toluene-2, 4-diisocyanate	0.02	0.14
o-Toluidine	5	22
Toxaphene, see Chlorinated camphene	—	—
Tributyl phosphate	—	5
1, 1, 1-Trichloroethane, see Methyl chloroform	—	—
1, 1, 2-Trichloroethane — Skin	10	45
Trichloroethylene	100	535
Trichloromethane, see Chloroform	—	—
Trichloronaphthalene — Skin	—	5
1, 2, 3-Trichloropropane	50	300
1, 1, 2-Trichloro 1, 2, 2-trifluoroethane	1,000	7,600
Triethylamine	25	100
Trifluoromonobromomethane	1,000	6,100
Trimethyl benzene	25	120
2, 4, 6-Trinitrophenol, see Picric acid	—	—
2, 4, 6-Trinitrophenyl-methylnitramine, see Tetryl	—	—
Trinitrotoluene — Skin	—	1.5
Triorthocresyl phosphate	—	0.1
Triphenyl phosphate	—	3
Tungsten & compounds, as W		
Soluble	—	1
Insoluble	—	5
Turpentine	100	560
Uranium (natural) soluble & insoluble compounds, as U	—	0.2
C Vanadium (V_2O_5) Dust	—	0.5
(V_2O_5) Fume	—	0.1
*Vinyl acetate	10	30
Vinyl benzene, see Styrene	—	—
**C Vinyl chloride		
Vinyl cyanide, see Acrylonitrile	—	—
Vinyl toluene	100	480
Warfarin	—	0.1
Xylene (xylol) — Skin	100	435
Xylidene — Skin	5	25
Yttrium	—	1
Zinc chloride fume	—	1
Zinc oxide fume	—	5
Zirconium compounds (as Zr)	—	5

a) Parts of vapor or gas per million parts of contaminated air by volume at 25°C and 760 mm. Hg. pressure.
b) Approximate milligrams of substance per cubic meter of air.
d) An atmosphere concentration of not more than 0.02 ppm, or personal protection may be necessary to avoid headache.
e) < 5-7m in diameter.
f) As sampled by method that does not collect vapor.
g) According to analytically determined composition.
h) For control of general room air, biologic monitoring is essential for personnel control.

Radioactivity: For permissible concentrations of radioisotopes in air, see U.S. Department of Commerce, National Bureau of Standards Handbook 69, "Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure," June 5, 1959. Also, see U.S. Department of Commerce National Bureau of Standards, Handbook 59, "Permissible Dose from External Sources of Ionizing Radiation," September 24, 1954, and addendum of April 15, 1958. A report, Basic Radiation Protection Criteria, published by the National Committee on Radiation Protection, revises and modernizes the concept of the NCRP standards of 1954, 1957 and 1958; obtainable as NCRP Rept. No. 39, P.O. Box 4867, Washington, D.C. 20008.

MINERAL DUSTS

Substance	m.p.p.c.f.[i]
SILICA, Crystalline	
**Quartz	—
**Cristobalite, Crystalline	—
Amorphous, including natural diatomaceous earth	20
SILICATES (less than 1% crystalline silica)	
**Asbestos, all types	
Mica	20
Perlite	30
Portland Cement	50
Soapstone	20
Talc (nonasbestiform)	20
Talc (fibrous) use asbestos limit	—
Tremolite (see Talc, fibrous)	—
Graphite (natural)	15
**"Inert" or Nuisance Particulates see Appendix D	~~50~~ 15 ~~30~~ or (~~10~~ mg/m³ whichever is the smaller) of total dust < 1% SiO_2

Conversion factors
mppcf x 35.3 = million particles per cubic meter
= particles per c.c.

i) Millions of particles per cubic foot of air, based on impinger samples counted by light-field technics.

**See Notice of Intended Changes for Mineral Dusts.

NOTICE OF INTENDED CHANGES (for 1971)

These substances, with their corresponding values, comprise those for which either a limit has been proposed for the first time, or for which a change in the "Adopted" listing has been proposed. In both cases, the proposed limits should be considered trial limits that will remain in this listing for a period of at least two years. If, after two years no evidence comes to light that questions the appropriateness of the values herein, the values will be reconsidered for the "Adopted" list. Documentation is available for each of these substances.

Substance	ppm[a]	Mg/m³[b]
†Acetaldehyde	100	180
†C Acetic anhydride	5	20
Allyl glycidyl ether	5	22

Substance	ppm[a]	mg/m³[b]
Ammonia	25	18
Ammonium chloride fume	—	10
†Bismuth telluride	—	10
†Bismuth telluride (Se-doped)	—	5
†Butane	500	1200
Butyl lactate	1	5
Camphor (symthetic)	2	12
†Caprolactam (2-Oxohexamethylenimine)	—	5
†Chloroform (trichloromethane)	25	120
Diazinon — Skin	—	0.1
†1, 2-Dibromoethane (ethylene dibromide) — Skin	20	145
2-N Dibutylaminoethanol — Skin	2	14
†1, 1-Dichloroethane	200	820
†Dichloroethyl ether — Skin	5	30
Diethylene triamine — Skin	1	4
†Diisobutyl ketone	25	150
†Diquat	—	0.5
†Ethylene glycol, particulate	—	10
†Ethylene glycol, vapor	100	260
†2-Ethoxyethanol — Skin	100	370
†Fluorine	1	2
C Formaldehyde	2	3
†Furfuryl alcohol	5	20
†Hexachlorocyclopentadiene	0.1	1
†Hexafluoroacetone	0.1	0.7
Iron pentacarbonyl	0.01	0.08
†Isophorone	10	55
†Isopropyl ether	250	1050
†Lead, inorganic compounds fumes & dusts	—	0.15
†Methylacrylonitrile — Skin	1	3
†Methyl bromide — Skin	15	60
Methyl chloride	100	210
†Methyl cyclohexanol	50	235
†o-Methyl cyclohexanone — Skin	50	230
Methylcyclopentadienyl manganese tricarbonyl (as Mn) — Skin	0.1	0.2
†Mineral wool fiber	—	D
†Paraffin wax fume	—	1
†Perlite	—	30mppcf
†C Phenylphosphine	0.05	0.25
Propylene glycol monomethyl ether	100	360
Rosin Core Solder, pyrolysis products (as formaldehyde)	—	0.1
†Silicon	—	10
C Subtilisins (Proteolytic enzymes) (as 100% pure crystalline enzyme)	—	0.0003
†Sulfur tetrafluoride	0.1	0.4
†Toluene	100	375
Vanadium (V_2O_5 Fume) as V	—	0.05
Vinyl bromide	250	1100
Vinyl chloride	200	770
Wood dust (nonallergenic)	—	5

a) Parts of vapor or gas per million parts of contaminated air by volume at 25°C and 760 mm. Hg. pressure.

b) Approximate milligrams of particulate per cubic meter of air.

†1971 Revision or Addition
Capital letters refer to Appendices

NOTICE OF INTENDED CHANGES (Cont'd)
MINERAL DUSTS

Substance	TLV
†Asbestos (all types)	5 fibers/ml > 5μm in length;[j]
†Coal dust (bituminous)	2 mg/m³ (respirable dust[k])
Cristobalite	Use one-half the value calculated from the count or mass formulae for quartz.
†'Inert' or Nuisance Particulates	10 mg/m³ or 30 mppcf (whichever is the smaller) of total dust < 1% SiO_2.
†Quartz	TLV in mppcf[l]: $\frac{300^{m)}}{\%\ \text{quartz} + 10}$ TLV for respirable dust in mg/m³: $\frac{10\ \text{mg/m}^{3m)}}{\%\ \text{Respirable quartz} + 2}$ TLV for "total dust," respirable and nonrespirable: $\frac{30\ \text{mg/m}^3}{\%\ \text{quartz} + 3}$
Silica, fused	Use quartz formulae
Tridymite	Use one-half the value calculated from formula for quartz.

j) As determined by the membrane filter method at 400-450 X magnification (4 mm objective) phase contrast illumination. Concentrations 5 fibers/ml but not to exceed 10, may be permitted for 15-minute periods each hour up to five times daily.

k) "Respirable dust as defined by the British Medical Research Council Criteria (1) and as sampled by a device producing equivalent results (2).
(1) Hatch, T.E. and Gross, P., Pulmonary Deposition and Retention of Inhaled Aerosols, p. 149. Academic Press, New York, New York, 1964.
(2) Interim Guide for Respirable Mass Sampling, AIHA Aerosol Technology Committee, AIHA J. 31, 2, 1970, p. 133.

m) The percentage of quartz in the formula is the amount determined from airborne samples, except in those instances in which other methods have been shown to be applicable.

n) Both concentration and percent quartz for the application of this limit are to be determined from the fraction passing a size-selector with the following characteristics:

Aerodynamic Diameter (μm) (unit density sphere)	% passing selector
≤ 2	90
2.5	75
3.5	50
5.0	25
10	0

APPENDIX A

A[1] Because of the high incidence of cancer, either in man or animals, no exposure or contact by any route, respiratory, oral or skin should be permitted for the compounds:

2-Acetylaminofluorene
4-Aminodiphenyl
Benzidine & its salts
Dichlorobenzidine
4-Dimethylaminoazobenzene
beta-Naphthylamine

4-Nitrodiphenyl
N-Nitrosodimethylamine
beta-Propiolactone

Because of the extremely high incidence of bladder tumors in workers handling beta-naphthylamine and the potential carcinogenic activity of the other compounds, the State of Pennsylvania prohibits the manufacture, use and other activities that involve human exposure without express approval by the Department of Health.

A[2] *Polytetrafluoroethylene* decomposition products.* Thermal decomposition of the fluorocarbon chain in air leads to the formation of oxidized products containing carbon, fluorine and oxygen. Because these products decompose in part by hydrolysis in alkaline solution, they can be quantitatively determined in air as fluoride to provide an index of exposure. No TLV is recommended pending determination of the toxicity of the products, but air concentrations should be minimal.

A[3] *Gasoline and/or Petroleum Distillates.* The composition of these materials varies greatly and thus a single TLV for all types of these materials is no longer applicable. In general, the aromatic hydrocarbon content will determine what TLV applies. Consequently the content of benzene, other aromatics and additives should be determined to arrive at the appropriate TLV (Elkins, et al. A.I.H.A.J. 24:99, 1963).

*Trade Names: Algoflon, Fluon, Halon, Teflon, Tetran.

APPENDIX B

B.1 THRESHOLD LIMIT VALUES FOR MIXTURES

When two or more hazardous substances are present, their combined effect, rather than that of either individually, should be given primary consideration. In the absence of information to the contrary, the effects of the different hazards should be considered as additive. That is, if the sum of the following fractions,

$$\frac{C_1}{T_1} + \frac{C_1}{T_2} + \ldots + \frac{C_n}{T_n}$$

exceeds unity, then the threshold limit of the mixture should be considered as being exceeded. C_1 indicates the observed atmospheric concentration, and T_1 the corresponding threshold limit (See Example 1A.a.).

Exceptions to the above rule may be made when there is a good reason to believe that the chief effects of the different harmful substances are not in fact additive, but *independent* as when purely local effects on different organs of the body are produced by the various components of the mixture. In such cases the threshold limit ordinarily is exceeded only when at least one member of the series $\left(\frac{C_1}{T_1} + \text{or} + \frac{C_2}{T_2} \text{ etc.}\right)$ itself has a value exceeding unity (See Example 1A.b.).

Antagonistic action or potentiation may occur with some combinations of atmospheric contaminants. Such cases at present must be determined individually. Potentiating or antagonistic agents are not necessarily harmful by themselves. Potentiating effects of exposure to such agents by routes other than that of inhalation is also possible, e.g. imbibed alcohol and inhaled narcotic (trichloroethylene). Potentiation is characteristically exhibited at high concentrations, less probably at low.

When a given operation or process characteristically emits a number of harmful dusts, fumes, vapors or gases, it will frequently be only feasible to attempt to evaluate the hazard by measurement of a single substance. In such cases, the threshold limit used for this substance should be reduced by a suitable factor, the magnitude of which will depend on the number, toxicity and relative quantity of the other contaminants ordinarily present.

Examples of processes which are typically associated with two or more harmful atmospheric contaminants are welding, automobile repair, blasting, painting, lacquering, certain foundry operations, diesel exhausts, etc. (Example 2.)

THRESHOLD LIMIT VALUES FOR MIXTURES

EXAMPLES

1A. General case, where air is analyzed for each component:

a. *Additive effects. (note: It is essential that the atmosphere be analyzed both qualitatively and quantitatively for each component present, in order to evaluate compliance or noncompliance with this calculated TLV.)*

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \frac{C_3}{T_3} + \ldots = 1$$

Example No. 1: Air contains 5 ppm of carbon tetrachloride (TLV, 10 ppm) 20 ppm of ethylene dichloride (TLV, 50 ppm) and 10 ppm of ethylene dibromide (TLV, 25 ppm)

Atmospheric concentration of mixture =

5 + 20 + 10 = 35 ppm of mixture

$$\frac{5}{10} + \frac{20}{50} + \frac{10}{25} = \frac{25 + 20 + 20}{50} = 1.3$$

Threshold Limit is exceeded. Furthermore, the TLV of this mixture may be calculated by reducing the total fraction to 1.0; i.e.

$$\text{TLV of mixture} = \frac{35}{1.3} = 27 \text{ ppm}$$

Example No. 2: Air contains 200 ppm of hexane (TLV = 500 ppm) 100 ppm of methylene chloride (TLV = 500 ppm) and 20 ppm of perchlorethylene (TLV = 100 ppm).

Atmospheric concentration of mixture =

200 + 100 + 20 = 320 ppm of mixture

$$\frac{200}{500} + \frac{100}{500} + \frac{20}{100} = \frac{200 + 100 + 100}{500} = \frac{400}{500} = 0.8$$

Threshold Limit is not exceeded. The TLV of this mixture =

$$\frac{320}{0.8} = 400 \text{ ppm}$$

1B. Special case when the source of contaiminant is a liquid mixture and the atmospheric composition is *assumed* to be similar to that of the original material; e.g. on a time weighted average exposure basis, all of the liquid (solvent) mixture eventually evaporates.

a. *Additive effects,* approximate solution

1. The percent composition (by weight) of the liquid mixture is known, the TLVs of the constituents must be listed in mg/M³.

NOTE: In orderto evaluate compliance with this TLV, field sampling instruments should be calibrated, in the laboratory, for response to this specific quantitative and qualtitative air-vapor mixture, and also to fractional concentrations of this mixture; e.g., 1/2 the TLV; 1/10 the TLV; 2 X the TLV; 10 X the TLV; etc.)

TLV of mixture =

$$\frac{1}{\frac{f_a}{TLV_a} + \frac{f_b}{TLV_b} + \frac{f_c}{TLV_c} + \ldots \frac{f_n}{TLV_n}}$$

Example No. 1: Liquid solvent contains (by weight) 50% heptane (TLV = 2000 mg/M³) 30% methylene chloride (TLV = 1740 mg/M³) 20% perchloroethylene (TLV = 670 mg/M³).

TLV of mixture =

$$\frac{1}{\frac{0.5}{2000} + \frac{0.3}{1740} + \frac{0.2}{670}} = \frac{1}{.00025 + .00017 + .0003}$$

$$= \frac{1}{.00072} = 1390 \text{ mg/M}^3$$

Of this mixture: 50% or 695 mg/M³ is heptane, 30% or 417 mg/M³ is methylene chloride and 20% or 278 mg/M³ is perchloroethylene.

These values can be converted to ppm as follows:

heptane:
2000 mg/M³ = 500 ppm
1 mg/M³ = 0.25 ppm
695 mg/M³ = 174 ppm

methylene chloride:
1740 mg/M³ = 500 ppm
1 mg/M³ = 0.287 ppm
417 mg/M³ = 119 ppm

perchlorethylene:
670 mg/M³ = 100 ppm
1 mg/M³ = 0.15 ppm
278 mg/M³ = 42 ppm

The TLV of this mixture =

174 + 119 + 42 = 335 ppm.

1B.b. General Exact Solution for Mixtures of N Components With Additive Effects and Different Vapor Pressures.

(1) $\frac{C_1}{T_1} + \frac{C_2}{T_2} + \ldots + \frac{C_n}{T_n} = 1;$

(2) $C_1 + C_2 + \ldots + C_n = T;$

(2.1) $\frac{C_1}{T} + \frac{C_2}{T} + \ldots + \frac{C_n}{T} = 1.$

By the Law of Partial Pressures,

(3) $C_1 = ap_1.$

And by Raoult's Law,

(4) $p_1 = F_1p_1°.$

Combine (3) and (4) to obtain

(5) $C_1 = aF_1p_1°.$

Combining (1), (2,1) and (5), we obtain

(6) $\frac{F_1p_1°}{T} + \frac{F_2p_2°}{T} + \ldots + \frac{F_np_n°}{T} =$

$\frac{F_1p_1°}{T_1} + \frac{F_2p_2°}{T_2} + \ldots + \frac{F_np_n°}{T_n} =$

and solving for T,

(6.1) $$T = \frac{F_1p_1° + F_2p_2° + \ldots + F_np_n°}{\frac{F_1p_1°}{T_1} + \frac{F_2p_2°}{T_2} + \ldots + \frac{F_np_n°}{T_n}}$$

or $\sum_{i=1}^{i=n} F_ip_i° = n F_1p_1°$

(6.2) $$T = \frac{i = 1}{\sum_{i=1}^{i=n} \frac{F_ip_i°}{T_1}}$$

T - Threshold Limit Value in ppm.
C - Vapor concentration in ppm.
p - Vapor pressure of component in solution.
p° - Vapor pressure of pure component.
F - Mol fraction of component in solution.
a - A constant of proportionality.
Subscripts 1,2, . . . n relate the above quantities to components 1,2, . . . n, respectively. Subscript i refers to an arbitrary component from 1 to n.
Absence of subscript relates the quantity to the mixture.

1B.c. Solution to be applied when there is a reservoir of the solvent mixture whose composition does not change appreciably by evaporation.

Exact Arithmetic Solution of Specific Mixture

Solvent		Mol. wt	Density	TLV	p° at 25°C	Mol fraction in half-and-half solution by volume
Trichloro-ethylene	(1)	131.4	1.46g/ml	100	73mm Hg	0.527
Methychloro-form	(2)	133.42	1.33g/ml	350	125mm Hg	0.473

$F_1p_1° = (0.527)\ (73) = 38.2$
$F_2p_2° = (0.473)\ (125) = 59.2$

$$T = \frac{38.2 + 59.2}{\frac{38.2}{100} + \frac{59.2}{350}} = \frac{(97.4)\ (350)}{133.8 + 59.2} = \frac{(97.4)\ (350)}{193.0} = 177$$

T = 177 ppm (Note difference in T.L.V. when account is taken of vapor pressure and not mol fraction in comparison with above example where such account is not taken).

2. A mixture of one part of (1) parathion (TLV, 0.1) and two parts of (2) EPN (TLV, 0.5).

$$\frac{C_1}{0.1} + \frac{C_2}{0.5} = \frac{C_m}{T_m} \quad C_2 = 2C_1$$

$$C_m = 3C_1$$

$$\frac{C_1}{0.1} + \frac{2C_1}{0.5} = \frac{3C_1}{T_m}$$

$$\frac{7C_1}{0.5} = \frac{3C_1}{T_m}$$

$$T_m = \frac{1.5}{7} = 0.21 \text{ mg/m}^3$$

1C. T.L.V. for Mixtures of Mineral Dusts.

For mixtures of biologically active mineral dusts the general formula for mixtures may be used. With the exception of asbestos, pure minerals are assigned TLV of 2.5, 20 or 50.

For a mixture containing 80% talc and 20% quartz, the TLV for 100% of the mixture "C" is given by:

$$TLV = \frac{1}{\frac{0.8}{20} + \frac{0.2}{2.5}} = 8.4 \text{ mppcf}$$

Essentially the same result will be obtained if the limit of the more (most) toxic component is used provided the effects are additive. In the above example the limit for 20% quartz is 10 mppcf.

For another mixture of 25% quartz 25% amorphous silica and 50% talc:

$$TLV = \frac{1}{\frac{0.25}{20} + \frac{0.25}{2.5} + \frac{0.5}{20}} = 7.3 \text{ mppcf}$$

The limit for 25% quartz approximates 8 mppcf.

APPENDIX C
PERMISSIBLE EXCURSIONS FOR TIME-WEIGHTED AVERAGE (TWA) LIMITS

The Excursion TLV Factor in the Table automatically defines the magnitude of the permissible excursion above the limit for those substances not given a "C" designation; i.e., the TWA limits. Examples in the Table show that nitrobenzene, the TLV for which is 1 ppm, should never be allowed to exceed 3 ppm. Similarly, carbon tetrachloride, TLV 10 ppm, should never be allowed to exceed 20 ppm. By contrast, those substances with a "C" designation are not subject to the excursion factor and must be kept at or below the TLV.

These limiting excursions are to be considered to provide a "rule-of-thumb" guidance for listed substances generally, and may not provide the most appropriate excursion for a particular substance. Efforts are being made to develop such specific excursions, when indicated to be significantly different from that recommended by the present excursion factors.

Substance	TLV	Excursion Factor	Max. Conc. Permitted for short time
	ppm		ppm
Nitrobenzene	1	3	3
Carbon tetrachloride	10	2	20
o-Dichlorobenzene	10	1.5	75
Acetone	1000	1.25	1250
Boron trifluoride	C 1	—	1
Butylamine	C 5	—	5
Styrene monomer	C100	—	100

For all substances:

		Excursion Factor	
TLV > 0-1	(ppm or mg/m^3),	Factor	= 3
TLV > 1-10	"	"	= 2
TLV > 10-100	"	"	= 1.5
TLV > 100-1000	"	"	= 1.25

BASIS FOR ASSIGNING LIMITING "C" VALUES

By definition in the Preface, a listed value bearing a "C" designation refers to a 'ceiling' value that should not be exceeded; all values should fluctuate below the listed value. This, in effect, makes the "C" designation a maximal allowable concentration (MAC). In general, the bases for assigning or not assigning a "C" value rest on whether excursions of concentration above a proposed limit *for periods up to 15 minutes* may result in a) intolerable irritation, b) chronic, or irreversible tissue change, or c) narcosis of sufficient degree to increase accident proness, impair self-rescue or materially reduce work efficiency.

APPENDIX D
Some "Inert" or Nuisance Particulates[p]
TLV, 30 mppcf or 10 mg/m^3

Alundum (Al_2O_3)	Kaolin
Calcium carbonate	Limestone
Cellulose (paper fiber)	Magnesite
Portland Cement	Marble
Corundum (Al_2O_3)	Pentaerythritol
Emery	Plaster of Paris
Glass, fibrous[q] or dust	Rouge
Glycerin Mist	Silicon
Graphite (synthetic)	Silicon Carbide
Gypsum	Starch
Vegetable oil mists (except castor, cashew nut, or similar irritant oils)	Sucrose
	Tin Oxide
	Titanium Dioxide

p) When toxic impurities are not present, e.g. quartz < 1%.
q) < 7 μm in diameter

APPENDIX E
Some Simple Asphyxiants - "Inert" Gases and Vapors[r]

Acetylene	Hydrogen
Argon	Methane
Butane	Neon
Ethane	Nitrogen
Ethylene	Nitrous Oxide
Helium	Propane

r) As defined in preface.

PREFACE — PHYSICAL AGENTS

These threshold limit values refer to levels of physical agents and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variations in individual susceptibility, exposure of an occasional individual at, or even below, the threshold limit may not prevent annoyance, aggravation of a pre-existing condition, or physiological damage.

Threshold limit values refer to levels of exposure for an 8-hour workday for a 40-hour work week. Exceptions are those limits which are given a ceiling value (C). They should be used as guides in the control of health hazards and should not be used as fine lines between safe and dangerous levels of exposures.

These threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and when possible, from a combination of the three.

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, (1) in the evaluation or control of the levels of physical agents in the community, (2) as proof or disproof of an existing physical disability, or (3) for adoption by countries whose working conditions differ from those in the United States of America.

These values are reviewed annually by the Committee on Threshold Limits for Physical Agents for revisions or additions, as further information becomes available.

Ceiling Value — There are some physical agents which produce physiological response from short intense exposure and whose threshold limit is more appropriately based on this particular response. Physical agents with this type of response are best controlled by a ceiling "C" limit which is a maximum level of exposure which should not be exceeded.

Notice of Intent — At the beginning of each year, proposed actions of the Committee for the forthcoming year are issued in the form of a "Notice of Intent." This notice provides not only an opportunity for comment, but solicits suggestions of physical agents to be added to the list. The suggestions should be accompanied by substantiating evidence.

As Legislative Code — The Conference recognizes that the Threshold Limit Values may be adopted in legislative codes and regulations. If so used, the intent of the concepts contained in the Preface should be maintained and provisions should be made to keep the list current.

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THRESHOLD LIMIT VALUES NOISE

These threshold limit values refer to sound pressure levels that represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect on their ability to hear and understand normal speech. The medical profession[1,2] has defined hearing impairment as an average hearing threshold levels in excess of 25 decibels (ANSI S3.6 — 1969) at 500, 1000, and 2000 Hz, and the limits which are given have been established to prevent a hearing loss in excess of this value. These values should be used as guides in the control of noise exposure and, due to individual susceptibility, should not be regarded as fine lines between safe and dangerous levels.

1. Guides for the Evaluation of Hearing Impairment. Transactions of the American Academy of Ophthalmology and Otolarygology, pp. 167-168 (March-April 1959).
2. Guides to the Evaluation of the Permanent Impairment; Ear, Nose, Throat and Related Structures. J. Am. Med. Assoc. 197:489 (August 1961).

Continuous and Intermittent

The sound level shall be determined by a sound level meter, meeting the standards of the American National Standards Institute and operating on the A-weighting network with slow meter response. Exposure shall not exceed that shown in Table I.

These values apply to total time of exposure per working day regardless of whether this is one continuous exposure or a number of short-term exposures but does not apply to impact or impulsive type of noises.

When the daily noise exposure is composed of two or more periods of noise exposure of different levels, their combined effect should be considered, rather than the individual effect of each. If the sum of the following fractions:

$$\frac{C1}{T1} + \frac{C2}{T2} + \cdots \frac{Cn}{Tn}$$

exceeds unity, then the mixed exposure should be considered to exceed the threshold limit value, C1 indicates the total time of exposure at a specified noise level, and T1 indicates the total exposure permitted at that level. Noise exposures of less than 90 dBA do not enter into the above calculations.

TABLE I
Permissible Noise Exposure

Duration per day Hours	Sound Level dBA[a)]
8	90
6	92
4	95
3	97
2	100
1 1/2	102
1	105
3/4	107
1/2	110
1/4	115-C*

[a)] Sound level in decibels as measured on a standard level meter operating on the A-weighing network with slow meter response.

* Ceiling Value: No exposure in excess of 115 dBA.

Impulsive or Impact Noise

It is recommended that exposure to impulsive or impact noise should not exceed 140 decibels peak sound pressure level-C.

6943Å LASERS

Eye Protection

The threshold limit values for exposure of the eye refer to levels of laser energy at the cornea under conditions to which nearly all workers may be exposed without adverse effects. The threshold limit values should be used as guides in the

control of exposures to the eye from Q-Switched, and Non-Q-Switched laser energy at 6943Å, and should not be regarded as fine lines between safe and dangerous levels. They are based on the best available information from experimental studies.

Adopted Values

The values apply to direct illumination or specular reflected laser energy (6943A) at the cornea and do not apply to laser energy at any other wave length or operational mode.

Mode	Energy Density Joules/cm^2
Q-Switched (In sec. - 1μ sec. pulse)	1×10^{-7}*
Non-Q-Switched (1μ sec. - 0.1 sec. pulse)	1×10^{-6}*

* Ceiling Value

CONTINUOUS WAVE LASERS

Eye Protection

The threshold limit values for exposure for the eye refer to levels of laser energy at the cornea under conditions to which nearly all workers may be exposed without adverse effects. These threshold limit values should be used as guides in the control of exposures to the eye from Continuous Wave laser energy in the 4000Å to 7500Å region of the spectra, and should not be regarded as fine lines between safe and dangerous levels. They are based on the best available information from experimental studies.

Adopted Values

The values apply to direct illumination of specular reflected continuous wave laser energy (4000Å to 7500Å) at the cornea and do not apply to laser energy at any other wave length or operational mode.

Mode	Power Density W/cm^2
Continuous Wave	
(> 0.1 sec.)	1×10^{-5} C*

* Ceiling Value

LASERS

Skin Protection

The Threshold limit values for exposure of the skin to levels of laser energy in the visible, near infrared, and infrared portions of the spectra are under conditions which it is believed nearly all workers may be exposed without adverse effects.

These values should be used as guides in the control of exposure to pulsed and continuous wave laser energy, and should not be regarded as fine lines between safe and dangerous levels. These threshold limit values are based on the best available information from experimental studies.

The notation "SKIN PROTECTION" refers to the potential risk of exposure of the skin to laser energy. These limits are not directly related to, or part of, the threshold limit value for eye protection and are intended to suggest that appropriate control measures may be necessary to prevent damage to the skin.

Adopted Values

The values apply to the maximum intensity of laser energy incident on the skin (excluding eyes) in the visible, near infrared and infrared wave lengths.

Mode	
Pulsed	0.1 Joules/cm^2* (Energy Density)
Continuous Wave	1.0 Watts/cm^2 (Power Density)

* Ceiling Value

NOTICE OF INTENT TO ESTABLISH THRESHOLD LIMIT VALUES

MICROWAVES

These Threshold Limit Values refer to microwave energy in the frequency range of 100 MHz to 100 GHz and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect.

These values should be used as guides in the control of exposure of microwaves and should not be regarded as a fine line between safe and dangerous levels. The values will be reviewed annually by the Committee on Physical Agents for revisions or additions as further information becomes available.

Recommended Values

The Threshold Limit Value for occupational microwave energy exposure where power densities are known and exposure time controlled is as follows:

1. For average power density levels up to but not exceeding 10 milliwatts per square centimeter, total exposure time shall be limited to the 8-hour workday (continuous exposure).
2. For average power density levels from 10 milliwatts per square centimeter up to but not exceeding 25 milliwatts per square centimeter, total exposure time shall be limited to no more than 10 minutes for any 60 minute period during an 8 hour workday (intermittent exposure).
3. For average power density levels in excess of 25 milliwatts per square centimeter, exposure is not permissible (ceiling value).

NOTE: For repetitively pulsed sources the average power density may be calculated by multiplying the peak power density by the duty cycle. The duty cycle is equal to the pulse duration in seconds times the pulse repetition rate in hertz.

ULTRAVIOLET RADIATION

These threshold limit values refer to ultraviolet radiation in the spectral region between 200 and 400 nm and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect. These values for exposure of the eye or the skin apply to ultraviolet radiation from arcs, gas, and vapor discharges, and incandescent sources, but do not apply to ultraviolet lasers or solar radiation. These levels should not be used for determining exposure of photosensitive individuals to ultraviolet radiation. These values should be used as guides in the control of exposure to continuous sources where the exposure duration shall not be less than 0.1 sec.

These values should be used as guides in the control of exposure to ultraviolet sources and should not be regarded as

a fine line between safe and dangerous levels. The values will be reviewed annually by the Committee on Physical Agents for revisions or additions as further information becomes available.

Recommended Values:

The threshold limit value for occupational exposure to ultraviolet radiation incident upon skin or eye where irradiance values are known and exposure time is controlled are as follows:

1. For the near ultraviolet spectral region (320 to 400 nm) total irradiance incident upon the unprotected skin or eye should not exceed 0.1 W/cm^2.
2. For the actinic ultraviolet spectral region (200 — 315 nm), radiant exposure incident upon the unprotected skin or eye should not exceed the values given in Table 1 within a 24-hour period.
3. To determine the effective irradiance of a broadband source weighted against the peak of the spectral effectiveness curve (270 nm), the following weighting formula should be used:

$$H_{eff} = \sum H_\lambda S_\lambda \Delta_\lambda$$

where:

H_{eff} = effective irradiance relative to a monochromatic source at 270 nm.

H_λ = spectral irradiance in W/cm^2/nm

S_λ = relative spectral effectiveness (unitless)

Δ_λ = band width in nanometers

4. Permissible exposure time in seconds for exposure to actinic ultraviolet radiation incident upon the unprotected skin or eye may be computed by dividing 0.003 J/cm by H_{eff} in W/cm^2. The exposure time may also be determined using Table 2 which provides exposure times corresponding to effective irradiances in μW/cm^2.

TABLE 1
Relative Spectral Effectiveness by Wavelength

Wavelength (nm)	TLV (mJ/cm^2)	Relative Spectral Effectiveness S_λ
200	100	0.03
210	40	0.075
220	25	0.12
230	16	0.19
240	10	0.30
250	7.0	0.43
254	6.0	0.5
260	4.6	0.65
270	3.0	1.0
280	3.4	0.88
290	4.7	0.64
300	10	0.30
305	50	0.06
310	200	0.015
315	1000	0.003

TABLE 2
Permissible Ultraviolet Exposures

Duration of Exposure Per Day	Effective Irradiance E_{eff} (μW/cm^2)
8 hrs	0.1
4 hrs	0.2
2 hrs	0.4
1 hr	0.8
30 min	1.7
15 min	3.3
10 min	5
5 min	10
1 min	50
30 sec	100
10 sec	300
1 sec	3,000
0.5 sec	6,000
0.1 sec	30,000

HEAT STRESS

These Threshold Limit Values refer to heat stress conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse health effects. The TLVs shown in Table I are based on the assumption that nearly all acclimatized, fully clothed workers with adequate water and salt intake should be able to function effectively under the given working conditions without exceeding a deep body temperature of 38° C (WHO technical report series #413, 1969 *Health Factors Involved in Working Under Conditions of Heat Stress).*

Since measurement of deep body temperature is impractical for monitoring the workers' heat load, the measurement of environmental factors is required which most nearly correlate with deep body temperature and other physiological responses to heat. At the present time Wet Bulb-Globe Temperature Index (WBGT) is the simplest and most suitable technique to measure the environmental factors. WBGT values are calculated by the following equations:

1. Outdoors with solar load:
   WBGT = 0.7WB + 0.2GT + 0.1 DB
2. Indoors or Outdoors with no solar load:
   WBGT = 0.7WB + 0.3GT

where:
WBGT = Wet Bulb-Globe Temperature Index
WB = Natural Wet-Bulb Temperature
DB = Dry-Bulb Temperature
GT = Globe Thermometer Temperature

The determination of WBGT requires the use of a black globe thermometer, a natural (static) wet-bulb thermometer, and a dry-bulb thermometer.

TABLE I
Permissible Heat Exposure Threshold Limit Values
(Values are given in °C. WBGT)

Work - Rest Regimen	Work Load		
	Light	Moderate	Heavy
Continuous work	30.0	26.7	25.0
75% Work — 25% Rest	30.6	28.0	25.9
50% Work — 50% Rest	31.4	29.4	27.9
25% Work — 75% Rest	32.2	31.1	30.0

Higher heat exposures than shown in Table I are permissible if the workers have been undergoing medical surveillance and it has been established that they are more tolerant to work in heat than the average worker. Workers should not be permitted to continue their work when their deep body temperature exceeds 38.0° C.

APPENDIX A

HEAT STRESS

I. *Measurement of the Environment*

The instruments required are a dry-bulb, a natural wet-bulb, a globe thermometer, and a stand. The measurement of the environmental factors shall be performed as follows:

A. The range of the dry and the natural wet bulb thermometer shall be −5° C to 50° C with an accuracy of ±0.5° C. The dry bulb thermometer must be shielded from the sun and the other radiant surfaces of the environment without restricting the airflow around the bulb. The wick of the natural wet-bulb thermometer shall be kept wet with distilled water for at least 1/2 hour before the temperature reading is made. It is not enough to immerse the other end of the wick into a reservoir of distilled water and wait until the whole wick becomes wet by capillarity. The wick shall be wetted by direct application of water from a syringe 1/2 hour before each reading. The wick shall extend over the bulb of the thermometer, covering the stem about one additional bulb length. The wick should always be clean and new wicks should be washed before using.

B. One globe thermometer, consisting of a 15 cm. (6-inch) diameter hollow copper sphere, painted on the outside with a matte black finish or equivalent shall be used. The bulb or sensor of a thermometer (range −5° C to 100° C with an accuracy of ±0.5° C) must be fixed in the center of the sphere. The globe thermometer shall be exposed at least 25 minutes before it is read.

C. One stand shall be used to suspend the three thermometers so that they do not restrict free air flow around the bulbs, and the wet-bulb and globe thermometer are not shaded.

D. It is permissible to use any other type of temperature sensor that gives identical reading to a mercury thermometer under the same conditions.

E. The thermometers must be so placed that the readings are representative of the condition where the men work or rest, respectively.

The methodology outlined above is more fully explained in the following publications:

1. "Prevention of Heat Casualties in Marine Corps Recruits, 1955-1960, with Comparative Incidence Rates and Climatic Heat Stresses in other Training Categories," by Captain David Minard, MC, USN, Research Report No. 4 Contract No. MR005.01-0001.01, Naval Medical Research Institute, Bethesda, Maryland, 21 February 1961.

2. "Heat Casualties in the Navy and Marine Corps, 1959-1962, with Appendices on the Field Use of the Wet Bulb-Globe

TABLE A
Assessment of Work Load

Average values of metabolic rate during different activities.

A. Body position and movement	Kcal./min.
Sitting	0.3
Standing	0.6
Walking	2.0-3.0
Walking up hill	add 0.8 per meter (yard) rise

B. Type of Work		Average Kcal./min.	Range Kcal./min.
Hand work			
	light	0.4	0.2-1.2
	heavy	0.9	
Work with one arm			
	light	1.0	0.7-2.5
	heavy	1.8	
Work with both arms			
	light	1.5	1.0-3.5
	heavy	2.5	
Work with body			
	light	3.5	2.5-15.0
	moderate	5.0	
	heavy	7.0	
	very heavy	9.0	

Light hand work: writing, hand knitting

Heavy hand work: typewriting

Heavy work with one arm; hammering in nails (shoemaker, upholsterer)

Light work with two arms: filing metal, planing wood, raking of a garden

Moderate work with the body: cleaning a floor, beating a carpet

Heavy work with the body: railroad track laying, digging, barking trees

Sample Calculation: Using a heavy hand tool on an assembly line

A. Walking along		2.0 Kcal./min.
B. Intermediate value between heavy work with two arms and light work with the body		3.0 Kcal./min.
		5.0 Kcal./min.
C. Add for basal metabolism		1.0 Kcal./min.
	Total	6.0 Kcal./min.

Adapted from Lehmann, G.E., A. Muller and H. Spitzer: Der Kalorienbedarf bei gewerblicher Arbeit. Arbeitsphysiol. *14*: 166, 1950.

Temperature Index," by Captain David Minard, MC, USN, and R. L. O'Brien, HMC, USN. Research Report No. 7, Contract No. MR005.01-0001.01, Naval Medical Research Institute, Bethesda, Maryland, 12 March 1964.

3. Minard, D.: Prevention of Heat Casualties in Marine Corps Recruits. Military Medicine *126(4)*: 261-272, 1961.

II. *Work Load Categories*

The heat produced by body and the environmental heat together determine the total heat load. Therefore, if work is to be performed under hot environmental conditions, the work-load category of each job shall be established and the heat exposure limit pertinent to the work load evaluated against the applicable standard in order to protect the worker from exposure beyond the permissible limit.

A. The work load category may be established by ranking each job into light, medium, and heavy categories on the basis of type of operation. Where the work load is ranked into one of said three categories, i.e.

(1) light work: e.g. sitting or standing to control machines, performing light hand or arm work,

(2) moderate work: e.g., walking about with moderate lifting and pushing,

(3) heavy work: e.g., pick and shovel work,

the permissible heat exposure limit for that work load shall be determined from Table I.

B. The ranking of the job may be performed either by measuring the worker's metabolic rate while performing his job or by estimating his metabolic rate by the use of the scheme shown in Table A. Tables available in the literature listed below and in other publications as well may also be utilized.

1. Per-Olaf Astrand and Kaare Rodahl: "Textbook of Work Physiology" McGraw-Hill Book Company, New York, San Francisco, 1970.

2. "Ergonomics Guide to Assessment of Metabloic and Cardiac Costs of Physical Work." Amer. Ind. Hyg. Assoc. J., 1971 (In Press).

3. Energy Requirements for Physical Work, Purdue Farm Cardiac Project. Agricultural Experiment Station. Research Progress Report No. 30, 1961.

4. J. V. G. A. Durnin and R. Passmore: "Energy, Work and Leisure," Heinemann Educational Books, Ltd., London, 1967.

III. *Work-Rest Regimen*

The permissible exposure limits specified in Table I and Diagram A are based on the assumption that the WBGT value of the resting place is the same or very close to that of the work place. If the resting place is air conditioned and its climate is kept at or below 24° C (75° F.) WBGT, the allowable resting time may be reduced by 25%. The permissible exposure limits for continuous work are applicable where there is a work-rest regimen of a 5 day work week and an 8-hour work day with a short morning and afternoon break (approximately 15 minutes) and a longer lunch break (approximately 30 minutes). Higher exposure limits are permitted if additional resting time is allowed. All breaks, including unscheduled pauses and administrative or operational waiting periods during work may be counted as rest time when additional rest allowance must be given because of high environmental temperatures.

It is a common experience that when the work on a job is self-paced, the workers will spontaneously limit their hourly work load to 30-50% of their maximum physical performance capacity. They do this either by setting an appropriate work speed or by interspersing unscheduled breaks. Thus the daily average of the workers' metabolic rate seldom exceeds 330 kcal/hr. However, within an 8-hour work shift there may be periods where the workers' hourly average metabolic rate will be higher.

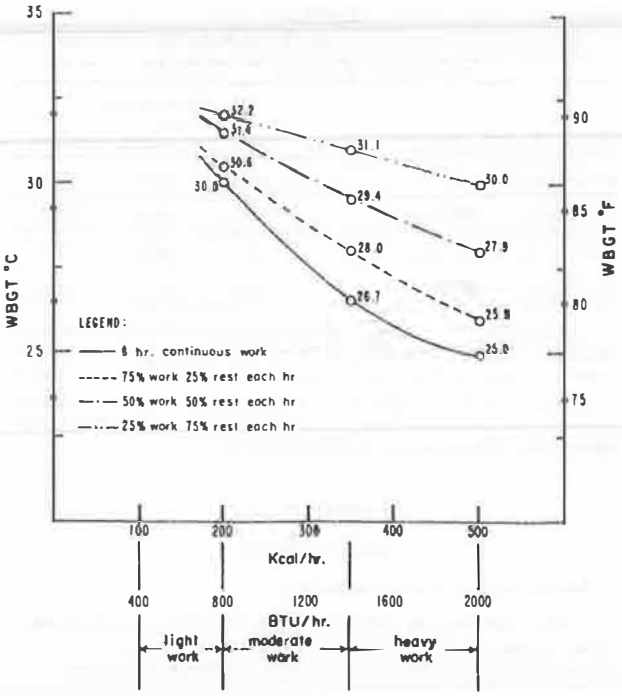

Diagram A — Permissible Heat Exposure Threshold Limit Value.

IV. *Water and Salt Supplementation*

During the hot season or when the worker is exposed to artificially generated heat, drinking water shall be made available to the workers in such a way that they are stimulated to frequently drink small amounts, i.e. one cup every 15-20 minutes (about 150 ml or 1/4 pint).

The water shall be kept reasonably cool (10°-15° C or 50.0°-60.0° F) and shall be placed close to the workplace so that the worker can reach it without abandoning the work area.

The workers should be encouraged to salt their food abundantly during the hot season and particularly during hot spells. If the workers are unacclimatized, salted drinking water shall be made available in a concentration of 0.1% (1g NaCl to 1.0 liter or 1 level tablespoon of salt to 10 quarts of water). The added salt shall be completely dissolved before the water is distributed, and the water shall be kept reasonably cool.

V. *Other Considerations*

A. Clothing: The permissible heat exposure TLVs are valid for light summer clothing as customarily worn by workers when working under hot environmental conditions. If special clothing is required for performing a particular job and this clothing is heavier or it impedes sweat evaporation or has higher insulation value, the worker's heat tolerance is reduced, and the permissible heat exposure limits indicated in Table I and

Diagram A are not applicable. For each job category where special clothing is required, the permissible heat exposure limit shall be established by an expert.

B. Acclimatization and Fitness: The recommended heat stress TLVs are valid for acclimated workers who are physically fit.

RADIATION

See U.S. Department of Commerce National Bureau of Standards, Handbook 59, "Permissible Dose from External Sources of Ionizing Radiation," September 24, 1954, and addendum of April 15, 1958. A report, Basic Radiation Protection Criteria, published by the National Committee on Radiation Protection, revises and modernizes the concept of the NCRP standards of 1954, 1957 and 1958; obtainable as NCRP Rept. No. 39, P.O. Box 4867, Washington, D.C. 20008.

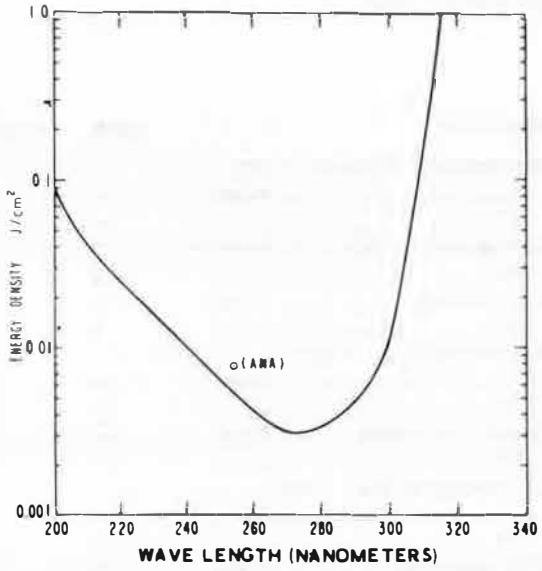

Figure 1 — Proposed Threshold Limit Values for Ultraviolet Radiation.

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1972

changes from 1971

Threshold Limit Values adopted at the Thirty-Fourth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 14-19, 1972, San Francisco, CA.

New Values

Substance	ppm	mg/m^3
Ammonium chloride fume	—	10
Appendix A[1a] and it chemicals		
Camphor (Synthetic)	2	12
Diazinon — skin	—	0.1
2-N-Dibutyaminoethanol — skin	2	14
Diethylene triamine (RV)	1	4
4-Dimethylaminoazobenzene	from	A[1] to A[2]
Iron pentacarbonyl	0.01	0.08
Nickel carbonyl add A[1a] to:	0.001	0.007
4-Nitrodiphenyl	—	A[1a]
Propylene glycolmonomethyl ether	100	360
Rosin core solder, pyrolysis products (as formadehyde)	—	0.1
Vinyl bromide	250	1100
Vinyl chloride (RV)	200	770
Wooddust (non allergenic)	—	5

Mineral Dusts

Christobalite, Crystalline — use one-half the value calculated from the count or mass formulae for quartz.

Quartz

TLV in mppcf:

$$\frac{300^{j)}}{\%\ \text{quartz} + 10}$$

TLV for respirable dust mg/m³:

$$\frac{10\ \text{mg/m}^{3k)}}{\%\ \text{Respirable quartz} + 2}$$

TLV for "total dust" respirable and nonrespirable:

$$\frac{30\ \text{mg/m}^3}{\%\ \text{quartz} + 3}$$

---

j) The percentage of quartz in the formula is the amount determined from airborne samples, except in those instances in which other methods have been shown applicable.

k) Both concentration and percent quartz for the application of this limit are to be determined from the fraction passing a size-selector with the following characteristics:

Aerodynamic Diameter (μm)	% Passing Sector
< 2	90
2.5	75
3.5	50
5.0	25
10	0

Appendix E
Some Nuisance Particulates[q)]

Alundum (Al_2O_3)
Calcium carbonate
Cellulose (paper fiber)
Portland Cement
Corundum (Al_2O_3)
Emery
Glass, fibrous[r)] dust
Glycerine mist
Graphite (synthetic)
Gypsum
Kaolin
Limestone
Magnesite
Marble
Pentaerythritol
Plaster of Paris
Rouge
Silicon Carbide
Starch
Sucrose
Tin oxide
Titantium dioxide
Vegetable oil mists (except castor, cashew nut, or similar irritant oils)

---

q) When toxic impurities are not present, e.g., quartz < 1%.

r) < 5-7 μm in diameter.

Revised Values

In 1971 the ppm and mg/m³ values had been omitted in the adopted listing for those substances which appeared on the Notice of Intended Changes (NIC). In 1972 the adopted values were returned to the alphabetical listing but parentheses were placed around the values for those substances listed in the NIC.

Substance		ppm	mg/m³
2-Acetylaminofluorene — skin	from:	—	A[1]
	TO	—	A[2]
Allyl alcohol — skin	from:	2	5
	TO	2	3*
Allyl chloride	from:	1	3
	TO	1	5*
4-Aminodiphenyl — skin	from:	—	A[1]
	TO	—	A[1b]
Benzidene — skin	from:	—	A[1]
	TO	—	A[1b]
Dichlorobenzidine — skin	from:	—	A[1]
	TO	—	A[1b]
C Formaldehyde	from:	5	6
	TO	2	3
Gasoline	from:	—	A[3]
	TO	—	B[2]
Methyl chloride		Delete: "C"	
β-Naphthylamine	from:	—	A[1]
	TO	—	A[1b]
N-Nitrosodimethylamine (dimethylnitrosoamine) — skin	from:	—	A[1]
	TO	—	A[2]
Oil mist, vapor	from:	—	g)A[3]
	TO	—	g)B[2]
Petroleum distillates (napatha)	from:	—	g)A[3]
	TO	—	g)B[2]
Polytetrafluoroethylene decomposition products	from:	—	A[2]
	TO	—	B[1]
β-Propiolactone	from:	—	A[1]
	TO	—	A[2]
Teflon® decomposition products	from:	—	A[2]
	TO	—	B[1]

Substance	ppm	mg/m³
C Vanadium (V_2O_5 dust)		
..... from:	—	0.5
(V_2O_5 fume) ..... from:	—	0.1
To: Vanadium (V_2O_5), as V		
Dust	—	0.5
C Fume	—	0.05

*Possible typo.
g) According to analytically determined composition.

Appendix E

Appendix D became Appendix E. The following substances are now listed with an E in the alphabetical listing.

Alundum
Calcium carbonate
Cellulose (paper fiber)
Corundum (Al_2O_3)
Emery
Glass fibrous[e] or dust
Glycerin mist
Graphite, synthetic
Gypsum
Kaolin
Limestone
Magnesite
Marble
Pentaerythritol
Plaster of Paris
Rouge
Silicon carbide
Starch
Sucrose
Tin oxide
Titanium dioxide

e) < 5-7 μm in diameter.

Appendix F

Appendix E became Appendix F. The following substances are now listed with a F in the alphabetical listing.

Acetylene Methane
Argon Neon
Ethane Nitrogen
Ethylene Nitrous oxide
Helium Propane
Hydorgen

Threshold Limit Values Airborne Contaminants Committee

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Physical Agents

To Notice of Intended Changes

6943Å Lasers

Eye
Skin

Continuous Wave Lasers

Eye
Skin

New Values

MICROWAVES

These Threshold Limit Values refer to microwave energy in the frequency range of 100 MHz to 100 GHz and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect.

These values should be used as guides in the control of exposure of microwaves and should not be regarded as a fine line between safe and dangerous levels. The values will be reviewed annually by the Committee on Physical Agents for revisions or additions as further information becomes available.

Recommended Values

The Threshold Limit Value for occupational microwave energy exposure where power densities are known and exposure time controlled is as follows:

1. For average power density levels up to but not exceeding 10 milliwatts per square centimeter, total exposure time shall be limited to the 8-hour workday (continuous exposure).

2. For average power density levels from 10 milliwatts per square centimeter up to but not exceeding 25 milliwatts per square centimeter, total exposure time shall be limited to no more than 10 minutes for any 60 minute period during an 8-hour workday (intermittent exposure).

3. For average power density levels in excess of 25 milliwatts per square centimeter, exposure is not permissible (ceiling value).

NOTE: For repetitively pulsed sources the average power density may be calculated by multiplying the peak power density by the duty cycle. The duty cycle is equal to the pulse duration in seconds times the pulse repetition in hertz.

ULTRAVIOLET RADIATION

These threshold limit values refer to ultraviolet radiation in the spectral region between 200 and 400 nm and represent conditions under which it believed that nearly all workers may be repeatedly exposed without adverse effect. These values for exposure of the eye or the skin apply to ultraviolet radiation from arcs, gas, and vapor discharges, and incandescent sources, but do not apply to ultraviolet lasers or solar radiation. These levels should not be used for determining exposure of photosensitive individuals to ultraviolet radiation. These values should be used as guides in the control of exposure to continuous sources where the exposure relation shall not be less than 0.1 sec.

These values should be used as guides in the control of exposure to ultraviolet sources and should not be regarded as a fine line between safe and dangerous levels. The values will be reviewed annually by the Committee on Physical Agents for revisions or additions as further information becomes available.

Recommended Values

The threshold limit value for occupational exposure to ultraviolet radiation incident upon skin or eye where irradiance values are known and exposure time is controlled are as follows:

1. For the near ultraviolet spectral region (320 to 400 mm) total irradiance incident upon the unprotected skin or eye should exceed 1 mw/cm^2 for periods greater than 10^3 seconds (approximately 16 minutes) and for exposure times less than 10^3 seconds should not exceed one J/cm^2.

2. For the actinic ultraviolet spectral region (200-315 mm), radiant exposure incident upon the unprotected skin or eye should not exceed the values given in Table 1 within an 8-hour period.

3. To determine the effective irradiance of a broadband source weighted against the peak of the spectral effectiveness curve (270 nm), the following weighting formula should be used:

$$E_{eff} = \sum E_\lambda S_\lambda \Delta_\lambda$$

where: E_{eff} = effective irradiance relative to a monochromatic source at 270 nm

E_λ = spectral irradiance in W/cm^2/nm

S_λ = relative spectral effectiveness (unitless)

Δ_λ = band width in nanometers

4. Permissible exposure time in seconds for exposure to actinic ultraviolet radiation incident upon the unprotected skin or eye may be computed by dividing 0.003 J/cm by E_{eff} in W/cm^2. The exposure time may also be determined using Table 2 which provides exposure times corresponding to effective irradiances in μW/cm^2.

TABLE 1

Wavelength (nm)	TLV (mJ/cm^2)	Relative Spectral Effectiveness S_λ
200	100	0.03
210	40	0.075
220	25	0.12
230	16	0.19
240	10	0.30
250	7.0	0.43
254	6.0	0.5
260	4.6	0.65
270	3.0	1.0
280	3.4	0.88
290	4.7	0.64
300	10	0.30
305	50	0.06
310	200	0.015
315	1000	0.003

TABLE 2

Duration of Exposure per Day	Effective Irradiance, E_{eff} ($\mu W/cm^2$)
8 hrs	0.1
4 hrs	0.2
2 hrs	0.4
1 hr	0.8
1/2 hr	1.7
15 min	3.3
10 min	5
5 min	10
1 min	50
30 sec	100
10 sec	300
1 sec	3000
0.5 sec	6000
0.1 sec	30000

TLV Committee for Physical Agents:

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Dr. Robert N. Thompson
Thomas K. Wilkinson
Eugene G. Wood
Ronald D. Dobbin

1973

changes from 1972

Threshold Limit Values adopted at the Thirty-Fifth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 20-25, 1973, Boston, MA.

New Values

Substance	ppm	mg/m^3
C Acetic Anhydride	5	20
Anisidine (o,p-isomers) — skin	0.1	0.5
Bismuth telluride	—	10
(Se-doped)	—	5
Butane	500	1200
Carbon dioxide	1973 Revised Documentation	
Demeton® — skin	0.01	0.1
Dichlorvos (DDVP) — skin	0.1	1
Dinitrobenzene (all isomers) — skin	0.15	1
Diquat	—	0.5
Ethylene glycol, particulate	—	10
Ethylene glycol, vapor	100	260
Germanium tetrahydride	0.2	0.6
Hexafluoroacetone	0.1	0.7
Isopropylether	250	1050
Lead, inorganic, fumes and dusts	—	0.15
Mercury (Alkyl compounds) — skin	0.001	0.01
Methyl acrylonitrile — skin	1	3
Methyl bromide — skin	15	60
Nicotine — skin	0.075	0.5
Osmium tetroxide	0.0002	0.002
C Phenylphosphine	0.05	0.25
Phosdrin (Mevinphos®) — skin	0.01	0.1
Propargyl alcohol	1	2
Silicon	—	10
Sulfur tetrafluoride	0.1	0.4
TEPP — skin	0.004	0.05
Toulene	100	375
Trinitrotoluene — skin	0.2	1.5

Revised Values

Substance		ppm	mg/m³
Acetaldehyde	from	200	360
	TO	100	180
C Allyl glycidyl ether	from	10	45
	TO	5	22
Ammonia	from	50	35
	TO	25	18
Copper fume	from	—	0.1
	TO		(1)*
C 1,2-Dibromoethane (ethylene dibromide) — skin	from	25	190
	To	20	145
1,1-Dichloroethane	from	100	400
	TO	200	320
Dichloroethyl ether — skin	from "C"	15	90
	TO	5	30
Diisobutyl ketone	from	50	290
	TO	25	150
2-Ethoxyethanol — skin	from	(200)	(740)
	TO	100	370
Fluorine	from	(0.1)	(0.2)
	TO	1	2
Furfuryl alcohol	from	(50)	(200)
	TO	(5)*	(20)*
Methylcyclohexanol	from	(100)	(470)
	TO	50	235
o-Methylcyclohexanone — skin	from	(100)	(460)
	TO	50	230
Vinyl chloride	from	200	770
	TO	200	510

* Also to the Notice of Intended Changes list.

Placed on Notice of Intended Changes list

Substance

Cadium oxide fume (as Cd)
Copper fume
Furfuryl alcohol
Iron oxide fume
Sodium hydroxide: add "C"

Mineral Dusts

Tridymite — Use one-half the value calculated from formulae for quartz.

Silica, fused — Use quartz formulae.

Coal dust (bitiminous) — 2 mg/m³ (respirable dust[p] fraction < 5% quartz). If > 5%, use respirable mass formulae.

p) "Respirable dust" as defined by the British Medical Research Council Criteria[1] and as sampled by a device producing equivalent results.[2]

1. Hatch, T.E. and P. Gross: *Pulmonary Deposition and Retention of Inhaled Aerosols*, p. 149, Academic Press, New York (1964).

2. AIHA Aerosol Technology Committee: Interim Guide for Respirable Mass Sampling. *AIHA J. 31(2)*:133 (1970).

TLV Airborne Contaminants Committee

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Physical Agents

New Values

HEAT STRESS

According to the Physical Agents Committee report immediately following this section, the heading for Heat Stress in the 1973 TLV booklet should state ADOPTED instead of NOTICE OF INTENT TO ESTABLISH... The heading was merely a reprint of the entire NIC from 1982. The following is the corrected text (as per report) for Heat Stress.

THRESHOLD LIMIT VALUES

HEAT STRESS

These Threshold Limit Values refer to heat stress conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse health effects. The TLVs shown in Table 1 are based on the assumption that nearly all acclimatized, fully clothed workers with adequate water and salt intake should be able to function effectively under the given working conditions without exceeding a deep body temperature of 38° C (WHO technical report series #412, 1969 *Health Factors Involved in Working Under Conditions of Heat Stress).*

Since measurement of deep body temperature is impractical for monitoring the workers' heat load, the measurement of environmental factors is required which most nearly correlate with deep body temperature and other physiological responses to heat. At the present time Wet Bulb-Globe Temperature Index (WBGT) is the simplest and most suitable technique to measure the environmental factors. WBGT values are calculated by the following equations:

1. Outdoors with solar load:
   WBGT = 0.7WB + 0.2GT + 0.1 DB
2. Indoors or Outdoors with no solar load:
   WBGT = 0.7WB + 0.3GT

where:
WBGT = Wet Bulb-Globe Temperature Index
WB = Natural Wet-Bulb Temperature
DB = Dry-Bulb Temperature
GT = Globe Thermometer Temperature

The determination of WBGT requires the use of a black globe thermometer, a natural (static) wet-bulb thermometer, and a dry-bulb thermometer.

TABLE 1
Permissible Heat Exposure Threshold Limit Values
(Values are given in °C. WBGT)

	Work Load		
Work - Rest Regimen	**Light**	**Moderate**	**Heavy**
Continuous work	30.0	26.7	25.0
75% Work — 25% Rest, Each hour	30.6	28.0	25.9
50% Work — 50% Rest, Each hour	31.4	29.4	27.9
25% Work — 75% Rest, Each hour	32.2	31.1	30.0

Higher heat exposures than shown in Table 1 are permissible if the workers have been undergoing medical surveillance and it has been established that they are more tolerant to work in heat than the average worker. Workers should not be permitted to continue their work when their deep body temperature exceeds 38.0° C.

APPENDIX G

HEAT STRESS

I. *Measurement of the Environment*

The instruments required are a dry-bulb, a natural wet-bulb, a globe thermometer, and a stand. The measurement of the environmental factors shall be performed as follows:

A. The range of the dry and the natural wet bulb thermometer shall be −5° C to 50° C with an accuracy of ±0.5° C. The dry bulb thermometer must be shielded from the sun and the other radiant surfaces of the environment without restricting the airflow around the bulb. The wick of the natural wet-bulb thermometer shall be kept wet with distilled water for at least 1/2 hour before the temperature reading is made. It is not enough to immerse the other end of the wick into a reservoir of distilled water and wait until the whole wick becomes wet by capillarity. The wick shall be wetted by direct application of water from a syringe 1/2 hour before each reading. The wick shall extend over the bulb of the thermometer, covering the stem about one additional bulb length. The wick should always be clean and new wicks should be washed before using.

B. One globe thermometer, consisting of a 15 cm. (6-inch) diameter hollow copper sphere, painted on the outside with a matte black finish or equivalent shall be used. The bulb or sensor of a thermometer (range −5° C to 100° C with an accuracy of ±0.5° C) must be fixed in the center of the sphere. The globe thermometer shall be exposed at least 25 minutes before it is read.

C. One stand shall be used to suspend the three thermometers so that they do not restrict free air flow around the bulbs, and the wet-bulb and globe thermometer are not shaded.

D. It is permissible to use any other type of temperature sensor that gives identical reading to a mercury thermometer under the same conditions.

E. The thermometers must be so placed that the readings are representative of the condition where the men work or rest, respectively.

The methodology outlined above is more fully explained in the following publications:

1. "Prevention of Heat Casualties in Marine Corps Recruits, 1955-1960, with Comparative Incidence Rates and Climatic Heat Stresses in other Training Categories," by Captain David Minard, MC, USN, Research Report No. 4 Contract No. MR005.01-0001.01, Naval Medical Research Institute, Bethesda, Maryland, 21 February 1961.

2. "Heat Casualties in the Navy and Marine Corps, 1959-1962, with Appendices on the Field Use of the Wet Bulb-Globe Temperature Index," by Captain David Minard, MC, USN, and R. L. O'Brien, HMC, USN. Research Report No. 7, Contract No. MR005.01-0001.01, Naval Medical Research Institute, Bethesda, Maryland, 12 March 1964.

3. Minard, D.: Prevention of Heat Casualties in Marine Corps Recruits. Military Medicine *126(4)*: 261-272, 1961.

II. *Work Load Categories*

The heat produced by body and the environmental heat together determine the total heat load. Therefore, if work is to be performed under hot environmental conditions, the workload category of each job shall be established and the heat exposure limit pertinent to the work load evaluated against the applicable standard in order to protect the worker from exposure beyond the permissible limit.

A. The work load category may be established by ranking each job into light, medium, and heavy categories on the basis of type of operation, where the work load is ranked into one of said three categories, i.e.

(1) light work: e.g., sitting or standing to control machines, performing light hand or arm work,

(2) moderate work: e.g., walking about with moderate lifting and pushing,

(3) heavy work: e.g., pick and shovel work,

the permissible heat exposure limit for that work load shall be determined from Table 1.

B. The ranking of the job may be performed either by measuring the worker's metabolic rate while performing his job or by estimating his metabolic rate by the use of the scheme shown in Table 2. Tables available in the literature listed below and in other publications as well may also be utilized.

1. Per-Olaf Astrand and Kaare Rodahl: "Textbook of Work Physiology" McGraw-Hill Book Company, New York, San Francisco, 1970.

2. "Ergonomies Guide to Assessment of Metabloic and Cardiac Costs of Physical Work." Amer. Ind. Hyg. Assoc. J. *32*:560, 1971.

3. Energy Requirements for Physical Work, Purdue Farm Cardiac Project. Agricultural Experiment Station. Research Progress Report No. 30, 1961.

4. J. V. G. A. Durnin and R. Passmore: "Energy, Work and Leisure," Heinemann Educational Books, Ltd., London, 1967.

TABLE 2
Assessment of Work Load

Average values of metabolic rate during different activities.

A. Body position and movement	Kcal./min.
Sitting	0.3
Standing	0.6
Walking	2.0-3.0
Walking up hill	add 0.8 per meter (yard) rise

B. Type of Work		Average Kcal./min.	Range Kcal./min.
Hand work			
	light	0.4	0.2-1.2
	heavy	0.9	
Work with one arm			
	light	1.0	0.7-2.5
	heavy	1.8	
Work with both arms			
	light	1.5	1.0-3.5
	heavy	2.5	
Work with body			
	light	3.5	2.5-15.0
	moderate	5.0	
	heavy	7.0	
	very heavy	9.0	

Light hand work: writing, hand knitting

Heavy hand work: typewriting

Heavy work with one arm; hammering in nails (shoemaker, upholsterer)

Light work with two arms: filing metal, planing wood, raking of a garden

Moderate work with the body: cleaning a floor, beating a carpet

Heavy work with the body: railroad track laying, digging, barking trees

Sample Calculation: Using a heavy hand tool on an assembly line

A. Walking along	2.0 Kcal./min.
B. Intermediate value between heavy work with two arms and light work with the body	3.0 Kcal./min.
	5.0 Kcal./min.
C. Add for basal metabolism	1.0 Kcal./min.
Total	6.0 Kcal./min.

Adapted from Lehmann, G.E., A. Muller and H. Spitzer: Der Kalorienbedarf bei gewerblicher Arbeit. Arbeitsphysiol. *14*: 166, 1950.

III. *Work-Rest Regimen*

The permissible exposure limits specified in Table 1 and Figure 1 are based on the assumption that the WBGT value of the resting place is the same or very close to that of the work place. If the resting place is air conditioned and its climate is kept at or below 24°C (75°F.) WBGT, the allowable resting time may be reduced by 25%. The permissible exposure limits for continuous work are applicable where there is a work-rest regimen of a 5-day work week and an 8-hour work day with a short morning and afternoon break (approximately 15 minutes) and a longer lunch break (approximately 30 minutes). Higher exposure limits are permitted if additional resting time is allowed. All breaks, including unscheduled pauses and administrative or operational waiting periods during work may be counted as rest time when additional rest allowance must be given because of high environmental temperatures.

It is a common experience that when the work on a job is self-paced, the workers will spontaneously limit their hourly work load to 30-50% of their maximum physical performance capacity. They do this either by setting an appropriate work speed or by interspersing unscheduled breaks. Thus the daily average of the workers' metabolic rate seldom exceeds 330 kcal/hr. However, within an 8-hour work shift there may be periods where the workers' hourly average metabolic rate will be higher.

IV. *Water and Salt Supplementation*

During the hot season or when the worker is exposed to artificially generated heat, drinking water shall be made available to the workers in such a way that they are stimulated

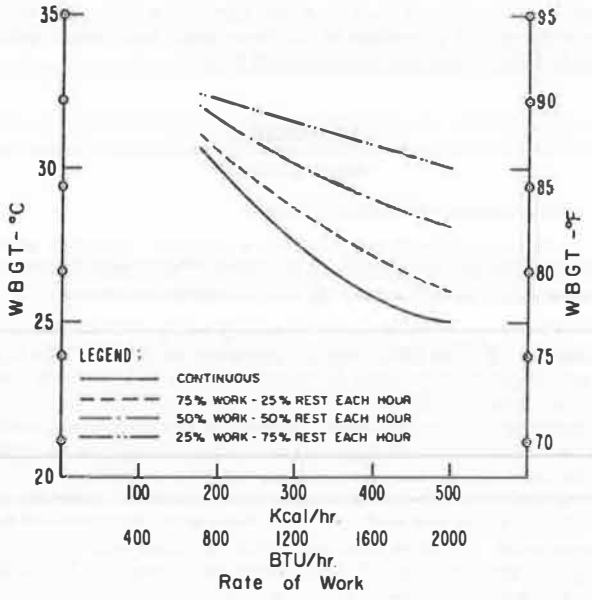

Figure 1 — Permissible Heat Exposure Threshold Limit Value.

to frequently drink small amounts, i.e., one cup every 15-20 minutes (about 150 ml or 1/4 pint).

The water shall be kept reasonably cool (10°-15°C or 50.0°-60.0°F) and shall be placed close to the workplace so that the worker can reach it without abandoning the work area.

The workers should be encouraged to salt their food abundantly during the hot season and particularly during hot spells. If the workers are unacclimatized, salted drinking water shall be made available in a concentration of 0.1% (1g NaCl to 1.0 liter or 1 level tablespoon of salt to 15 quarts of water). The added salt shall be completely dissolved before the water is distributed, and the water shall be kept reasonably cool.

V. *Other Considerations*

A. Clothing: The permissible heat exposure TLVs are valid for light summer clothing as customarily worn by workers when working under hot environmental conditions. If special clothing is required for performing a particular job and this clothing is heavier or it impedes sweat evaporation or has higher insulation value, the worker's heat tolerance is reduced, and the permissible heat exposure limits indicated in Table 1 and Figure 1 are not applicable. For each job category where special clothing is required, the permissible heat exposure limit shall be established by an expert.

B. Acclimatization and Fitness: The recommended heat stress TLVs are valid for acclimated workers who are physically fit.

The following is the corrected text (as per report) for Ultraviolet Radiation.

ULTRAVIOLET RADIATION*

These threshold limit values refer to ultraviolet radiation in the spectral region between 200 and 400 nm and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect. These values for exposure of the eye or the skin apply to ultraviolet radiation from arcs, gas, and vapor discharges, fluorescent, and incandescent sources, but do not apply to ultraviolet lasers* or solar radiation. These levels should not be used for determining exposure of photosensitive individuals to ultraviolet radiation. These values should be used as guides in the control of exposure to continuous sources where the exposure duration shall not be less than 0.1 sec.

These values should be used as guides in the control of exposure to ultraviolet sources and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The threshold limit value for occupational exposure to ultraviolet radiation incident upon skin or eye where irradiance values are known and exposure time is controlled are as follows:

1. For the near ultraviolet spectral region (320 to 400 nm) total irradiance incident upon the unprotected skin or eye should not exceed 1 mw/cm^2 for periods greater than 10^3 seconds (approximately 16 minutes) and for exposure times less than 10^3 seconds should not exceed one J/cm^2.
2. For the actinic ultraviolet spectral region (200 — 315 nm), radiant exposure incident upon the unprotected skin or eye should not exceed the values given in Table 8 within an 8-hour period.
3. To determine the effective irradiance of a broadband source weighted against the peak of the spectral effectiveness curve (270 nm), the following weighting formula should be used:

$$E_{eff} = \sum E_\lambda S_\lambda \Delta_\lambda$$

where:

E_{eff} = effective irradiance relative to a monochromatic source at 270 nm

E_λ = spectral irradiance in W/cm^2/nm

S_λ = relative spectral effectiveness (unitless)

Δ_λ = band width in nanometers

4. Permissible exposure time in seconds for exposure to actinic ultraviolet radiation incident upon the unprotected skin or eye may be computed by dividing 0.003 J/cm^2 by E_{eff} in W/cm^2. The exposure time may also be determined using Table 9 which provides exposure times corresponding to effective irradiances in μW/cm^2.

TABLE 8
Relative Spectral Effectiveness by Wavelength

Wavelength (nm)	TLV (mJ/cm^2)	Relative Spectral Effectiveness S_λ
200	100	0.03
210	40	0.075
220	25	0.12
230	16	0.19
240	10	0.30
250	7.0	0.43
254	6.0	0.5
260	4.6	0.65
270	3.0	1.0
280	3.4	0.88
290	4.7	0.64
300	10	0.30
305	50	0.06
310	200	0.015
315	1000	0.003

*See Laser TLVs.

*Mumford, W.W., "Heat Stress Due to R.F. Radiation, "Proceedings of IEEE, Vol. 57, No. 2, Feb. 1969, pp. 171-178.

TABLE 9
Permissible Ultraviolet Exposures

Duration of Exposure Per Day	Effective Irradiance E_{eff} ($\mu W/cm^2$)
8 hrs	0.1
4 hrs	0.2
2 hrs	0.4
1 hr	0.8
30 min	1.7
15 min	3.3
10 min	5
5 min	10
1 min	50
30 sec	100
10 sec	300
1 sec	3,000
0.5 sec	6,000
0.1 sec	30,000

All the preceding TLVs for ultraviolet energy apply to sources which subtend an angle less than 80°. Sources which subtend a greater angle need to be measured only an angle of 80°.

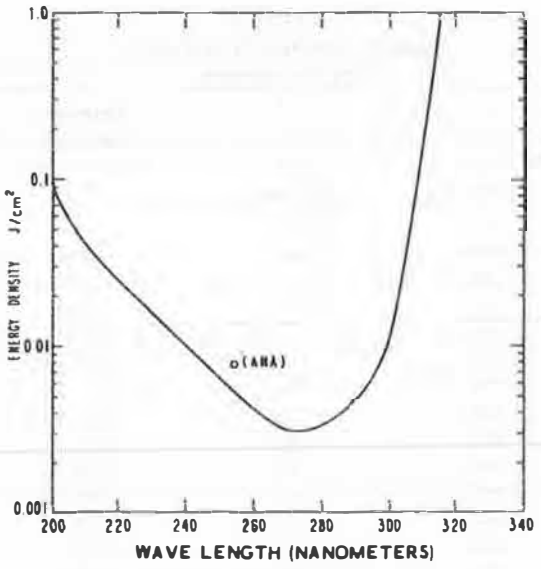

Figure 7 — Threshold Limit Values for Ultraviolet Radiation.

Revised Values
LASERS

The threshold limit values are for exposure to laser radiation under conditions to which nearly all workers may be exposed without adverse effects. The values should be used as guides in the control of exposures and should not be regarded as fine lines between safe and dangerous levels. They are based on the best available information from experimental studies.

Limiting Apertures

The TLVs expressed as radiant exposure or irradiance in this section may be averaged over an aperture of 1 mm except for TLVs for the eye in the spectral range of 400-1400 nm, which should be averaged over a 7 mm limiting aperture (pupil). No modification of the TLVs is permitted for pupil sizes less than 7 mm.

The TLVs for "extended sources" apply to sources which subtend an angle greater than τ (Table 5) which varies with exposure time. This angle is *not* the beam divergence of the source.

Correction Factors A (CFA) for Eye Exposure

All TLVs in Tables 3 and 4 are to be used as given for wavelengths 400 nm to 700 nm. At all wavelengths greater than 1.06 μm and less than 1.4 μm the TLVs are to be increased by a factor of 5. TLV at wavelengths between 700 nm and 1.06 μm are to be increased by a uniformly extrapolated factor as shown in Figure 2.

Repetitively Pulsed Lasers

Since there are few experimental data for multiple pulses, caution must be used in the evaluation of such exposures. The protection standards for irradiance or radiant exposure in multiple pulse trains have the following limitations:

(1) The exposure from any single pulse in the train is limited to the protection standard for a single comparable pulse.

(2) The average irradiance for a group of pulses is limited to the protection standard as given in Tables 3, 4, or 6 of a single pulse of the same duration as the entire pulse group.

(3) When the Instantaneous Pulse Repetition Frequency (PRF) of any pulses within a train exceeds one, the protection standard applicable to each pulse is reduced as shown in Figure 6 for pulse durations less than 10^{-5} second. For pulses of greater duration, the following formula should be followed:

$$\text{Standard}\left(\begin{matrix}\text{single pulse}\\ \text{in train}\end{matrix}\right) = \frac{\text{Standard (pulse } n\tau)}{n}$$

where:

n = number of pulses in train

τ = duration of a single pulse in the train

Standard ($n\tau$) = protection standard of one pulse having a duration equal to $n\tau$ seconds.

TABLE 3
Threshold Limit Value for Direct Ocular Exposures (Intrabeam Viewing) from a Laser Beam

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
UVC	200 nm to 280 nm	10^{-3} to 3×10^{4}	3 mJ • cm^{-2}
UVB	280 nm to 302 nm	"	3 "
	303 nm	"	4 "
	304 nm	"	6 "
	305 nm	"	10 "
	306 nm	"	16 "
	307 nm	"	25 "
	308 nm	"	40 "
	309 nm	"	63 "
	310 nm	"	100 "
	311 nm	"	160 "
	312 nm	"	250 "
	313 nm	"	400 "
	314 nm	"	630 "
	315 nm	"	1.0 J • cm^{-2}
UVA	315 nm to 400 nm	10 to 10^{3}	1.0 J • cm^{-2}
	" "	10^{3} to 3×10^{4}	1.0 mW • cm^{-2}
Light	400 nm to 700 nm	10^{-9} to 1.8×10^{-5}	5×10^{-7} J• cm^{-2}
	400 nm to 700nm	1.8×10^{-5} to 10	$(1.8\ t/\sqrt{t})$ mJ • cm^{-2}
	400 nm to 700 nm	10 to 10^{4}	10 mJ • cm^{-2}
	400 nm to 700 nm	10^{4} to 3×10^{4}	10^{-6} W • cm^{-2}
Infrared A	700 nm to 1.06 μm	10^{-9} to 10^{2}	[light TLV's] × [CFA]
"	1.06 μm to 1.40 μm	10^{-9} to 10^{2}	(light TLV) × 5
	700 nm to 1.06 μm	10^{2} to 3×10^{4}	10^{-4} [CFA] W • cm^{-2}
	1.06 μm to 1.4 μm	" "	5×10^{-4} W • cm^{2}
Infrared B & C	1.4 μm to 10^{3} μm	10^{-9} to 10^{-7}	10^{-2} J • cm^{-2}
	" "	10^{-7} to 10	$0.56\sqrt[4]{t}$ J • cm^{-2}
	" "	10 to 3×10^{4}	0.1 W • cm^{-2}

NOTE: To aid in the determination of TLV's for exposure durations requiring calculations of fractional powers Figures 3, 4 and 6 may be used.

TABLE 4
Threshold Limit Values for Viewing a Diffuse Reflection of a Laser Beam or an Extended Source Laser

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
UV	200 nm to 400 nm	10^{-3} to 3×10^{4}	Same as Table 3
Light	400 nm to 700 nm	10^{-9} to 10	$10\sqrt[3]{t}$ J • cm^{-2} • sr^{-1}
	400 nm to 700 nm	10 to 10^{4}	20 J • cm^{-2} • sr^{-1}
	400 nm to 700 nm	10^{4} to 3×10^{4}	2×10^{-3} W • cm^{-2} • sr^{-1}
Infrared A	700 nm to 1.06 μm	10^{-7} to 10	CFA × $10\sqrt[3]{t}$ J • cm^{-2} • sr^{-1}
	" "	10 to 10^{2}	CFA × 20 J • cm^{-2} • sr^{-1}
	" "	10^{2} to 3×10^{4}	CFA × W • cm^{-2} • sr^{-1}
	1.06 μm to 1.4 μm	10^{-9} to 10	$50 \times \sqrt[3]{t}$ J • cm^{-2} • sr^{-1}
	" "	10 to 10^{2}	10 J • cm^{-2} • sr^{-1}
	" "	10^{2} to 3×10^{4}	1.0 W • cm^{-2} • sr^{-1}
Infrared B & C	1.4 μm to 1 mm	10^{-9} to 3×10^{4}	Same as Table 3

NOTE: To aid in the determination of TLV's for exposure durations requiring calculations of fractional powers Figures 3, 4 and 6 may be used.

TABLE 5
Limiting Angle to Extended Source Which May Be Used for Applying Extended Source TLVs

Exposure Duration(s)	Angle × (mrad)
10^{-9}	8.0
10^{-8}	5.4
10^{-7}	3.7
10^{-6}	2.5
10^{-5}	1.7
10^{-4}	2.2
10^{-3}	3.6
10^{-2}	5.7
10^{-1}	9.2
1.0	15
10	24
10^{2}	24
10^{3}	24
10^{4}	24

TABLE 6
Threshold Limit Value for Skin Exposure from a Laser Beam

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
UV	200 nm to 400 nm	10^{-3} to 3×10^{4}	Same as Table 3
Light &	400 nm to 1400 nm	10^{-9} to 10^{-7}	2×10^{-2} J • cm^{-2}
Infrared A	" "	10^{-7} to 10	1.1 $\sqrt[4]{t}$ J • cm^{-2}
	" "	10 to 3×10^{4}	0.2 W • cm^{-2}
Infrared B & C	1.4 μm to 1 mm	10^{-9} to 3×10^{4}	Same as Table 3

NOTE: To aid in the determination of TLV's for exposure durations requiring calculations of fractional powers Figures 3, 4, and 6 may be used.

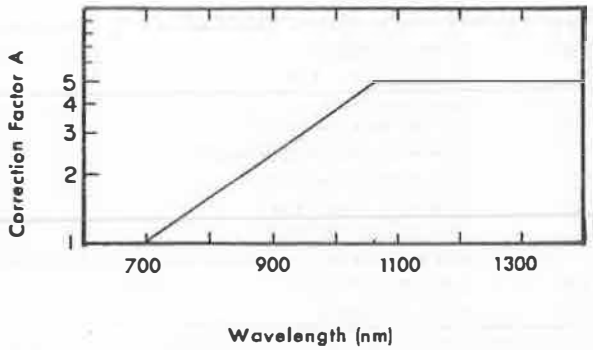

Figure 2 — TLV correction factors for laser wavelengths (eye).

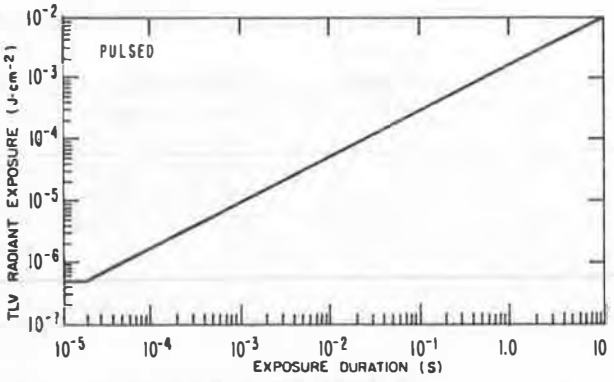

Figure 3a — TLV for intrabeam (direct) viewing of laser beam (400-700 nm).

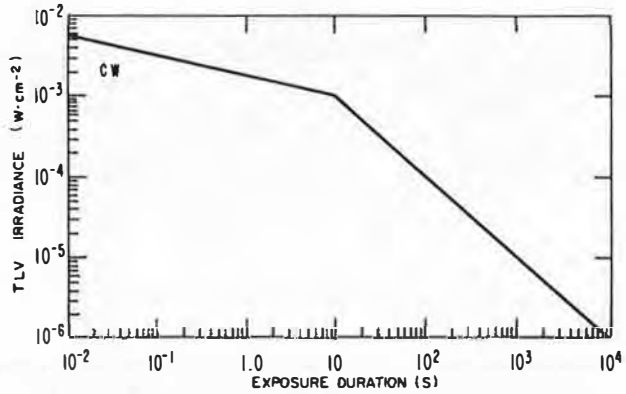

Figure 3b — TLV for intrabeam (direct) viewing of CW laser beam (400-700 nm).

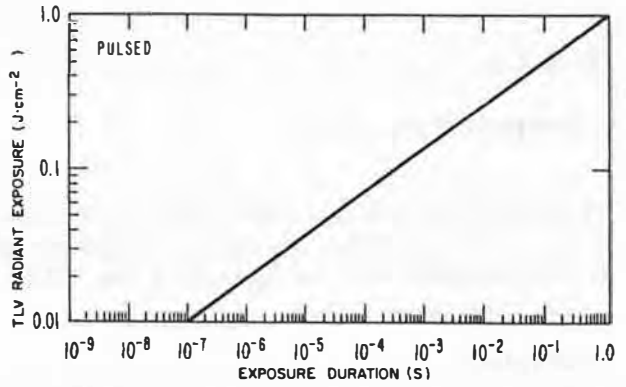

Figure 4a — TLV for laser exposure of skin and eyes for far-infrared radiation (wavelengths greater than 1.4 μm).

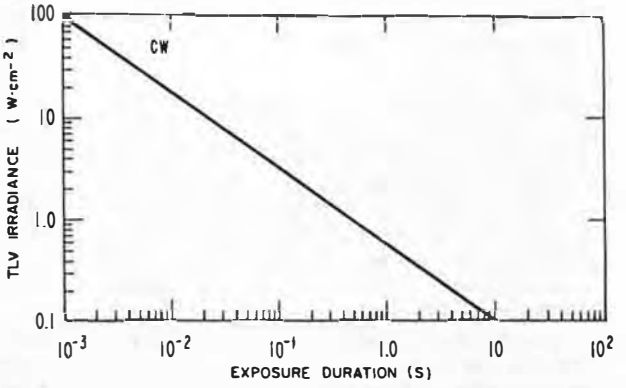

Figure 4b — TLV for CW laser exposure of skin and eyes for far-infrared radiation (wavelengths greater than 1.4 μm).

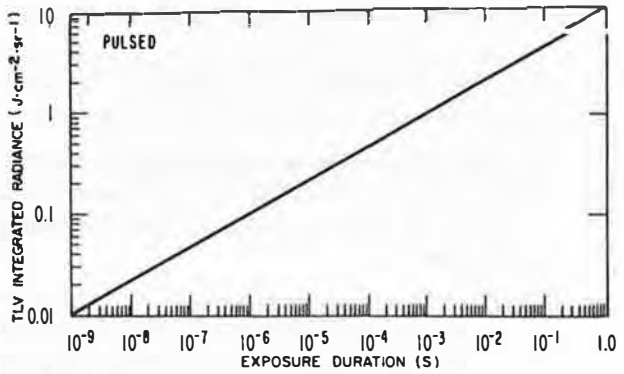

Figure 5a — TLV for extended sources or diffuse reflections of laser radiation (400-700 nm).

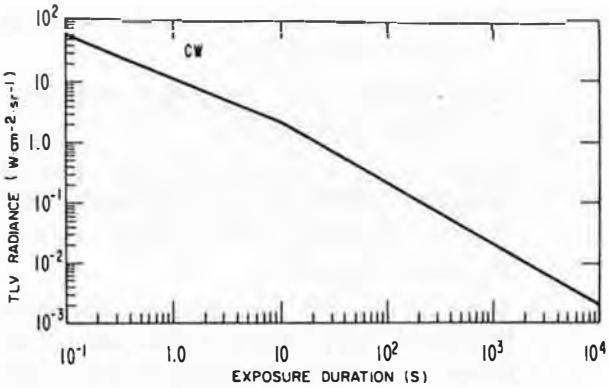

Figure 5b — TLV for extended sources or diffused reflections of laser radiation (400-700 nm), cw.

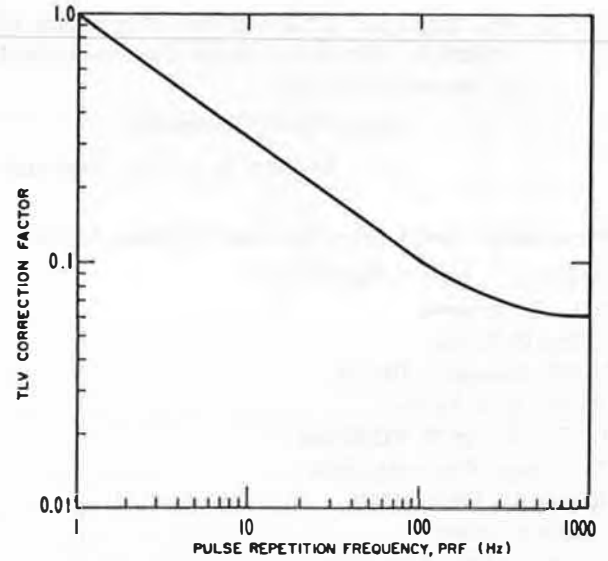

Figure 6 — Multiplicative correction factor for repetitively pulsed lasers having pulse durations less than 10^{-5} second. TLV for a single pulse of the pulse train is multiplied by the above correction factor for PRF greater than 1000 H_z is 0.06.

Report of Committee on Physical Agents

1. Recommend the adoption of the heat stress threshold limit values which were published as a notice of intent in 1972.
2. Recommend the adoption of the UV threshold limit values which were published as a notice of intent in 1972 with the following changes:
   (1) Define acceptance angle as follows — All the preceding TLVs for ultraviolet energy apply to sources which subtend an angle less than 80°. Sources which subtend a greater angle need to be measured only over an angle of 80°.
   (2) Add "fluorescent" to list of sources in the first paragraph.
   (3) Add footnote to "excursion of lasers," to say "see laser TLV."
3. Recommend the adoption of a notice of intent to change the UV threshold limit values by dropping "Solar radiation" from the first paragraph.
4. Recommend the adoption of the laser threshold limit values which were published as a notice of intent in 1972 with minor changes in some tables in order to be consistent with the ANSI Z-136 Laser Safety Standard.
5. Recommend the adoption of a notice of *intent to change the Noise* threshold limit values as in Table I.

Respectfully submitted,

/s/ Herbert H. Jones, Chairman

Threshold Limit Committee for Physical Agents

Herbert H. Jones, *Chairman*
Peter A. Breysse
Irving H. Davis
LCDR Joseph J. Drozd
Dr. David A. Fraser
Lt. Col. Owen H. Kittilstad
Dr. Ernest Mastromatteo
William A. Palmisano
David H. Sliney
Dr. Robert N. Thompson
Thomas K. Wilkinson
Eugene G. Wood
Ronald D. Dobbin

TABLE I
Threshold Limit Values

Duration per Day Hours	Sound level[a] dBA
16	80
8	85
4	90
2	95
1	100
1/2	105
1/4	110
1/8	115*

* No exposure to continuous or intermittent in excess of 115 dBA

[a] Sound level in decibles as measured on a sound level meter, conforming as a minimum to the requirements of the American National Standard Specification for Sound Level Meters, S1.4 (1971) Type S2A, operating the A-weighted network slow meter response.

1974

changes from 1973

Threshold Limit Values Adopted at the Thirty-Sixth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 12-17, 1974, Miami Beach, FL.

New Values

Substance	ppm	mg/m^3
Bagon (Propaxur)	—	0.5
C Cadmium oxide fume (as Cd)	—	0.5
Caprolactam		
Dust	—	1
Vapor	5	20
bis-Chloromethyl ether	0.001	A[1a]
o-Chlorotoluene	50	250
Cyclohexylamine — skin	10	40
Disyston — skin	—	0.1
C Ethylidene norborene	5	25
Furfuryl alcohol	5	20
Hexachlorocyclopentadiene	0.1	0.11
Manganese cyclopentadienyl tricarbonyl (as Mn) — skin	—	0.1
C Methyl ethyl ketone peroxide	0.2	1.5
4,4'-Methylene bis(2-chloraniline) — skin	0.02	A[2]
C Methylene bis(4-cyclohexylisocyanate)	~~0.1~~	0.11
Paraffin wax fume	—	0.2
Phorate (Thimet®) — skin	—	0.05
C Potassium hydroxide	—	2
Propyl alcohol	*Add:* skin notation	

Substance	ppm	mg/m³
Silane (see Silicon tetrahydride)	0.5	0.7
Zinc stearate	—	E
Mineral Dusts		
Silicates (< 1% quartz)		
Asbestos	5 fibers/cc 5 μ in length;[n]	A[1a]
Mineral wool fiber		10 mg/m³
Tripoli	Use respirable mass quartz formula.	

n) As determined by the membrane filter method at 400-450X magnification (4mm objective) phase contrast illumination.

Revised Values

Substance		ppm	mg/m³
Allyl alcohol	from	2	3
	TO	2	5
Allyl chloride	from	1	5
	TO	1	3
Chloroform (trichloromethane)	from	(50)	(240)
	TO	25	120
Chromium metal and insoluble salts	from	A[1a]	(1)
	TO: Chromates, certain insoluble forms	—	A[1a]
Cotton dust (raw)	from	—	(1)
	TO	—	0.2[m]
Dioxane (Diethylene dioxide) — skin	from	(100)	(360)
	TO	50	180
Silicon	from	—	10
	TO	—	E
Toluene-2,4-diisocyanate	from	0.02	0.14
	TO	0.02	0.12

m) Lint free dust as measured by the vertical elutriator, cotton-dust sampler described in the *Transactions of the National Conference on Cotton Dust*, J.R. Lynch, p. 33, May 2, 1970.

Placed on Notice of Intended Changes list

Arsenic, inorganic compounds (as As)
Benzene
Butane
n-Butane
Cadmium (metal dust and soluble salts)
Heptane
Hexane
Isobutyl alcohol
Methylcyclohexane
Nickel, soluble compounds (as Ni)
Octane
Pentane
Phosgene (carbonyl chloride)
Stoddard solvent
Vinyl chloride

Deletions

2-Acetylaminofluorene — skin
4-Dimethylaminoazobenzene
Nitrogen — from Appendix F and alphabetical listing

TLV Committee for Airborne Contaminants:

Herbert E. Stokinger, Ph.D., *Chairman*
Hector P. Blejer, M.D., DIH
Paul E. Caplan, P.E., MPH
Hervey B. Elkins, Ph.D.
W. G. Fredrick, Sc.D.
Bernard Grabois, P.E.
Paul Gross, M.D.
John W. Knauber, MPH
Jesse Lieberman, P.E.
Keith R. Long, M.D.
Frederick T. McDermott, P.E.
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Keith R. Long, M.D.
Frederick T. McDermott, P.E.
E. Mastromatteo, M.D.,
Col. Walter W. Melvin, Jr., M.D.
Lt. Col. Marshall Steinberg, Ph.D.
William D. Wagner, *Recording Secretary*
Ralph C. Wands, M.S.

Liaison Members

David A. Padden, Labor Union
James F. Morgan, Industry
Theodore R. Torkelson, Sc.D., Alternate
Mitchell R. Zavon, Industry

Report of Committee on Physical Agents

The Committee published *A Guide for Control of Laser Harards* and this is available from the Secretary-Treasurer's office and will sell for $2.75.

The membership adopted the following recommendations for changes in TLV:

1. Extend the coverage of the UV-TLV to include solar radiation as given in the Notice of Intended Changes (1973).

2. Insert the following statement in the UV-TLV,

   "Conditioned (tanned) individuals can tolerate skin exposure in excess of the TLV without erythmeter effects. However, suc higher levels may not protect persons against skin cancer."

3. Add the following paragraph to the noise TLV,

   "It should be recognized that the application of the TLV for noise will not protect all workers from the adverse effects of noise exposure. A hearing conservation program with audiometric testing is necessary when workers are exposed in excess of the TLV."

TLV Committee for Physical Agents:

Herbert H. Jones, *Chairman*
Peter A. Breysse
Tom Cummins
Irving H. Davis
LCDR Joseph J. Drozd
Dr. David A. Fraser
Maj. George S. Kush
Dr. Wordie H. Parr
David H. Sliney
Dr. Robert N. Thompson
Thomas K. Wilkinson
Eugene G. Wood
Ronald D. Dobbin
Lt. Col. Robert T. Wangemann

1975

changes from 1974

Threshold Limit Values Adopted at the Thirty-Seventh Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 31 - June 6, 1975, Minneapolis, MN.

New Values

Substance	ppm	mg/m^3
Asbestos (all forms)	—	A[1a]
Biphenyl	0.2	1
Carbon tetrabromide	0.1	1.4
Cesium hydroxide	—	2
Chlorodifluoromethane	1000	3500
Chlorpyrifos (Dorsban®) — skin	—	0.2
o-Chlorostyrene	50	285
2-Chloro-6-(trichloromethyl) pyridine (N-Serve®)	—	10
Clopidol (Coyden®)	—	10
Copper fume	—	0.2
Crufomate (Ruelene®)	—	50
Cyanogen	—	20
Dicyclopentadienyl iron	—	10
Diethylphthalate	—	5
3,5-Dinitro-o-toluamide (Zoalene®)	—	5
2,6-Ditert-butyl-p-cresol	—	10
Formamide	20	30
Iron oxide fume	B[4]	5
Picloram (Tordon®)	—	10
C Sodium hydroxide	—	2
C Subtilisins (Proteolytic enzymes as 100% pure crystalline enzymes)	—	0.00006[o]
Tricyclohexyltin hydroxide (Plictran®)	—	5
Vinylidene chloride	10	40

o) Based on "high volume" sampling.

Revised Values

Substance	ppm	mg/m^3
Coal tar pitch volatiles — change to: Particulate polycyclic organic matter (PPOM) as benzene solubles	—	0.2
1,1-Dichloroethane from	200	320
TO	200	820*
Nicotine from	0.075	0.5
TO	—	0.5
4-Nitrodiphenyl from	—	A[1a]
TO	—	A[1b]
Paraffin wax fume from	—	0.2
TO	—	2

* Typo made in 1973 corrected.

Mineral Dusts

Tripoli — Use respirable[p] mass quartz formula

p) "Respirable dust" as defined by the British Medical Research Council Criteria[1] and as sampled by a device producing equivalent results.[2]

1. Hatch, T.F. and P. Gross: *Pulmonary Deposition and Retention of Inhaled Aerosols*, p. 149. Academic Press, New York (1964).
2. AIHA Aerosol Technology Committee: Interim Guide for Respirable Mass Sampling. *AIHA J. 31(2)*:133 (1970).

Placed on Notice of Intended Changes list

Antimony and compounds (as Sb)
Cobalt, metal, fume and dust
Ethylene chlorohydrin
2-Hexanone (Methybutyl ketone)
Hydrazine
Nickel carbonyl
Phthalic anhydride

Deletions

Coal tar (Naptha)
Nickel soluble compounds (as Ni)

TLV Committee for Airborne Contaminants:

Herbert E. Stokinger, Ph.D., *Chairman*
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Paul E. Caplan, P.E., MPH
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Meier Schneider, P.E., CIH
Lt. Col. Marshall Steinberg, Ph.D.
Gordon J. Stopps
John F. Summersett
William D. Wagner, *Recording Secretary*
Ralph C. Wands, M.S.

Consultants

James F. Morgan
Theodore R. Torkelson, Sc.D.
Mitchell R. Zavon, M.D.

Report of Threshold Limit Values Committee on Physical Agents

New Values

No new values were adopted in 1975.

Notice of Intended Changes

These physical agents, with their corresponding values, comprise those for which either a limit has been proposed for the first time, or for which a change in the "adopted" listing has been proposed. In both cases, the proposed limits should be considered trial limits that will remain in the listing for a period of at least one year. If, after one year, no evidence comes to light that questions the appropriateness of the values herein, the values will be reconsidered for the "adopted" list.

Notice of Intent to establish threshold limit values

LIGHT

These Threshold Limit Values refer to visible radiation in the wavelength range of 400 nm to 700 nm and represent conditions under which it is believed that nearly all workers may be exposed without adverse effect.

These values should be used as guides in the control of exposure to light and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The Threshold Limit Value for occupational exposure to light where luminances are known and exposure durations exceeding 10 seconds in any eight-hour workday is as follows:

1. The average luminance of objects continuously viewed shall not exceed 1 candela cm^{-2}.

This TLV is not to be used for short exposure durations or pulsed light sources.

NOISE

These Threshold Limit Values refer to sound pressure levels and durations of exposure that represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect on their ability to hear and understand normal speech. The medical profession has defined hearing impairment as an average hearing threshold level in excess of 25 decibels (ANSI-S3.6-1969) at 500, 1000, and 2000 Hz, and the limits which are given have been established to prevent a hearing loss in excess of this level. The values should be used as guides in the control of noise exposure and, due to individual susceptibility, should not be regarded as fine lines between safe and dangerous levels.

Impulsive or Impact Noise

It is recommended that exposure to impulsive or impact noise should not exceed those listed in Table II. Impulsive or impact noise is considered to be those variations in noise levels that involve

maxima at intervals of greater than one per second. Where the intervals are less than one second, it should be considered continuous.

TABLE II
Threshold limit values impulsive or impact noise

Sound Level dB*	Number of Impulses or Impacts per day
140	100
130	1000
120	10,000

* Decibels peak sound pressure level

Notice of intent to change TLV for

LASERS

TLVs for Lasers would be changed for ocular exposure to visible and IR-A laser radiation for durations greater than 10s. Also to be changed would be TLVs for skin exposure to IR-A laser radiation. All other laser TLVs would remain unchanged. The sections of Tables 3, 4, and 6 that would have changes are as follows:

TABLE 3
Threshold Limit Value for Direct Ocular Exposures (Intrabeam Viewing) from a Laser Beam

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
Light	400 nm to 700 nm	10^{-9} to 1.8×10^{-5}	5×10^{-7} J • cm^{-2}
	400 nm to 700nm	1.8×10^{-5} to 10	$1.8\ (t/\sqrt[4]{t})$ mJ • cm^{-2}
	400 nm to 549 nm	10 to 10^{4}	10 mJ • cm^{-2}
	550 nm to 700 nm	10 to T_1	$1.8\ (t/\sqrt[4]{t})$ mJ • cm^{-2}
	550 nm to 700 nm	T_1 to 10^{4}	$10\ C_B$ mJ • cm^{-2}
	400 nm to 700 nm	10^{4} to 3×10^{4}	$C_B\ \mu$W • cm^{-2}
IR-A	700 nm to 1059 nm	10^{-9} to 1.8×10^{-5}	$5\ C_A \times 10^{-7}$ J • cm^{-2}
	700 nm to 1059 nm	1.8×10^{-5} to 10^{3}	$1.8\ C_A\ (t/\sqrt[4]{t})$ mJ • cm^{-2}
	1060 nm to 1400 nm	10^{-9} to 10^{-4}	5×10^{-6} J • cm^{-2}
	1060 nm to 1400 nm	10^{-4} to 10^{3}	$9(t/\sqrt[4]{t})$ mJ • cm^{-2}
	700 nm to 1400 nm	10^{3} to 3×10^{4}	$320\ C_A\ \mu$W • cm^{-2}

C_A — See Fig. 2, Laser TLV listing.
$C_B = 1$ for λ = 400 to 550 nm; $C_B = 10^{[0.015\ (\lambda\ -\ 550)]}$ for λ = 550 to 700 nm.
$T_1 = 10$ s for λ = 400 to 550 nm; $T_1 = 10 \times 10^{[0.02\ (\lambda\ -\ 550)]}$ for λ = 550 to 700 n.

TABLE 4
Threshold Limit Values for Viewing a Diffuse Reflection of a Laser Beam or an Extended Source Laser

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
Light	400 nm to 700 nm	10^{-9} to 10	$10\sqrt[3]{t}$ J • cm^{-2} • sr^{-1}
	400 nm to 549 nm	10 to 10^{4}	21 J • cm^{-2} • sr^{-1}
	550 nm to 700 nm	10 to T_1	$3.83\ (t/\sqrt[4]{t})$ J • cm^{-2} • sr^{-1}
	550 nm to 700 nm	T_1 to 10^{4}	$21/C_B$ J • cm^{-2} • sr^{-1}
	400 nm to 700 nm	10^{4} to 3×10^{4}	$2.1/C_B \times 10^{-3}$ W • cm^{-2} • sr^{-1}
IR-A	700 nm to 1400 nm	10^{-9} to 10	$10\ C_A\sqrt[3]{t}$ J • cm^{-2} • sr^{-1}
	700 nm to 1400 nm	10 to 10^{3}	$3.83\ C_A\ (t/\sqrt[4]{t})$ J • cm^{-2} • sr^{-1}
	700 nm to 1400 nm	10^{3} to 3×10^{4}	$0.64\ C_A$ W • cm^{-2} • sr^{-1}

C_A, C_B and T_1 are the same as in footnote to Table 3.

TABLE 6
Threshold Limit Value for Skin Exposure from a Laser Beam

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
Light & IR-A	400 nm to 1400 nm	10^{-9} to 10^{-7}	$2\ C_A \times 10^{-2}\ J \bullet cm^{-2}$
	" "	10^{-7} to 10	$1.1\ C_A \sqrt[4]{t}\ J \bullet cm^{-2}$
	" "	10 to 3×10^4	$0.2\ C_A\ W \bullet cm^{-2}$

C_A = 1.0 for λ = 400-700 nm; see Figure 2 Laser TLV list for greater wavelength values.

Notice of intent to study

These agents comprise those which the Physical Agents Committee of ACGIH proposes to study during this year to determine the feasibility of establishing proposed TLVs in 1976. Comments and suggestions, accompanied by substantitive evidence, are solicited.

Radiofrequency Radiation. Specifically, that of the spectrum from 10 MHz to 100 MHz.

Ultrasonic Energy. Specifically, accoustic energy at frequencies above 10 kHz.

Magnetic Fields. Both pulsed and continuous.

Microwave Radiation. Specifically from 100 GHz to 300 GHz.

Laser Radiation. Specifically ultraviolet radiation for pulsed exposure, and repetitively pulsed Light and IR-A laser exposures.

TLV Committee for Physical Agents:

Herbert H. Jones, *Chairman*
Peter A. Breysse
Tom Cummins
Irving H. Davis
LCDR Joseph J. Drozd
Dr. David A. Fraser
Maj. George S. Kush
Dr. Wordie H. Parr
David H. Sliney
Dr. Robert N. Thompson
Thomas K. Wilkinson
Eugene G. Wood
Ronald D. Dobbin
Lt. Col. Robert T. Wangemann

1976

changes from 1975

Threshold Limit Values adopted at the Thrity-Eighth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 17-21, 1976, Atlanta, GA.

EDITOR'S NOTE: The first STEL list was published in 1976. These tentative values were placed next to adopted values, however no STEL values were given for those substances on the Notice of Intended Change list. The 1976 booklet also listed the TWA and STEL values with each synonium. Because of the extensive change in the booklet for 1976, the full text is included following the highlights listed below.

New Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Bromochloromethane	200	1050		
Calcium cyanamide	—	0.5	—	1
Captan	—	5	—	15
Carbofuran (Furodan)	—	0.1	0.1	
2-Chloroethanol (Ethylene chlorohydrin)	1	3	1	3
Chloroethylene	A[1c]	—	A[1c]	—
DDVP, (Dichlorvos)	0.1	1	0.3	3
1,2-Diaminoethane, see Ethylenediamine	10	25	10	25
Dichloromethane, see Methylene chloride	200	720	200*	720*
1,2-Dichloropropane, see Propylene dichloride	75	350	110	525

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Dicyclopentadiene	5	30	3	30
Diethylene triamine	—	1	—	4
Disulfuram	—	2	—	5
Dyfonate	—	0.1	—	0.1
Ethion (Nialate®) — TO skin	—	0.4	—	0.4
Fensulfothion (Dasanit)	—	0.1	—	0.1
Hydrogenated terphenyls	0.5	5	0.5	5
Iodoform	0.2	3	0.4	0.6
Nickel, soluble compounds (as Ni)	—	0.1	—	0.3
Nonane	200	1050	250	1300
Pentane	600	1800	750	2250
Resorcinol	10	45	20	90
C Sodium azide	0.1	0.3	—	—
4,4-Thiobis (6-tert. butyl-m-cresol)	—	10	—	20
Welding fumes	—	5,B4	—	5,B4
C m-Xylene α,α′-diamine	—	0.1	—	—

* Note STEL differ between synonyms.

Revised Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Butane from	(500)	(1200)		
TO	600	1400	750	1610
n-Butyl alcohol — skin from	(100)	(300)		
TO "C"	50	150		
n-Butyl lactate	5	25	5	25
Cadmium, dusts and salts (as Cd) from	—	0.05		
TO	—	0.15	—	—
Chlorobromomethane TO: Bromochloromethane	200	1050	250	1300
Coal tar pitch volatiles from	—	—		
TO	—	A[1a]	—	A[1a]
Crufomate from	—	50		
TO	—	5	—	—
Dichlorobenzidine from	A[1b]	—		
TO	A[2]	—	—	—
C Ethylene chlorohydrin — skin from	(5)	(16)		
TO "C"	1	3	—	—
Ethylidene chloride, see 1,1-Dichloroethane from	200	320*		
TO	200	820*	250	400**
Heptane (n-Heptane) from	(500)	(2000)		
TO	400	1600	500	2000
Hexane (n-Hexane) from	(500)	(1800)		
TO	100	360	125	450
2-Hexanone, see Methyl butyl ketone — skin from	(100)	(410)		
TO	25	100	40	150
Isobutyl alcohol	(100)	(300)		
TO	50	150	75	225
Isophorone from	(10)	(50)		
TO "C"	5	25	—	—
Methyl butyl ketone, see 2-Hexanone from	—	—		
TO	25	100	40	150
Methylcyclohexane	~~500~~ 400	~~1200~~ 1600		
TO	400	1600	500	2000
Methylene chloride from	(100)	(360)		
TO	200	720	250**	900**
Nickel carbonyl from	(0.001,A[1a])	(0.007)		
TO	0.05	0.35	0.05	0.35
Octane	(400)	(1900)		
TO	300	1450	375	1800
Particulate polycyclic organic matter (PPOM) as benzene solubles	—	0.2		
To: Particulate polycyclic aromatic hydrocarbons (PPAH) as benzene solubles	—	0.2A[1a]	—	0.2A[1a]
Phosgene (carbonyl chloride)	0.1	0.4	0.05	0.2
Phthalic anhydride from	(2)	(12)		
TO	1	6	4	24
Propyne, see Methyl-acetylene from	—	—		
TO	1000	1650	1250	2050
Stoddard solvent from	(200)	(1150)		
TO	100	575	150	720

* Error in transfer of value from the NIC to the adopted list in 1973 and carried through until 1978. The 320 has been corrected to 820 in this listing.

** The STEL does not agree with its synonym.

Placed on Notice of Intended Changes list

Calcium oxide
Chloroform (trichloromethane)
Dichloromonofluoromethane
Paraquat
Trinitrotoluene

Ceiling limit and STEL

The definition of a ceiling limit is the concentration that should not exceed even instantaneously, therefore no STEL should be listed with those substances assigned a ceiling limit. The 1976 TLV booklet erroneously lists a tentative STEL with the following substances.

Acetic anhydride
Boron trifluoride
n-Butyl alcohol
Butylamine
Cadmium oxide fume, as Cd
Chlorine trifluoride
Chloroacetaldehyde
Dichloroacetylene
o-Dichlorobenzene
1,1-Dichloro-1-nitroethane

Diglycidyl ether
Ethylene chlorohydrin
Ethylene glycol dinitrate and/or Nitroglycerin
Ethylidene Norbornene
Formaldehyde
Gluteraldehyde, activated or unactivated
Hydrogen chloride
Iodine
Isophorone
Maganese & compounds, as Mn
Methylene bisphenyl isocyanate
Methylene bis (4-cyclohexylisocyante)
Methyl ethyl ketone peroxide
Methyl silicate
α-Methyl styrene
Monomethyl hydrazine
Nitrogen dioxide
Phenylphosphine
Potassium hydroxide
Sodium azide
Sodium hydroxide
Subtilisins (Proteolytic enzymes as 100% pure crystalline enzyme)
Terphenyls
Toulene-2,4-dilsocyanate
Vanadium (V_2O_5) Fume, as V
m-Xylene α,α'-diamine

EDITOR'S NOTE: Calcium hydroxide should not have been placed in the alphabetical listing of adopted values at a TWA of 5 mg/m^3 as well as the additional indication to see NIC. Calcium hydroxide first appeared on the NIC as a *new* substance this year at the 5 mg/m^3 TWA.

Airborne Contaminants TLV Committee

Herbert E. Stokinger, Ph.D., *Chairman*
Hector P. Blejer, M.D., DIH
Paul E. Caplan, P.E., MPH
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Paul Gross, M.D.
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William D. Wagner, *Recording Secretary*
Ralph C. Wands, M.S.

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James F. Morgan
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Development of short-term exposure limits (STEL)

PAUL E. CAPLAN, P.E., MPH
Committee Member

The need for Short-Term Exposure Limits was first considered by the TLV Committee in 1971, when its Chairman, Dr. Herbert Stokinger, appointed an ad hoc committee at its November 1971 plenary session. This subcommittee consisted of Dr. William Fredrick, Dr. Hector Blejer and Mr. Paul Caplan, Chairman. Subsequently, Mr. Jack Knauber, Mr. Jesse Lieberman, and Dr. Theodore Torkelson were added to the subcommittee.

In 1972 the Executive Board of the ACGIH requested that the TLV Committee consider developing STELs for inclusion in the published TLV booklet. The charge to the committee at the May 3, 1973 TLV Committee plenary meeting was:

1. To evaluate the TLV list as to the substances for which an "STL" is applicable.
2. Substances of greater prominence (production and use volumes, exposure time and frequency) will receive first priority for development of an STL.
3. Annotations in the TLV booklet (Preface) will include reference to the STL concept.
4. Incorporate STL concept in Appendix D "excursion of actions" including modification of "for all substances" statement.

Previous to this time, several organizations had developed lists of short term limits. These included:

1. "Short-Term Limits for Exposure to Airborne Contaminants." A "Documentation" and "Supplement" by the Pennsylvania Department of Health, 1967-1969.
2. "Emergency Exposure Limits" by the Toxicology Committee of the American Industrial Hygiene Association; *AIHAJ*. November/December, 1964.

3. "Basis for Establishing Guides for Short-Term Exposures of the Public to Air Pollutants," by the Committee on Toxicology of the National Academy of Sciences-National Research Council, May 1971.

The purposes of these short-term or Emergency Limits were generally to give guidance to industrial hygienists in the management of *single* brief exposures to airborne contaminents usually as the result of unplanned or accidental incidents.

In November of 1973, the STL subcommittee reported to the TLV Committee and recommended that a third category of TLVs be established (in addition to TLV-TWA, TLV-C) namely the TLV-EL, Excursion Limit. The maximum concentration to which workers can be exposed *for a period up to 15 minutes* continuously without suffering from:

1. "Intolerable irritation" (subsequently changed to "irritation").
2. Chronic or irreversible tissue change.
3. Narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work efficiency with no more than four excursions per day permitted and provided the daily TLV-TWA is also not exceeded.

It further recommended "for some substances, e.g., irritant gasses, only one category," the "ceiling" level, may be relevent. For some chemicals, such as lead fume, two categories may be relevent, the TLV-TWA and the TLV-EL. For other substances, perhaps two other categories may be relevent, (the TLV-TWA and the TLV-C). Thus, a substance may have one, two, or three relevent specific categories, depending upon its physiological reactions.

As a first attempt at developing "proposed 'STELs' " (name now changed from "ELs" to "STELs") for the more than 450 compounds in the TLV booklet, the subcommittee chairman assigned responsibility to the 5 members (each for specific groups of chemicals) for development of assigned STELs as part of the "Notice of Intended Changes" in the 1975 Booklet. The following references for "Justification of appropriateness of values" were used for a first "best estimate":

a) TLV Approved List of 1973.
b) TLV list of "Intended Changes" for 1973.
c) TLV "C" on Approved List for 1973.
d) TLV "C" on Intended Changes list for 1973.
e) Use of "Excursion Factors" (from 3 to 1.25) as recommended in the 1973 booklet.
f) Short-Term Exposure Limits of Pennsylvania Department of Health.
g) OSHA limits of October 17, 1972, *Federal Register,* 1973.
h) Carcinogen standards of OSHA in *Federal Register,* November 1973.
i) Criteria Documents of NIOSH.
j) ANSI standards.
k) California Hygienic Standards.
l) Emergency Limits of OSHA and NIOSH.
m) "Grabois" factor (STE $\approx 2 \times$ TWA; C $\approx 3 \times$ TWA).
n) Documentation of TLVs.

Of specific interest, was Mr. Bernard Grabois' (member of TLV committee) suggestion that, if no other data was available, a reasonable STEL would be $2 \times$ TWA.

Since Mr. Grabois had expressed an interest in the STELs, he was appointed as a subcommittee member, until his retirement from the TLV Committee and the New York State Department of Labor in 1974. Mr. Meier Schneider and Mr. Ralph Wands were appointed to the subcommittee to replace Grabois and Dr. Torkelson (who assumed chairmanship of the Halogenated Hydrocarbons Subcommittee in late 1973). Completed assignments were compiled by the subcommittee chairman in late 1973 and 1974, with each recommended STEL value accompanied by notations of justification. Comments from other ACGIH members on the rationale of STELs were also reviewed.

In April 1974 a review of the approximately 520 compounds in the TLV booklet for 1973 indicated (by concensus) that 425 compounds were amendable to the "excursion factor" as a first "best estimate"; and the remaining 95 compounds needed further evaluation by the subcommittee.

In 1975 the subcommittee continued to develop STELs to be presented at the next annual ACGIH meeting. The TLV committee report (1975) recommended that the preface of the 1975 Booklet include the STEL concept. However, it was not added until 1976, when specific "Tentative Values" for STELs were listed in the booklet. Comments on

"the specific listed values" or "problems in the use or interpretation of STELs" started to come to the TLV Committee chairman and the subcommittee chairman. Some of the comments involved:

1. The effects of novel work schedules on TLVs.
2. Misuse of the "excursion factor" as "rule of thumb" estimates.
3. Inconsistancies, errors, and misprints in the listings as observed by several corporate staffs.
4. Misgivings in the development and use of STELs.

Some of the major concerns, both from TLV committee members and industrial hygienists outside the Committee, appeared to be:

1. The "Excursion Factors" were used too frequently and were not always appropriate.
2. An attempt was being made to create a STEL for every substance.
3. The interpretation of the phrase "up to 15 minutes, no more than 4 times per day" was not specific enough.
4. Some felt short excursions (of a few seconds or minutes) above the STEL should be "allowed."
5. Industry could not feasibly live with "prohibitions of *any* exposure above the STEL."
6. Monitoring systems were not capable of measuring short excursions (few seconds) above the STEL level.

The subcommittee's responses to the above were essentially that:

1. Excursion factors were used only as a first "best estimate" if no other pertenent references could be found. When more relevent data were received, STELs would be modified.
2. The subcommittee agreed that not all substances, in fact, need a STEL value. It requested of all authors of future "Documentations of TLVs" that they address the issue, explicitly, of whether or not a STEL was appropriate, based on existing toxicological data, and if so, what value was appropriate.
3. Emphasis was repeated that the definition of the STEL did *not* make it a 15-minute TWA. It was, in fact, a ceiling value that could not be exceeded for *any time period* up to 15 minutes (not one second or one minute); and then no more than four such periods per working day.
4. The evaluation for compliance was purposely omitted, both because the value was derived totally on a physiological basis (not a sampling and analysis basis) and because this is a guideline (as are all TLVs), not an enforceable standard.
5. If this guideline level will be exceeded routinely in a work operation (as shown by previous experiences), additional protection should be provided by other control means, such as respirators, administrative practices, work practices, etc.
6. Other time frames for STELs, such as 10-second exposures, 1 minute, 10 minutes, etc., with allowances of 50 to 100% above the STEL, probably would make standards development and enforcement too complicated in interpretation and application.

One subcommittee member, Ralph Wands, suggested that criteria, for which STELs are to be established, should be developed and published. In April 1978 a list of "Guidelines of an STEL value, relative to the TLV-TWA" was prepared by the subcommittee chairman and distributed to the members. It suggested a range of factors to be applied to the TWA based on physiological actions. There was wide disagreement, inside the subcommittee, on the proposed factors. However, it should serve as a starting point for future developments.

Equally important, in the opinion of the subcommittee chairman, to the assignment of STEL values, is the necessity for agreement concensus in "terminology" useage by the several official and professional organizations involved in workplace standards development and implementation.

Physical Agents TLV Committee report

1. Recommends the adoption of the changes in the Laser TLV given in the Notice of Intended Changes in 1975.

2. Recommends the adoption of the changes in the Impact Noise TLV given in the Notice of Intended Changes in 1975.
3. Recommends that a notice of intent to establish a TLV for ultrasound as given in the attached copy to be adopted. (See complete text of the 1976 TLV booklet following this report.)
4. Recommends that changes be made in the Notice of Intent to establish a TLV for Light adopted in 1975 as outlined in the attached copy. (See complete text.)
5. Recommends that a Notice of Intent to Change the TLV for Microwaves as given in the attached copy be adopted. (See complete text.)

/s/ Herbert H. Jones
Chairman

Revised Values

LASERS

Tables 3 and 4, that portion from the first listing of Light through last listing for IR-A, plus footnotes. Table 6, that portion covering Light and IR-A, plus footnote. Complete tables can be found in complete text of the 1976 TLV booklet following this report.

IMPACT NOISE

See full text of the 1976 TLV booklet following.

Physical Agents TLV Committee

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Threshold limit values for chemical substances and physical agents in the workroom environment with intended changes for 1976

PREFACE
CHEMICAL CONTAMINANTS

Threshold limit values refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variation in individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit; a smaller percentage may be affected more seriously by aggravation of a pre-existing condition or by development of an occupational illness.

Simple tests are now available (J. Occup. Med. 15: 564, 1973; Ann. N.Y. Acad. Sci., *151, Art. 2:* 968, 1968) that may be used to detect those individuals hypersusceptible to a variety of industrial chemicals (respiratory irritants, hemolytic chemicals, organic isocyanates, carbon disulfide). These tests may be used to screen out by appropriate job placement the hyperreactive worker and thus in effect improve the "coverage" of the TLVs.

Three categories of Threshold Limit Values (TLVs) are specified herein, as follows:

a) Threshold Limit Value-Time Weighted Average (TLV-TWA) — the time-weighted average concentration for a normal 8-hour workday or 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

b) Threshold Limit Value-Short Term Exposure Limit (TLV-STEL) — the maximal concentration to which workers can be exposed for a period up to 15 minutes continuously without suffering from 1) irritation, 2) chronic or irreversible tissue change, or 3) narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work efficiency, provided that no more than four excursions per day are permitted, with at least 60 minutes between exposure periods, and provided that the daily TLV-TWA also is not exceeded. The STEL should be considered a maximal allowable concentration, or absolute ceiling, not to be exceeded at any time during the 15-minute excursion period. STELs are based on one or more of the following criteria: (1) Adopted TLVs including those with a "C" or "ceiling" limit. (2) TWA-TLV Excursion Factors listed in Appendix D. (3) Pennsylvania Short-Term Limits for Exposure to Airborne Contaminants (Penna. Dept. of Hlth., Chapter 4, Art. 432, Rev. Jan. 25, 1968). (4) OSHA Occupational Safety and Health Standards, Fed. Reg. Vol. 36, No. 105, May 29, 1971. The TWA-STEL should not be used as engineering design criterion or considered as an emergency exposure level (EEL).

c) Threshold Limit Value-Ceiling (TLV-C) — the concentration that should not be exceeded even instantaneously.

For some substances, e.g., irritant gases, only one category, the TLV-Ceiling, may be relevant. For other substances, either two or three categories may be relevant, depending upon their physiologic action. It is important to observe that if any one of these three TLVs is exceeded, a potential hazard from that substance is presumed to exist.

The TLV-TWA should be used as guides in the control of health hazards and should not be used as fine lines between

safe and dangerous concentrations. [Exceptions are those substances in Category c), which have been designated "C" or Ceiling limit.]

Time-weighted averages permit excursions above the limit provided they are compensated by equivalent excursions below the limit during the workday. In some instances it may be permissible to calculate the average concentration for a workweek rather than for a workday. The degree of permissible excursion is related to the magnitude of the threshold limit value of a particular substance as given in Appendix D. The relationship between threshold limit and permissible excursion is a rule of thumb and in certain cases may not apply. The amount by which threshold limits may be exceeded for short periods without injury to health depends upon a number of factors such as the nature of the contaminant, whether very high concentrations — even for short periods — produce acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such periods. All-factors must be taken into consideration in arriving at a decision as to whether a hazardous condition exists.

Threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and, when possible, from a combination of the three. The basis on which the values are established may differ from substance to substance; protection against impairment of health may be a guiding factor for some, whereas reasonable freedom from irritation, narcosis, nuisance or other forms of stress may form the basis for others.

The amount and nature of the information available for establishing a TLV varies from substance to substance; consequently, the precision of the estimated TLV is also subject to variation and the latest *Documentation* should be consulted in order to assess the extent of the data available for a given substance.

The committee holds to the opinion that limits based on physical irritation should be considered no less binding than those based on physical impairment. There is increasing evidence that physical irritation may initiate, promote or accelerate physical impairment through interaction with other chemical or biologic agents.

In spite of the fact that serious injury is not believed likely as a result of exposure to the threshold limit concentrations, the best practice is to maintain concentrations of all atmospheric contaminants as low as is practical.

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, (1) as a relative index of hazard or toxicity, (2) in the evaluation or control of community air pollution nuisances, (3) in estimating the toxic potential of continuous, uninterrupted exposures or other extended work periods, (4) as proof or disproof of an existing disease or physical condition, or (5) for adoption by countries whose working conditions differ from those in the United States of America and where substances and processes differ.

Ceiling vs Time-Weighted Average Limits. Although the time-weighted average concentration provides the most satisfactory, practical way of monitoring airborne agents for compliance with the limits, there are certain substances for which it is inappropriate. In the latter group are substances which are predominantly fast acting and whose threshold limit is more appropriately based on this particular response. Substances with this type of response are best controlled by a ceiling "C" limit that should not be exceeded. It is implicit in these definitions that the manner of sampling to determine noncompliance with the limits for each group must differ; a single brief sample, that is applicable to a "C" limit, is not appropriate to the time-weighted limit; here, a sufficient number of samples are needed to permit a time-weighted average concentration throughout a complete cycle of operations or throughout the work shift.

Whereas the ceiling limit places a definite boundary which concentrations should not be permitted to exceed, the time-weighted average limit requires an explicit limit to the excursions that are permissible above the listed values. The magnitude of these excursions may be pegged to the magnitude of the threshold limit by an appropriate factor shown in Appendix D. It should be noted that the same factors are used by the Committee in determining the magnitude of the value of the STELs, or whether to include or exclude a substance for a "C" listing.

"Skin" Notation. Listed substances followed by the designation "Skin" refer to the potential contribution to the overall exposure by the cutaneous route including mucous membranes and eye, either by airborne, or more particularly, by direct contact with the substance. Vehicles can alter skin absorption. This attention-calling designation is intended to suggest appropriate measures for the prevention of cutaneous absorption so that the threshold limit is not invalidated.

Mixtures. Special consideration should be given also to the application of the TLVs in assessing the health hazards which may be associated with exposure to mixtures of two or more substances. A brief discussion of basic considerations involved in developing threshold limit values for mixtures, and methods for their development, amplified by specific examples are given in Appendix C.

Nuisance Particulates. In contrast to fibrogenic dusts which cause scar tissue to be formed in lungs when inhaled in excessive amounts, so-called "nuisance" dusts have a long history of little adverse effect on lungs and do not produce significant organic disease or toxic effect when exposures are kept under reasonable control. The nuisance dusts have also been called (biologically) "inert" dusts, but the latter term is inappropriate to the extent that there is no dust which does not evoke some cellular response in the lung when inhaled in sufficient amount. However, the lung-tissue reaction caused by inhalation of nuisance dusts has the following characteristics: (1) The architecture of the air spaces remains intact. (2) Collagen (scar tissue) is not formed to a significant extent. (3) The tissue reaction is potentially reversible.

Excessive concentrations of nuisance dusts in the workroom air may seriously reduce visibility, may cause unpleasant deposits in the eyes, ears and nasal passages (Portland Cement dust), or cause injury to the skin or mucous membranes by chemical or mechanical action per se or by the rigorous skin cleansing procedures necessary for their removal.

A threshold limit of 10 mg/m^3, or 30 mppcf, of total dust $< 1\%$ quartz is recommended for substances in these categories and for which no specific threshold limits have been assigned. This limit, for a normal workday, does not apply to brief exposures at higher concentrations. Neither does it apply to those substances which may cause physiologic impairment at lower concentrations but for which a threshold limit has ot yet been adopted. Some nuisance particulates are given in Appendix E.

Simple Asphyxiants — "Inert" Gases or Vapors. A number of gases and vapors, when present in high concentrations in air, act primarily as simple asphyxiants without other significant physiologic effects. A TLV may not be recommended for each simple asphyxiant because the limiting factor is the available oxygen. The minimal oxygen content should be 18 percent by volume under normal atmospheric pressure (equivalent to a partial pressure, pO_2 of 135 mm Hg). Atmospheres deficient in O_2 do not provide adequate warning and most simple asphyxiants are odorless. Several simple asphyxiants

present an explosion hazard. Account should be taken of this factor in limiting the concentration of the asphyxiant. Specific examples are listed in Appendix F.

Physical Factors. It is recognized that such physical factors as heat, ultraviolet and ionizing radiation, humidity, abnormal pressure (altitude) and the like may place added stress on the body so that the effects from exposure at a threshold limit may be altered. Most of these stresses act adversely to increase the toxic response of a substance. Although most threshold limits have built-in safety factors to guard against adverse effects to moderate deviations from normal environments, the safety factors of most substances are not of such a magnitude as to take care of gross deviations. For example, continuous work at temperatures above 90° F, or overtime extending the workweek more than 25%, might be considered gross deviations. In such instances judgment must be exercised in the proper adjustments of the Threshold Limit Values. Brief & Scala (AIHAJ. 26, 467, 1975) have proposed formulae for calculating the TLV Reducation Factor for Novel Work Schedules, i.e. 10-hr workday.

Biologic Limit Values (BLVs). Other means exist and may be necessary for monitoring worker exposure other than reliance on the Threshold Limit Values for industrial air, namely, the Biologic Limit Values. These values represent limiting amounts of substances (or their effects) to which the worker may be exposed without hazard to health or well-being as determined in his tissues and fluids or in his exhaled breath. The biologic measurements on which the BLVs are based can furnish two kinds of information useful in the control of worker exposure: (1) measure of the individual worker's over-all exposure; (2) measure of the worker's individual and characteristic response. Measurements of response furnish a superior estimate of the physiologic status of the worker, and may be made of (a) changes in amount of some critical biochemical constituent, (b) changes in activity of a critical enzyme, (c) changes in some physiologic function. Measurement of exposure may be made by (1) determining in blood, urine, hair, nails, in body tissues and fluids, the amount of substance to which the worker was exposed; (2) determination of the amount of the metabolite(s) of the substance in tissues and fluids; (3) determination of the amount of the substance in the exhaled breath. The biologic limits may be used as an adjunct to the TLVs for air, or in place of them. The BLVs, and their associated procedures for determining compliance with them, should thus be regarded as an effective means of providing health surveillance of the worker.

Unlisted substances. There are a number of reasons why a substance does not appear in the Threshold Limit list; either insufficient information is available or it has not been brought to the attention of the Threshold Limits Committee from which a limit can be developed, or it is a substance that could be included in the Appendices E and F pertaining to Nuisance Particulates and Simple Asphyxiants. Substances appearing in these appendices serve as examples only; the appendices are not intended to be inclusive.

"Notice of Intent." At the beginning of each year, proposed actions of the Committee for the forthcoming year are issued in the form of a "Notice of Intended Changes." This Notice provides not only an opportunity for comment, but solicits suggestions of substances to be added to the list. The suggestions should be accompanied by substantiating evidence. The list of Intended Changes follows the Adopted Values in the TLV booklet.

Legal Status. By publication in the Federal Register (Vol. 36, No. 105, May 29, 1971) the Threshold Limit Values for 1968 are now official federal standards for industrial air.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Abate	—	10	—	20
Acetaldehyde	100	180	150	270
Acetic acid	10	25	15	37
C Acetic anhydride	5	20	5	20
Acetone	1,000	2,400	1,250	3,000
Acetonitrile	40	70	60	105
Acetylene	F	—	—	—
Acetylene dichloride, see 1, 2-Dichloroethylene	200	790	250	1,000
Acetylene tetrabromide	1	14	1.25	17.5
Acrolein	0.1	0.25	0.3	0.75
Acrylamide — Skin	—	0.3	—	0.6
Acrylonitrile — Skin	20	45	30	68
Aldrin — Skin *	—	0.25	—	0.75
Allyl alcohol — Skin	2	5	4	10
Allyl chloride	1	3	2	6
Allyl glycidyl ether (AGE) — Skin	5	22	10	44
Allyl propyl disulfide	2	12	3	18
Alundum (Al_2O_3)	—	E	—	20
4-Aminodiphenyl — Skin	—	A1b	—	A1b
2-Aminoethanol, see Ethanolamine	3	6	6	12
2-Aminopyridine	0.5	2	1.5	6
Ammonia	25	18	35	27
Ammonium chloride-fume	—	10	—	20
Ammonium sulfamate (Ammate)	—	10	—	20
n-Amyl acetate	100	525	150	790
sec-Amyl acetate	125	650	150	810
Aniline — Skin	5	19	5	19
Anisidine (o-p-isomers	0.1	0.5	0.1	0.50
**Antimony & Compounds (as Sb)	—	(0.5)	—	(0.75)
ANTU (α-Naphthyl thiourea)	—	0.3	—	0.9
Argon	F	—	F	F
**Arsenic & compounds (as As)	—	(0.5)	—	(0.5)
Arsine	0.05	0.2	0.05	0.2
Asbestos (all forms)	—	A1a	A1a	A1a
Asphalt (petroleum) fumes	—	5	—	10
Azinphos methyl — Skin	—	0.2	—	0.6
Baygon (propoxur)	—	0.5	—	1.5
Barium (soluble compounds)	—	0.5	—	0.5
**C Benzene — Skin	(10)	(32)	(25)	(80)
Benzidine production — Skin	—	A1b	—	A1b
p-Benzoquinone, see Quinone	0.1	0.4	0.3	1.2

Capital letters refer to Appendices.
Footnotes (a thru h) see Page 435.
**See Notice of Intended Changes.
*1976 Addition.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Benzoyl peroxide	—	5	—	5
Benz(a)pyrene	—	A2	—	A2
Benzyl chloride	1	5	1	5
Beryllium	—	0.002	—	0.025
Biphenyl	0.2	1	0.2	1
Bismuth telluride	—	10	—	20
Bismuth telluride, Se-doped	—	5	—	10
Boron oxide	—	10	—	20
Boron tribromide	1	10	3	30
C Boron trifluoride	1	3	1	3
Bromine	0.1	0.7	0.3	2
Bromine pentafluoride	0.1	0.7	0.3	2
Bromochloromethane	200	1,050	250	1,300
Bromoform — Skin	0.5	5	0.5	5
Butadiene (1, 3-butadiene)	1,000	2,200	1,250	2,750
*Butane	600	1,400	750	1,610
Butanethiol, see Butyl mercaptan	0.5	1.5	0.5	1.5
2-Butanone	200	590	300	885
2-Butoxy ethanol (Butyl Cellosolve) — Skin	50	240	150	720
n-Butyl acetate	150	710	200	950
sec-Butyl acetate	200	950	250	1,190
tert-Butyl acetate	200	950	250	1,190
*C n-Butyl alcohol — Skin	50	150	50	150
sec-Butyl alcohol	150	450	150	450
tert-Butyl alcohol	100	300	150	450
C Butylamine — Skin	5	15	5	15
C tert-Butyl chromate (as CrO_3) — Skin	—	0.1	—	0.1
n-Butyl glycidyl ether (BGE)	50	270	50	270
*n-Butyl lactate	5	25	5	25
Butyl mercaptan	0.5	1.5	0.5	1.5
p-tert-Butyltoluene	10	60	20	120
*Cadmium, dust & salts, as Cd	—	0.05	—	0.15
C Cadmium oxide fume, as Cd	—	0.05	—	0.05
Calcium carbonate	—	E	—	20
Calcium arsenate, as As	—	1	—	1
Calcium cyanamide	—	0.5	—	1
**Calcium hydroxide	—	5	—	—
**Calcium oxide	—	(5)	—	(5)
Camphor, synthetic	2	12	3	18
Caprolactam Dust	—	1	—	3
Vapor	5	20	10	40
*Captan	—	5	—	15
Carbaryl (Sevin®)	—	5	—	10
*Carbofuran (Furadan®)	—	0.1	—	0.1
Carbon black	—	3.5	—	7
Carbon dioxide	5,000†	9,000	15,000	18,000
Carbon disulfide — Skin	20	60	30	90
Carbon monoxide	50	55	400	440

Capital letters refer to Appendices.
†See 1974 Revised Documentation.
*1976 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Carbon tetrabromide	0.1	1.4	0.3	4.2
Carbon tetrachloride — Skin	10	65	25	160
Cellulose (paper fiber)	—	E	—	20
Cesium hydroxide	—	2	—	2
Chlordane — Skin	—	0.5	—	2
Chlorinated camphene — Skin	—	0.5	—	1
Chlorinated diphenyl oxide	—	0.5	—	1.5
Chlorine	1	3	3	9
Chlorine dioxide	0.1	0.3	0.3	0.9
C Chlorine trifluoride	0.1	0.4	0.1	0.4
C Chloroacetaldehyde	1	3	1	3
α-Chloroacetophenone (Phenacyl chloride)	0.05	0.3	0.05	0.3
Chlorobenzene (Monochlorobenzene)	75	350	75	350
o-Chlorobenzylidene malonoitrile — Skin	0.05	0.4	0.05	0.4
Chlorobromomethane	200	1,050	250	1,300
2-Chloro-1, 3-butadiene, see β Chloroprene	25	90	35	135
Chlorodifluoromethane	1,000	3,500	1,250	4,375
Chlorodiphenyl (42% Chlorine) — Skin	—	1	—	1
Chlorodiphenyl (54% Chlorine) — Skin	—	0.5	—	1
1-Chloro, 2, 3-epoxy-propane (Epichlor-hydrin)	5	19	10	38
2-Chloroethanol (Ethylene chlorohydrin)	1	3	1	3
Chloroethylene (Vinyl chloride)	A1c	—	A1c	—
**Chloroform (Trichloromethane)	(25)	(120)	25A2	—
bis-Chloromethyl ether	0.001	A1a	0.001	A1a
1-Chloro-1-nitro-propane	20	100	20	100
Chloropicrin	0.1	0.7	0.1	0.7
β-Chloroprene — Skin	25	90	35	135
Chlorpyrifos (Dursban®) — Skin	—	0.2	—	0.6
o-Chlorostyrene	50	285	75	430
o-Chlorotoluene — Skin	50	250	75	375
2-Chloro-6-(trichloromethyl pyridine (N-Serve®)	—	10	—	20
Chromates, certain insoluble forms	—	A1a	—	A1a
Chromic acid and Chromates, as Cr	—	0.05	—	—
Chromium, Sol. chromic, chromous salts, as Cr	—	0.5	—	0.5
Chromium metal	—	1.0	—	—
Clopidol (Coyden®)	—	10	—	20

Capital letters refer to Appendices.
Footnotes (a thru h) see Page 435.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Coal tar pitch volatiles (See Particulate polycyclic aromatic hydrocarbons)	—	A1a	—	A1a
**Cobalt metal, dust and fume	—	(0.1)	—	(0.1)
Copper fume	—	0.2	—	0.2
Dusts & Mists	—	1	—	2
Corundum (Al_2O_3)	—	E	—	E
Cotton dust, raw	—	0.2[m]	—	0.6
Crag® herbicide	—	10	—	20
Cresol, all isomers — Skin	5	22	5	22
Crotonaldehyde	2	6	6	18
Crufomate®	—	5	—	20
Cumene — Skin	50	245	75	365
Cyanide, as CN — Skin	—	5	—	5
Cyanogen	10	20	10	20
Cyclohexane	300	1,050	375	1,300
Cyclohexanol	50	200	50	200
Cyclohexanone	50	200	50	200
Cyclohexene	300	1,015	300	1,015
Cyclohexylamine — Skin	10	40	10	40
Cyclopentadiene	75	200	150	400
2, 4-D (2, 4-Diphenoxy-acetic acid)	—	10	—	20
DDT (Dichlorodiphenyl-trichloroethane)	—	1	—	3
DDVP, See Dichlorvos	0.1	1	0.3	3
Decaborane — Skin	0.05	0.3	0.15	0.9
Demeton® — Skin	0.01	0.1	0.03	0.3
Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone)	50	240	75	360
1, 2-Diaminoethane, See Ethylenediamine	10	25	10	25
Diazinon — Skin	—	0.1	—	0.3
Diazomethane	0.2	0.4	0.2	0.4
Diborane	0.1	0.1	0.1	0.1
1, 2-Dibromoethane (Ethylene dibromide) — Skin	20	145	30	220
Dibrom®	—	3	—	6
2-N-Dibutylaminoethanol — Skin	2	14	4	28
Dibutyl phosphate	1	5	2	10
Dibutyl phthalate	—	5	—	10
C Dichloracetylene	0.1	0.4	0.1	0.4
C o-Dichlorobenzene	50	300	50	300
p-Dichlorobenzene	75	450	110	675
Dichlorobenzidine — Skin	—	A2	—	A2
Dichlorodifluoromethane	1,000	4,950	1,250	6,200
1, 3-Dichloro-5, 5-dimethyl hydantoin	—	0.2	—	0.4
1, 1-Dichloroethane	200	820	250	1,025
1, 2-Dichloroethane	50	200	75	300
1, 2-Dichloroethylene	200	790	250	1,000

Capital letters refer to Appendices.
m) See p. 436.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Dichloroethyl ether — Skin	5	30	10	60
*Dichloromethane, see Methylene chloride	200	720	200	720
**Dichloromonofluoro-methane	(1,000)	(4,200)	(1,250)	(5,250)
C 1, 1-Dichloro-1-nitroethane	10	60	10	60
1, 2-Dichloropropane, see Propylene dichloride	75	350	110	525
Dichlorotetrafluoro-ethane	1,000	7,000	1,250	8,750
Dichlorvos (DDVP) — Skin	0.1	1	0.3	3
*Dicyclopentadiene	5	30	5	30
Dicyclopentadienyl iron	—	10	—	20
Dieldrin — Skin	—	0.25	—	0.75
Diethylamine	25	75	25	75
Diethylaminoethanol — Skin	10	50	10	50
Diethylene triamine — Skin	1	4	1	4
Diethyl ether, see Ethyl ether	400	1,200	500	1,500
Diethyl phthalate	—	5	—	10
Difluorodibromomethane	100	860	150	1,290
C Diglycidyl ether (DGE)	0.5	2.8	0.5	2.8
Dihydroxybenzene, see Hydroquinone	—	2	—	3
Diisobutyl ketone	25	150	25	150
Diisopropylamine — Skin	5	20	5	20
Dimethoxymethane, see Methylal	1,000	3,100	1,250	3,875
Dimethyl acetamide — Skin	10	35	15	50
Dimethylamine	10	18	10	18
Dimethylaminobenzene, see Xylidene	5	25	10	50
Dimethylaniline (N-Dimethylaniline) — Skin	5	25	10	50
Dimethylbenzene, see Xylene	100	435	150	650
Dimethyl-1, 2-dibromo-2-dichloro-ethyl phosphate, see Dibrom	—	3	—	6
Dimethylformamide — Skin	10	30	20	60
2, 6-Dimethylheptanone, see Diisobutyl ketone	25	150	25	150
1, 1-Dimethylhydrazine — Skin	0.5	1	1	2
Dimethylphthalate	—	5	—	10
**Dimethyl sulfate — Skin	(0.01)	(A2)	A2	—

Capital letters refer to Appendices.
*1976 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Dinitrobenzene (all isomers) — Skin	0.15	1	0.5	3
Dinitro-o-cresol — Skin	—	0.2	—	0.6
3, 5-Dinitro-o-toluamide (Zoalene®)	—	5	—	10
Dinitrotoluene — Skin	—	1.5	—	5
Dioxane, tech. grade — Skin	50	180	50	180
Diphenyl, see Biphenyl	0.2	1	0.6	3
Diphenylamine	—	10	—	20
Diphenylmethane diisocyanate, see Methylene-bisphenyl isocyanate (MDI)	0.02	0.2	0.02	0.2
Dipropylene glycol methyl ether — Skin	100	600	150	900
Diquat	—	0.5	—	1
Di-sec, octyl phthalate (Di-2-ethylhexyl-phthalate)	—	5	—	10
*Disulfuram	—	2	—	5
Disyston — Skin	—	0.1	—	0.3
2, 6-Ditert. butyl-p-cresol	—	10	—	20
*Dyfonate	—	0.1	—	0.1
Emery	—	E	—	20
Endosulfan (Thiodan®) — Skin	—	0.1	—	0.3
Endrin — Skin	—	0.1	—	0.3
Epichlorhydrin — Skin	5	20	10	40
EPN — Skin	—	0.5	—	1.5
1, 2-Epoxypropane, see Propylene oxide	100	240	150	360
2, 3-Epoxy-1-propanol, see Glycidol	50	150	65	190
Ethane	F	—	F	—
Ethanethiol, see Ethyl mercaptan	0.5	1	1.5	3
Ethanolamine	3	6	6	12
*Ethion (Nialate®) — Skin	—	0.4	—	0.4
2-Ethoxyethanol — Skin	100	370	150	560
2-Ethoxyethyl acetate (Cellosolve acetate) — Skin	100	540	150	810
Ethyl acetate	400	1,400	400	1,400
Ethyl acrylate — Skin	25	100	25	100
Ethyl alcohol (Ethanol)	1,000	1,900	1,000	1,900
Ethylamine	10	18	10	18
Ethyl sec-amyl ketone (5-Methyl-3-heptanone)	25	130	25	130
Ethyl benzene	100	435	125	545
Ethyl bromide	200	890	250	1,110
Ethyl butyl ketone (3-Heptanone)	50	230	75	345
Ethyl chloride	1,000	2,600	1,250	3,250
Ethyl ether	400	1,200	500	1,500
Ethyl formate	100	300	150	450
Ethyl mercaptan	0.5	1	0.5	1

Capital letters refer to Appendices.
*1976 Addition

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Ethyl silicate	100	850	150	1,275
Ethylene	F	—	F	—
*C Ethylene chlorohydrin — Skin	1	3	1	3
Ethylene diamine	10	25	10	25
Ethylene dibromide, see 1, 2-Dibromoethane	20	145	30	220
Ethylene dichloride, see 1, 2-Dichloroethane	50	200	75	300
Ethylene glycol, Particulate	—	10	—	20
Vapor	100	260	125	325
C Ethylene glycol dinitrate and/or Nitroglycerin — Skin	0.2[d]	—	0.2	—
Ethylene glycol monomethyl ether acetate (Methyl cellosolve acetate) — Skin	25	120	40	180
Ethylene oxide	50	90	75	135
Ethyleneimine — Skin	0.5	1	0.5	1
Ethylidene chloride, see 1, 1-Dichloroethane	200	320	250	400
C Ethylidene norbornene	5	25	5	25
N-Ethylmorpholine — Skin	20	94	20	94
*Fensulfothion (Dasanit)	—	0.1	—	0.1
Ferbam	—	10	—	20
Ferrovanadium dust	—	1	—	3
Fluoride (as F)	—	2.5	—	2.5
Fluorine	1	2	2	4
Fluorotrichloromethane	1,000	5,600	1,250	7,000
C Formaldehyde	2	3	2	3
Formamide	20	30	30	45
Formic acid	5	9	5	9
Furfural — Skin	5	20	15	60
Furfuryl alcohol — Skin.	5	20	10	40
Gasoline	—	B2	—	B2
Germanium tetrahydride.	0.2	0.6	0.6	1.8
Glass, fibrous[e] or dust	—	E	—	E
**C Glutaraldehyde, activated or unactivated	—	(0.25)	—	(0.25)
Glycerin mist	—	E	—	E
Glycidol (2, 3-Epoxy-1-propanol)	50	150	75	225
Glycol monoethyl ether, see 2-Ethoxyethanol	100	370	150	560
Graphite (Synthetic)	—	E	—	—
Guthion®, see Azinphos-methyl	—	0.2	—	0.6
Gypsum	—	E	—	20
Hafnium	—	0.5	—	1.5
Helium	F	—	F	—
Heptachlor — Skin	—	0.5	—	1.5
*Heptane (n-Heptane)	400	1,600	500	2,000
Hexachlorocyclopentadiene	0.01	0.11	0.03	0.33

Capital letters refer to Appendices.
Footnotes (a thru h) see Page 435.
*1976 Addition
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Hexachloroethane — Skin	1	10	3	30
Hexachloronaphthalene — Skin	—	0.2	—	0.6
Hexafluoroacetone	0.1	0.7	0.3	2.1
*Hexane (n-hexane)	100	360	125	450
*2-Hexanone, see Methyl butyl ketone — Skin	25	100	40	150
Hexone (Methyl isobutyl ketone) — Skin	100	410	125	510
sec-Hexyl acetate	50	300	50	300
**Hydrazine — Skin	(1)	(1.3)	0.3	0.4
Hydrogen	F	—	F	—
*Hydrogenated terphenyls	0.5	5	0.5	5
Hydrogen bromide	3	10	3	10
C Hydrogen chloride	5	7	5	7
Hydrogen cyanide — Skin	10	11	15	16
Hydrogen fluoride	3	2	3	2
Hydrogen peroxide	1	1.4	2	2.8
Hydrogen selenide	0.05	0.2	0.05	0.2
Hydrogen sulfide	10	15	15	27
Hydroquinone	—	2	—	4
Indene	10	45	15	27
Indium & Compounds, as In	—	0.1	—	0.3
C Iodine	0.1	1	0.1	1
*Iodoform	0.2	3	0.4	0.6
Iron oxide fume	B4	5	—	10
Iron pentacarbonyl	0.01	0.08	0.01	0.08
Iron salts, soluble, as Fe	—	1	—	2
Isoamyl acetate	100	525	125	655
Isoamyl alcohol	100	360	125	450
Isobutyl acetate	150	700	187	875
*Isobutyl alcohol	50	150	75	225
*C Isophorone	5	25	5	25
Isopropyl acetate	250	950	310	1,185
Isopropyl alcohol — Skin	400	980	500	1,225
Isopropylamine	5	12	10	24
Isopropyl ether	250	1,050	310	1,320
Isopropyl glycidyl ether (IGE)	50	240	75	360
Kaolin	—	E	—	20
Ketene	0.5	0.9	1.5	2.7
Lead, inorg., fumes & dusts, as Pb	—	0.15	—	0.45
Lead arsenate, as Pb	—	0.15	—	0.45
Limestone	—	E	—	20
Lindane — Skin	—	0.5	—	1.5
Lithium hydride	—	0.025	—	0.025
L.P.G. (Liquified petroleum gas)	1,000	1,800	1,250	2,250
Magnesite	—	E	—	20
Magnesium oxide fume	—	10	—	10
Malathion — Skin	—	10	—	10
Maleic anhydride	0.25	1	0.25	1
C Manganese & Compounds, as Mn	—	5	—	5

Capital letters refer to Appendices.
*1976 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Manganese cyclopentadienyl tricarbonyl (as Mn) — Skin	—	0.1	—	0.3
Marble	—	E	—	20
Mercury (Alkyl compounds) — Skin, As Hg	0.001	0.01	0.003	0.03
Mercury (All forms except alkyl) as Hg	—	0.05	—	0.15
Mesityl oxide	25	100	25	100
Methane	F	—	F	—
Methanethiol, see Methyl mercaptan	0.5	1	0.5	1
Methoxychlor	—	10	—	10
2-Methoxyethanol — Skin (Methyl cellosolve)	25	80	35	120
Methyl acetate	200	610	250	760
Methyl acetylene (propyne)	1,000	1,650	1,250	2,060
Methyl acetylene-propadiene mixture (MAPP)	1,000	1,800	1,250	2,250
Methyl acrylate — Skin	10	35	10	35
Methyl acrylonitrile — Skin	1	3	2	6
Methylal (dimethoxymethane)	1,000	3,100	1,250	3,875
Methyl alcohol (methanol) — Skin	200	260	250	310
Methylamine	10	12	10	12
Methyl amyl alcohol, see Methyl isobutyl carbinol	25	100	40	150
Methyl 2-cyanoacrylate	2	8	4	16
Methyl isoamyl ketone	100	475	150	710
Methyl n-amyl ketone (2-Heptanone)	100	465	150	710
Methyl bromide — Skin	15	60	15	60
Methyl butyl ketone, see 2-Hexanone	25	100	40	150
Methyl cellosolve — Skin see 2-Methoxyethanol	25	80	35	120
Methyl cellosolve acetate — Skin, see Ethylene glycol monomethyl ether acetate	25	120	35	150
Methyl chloride	100	210	125	260
Methyl chloroform	350	1,900	450	2,375
*Methylcyclohexene	400	1,600	500	2,000
Methylcylohexanol	50	235	75	350
o-Methycyclohexanone — Skin	50	230	75	345
Methylcyclopentadienyl manganese tricarbonyl (as Mn) — Skin	0.1	0.2	0.3	0.6
Methyl demeton — Skin	—	0.5	—	1.5

Capital letters refer to Appendices.
Footnotes (a thru h) see Page 435.
*1976 Addition.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
C Methylene bisphenyl isocyanate (MDI)	0.02	0.2	0.02	0.2
*Methylene chloride (dichloromethane)	200	720	250	900
4, 4'-Methylene bis (2-chloraniline) — Skin	0.02A2	—	0.02A2	—
C Methylene bis (4-cyclohexylisocyanate)	0.01	0.11	0.01	0.11
Methyl ethyl ketone (MEK), see 2-Butanone	200	590	250	740
C Methyl ethyl ketone peroxide	0.2	1.5	0.2	1.5
Methyl formate	100	250	150	375
Methyl iodide — Skin	5	28	10	56
Methyl isobutyl carbinol — Skin	25	100	40	150
Methyl isobutyl ketone, see Hexone	100	410	125	510
Methyl isocyanate — Skin	0.02	0.05	0.02	0.05
Methyl mercaptan	0.5	1	0.5	1
Methyl methacrylate	100	410	125	510
Methyl parathion — Skin	—	0.2	—	0.6
Methyl propyl ketone, see 2-Pentanone	200	700	250	875
C Methyl silicate	5	30	5	30
C α-Methyl styrene	100	480	100	480
Molybdenum, as Mo Soluble compounds	—	5	—	10
Insoluble compounds	—	10	—	20
Monomethyl aniline — Skin	2	9	4	18
C Monomethyl hydrazine — Skin	0.2	0.35	0.2	0.35
Morpholine — Skin	20	70	30	105
Naphthalene	10	50	15	75
β-Naphthylamine	—	A1b	—	A1b
Neon	F	—	F	—
*Nickel carbonyl	0.05	0.35	0.05	0.35
Nickel metal	—	1	—	—
*Nickel, soluble compounds (as Ni)	—	0.1	—	0.3
Nicotine — Skin	—	0.5	—	1.5
Nitric acid	2	5	4	10
Nitric oxide	25	30	35	45
p-Nitroaniline — Skin	1	6	2	12
Nitrobenzene — Skin	1	5	2	10
p-Nitrochlorobenzene — Skin	—	1	—	2
4-Nitrodiphenyl	—	A1b	—	A1b
Nitroethane	100	310	150	465
C Nitrogen dioxide	5	9	5	9
Nitrogen trifluoride	10	29	15	45
Nitroglycerin[d] — Skin	0.2	2	0.2	2
Nitromethane	100	250	150	375
1-Nitropropane	25	90	35	135
2-Nitropropane	25	90	25	90

Capital letters refer to Appendices.
*1976 Addition.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
N-Nitrosodimethylamine (dimethylnitrosoamine) — Skin	—	A2	—	A2
Nitrotoluene — Skin	5	30	10	60
Nitrotrichloromethane, see Chloropicrin	0.1	0.7	0.3	2
Nitrous oxide	F	—	F	—
*Nonane	200	1,050	250	1,300
Octachloronaphthalene — Skin	—	0.1	—	0.3
*Octane	300	1,450	375	1,800
Oil mist, particulate	—	5[f]	—	10
Oil mist, vapor	[g]B3	—	B3	—
Osmium tetroxide, as Os	0.0002	0.002	0.0006	0.006
Oxalic acid	—	1	—	2
Oxygen difluoride	0.05	0.1	0.15	0.3
Ozone	0.1	0.2	0.3	0.6
Paraffin wax fume	—	2	—	6
**Paraquat — Skin	—	(0.5)	—	0.5
Parathion — Skin	—	0.1	—	0.3
Particulate polycyclic aromatic hydrocarbons (PPAH) as benzene solubles	—	0.2A1a	—	0.2A1a
Pentaborane	0.005	0.01	0.015	0.03
Pentachloronaphthalene — Skin	—	0.05	—	1.5
Pentachlorophenol — Skin	—	0.5	—	1.5
Pentaerythritol	—	E	—	20
*Pentane	600	1,800	750	2,250
2-Pentanone	200	700	250	875
Perchloroethylene — Skin	100	670	150	1,000
Perchloromethyl mercaptan	0.1	0.8	0.1	0.8
Perchloryl fluoride	3	14	6	28
Petroleum distillates (naphtha)	[g]B3	—	B3	—
Phenol — Skin	5	19	10	38
Phenothiazine — Skin	—	5	—	10
p-Phenylene diamine — Skin	—	0.1	—	0.1
Phenyl ether (vapor)	1	7	2	14
Phenyl ether-Diphenyl mixture (vapor)	1	7	2	14
Phenylethylene, see Styrene	100	420	125	525
Phenyl glycidyl ether (PGE)	10	60	15	90
Phenylhydrazine — Skin	5	22	10	44
C Phenylphosphine	0.05	0.25	0.05	0.25
Phorate (Thimet®) — Skin	—	0.05	—	0.15
Phosdrin (Mevinphos®) — Skin	0.01	0.1	0.03	0.3
*Phosgene (carbonyl chloride)	0.10	0.4	0.05	0.2

Capital letters refer to Appendices.
Footnotes (a thru h) see Page 435.
*1976 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Phosphine	0.3	0.4	1	1
Phosphoric acid	—	1	—	3
Phosphorus (yellow)	—	0.1	—	0.3
Phosphorus pentachloride	—	1	—	3
Phosphorus pentasulfide	—	1	—	3
Phosphorus trichloride	0.5	3	0.5	3
*Phthalic anhydride	1	6	4	24
Picloram (Tordon®)	—	10	—	20
Picric acid — Skin	—	0.1	—	0.3
Pival® (2-Pivalyl-1, 3-indandione)	—	0.1	—	0.3
Plaster of Paris	—	E	—	20
Platinum (Soluble salts) as Pt	—	0.002	—	0.002
Polychlorobiphenyls, see Chlorodiphenyls	—	—	—	3
Polytetrafluoroethylene decomposition products	—	B1	—	B1
C Potassium hydroxide	—	2	—	2
Propane	F	—	F	—
β-Propiolactone	—	A2	—	A2
Propargyl alcohol — Skin	1	2	3	6
n-Propyl acetate	200	840	250	1,050
Propyl alcohol — Skin	200	500	250	625
n-Propyl nitrate	25	110	40	140
Propylene	F	—	F	—
Propylene dichloride (1, 2-Dichloropropane)	75	350	115	525
Propylene glycol monomethyl ether	100	360	150	450
Propylene imine — Skin	2	5	2	5
Propylene oxide	100	240	150	360
Propyne, see Methyl-acetylene	1,000	1,650	1,250	2,050
Pyrethrum	—	5	—	10
Pyridine	5	15	10	30
Quinone	0.1	0.4	0.3	1
RDX — Skin	—	1.5	—	3
*Resorcinol	10	45	20	90
Rhodium, Metal fume and dusts (as Rh)	—	0.1	—	0.3
Soluble salts	—	0.001	—	0.003
Ronnel	—	10	—	10
Rosin core solder pyrolysis products (as formaldehyde)	—	0.1	—	0.3
Rotenone (commercial)	—	5	—	10
Rouge	—	E	—	20
Selenium compounds (as Se)	—	0.2	—	0.2
Selenium hexafluoride, as Se	0.05	0.4	0.05	0.4
Sevin® (see Carbaryl)	—	5	—	10
Silane (see Silicon tetrahydride)	0.05	0.7	1	1.5
Silicon	—	E	—	20
Silicon carbide	—	E	—	20
Silicon tetrahydride (Silane)	0.5	0.7	1	1.5
Silver, metal and soluble compounds, as Ag	—	0.01	—	0.03
*C Sodium azide	0.1	0.3	0.1	0.3
Sodium fluoroacetate (1080) — Skin	—	0.05	—	0.15
C Sodium hydroxide	—	2	—	2
Starch	—	E	—	20
Stibine	0.1	0.5	0.3	1.5
*Stoddard solvent	100	575	150	720
Strychnine	—	0.15	—	0.45
Styrene, monomer (Phenylethylene)	100	420	125	525
**Succinaldehyde (see Glutaraldehyde)	—	(0.25)	—	—
C Subtilisins (Proteolytic enzymes as 100% pure crystalline enzyme)	—0.00006[o]		—	0.00006
Sucrose	—	E	—	20
Sulfur dioxide	5	13	5	13
Sulfur hexafluoride	1,000	6,000	1,250	7,500
Sulfuric acid	—	1	—	1
Sulfur monochloride	1	6	3	18
Sulfur pentafluoride	0.025	0.25	0.075	0.75
Sulfur tetrafluoride	0.1	0.4	0.3	1
Sulfuryl fluoride	5	20	10	40
Systox, see Demeton®	0.01	0.1	0.03	0.3
2, 4, 5-T	—	10	—	20
Tantalum	—	5	—	10
TEDP — Skin	—	0.2	—	0.6
Teflon® decomposition products	—	B1	—	B1
Tellurium	—	0.1	—	0.1
Tellurium hexafluoride, as Te	0.02	0.2	0.02	0.2
TEPP — Skin	0.004	0.05	0.012	0.15
C Terphenyls	1	9	1	9
1, 1, 1, 2-Tetrachloro-2, 2-difluoroethane	500	4,170	625	5,210
1, 1, 2, 2-Tetrachloro-1, 2-difluoroethane	500	4,170	625	5,210
1, 1, 2, 2-Tetrachloroethane — Skin	5	35	10	70
Tetrachloroethylene, see Perchloroethylene	100	670	150	1,000
Tetrachloromethane, see Carbon tetrachloride	10	65	20	130
Tetrachloronaphthalene — Skin	—	2	—	4
Tetraethyl lead (as Pb) — Skin	—	0.100[h]	—	0.3
Tetrahydrofuran	200	590	250	700

Capital letters refer to Appendices.
*1976 Addition.

Capital letters refer to Appendices.
Footnotes (a thru h) see Page 435.
o) See Page 436.
*1976 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	TENTATIVE VALUES STEL ppm[a]	STEL mg/m³[b]
Tetramethyl lead as (Pb) — Skin	—	0.150[h]	—	0.45
Tetramethyl succinonitrile — Skin	0.5	3	1.5	9
Tetranitromethane	1	8	1	8
Tetryl (2, 4, 6-trinitrophenyl-methylnitramine) — Skin	—	1.5	—	3.0
Thallium (soluble compounds) — Skin (as Tl)	—	0.1	—	0.1
*4, 4'-Thiobis (6-tert. butyl-m-cresol)	—	10	—	20
Thiram®	—	5	—	10
Tin (inorganic compounds, except SnH_4 and SnO_2) as Sn	—	2	—	4
Tin (organic compounds) — Skin (as Sn)	—	0.1	—	0.2
Tin oxide	—	E	—	20
Titanium dioxide	—	E	—	20
Toluene (toluol) — Skin	100	375	150	560
C Toluene-2, 4-diisocyanate (TDI)	0.02	0.14	0.02	0.14
o-Toluidine	5	22	10	44
Toxaphene, see Chlorinated camphene	—	0.5	—	1.5
Tributyl phosphate	—	5	—	5
1, 1, 1-Trichloroethane, see Methyl chloroform	350	1,900	440	2,380
1, 1, 2-Trichloroethane — Skin	10	45	20	90
Trichloroethylene	100	535	150	800
**Trichloromethane, see Chloroform	(25)	(120)	25A2	—
Trichloronaphthalene — Skin	—	5	—	10
1, 2, 3-Trichloropropane	50	300	150	450
1, 1, 2-Trichloro 1, 2, 2-trifluoroethane	1,000	7,600	1,250	9,500
Triethylamine	25	100	40	150
Tricyclohexyltin hydroxide (Plictran®)	—	5	—	10
Trifluoromonobromo-methane	1,000	6,100	1,200	7,625
Trimethyl benzene	25	120	135	180
2, 4, 6-Trinitrophenol, see Picric acid	—	0.1	—	0.3
2, 4, 6-Trinitrophenyl-methylnitramine, see Tetryl	—	1.5	—	3.0
**Trinitrotoluene (TNT) — Skin	—	(1.5)	—	4.5
Triorthocresyl phosphate	—	0.1	—	0.3
Triphenyl phosphate	—	3	—	6
Tungsten & compounds, as W				
Soluble	—	1	—	3
Insoluble	—	5	—	10
Turpentine	100	560	150	840
Uranium (natural) soluble & insoluble compounds, as U	—	0.2	—	0.6
Vanadium (V_2O_5) as V Dust	—	0.5	—	1.5
C Fume	—	0.05	—	0.05
Vinyl acetate	10	30	20	60
Vinyl benzene, see Styrene	100	420	150	630
Vinyl bromide	250	1,100	250	1,100
**Vinyl chloride	(200)	(510)	A1c	A1c
Vinyl cyanide, see Acrylonitrile	20	45	30	70
Vinylidene chloride	10	40	20	80
Vinyl toluene	100	480	150	720
Warfarin	—	0.1	—	0.3
*Welding fumes (Total particulate)	—	5, B4	—	5, B4
Wood dust (nonallergenic)	—	5	—	10
Xylene (o-, m-, p-isomers) — Skin	100	435	150	655
*C m-Xylene α, α'-diamine	—	0.1	—	0.1
Xylidene — Skin	5	25	10	50
Yttrium	—	1	—	3
Zinc chloride fume	—	1	—	2
Zinc oxide fume	—	5	—	10
Zinc stearate	—	E	—	20
Zirconium compounds (as Zr)	—	5	—	10

Capital letters refer to Appendices.
*1976 Addition
**See Notice of Intended Changes.

a) Parts of vapor or gas per million parts of contaminated air by volume at 25°C and 760 mm. Hg. pressure.
b) Approximate milligrams of substance per cubic meter of air.
d) An atmosphere concentration of not more than 0.02 ppm, or personal protection may be necessary to avoid headache for intermittent exposure.
e) $< 7\ \mu m$ in diameter.
f) As sampled by method that does not collect vapor.
g) According to analytically determined composition.
h) For control of general room air, biologic monitoring is essential for personnel control.

Radioactivity: For permissible concentrations of radioisotopes in air, see U.S. Department of Commerce, National Bureau of Standards Handbook 69, "Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure," June 5, 1969. Also, see U.S. Department of Commerce National Bureau of Standards, Handbook 59, "Permissible Dose from External Sources of Ionizing Radiation," September 24, 1954, and addendum of April 15, 1958. A report, Basic Radiation Protection Criteria, published by the National Committee on Radiation Protection, revises and modernizes the concept of the NCRP standards of 1954, 1957 and 1958; obtainable as NCRP Rept. No. 39, P.O. Box 4867, Washington, D.C. 20008.

MINERAL DUSTS

Substance

SILICA, SiO_2

Crystalline

Quartz — TLV in mppcf[i]:

$$\frac{300^{j}}{\%\ \text{quartz} + 10}$$

TLV for respirable dust in mg/m³:

$$\frac{10\ \text{mg/m}^{3k}}{\%\ \text{Respirable quartz} + 2}$$

TLV for "total dust," respirable and nonrespirable:

$$\frac{30\ \text{mg/m}^3}{\%\ \text{quartz} + 3}$$

Cristobalite ..... Use one-half the value calculated from the count or mass formulae for quartz.

Tridymite ..... Use one-half the value calculated from formulae for quartz.

Silica, fused ..... Use quartz formulae.

Tripoli ..... Use respirable[p] mass quartz formula.

****Amorphous** ..... 20 mppcf[i]

SILICATES (<1% quartz)

Asbestos, all forms†	5 fibers/cc> 5μm in length;[n] A1a
Graphite (natural)	15 mppcf
Mica	20 mppcf
Mineral wool fiber	10 mg/m³
Perlite	30 mppcf
Portland Cement	30 mppcf
Soapstone	20 mppcf
Talc (nonasbestiform)	20 mppcf
Talc (fibrous) use Asbestos limit.	
Tremolite, see Asbestos.	

COAL DUST

2 mg/m³ (respirable dust fraction < 5% quartz).
If > 5% quartz, use respirable mass formula.

NUISANCE PARTICULATES

(see Appendix E)

30 mppcf or 10 mg/m³[l]
of total dust < 1% quartz, or 5 mg/m³ respirable dust.

Conversion factors:
mppcf × 35.3 = Million particles per cubic meter
= particles per c.c.

i) Millions of particles per cubic foot of air, based on impringer samples counted by light-field technics.

j) The percentage of quartz in the formula is the amount determined from airborne samples, except in those instances in which other methods have been shown to be applicable.

k) Both concentration and percent quartz for the application of this limit are to be determined from the fraction passing a size-selector with the following characteristics:

Aerodynamic Diameter (μm) (unit density sphere)	% passing selector
≤ 2	90
2.5	75
3.5	50
5.0	25
10	0

†A more stringent TLV for crocidolite may be required.

l), n) See p. 00.

**See Notice of Intended Changes.

l) containing <1% quartz; if quartz content >1%, use formulae for quartz.

m) Lint-free dust as measured by the vertical-elutriator, cotton-dust sampler described in the Transactions of the National Conference on Cotton Dust, Jr. R. Lynch, pg. 33, May 2, 1970.

n) As determined by the membrane filter method at 400-450X magnification (4 mm objective) phase contrast illumination.

o) Based on "high volume" sampling.

p) "Respirable" dust as defined by the British Medical Research Council Criteria (1) and as sampled by a device producing equivalent results (2).
(1) Hatch, T.E. and Gross, P., Pulmonary Deposition and Retention of Inhaled Aerosols, p. 149. Academic Press, New York, New York 1964.
(2) Interim Guide for Respirable Mass Sampling, AIHA Aerosol Technology Committee, AHIA J. 31:2, 1970, p. 133.

NOTICE OF INTENDED CHANGES (for 1976)

These substances, with their corresponding values, comprise those for which either a limit has been proposed for the first time, or for which a change in the "Adopted" listing has been proposed. In both cases, the proposed limits should be considered trial limits that will remain in the listing for a period of at least two years. If, after two years no evidence comes to light that questions the appropriateness of the values herein, the values will be reconsidered for the "Adopted" list. Documentation is available for each of these substances.

Substance	ppm[a]	mg/m³[b]
†Aliphatic solvent "140 Flash"	25	150
Antimony trioxide, handling & use, as Sb	—	0.5
Antimony trioxide production	—	A2, 0.05
Arsenic trioxide production	—	A1a, 0.05
†Atrazine	—	10
Benzene — Skin	A2, 10	A2, 30
Borates, tetra, sodium salts, Anhydrous	—	1
Decahydrate	—	5
Pentahydrate	—	1
†Butyl acrylate	10	55
C Cadmium oxide production	—	A2, 0.05
†Calcium hydroxide	—	5
†Calcium Oxide	—	2
Captafol (Difolatan®) — Skin	—	0.1
†Carbonyl fluoride	5	15
Catechol (Pyrocatechol)	5	20
†Chloroform	A2, 10	50
Chromite ore processing (as Cr)	—	A1a, 0.05
†Cobalt metal, fume and dust (as Co)	—	0.05
Cyanamide	—	2
†Dichloromonofluoromethane	500	2,100
Dicrotophos (Bidrin®) — Skin	—	0.25
†Dimethyl carbamyl chloride	A2	A2
C Dimethyl sulfate	A2, 1	A2, 5
Dioxathion (Delnav®)	—	0.2
Diuron	—	10
†Glutaraldehyde (Activated and unactivated)	0.3	1.2
†Hexamethyl phosphoramide — Skin	A2	A2
Hydrazine	0.1	0.1
Isophorone diisocyanate — Skin	0.01	0.06
†Manganese tetroxide	—	1

Capital letters refer to Appendices.

†1976 Revision or Addition.

Substance	ppm[a]	mg/m³[b]
Methomyl (Lannate®) — Skin	—	2.5
†4,4'-Methylene dianiline	—	A2
†N, Methyl-2-pyrrolidone	100	400
Monocrotophos (Azodrin®)	—	0.25
Nickel carbonyl	0.05	0.35
†Nickel sulfide roasting, as Ni	—	A1a, 1
†Paraquat, respirable sizes	—	0.1
†Phenyl mercaptan	0.5	2
†Phosgene	0.1	0.4
Phthalic anhydride	1	6
m-Phthalodinitrile	—	5
†C Propylene glycol dinitrate — Skin	0.2	2
Rubber solvent	400	1,600
†"60 Solvent"	100	450
†"70 Solvent"	50	300
†Thioglycolic acid	1	5
C 1, 2, 4-Trichlorobenzene	5	40
†Trimethyl phosphite	0.5	2.6
†C 2, 4, 6-Trinitrotoluene (TNT)	—	0.5
†Valeraldehyde	50	175
Vinyl chloride	Pending, A1c	—
Vinyl cyclohexene dioxide	10	60
†VM & P Naphtha	400	1,800
Zinc chromate, as Cr	—	0.05A2

NOTICE OF INTENDED CHANGES
MINERAL DUSTS

Substance	TLV
†Silica, amorphous	5 mg/m³ Total dust (all sampled sizes) 2 mg/m³ Respirable dust (< 5 μm)
†Diatomaceous earth, natural	1.5 mg/m³, Respirable dust

NOTICE OF INTENDED CHANGES
APPENDIX A
CARCINOGENS

The Committee lists below those substances in industrial use that have proven carcinogenic in man, or have induced cancer in animals under appropriate experimental conditions. Present listing of those substances carcinogenic for man takes three forms: Those for which a TLV has been assigned (1a), those for which environmental conditions have not been sufficiently defined to assign a TLV (1b), and (1c), those whose reassignment of a TLV is awaiting more definitive data, and hence should be treated as a 1-b carcinogen.

A1a. *Human Carcinogens.* Substances or substances associated with industrial processes, recognized to have carcinogenic or cocarcinogenic potential, with an assigned TLV*:

	TLV
Arsenic trioxide production	As_2O_3, 0.05 mg/m³ as As SO_2, C 5.0 ppm Sb_2O_3, 0.05 mg/m³ as Sb
Asbestos, all forms*	5 fibers/cc, > 5 μm in length
bis (Chloromethyl) ether	0.001 ppm
Chromite ore processing	0.05 mg/m³ as Cr
Nickel sulfide roasting, fume & dust	1.0 mg/m³ as Ni
Particulate Polycyclic Aromatic Hydrocarbons (PPAH)	0.2 mg/m³, as benzene solubles

1b. *Human Carcinogens.* Substances or substances associated with industrial processes, recognized to have carcinogenic potential without an assigned TLV:

4-Aminodiphenyl (p-Xenylamine)
Benzidine production
beta-Naphthylamine
4-Nitrodiphenyl

1c. *Human Carcinogens.* Substances with recognized carcinogenic potential awaiting reassignment of TLV pending further data acquisition:

Vinyl chloride

For the substances in 1b, no exposure or contact by any route — respiratory, skin or oral, as detected by the most sensitive methods — shall be permitted.
"No exposure or contact" means hermitizing the process or operation by the best practicable engineering methods. The worker should be properly equipped to insure virtually no contact with the carcinogen.

A2. *Industrial Substances Suspect of Carcinogenic Potential for MAN.* Chemical substances or substances associated with industrial processes, which are suspect of inducing cancer, based on either (1) limited epidemiologic evidence, exclusive of clinical reports of single cases, or (2) demonstration of carcinogenesis in one or more animal species by appropriate methods.

Antimony trioxide production*	0.5 mg/m³
Benzene — Skin	10 ppm
Benz(a)pyrene	—
Beryllium	2.0 μg/m³
Cadmium oxide production	0.05 mg/m³
Chloroform	10 ppm
Chromates of lead and zinc (as Cr)	0.5 mg/m³
3, 3'-Dichlorobenzidine	—
Dimethylcarbamyl chloride	—
1, 1-Dimethyl hydrazine	0.5 ppm
Dimethyl sulfate	1 ppm
Eqichlorhydrin	5 ppm
Hexamethyl phosphoramide — Skin	—
Hydrazine	0.1 ppm
4, 4'-Methylene bis (2-chloroaniline) — Skin	0.02 ppm
4, 4'-Methylene dianiline	—
Monomethyl hydrazine	0.2 ppm
Nitrosamines	—
Propane sultone	—
beta-Propiolactone	—
Thallium	0.1 mg/m³
Vinyl cyclohexene dioxide	10 ppm

For the above, worker exposure by all routes should be carefully controlled to levels consistent with the animal and human experience data (see Documentation), including those substances with a listed TLV.

Capital letters refer to Appendices.
†1976 Revision or Addition.

*Cigarette smoking can enhance the incidence of bronchogenic carcinoma from this and others of these substances or processes.

A3. *Guidelines for the Classification of Experimental ANIMAL Carcinogens.* The following guidelines are offered in the present state of knowledge as an aid in classifying substances in the occupational environment found to be carcinogenic in experimental animals. A need was felt by the Threshold Limits Committee for such a classification in order to take the first step in developing an appropriate TLV for occupational exposure.

Determination of Approximate Threshold of Response Requirement. In order to determine in which category to classify an experimental carcinogen for the purpose of assigning an industrial air limit (TLV), an approximate threshold of neoplastic response must be determined. Because of practical experimental difficulties, a precisely defined threshold cannot be attained. For the purposes of standard-setting, this is of little moment, as an appropriate risk, or safety, factor can be applied to the approximate threshold, the magnitude of which is dependent on the degree of potency of the carcinogenic response.

To obtain the best 'practical' threshold of neoplastic response, dosage decrements should be less than logarithmic. This becomes particularly important at levels greater than 10 ppm (or corresponding mg/m^3). Accordingly, after a range-finding determination has been made by logarithmic decreases, two additional dosage levels are required within the levels of "effect" and "no effect" to approximate the true threshold of neoplastic response.

The second step should attempt to establish metabolic relationship between animal and man for the particular substance found carcinogenic in animals. If the metabolic pathways are found comparable, the substance should be classed highly suspect as a carcinogen for man. If no such relation is found, the substance should remain listed as an experimental animal carcinogen until evidence to the contrary is found.

Proposed Classification of Experimental Animal Carcinogens. Substances occurring in the occupational environment found carcinogenic for animals may be grouped into three classes, those of high, intermediate and low potency. In evaluating the incidence of animal cancers, significant incidence of cancer is defined as a neoplastic response which represents, in the judgment of the Committee, a significant excess of cancers above that occurring in negative controls.

EXCEPTIONS: No substance is to be considered an occupational carcinogen of any practical significance which reacts by the respiratory route at or above 1000 mg/m^3 for the mouse, 2000 mg/m^3 for the rat; by the dermal route, at or above 1500 mg/kg for the mouse, 3000 mg/kg for the rat; by the gastrointestinal route at or above 500 mg/kg/d for a lifetime, equivalent to about 100 g T.D. for the rat 10g T.D. for the mouse.

These dosage limitations exclude such substances as dioxane and trichlorethylene from consideration as carcinogens.

Examples: Dioxane — rats, hepatocellular and nasal tumors from 1015 mg/kg/d, oral

Trichloroethylene — female mice, tumors (30/98 @ 900 mg/kg/d), oral

A3a. *INDUSTRIAL SUBSTANCES OF HIGH CARCINOGENIC POTENCY IN EXPERIMENTAL ANIMALS*

1. A substance to qualify as a carcinogen of high potency must fulfill one of the three following conditions in two animal species:

1a. *Respiratory.* Elicit cancer from (1) dosages below 1 mg/m^3 (or equivalent ppm) via the respiratory tract in 6- 7-hour daily repeated inhalation exposures throughout lifetime; or (2) from a single intratracheally administered dose not exceeding 1 mg of particulate, or liquid, per 100 ml or less of animal minute respiratory volume;

Examples: bis-Chloromethyl ether, malignant tumors, rats, @ 0.47 mg/m^3 (0.1 ppm) in 2 years;

Hexamethyl phosphoramide, nasal squamous cell carcinoma, rats @ 0.05 ppm, in 13 months.

1b. *Dermal.* Elicit cancer within 20 weeks by skin-painting, twice weekly at 2 mg/kg body weight or less per application for a total dose equal to or less than 1.5 mg, in a biologically inert vehicle;

Examples: 7,12-Dimethylbenz(a)anthracene — skin tumors @ 0.12-0.8 mg T.D. in four weeks

Benz(a)pyrene, mice 12 μg, 3X/wk for 18 mos. T.D. 2.6 mg, 90.9% skin tumors

OR

1c. *Gastrointestinal.* Elicit cancer by daily intake via the gastrointestinal tract, within six months, with a six-month holding period, at a dosage below 1 mg/kg body weight per day; total dose, rat ≤ 50 mg; mouse, ≤ 3.5 mg;

Examples: 7,12-Dimethylbenz(a)anthracene — mammary tumors from 10 mg 1X

3-Methylcholanthrene — Tumors @ 3 sites from 8 mg in 89 weeks.

Benz(a)pyrene, mice, 3.9% leukemias, from 30 mg T.D. 198 days.

2. Elicit cancer by all three routes in at least two animal species at does levels prescribed for high or intermediate potency.

A3b. *INDUSTRIAL SUBSTANCES OF INTERMEDIATE CARCINOGENIC POTENCY IN EXPERIMENTAL ANIMALS*

To qualify as a carcinogen of intermediate potency, a substance should elicit cancer in two animal species at dosages intermediate between those described in A3a and A3c by two routes of administration.

Example: Carbamic acid ethyl ester
Dermal, mammary tumors, mice, 100%, 63 weeks, 500-1400 mg T.D. Gastrointestinal, various type tumors, mice 42 weeks, 320 mg T.D.

Gastrointestinal, various type tumors, rats, 60 weeks, 110-930 mg T.D.

A3c. *INDUSTRIAL SUBSTANCES OF LOW CARCINOGENIC POTENCY IN EXPERIMENTAL ANIMALS*

To qualify as a carcinogen of low potency, a substance should elicit cancer in one animal species by any *one* of

three routes of administration at the following prescribed dosages and conditions:

1a. *Respiratory.* Elicit cancer from (1) dosages greater than 10 mg/m^3 (or equivalent ppm) via the respiratory tract in 6- 7-hour, daily repeated inhalation exposures, for 12 months' exposure and 12 months' observation period; or (2) from intratracheally administered dosages totaling more than 10 mg of particulate or liquid per 100 ml or more of animal minute respiratory volume;

Examples: Beryl (beryllium aluminum silicate) malig. lung tumors, rats, @ 15 mg/m^3 @ 17 months

Benzidine, var. tumors, rats, 10-20 mg/m^3 @ > 13 mos.

OR

1b. *Dermal.* Elicit cancer by skin-painting of mice in twice-weekly dosages of > 10 mg/kg body weight in a biologically inert vehicle for at least 75 weeks, i.e., ≥ 1.5g T.D.

Examples: Shale tar, mouse, 0.1 ml × 50 – g T.D. 59/60 skin tumors.

Arsenic trioxide, man, dose unknown, but estimated to be high

1c. *Gastrointestinal.* Elicit cancer from daily oral dosages of 50 mg/kg/day or greater during the lifetime of the animal.

APPENDIX B

B1 *Polytetrafluoroethylene* decomposition products.* Thermal decomposition of the fluorocarbon chain in air leads to the formation of oxidized products containing carbon, fluorine and oxygen. Because these products decompose in part by hydrolysis in alkaline solution, they can be quantitatively determined in air as fluoride to provide an index of exposure. No TLV is recommended pending determination of the toxicity of the products, but air concentrations should be minimal.

B2 *Gasoline.* The composition of gasoline varies greatly and thus a single TLV for all types of these materials is no longer applicable. In general, the aromatic hydrocarbon content will determine what TLV applies. Consequently the content of benzene, other aromatics and additives should be determined to arrive at the appropriate TLV (Elkins, et al. A.I.H.A.J. *24*:99, 1963); Runion, ibid, *36*, 338, 1975).

Notice of intended changes

B3 *Petroleum Distillates.* For petroleum distillates for which no specific TLV's are listed, approximate values can be obtained by use of the following equation:

$$TLV = \frac{100}{\frac{\%Al}{3.6(200 - B.P.\,^\circ C.) + 20} + \frac{\%Ar}{1.3(200 - B.P.\,^\circ C) + 10}}\ ppm$$

where Al = aliphatic component
Ar = aromatic component
B.P. = mean boiling point in degrees centigrade (normally the 50% distillation temperature).

The equation cannot be used if the benzene content of the fraction exceeds 1%, nor if the mean boiling point is above 200° C.

It may also lead to error if there are large amounts of hexane or cyclohexane in the distillate.

If the molecular weight (average) is not known for the mixture, it can be approximated by the following equation:

$$M.W. = \%Al + 0.88\%Ar + 0.5(B.P.^\circ C. - 100)$$

B4 *Welding Fumes* —

Total Particulate (NOC) TLV, 5 mg/m^3*

Welding fumes cannot be classified simply. The composition and quantity of both are dependent on the alloy being welded and the process and electrodes used. Reliable analysis of fumes cannot be made without considering the nature of the welding process and system being examined; reactive metals and alloys such as aluminum and titanium are arc-welded in a protective, inert atmosphere such as argon. These arcs create relatively little fume, but an intense radiation which can produce ozone. Similar processes are used to arc-weld steels, also creating a realtively low level of fumes. Ferrous alloys also are arc-welded in oxidizing environments which generate considerable fume, and can produce carbon monoxide instead of ozone. Such fumes generally are composed of discreet particles of amorphous slags containing iron, manganese, silicon and other metallic constituents depending on the alloy system involved. Chromium and nickel compounds are found in fumes when stainless steels are arc-welded. Some coated and flux-cored electrodes are formulated with fluorides and the fumes associated with them can contain significantly more fluorides than oxides. Because of the above factors, arc-welding fumes frequently must be tested for individual constituents which are likely to be present to determine whether specific TLV's are exceeded. Conclusions based on total fume concentration are generally adequate if no toxic elements are present in welding rod, metal, or metal coating and conditions are not conducive to the formation of toxic gases.

Most welding, even with primitive ventilation, does not produce exposures inside the welding helmet above 5 mg/m^3. That which does, should be controlled.

APPENDIX C

C.1 THRESHOLD LIMIT VALUES FOR MIXTURES

When two or more hazardous substances are present, their combined effect, rather than that of either individually, should be given primary consideration. In the absence of information to the contrary, the effects of the different hazards should be considered as additive. That is, if the sum of the following fractions,

$$\frac{C_1}{T_1} + \frac{C_1}{T_2} + \cdots \frac{C_n}{T_n}$$

exceeds unity, then the threshold limit of the mixture should be considered as being exceeded. C_1 indicates the observed atmospheric concentration, and T_1 the corresponding threshold limit (See Example 1A.a. and 1A.c.).

Exceptions to the above rule may be made when there is a good reason to believe that the chief effects of the different

*Trade Names: Algoflon, Fluon, Halon, Teflon, Tetran.

harmful substances are not in fact additive, but *independent* as when purely local effects on different organs of the body are produced by the various components of the mixture. In such cases the threshold limit ordinarily is exceeded only when at least one member of the series $\left(\frac{C_1}{T_1} + \text{or} + \frac{C_2}{T_2} \text{ etc.}\right)$ itself has a value exceeding unity (See Example 1A.c.).

Antagonistic action or potentiation may occur with some combinations of atmospheric contaminants. Such cases at present must be determined individually. Potentiating or antagonistic agents are not necessarily harmful by themselves. Potentiating effects of exposure to such agents by routes other than that of inhalation is also possible, e.g. imbibed alcohol and inhaled narcotic (trichloroethylene). Potentiation is characteristically exhibited at high concentrations, less probably at low.

When a given operation or process characteristically emits a number of harmful dusts, fumes, vapors or gases, it will frequently be only feasible to attempt to evaluate the hazard by measurement of a single substance. In such cases, the threshold limit used for this substance should be reduced by a suitable factor, the magnitude of which will depend on the number, toxicity and relative quantity of the other contaminants ordinarily present.

Examples of processes which are typically associated with two or more harmful atmospheric contaminants are welding, automobile repair, blasting, painting, lacquering, certain foundry operations, diesel exhausts, etc.

C.1A *Examples of THRESHOLD LIMIT VALUES FOR MIXTURES*

The following formulae apply only when the components in a mixture have similar toxicologic effects; they should not be used for mixtures with widely differing reactivities, e.g. hydrogen cyanide & sulfur dioxide. In such case the formula for Independent Effects (1A.c.) should be used.

1A.a. General case, where air is analyzed for each component:

a. *Additive effects (Note: It is essential that the atmosphere be analyzed both qualitatively and quantitatively for each component present, in order to evaluate compliance or noncompliance with this calculated TLV.)*

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \frac{C_3}{T_3} + \ldots = 1$$

Example No. 1A.a.: Air contains 5 ppm of carbon tetrachloride (TLV = 10 ppm) 20 ppm of 1, 2-dichloroethane (TLV = 50 ppm) and 10 ppm of 1, 2-dibromoethane (TLV = 20 ppm)

Atmospheric concentration of mixture = 5 + 20 + 10 = 35 ppm of mixture

$$\frac{5}{10} + \frac{20}{50} + \frac{10}{20} = \frac{25 + 20 + 25}{50} = 1.4$$

Threshold Limit is exceeded. Furthermore, the TLV of this mixture may be calculated by reducing the total fraction to 1.0; i.e.

$$\text{TLV of mixture} = \frac{35}{1.4} = 25 \text{ ppm}$$

1A.b. Special case when the source of contaiminant is a liquid mixture and the atmospheric composition is *assumed* to be similar to that of the original material; e.g. on a time-weighted average exposure basis, all of the liquid (solvent) mixture eventually evaporates.

Additive effects (approximate solution)

1. The percent composition (by weight) of the liquid mixture is known, the TLVs of the constituents must be listed in mg/m^3.

(Note: In order to evaluate compliance with this TLV, field sampling instruments should be calibrated, in the laboratory, for response to this specific quantitative and qualitative air-vapor mixture, and also to fractional concentrations of this mixture; e.g., 1/2 the TLV; 1/10 the TLV/ 2 × the TLV; 10 × the TLV; etc.)

$$\text{TLV of mixture} = \frac{1}{\frac{f_a}{TLV_a} + \frac{f_b}{TLV_b} + \frac{f_c}{TLV_c} + \ldots \frac{f_n}{TLV_n}}$$

Example No. 1: Liquid contains (by weight)
50% heptane: TLV = 400 ppm or 1600 mg/m^3
1 mg/m^3 ≡ 0.25 ppm
30% methylene chloride: TLV = 200 ppm or 720 mg/m^3
1 mg/m^3 ≡ 0.28 ppm
20% perchloroethylene: TLV = 100 ppm or 670 mg/m^3
1 mg/m^3 ≡ 0.15 ppm

$$\text{TLV of Mixture} = \frac{1}{\frac{0.5}{1600} + \frac{0.3}{720} + \frac{0.2}{670}}$$

$$= \frac{1}{0.00031 + 0.00042 + 0.00030}$$

$$= \frac{1}{0.00103} = 970 \text{ mg/m}^3$$

of this mixture
50% or (970) (0.5) = 485 mg/m^3 is heptane
30% or (970) (0.3) = 291 mg/m^3 is methylene chloride
20% or (970) (0.2) = 194 mg/m^3 is perchloroethylene

These values can be converted to ppm as follows:

heptane: 485 mg/m^3 × 0.25 ppm (≡ 1 mg/m^3) = 121 ppm
methylene chloride: 291 mg/m^3 × 0.28 ppm (≡ 1 mg/m^3) = 81 ppm
perchloroethylene: 194 mg/m^3 × 0.15 ppm (≡ 1 mg/m^3) = 29 ppm

TLV of mixture = 121 + 81 + 29 = 231 ppm, or 970 mg/m^3

Example No. 2. Liquid solvent contains (by weight)

50% isopropyl alcohol: TLV = 400 ppm or 980 mg/m^3
1 mg/m^3 ≡ 0.41 ppm
30% dichloroethane: TLV = 50 ppm or 200 mg/m^3
1 mg/m^3 ≡ 0.25 ppm
20% perchloroethylene: TLV = 100 ppm or 670 mg/m^3
1 mg/m^3 ≡ 0.15 ppm

$$\text{TLV of Mixture} = \frac{1}{\frac{0.5}{980} + \frac{0.3}{200} + \frac{0.2}{670}}$$

$$= \frac{1}{0.00051 + 0.0015 + 0.000298}$$

$$= \frac{1}{0.002308} = 433 \text{ mg/m}^3$$

of this mixture
50% or (433) (0.5) = 2.6 mg/m^3 is isopropyl alcohol
30% or (433) (0.3) = 130 mg/m^3 is dichloroethane
20% or (433) (0.2) = 87 mg/m^3 is perchloroethylene

These values can be converted to ppm as follows:

$$\text{isopropyl alcohol: } 216 \frac{\text{mg}}{\text{m}^3} \times 0.41 \text{ ppm } (\equiv \text{mg/m}^3) = 89 \text{ ppm}$$

$$\text{dichloroethane: } 130 \frac{\text{mg}}{\text{m}^3} \times 0.25 \text{ ppm } (\equiv \text{mg/m}^3) = 33 \text{ ppm}$$

$$\text{perchloroethylene: } 87 \frac{\text{mg}}{\text{m}^3} \times 0.15 \text{ ppm } (\equiv \text{mg/m}^3) = 13 \text{ ppm}$$

TLV of mixture = 89 + 33 + 13 = 135 ppm or 433 mg/m^3

1A.c. *Independent effects.*
Air contains 0.15 mg/m^3 of lead (TLV, 0.15) and 0.7 mg/m^3 of sulfuric acid (TLV, 1).

$$\frac{0.15}{0.15} = 1; \qquad \frac{0.7}{1} = 0.7$$

Threshold limit is not exceeded.

1B. TLV for Mixtures of Mineral Dusts.

For mixtures of biologically active mineral dusts the general formula for mixtures may be used.

For mixture containing 80% nonasbestiform talc and 20% quartz, the TLV for 100% of the mixture is given by:

$$\text{TLV} = \frac{1}{\frac{0.8}{20} + \frac{0.2}{2.7}} = 9 \text{ mppcf}$$

TLV of asbestiform talc (pure) = 20 mppcf
TLV of quartz (pure) =

$$\frac{300}{100 + 10} = \frac{300}{110} = 2.7 \text{ mppcf}$$

Essentially the same resultwill be obtained if the limit of the more (most) toxic component is used provided the effects are additive. In the above example the limit for 20% quartz is 10 mppcf.

For another mixture of 25% quartz, 25% amorphous silica and 50% talc:

25% quartz — TLV (pure) = 2.7 mppcf
25% amorphous silica — TLV (pure) = mppcf
50% talc TLV (pure) = 20 mppcf

$$\text{TLV} = \frac{1}{\frac{0.25}{2.7} + \frac{0.25}{20} + \frac{0.5}{20}} = 8 \text{ mppcf}$$

The limit for 25% quartz approximates 9 mppcf.

APPENDIX D
PERMISSIBLE EXCURSIONS FOR TIME-WEIGHTED AVERAGE (TWA) LIMITS

The Excursion TLV Factor in the Table automatically defines the magnitude of the permissible excursion above the limit for those substances not given a "C" designation; i.e., the TWA limits. Examples in the Table show that nitrobenzene, the TLV for which is 1 ppm, should never be allowed to exceed 3 ppm. Similarly, carbon tetrachloride, TLV = 10 ppm, should never be allowed to exceed 20 ppm. By contrast, those substances with a "C" designation are not subject to the excursion factor and must be kept at or below the TLV ceiling.

These limiting excursions are to be considered to provide a "rule-of-thumb" guidance for listed substances generally, and may not provide the most appropriate excursion for a particular substance e.g., the permissible excursion for CO is 400 ppm for 15 minutes.

For appropriate excursions for 142 substances consult Pa. Rules & Regs. Chap. 4, Art. 432, and "Acceptable Concentrations," ANSI.

Substance	TLV	Excursion Factor	Max. Conc. Permitted for short time
Nitrobenzene	1	3	3
Carbon tetrachloride	10	2	20
Trimethyl benzene	25	1.5	40
Acetone	1000	1.25	1250
Boron trifluoride	C 1	—	1
Butylamine	C 5	—	5

EXCURSION FACTORS

For all substances not bearing C notation

TLV > 0-1	(ppm or mg/m^3),	Excursion Factor	= 3
TLV > 1-10	"	"	= 2
TLV > 10-100	"	"	= 1.5
TLV > 100-1000	"	"	= 1.25

The number of times the excursion above the TLV is permitted is governed by conformity with the Time-Weighted Average TLV.

INTERPRETATION OF MEASURED PEAK CONCENTRATIONS

With increasing use of rapid, direct-reading analytical instruments for airborne contaminants in the work area, the question of interpretation of essentially "instantaneous" peaks arises. Although no general statement can be made covering all occupational substances, the following guidelines should prove helpful, assuming peak excursions conform to time-weighted average TLV as stated above.

The toxicologic importance of momentary peak concentrations depends on whether the substance is fast of slow acting. If slow acting, as for quartz, lead, or carbon monoxide, momentary peaks are of no toxicologic concern provided, of course, they are not astronomic. On the other hand, fast-acting substances that rapidly produce disabling narcosis, e.g., H_2S, or intolerable irritation or asphyxiation, NH_3, SO_2, CO_2, or initiate sensitization — the organic isocyanates, even "instantaneous" peaks appreciably above the permissible excursion, should not be permitted, unless information exists to the contrary. Other more specific excursions will be developed in the future.

APPENDIX E
Some Nuisance Particulates[q]
TLV, 30 mppcf or 10 mg/m^3

Alundum (Al_2O_3)
Calcium carbonate
Calcium silicate
Cellulose (paper fiber)
Portland Cement
Corundum (Al_2O_3)
Emery
Kaolin
Limestone
Magnesite
Marble
Mineral Wool Fiber
Pentaerythritol
Plaster of Paris

Glass, fibrous[r] or dust
Glycerin Mist
Graphite (synthetic)
Gypsum
Vegetable oil mists
(except castor, cashew nut, or similar irritant oils)
Rouge
Silicon
Silicon Carbide
Starch
Sucrose
Tin Oxide
Titanium Dioxide
Zinc Stearate
Zinc oxide dust

q) When toxic impurities are not present, e.g. quartz < 1%, and when determined by appropriate methods (cf p. 00.)
r) < 7 μm in diameter

APPENDIX F
Some Simple Asphyxiants[s]

Acetylene
Argon
Butane
Ethane
Ethylene
Helium
Hydrogen
Methane
Neon
Nitrous oxide
Propane
Propylene

s) As defined in preface.

APPENDIX G

Calculations for Conversion of Particle Count Concentration (by Standard Light Field — Midget Impinger Techniques), in mppcf, to Respirable Mass Concentration (by Respirable Sampler) in mg/m^3.†

1. In 1967, Jacobsen and Tomb,† derived an empirical relationship of 5.6 mppcf to 1 milligram of respirable dust per cubic meter of air, based on 23 sets of samples, mostly coal dust. The following calculation results in an equivalence of 6.37 mppcf to 1 mg/m^3 of respirable dust. Thus, an approximate ratio of 6 mppcf to 1 mg/m^3 of respirable dust is suggested for conversion of TLVs from a count to a mass basis when the density and mass median diameter have not been determined.
2. Basic assumptions:
   a) Average density for silica containing dusts $\approx$ 2.5 gms/cm^3 (2500 mg/cm^3). Pulmonary significant dust densities may vary from 1.2 gm/cm^3 for coal dust to 3.1 gm/cm^3 for Portland Cement. Silica densities vary from 2.2 (amorphous) to 2.3 (cristobalite and tridymite) to 2.5 (alpha-quartz.) gms per cm^3.
   b) The mass median diameter (mmd) of particles collected in midget impinger samplers and counted by the standard light field technique, *and* collected in a respirable sampler is approximately 1.5 μm or 1.5 $\times$ 10^{-4} cm. This assumption is, or course, quite arbitrary since the mmd of all dust clouds is quite variable, depending on many independent parameters, such as source of dust, age of dust cloud, meteorlogical conditions, etc.
3. Calculation:
   a) vol. per particle: $4/3\ \pi\ r^3$, $r = 0.75 \times 10^{-4}$ cm
      $= 4/3 \bullet \pi \bullet (0.75 \times 10^{-4})^3$
      $= 1.77 \times 10^{-12}$ cm^3
   b) wt. per particle = vol. $\times$ density
      $= 1.77 \times 10^{-12}$ cm$^3 \times 2.5 \times 10^3$ mg/cm^3
      $= 4.425 \times 10^{-9}$ mg/particle
   c) 1 particle/ft.^{3} = 35.5 part./m^3
      (since 35.5 cu ft = 1 cu m.)
      10^6 part.ft^3 = mppcf = 35.5×10^6 part./m^3
      wt. of 1 mppcf $\equiv 35.5 \times 10^6$ part./m$^3 \times 4.425 \times 10^{-9}$ mg/part.
      1 mppcf $\equiv$ 0.157 mg/m^3
      or
      6.37 mppcf $\equiv$ 1 mg/m
      or approximately 6 mppcf $\equiv$ 1 mg/m^3.
4. Equivalent TLVs in mppcf and mg/m^3 (respirable mass) for Mineral Dusts.

Substance	Threshold Limit Value		
	Count mppcf	Resp. Mass mg/m^3	Total Mass* mg/m^3
Silica (SiO_2)			
Amorphous	20	(3)**	(6)
Cristobalite	1.5	0.05	0.15
Fused silica	3	0.1	0.3
Quartz	3	0.1	0.3
Tridymite	1.5	0.05	0.15
Coal Dust	(12)	2	(4)
Diatomaceous earth, natural	—	1.5	—
Graphite	15	(2.5)	(5)
Mica	20	(3)	(6)
Mineral wool fiber	—	(5)	10
Nuisance particulates	30	(5)	10
Perlite	30	(5)	(10)
Portland Cement	30	(5)	(10)
Soapstone	20	(3)	(6)
Talc (nonasbestiform)	20	(3)	(6)
Tripoli	(3)	0.1	(0.3)

*Unless otherwise specified, respirable mass is presumed to equal approximately 50% of total mass.
**All values in parentheses ( ) represent newly calculated values based on equivalence of 6 mppcf $\equiv$ 1 mg/m^3 respirable mass and respirable mass = 50% total mass.

PREFACE — PHYSICAL AGENTS

These threshold limit values refer to levels of physical agents and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variations in individual susceptibility, exposure of an occasional individual at, or even below, the threshold limit may not prevent annoyance, aggravation of a pre-existing condition, or physiological damage.

These threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and when possible, from a combination of the three.

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, (1) in the evaluation or control of the levels of physical agents in the community, (2) as proof or disproof of an existing physical disability, or (3) for adoption by countries whose working conditions differ from those in the United States of America.

These values are reviewed annually by the Committee on Threshold Limits for Physical Agents for revisions or additions, as further information becomes available.

Notice of Intent — At the beginning of each year, proposed actions of the Committee for the forthcoming year are issued in the form of a "Notice of Intent." This notice provides not only an opportunity for comment, but solicits suggestions of physical agents to be added to the list. The suggestions should be accompanied by substantiating evidence.

†"Relationship Between Gravimetric Respirable Dust Concentration and Midget Impinger Number Concentration," by Murray Jacobson and T.F. Tomb, AIHAJ, 28: Nov.-Dec. 1967.

As Legislative Code — The Conference recognizes that the Threshold Limit Values may be adopted in legislative codes and regulations. If so used, the intent of the concepts contained in the Preface should be maintained and provisions should be made to keep the list current.

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THRESHOLD LIMIT VALUES

HEAT STRESS

These Threshold Limit Values refer to heat stress conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse health effects. The TLVs shown in Table 1 are based on the assumption that nearly all acclimatized, fully clothed workers with adequate water and salt intake should be able to function effectively under the given working conditions without exceeding a deep body temperature of 38° C (WHO technical report series #412, 1969 *Health Factors Involved in Working Under Conditions of Heat Stress;* F.N. Dukes-Dobos and A. Henschel: *"Development of Permissible Heat Exposure Limits for Occupational Work."* ASHRAE Journal, Vol. 15: No. 9, September 1973, pp. 57-62.)

Since measurement of deep body temperature is impractical for monitoring the workers' heat load, the measurement of environmental factors is required which most nearly correlate with deep body temperature and other physiological responses to heat. At the present time Wet Bulb-Globe Temperature Index (WBGT) is the simplest and most suitable technique to measure the environmental factors. WBGT values are calculated by the following equations:

1. Outdoors with solar load:
   WBGT = 0.7WB + 0.2GT + 0.1 DB
2. Indoors or Outdoors with no solar load:
   WBGT = 0.7WB + 0.3GT

where:

WBGT = Wet Bulb-Globe Temperature Index
WB = Natural Wet-Bulb Temperature
DB = Dry-Bulb Temperature
GT = Globe Thermometer Temperature

The determination of WBGT requires the use of a black globe thermometer, a natural (static) wet-bulb thermometer, and a dry-bulb thermometer.

TABLE 1
Permissible Heat Exposure Threshold Limit Values
(Values are given in °C. WBGT)

	Work Load		
Work - Rest Regimen	Light	Moderate	Heavy
Continuous work	30.0	26.7	25.0
75% Work — 25% Rest, Each hour	30.6	28.0	25.9
50% Work — 50% Rest, Each hour	31.4	29.4	27.9
25% Work — 75% Rest, Each hour	32.2	31.1	30.0

Higher heat exposures than shown in Table 1 are permissible if the workers have been undergoing medical surveillance and it has been established that they are more tolerant to work in heat than the average worker. Workers should not be permitted to continue their work when their deep body temperature exceeds 38.0° C.

APPENDIX G

HEAT STRESS

I. *Measurement of the Environment*

The instruments required are a dry-bulb, a natural wet-bulb, a globe thermometer, and a stand. The measurement of the environmental factors shall be performed as follows:

A. The range of the dry and the natural wet bulb thermometer shall be −5° C to 50° C with an accuracy of ±0.5° C. The dry bulb thermometer must be shielded from the sun and the other radiant surfaces of the environment without restricting the airflow around the bulb. The wick of the natural wet-bulb thermometer shall be kept wet with distilled water for at least 1/2 hour before the temperature reading is made. It is not enough to immerse the other end of the wick into a reservoir of distilled water and wait until the whole wick becomes wet by capillarity. The wick shall be wetted by direct application of water from a syringe 1/2 hour before each reading. The wick shall extend over the bulb of the thermometer, covering the stem about one additional bulb length. The wick should always be clean and new wicks should be washed before using.

B. One globe thermometer, consisting of a 15 cm. (6-inch) diameter hollow copper sphere, painted on the outside with a matte black finish or equivalent shall be used. The bulb or sensor of a thermometer (range −5° C to 100° C with an accuracy of ±0.5° C) must be fixed in the center of the sphere. The globe thermometer shall be exposed at least 25 minutes before it is read.

C. One stand shall be used to suspend the three thermometers so that they do not restrict free air flow around the bulbs, and the wet-bulb and globe thermometer are not shaded.

D. It is permissible to use any other type of temperature sensor that gives identical reading to a mercury thermometer under the same conditions.

E. The thermometers must be so placed that the readings are representative of the condition where the men work or rest, respectively.

The methodology outlined above is more fully explained in the following publications:

1. "Prevention of Heat Casualties in Marine Corps Recruits, 1955-1960, with Comparative Incidence Rates and Climatic Heat Stresses in other Training Categories," by Captain David Minard, MC, USN, Research Report No. 4 Contract No. MR005.01-0001.01, Naval Medical Research Institute, Bethesda, Maryland, 21 February 1961.

2. "Heat Casualties in the Navy and Marine Corps, 1959-1962, with Appendices on the Field Use of the Wet Bulb-Globe Temperature Index," by Captain David Minard, MC, USN, and R. L. O'Brien, HMC, USN. Research Report No. 7, Contract No. MR005.01-0001.01, Naval Medical Research Institute, Bethesda, Maryland, 12 March 1964.

3. Minard, D.: Prevention of Heat Casualties in Marine Corps Recruits. Military Medicine *126(4)*: 261-272, 1961.

TABLE 2
Assessment of Work Load

Average values of metabolic rate during different activities.

A. Body position and movement	Kcal./min.
Sitting	0.3
Standing	0.6
Walking	2.0-3.0
Walking up hill	add 0.8 per meter (yard) rise

B. Type of Work		Average Kcal./min.	Range Kcal./min.
Hand work			
	light	0.4	0.2-1.2
	heavy	0.9	
Work with one arm			
	light	1.0	0.7-2.5
	heavy	1.8	
Work with both arms			
	light	1.5	1.0-3.5
	heavy	2.5	
Work with body			
	light	3.5	2.5-15.0
	moderate	5.0	
	heavy	7.0	
	very heavy	9.0	

Light hand work: writing, hand knitting

Heavy hand work: typewriting

Heavy work with one arm; hammering in nails (shoemaker, upholsterer)

Light work with two arms: filing metal, planing wood, raking of a garden

Moderate work with the body: cleaning a floor, beating a carpet

Heavy work with the body: railroad track laying, digging, barking trees

Sample Calculation: Using a heavy hand tool on an assembly line

A. Walking along	2.0 Kcal./min.
B. Intermediate value between heavy work with two arms and light work with the body	3.0 Kcal./min.
	5.0 Kcal./min.
C. Add for basal metabolism	1.0 Kcal./min.
Total	6.0 Kcal./min.

Adapted from Lehmann, G.E., A. Muller and H. Spitzer: Der Kalorienbedarf bei gewerblicher Arbeit. Arbeitsphysiol. *14*: 166, 1950.

II. *Work Load Categories*

The heat produced by body and the environmental heat together determine the total heat load. Therefore, if work is to be performed under hot environmental conditions, the work-load category of each job shall be established and the heat exposure limit pertinent to the work load evaluated against the applicable standard in order to protect the worker from exposure beyond the permissible limit.

A. The work load category may be established by ranking each job into light, medium, and heavy categories on the basis of type of operation. Where the work load is ranked into one of said three categories, i.e.

(1) light work (up to 200 Kcal/hr or 800 Btu/hr): e.g. sitting or standing to control machines, performing light hand or arm work,

(2) moderate work (200-350 Kcal/hr or 800-1400 Btu/hr): e.g., walking about with moderate lifting and pushing,

(3) heavy work (350-500 Kcal/hr or 1400-2000 Btu/hr): e.g., pick and shovel work,

the permissible heat exposure limit for that work load shall be determined from Table 1.

B. The ranking of the job may be performed either by measuring the worker's metabolic rate while performing his job or by estimating his metabolic rate by the use of the scheme shown in Table 2. Tables available in the literature listed below and in other publications as well may also be utilized. When this method is used the permissible heat exposure limit can be determined by Figure 1.

1. Per-Olaf Astrand and Kaare Rodahl: "Textbook of Work Physiology" McGraw-Hill Book Company, New York, San Francisco, 1970.

2. "Ergonomies Guide to Assessment of Metabloic and Cardiac Costs of Physical Work." Amer. Ind. Hyg. Assoc. J. *32*:560, 1971.

3. Energy Requirements for Physical Work, Purdue Farm Cardiac Project. Agricultural Experiment Station. Research Progress Report No. 30, 1961.

4. J. V. G. A. Durnin and R. Passmore: "Energy, Work and Leisure," Heinemann Educational Books, Ltd., London, 1967.

III. *Work-Rest Regimen*

The permissible exposure limits specified in Table 1 and Figure 1 are based on the assumption that the WBGT value of the resting place is the same or very close to that of the work place. Where the WBGT of the work area is different from that of the rest area a time-weighted average value should be used for both environmental and metabolic heat. When time-weighted averge values are used the appropriate curve on Figure 1 is the solid line labeled "continuous."

The time-weighted average metabolic rate (M) shall be determined by the equation:

$$\text{Av. } M = \frac{(M_1) \times (t_2) + (M_2) \times (t_2) + \ldots + (M_n) \times (t_n)}{(t_1) + (t_2) + \ldots + (t_n)}$$

Where M_1 M_2, M_n are estimated or measured metabolic rates for the various activities of the worker during the total time period. t_1, t_2, t_n are the elapsed times in minutes spent at the corresponding metabolic rate as determined by a time study.

The time-weighted average WBGT shall be determined by the equation:

$$\text{Av. WBGT} = \frac{(WBGT_1) \times (t_1) + (WBGT_2) \times t_2 + \ldots + (WBGT_n) \times (t_n)}{(t_1) + (t_2) + \ldots + (t_n)}$$

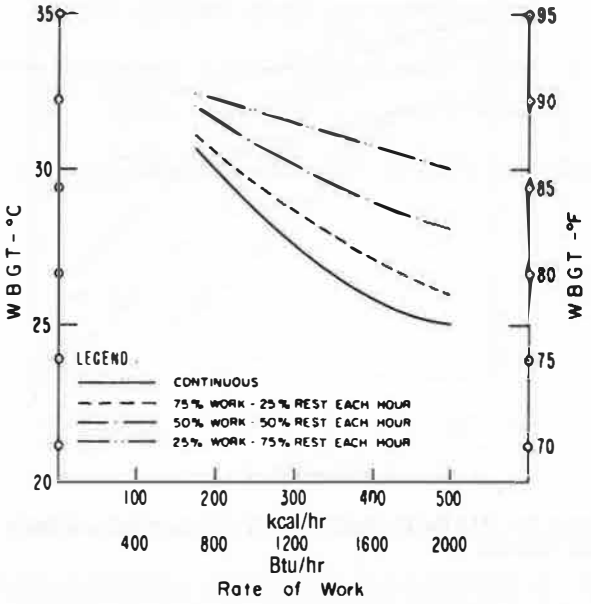

Figure 1 — Permissible Heat Exposure Threshold Limit Value.

where $WBGT_1$, $WBGT_2$, $WBGT_n$ are calculated values of WBGT for the various work and rest areas occupied during total time periods. t_1, t_2, t_n are the elapsed times in minutes spent in the corresponding areas which are determined by a time study. Where exposure to hot environmental conditions is continuous for several hours or the entire work day, the time-weighted average i.e., $t_1 + t_2 + \ldots t_n = 60$ minutes. Where the exposure is intermittent, the time-weighted averages shall be calculated as two-hour time-weighted averages, i.e., $t_1 + t_2 + \ldots t_n = 120$ minutes.

The permissible exposure limits for continuous work are applicable where there is a work-rest regimen of a 5-day work week and an 8-hour work day with a short morning and afternoon break (approximately 15 minutes) and a longer lunch break (approximately 30 minutes). Higher exposure limits are permitted if additional resting time is allowed. All breaks, including unscheduled pauses and administrative or operational waiting periods during work may be counted as rest time when additional rest allowance must be given because of high environmental temperatures.

It is a common experience that when the work on a job is self-paced, the workers will spontaneously limit their hourly work load to 30-50% of their maximum physical performance capacity. They do this either by setting an appropriate work speed or by interspersing unscheduled breaks. Thus the daily average of the workers' metabolic rate seldom exceeds 330 kcal/hr. However, within an 8-hour work shift there may be periods where the workers' hourly average metabolic rate will be higher.

IV. *Water and Salt Supplementation*

During the hot season or when the worker is exposed to artificially generated heat, drinking water shall be made available to the workers in such a way that they are stimulated to frequently drink small amounts, i.e. one cup every 15-20 minutes (about 150 ml or 1/4 pint).

The water shall be kept reasonably cool (10°-15° C or 50.0°-60.0° F) and shall be placed close to the workplace so that the worker can reach it without abandoning the work area.

The workers should be encouraged to salt their food abundantly during the hot season and particularly during hot spells. If the workers are unacclimatized, salted drinking water shall be made available in a concentration of 0.1% (1g NaCl to 1.0 liter or 1 level tablespoon of salt to 15 quarts of water). The added salt shall be completely dissolved before the water is distributed, and the water shall be kept reasonably cool.

V. *Other Considerations*

A. Clothing: The permissible heat exposure TLVs are valid for light summer clothing as customarily worn by workers when working under hot environmental conditions. If special clothing is required for performing a particular job and this clothing is heavier or it impedes sweat evaporation or has higher insulation value, the worker's heat tolerance is reduced, and the permissible heat exposure limits indicated in Table 1 and Figure 1 are not applicable. For each job category where special clothing is required, the permissible heat exposure limit shall be established by an expert.

B. Acclimatization and Fitness: The recommended heat stress TLVs are valid for acclimated workers who are physically fit.

IONIZING RADIATION

See U.S. Department of Commerce National Bureau of Standards, Handbook 59, "Permissible Dose from External Sources of Ionizing Radiation," September 24, 1954, and addendum of April 15, 1958. A report, Basic Radiation Protection Criteria, published by the National Committee on Radiation Protection, revises and modernizes the concept of the NCRP standards of 1954, 1957 and 1958; obtainable as NCRP Rept. No. 39, P.O. Box 4867, Washington, D.C. 20008.

LASERS

The threshold limit values are for exposure to laser radiation under conditions to which nearly all workers may be exposed without adverse effects. The values should be used as guides in the control of exposures and should not be regarded as fine lines between safe and dangerous levels. They are based on the best available information from experimental studies.

Limiting Apertures

The TLVs expressed as radiant exposure or irradiance in this section may be averaged over an aperture of 1 mm except for TLVs for the eye in the spectral range of 400-1400 nm, which should be averaged over a 7 mm limiting aperture (pupil); and except for all TLVs for wavelengths between 0.1-1 mm where the limiting aperture is 10 mm. No modification of the TLVs is permitted for pupil sizes less than 7 mm.

The TLVs for "extended sources" apply to sources which subtend an angle greater than α (Table 5) which varies with exposure time. This angle is *not* the beam divergence of the source.

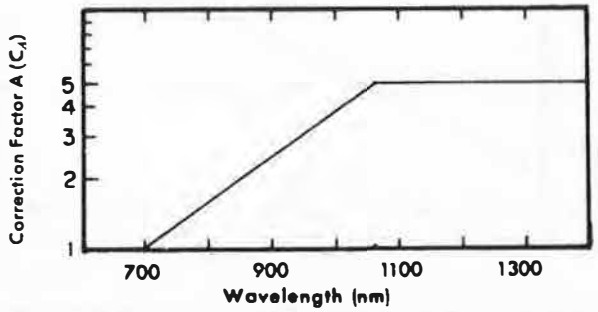

Figure 2 — TLV correction factors for laser wavelengths (eye).

Correction Factors A and B (C_A and C_B) for Eye Exposure

All TLVs in Tables 3 and 4 are to be used as given for wavelengths 400 nm to 700 nm. At all wavelengths greater than 1.06 μm and less than 1.4 μm the TLVs are to be increased by a factor of 5. TLV at wavelengths between 700 nm and 1.06 μm are to be increased by a uniformly extrapolated factor as shown in Figure 2. For certain exposure durations at wavelengths between 700-800 nm, correction factor C_B is applied.

Repetitively Pulsed Lasers

Since there are few experimental data for multiple pulses, caution must be used in the evaluation of such exposures. The protection standards for irradiance or radiant exposure in multiple pulse trains have the following limitations:

(1) The exposure from any single pulse in the train is limited to the protection standard for a single comparable pulse.

(2) The average irradiance for a group of pulses is limited to the protection standard as given in Tables 3, 4, or 6 of a single pulse of the same duration as the entire pulse group.

(3) When the Instantaneous Pulse Repetition Frequency (PRF) of any pulses within a train exceeds one, the protection standard applicable to each pulse is reduced as shown in Figure 6 for pulse durations less than 10^{-5} second. For pulses of greater duration, the following formula should be followed:

$$\text{Standard}\left(\begin{matrix}\text{single pulse}\\ \text{in train}\end{matrix}\right) = \frac{\text{Standard (pulse } n\tau)}{n}$$

where:

n = number of pulses in train

τ = duration of a single pulse in the train

Standard ($n\tau$) = protection standard of one pulse having a duration equal to $n\tau$ seconds.

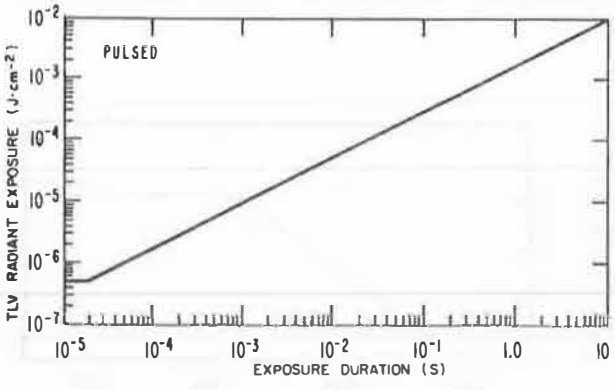

Figure 3a — TLV for intrabeam (direct) viewing of laser beam (400-700 nm).

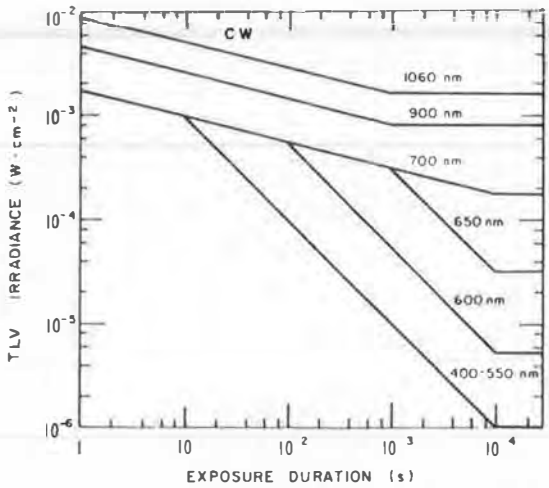

Figure 3b — TLV for intrabeam (direct) viewing of CW laser beam (400-1400 nm).

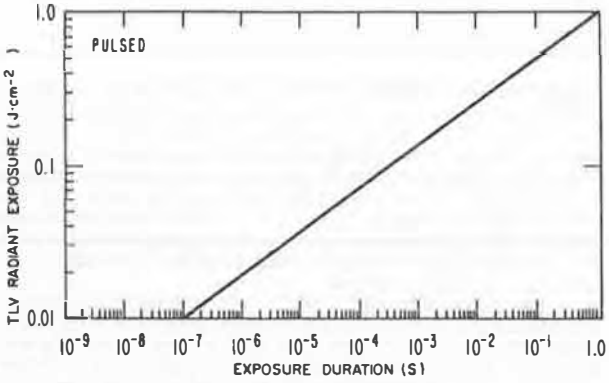

Figure 4a — TLV for laser exposure of skin and eyes for far-infrared radiation (wavelengths greater than 1.4 μm).

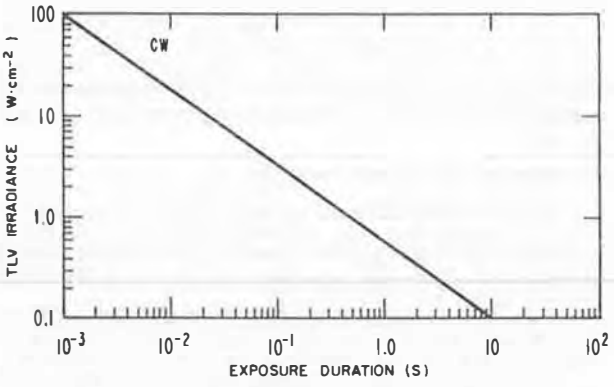

Figure 4b — TLV for CW laser exposure of skin and eyes for far-infrared radiation (wavelengths greater than 1.4 μm).

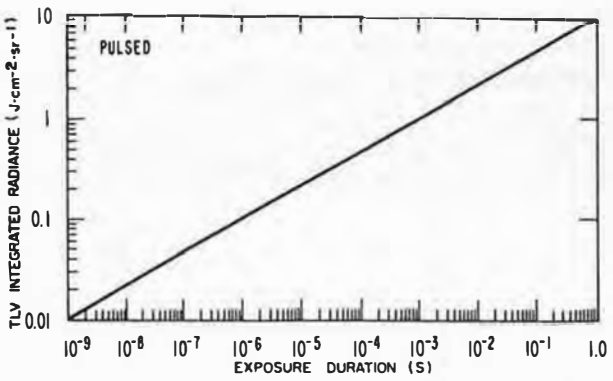

Figure 5a — TLV for extended sources or diffuse reflections of laser radiation (400-700 nm).

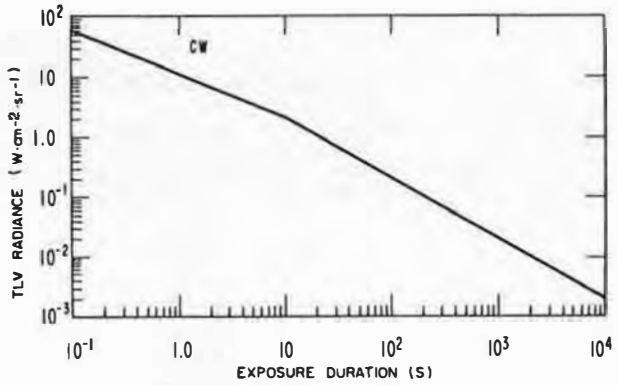

Figure 5b — TLV for extended sources or diffuse reflections for laser radiation (400-1400 nm), cw.

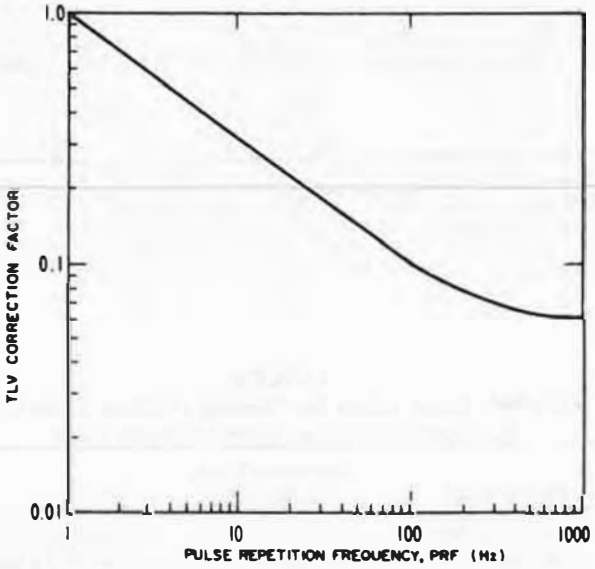

Figure 6 — Multiplicative correction factor for repetitively pulsed lasers having pulse durations less than 10^{-5} second. TLV for a single pulse of the pulse train is multiplied by the above correction factor for PRF greater than 1000 H_z is 0.06.

TABLE 3
Threshold Limit Value for Direct Ocular Exposures (Intrabeam Viewing) from a Laser Beam

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
UVC	200 nm to 280 nm	10^{-2} to 3×10^{4}	3 mJ • cm^{-2}
UVB	280 nm to 302 nm	"	3 "
	303 nm	"	4 "
	304 nm	"	6 "
	305 nm	"	10 "
	306 nm	"	16 "
	307 nm	"	25 "
	308 nm	"	40 "
	309 nm	"	63 "
	310 nm	"	100 "
	311 nm	"	160 "
	312 nm	"	250 "
	313 nm	"	400 "
	314 nm	"	630 "
	315 nm	"	1.0 J • cm^{-2}
UVA	315 nm to 400 nm	10 to 10^{3}	1.0 J • cm^{-2}
	" "	10^{3} to 3×10^{4}	1.0 mW • cm^{-2}
Light	400 nm to 700 nm	10^{-9} to 1.8×10^{-5}	5×10^{-7} J• cm^{-2}
	400 nm to 700nm	1.8×10^{-5} to 10	1.8 $(t/\sqrt[4]{t})$ mJ • cm^{-2}
	400 nm to 549 nm	10 to 10^{4}	10 mJ • cm^{-2}
	550 nm to 700 nm	10 to T_1	1.8 $(t/\sqrt[4]{t})$ mJ • cm^{-2}
	550 nm to 700 nm	T_1 to 10^{4}	10 C_B mJ • cm^{-2}
	400 nm to 700 nm	10^{4} to 3×10^{4}	C_B μW • cm^{-2}
IR-A	700 nm to 1059 nm	10^{-9} to 1.8×10^{-5}	5 $C_A \times 10^{-7}$ J • cm^{-2}
	700 nm to 1059 nm	1.8×10^{-5} to 10^{3}	1.8 C_A $(t/\sqrt[4]{t})$ mJ • cm^{-2}
	1060 nm to 1400 nm	10^{-9} to 10^{-4}	5×10^{-6} J • cm^{-2}
	1060 nm to 1400 nm	10^{-4} to 10^{3}	9$(t/\sqrt[4]{t})$ mJ • cm^{-2}
	700 nm to 1400 nm	10^{3} to 3×10^{4}	320 C_A μW • cm^{-2}
IR-B & C	1.4 μm to 10^{3} μm	10^{-9} to 10^{-7}	10^{-2} J • cm^{-2}
	" "	10^{-7} to 10	0.56 $\sqrt[4]{t}$ J • cm^{-2}
	" "	10 to 3×10^{4}	0.1 W • cm^{-2}

C_A — See Fig. 2, Laser TLV listing.
C_B = 1 for λ = 400 to 550 nm; $C_B = 10^{[0.015\ (\lambda\ -\ 550)]}$ for λ = 550 to 700 nm.
T_1 = 10 s for λ = 400 to 550 nm; $T_1 = 10 \times 10^{[0.02\ (\lambda\ -\ 550)]}$ for λ = 550 to 700 n.

TABLE 4
Threshold Limit Values for Viewing a Diffuse Reflection of a Laser Beam or an Extended Source Laser

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
UV	200 nm to 400 nm	10^{-3} to 3×10^{4}	Same as Table 3
Light	400 nm to 700 nm	10^{-9} to 10	10 $\sqrt[9]{t}$ J • cm^{-2} • sr^{-1}
	400 nm to 549 nm	10 to 10^{4}	21 J • cm^{-2} • sr^{-1}
	550 nm to 700 nm	10 to T_1	3.83 $(t/\sqrt[4]{t})$ J • cm^{-2} • sr^{-1}
	550 nm to 700 nm	T_1 to 10^{4}	21/C_B J • cm^{-2} • sr^{-1}
	400 nm to 700 nm	10^{4} to 3×10^{4}	$2.1/C_B \times 10^{-3}$ W • cm^{-2} • sr^{-1}
IR-A	700 nm to 1400 nm	10^{-9} to 10	10 C_A $\sqrt[3]{t}$ J • cm^{-2} • sr^{-1}
	700 nm to 1400 nm	10 to 10^{3}	3.83 C_A $(t/\sqrt[4]{t})$ J • cm^{-2} • sr^{-1}
	700 nm to 1400 nm	10^{3} to 3×10^{4}	0.64 C_A W • cm^{-2} • sr^{-1}
IR-B & C	1.4 μm to 1 mm	10^{-9} to 3×10^{4}	Same as Table 3

C_A, C_B and T_1 are the same as in footnote to Table 3.

TABLE 5
Limiting Angle to Extended Source
Which May Be Used for Applying Extended Source TLVs

Exposure Duration(s)	Angle α (mrad)
10^{-9}	8.0
10^{-8}	5.4
10^{-7}	3.7
10^{-6}	2.5
10^{-5}	1.7
10^{-4}	2.2
10^{-3}	3.6
10^{-2}	5.7
10^{-1}	9.2
1.0	15
10	24
10^{2}	24
10^{3}	24
10^{4}	24

TABLE 6
Threshold Limit Value for Skin Exposure from a Laser Beam

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
UV	200 nm to 400 nm	10^{-3} to 3×10^{4}	Same as Table 3
Light &	400 nm to 1400 nm	10^{-9} to 10^{-7}	$2\ C_A \times 10^{-2}$ J • cm^{-2}
IR-A	" "	10^{-7} to 10	$1.1\ C_A \sqrt{t}$ J • cm^{-2}
IR-B & C	1.4 μm to 1 mm	10^{-9} to 3×10^{4}	Same as Table 3

C_A = 1.0 for λ = 400-700 nm; see Figure 2 Laser TLV list for greater wavelength values.
NOTE: To aid in the determination of TLV's for exposure durations requiring calculations of fractional powers Figures 3, 4, 5 and 6 may be used.

MICROWAVES*

These Threshold Limit Values refer to microwave energy in the frequency range of 100 MHz to 100 GHz and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect.

These values should be used as guides in the control of exposure of microwaves and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values

The Threshold Limit Value for occupational microwave energy exposure where power densities are known and exposure time controlled is as follows:

1. For average power density levels up to but not exceeding 10 milliwatts per square centimeter, total exposure time shall be limited to the 8-hour workday (continuous exposure).
2. For average power density levels from 10 milliwatts per square centimeter up to but not exceeding 25 milliwatts per square centimeter, total exposure time shall be limited to no more than 10 minutes for any 60 minute period during an 8-hour workday (intermittent exposure).
3. For average power density levels in excess of 25 milliwatts per square centimeter, exposure is not permissible.

NOTE: For repetitively pulsed sources the average power density may be calculated by multiplying the peak power density by the duty cycle. The duty cycle is equal to the pulse duration in seconds times the pulse repetition rate in hertz.

*See Notice of Intended Changes; Notice of Intent to Study.

NOISE

These threshold limit values refer to sound pressure levels and durations of exposure that represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect on their ability to hear and understand normal speech. The medical profession has defined hearing impairment as an average hearing threshold level in excess of 25 decibels (ANSI-S3, 6-1969) at 500, 1000, and 2000 Hz, and the limits which are given have been established to prevent a hearing loss in excess of this level. The values should be used as guides in the control of noise exposure and, due to individual susceptibility, should not be regarded as fine lines between safe and dangerous levels.

Continuous or Intermittent

The sound level shall be determined by a sound level meter, conforming as a minimum to the requirements of the American National Standard Specification for Sound Level Meters, S1.4 (1971) Type S2A, and set to use the A-weighted network with slow meter response. Duration of exposure shall not exceed that shown in Table 7.

These values apply to total duration of exposure per working day regardless of whether this is one continuous exposure or a number of short-term exposures but does not apply to impact or impulsive type of noise.

When the daily noise exposure is composed of two or more periods of noise exposure of different levels, their combined effect should be considered, rather than the individual effect of each. If the sum of the following fractions:

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \cdots \frac{C_n}{T_n}$$

exceeds unity, then, the mixed exposure should be considered to exceed the threshold limit value. C_1 indicates the total duration of exposure at a specific noise level, and T_1 indicates the total duration of exposure permitted at that level. All on-the-job noise exposures of 80 dBA or greater shall be used in the above calculations.

TABLE 7
Threshold Limit Values

Duration per day Hours	Sound Level dBA[a)]
16	80
8	85
4	[c]
2	95
1	100
1/2	105
1/4	110
1/8	115*

*No exposure to continuous or intermittent in excess of 115 dBA.
[a)]Sound level in decibels as measured on a sound level meter, conforming as a minimum to the requirements of the American National Standard Specification for Sound Level Meters, S1.4 (1971) Type S2A, and set to use the A-weighted network with slow meter response.

IMPULSIVE OR IMPACT NOISE

It is recommended that exposure to impulsive or impact noise shall not exceed the limits listed in Table 8 or taken from Figure 7. No exposures in excess of 140 decibels peak sound pressure level are permitted. Impulsive or impact noise is considered to be those variations in noise levels that involve maxima at intervals of greater than one per second. Where the intervals are less than one second, it should be considered continuous.

TABLE 8
Threshold Limit Values
Impulsive or Impact Noise

Sound Level dB**	Permitted Number of Impulses or Impacts per day
140	100
130	1,000
120	10,000

*It should be recognized that the application of the TLV for noise will not protect all workers from the adverse effects of noise exposure. A hearing conservation program with audiometric testing is necessary when workers are exposed to noise at or above the TLV levels.
**Decibels peak sound pressure level.

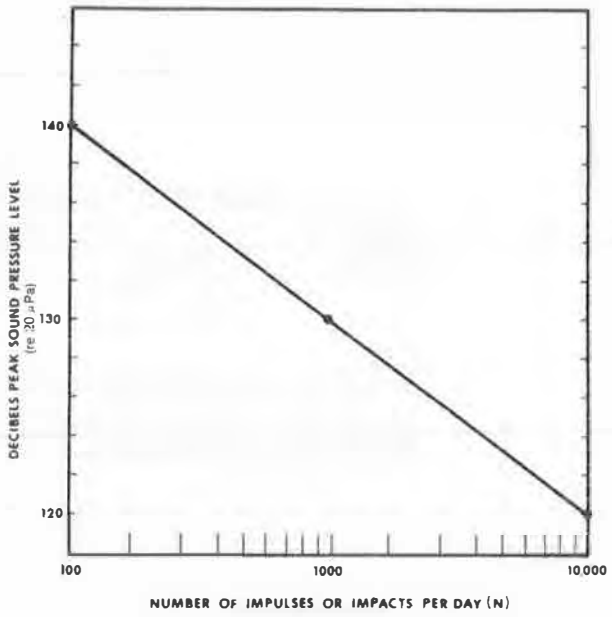

Figure 7 — Threshold Limit Values for Impulse/Impact noise.

ULTRAVIOLET RADIATION*

These threshold limit values refer to ultraviolet radiation in the spectral region between 200 and 400 nm and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect. These values for exposure of the eye or the skin apply to ultraviolet radiation from arcs, gas, and vapor discharges, fluorescent, and incandescent sources, and solar radiation, but do not apply to ultraviolet lasers.* These levels should not be used for determining exposure of photosensitive individuals to ultraviolet radiation. These values should be used as guides in the control of exposure to continuous sources where the exposure duration shall not be less than 0.1 sec.

*See Laser TLVs.
*Mumford, W.W., "Heat Stress Due to R.F. Radiation, "Proceedings of IEEE, Vol. 57, No. 2, Feb. 1969, pp. 171-178.

These values should be used as guides in the control of exposure to ultraviolet sources and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The threshold limit value for occupational exposure to ultraviolet radiation incident upon skin or eye where irradiance values are known and exposure time is controlled are as follows:

1. For the near ultraviolet spectral region (320 to 400 nm) total irradiance incident upon the unprotected skin or eye should not exceed 1 mw/cm^2 for periods greater than 10^3 seconds (approximately 16 minutes) and for exposure times less than 10^3 seconds should not exceed one J/cm^2.
2. For the actinic ultraviolet spectral region (200 — 315 nm), radiant exposure incident upon the unprotected skin or eye should not exceed the values given in Table 9 within an 8-hour period.
3. To determine the effective irradiance of a broadband source weighted against the peak of the spectral effectiveness curve (270 nm), the following weighting formula should be used:

$$E_{eff} = \sum E_\lambda S_\lambda \Delta\lambda$$

where:

E_{eff} = effective irradiance relative to a monochromatic source at 270 nm in W/cm^2 (J/s/cm^2)

E_λ = spectral irradiance in W/cm^2/nm

S_λ = relative spectral effectiveness (unitless)

$\Delta\lambda$ = band width in nanometers

4. Permissible exposure time in seconds for exposure to actinic ultraviolet radiation incident upon the unprotected skin or eye may be computed by dividing 0.003 J/cm^2 by E_{eff} in W/cm^2. The exposure time may also be determined using Table 10 which provides exposure times corresponding to effective irradiances in μW/cm^2.

TABLE 9
Relative Spectral Effectiveness by Wavelength

Wavelength (nm)	TLV (mJ/cm^2)**	Relative Spectral Effectiveness S_λ
200	100	0.03
210	40	0.075
220	25	0.12
230	16	0.19
240	10	0.30
250	7.0	0.43
254	6.0	0.5
260	4.6	0.65
270	3.0	1.0
280	3.4	0.88
290	4.7	0.64
300	10	0.30
305	50	0.06
310	200	0.015
315	1000	0.003

**1 m J/cm^{-3} = J/cm^2

TABLE 10
Permissible Ultraviolet Exposures

Duration of Exposure Per Day	Effective Irradiance E_{eff} (μW/cm^2)***
8 hrs	0.1
4 hrs	0.2
2 hrs	0.4
1 hr	0.8
30 min	1.7
15 min	3.3
10 min	5
5 min	10
1 min	50
30 sec	100
10 sec	300
1 sec	3,000
0.5 sec	6,000
0.1 sec	30,000

***1μW/cm^2 = 10^{-6} W/cm^2

All the preceding TLVs for ultraviolet energy apply to sources which subtend an angle less than 80°. Sources which subtend a greater angle need to be measured only an angle of 80°.

Conditioned (tanned) individuals can tolerate skin exposure in excess of the TLV without erythemal effects. However, such conditioning may not protect persons against skin cancer.

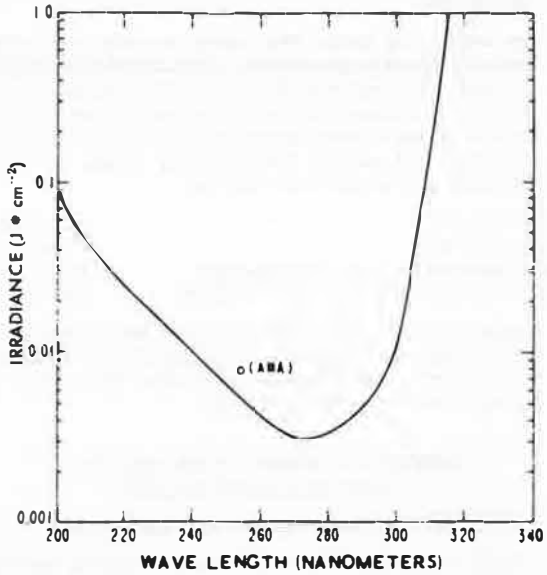

Figure 8 — Threshold Limit Values for Ultraviolet Radiation.

NOTICE OF INTENDED CHANGES (for 1976)

These physical agents, with their corresponding values, comprise those for which either a limit has been proposed for the first time, or for which a change in the 'Adopted" listing has been proposed. In both cases, the proposed limts should be considered trial limits that will remain in the listing for a period of at least one year. If after one year no evidence comes to light that questions the appropriateness of the values herein the values will be reconsidered for the "Adopted" list.

MICROWAVES

These Threshold Limit Values refer to microwave energy in the frequency range of 300 MHz to 300 GHz and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect.

Under conditions of moderate to severe heat stress the recommended values may need to be reduced.* Therefore, these values should be used as guides in the control of exposure to microwave energy and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The Threshold Limit Value for occupational exposure to microwave energy, where power density or field intensity is known and exposure time is controlled, is as follows:

1. For exposure to continuous wave (CW) sources, the power density level shall not exceed 10 milliwatts per square centimeter (mW/cm^2) for continuous exposure, and the total exposure time shall be limited to an 8-hour workday. This power density is approximately equivalent to a free-space electric field strength of 200 volts-per-meter rms (V/m) and a free-space magnetic field strength of 0.5 ampere-per-meter rms (A/m).
2. Exposures to CW power density levels greater than 10 mW/cm^2 are permissible up to a maximum of 25 mW/cm^2 based upon an average energy density of 1 milliwatt-hour per square centimeter (MWh/cm^2) averaged over any 0.1 hour period. For example, at 25 mW/cm^2, the permissible exposure duration is approximately 2.4 minutes in any 0.1 hour period.
3. For repetitively pulsed microwave sources, the average field strength or power density is calculated by multiplying the peak-pulse value by the duty cycle. The duty cycle is equal to the pulse duration in seconds times the pulse repetition rate in Hertz. Exposure during an 8-hour workday shall not exceed the following values which are averaged over any 0.1 hour period:

Power Density	10 mW/cm^2
Energy Density	1 mWh/cm^2
Mean Squared Electric Field Strength	40,000 V^2/m^2
Mean Squared Magnetic Field Strength	0.25 A^2/m^2

4. Exposure is not permissible in CW or repetitively pulsed fields with an average power density in excess of 25 mW/cm^2 or approximate equivalent free-space field strengths of 300 V/m or 0.75 A/m.

NOTICE OF INTENT TO ESTABLISH THRESHOLD LIMIT VALUES

LIGHT AND NEAR-INFRARED RADIATION

These Threshold Limit Values refer to visible and near-infrared radiation in the wavelength range of 400 nm to 1400 nm and represent conditions under which it is believed that nearly all workers may be exposed without adverse effect. These values should be used as guides in the control of exposure to light and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The Threshold Limit Value for occupational exposure to broad-band light and near-infrared radiation for the eye apply to exposure in any eight-hour workday and require knowledge of the spectral radiance (L_λ) and total irradiance (E) of the source as measured at the position(s) of the eye of the worker. Such detailed spectral data of a white light source is generally only required if the luminance of the source exceeds 1 cd cm^{-2}. At luminances less than this value the TLV would not be exceeded.

The TLV's are:

1. To protect against retinal thermal injury, the spectral radiance of the lamp weighted against the function R (Table 14) should not exceed:

$$\sum_{400}^{1400} L_\lambda R_\lambda \Delta\lambda \leq \sqrt{t/\alpha t} \qquad (1)$$

where L_λ is in W cm^{-2} sr^{-1} and t is the viewing duration (or pulse duration if the lamp is pulsed) limited to 1 μs to 10 s, and α is the angular subtense of the source in radians. If the lamp is oblong, α refers to the longest dimension that can be viewed. For instance, at a viewing distance r = 100 cm from a tubular lamp of length l = 50 cm, the viewing angle is:

$$\alpha = l/r = 50/100 = 0.5 \text{ rad} \qquad (2)$$

2. To protect against retinal injury from chronic blue-light exposure the integrated spectral radiance of the lamp weighted against the blue-light hazard function B_λ (Table 14) should not exceed:

$$\sum_{400}^{1400} L_\lambda \, t \, B_\lambda \, \Delta\lambda \leq 100 \text{ J}cm^{-2} sr^{-1} \; (t \leq 10^4 s) \qquad (3a)$$

$$\sum_{400}^{1400} L_\lambda \, B_\lambda \, \Delta\lambda \leq 10^{-2} \text{ W}cm^{-2} sr^{-1} \; (t > 10^4 s) \qquad (3b)$$

For a source radiance L which exceeds 2 mW cm^{-2} sr^{-1} in the blue spectral region, the permissible exposure duration t_{max} in seconds is simply:

$$t_{max} = 100 \text{ J } cm^{-2} sr^{-1}/L \text{ (blue)} \qquad (4)$$

The latter limits are greater than the maximum permissible exposure limits for 440 nm laser radiation (see Laser TLV) because a 2-3 mm pupil is assumed rather than a 7 mm pupil for the Laser TLV.

3. *Infrared Radiation:* To avoid possible delayed effects upon the lens of the eye (cataractogenesis), the infrared radiation ($\lambda > 770$ nm) should be limited to 10 mWcm^{-2}. For an infrared heat lamp or any near-infrared source where a strong visual stimulus is absent, the near infrared (770-1400 nm) radiance as viewed by the eye should be limited to:

$$\sum_{770}^{1400} E_\lambda \, \Delta_\lambda = 600/\alpha \qquad (5)$$

for extended duration viewing conditions. This limit is based upon a 7 mm pupil diameter.

TABLE 11
Spectral Weighting Functions for Assessing Retinal Hazards from Broad - Band Optical Sources

Wavelength (nm)	Blue-Light Hazard Function B_λ	Burn Hazard Function R_λ
400	0.10	1.0
405	0.20	2.0
410	0.40	4.0
415	0.80	8.0
420	0.90	9.0
425	0.95	9.5
430	0.98	9.8
435	1.0	10
440	1.0	10
445	0.97	9.7
450	0.94	9.4
455	0.90	9.0
460	0.80	8.0
465	0.70	7.0
470	0.62	6.2
475	0.55	5.5
480	0.45	4.5
485	0.40	4.0
490	0.22	2.2
495	0.16	1.6
500-600	$10^{[(450-\lambda)/50]}$	1.0
600-700	0.001	1.0
700-1060	0.001	$10^{[(\lambda-700)/515]}$
1060-1400	0.001	0.2

AIRBORNE UPPER SONIC AND ULTRASONIC ACOUSTIC RADIATION

These threshold limit values refer to sound pressure levels that represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect. The values listed in Table 15 should be used as guides in the control of noise exposure and, due to individual susceptibility, should not be regarded as fine lines between safe and dangerous levels. The levels for the third octave bands centered below 20 kHz are below those which cause subjective effects. Those levels for 1/3 octaves above 20 kHz are for prevention of possible hearing losses from subharmonics of these frequencies.

TABLE 12
Permissible Ultrasound Exposure Levels

Mid-Frequency of Third-Octave Band kHz	One-Third Octave - Band Level in dB reference 0.0002 dynes/cm^2
10	80
12.5	80
16	80
20	105
25	110
31.5	115
40	115
50	115

NOTICE OF INTENT TO STUDY

These agents comprise those which the Physical Agents Committee of ACGIH proposes to study during this year to determine the feasibility of establishing proposed TLVs in 1976. Comments and suggestions, accompanied by substantitive evidence, are solicited.

1. *Radiofrequency Radiation.* Specifically, that portion of the spectrum from 10 MHz to 100 MHz.
2. *Microwave Radiation.* Specifically from 100 GHz to 300 GHz.
3. *Magnetic Fields.* Both pulsed and continuous.
4. *Laser Radiation.* Specifically ultraviolet radiation for pulsed exposures, and repetitively pulsed light and infrared-A laser exposures.
5. *Ultrasonic Energy.* Specifically, acoustic energy at frequencies above 10 kHz.
6. *Vibration.* Segmental and whole-body.

1977

changes from 1976

Threshold Limit Values adopted at the Thirty-Ninth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 22-27, 1977, New Orleans, LA.

New Values

Substance	TWA ppm	TWA mg/m^3
Benzene — skin	10,A2	30,A2
Benzo(a)pyrene	—	A2
Borates, tetra, sodium salts,		
Anhydrous	—	1
Decahydrate	—	5
Pentahydrate	—	1
Calcium hydroxide	—	5
Captafol (Difolatan®) — skin	—	0.1
Catechol (Pyrocatechol)	5	20
Cyanamide	—	2
Dicrotophos (Bidrin®) — skin	—	0.25
Dimethyl sulfate — skin	0.1,A2	0.5,A2
Dioxathion (Delnav®)	—	0.2
Diuron	—	10
C Hexylene glycol	25	125
Hydrazine — skin	0.1	0.1
Isophorone diisocyanate — skin	0.01	0.06
Lead chromate (as Cr)	—	0.05,A2
Methomyl (Lannate®) — skin	—	2.5
Monocrotophos (Azodrin®)	—	0.25
Nickel Metal	—	1
m-Phthalodinitrile	—	5

Substance	TWA ppm	TWA mg/m³
Propane sultone	A2	A2
Rubber solvent	400	1600
Vinyl cyclohexene dioxide	10	60
Zinc chromate (as Cr)	—	0.05, A2

Revised Value

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Chromates, certain insoluble forms				
from	—	A,1a		
TO	—	0.05,A1a		
Iron oxide from	—	B4		
TO	—	B3		
Welding fumes (Total particulate				
from	—	5,B4	—	5,B4
TO	—	5,B3	—	B3

Appendix A2

The following substances were added to the Appendix A2 listing, but the A2 designation was not carried in the alphabetical listing.

Beryllium
1,1-Dimethyl hydrazine
Vinyl cyclohexene dioxide

Placed on Notice of Intended Changes list

Vinyl bromide

STEL Values deleted for

Aniline
Anisidine (o-, p-isomers)
Arsine
Barium (soluble compounds)
Benzoyl peroxide
Benzyl chloride
Biphenyl
Boron trifluoride
Bromoform — skin
Butanethiol
n-Butyl alcohol — skin
sec-Butyl alcohol
Butylamine — skin
tert-Butyl chromates (as CrO_3) — skin
n-Butyl glycidyl ether
n-Butyl lactate
Butyl mercaptan
Cadmium oxide fume (as Cd)
Calcium arsenate (as As)
Carbofuran (Furadan®)
Cesium hydroxide
Chlorine trifluoride
Chloroacetaldehyde
α-Chloroacetophenone (phenacyl chloride)
Chlorobenzene (monochlorobenzene)
o-Chlorobenzylidene malonoitrile — skin
Chlorodiphenyl (42% chlorine) — skin
2-Chloroethanol (Ethylene chlorohydrin)
bis-Chloromethyl ether
1-Chloro-1-nitro-propane
Chloropicrin
Chromic acid and Chromates (as Cr)
Chromium, Soluble chromic, chromous salts (as Cr)
Copper fume
Cresol, all isomers — skin
Cyanide, as CN — skin
Cyanogen
Cyclohexanol
Cyclohexanone
Cyclohexene
Cyclohexylamine — skin
1,2-Diaminoethane
Diazomethane
Diborane
Dichloracetylene
o-Dichlorobenzene
1,1-Dichloro-1-nitroethane
Dicyclopentadiene
Diethylamine
Diethylaminoethanol — skin
Diethylene triamine — skin
Diglycidyl ether (DGE)
Diisobutyl ketone
Diisopropylamine — skin
Dimethylamine
2,6-Dimethyiheptanone, see Diisobutyl ketone
Dioxane, tech. grade — skin
Diphenyl methane diisocyanate
Dyfonate
Ethion (Nialate®) — skin
Ethyl acetate
Ethyl acrylate
Ethyl alcohol (Ethanol)
Ethylamine
Ethyl sec-amyl ketone (4-Methyl-3-heptanone)
Ethyl mercaptan
Ethyl silicate
Ethylene chlorohydrin — skin
Ethylene diamine
Ethylene glycol dinitrate and/or Nitroglycerin — skin
Ethylenimine — skin
Ethylidene norbornene
N-Ethylmorpholine — skin
Fensulfothion (Dasanit)
Fluoride (as F)
Formaldehyde
Formic acid
sec-Hexyl acetate
Hydrogenated terphenyls
Hydrogen bromide
Hydrogen chloride
Hydrogen fluoride
Hydrogen selenide
Iodine
Iron pentacarbonyl
Isophorone
Lithium hydride
Magnesium oxide fume
Malathion

Maleic anhydride
Manganese and compounds (as Mn)
Mesityl oxide
Methanethiol
Methoxychlor
Methyl acrylate
Methylamine
Methyl bromide — skin
Methylene bisphenyl isocyante (MDI)
Methylene bis (4-cyclohexylisocyanate)
Methyl ethyl ketone peroxide
Methyl isocyanate — skin
Methyl mercaptan
Methyl silicate
α-Methyl styrene
Monomethyl hydrazine — skin
Nickel carbonyl
Nitrogen dioxide
Nitroglycerin[d] — skin
2-Nitropropane
Perchloromethyl mercaptan
p-Phenylene diamine — skin
Phenylphosphine
Phosgene (carbonyl chloride)
Phosphorus trichloride
Platinum (soluble salts), as Pt
Potassium hydroxide
Propylene imine — skin
Ronnel
Selenium compounds (as Se)
Sodium azide
Sodium hydroxide
Subtillisins (Proteolytic enzymes as 100% pure crystalline enzyme)
Sulfur dioxide
Sulfuric acid
Tellurium
Tellurium hexaflouride, as Te
Terphenyls
Tetranitromethane
Thallium, soluble compounds (as Tl) — skin
Toluene-2,4-diisocyanate (TDI)
Vandium (V_2O_5), as V fume
m-Xylene α,α'-diamine

Deletions

Nitrous oxide — from Appendix F and entire alphabetical listings.
Oil mist, vapor — from entire alphabetical listings.
Petroleum distillates (naphtha) — from entire alphabetical listings.

Airborne Contaminants TLV Committee:

Hervey B. Elkins, Ph.D., *Chairman*
Charles E. Adkins
Hector P. Blejer, M.D.
Paul E. Caplan, P.E., MPH
Paul Gross, M.D.
John W. Knauber, MPH
Jesse Lieberman, P.E.
Trent R. Lewis, Ph.D.
Keith R. Long, Ph.D.
Frederick T. McDermott, P.E.
Floyd A. Madsen
Col. Walter W. Melvin, Jr., M.D.
Leonard D. Pagnotto, *Secretary*
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Herbert E. Stokinger, Ph.D.
William D. Wagner
Ralph C. Wands
David H. Wegman, M.D.

Consultants

E. Mastromatteo, M.D.
James F. Morgan
Marshall Steinberg, Ph.D.
Theodore R. Torkelson, Sc.D.
Mitchell R. Zavon, M.D.

Physical Agent TLV committee report

The committee held one meeting during the year, September 22 at the National Institute of Health, Bethesda, Maryland.

For the first time since the formation of the committee there were no recommendations for the new TLVs or notices of intent to establish a TLV. The committee sees the need for TLVs for vibration, radio frequency radiation from 10 in Hz to 100 Hz, hyperbaric environments, magnetic fields and ultrasonics. The committee is also trying to develop a recommendation on how to evaluate a mixed noise exposure that is impact plus continuous.

The second edition of the *Laser Guide* was published during the year.

/s/ Herbert H. Jones
Chairman

Physical Agents TLV Committee:

Herbert H. Jones, *Chairman*
Peter A. Breysse
Gerald V. Coles
Thomas Cummins
Irving H. Davis
Ronald D. Dobbin
LCDR Joseph J. Drozd
Maj. George S. Kush
Edward J. Largent
William E. Murray

Dr. Wordie H. Parr
David H. Sliney
Lt. Col. Robert T. Wangemann
Thomas K. Wilkinson, USPHS

1978

changes from 1977

Threshold Limit Values adopted at the Fortieth Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 7-12, 1978, Los Angeles, CA.

New Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Antimony trioxide, handling and use (as Sb)	—	0.5	—	—
Atrazine	—	10		
Butyl acrylate	10	55		
Calcium hydroxide	—	5		
Calcium oxide	—	2		
Carbonyl chloride	0.1	0.4		
Carbonyl fluoride	5	15		
Chlorodiphenyl (42% chlorine) — skin	—	—	—	2
Chloroform (trichloromethane)	10,A2	50,A2	—	—
Chloropicrin	—	—	0.3	2
Chromite ore processing (Chromate, as Cr)	—0.05,A1a		—	—
Dimethyl carbamyl chloride	A2	A2	—	—
Ethylmercaptan	—	—	2	3
Hexamethyl phosphoramide — skin	A2	A2	—	—
Manganese tetroxide	—	1	—	—
Nickel sulfide roasting, fume & dust (as Ni)	—	1,A1a	—	—
Phenyl mercaptan	0.5	2	—	—
C Propylene glycol dinitrate — skin	0.2	2	—	—
Thioglycolic acid	1	5	—	—
C 1,2,4-Trichloro benzene	5	40	—	—
Valeraldehyde	50	175	—	—

Revised Values

Substance		TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
2-Aminoethanol	from	3	6		
	TO	3	8	6	15
Biphenyl	from	0.2	1		
	TO	0.2	1.5	0.6	4
Carbon tetrachloride — skin	from	10	65	25	160
	TO	10	65	20	130
Dimethylbenzene		*Add:* skin			
Dimethyl sulfate		*Add:* "C"			
Diphenylmethane diisocyanate		*Add:* "C"			
Ethylidene Chloride	from	200	320		
	TO	200	810	—	—
See 1,1-Dichloroethane		250	400		
	TO	250	1010	—	—
Ethylene glycol dinitrate and/or Nitroglycerin — skin	from	0.2[d]	—		
	TO "C"	0.2[d]	2	—	—
Glass, fibrous[e] or dust	from	—	E		
	TO	—	10	—	—
Hydrazine — skin	from	0.1	0.1		
	TO	0.1,A2	0.1,A2	—	—
Indene	from	10	45	15	27
	TO	10	45	15	70
Iodoform		0.2	3	0.4	0.6
	TO	0.6	10	1	20
Nitroglycerin[d] — skin			*Add:* C		
Paraquat — skin	from	—	(0.5)		
TO: Paraquat, respirable sizes		—	0.1	—	—
n-Propyl nitrate	from	25	110	40	140
	TO	25	105	40	470
Trichloromethane		10,A2	50,A2		
C Trinitrotoluene — skin		—	0.5	—	—

d) An atmospheric concentration of not more than 0.02 ppm, or personal protection may be necessary to avoid headache for intermittent exposure.

e) < 7 μm in diameter.

Placed on Notice of Intended Changes list:

Acrylonitrile
Aniline
Asbestos (all forms)
Cadmium oxide production (as Cd)
Carbon disulfide — skin
Chloroethylene (Vinyl chloride)
β-Chloroprene — skin
1,2-Dibromoethane (ethylene dibromide) — skin
1,2-Dichloroethane
Dichloromethane, see Methylene chloride
Epichlorhydrin
Ethylene dibromide
Ethylene dichloride
Hydrogen cyanide — skin
2-Nitropropane
Phosphorus pentachloride
Silver, metal and soluble compounds, as Ag
Sulfur dioxide
C Terphenyls
C Toluene-2,4-diisocyanate (TDI)
Talc (fibrous) use asbestos limit
Tremolite

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Mitchell R. Zavon, M.D.

Physical agents TLV committee report

No new adopted values, nor new notice of intent to establish TLVs.

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Thomas K. Wilkinson

1979

changes from 1978

Threshold Limit Values adopted at the Forty-First Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 27 - June 1, 1979, Chicago, IL.

New Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Aluminum metal and oxide	—	10	—	20
Aluminum pyro powders	—	5	—	—
Aluminum welding fumes	—	5	—	—
Aluminum, soluble salts	—	2	—	—
Aluminum, alkyls (NOC)*	—	2	—	—
3-Amino 1,2,4-triazole	A2	A2	—	—
Benomyl	0.8	10	1.3	15
Bromacil	1	10	2	20
Manganese fume (as Mn)	—	1	—	3
n-Phenyl-beta-naphthylamine	A2	A2	—	—
Trimethyl phosphate	0.5	2.6	—	—
VM & P naptha	300	1350	400	1800

* NOC = Not otherwise classified

Revised Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Beryllium from	—	0.002	—	0.025
TO	—0.002,A2		—	—
Ethyl silicate	10	85	30	225
C Glutaraldehyde, activated or unactivated from	—	(0.25)		
C To: Glutaraldehyde	0.2	0.7	—	—
Methlylcyclopentadienyl manganese tricarbonyl (as Mn) — skin	*Delete:* ppm values			
Selenium hexafluoride (as Se)	*Delete:* STEL values			
1,2,4-Trichlorobenzene	*Delete:* C			

Placed on Notice of Intended Change list:

Acetone
Butane
2-Butoxyethanol (butyl cellosolve) — skin
sec-Butyl alcohol
n-Butyl glycidyl ether (BGE)
Carbon tetrachloride — skin
Carbonyl fluoride

1-Chloro-1-nitropropane
Chromates, certain insoluble forms
Chromic acid and Chromates, (as Cr)
Cyclohexanone
Diethylamine
Diglycidyl ether (DGE)
Dioxane, tech. grade — skin
2-Ethoxyethanol — skin
2-Ethyxoyethyl acetate (cellosolve acetate) — skin
Ethyl acrylate
Ethylene glycol, vapor
Ethylene glycol dinitrate and/or nitroglycerin — skin
Ethylene oxide
Furfural — skin
Glycidol (2,3-Epoxy-1-propanol)
Hexane (n-hexane)
Hexone (methyl isobutyl ketone) — skin
Mesityl oxide
Methyl n-amyl ketone (2-Heptanone)
Methyl bromide
Methyl butyl ketone, see 2-Hexanone — skin
Methyl chloride
Methyl iodide — skin
Methyl silicate
α-Methyl styrene
Nitrogen dioxide
Nitroglycerin — skin
1-Nitropropane
Phenyl ether-Diphenyl mixture (vapor)
β-Propiolactone
Propylene glycol dinitrate — skin
Propylene oxide
Styrene, monomer (Phenylethylene)
Tributyl phosphate
Trichloroethylene
Vanadium (V_2O_5) as V
  Dust
  C Fume
Vinyl benzene, see Styrene
Vinyl cyanide, see Acrylonitrile — skin
Vinyl toluene
Wood dust (non-allergenic)

Airborne Contaminants TLV Committee

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Theodore R. Torkelson
Ralph C. Wands
Mitchell R. Zavon, M.D.

Physical Agents TLV Committee report

New Values

None.

Revised Values

None.

Notice of Intent to Establish TLV

None.

Physical Agents TLV Committee

Herbert H. Jones, *Chairman*
Peter A. Breysse
Thomas Cummings
Irving H. Davis
Ronald D. Dobbin
LCDR Joseph J. Drozd
Dr. Allan P. Heins
LCDR Richard Johnson
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William E. Murray
Dr. Wordie H. Parr
David H. Sliney
LTC Robert T. Wangemann
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Gerald V. Coles

1980

changes from 1979

Threshold Limit Values adopted at the Forty-Second Annual Meeting of the American Confer-

ence of Governmental Industrial Hygienists, May 18-23, 1980, Houston, TX.

New Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Acetylsalicylic acid (Asprin)	—	5	—	—
Aluminum oxide (Al_2O_3)	—	E	—	20
Baytex, see Fenthion	—	0.1	—	0.3
Benzene	—	—	25,A2	75,A2
o-sec-Butylphenol — skin	5	30	—	—
Chloroacetyl chloride — skin	0.05	0.2	—	—
Chloroform	—	—	50	225
C Cyanogen chloride	0.3	0.6	—	—
Cyclonite — skin	—	1.5	—	3
Dichloropropene — skin	1	5	10	50
2,2-Dichloropropionic acid	1	6	—	—
Diethylamine	3	15	—	—
Divinyl benzene	10	50	—	—
Fenthion	—	0.1	—	0.3
Hydrogen fluoride (as F)	—	—	6	5
2-Hydroxypropyl acrylate — skin		0.5	3	
N-Isopropylaniline — skin	2	10	5	20
4,4-Methylene dianiline — skin	0.1	0.8	0.5	4
C Methyl hydrozine — skin	0.2,A2	0.35,A2	—	—
Propionic acid	10	30	15	45
Silver, metal	—	0.01	—	—
Sodium bisulfite	—	5	—	—
Sodium 2,4-dichloro-phenoxyethyl sulfate	—	10	—	20
Sodium metabisulfite	—	5	—	—
Tetrasodium pyrophosphate	—	5	—	—
Trichloroacetic acid	1	5	—	—
Triphenyl amine	—	5	—	—

Mineral Dusts

Asbestos	
Amosite	0.5 fibers > 5 μ m/cc, A1a
Chrysotile	2 fibers > 5 μm/cc, A1a
Crocidolite	0.2 fibers > 5 μ m/cc, A1a
Other forms	2 fibers > 5 μ m/cc, A1a

Revised Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Aniline — skin				
To: Aniline & homologues — skin	2	10	5	20
Antimony & compounds (as Sb)				
retain	—	5	—	—
Antimony trioxide production				
from	—	(0.5,A2)		
TO	—	A2	—	—
Arsenic & compounds (as As)				
To: Arsenic & soluble compounds (as As)	—	0.2	—	—
Arsenic trioxide production (as As)	—	A2	—	—
Carbon disulfide — skin	10	30	—	—
2-Chloro-1,3-buladiene, see β-Chloroprene — skin	10	45	—	—
1-Chloro,2,3-epoxy-propane (Epichlorohydrin) — skin	2	8	5	19
Chloroethylene, see Vinyl chloride	5,A1a	10,A1a	—	—
β-Chloroprene — skin	10	45		
1,2-Dichloroethane, see Ethylene dichloride	10	40	15	60
Dichlorofluoromethane	10	40	—	—
1,1-Dimethylhydrazine — skin				
from	0.5		1	12
TO	*Add:* A2			
Dimethyl sulfate	*Delete:* "C"			
Epichlorohydrin — skin	2	10	5	20
Ethylene dichloride, see 1,2-Dichloroethane				
To: Ethylene dichloride	10	40	15	60
C Hydrogen cyanide — skin	10	10	—	—
C 2-Nitropropane	25,A2	90,A2	—	—
Phosphorus pentachloride	0.1	1	—	—
Sulfur dioxide	2	5	5	10
C Terphenyls	0.5	5	—	—
Vinyl bromide	5,A2	20,A2	—	—
Vinyl chloride	5,A1a	10,A1a	—	—

Placed on Notice of Intended Change list:

Benzidine production — skin
o-Chlorobenzylidene malononitrile — skin
N-Ethylmorpholine — skin
Fluorotrichloromethane
Furfuryl alcohol — skin
Gasoline
Hexachloroethane — skin
Iron pentacarbonyl (as Fe)
Lead arsenate (as Pb)
Mercury (all forms except alkyl), as Hg
Methyl isoamyl ketone
Monomethyl aniline — skin
p-Nitroaniline — skin
p-Nitrochlorobenzene — skin
Nitrotoluene
Perchloroethylene — skin
Phenylethylene, see Styrene monomer
Phenyl glycidyl ether (PGE)
Phosphorus trichloride
Propylene imine — skin
Rhodium, metal fume and dusts (as Rh)
Silane, see Silicon tetrahydride
Silicon tetrahydride (silane)
Stoddard solvent
1,1,2,2-Tetrachloroethane — skin
Tin, inorganic compounds, except SnH_4 and SnO_2 (as Sn)
Tin oxide (as Sn)
o-Toluidine
Trichlorofluoromethane
Trimethyl phosphite
2,4,6-Trinitrotoluene (TNT)
Xylidene — skin

Deletions

Alundum®, completely from alphabetical listing
Appendix D
Benomyl, ppm value only
Calcium arsenate (as As), completely from alphabetical listing
Carundum (Al_2O_3), now Aluminim oxide
Mercury (Alkyl compounds) (as Hg) — skin, ppm value only
Methylcyclopentadienyl manganese Tricarbonyl (as Mn) —skin, Delete ppm value

Airborne Contaminants TLV Committee:

Hervey B. Elkins, Ph.D., *Chairman through April 30, 1980*
COL Vernon L. Carter, *Chairman, appointed May 1980*
Charles E. Adkins
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Mitchell R. Zavon, M.D.

Physical Agents Committee report

New Values

None.

Revised Values

None.

NOTICE OF INTENT TO ESTABLISH THRESHOLD LIMIT VALUES

LIGHT AND NEAR-INFRARED RADIATION

These Threshold Limit Values refer to visible and near-infrared radiation in the wavelength range of 400 nm to 1400 nm and represent conditions under which it is believed that nearly all workers may be exposed without adverse effect. These values should be used as guides in the control of exposure to light and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The Threshold Limit Value for occupational exposure to broad-band light and near-infrared radiation for the eye apply to exposure in any eight-hour workday and require knowledge of the spectral radiance (L_λ) and total irradiance (E) of the source as measured at the position(s) of the eye of the worker. Such detailed spectral data of a white light source is generally only required if the luminance of the source exceeds 1 cd cm^{-2}. At luminances less than this value the TLV would not be exceeded.

The TLV's are:

1. To protect against retinal thermal injury, the spectral radiance of the lamp weighted against the function R (Table 11) should not exceed:

$$\sum_{400}^{1400} L_\lambda R_\lambda \Delta\lambda \leq 1/\alpha t^{1/2} \qquad (1)^*$$

where L_λ is in W cm^{-2} sr^{-1} and t is the viewing duration (or pulse duration if the lamp is pulsed) limited to 1 μs to 10 s, and α is the angular subtense of the source in radians. If the lamp is oblong, α refers to the longest dimension that can be viewed. For instance, at a viewing distance r = 100 cm from a tubular lamp of length l = 50 cm, the viewing angle is:

$$\alpha = l/r = 50/100 = 0.5 \text{ rad} \qquad (2)$$

2. To protect against retinal photochemical injury from chronic blue-light exposure the integrated spectral radiance of light source weighted against the blue-light hazard function B_λ (Table 11) should not exceed:

$$\sum_{400}^{1400} L_\lambda \, t \, B_\lambda \Delta\lambda \leqq 100 \text{ Jcm}^{-2} \text{ sr}^{-1} \; (t \leq 10^4 \text{s}) \qquad (3a)$$

$$\sum_{400}^{1400} L_\lambda \, B_\lambda \Delta\lambda \leqq 10^{-2} \text{ Wcm}^{-2} \text{ sr}^{-1} \; (t > 10^4 \text{s}) \qquad (3b)$$

For a source radiance L which exceeds 10 mW cm^{-2} sr^{-1} in the blue spectral region, the permissible exposure duration t_{max} in seconds is simply:

$$t_{max} = 100 \text{ J cm}^{-2} \text{ sr}^{-1}/\text{L (blue)} \qquad (4)$$

The latter limits are greater than the maximum permissible exposure limits for 440 nm laser radiation (see Laser TLV) because a 2-3 mm pupil is assumed rather than a 7 mm pupil for the Laser TLV.

For a light source subtending an angle α less than 11 mrd (0.011 radian) the above limits are relaxed such that the spectral irradiance weighted against the blue-light hazard function Bλ should not exceed:

$$\sum_{400}^{1400} E_\lambda \bullet t \bullet B_\lambda \bullet \Delta\lambda \leq 10 \text{ mJ} \bullet \text{cm}^{-2} \; (t \leq 10^4 \text{s}) \qquad (5a)$$

$$\sum_{400}^{1400} E_\lambda \bullet B_\lambda \bullet \Delta\lambda \leq 1\ \mu W \bullet cm^{-2}\ (t \geq 10^4 s) \qquad (5b)$$

For a source where the blue light weighted irradiance E (blue) exceeds 1 $\mu W \bullet cm^{-2}$ is the maximum permissible exposure duration T_{max} in seconds is:

$$t_{max} = 10\ mJ \bullet cm^{-2} / E\ (blue) \qquad (6)$$

3. *Infrared Radiation:* To avoid possible delayed effects upon the lens of the eye (cataractogenesis), the infrared radiation ($\lambda > 770$ nm) should be limited to 10 $mWcm^{-2}$. For an infrared heat lamp or any near-infrared source where a strong visual stimulus is absent, the near infrared (770-1400 nm) radiance as viewed by the eye should be limited to:

$$\sum_{770}^{1400} L_\lambda \Delta_\lambda = 0.6/\alpha \qquad (7)^*$$

for extended duration viewing conditions. This limit is based upon a 7 mm pupil diameter.

*Formulae (1) and (7) are empirical and are not, strictly speaking, dimensionally correct. To make the formulae dimensionally correct, one would have to insert a dimensional correction factor k in the right hand numerator in each formula. For formula (1) this would be $k_1 = 1\ W \bullet rad \bullet s^{1/2}/(cm^2 \bullet sr)$, and for formula (7) $k_2 = 1\ W \bullet rad/(cm^{-2} \bullet sr)$.

TABLE 11
Spectral Weighting Functions for Assessing Retinal Hazards from Broad - Band Optical Sources

Wavelength (nm)	Blue-Light Hazard Function B_λ	Burn Hazard Function R_λ
400	0.10	1.0
405	0.20	2.0
410	0.40	4.0
415	0.80	8.0
420	0.90	9.0
425	0.95	9.5
430	0.98	9.8
435	1.0	10
440	1.0	10
445	0.97	9.7
450	0.94	9.4
455	0.90	9.0
460	0.80	8.0
465	0.70	7.0
470	0.62	6.2
475	0.55	5.5
480	0.45	4.5
485	0.40	4.0
490	0.22	2.2
495	0.16	1.6
500-600	$10^{[(450-\lambda)/50]}$	1.0
600-700	0.001	1.0
700-1049	0.001	$10^{[(700-\lambda)/505]}$
1050-1400	0.001	0.2

PULSED ULTRAVIOLET LASER EXPOSURES FOR EXPOSURE DURATION LESS THAN ONE MILLISECOND

TLVs for pulsed Ultraviolet Laser Exposures for Exposure Durations Less than One Millisecond. These changes would expand the scope of the present TLVs for Laser radiation to include pulsed ultraviolet laser exposure.

1. Table 3 would be modified such that the lower exposure duration limit of 10^{-3}s now given for the UVC and UVB be changed to 10^{-9}s. An additional notation would be made to the right side of the TLV column:

   "Not to exceed $0.56\ t^{1/4}\ J \cdot cm^{-9}$ for $t \leq 10$ s."

2. Tables 4 and 6 would be modified such that the lower exposure duration of 10^{-3}s now given for the UV be changes to 10^{-9}s.

Physical Agents TLV Committee

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LTC Robert T. Wangemann
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Consultants

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1981

changes from 1980

Threshold Limit Values adopted at the Forty-third Annual Meeting of the American Conference of Governmental Industrial Hygienists, May 24-29, 1981, Portland, OR.

New Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Acrylic acid	10	30	—	—
Chloropentafluoroethane	1000	6320	—	—
Chromium metal	—	0.5	—	—
Chromium (II) compounds, as Cr	—	0.5	—	—
Chromium (III) compounds, as Cr	—	0.5	—	—
Chromium (VI) compounds, as Cr				
Water soluble compounds	—	0.05	—	—
Certain water insoluble compounds	—	0.05,A1a	—	—
Crysene	A2	A2	—	—
Cyclopentane	600	1720	900	2580
Diethyl ketone	200	705	—	—
Dipropyl ketone	50	235	—	—
Isopropoxyethanol	25	105	75	320
Methacrylic acid	20	70	—	—
Methyl isopropyl ketone	200	705	—	—
Platinum, metal	—	1	—	—
Trimellitic anhydride	0.005	0.04	—	—
Wood dust (certain hard woods as beech & oak)	—	1	—	—
Soft wood	—	5	—	10

Revised Values

Substance	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³
Benomyl	0.8	10	1.3	15
Butane	800	1900	—	—
2-Butoxyethanol — skin	25	120	75	360
sec-Butyl alcohol	100	305	150	455
n-Butyl glycidyl ether (BGE)	25	235	—	—
Carbon tetrachloride — skin	5,A2	30,A2	20,A2	125,A2
Carbonyl fluoride	2	5	5	15
Chloroform	*Add:* A2 to STEL			
bis-Chloromethyl ether	from	—	—	—	A1a
TO	0.001, A1a	0.005, A1a	—	—
1-Chloro-1-nitropropane	2	10	—	—
Coal tar pitch volatiles as benzene solubles	*Delete:* A1a from STEL			
Cyclohexanone	25	100	100	400
1,1-Dichloro-1-nitroethane	2	10	10	60
Diethylamine	10	30	25	75
Diglycidyl ether	0.1	0.5	—	—
Dioxane, tech. grade — skin	25	90	100	360
2-Ethoxyethanol — skin	50	185	100	370
2-Ethoxyethyl acetate — skin	50	270	100	540
Ethyl acrylate — skin	5	20	25	100
C Ethylene glycol, vapor	50	125	—	—
Furfuryl — skin	2	8	10	40
Glycidol	25	75	100	300
Mesityl oxide	15	60	25	100
Methyl n-amyl ketone	50	235	100	465
Methyl bromide — skin	5	20	15	60
Methyl n-butyl ketone — skin Delete skin notation	5	20	—	—
Methyl chloride	50	105	100	205
Methylene chloride	100	360	500	1700
Methyl iodide — skin	2,A2	10,A2	5,A2	30,A2
Methyl isobutyl ketone	50	205	75	300
Methyl silicate	1	6	5	30
α-Methyl styrene	50	240	100	485
Nitrogen dioxide	3	6	5	10
β-Propiolactone	0.5,A2	1.5,A2	1,A2	3,A2
Propylene oxide	20	50		
Quinone	0.1	0.4	0.3	2
TO	0.1	0.4	0.3	1
Silver, soluble compounds, as Ag	*Delete:* STEL			
Styrene, monomer	50	215	100	425
Tributyl phosphate	0.2	2.5	0.4	5
Vinyl cyclohexene dioxide	*Add:* A2			
Vinyl toluene	50	240	100	485

Appendix change:

Acetylene from F to E
Aluminum oxide (Al_2O_3) from F to D
Argon from F to E and delete in STEL column
Calcium carbonate/marble from E to D
Cellolose (paper fiber) from E to D
Emery from E to D
Ethane from F to E
Ethylene from F to E and delete in STEL column
Glycerin mist from E to D
Graphite (synthetic) from E to D
Gypsum from E to D
Helium from F to E and delete in STEL column
Hydrogen from F to E
Kaolin from E to D
Limestone from E to D
Magnesite from E to D
Marble/Calcium carbonate from E to D
Methane from F to E
Neon from F to E
Pentaerythritol from E to D
Plaster of Paris from E to D
Propane from F to E
Propylene from F to E
Rouge from E to D
Silicon from E to D
Silicon carbide from E to D
Starch From E to D
Sucrose from E to D
Titanitum dioxide (as Ti) from E to D
Zinc sterate form E to D

Place on Notice of Intended Change list:

Atrazine
Fenthion
Formaldehyde
Furfural alcohol — skin
2-Nitropropane
Phenylhydrazine
Triethylamine
2,4,6-Trinitrotoluene (TNT)

Physical agents TLV committee report

New Values

None.

Revised Values

None.

Notice of intent to establish TLVs

RADIOFREQUENCY/MICROWAVE RADIATION

See the full text of the 1981 TLV booklet that follows.

Threshold Limit Values for chemical substances and physical agents in the workroom environment with intended changes for 1981

PREFACE
CHEMICAL SUBSTANCES

Threshold limit values refer to airborne concentrations of substances and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variation in individual susceptibility, however, a small percentage of workers may experience discomfort from some substances at concentrations at or below the threshold limit; a smaller percentage may be affected more seriously by aggravation of a pre-existing condition or by development of an occupational illness.

Threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and, when possible, from a combination of the three. The basis on which the values are established may differ from substance to substance; protection against impairment of health may be a guiding factor for some, whereas reasonable freedom from irritation, narcosis, nuisance or other forms of stress may form the basis for others.

The amount and nature of the information available for establishing a TLV varies from substance to substance; consequently, the precision of the estimated TLV is also subject to variation and the latest *Documentation* should be consulted in order to assess the extent of the data available for a given substance.

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, (1) as a relative index of hazard or toxicity, (2) in the evaluation or control of community air pollution nuisances, (3) in estimating the toxic potential of continuous, uninterrupted exposures or other extended work periods, (4) as proof or disproof of an existing disease or physical condition, or (5) for adoption by countries whose working conditions differ from those in the United States of America and where substances and processes differ.

The TLV-TWA should be used as guides in the control of health hazards and should not be used as fine lines between safe and dangerous concentrations.

In spite of the fact that serious injury is not believed likely as a result of exposure to the threshold limit concentrations, the best practice is to maintain concentrations of all atmospheric contaminants as low as is practical.

Legal Status. The Threshold Limit Values, as issued by ACGIH, are recommendations and should be used as guidelines for good practices. Wherever these values (of whatever year) have been used or included by reference in Federal and/or State statutes and registers, the TLVs do have the force and effects of law.

"Notice of Intent." At the beginning of each year, proposed actions of the Committee for the forthcoming year are issued in the form of a "Notice of Intended Changes." This Notice provides not only an opportunity for comment, *but solicits suggestions of substances to be added to the list*. The suggestions *should be accompanied by substantiating evidence*. The list of Intended Changes follows the Adopted Values in the TLV booklet. Values listed in parenthesis in the "Adopted" list are to be used during the period in which a proposed change for that Value is listed in the Notice of Intended Changes.

Definitions. Three categories of Threshold Limit Values (TLVs) are specified herein, as follows:

a) The Threshold Limit Value-Time Weighted Average (TLV-TWA) — the time-weighted average concentration for a normal 8-hour workday and a 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.

b) Threshold Limit Value-Short Term Exposure Limit (TLV-STEL) — the maximal concentration to which workers can be exposed for a period up to 15 minutes continuously without suffering from 1) irritation, 2) chronic or irreversible tissue change, or 3) narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work efficiency, provided that no more than four excursions per day are permitted, with at least 60 minutes between exposure periods, and provided that the daily TLV-TWA also is not exceeded. The STEL should be considered a maximal allowable concentration, or ceiling, not to be exceeded at any time during the 15-minute excursion period.

c) Threshold Limit Value-Ceiling (TLV-C) — the concentration that should not be exceeded even instantaneously.

For some substances, e.g., irritant gases, only one category, the TLV-Ceiling, may be relevant. For other substances, either two or three categories may be relevant, depending upon their physiologic action. It is important to observe that if any one of these three TLVs is exceeded, a potential hazard from that substance is presumed to exist.

The committee holds to the opinion that limits based on physical irritation should be considered no less binding than those based on physical impairment. There is increasing evidence that physical irritation may initiate, promote or accelerate physical impairment through interaction with other chemical or biologic agents.

Time-Weighted Average vs Ceiling Limits. Time-weighted averages permit excursions above the limit provided they are compensated by equivalent excursions below the limit during the workday. In some instances it may be permissible to calculate the average concentration for a workweek rather than for a workday. The relationship between threshold limit and permissible excursion is a rule of thumb and in certain cases may not apply. The amount by which threshold limits may be exceeded for short periods without injury to health depends upon a number of factors such as the nature of the contaminant, whether very high concentrations — even for short periods — produce acute poisoning, whether the effects are cumulative, the frequency with which high concentrations occur, and the duration of such

periods. All-factors must be taken into consideration in arriving at a decision as to whether a hazardous condition exists.

Although the time-weighted average concentration provides the most satisfactory, practical way of monitoring airborne agents for compliance with the limits, there are certain substances for which it is inappropriate. In the latter group are substances which are predominantly fast acting and whose threshold limit is more appropriately based on this particular response. Substances with this type of response are best controlled by a ceiling "C" limit that should not be exceeded. It is implicit in these definitions that the manner of sampling to determine noncompliance with the limits for each group must differ; a single brief sample, that is applicable to a "C" limit, is not appropriate to the time-weighted limit; here, a sufficient number of samples are needed to permit a time-weighted average concentration throughout a complete cycle of operations or throughout the work shift.

Whereas the ceiling limit places a definite boundary which concentrations should not be permitted to exceed, the time-weighted average limit requires an explicit limit to the excursions that are permissible above the listed values. It should be noted that the same factors are used by the Committee in determining the magnitude of the value of the STELs, or whether to include or exclude a substance for a "C" listing.

"Skin" Notation. Listed substances followed by the designation "Skin" refer to the potential contribution to the overall exposure by the cutaneous route including mucous membranes and eye, either by airborne, or more particularly, by direct contact with the substance. Vehicles can alter skin absorption. This attention-calling designation is intended to suggest appropriate measures for the prevention of cutaneous absorption so that the threshold limit is not invalidated.

Mixtures. Special consideration should be given also to the application of the TLVs in assessing the health hazards which may be associated with exposure to mixtures of two or more substances. A brief discussion of basic considerations involved in developing threshold limit values for mixtures, and methods for their development, amplified by specific examples are given in Appendix C.

Nuisance Particulates. In contrast to fibrogenic dusts which cause scar tissue to be formed in lungs when inhaled in excessive amounts, so-called "nuisance" dusts have a long history of little adverse effect on lungs and do not produce significant organic disease or toxic effect when exposures are kept under reasonable control. The nuisance dusts have also been called (biologically) "inert" dusts, but the latter term is inappropriate to the extent that there is no dust which does not evoke some cellular response in the lung when inhaled in sufficient amount. However, the lung-tissue reaction caused by inhalation of nuisance dusts has the following characteristics: (1) The architecture of the air spaces remains intact. (2) Collagen (scar tissue) is not formed to a significant extent. (3) The tissue reaction is potentially reversible.

Excessive concentrations of nuisance dusts in the workroom air may seriously reduce visibility, may cause unpleasant deposits in the eyes, ears and nasal passages (Portland Cement dust), or cause injury to the skin or mucous membranes by chemical or mechanical action per se or by the rigorous skin cleansing procedures necessary for their removal.

A threshold limit of 10 mg/m^3, or 30 mppcf, of total dust < 1% quartz, or, 5 mg/m^3 respirable dust is recommended for substances in these categories and for which no specific threshold limits have been assigned. This limit, for a normal workday, does not apply to brief exposures at higher concentrations. Neither does it apply to those substances which may cause physiologic impairment at lower concentrations but for which a threshold limit has not yet been adopted. Some nuisance particulates are given in Appendix D.

Simple Asphyxiants — "Inert" Gases or Vapors. A number of gases and vapors, when present in high concentrations in air, act primarily as simple asphyxiants without other significant physiologic effects. A TLV may not be recommended for each simple asphyxiant because the limiting factor is the available oxygen. The minimal oxygen content should be 18 percent by volume under normal atmospheric pressure (equivalent to a partial pressure, pO_2 of 135 mm Hg). Atmospheres deficient in O_2 do not provide adequate warning and most simple asphyxiants are odorless. Several simple asphyxiants present an explosion hazard. Account should be taken of this factor in limiting the concentration of the asphyxiant. Specific examples are listed in Appendix E.

Physical Factors. It is recognized that such physical factors as heat, ultraviolet and ionizing radiation, humidity, abnormal pressure (altitude) and the like may place added stress on the body so that the effects from exposure at a threshold limit may be altered. Most of these stresses act adversely to increase the toxic response of a substance. *Although most threshold limits have built-in safety factors to guard against adverse effects to moderate deviations* from normal environments, the safety factors of most substances are not of such a magnitude as to take care of gross deviations. For example, continuous work at temperatures above 90°F, or overtime extending the workweek more than 25%, might be considered gross deviations. In such instances judgment must be exercised in the proper adjustments of the Threshold Limit Values.

Biologic Limit Values (BLVs). Other means exist and may be necessary for monitoring worker exposure other than reliance on the Threshold Limit Values for industrial air, namely, the Biologic Limit Values. These values represent limiting amounts of substances (or their effects) to which the worker may be exposed without hazard to health or well-being as determined in *his* tissues and fluids or in *his* exhaled breath. The biologic measurements on which the BLVs are based can furnish two kinds of information useful in the control of worker exposure: (1) measure of the individual worker's over-all exposure; (2) measure of the worker's individual and characteristic response. Measurements of response furnish a superior estimate of the physiologic status of the worker, and may be made of (a) changes in amount of some critical biochemical constituent, (b) changes in activity of a critical enzyme, (c) changes in some physiologic function. Measurement of exposure may be made by (1) determining in blood, urine, hair, nails, in body tissues and fluids, the amount of substance to which the worker was exposed; (2) determination of the amount of the metabolite(s) of the substance in tissues and fluids; (3) determination of the amount of the substance in the exhaled breath. The biologic limits may be used as an adjunct to the TLVs for air, *or in place of them*. The BLVs, and their associated procedures for determining compliance with them, should thus be regarded as an effective means of providing health surveillance of the worker.

Tests are available (*J. Occup. Med. 15*:564, 1973; *Ann. N.Y. Acad. Sci. 151, Art. 2*:968, 1968) that may be used to detect those individuals hypersusceptible to a variety of industrial chemicals (respiratory irritants, hemolytic chemicals, organic isocyanates, carbon disulfide).

Unlisted Substances. Many substances present or handled in industrial processes do not appear on the TLV list. In

a number of instances the material is rarely present as a particulate, vapor or other airborne contaminant, and a TLV is not necessary. In other cases sufficient information to warrant development of a TLV, even on a tentative basis, is not available to the Committee. Other substances, of low toxicity, could be included in Appendix D pertaining to nuisance particulates. This list (as well as Appendix E) is not meant to be all inclusive; the substances serve only as examples.

In addition there are some substances of not in considerable toxicity, which have been omitted primarily because only a limited number of workers (e.g., employees of a single plant) are known to have potential exposure to possibly harmful concentrations.

	ADOPTED VALUES			
	TWA		STEL	
Substance	ppm[a]	mg/m³[b]	ppm[a]	mg/m³[b]
Abate	—	10	—	20
Acetaldehyde	100	180	150	270
Acetic acid	10	25	15	37
C Acetic anhydride	5	20	—	—
** Acetone	(1,000)	(2,400)	(1,250)	(3,000)
Acetonitrile — Skin	40	70	60	105
Acetylene	E	—	—	—
Acetylene dichloride, see 1, 2-Dichloroethylene				
Acetylene tetrabromide	1	15	1.5	20
Acetylsalicylic acid (Asprin)	—	5	—	—
Acrolein	0.1	0.25	0.3	0.8
Acrylamide — Skin	—	0.3	—	0.6
* Acrylic acid	10	30	—	—
** Acrylonitrile — Skin	(A1b)	(A1b)	—	—
Aldrin — Skin	—	0.25	—	0.75
Allyl alcohol — Skin	2	5	4	10
Allyl chloride	1	3	2	6
Allyl glycidyl ether (AGE) — Skin	5	22	10	44
Allyl propyl disulfide	2	12	3	18
Aluminum metal and oxide	—	10	—	20
Aluminum pyro powders	—	5	—	—
Aluminum welding fumes	—	5	—	—
Aluminum, soluble salts	—	2	—	—
Aluminum, alkyls (NOC)*	—	2	—	—
Aluminum oxide (Al_2O_3)	—	D	—	20
4-Aminodiphenyl — Skin	—	A1b	—	A1b
2-Aminoethanol, see Ethanolamine				
2-Aminopyridine	0.5	2	2	4
3-Amino 1, 2, 4-triazole	A2	A2	—	—
Ammonia	25	18	35	27
Ammonium chloride-fume	—	10	—	20
Ammonium sulfamate (Ammate)	—	10	—	20
n-Amyl acetate	100	530	150	800
sec-Amyl acetate	125	670	150	800
Aniline & homologues — Skin	2	10	5	20
Anisidine (o-, p-isomers) — Skin	0.1	0.5	—	—
Antimony & compounds, as Sb	—	0.5	—	—
Antimony trioxide, handling and use, as Sb	—	0.5	—	—
Antimony trioxide production	—	A2	—	—
ANTU (α-Naphthyl thiourea)	—	0.3	—	0.9
Argon	E	—	—	—
Arsenic & soluble compounds, as As	—	0.2	—	—
Arsenic trioxide production	—	A2	—	—
Arsine	0.05	0.2	—	—
Asbestos, see MINERAL DUSTS	—	A1a	—	A1a
Asphalt (petroleum) fumes	—	5	—	10
** Atrazine	—	(10)	—	—
Azinphos-methyl — Skin	—	0.2	—	0.6
Barium (soluble compounds), as Ba	—	0.5	—	—
Baygon (propoxur)	—	0.5	—	2
Baytex, see Fenthion				
Benomyl	0.8	10	1.3	15
Benzene	10, A2	30, A2	25, A2	75, A2
** Benzidine production — Skin	—	(A1b)	—	(A1b)
p-Benzoquinone, see Quinone				
Benzoyl peroxide	—	5	—	—
Benzo(a)pyrene	—	A2	—	A2
Benzyl chloride	1	5	—	—
Beryllium	—	0.002, A2	—	—
Biphenyl	0.2	1.5	0.6	4
Bismuth telluride	—	10	—	20
Bismuth telluride, Se-doped	—	5	—	10
Borates, tetra, sodium salts, Anhydrous	—	1	—	—
Decahydrate	—	5	—	—
Pentahydrate	—	1	—	—
Boron oxide	—	10	—	20
Boron tribromide	1	10	3	30
C Boron trifluoride	1	3	—	—
Bromacil	1	10	2	20
Bromine	0.1	0.7	0.3	2
Bromine pentafluoride	0.1	0.7	0.3	2
Bromochloromethane, see Chlorobromomethane				
Bromoform — Skin	0.5	5	—	—
Butadiene (1, 3-butadiene)	1,000	2,200	1,250	2,750
* Butane	800	1,900	—	—

Capital letters refer to Appendices.
Footnotes (a thru f) see Page 473.
*1981 Addition
**See Notices of Intended Changes.

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Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Butanethiol, see Butyl mercaptan				
2-Butanone, see Methyl ethyl ketone (MEK)				
* 2-Butoxyethanol — Skin	25	120	75	360
n-Butyl acetate	150	710	200	950
sec-Butyl acetate	200	950	250	1,190
tert-Butyl acetate	200	950	250	1,190
Butyl acrylate	10	55	—	—
C n-Butyl alcohol — Skin	50	150	—	—
* sec-Butyl alcohol	100	305	150	455
tert-Butyl alcohol	100	300	150	450
C Butylamine — Skin	5	15	—	—
Butyl Cellosolve,® see 2-Butoxyethanol				
C tert-Butyl chromate, as CrO_3 — Skin	—	0.1	—	—
* n-Butyl glycidyl ether (BGE)	25	135	—	—
n-Butyl lactate	5	25	—	—
Butyl mercaptan	0.5	1.5	—	—
o-sec-Butylphenol — Skin	5	30	—	—
p-tert-Butyltoluene	10	60	20	120
Cadmium, dust & salts, as Cd	—	0.05	—	0.2
C Cadmium oxide fume, as Cd	—	0.05	—	—
** Cadmium oxide production, as Cd	—	(A2)	—	—
Calcium carbonate/ marble	—	D	—	20
Calcium cyanamide	—	0.5	—	1
Calcium hydroxide	—	5	—	—
Calcium oxide	—	2	—	—
Camphor, synthetic	2	12	3	18
Caprolactam Dust	—	1	—	3
Vapor	5	20	10	40
Captafol (Difolatan®) — Skin	—	0.1	—	—
Captan	—	5	—	15
Carbaryl (Sevin®)	—	5	—	10
Carbofuran (Furadan®)	—	0.1	—	—
Carbon black	—	3.5	—	7
Carbon dioxide	5,000	9,000	15,000	27,000
Carbon disulfide — Skin	10	30	—	—
Carbon monoxide	50	55	400	440
Carbon tetrabromide	0.1	1.4	0.3	4
* Carbon tetrachloride — Skin	5, A2	30, A2	20, A2	125, A2
Carbonyl chloride, see Phosgene				
* Carbonyl fluoride	2	5	5	15
Catechol (Pyrocatechol)	5	20	—	—
Cellosolve® acetate, see 2-Ethoxyethyl acetate				
Cellulose (paper fiber)	—	D	—	20
Cesium hydroxide	—	2	—	—
Chlordane — Skin	—	0.5	—	2

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*1981 Addition.
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Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Chlorinated camphene — Skin	—	0.5	—	1
Chlorinated diphenyl oxide	—	0.5	—	2
Chlorine	1	3	3	9
Chlorine dioxide	0.1	0.3	0.3	0.9
C Chlorine trifluoride	0.1	0.4	—	—
C Chloroacetaldehyde	1	3	—	—
α-Chloroacetophenone (Phenacyl chloride)	0.05	0.3	—	—
Chloroacetyl chloride	0.05	0.2	—	—
Chlorobenzene (Monochlorobenzene)	75	350	—	—
** o-Chlorobenzylidene malononitrile — Skin	(0.05)	(0.4)	—	—
Chlorobromomethane	200	1,050	250	1,300
2-Chloro-1, 3-butadiene, see β Chloroprene				
Chlorodifluoromethane	1,000	3,500	1,250	4,375
Chlorodiphenyl (42% Chlorine) — Skin	—	1	—	2
Chlorodiphenyl (54% Chlorine) — Skin	—	0.5	—	1
1-Chloro, 2, 3-epoxy-propane, see Epichlorohydrin				
2-Chloroethanol, see Ethylene chlorohydrin				
Chloroethylene, see Vinyl chloride				
Chloroform	10, A2	50, A2	50, A2	225, A2
bis-Chloromethyl ether	0.001, A1a	0.005, A1a	—	—
* 1-Chloro-1-nitropropane	2	10	—	—
* Chloropentafluoroethane	1,000	6,320	—	—
Chloropicrin	0.1	0.7	0.3	2
β-Chloroprene — Skin	10	45	—	—
o-Chlorostyrene	50	285	75	430
o-Chlorotoluene — Skin	50	250	75	375
2-Chloro-6-(trichloromethyl) pyridine (N-Serve®)	—	10	—	20
Chlorpyrifos (Dursban®) — Skin	—	0.2	—	0.6
* Chromium metal	—	0.5	—	—
* Chromium (II) compounds, as Cr	—	0.5	—	—
* Chromium (III) compounds, as Cr	—	0.5	—	—
* Chromium (VI) compounds, as Cr Water soluble Cr VI compounds	—	0.05	—	—
Certain water insoluble Cr VI compounds	—	0.05, A1a	—	—
Chromite ore processing (chromate), as Cr	—	0.05, A1a	—	—

Capital letters refer to Appendices.
Footnotes (a thru f) see Page 473.
*1981 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Chromium, soluble chromic, chromous salts, as Cr	—	0.5	—	—
* Chrysene	A2	A2	—	—
Clopidol (Coyden®)	—	10	—	20
Coal tar pitch volatiles, as benzene solubles	—	0.2, A1a	—	—
** Cobalt, metal, dust & fume, as Co	—	(0.1)	—	—
Copper fume	—	0.2	—	—
Dusts & mists, as Cu	—	1	—	2
Cotton dust, raw	—	0.2[k]	—	0.6
Crag® herbicide, see Sodium 2, 4-dichloro-phenoxyethyl sulfate				
Cresol, all isomers — Skin	5	22	—	—
Crotonaldehyde	2	6	6	18
Crufomate®	—	5	—	20
Cumene — Skin	50	245	75	365
Cyanamide	—	2	—	—
Cyanides, as CN — Skin	—	5	—	—
Cyanogen	10	20	—	—
Cyanogen chloride	0.3	0.6	—	—
Cyclohexane	300	1,050	375	1,300
Cyclohexanol	50	200	—	—
* Cyclohexanone	25	100	100	400
Cyclohexene	300	1,015	—	—
Cyclohexylamine — Skin	10	40	—	—
Cyclonite — Skin	—	1.5	—	3
Cyclopentadiene	75	200	150	400
* Cyclopentane	600	1,720	900	2,580
2, 4-D (2, 4-Dichloro-phenoxy-acetic acid)	—	10	—	20
DDT (Dichlorodiphenyl-trichloroethane)	—	1	—	3
DDVP, see Dichlorvos				
Decaborane — Skin	0.05	0.3	0.15	0.9
Demeton® — Skin	0.01	0.1	0.03	0.3
Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone)	50	240	75	360
1, 2-Diaminoethane, see Ethylenediamine				
Diazinon — Skin	—	0.1	—	0.3
Diazomethane	0.2	0.4	—	—
Diborane	0.1	0.1	—	—
1, 2-Dibromoethane, see Ethylene dibromide				
Dibrom®	—	3	—	6
2-n-Dibutylaminoethanol — Skin	2	14	4	28
Dibutyl phosphate	1	5	2	10
Dibutyl phthalate	—	5	—	10
C Dichloroacetylene	0.1	0.4	—	—
C o-Dichlorobenzene	50	300	—	—
p-Dichlorobenzene	75	450	110	675
3, 3'-Dichlorobenzidene — Skin	—	A2	—	A2

Capital letters refer to Appendices.
*1981 Addition.
**See Notice of Intended Changes.
k) See p. 474.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Dichlorodifluoromethane	1,000	4,950	1,250	6,200
1, 3-Dichloro-5, 5-dimethyl hydantoin	—	0.2	—	0.4
1, 1-Dichloroethane	200	810	250	1,010
1, 2-Dichloroethane, see Ethylene dichloride				
1, 1-Dichloroethylene, see Vinylidene chloride				
1, 2-Dichloroethylene	200	790	250	1,000
Dichloroethyl ether — Skin	5	30	10	60
Dichlorofluoromethane	10	40	—	—
Dichloromethane, see Methylene chloride				
* 1, 1-Dichloro-1-nitroethane	2	10	10	60
1, 2-Dichloropropane, see Propylene dichloride				
Dichloropropene — Skin	1	5	10	50
2, 2-Dichloropropionic acid	1	6	—	—
Dichlorotetrafluoro-ethane	1,000	7,000	1,250	8,750
Dichlorvos (DDVP) — Skin	0.1	1	0.3	3
Dicrotophos (Bidrin®) — Skin	—	0.25	—	—
Dicyclopentadiene	5	30	—	—
Dicyclopentadienyl iron	—	10	—	20
Dieldrin — Skin	—	0.25	—	0.75
Diethanolamine	3	15	—	—
* Diethylamine	10	30	25	75
Diethylaminoethanol — Skin	10	50	—	—
Diethylene triamine — Skin	1	4	—	—
Diethyl ether, see Ethyl ether				
* Diethyl ketone	200	705	—	—
Diethyl phthalate	—	5	—	10
Difluorodibromomethane	100	860	150	1,290
* Diglycidyl ether (DGE)	0.1	0.5	—	—
Dihydroxybenzene, see Hydroquinone				
Diisobutyl ketone	25	150	—	—
Diisopropylamine—Skin	5	20	—	—
Dimethoxymethane, see Methylal				
Dimethyl acetamide — Skin	10	35	15	50
Dimethylamine	10	18	—	—
Dimethylaminobenzene, see Xylidene				
Dimethylaniline (N, N-Dimethylaniline) — Skin	5	25	10	50
Dimethylbenzene, see Xylene				

Capital letters refer to Appendices.
Footnotes (a thru f) see Page 473.
*1981 Addition.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Dimethyl carbamyl chloride	A2	A2	—	—
Dimethyl-1, 2-dibromo-2-dichloroethyl phosphate, see Dibrom				
Dimethylformamide — Skin	10	30	20	60
2, 6-Dimethyl-4-heptanone, see Diisobutyl ketone				
1, 1-Dimethylhydrazine — Skin	0.5, A2	1, A2	1, A2	2, A2
Dimethylphthalate	—	5	—	10
Dimethyl sulfate — Skin	0.1, A2	0.5, A2	—	—
Dinitrobenzene (all isomers) — Skin	0.15	1	0.5	3
Dinitro-o-cresol — Skin	—	0.2	—	0.6
3, 5-Dinitro-o-toluamide (Zoalene®)	—	5	—	10
Dinitrotoluene — Skin	—	1.5	—	5
* Dioxane, tech. grade — Skin	25	90	100	360
Dioxathion (Delnav®) — Skin	—	0.2	—	—
Diphenyl, see Biphenyl				
Diphenylamine	—	10	—	20
Diphenylmethane diisocyanate, see Methylene bisphenyl isocyanate (MDI)				
Dipropylene glycol methyl ether — Skin	100	600	150	900
* Dipropyl ketone	50	235	—	—
Diquat	—	0.5	—	1
Di-sec, octyl phthalate (Di-2-ethylhexyl-phthalate)	—	5	—	10
Disulfiram	—	2	—	5
Disulfoton (Disyston®)	—	0.1	—	0.3
2, 6-Ditert. butyl-p-cresol	—	10	—	20
Diuron	—	10	—	—
* Divinyl benzene	10	50	—	—
Dyfonate — Skin	—	0.1	—	—
Emery	—	E	—	20
Endosulfan (Thiodan®) — Skin	—	0.1	—	0.3
Endrin — Skin	—	0.1	—	0.3
Epichlorohydrin — Skin	2	10	5	20
EPN — Skin	—	0.5	—	2
1, 2-Epoxypropane, see Propylene oxide				
2, 3-Epoxy-1-propanol, see Glycidol				
Ethane	E	—	—	—
Ethanethiol, see Ethyl mercaptan				
Ethanolamine	3	8	6	15
Ethion (Nialate®) — Skin	—	0.4	—	—
* 2-Ethoxyethanol — Skin	50	185	100	370
* 2-Ethoxyethyl acetate — Skin	50	270	100	540

Capital letters refer to Appendices.
*1981 Addition.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Ethyl acetate	400	1,400	—	—
* Ethyl acrylate — Skin	5	20	25	100
Ethyl alcohol (Ethanol)	1,000	1,900	—	—
Ethylamine	10	18	—	—
Ethyl amyl ketone	25	130	—	—
Ethyl benzene	100	435	125	545
Ethyl bromide	200	890	250	1,110
Ethyl butyl ketone	50	230	75	345
Ethyl chloride	1,000	2,600	1,250	3,250
Ethylene	E	—	—	—
C Ethylene chlorohydrin — Skin	1	3	—	—
Ethylenediamine	10	25	—	—
** Ethylene dibromide	(A1b)	(A1b)	—	—
Ethylene dichloride	10	40	15	60
Ethylene glycol, Particulate	—	10	—	20
*C Vapor	50	125	—	—
** Ethylene glycol dinitrate — Skin	(0.02)	(0.1)	(0.05)	(0.3)
Ethylene glycol methyl ether acetate — Skin	25	120	35	170
** Ethylene oxide	(10)	(20)	—	—
Ethyleneimine — Skin	0.5	1	—	—
Ethyl ether	400	1,200	500	1,500
Ethyl formate	100	300	150	450
Ethylidene chloride, see 1, 1-Dichloroethane				
C Ethylidene norbornene	5	25	—	—
Ethyl mercaptan	0.5	1	2	3
** N-Ethylmorpholine — Skin	(20)	(95)	—	—
Ethyl silicate	10	85	30	255
Fensulfothion (Dasanit)	—	0.1	—	—
** Fenthion	—	(0.1)	—	(0.3)
Ferbam	—	10	—	20
Ferrovanadium dust	—	1	—	0.3
Fluoride, as F	—	2.5	—	—
Fluorine	1	2	2	4
Fluorotrichloromethane, see Trichlorofluoromethane				
**C Formaldehyde	(2)	(3)	—	—
Formamide	20	30	30	45
Formic acid	5	9	—	—
* Furfural — Skin	2	8	10	40
** Furfuryl alcohol — Skin	(5)	(20)	(10)	(40)
** Gasoline	—	(B2)	—	(B2)
Germanium tetrahydride	0.2	0.6	0.6	1.8
Glass, fibrous[e] or dust	—	10	—	—
C Glutaraldehyde	0.2	0.7	—	—
Glycerin mist	—	D	—	—
* Glycidol	25	75	100	300
Glycol monoethyl ether, see 2-Ethoxyethanol				
Graphite (Synthetic)	—	D	—	—
Guthion®, see Azinphos-methyl				

Capital letters refer to Appendices.
*1981 Addition.
**See Notice of Intended Changes.
Footnotes (a thru f) see Page 473.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Gypsum	—	D	—	20
Hafnium	—	0.5	—	1.5
Helium	E	—	—	—
Heptachlor — Skin	—	0.5	—	2
Heptane (n-Heptane)	400	1,600	500	2,000
3-Heptanone, see Ethyl butyl ketone				
Hexachlorocyclopentadiene	0.01	0.1	0.03	0.3
** Hexachloroethane — Skin	(1)	(10)	(3)	(30)
Hexachloronaphthalene — Skin	—	0.2	—	0.6
Hexafluoroacetone	0.1	0.7	0.3	2
** Hexane (n-hexane)	(100)	(360)	(125)	(450)
Hexamethyl phosphoramide — Skin	A2	A2	—	—
2-Hexanone, see Methyl n-butyl ketone				
Hexone, see Methyl isobutyl ketone				
sec-Hexyl acetate	50	300	—	—
C Hexylene glycol	25	125	—	—
Hydrazine — Skin	0.1, A2	0.1, A2	—	—
Hydrogen	E	—	—	—
Hydrogenated terphenyls	0.5	5	—	—
Hydrogen bromide	3	10	—	—
C Hydrogen chloride	5	7	—	—
C Hydrogen cyanide — Skin	10	10	—	—
Hydrogen fluoride, as F	3	2.5	6	5
Hydrogen peroxide	1	1.5	2	3
Hydrogen selenide, as Se	0.05	0.2	—	—
Hydrogen sulfide	10	14	15	21
Hydroquinone	—	2	—	4
2-Hydroxypropyl acrylate — Skin	0.5	3	—	—
Indene	10	45	15	70
Indium & compounds, as In	—	0.1	—	0.3
C Iodine	0.1	1	—	—
Iodoform	0.6	10	1	20
Iron oxide fume (Fe_2O_3), as Fe	B3	5	—	10
** Iron pentacarbonyl, as Fe	(0.01)	(0.08)	—	—
Iron salts, soluble, as Fe	—	1	—	2
Isoamyl acetate	100	525	125	655
Isoamyl alcohol	100	360	125	450
Isobutyl acetate	150	700	187	875
Isobutyl alcohol	50	150	75	225
C Isophorone	5	25	—	—
Isophorone diisocyanate — Skin	0.01	0.09	—	—
* Isopropoxyethanol	25	105	75	320
Isopropyl acetate	250	950	310	1,185
Isopropyl alcohol	400	980	500	1,225
Isopropylamine	5	12	10	24
N-Isopropylaniline — Skin	2	10	5	20

Capital letters refer to Appendices.
*1981 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Isopropyl ether	250	1,050	310	1,320
Isopropyl glycidyl ether (IGE)	50	240	75	360
Kaolin	—	D	—	20
Ketene	0.5	0.9	1.5	3
Lead, inorg., fumes & dusts, as Pb	—	0.15	—	0.45
** Lead arsenate, as Pb	—	(0.15)	—	(0.45)
Lead chromate, as Cr	—	0.05, A2	—	—
Limestone	—	D	—	20
Lindane — Skin	—	0.5	—	1.5
Lithium hydride	—	0.025	—	—
L.P.G. (Liqulfied petroleum gas)	1,000	1,800	1,250	2,250
Magnesite	—	D	—	20
Magnesium oxide fume	—	10	—	—
Malathion — Skin	—	10	—	—
Maleic anhydride	0.25	1	—	—
C Manganese & compounds, as Mn	—	5	—	—
Manganese fume, as Mn	—	1	—	3
Manganese cyclopentadienyl tricarbonyl, as Mn — Skin	—	0.1	—	0.3
Manganese tetroxide	—	1	—	—
Marble/calcium carbonate	—	D	—	20
Mercury (Alkyl compounds) — Skin, as Hg	—	0.01	—	0.03
** Mercury (All forms except alkyl), as Hg	—	(0.05)	—	(0.15)
* Mesityl oxide	15	60	25	100
* Methacrylic acid	20	70	—	—
Methane	E	—	—	—
Methanethiol, see Methyl mercaptan				
Methomyl (Lannate®) — Skin	—	2.5	—	—
Methoxychlor	—	10	—	—
2-Methoxyethanol — Skin	25	80	35	120
Methyl acetate	200	610	250	760
Methyl acetylene	1,000	1,650	1,250	2,040
Methyl acetylene-propadiene mixture (MAPP)	1,000	1,800	1,250	2,250
Methyl acrylate — Skin	10	35	—	—
Methylacrylonitrile — Skin	1	3	2	6
Methylal	1,000	3,100	1,250	3,875
Methyl alcohol (methanol) — Skin	200	260	250	310
Methylamine	10	12	—	—
Methyl amyl alcohol, see Methyl isobutyl carbinol				
* Methyl n-amyl ketone	50	235	100	465

Capital letters refer to Appendices.
*1981 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
* Methyl bromide — Skin	5	20	15	60
* Methyl n-butyl ketone	5	20	—	—
Methyl Cellosolve®, see 2-Methoxyethanol				
Methyl Cellosolve® acetate, see Ethylene glycol monomethyl ether acetate				
* Methyl chloride	50	105	100	205
Methyl chloroform	350	1,900	450	2,450
Methyl 2-cyanoacrylate	2	8	4	16
Methylcyclohexane	400	1,600	500	2,000
Methylcyclohexanol	50	235	75	350
o-Methylcyclohexanone — Skin	50	230	75	345
Methylcyclopentadienyl manganese tricarbonyl, as Mn — Skin	—	0.2	—	0.6
Methyl demeton — Skin	—	0.5	—	1.5
C Methylene bisphenyl isocyanate (MDI)	0.02	0.2	—	—
* Methylene chloride	100	360	500	1,700
4, 4′-Methylene bis (2-chloroaniline) — Skin	0.02, A2	0.22, A2	—	—
C Methylene bis (4-cyclohexylisocyanate)	0.01	0.11	—	—
4, 4-Methylene dianiline — Skin	0.1	0.8	0.5	4
Methyl ethyl ketone (MEK)	200	590	300	885
C Methyl ethyl ketone peroxide	0.2	1.5	—	—
Methyl formate	100	250	150	375
5-Methyl-3-heptanone, see Ethyl amyl ketone				
C Methyl hydrazine — Skin	0.2, A2	0.35, A2	—	—
* Methyl iodide — Skin	2, A2	10, A2	5, A2	30, A2
** Methyl isoamyl ketone	(100)	(475)	(150)	(710)
Methyl isobutyl carbinol — Skin	25	100	40	165
* Methyl isobutyl ketone	50	205	75	300
Methyl isocyanate — Skin	0.02	0.05	—	—
* Methyl isopropyl ketone	200	705	—	—
Methyl mercaptan	0.5	1	—	—
Methyl methacrylate	100	410	125	510
Methyl parathion — Skin	—	0.2	—	0.6
Methyl propyl ketone	200	700	250	875
* Methyl silicate	1	6	5	30
* α-Methyl styrene	50	240	100	485
Molybdenum, as Mo Soluble compounds	—	5	—	10
Insoluble compounds	—	10	—	20
Monocrotophos (Azodrin®)	—	0.25	—	—
** Monomethyl aniline — Skin	(2)	(9)	(4)	(18)
Morpholine — Skin	20	70	30	105

Capital letters refer to Appendices.
*1981 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Naphthalene	10	50	15	75
β-Naphthylamine	—	A1b	—	A1b
Neon	E	—	—	—
Nickel carbonyl, as Ni	0.05	0.35	—	—
Nickel, metal	—	1	—	—
Soluble compounds, as Ni	—	0.1	—	0.3
Nickel sulfide roasting, fume & dust, as Ni	—	1, A1a	—	—
Nicotine — Skin	—	0.5	—	1.5
Nitric acid	2	5	4	10
Nitric oxide	25	30	35	45
** p-Nitroaniline — Skin	(1)	(6)	(2)	(12)
Nitrobenzene — Skin	1	5	2	10
** p-Nitrochlorobenzene — Skin	—	(1)	—	(2)
4-Nitrodiphenyl	—	A1b	—	A1b
Nitroethane	100	310	150	465
* Nitrogen dioxide	3	6	5	10
Nitrogen trifluoride	10	30	15	45
** Nitroglycerin (NG) — Skin	(0.02)	(0.2)	(0.05)	(0.5)
Nitromethane	100	250	150	375
** 1-Nitropropane	(25)	(90)	(35)	(135)
**C 2-Nitropropane	(25, A2)	(90, A2)	—	—
N-Nitrosodimethylamine (dimethylnitrosoamine) — Skin	—	A2	—	A2
** Nitrotoluene — Skin	(5)	(30)	(10)	(60)
Nitrotrichloromethane, see Chloropicrin				
Nonane	200	1,050	250	1,300
Octachloronaphthalene — Skin	—	0.1	—	0.3
Octane	300	1,450	375	1,800
Oil mist, mineral	—	5[e]	—	10
Osmium tetroxide, as Os	0.0002	0.002	0.0006	0.006
Oxalic acid	—	1	—	2
Oxygen difluoride	0.05	0.1	0.15	0.3
Ozone	0.1	0.2	0.3	0.6
Paraffin wax fume	—	2	—	6
Paraquat, respirable sizes	—	0.1	—	—
Parathion — Skin	—	0.1	—	0.3
Particulate polycyclic aromatic hydro-carbons (PPAH), see Coal tar pitch volatiles				
Pentaborane	0.005	0.01	0.015	0.03
Pentachloronaphthalene	—	0.5	—	2
Pentachlorophenol — Skin	—	0.5	—	1.5
Pentaerythritol	—	D	—	20
Pentane	600	1,800	750	2,250
2-Pentanone, see Methyl propyl ketone				
** Perchloroethylene —				

Capital letters refer to Appendices.
Footnotes (a thru f) see Page 473.
*1981 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Skin	(100)	(670)	(150)	(1,000)
Perchloromethyl mercaptan	0.1	0.8	—	—
Perchloryl fluoride	3	14	6	28
Phenol — Skin	5	19	10	38
Phenothiazine — Skin	—	5	—	10
N-Phenyl-beta-naphthylamine	A2	A2	—	—
p-Phenylene diamine — Skin	—	0.1	—	—
Phenyl ether (vapor)	1	7	2	14
Phenylethylene, see Styrene, monomer				
** Phenyl glycidyl ether (PGE)	(10)	(60)	(15)	(90)
** Phenylhydrazine — Skin	(5)	(20)	(10)	(45)
Phenyl mercaptan	0.5	2	—	—
C Phenylphosphine	0.05	0.25	—	—
Phorate (Thimet®) — Skin	—	0.05	—	0.2
Phosdrin (Mevinphos®) — Skin	0.01	0.1	0.03	0.3
Phosgene	0.1	0.4	—	—
Phosphine	0.3	0.4	1	1
Phosphoric acid	—	1	—	3
Phosphorus (yellow)	—	0.1	—	0.3
Phosphorus pentachloride	0.1	1	—	—
Phosphorus pentasulfide	—	1	—	3
** Phosphorus trichloride	(0.5)	(3)	—	—
Phthalic anhydride	1	6	4	24
m-Phthalodinitrile	—	5	—	—
Picloram (Tordon®)	—	10	—	20
Picric acid — Skin	—	0.1	—	0.3
Pival® (2-Pivalyl-1, 3-indandione)	—	0.1	—	0.3
Plaster of Paris	—	D	—	20
* Platinum, metal	—	1	—	—
Soluble salts, as Pt	—	0.002	—	—
Polychlorobiphenyls, see Chlorodiphenyls				
Polytetrafluoroethylene decomposition products	—	B1	—	B1
C Potassium hydroxide	—	2	—	—
Propane	E	—	—	—
Propane sultone	A2	A2	—	—
Propargyl alcohol—Skin	1	2	3	6
* β-Propiolactone	0.5, A2	1.5, A2	1, A2	3, A2
* Propionic acid	10	30	15	45
n-Propyl acetate	200	840	250	1,050
Propyl alcohol — Skin	200	500	250	625
n-Propyl nitrate	25	105	40	470
Propylene	E	—	—	—
Propylene dichloride	75	350	110	510
** Propylene glycol dinitrate (PGDN) — Skin	(0.02)	(0.1)	(0.05)	(0.3)

Capital letters refer to Appendices.
Footnotes (a thru f) see Page 473.
*1981 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Propylene glycol monomethyl ether	100	360	150	540
** Propylene imine — Skin	(2)	(5)	—	—
* Propylene oxide	20	50	—	—
Propyne, see Methyl acetylene				
Pyrethrum	—	5	—	10
Pyridine	5	15	10	30
Quinone	0.1	0.4	0.3	2
RDX, see Cyclonite				
Resorcinol	10	45	20	90
** Rhodium, metal fume & dusts, as Rh	—	(0.1)	—	(0.3)
Soluble salts, as Rh	—	0.001	—	0.003
Ronnel	—	10	—	—
Rosin core solder pyrolysis products, as formaldehyde	—	0.1	—	0.3
Rotenone (commercial)	—	5	—	10
Rouge	—	D	—	20
Rubber solvent (Naphtha)	400	1,600	—	—
Selenium compounds, as Se	—	0.2	—	—
Selenium hexafluoride, as Se	0.05	0.2	—	—
Sevin®, see Carbaryl				
Silane, see Silicon tetrahydride				
Silicon	—	D	—	20
Silicon carbide	—	D	—	20
** Silicon tetrahydride	(0.5)	(0.7)	(1)	(1.5)
Silver, metal	—	0.1	—	—
* Soluble compounds, as Ag	—	0.01	—	—
C Sodium azide	0.1	0.3	—	—
Sodium bisulfite	—	5	—	—
Sodium 2, 4-dichloro-phenoxyethyl sulfate	—	10	—	20
Sodium fluoroacetate (1080) — Skin	—	0.05	—	0.15
C Sodium hydroxide	—	2	—	—
Sodium metabisulfite	—	5	—	—
Starch	—	D	—	20
Stibine	0.1	0.5	0.3	1.5
** Stoddard solvent	100	(575)	(125)	(720)
Strychnine	—	0.15	—	0.45
* Styrene, monomer	50	215	100	425
C Subtilisins (Proteolytic enzymes as 100% pure crystalline enzyme)	—	0.00006[m]	—	—
Sucrose	—	D	—	20
Sulfur dioxide	2	5	5	10
Sulfur hexafluoride	1,000	6,000	1,250	7,500
Sulfuric acid	—	1	—	—
Sulfur monochloride	1	6	3	18
Sulfur pentafluoride	0.025	0.25	0.075	0.75
Sulfur tetrafluoride	0.1	0.4	0.3	1

Capital letters refer to Appendices.
*1981 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Sulfuryl fluoride	5	20	10	40
Systox, see Demeton®				
2, 4, 5-T	—	10	—	20
Tantalum	—	5	—	10
TEDP — Skin	—	0.2	—	0.6
Teflon® decomposition products	—	B1	—	B1
Tellurium & compounds, as Te	—	0.1	—	—
Tellurium hexafluoride, as Te	0.02	0.2	—	—
TEPP — Skin	0.004	0.05	0.01	0.2
C Terphenyls	0.5	5	—	—
1, 1, 1, 2-Tetrachloro-2, 2-difluoroethane	500	4,170	625	5,210
1, 1, 2, 2-Tetrachloro-1, 2-difluoroethane	500	4,170	625	5,210
** 1, 1, 2, 2-Tetrachloroethane — Skin	(5)	(35)	(10)	(70)
Tetrachloroethylene, see Perchloroethylene				
Tetrachloromethane, see Carbon tetrachloride				
Tetrachloronaphthalene	—	2	—	4
Tetraethyl lead, as Pb — Skin	—	0.100[n]	—	0.3
Tetrahydrofuran	200	590	250	735
Tetramethyl lead, as Pb — Skin	—	0.150[n]	—	0.5
Tetramethyl succinonitrile — Skin	0.5	3	2	9
Tetrasodium pyrophosphate	—	5	—	—
Tetranitromethane	1	8	—	—
Tetryl (2, 4 6-trinitrophenyl-methylnitramine) — Skin	—	1.5	—	3.0
Thallium, soluble compounds, as Tl — Skin	—	0.1	—	—
4, 4'-Thiobis (6-tert. butyl-m-cresol)	—	10	—	20
Thioglycolic acid	1	5	—	—
Thiram®	—	5	—	10
** Tin, inorganic compounds, except SnH_4 and SnO_2, as Sn	—	(2)	—	(4)
Tin, organic compounds, as Sn — Skin	—	0.1	—	0.2
** Tin oxide, as Sn	—	(D)	—	(20)
Titanium dioxide, as Ti	—	D	—	20
Toluene (toluol) — Skin	100	375	150	560
**C Toluene-2, 4-diisocyanate (TDI)	(0.02)	(0.14)	—	—
** o-Toluidine	(5)	(22)	(10)	(44)
Toxaphene, see Chlorinated camphene				

Capital letters refer to Appendices.
**See Notice of Intended Changes.
m) See Page 474.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
* Tributyl phosphate	0.2	2.5	0.4	5
Trichloroacetic acid	1	5	—	—
1, 2, 4-Trichlorobenzene	5	40	—	—
1, 1, 1-Trichloroethane, see Methyl chloroform				
1, 1, 2-Trichloroethane — Skin	10	45	20	90
** Trichloroethylene	(100)	(535)	(150)	(800)
** Trichlorofluoromethane	(1,000)	(5,600)	(1,250)	(7,000)
Trichloromethane, see Chloroform				
Trichloronaphthalene	—	5	—	10
Trichloronitromethane, see Chloropicrin				
1, 2, 3-Trichloropropane	50	300	75	450
1, 1, 2-Trichloro 1, 2, 2-trifluoroethane	1,000	7,600	1,250	9,500
Tricyclohexyltin hydroxide (Plictran®)	—	5	—	10
** Triethylamine	(25)	(100)	(40)	(160)
Trifluorobromomethane	1,000	6,100	1,200	7,300
* Trimellitic anhydride	0.005	0.04	—	—
Trimethyl benzene	25	125	35	170
** Trimethyl phosphite	(0.5)	(2.6)	—	—
2, 4, 6-Trinitrophenol, see Picric acid				
2, 4, 6-Trinitrophenyl-methylnitramine, see Tetryl				
**C 2, 4, 6-Trinitrotoluene (TNT)	—	(0.5)	—	—
Triorthocresyl phosphate	—	0.1	—	0.3
Triphenyl amine	—	5	—	—
Triphenyl phosphate	—	3	—	6
Tungsten & compounds, as W				
Soluble	—	1	—	3
Insoluble	—	5	—	10
Turpentine	100	560	150	840
Uranium (natural), soluble & insoluble compounds, as U	—	0.2	—	0.6
** Vanadium (V_2O_5), as V				
Dust	—	(0.5)	—	(1.5)
C Fume	—	(0.05)	—	—
Valeraldehyde	50	175	—	—
Vinyl acetate	10	30	20	60
Vinyl benzene, see Styrene				
Vinyl bromide	5, A2	20, A2	—	—
Vinyl chloride	5, A1a	10, A1a	—	—
Vinyl cyanide, see Acrylonitrile				
Vinyl cyclohexene dioxide	10	60	—	—
Vinylidene chloride	10	40	20	80
* Vinyl toluene	50	240	100	485
VM & P Naphtha	300	1,350	400	1,800

Capital letters refer to Appendices.
Footnotes (a thru f) see Page 473.
*1981 Addition.
**See Notice of Intended Changes.

Substance	ADOPTED VALUES TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Warfarin	—	0.1	—	0.3
Welding fumes (NOC)†	—	5 B3	—	B3
* Wood dust (certain hard woods as beech & oak)	—	1	—	—
Soft wood	—	5	—	10
Xylene (o-, m-, p-isomers) — Skin	100	435	150	655
C m-Xylene α, α'-diamine	—	0.1	—	—
** Xylidene — Skin	(5)	(25)	(10)	(50)
Yttrium	—	1	—	3
Zinc chloride fume	—	1	—	2
Zinc chromate, as Cr	—	0.05, A2	—	—
Zinc oxide fume	—	5	—	10
Zinc stearate	—	D	—	20
Zirconium compounds, as Zr	—	5	—	10

Capital letters refer to Appendices.
*1981 Addition.
**See Notice of Intended Changes.

a) Parts of vapor or gas per million parts of contaminated air by volume at 25°C and 760 mm Hg pressure.
b) Approximate milligrams of substance per cubic meter of air.
d) < 7 μm in diameter.
e) As sampled by method that does not collect vapor.
f) For control of general room air, biologic monitoring is essential for personnel control.

Radioactivity: The Committee accepts the philosophy and recommendations of the National Council on Radiation Protection and Measurements (NCRP) for the ionizing radiation TLV. The NCRP is charted by Congress to, in part, collect, analyze, develop and disseminate information and recommendations about protection against radiation and about radiation measurements, quantities and units, including development of basic concepts in these areas. NCRP Report No. 39 (reference 1) provides basic philosophy and concepts leading to protection criteria established in the same report. Other NCRP reports address specific areas of radiation protection and, collectively, provide an excellent basis for establishing a sound program for radiation control. The Committee recommends the listed references as substantative documentation of a sound basis for ionizing radiation protection. The Committee also strongly recommends that all exposures to ionizing radiations be kept low as reasonably achievable within the stated guidance.

References:

1. *Basic Radiation Protection Criteria.* NCRP Report No. 39, issued January 15, 1971.
2. *Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure.* US Department of Commerce, National Bureau of Standards Handbook 69, issued June 5, 1959, with Addendum 1 issued August 1963. Available as NCRP Report No. 22.

The above documents, as well as information on numerous other NCRP Reports addressing specific subjects in ionizing radiation protection are available from: NCRP Publications, PO Box 30175, Washington, DC 20014.

MINERAL DUSTS

Substance	TLV
SILICA, SiO_2	
Crystalline	
Quartz	TLV in mppcf[g]: $\frac{300^{h}}{\%\ \text{quartz} + 10}$ TLV for respirable dust in mg/m³: $\frac{10\ \text{mg/m}^3\ [i]}{\%\ \text{Respirable quartz} + 2}$ TLV for "total dust," respirable and nonrespirable: $\frac{30\ \text{mg/m}^3}{\%\ \text{quartz} + 3}$
Cristobalite	Use one-half the value calculated from the count or mass formulae for quartz.
Tridymite	Use one-half the value calculated from formulae for quartz.
Silica, fused	Use quartz formulae.
Tripoli	Use respirable[n] mass quartz formula
**Amorphous	(20 mppcf[g])
SILICATES (< 1% quartz)	
Asbestos	
Amosite	0.5 fiber > 5μm/cc, A1a
Chrysotile	2 fibers > 5μm/cc, A1a
Crocidolite	0.2 fiber > 5μm/cc, A1a
Other forms	2 fibers > 5μm/cc, A1a
Mica	20 mppcf
Mineral wool fiber	10 mg/m³
Perlite	30 mppcf
Portland Cement	30 mppcf
Soapstone	20 mppcf
**Talc (nonasbestiform)	(20 mppcf)
**Talc (fibrous), (use Asbestos limit.)	
COAL DUST	
2 mg/m³ (respirable dust fraction < 5% quartz). If > 5% quartz, use respirable mass formula.	

NUISANCE PARTICULATES
(see Appendix D)

30 mppcf or 10 mg/m³[j]
of total dust < 1% quartz, or, 5 mg/m³ respirable dust.

Conversion factors:
mppcf × 35.3 = Million particles per cubic meter
= particles per cc

g) Millions of particles per cubic foot of air, based on impinger samples counted by light-field technics.

**See notice of intended changes

h) The percentage of quartz in the formula is the amount determined from airborne samples, except in those instances in which other methods have been shown to be applicable.

i) Both concentration and percent quartz for the application of this limit are to be determined from the fraction passing a size-selector with the following characteristics:

Aerodynamic Diameter (μm) (unit density sphere)	% passing selector
≤ 2	90
2.5	75
3.5	50
5.0	25
10	0

j) containing < 1% quartz; (if quartz content > 1%, use formulae for quartz.)

k) Lint-free dust as measured by the vertical elutriator, cotton-dust sampler described in the *Transactions of the National Conference on Cotton Dust*, p. 33 by J. R. Lynch, (May 2, 1970).

l) As determined by the membrane filter method at 400–450X magnification (4 mm objective) phase contrast illumination.

m) Based on "high volume" sampling.

n) "Respirable" dust as defined by the British Medical Research Council Criteria, [1] and as sampled by a device producing equivalent results. [2]

(1) Hatch, T. E. and Gross: *Pulmonary Deposition and Retention of Inhaled Aerosols*, p. 149. Academic Press, New York, (1964).

(2) AIHA Aerosol Technology Committee: Interim Guide for Respirable Mass Sampling. *Am. Ind. Hyg. Assoc. J. 31(2)*:133 (1970).

NOTICE OF INTENDED CHANGES (for 1981)

These substances, with their corresponding values, comprise those for which either a limit has been proposed for the first time, or for which a change in the "Adopted" listing has been proposed. In both cases, the proposed limits should be considered trial limits that will remain in the listing for a period of at least two years. If, after two years no evidence comes to light that questions the appropriateness of the values herein, the values will be reconsidered for the "Adopted" list. Documentation is available for each of these substances.

Substance	TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Acetone	750	1780	1000	2375
Acrylonitrile	2, A1a	4.5, A1a	—	—
† Atrazine	—	5	—	—
Benzidine — Skin	—	A1b	—	—
Cadmium oxide production	—	0.05	—	—
C o-Chlorobenzylidene malononitrile	0.05	0.4	—	—
Chloromethyl methyl ether	A2	A2	—	—
Chromyl chloride	0.025	0.15	—	—
† Cobalt carbonyl, as Co	—	0.1	—	—
† Cobalt hydrocarbonyl, as Co	—	0.1	—	—
Cobalt metal, dust & fume, as Co	—	0.05	—	0.1
Enflurane	75	575	—	—
Ethylene dibromide — Skin	A2	A2	—	—
† Ethylene glycol dinitrate (EGDN) — Skin	0.05	0.3	0.1	0.6
† Ethylene oxide	5, A2	10, A2	—	—
N-Ethylmorpholine — Skin	5	23	20	95
† Fenthion	—	0.2	—	—
† Formaldehyde	A2	A2	—	—
Furfuryl alcohol — Skin	10	40	15	60
Gasoline	300	900	500	1500
Halothane	50	400	—	—
Hexachlorobutadiene	0.02, A2	0.24, A2	—	—
Hexachloroethane — Skin	10	100	—	—
Hexane (n-Hexane)	50	180	—	—
Other isomers	500	1,800	1,000	3,600
Iron pentacarbonyl, as Fe	0.1	0.8	0.2	0.16
Isooctyl alcohol	50	270	—	—
Lead arsenate, as $Pb_3(AsO_4)_2$	—	0.15	—	0.45
Mercury (All forms except alkyl) — Skin, as Hg Vapor	—	0.05	—	—
Aryl & inorganic compounds	—	0.1	—	—
4-Methoxyphenol	—	5	—	—
N-Methyl aniline — Skin	0.5	2	1	5
Methyl isoamyl ketone	50	240	—	—
p-Nitroaniline — Skin	—	3	—	—
p-Nitrochlorobenzene — Skin	0.5	3	—	—
† Nitroglycerin (NG) — Skin	0.05	0.5	0.1	1
1-Nitropropane	15	55	25	90
† 2-Nitropropane	5, A2	35, A2	20, A2	70, A2
Nitrotoluene — Skin	2	11	—	—
Perchloroethylene — Skin	50	335	—	—
Persulfates, alkali metal, as S_2O_8	—	2	—	—
Phenyl glycidyl ether (PGE)	1	6	—	—
† Phenylhydrazine — Skin	5, A2	20, A2	10, A2	45, A2
Phosphorus oxychloride	0.1	0.6	0.5	3
Phosphorus trichloride	0.2	1.5	0.5	3
Piperazine dihydrochloride	—	5	—	—
† Propylene glycol dinitrate (PGDN) — Skin	0.05	0.3	0.1	0.6
Propylene imine — Skin	2, A2	5, A2	—	—
Rhodium, metal	—	1	—	—
Insoluble compounds, as Rh	—	0.1	—	0.3

Capital letters refer to Appendices.
†1981 Revision or Addition.

Capital letters refer to Appendices.
†1981 Revision or Addition.

Substance	TWA ppm[a]	TWA mg/m³[b]	STEL ppm[a]	STEL mg/m³[b]
Silicon tetrahydride (Silane)	5	7	—	—
Stoddard solvent	100	525	200	1,050
1, 1, 2, 2-Tetrachloroethane — Skin	1	7	5	35
Tin, tin oxide & inorganic compounds, except SnH_4, as Sn	—	2	—	4
o-Tolidine	A2	A2	—	—
Toluene-2, 4-diisocyanate (TDI)	0.005	0.04	0.02	0.15
o-Toluidine	2	9	—	—
Trichloroethylene	50	270	150	805
C Trichlorofluoromethane	1,000	5,600	—	—
† Triethylamine	10	40	15	60
† Trimethylamine	10	40	15	60
Trimethyl phosphite	2	10	5	25
2, 4, 6-Trinitrotoluene (TNT) — Skin	—	0.5	—	3
Vanadium, as V_2O_5, dust & fume	—	0.05	—	—
Xylidine — Skin	2	10	—	—

Capital letters refer to Appendices.
†1981 Revision or Addition.

NOTICE OF INTENDED CHANGES
MINERAL DUSTS

Substance	TLV
Diatomaceous earth, natural	1.5 mg/m³, Respirable dust
Silica, amorphous	6 mg/m³, Total dust (all sampled sizes) 3 mg/m³, Respirable dust (< 5 μm)
Talc (containing no fibers)	15 mppcf or 2 mg/m³, Respirable Dust
Talc (fiber-containing)	2 fibers/cc, > 5 μm in length

APPENDIX A
Carcinogens

The Committee lists below those substances in industrial use that have proven carcinogenic in man, or have induced cancer in animals under appropriate experimental conditions. Present listing of those substances carcinogenic for man takes two forms: Those for which a TLV has been assigned (1a) and those for which environmental conditions have not been sufficiently defined to assign a TLV (1b).

A1a. *Human Carcinogens*. Substances, or substances associated with industrial processes, recognized to have carcinogenic or cocarcinogenic potential, with an assigned TLV:

	TLV
Acrylonitrile	2 ppm
Asbestos	
Amosite	0.5 fiber > 5μm/cc
Chrysotile	2 fibers > 5μm/cc
Crocidolite	0.2 fiber > 5μm/cc
Other forms	2 fibers > 5μm/cc
bis (Chloromethyl) ether	0.001 ppm
Chromite ore processing (chromate)	0.05 mg/m³, as Cr
†† Chromium (VI), certain water insoluble compounds	0.05 mg/m³, as Cr
Coal tar pitch volatiles	0.2 mg/m³, as benzene solubles
Nickel sulfide roasting, fume & dust	1.0 mg/m³, as Ni
Vinyl chloride	5 ppm

* * *

A1b. *Human Carcinogens*. Substances, or substances associated with industrial processes, recognized to have carcinogenic potential without an assigned TLV:

** Acrylonitrile
4-Aminodiphenyl (p-Xenylamine)
Benzidine — Skin
** Chloromethyl methyl ether
** Ethylene dibromide
β-Naphthylamine
4-Nitrodiphenyl

For the substances in 1b, no exposure or contact by any route — respiratory, skin or oral, as detected by the most sensitive methods — shall be permitted. The worker should be properly equipped to insure virtually no contact with the carcinogen.

A2. *Industrial Substances Suspect of Carcinogenic Potential for MAN*. Chemical substances or substances associated with industrial processes, which are suspect of inducing cancer, based on either (1) limited epidemiologic evidence, exclusive of clinical reports of single cases, or (2) demonstration of carcinogenesis in one or more animal species by appropriate methods.

3-Amino 1, 2, 4-triazole	
Antimony trioxide production*	—
Arsenic trioxide production	—
Benzene	10 ppm
Benzo(a)pyrene	—
Beryllium	2.0 μg/m³
Cadmium oxide production	—
†† Carbon tetrachloride — Skin	5 ppm
Chloroform	10 ppm

*Cigarette smoking can enhance the incidence of respiratory cancers from this or others of these substances or processes.
†1981 Addition.
††1981 Adoption.
**See Notice of Intended Changes.

Chloromethyl methyl ether	——
Chromates of lead and zinc, as Cr	0.05 mg/m³
†† Chrysene	——
3, 3′-Dichlorobenzidine — Skin	——
Dimethylcarbamyl chloride	——
1, 1-Dimethyl hydrazine — Skin	0.5 ppm
Dimethyl sulfate — Skin	0.1 ppm
Ethylene dibromide — Skin	——
† Ethylene oxide	5 ppm
† Formaldehyde	——
Hexachlorobutadiene	0.02 ppm
Hexamethyl phosphoramide — Skin	——
Hydrazine — Skin	0.1 ppm
4, 4′-Methylene bis (2-chloroaniline) — Skin	0.02 ppm
C Methyl hydrazine — Skin	0.2 ppm
†† Methyl iodide — Skin	2 ppm
† 2-Nitropropane	10 ppm
N-Nitrosodimethylamine — Skin	——
N-Phenyl-beta-naphthylamine	——
† Phenylhydrazine — Skin	5 ppm
Propane sultone	——
†† beta-Propiolactone	0.5 ppm
Propylene imine — Skin	2 ppm
o-Tolidine	——
Vinyl bromide	5 ppm
Vinyl cyclohexene dioxide	10 ppm

†1981 Addition.
††1981 Adoption.

For the above, worker exposure by all routes should be carefully controlled to levels consistent with the animal and human experience data (see Documentation), including those substances with a listed TLV.

THE COMMITTEE GUIDELINES FOR CLASSIFICATION OF EXPERIMENTAL ANIMAL CARCINOGENS

The following guidelines are offered in the present state of knowledge as an aid in classifying substances in the occupational environment found to be carcinogenic in experimental animals. A need was felt by the Threshold Limits Committee for such a classification in order to take the first step in developing an appropriate TLV for occupational exposure.

Determination of Approximate Threshold of Response Requirement. In order to determine in which category to classify an experimental carcinogen for the purpose of assigning an industrial air limit (TLV), an approximate threshold of neoplastic response must be determined. Because of practical experimental difficulties, a precisely defined threshold cannot be attained. For the purposes of standard-setting, this is of little moment, as an appropriate risk, or safety, factor can be applied to the approximate threshold, the magnitude of which is dependent on the degree of potency of the carcinogenic response.

To obtain the best 'practical' threshold of neoplastic response, dosage decrements should be less than logarithmic. This becomes particularly important at levels greater than 10 ppm (or corresponding mg/m³). Accordingly, after a range-finding determination has been made by logarithmic decreases, two additional dosage levels are required within the levels of "effect" and "no effect" to approximate the true threshold of neoplastic response.

The second step should attempt to establish a metabolic relationship between animal and man for the particular substance found carcinogenic in animals. If the metabolic pathways are found comparable, the substance should be classed highly suspect as a carcinogen for man. If no such relation is found, the substance should remain listed as an experimental animal carcino gen until evidence to the contrary is found.

Proposed Classification of Experimental Animal Carcinogens. Substances occurring in the occupational environment found carcinogenic for animals may be grouped into three classes, those of high, intermediate and low potency. In evaluating the incidence of animal cancers, significant incidence of cancer is defined as a neoplastic response which represents, in the judgment of the Committee, a significant excess of cancers above that occurring in negative controls.

EXCEPTIONS: No substance is to be considered an occupational carcinogen of any practical significance which reacts by the respiratory route at or above 1000 mg/m³ for the mouse, 2000 mg/m³ for the rat; by the dermal route, at or above 1500 mg/kg for the mouse, 3000 mg/kg for the rat; by the gastrointestinal route at or above 500 mg/kg/d for a lifetime, equivalent to about 100 g T.D. for the rat, 10 g T.D. for the mouse.

These dosage limitations exclude such substances as dioxane and trichlorethylene from consideration as carcinogens.

Examples: Dioxane — rats, hepatocellular and nasal tumors from 1015 mg/kg/d, oral
Trichloroethylene — female mice, tumors (30/98 @ 900 mg/kg/d), oral

A. *Industrial Substances of High Carcinogenic Potency in Experimental Animals.*

1. A substance to qualify as a carcinogen of high potency must fulfill one of the three following conditions in two animal species:

1a. *Respiratory*. Elicit cancer from (1) dosages below 1 mg/m³ (or equivalent ppm) via the respiratory tract in 6- 7-hour daily repeated inhalation exposures throughout lifetime; or (2) from a single intratracheally administered dose not exceeding 1 mg of particulate, or liquid, per 100 ml or less of animal minute respiratory volume;

Examples: bis-Chloromethyl ether, malignant tumors, rats, @ 0.47 mg/m³ (0.1 ppm) in 2 years;
Hexamethyl phosphoramide, nasal squamous cell carcinoma, rats, @ 0.05 ppm, in 13 months

OR

1b. *Dermal*. Elicit cancer within 20 weeks by skin-painting, twice weekly at 2 mg/kg body weight

or less per application for a total dose equal to or less than 1.5 mg, in a biologically inert vehicle;

Examples: 7, 12-Dimethylbenz(a)anthracene — skin tumors @ 0.12-0.8 mg T.D. in four weeks

Benzo(a)pyrene, mice 12 μg, 3X/wk for 18 mos. T.D. 2.6 mg, 90.9% skin tumors

OR

1c. *Gastrointestinal*. Elicit cancer by daily intake via the gastrointestinal tract, within six months, with a six-month holding period, at a dosage below 1 mg/kg body weight per day; total dose, rat, ≦ 50 mg; mouse, ≦ 3.5 mg;

Examples: 7, 12-Dimethylbenz(a)anthracene — mammary tumors from 10 mg 1X

3-Methylcholanthrene — Tumors @ 3 sites from 8 mg in 89 weeks

Benzo(a)pyrene, mice, 3.9% leukemias, from 30 mg T.D. 198 days

2. Elicit cancer by all three routes in at least two animal species at dose levels prescribed for high or intermediate potency.

B. *Industrial Substances of Intermediate Carcinogenic Potency in Experimental Animals.*

To qualify as a carcinogen of intermediate potency, a substance should elicit cancer in two animal species at dosages intermediate between those described in A and C by two routes of administration.

Example: Carbamic acid ethyl ester
Dermal, mammary tumors, mice, 100%, 63 weeks, 500–1400 mg T.D. Gastrointestinal, various type tumors, mice 42 weeks, 320 mg T.D.

Gastrointestinal, various type tumors, rats, 60 weeks, 110–930 mg T.D.

C. *Industrial Substances of Low Carcinogenic Potency in Experimental Animals.*

To qualify as a carcinogen of low potency, a substance should elicit cancer in one animal species by any *one* of three routes of administration at the following prescribed dosages and conditions:

1a. *Respiratory*. Elicit cancer from (1) dosages greater than 10 mg/m³ (or equivalent ppm) via the respiratory tract in 6-7-hour, daily repeated inhalation exposures, for 12 months' exposure and 12 months' observation period; or (2) from intratracheally administered dosages totaling more than 10 mg of particulate or liquid per 100 ml or more of animal minute respiratory volume;

Examples: Beryl (beryllium aluminum silicate) malig. lung tumors, rats, @ 15 mg/m³ @ 17 months

Benzidine, var. tumors, rats, 10–20 mg/m³ @ > 13 mos.

OR

1b. *Dermal*. Elicit cancer by skin-painting of mice in twice weekly dosages of > 10 mg/kg body weight in a biologically inert vehicle for at least 75 weeks, i.e., ≧ 1.5g T.D.

Examples: Shale tar, mouse, 0.1 ml × 50 = 5g T.D. 59/60 skin tumors

Arsenic trioxide, man, dose unknown, but estimated to be high

1c. *Gastrointestinal*. Elicit cancer from daily oral dosages of 50 mg/kg/day or greater during the lifetime of the animal.

APPENDIX B
SUBSTANCES OF VARIABLE COMPOSITION

B1 *Polytetrafluoroethylene* decomposition products*. Thermal decomposition of the fluorocarbon chain in air leads to the formation of oxidized products containing carbon, fluorine and oxygen. Because these products decompose in part by hydrolysis in alkaline solution, they can be quantitatively determined in air as fluoride to provide an index of exposure. No TLV is recommended pending determination of the toxicity of the products, but air concentrations should be minimal.

B2 *Welding Fumes — Total Particulate (NOC)†*
TLV, 5 mg/m³

Welding fumes cannot be classified simply. The composition and quantity of both are dependent on the alloy being welded and the process and electrodes used. Reliable analysis of fumes cannot be made without considering the nature of the welding process and system being examined; reactive metals and alloys such as aluminum and titanium are arc-welded in a protective, inert atmosphere such as argon. These arcs create relatively little fume, but an intense radiation which can produce ozone. Similar processes are used to arc-weld steels, also creating a relatively low level of fumes. Ferrous alloys also are arc-welded in oxidizing environments which generate considerable fume, and can produce carbon monoxide instead of ozone. Such fumes generally are composed of discreet particles of amorphous slags containing iron, manganese, silicon and other metallic constituents depending on the alloy system involved. Chromium and nickel compounds are found in fumes when stainless steels are arc-welded. Some coated and flux-cored electrodes are formulated with fluorides and the fumes associated with them can contain significantly more fluorides than oxides. Because of the above factors, arc-welding fumes frequently must be tested for individual constituents which are likely to be present to determine whether specific TLV's are exceeded. Conclusions based on total fume concentration are generally adequate if no toxic elements are present in welding rod, metal, or metal coating and conditions are not conducive to the formation of toxic gases.

Most welding, even with primitive ventilation, does not produce exposures inside the welding helmet above 5 mg/m³. That which does, should be controlled.

APPENDIX C
MIXTURES

C.1 THRESHOLD LIMIT VALUES FOR MIXTURES

When two or more hazardous substances, which act upon the same organ system, are present, their combined effect, rather than that of either individually, should be given

primary consideration. In the absence of information to the contrary, the effects of the different hazards should be considered as additive. That is, if the sum of the following fractions,

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \ldots \frac{C_n}{T_n}$$

exceeds unity, then the threshold limit of the mixture should be considered as being exceeded. C_1 indicates the observed atmospheric concentration, and T_1 the corresponding threshold limit (See Example 1A.a. and 1A.c.).

Exceptions to the above rule may be made when there is a good reason to believe that the chief effects of the different harmful substances are not in fact additive, but *independent* as when purely local effects on different organs of the body are produced by the various components of the mixture. In such cases the threshold limit ordinarily is exceeded only when at least one member of the series $\left(\frac{C_1}{T_1} + \text{or} + \frac{C_2}{T_2} \text{ etc.}\right)$ itself has a value exceeding unity (See Example 1A.c.).

Synergistic action or potentiation may occur with some combinations of atmospheric contaminants. Such cases at present must be determined individually. Potentiating or synergistic agents are not necessarily harmful by themselves. Potentiating effects of exposure to such agents by routes other than that of inhalation is also possible, e.g. imbibed alcohol and inhaled narcotic (trichloroethylene). Potentiation is characteristically exhibited at high concentrations, less probably at low.

When a given operation or process characteristically emits a number of harmful dusts, fumes, vapors or gases, it will frequently be only feasible to attempt to evaluate the hazard by measurement of a single substance. In such cases, the threshold limit used for this substance should be reduced by a suitable factor, the magnitude of which will depend on the number, toxicity and relative quantity of the other contaminants ordinarily present.

Examples of processes which are typically associated with two or more harmful atmospheric contaminants are welding, automobile repair, blasting, painting, lacquering, certain foundry operations, diesel exhausts, etc.

C.1A Examples of THRESHOLD LIMIT VALUES FOR MIXTURES

The following formulae apply only when the components in a mixture have similar toxicologic effects; they should not be used for mixtures with widely differing reactivities, e.g. hydrogen cyanide & sulfur dioxide. In such case the formula for Independent Effects (1A.c.) should be used.

1A.a. General case, where air is analyzed for each component:

a. *Additive effects. (Note: It is essential that the atmosphere be analyzed both qualitatively and quantitatively for each component present, in order to evaluate compliance or noncompliance with this calculated TLV.)*

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \frac{C_3}{T_3} + \ldots = 1$$

Example No. 1A.a.: Air contains 400 ppm of acetone (TLV = 1000 ppm) 150 ppm of sec-butyl acetate (TLV = 200 ppm) and 100 ppm of 2-butanone (TLV = 200 ppm)

Atmospheric concentration of mixture = 400 + 150 + 100 = 650 ppm of mixture

$$\frac{400}{1000} + \frac{150}{200} + \frac{100}{200} = 0.4 + 0.75 + 0.5 = 1.65$$

Threshold Limit is exceeded.

1A.b. Special case when the source of contaminant is a liquid mixture and the atmospheric composition is *assumed* to be similar to that of the original material; e.g. on a time-weighted average exposure basis, all of the liquid (solvent) mixture eventually evaporates.

Additive effects (approximate solution)

1. The percent composition (by weight) of the liquid mixture is known, the TLVs of the constituents must be listed in mg/m³.

(Note: In order to evaluate compliance with this TLV, field sampling instruments should be calibrated, in the laboratory, for response to this specific quantitative and qualitative air-vapor mixture, and also to fractional concentrations of this mixture; e.g., 1/2 the TLV; 1/10 the TLV; 2 × the TLV; 10 × the TLV; etc.)

TLV of mixture =

$$\frac{1}{\frac{f_a}{TLV_a} + \frac{f_b}{TLV_b} + \frac{f_c}{TLV_c} + \ldots \frac{f_n}{TLV_n}}$$

Example No. 1: Liquid contains (by weight)
50% heptane: TLV = 400 ppm or 1600 mg/m³
1 mg/m³ ≡ 0.25 ppm
30% methyl chloroform: TLV = 350 ppm or 1900 mg/m³
1 mg/m³ ≡ 0.18 ppm
20% perchloroethylene: TLV = 100 ppm or 670 mg/m³
1 mg/m³ ≡ 0.15 ppm

$$\text{TLV of Mixture} = \frac{1}{\frac{0.5}{1600} + \frac{0.3}{1900} + \frac{0.2}{670}}$$

$$= \frac{1}{0.00031 + 0.00016 + 0.00030}$$

$$= \frac{1}{0.00077} = 1300 \text{ mg/m}^3$$

of this mixture
50% or (1300) (0.5) = 650 mg/m³ is heptane
30% or (1300) (0.3) = 390 mg/m³ is methyl chloroform
20% or (1300) (0.2) = 260 mg/m³ is perchloroethylene

These values can be converted to ppm as follows:

heptane: 650 mg/m³ × 0.25 = 162 ppm
methyl chloroform: 390 mg/m³ × 0.18 = 70 ppm
perchloroethylene: 260 mg/m³ × 0.15 = 39 ppm

TLV of mixture = 162 + 70 + 39 = 271 ppm, or 1300 mg/m³

These values can be converted to ppm as follows:

heptane: 468 mg/m³ × 0.25 = 117 ppm
methyl chloroform: 281 mg/m³ × 0.18 = 51 ppm
perchloroethylene: 187 mg/m³ × 0.15 = 29 ppm

TLV of mixture = 117 + 51 + 29 = 197 ppm, or 935 mg/m³

1A.c. *Independent effects.*
Air contains 0.15 mg/m³ of lead (TLV, 0.15) and 0.7 mg/m³ of sulfuric acid (TLV, 1).

$$\frac{0.15}{0.15} = 1; \qquad \frac{0.7}{1} = 0.7$$

Threshold limit is not exceeded.

1B. TLV for Mixtures of Mineral Dusts.

For mixtures of biologically active mineral dusts the general formula for mixtures may be used.

For mixture containing 80% nonasbestiform talc and 20% quartz, the TLV for 100% of the mixture is given by:

$$TLV = \frac{1}{\frac{0.8}{20} + \frac{0.2}{2.7}} = 9 \text{ mppcf}$$

TLV of asbestiform talc (pure) = 20 mppcf
TLV of quartz (pure) =

$$\frac{300}{100 + 10} = \frac{300}{110} = 2.7 \text{ mppcf}$$

Essentially the same result will be obtained if the limit of the more (most) toxic component is used provided the effects are additive. In the above example the limit for 20% quartz is 10 mppcf.

For another mixture of 25% quartz, 25% amorphous silica and 50% talc:

25% quartz — TLV (pure) = 2.7 mppcf
25% amorphous silica — TLV (pure) = 20 mppcf
50% talc TLV (pure) = 20 mppcf

$$TLV = \frac{1}{\frac{0.25}{2.7} + \frac{0.25}{20} + \frac{0.5}{20}} = 8 \text{ mppcf}$$

The limit for 25% quartz approximates 9 mppcf.

APPENDIX D
Some Nuisance Particulates[o]

TLV, 30 mppcf or 10 mg/m³ of total dust < 1% quartz, or, 5 mg/m³ respirable dust

Aluminum oxide (Al_2O_3)	Gypsum
Calcium carbonate	Kaolin
Calcium silicate	Limestone
Cellulose (paper fiber)	Magnesite
Emery	Marble
Glycerin Mist	Mineral Wool Fiber
Graphite (synthetic)	Pentaerythritol
Plaster of Paris	Titanium Dioxide
Portland Cement	Vegetable oil mists (except castor, cashew nut, or similar irritant oils)
Rouge	Zinc Stearate
Silicon	Zinc oxide dust
Silicon Carbide	
Starch	
Sucrose	

o) When toxic impurities are not present, e.g. quartz < 1%.

APPENDIX E
Some Simple Asphyxiants[p]

Acetylene	Helium	Propane
Argon	Hydrogen	Propylene
Ethane	Methane	
Ethylene	Neon	

p) As defined in preface.

APPENDIX F
Conversion of mppcf to Mass Concentration

Calculations for Conversion of Particle Count Concentration (by Standard Light Field — Midget Impinger Techniques), in mppcf, to Respirable Mass Concentration (by Respirable Sampler) in mg/m³.[1]

1. In 1967, Jacobsen and Tomb,[1] derived an empirical relationship of 5.6 mppcf to 1 milligram of respirable dust per cubic meter of air, based on 23 sets of samples, mostly coal dust. Studies on conversion factors have been undertaken and preliminary evidence suggests that the application of any single conversion factor may not be adequate for use in risk assessments, epidemiology studies, or setting TLVs.

   The following calculation results in an equivalence of 6.37 mppcf to 1 mg/m³ of respirable dust. Thus, an approximate ratio of 6 mppcf to 1 mg/m³ of respirable dust is suggested for conversion of TLVs from a count to a mass basis when the density and mass median diameter have not been determined.

2. Basic assumptions:

   a) Average density for silica containing dusts ≈ 2.5 g/cm³ (2500 mg/cm³). Pulmonary significant dust densities may vary from 1.2 g/cm³ for coal dust to 3.1 g/cm³ for Portland Cement. Silica densities vary from 2.2 (amorphous) to 2.3 (cristobalite and tridymite) to 2.5 (alpha-quartz.) gms per cm³.

   b) The mass median diameter (mmd) of particles collected in midget impinger samplers and counted by the standard light field technique, *and* collected in a respirable sampler is approximately 1.5 μm or 1.5×10^{-4} cm. This assumption is, of course, quite arbitrary since the mmd of all dust clouds is quite variable, depending on many independent parameters, such as source of dust, age of dust cloud, meteorological conditions, processes and equipment changes, etc. If the density and the mass median diameter of the dust particles are known, the nomograph in Figure 1 can be used to convert dust count concentrations (mppcf) to respirable mass concentrations (mg/m³).

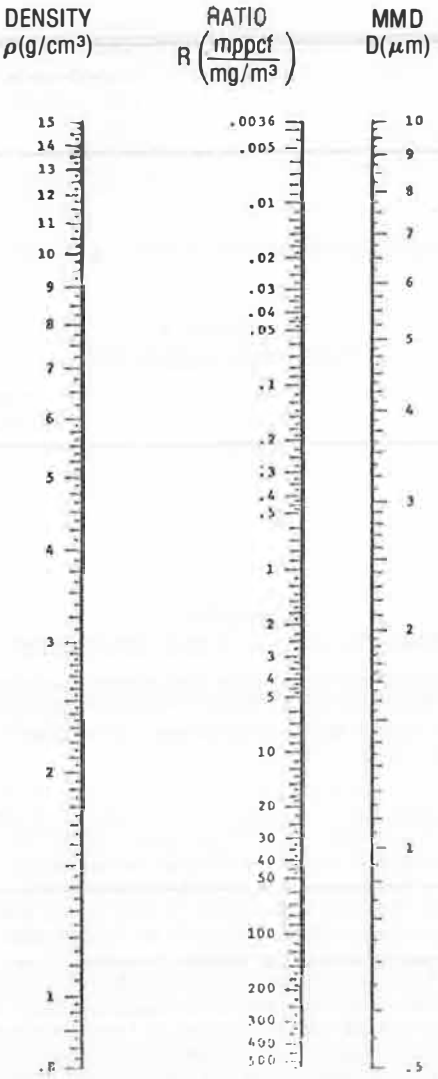

Figure 1 — Ratio of Particle Count — mppcf to Respirable Mass Concentration — mg/m³ (as function of density and mmd)†

†Prepared by P. E. Caplan and R. J. Smith

3. Calculation:

a) vol. per particle: $4/3\ \pi\ r^3$; $r = 0.75 \times 10^{-4}$ cm
$= 4/3 \cdot \pi \cdot (0.75 \times 10^{-4})^3$
$= 1.77 \times 10^{-12}$ cm³

b) wt. per particle = vol. × density
$= 1.77 \times 10^{-12}$ cm³ $\times\ 2.5 \times 10^{3}$ mg/cm³
$= 4.425 \times 10^{-9}$ mg/particle

c) 1 particle/ft.³ = 35.3 part./m³
(since 35.5 cu ft = 1 cu m.)
10^6 part./ft³ = mppcf = 35.3×10^6 part./m³
wt. of 1 mppcf ≡ 35.5×10^6 part./m³ $\times\ 4.425 \times 10^{-9}$ mg/part.
1 mppcf ≡ 0.157 mg/m³

or
6.37 mppcf ≡ 1 mg/m³
or approximately 6 mpccf ≡ 1 mg/m³.

Table 1

Equivalent TLVs in mppcf and mg/m³ (Respirable Mass) for Mineral Dusts†

Substance	Threshold Limit Value		
	Count mppcf	Resp. Mass mg/m³	Total Mass* mg/m³
Silica (SiO_2)			
Amorphous	20	(3)**	(6)
Cristobalite	1.5	0.05	0.15
Fused silica	3	0.1	0.3
Quartz	3	0.1	0.3
Tridymite	1.5	0.05	0.15
Coal Dust	(12)	2	(4)
Diatomaceous earth, natural	—	1.5	—
Graphite (natural)	15	(2.5)	(5)
Mica	20	(3)	(6)
Mineral wool fiber	—	(5)	10
Nuisance particulates	30	(5)	10
Perlite	30	(5)	(10)
Portland Cement	30	(5)	(10)
Soapstone	20	(3)	(6)
Tripoli	(3)	0.1	(0.3)

†Assuming that the mass median diameter is 1.5μm and density is 2.5 g/cm³.
*Unless otherwise specified, respirable mass is presumed to equal approximately 50% of total mass.
**All values in parentheses ( ) represent newly calculated values based on equivalence of 6 mppcf ≡ 1 mg/m³ respirable mass and respirable mass ≡ 50% total mass.

Reference

1. Jacobson, M. and T. F. Tomb: Relationship Between Gravimetric Respirable Dust Concentration and Midget Impinger Number Concentration. *Am. Ind. Hyg. Assoc. J. 28*:554 (Nov.-Dec. 1967).

APPENDIX G
Chemical Substances Under Study

Acetonitrile
Acetophenone
Acetyl acetone
Allyl chloride
Asbestos
Bismuth telluride
Carbonyl fluoride
Chlorinated naphthalenes
Chlorine
bis-Chloromethyl ether
Chloromethyl methyl ether
Copper dust & fume
Diatomaceous earth
4,4'-Diphenylmethane diisocyanate (MDI)
Epichlorohydrin
Ethyl chloride
Grain dust
Hexafluoroacetone
Hexamethylene diisocyanate (HMDI)
Isooctyl alcohol
Methyl methacrylate
Nickel, metal & soluble compounds
Nitrous oxide
Osmium tetroxide
Propylene chloride
Proylene oxide
Rhodium
Silica, amorphous
Silicon tetrahydride (Silane)
Styrene, monomer

Ethylene dichloride
Ethylene glycol monobutyl ether
Ethylene glycol monoethyl ether
Ethylene glycol monomethyl ether
Ethylene oxide
Formaldehyde
2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)
Tin hydride
Toluene-2,6-diisocyanate
1,2,3-Trichloropropane
Trimellitic anhydride
Vinylidine chloride
Welding fumes

PREFACE

PHYSICAL AGENTS

These threshold limit values refer to levels of physical agents and represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect. Because of wide variations in individual susceptibility, exposure of an occasional individual at, or even below, the threshold limit may not prevent annoyance, aggravation of a pre-existing condition, or physiological damage.

These threshold limits are based on the best available information from industrial experience, from experimental human and animal studies, and when possible, from a combination of the three.

These limits are intended for use in the practice of industrial hygiene and should be interpreted and applied only by a person trained in this discipline. They are not intended for use, or for modification for use, (1) in the evaluation or control of the levels of physical agents in the community, (2) as proof or disproof of an existing physical disability, or (3) for adoption by countries whose working conditions differ from those in the United States of America.

These values are reviewed annually by the Committee on Threshold Limits for Physical Agents for revisions or additions, as further information becomes available.

Notice of Intent — At the beginning of each year, proposed actions of the Committee for the forthcoming year are issued in the form of a "Notice of Intent." This notice provides not only an opportunity for comment, but solicits suggestions of physical agents to be added to the list. The suggestions should be accompanied by substantiating evidence.

As Legislative Code — The Conference recognizes that the Threshold Limit Values may be adopted in legislative codes and regulations. If so used, the intent of the concepts contained in the Preface should be maintained and provisions should be made to keep the list current.

THRESHOLD LIMIT VALUES

HEAT STRESS

These Threshold Limit Values refer to heat stress conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse health effects. The TLVs shown in Table 1 are based on the assumption that nearly all acclimatized, fully clothed workers with adequate water and salt intake should be able to function effectively under the given working conditions without exceeding a deep body temperature of 38°C.[1, 2]

Since measurement of deep body temperature is impractical for monitoring the workers' heat load, the measurement of environmental factors is required which most nearly correlate with deep body temperature and other physiological responses to heat. At the present time Wet Bulb Globe Temperature Index (WBGT) is the simplest and most suitable technique to measure the environmental factors. WBGT values are calculated by the following equations:

TABLE 1

Permissible Heat Exposure Threshold Limit Values
(Values are given in °C. WBGT)

	Work Load		
Work — Rest Regimen	Light	Moderate	Heavy
Continuous work	30.0	26.7	25.0
75% Work — 25% Rest, Each hour	30.6	28.0	25.9
50% Work — 50% Rest, Each hour	31.4	29.4	27.9
25% Work — 75% Rest, Each hour	32.2	31.1	30.0

1. Outdoors with solar load:
   $WBGT = 0.7\ NWB + 0.2\ GT + 0.1\ DB$
2. Indoors or Outdoors with no solar load:
   $WBGT = 0.7\ NWB + 0.3\ GT$

where:

WBGT = Wet Bulb Globe Temperature Index
NWB = Natural Wet-Bulb Temperature
DB = Dry-Bulb Temperature
GT = Globe Temperature

The determination of WBGT requires the use of a black globe thermometer, a natural (static) wet-bulb thermometer, and a dry-bulb thermometer.

Higher heat exposures than shown in Table 1 are permissible if the workers have been undergoing medical surveillance and it has been established that they are more tolerant to work in heat than the average worker. Workers should not be permitted to continue their work when their deep body temperature exceeds 38.0°C.

EVALUATION AND CONTROL

I. *Measurement of the Environment*

The instruments required are a dry-bulb, a natural wet-bulb, a globe thermometer, and a stand. The measurement of the environmental factors shall be performed as follows:

A. The range of the dry and the natural wet bulb thermometer shall be −5°C to 50°C with an accuracy of ±0.5°C. The dry bulb thermometer must be shielded from the sun and the other radiant surfaces of the environment without restricting the airflow around the bulb. The wick of the natural wet-bulb thermometer shall be kept wet with distilled water for at least 1/2 hour before the temperature reading is made. It is not enough to immerse the other end of the wick into a reservoir of distilled water and wait until the whole wick becomes wet by capillarity. The wick shall be wetted by direct application of water from a syringe 1/2 hour before

TABLE 2

Assessment of Work Load[9]

Average values of metabolic rate during different activities.

A. Body position and movement	kcal/min
Sitting	0.3
Standing	0.6
Walking	2.0–3.0
Walking up hill	add 0.8 per meter (yard) rise

B. Type of Work		Average kcal/min	Range kcal/min
Hand work			
	light	0.4	0.2–1.2
	heavy	0.9	
Work with one arm			
	light	1.0	0.7–2.5
	heavy	1.8	
Work with both arms			
	light	1.5	1.0–3.5
	heavy	2.5	
Work with body			
	light	3.5	2.5–15.0
	moderate	5.0	
	heavy	7.0	
	very heavy	9.0	

TABLE 3

Activity Examples[9]

Light hand work: writing, hand knitting

Heavy hand work: typewriting

Heavy work with one arm: hammering in nails (shoemaker, upholsterer)

Light work with two arms: filing metal, planing wood, raking of a garden

Moderate work with the body: cleaning a floor, beating a carpet

Heavy work with the body: railroad track laying, digging, barking trees

Sample Calculation

Assembly line work using a heavy hand tool.

A. Walking along	2.0 kcal/min
B. Intermediate value between heavy work with two arms and light work with the body	3.0 kcal/min
	5.0 kcal/min
C. Add for basal metabolism	1.0 kcal/min
Total	6.0 kcal/min

each reading. The wick shall extend over the bulb of the thermometer, covering the stem about one additional bulb length. The wick should always be clean and new wicks should be washed before using.

B. A globe thermometer, consisting of a 15 cm. (6-inch) diameter hollow copper sphere painted on the outside with a matte black finish or equivalent, shall be used. The bulb or sensor of a thermometer (range −5°C to 100°C with an accuracy of ±0.5°C) must be fixed in the center of the sphere. The globe thermometer shall be exposed at least 25 minutes before it is read.

C. A stand shall be used to suspend the three thermometers so that they do not restrict free air flow around the bulbs, and the wet-bulb and globe thermometer are not shaded.

D. It is permissible to use any other type of temperature sensor that gives identical reading as that of a mercury thermometer under the same conditions.

E. The thermometers must be so placed that the readings are representative of the condition where the men work or rest, respectively.

The methodology outlined above is more fully explained by Minard.[3–4]

II. *Work Load Categories*

Heat produced by the body and the environmental heat together determine the total heat load. Therefore, if work is to be performed under hot environmental conditions, the workload category of each job shall be established and the heat exposure limit pertinent to the work load evaluated against the applicable standard in order to protect the worker from exposure beyond the permissible limit.

A. The work load category may be established by ranking each job into light, medium, and heavy categories on the basis of type of operation. Where the work load is ranked into one of said three categories, i.e.

(1) light work (up to 200 kcal/hr or 800 Btu/hr): e.g., sitting or standing to control machines, performing light hand or arm work,

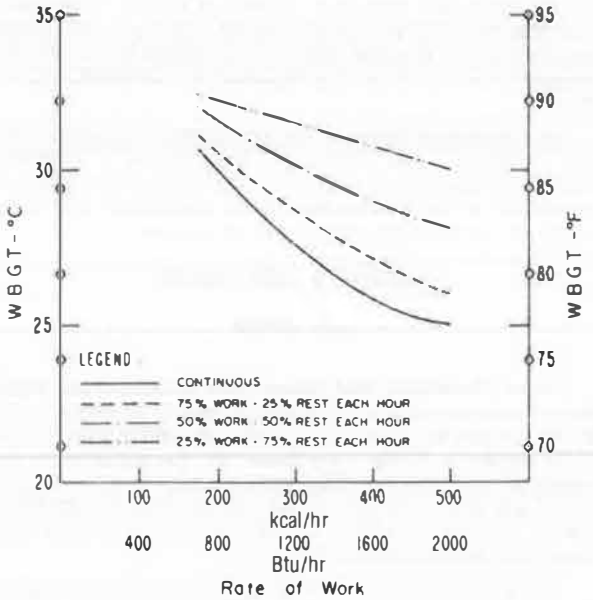

Figure 1 — Permissible Heat Exposure Threshold Limit Value

(2) moderate work (200–350 kcal/hr or 800–1400 Btu/hr): e.g., walking about with moderate lifting and pushing,

(3) heavy work (350–500 kcal/hr or 1400–2000 Btu/hr): e.g., pick and shovel work,

the permissible heat exposure limit for that work load shall be determined from Table 1.

B. The ranking of the job may be performed either by measuring the worker's metabolic rate while performing his job or by estimating his metabolic rate with the use of Tables 2 and 3. Additional tables available in the literature[5–8] may be utilized also. When this method is used the permissible heat exposure limit can be determined by Figure 1.

III. *Work-Rest Regimen*

The permissible exposure limits specified in Table 1 and Figure 1 are based on the assumption that the WBGT value of the resting place is the same or very close to that of the work place. Where the WBGT of the work area is different from that of the rest area a time-weighted average value should be used for both environmental and metabolic heat. When time-weighted average values are used the appropriate curve on Figure 1 is the solid line labeled "continuous."

The time-weighted average metabolic rate (M) shall be determined by the equation:

$$\text{Av. } M = \frac{M_1 \times t_1 + M_2 \times t_2 + \ldots + M_n \times t_n}{t_1 + t_2 + \ldots + t_n}$$

where M_1, M_2 . . . and M_n are estimated or measured metabolic rates for the various activities and rest periods of the worker during the time periods t_1, t_2 . . . and t_n (in minutes) as determined by a time study.

The time-weighted average WBGT shall be determined by the equation:

$$\text{Av. WBGT} = \frac{WBGT_1 \times t_1 + WBGT_2 \times t_2 + \ldots + WBGT_n \times t_n}{t_1 + t_2 + \ldots + t_n}$$

where $WBGT_1$, $WBGT_2$ . . . and $WBGT_n$ are calculated values of WBGT for the various work and rest occupied during total time periods t_1, t_2 . . . and t_n are the elapsed times in minutes spent in the corresponding areas which are determined by a time study. Where exposure to hot environmental conditions is continuous for several hours or the entire work day, the time-weighted averages shall be calculated as hourly time-weighted average i.e., $t_1 + t_2 + \ldots + t_n = 60$ minutes. Where the exposure is intermittent, the time-weighted averages shall be calculated as two-hour time-weighted averages, i.e., $t_1 + t_2 + \ldots + t_n = 120$ minutes.

The permissible exposure limits for continuous work are applicable where there is a work-rest regimen of a 5-day work week and an 8-hour work day with a short morning and afternoon break (approximately 15 minutes) and a longer lunch break (approximately 30 minutes). Higher exposure limits are permitted if additional resting time is allowed. All breaks, including unscheduled pauses and administrative or operational waiting periods during work may be counted as rest time when additional rest allowance must be given because of high environmental temperatures.

IV. *Water and Salt Supplementation*

During the hot season or when the worker is exposed to artificially generated heat, drinking water shall be made available to the workers in such a way that they are stimulated to frequently drink small amounts, i.e., one cup every 15–20 minutes (about 150 ml or 1/4 pint).

The water shall be kept reasonably cool (10°–15°C or 50.0°–60.0°F) and shall be placed close to the workplace so that the worker can reach it without abandoning the work area.

The workers should be encouraged to salt their food abundantly during the hot season and particularly during hot spells. If the workers are unacclimatized, salted drinking water shall be made available in a concentration of 0.1% (1g NaCl to 1.0 liter or 1 level tablespoon of salt to 15 quarts of water). The added salt shall be completely dissolved before the water is distributed, and the water shall be kept reasonably cool.

V. *Other Considerations*

A. *Clothing:* The permissible heat exposure TLVs are valid for light summer clothing as customarily worn by workers when working under hot environmental conditions. If special cothing is required for performing a particular job and this clothing is heavier or it impedes sweat evaporation or has higher insulation value, the worker's heat tolerance is reduced, and the permissible heat exposure limits indicated in Table 1 and Figure 1 are not applicable. For each job category where special clothing is required, the permissible heat exposure limit shall be established by an expert.

B. *Acclimatization and Fitness:* Acclimatization to heat involves a series of physiological and psychological adjustments that occur in an individual during his first week of exposure to hot environmental conditions. The recommended heat stress TLVs are valid for acclimated workers who are physically fit. Extra caution must be employed when unacclimated or physically un-fit workers must be exposed to heat stress conditions.

References:

1. *Health Factors Involved in Working Under Conditions of Heat Stress*. WHO Technical Report Series No. 412 (1969).
2. **Dukes-Dobos, F. N. and A. Henschel:** Development of Permissible Heat Exposure Limits for Occupational Work. *ASHRAE Journal 15(9)*:57–62 (Sept. 1973).
3. **Minard, D.:** *Prevention of Heat Casualties in Marine Corps Recruits, Period of 1955–60, with Comparative Incidence Rates and Climatic Heat Stresses in Other Training Categories*. Research Report No. 4, Contract No. MR 005.01-0001.01, Naval Medical Research Institue, Bethesda, MD (Feb. 21, 1961). Published in *Military Medicine 126(44)*:261–272 (April 1961).
4. **Minard, D. and R. L. O'Brien:** *Heat Casualties in the Navy and Marine Corps 1959–1962 with Appendices on the Field Use of the Wet Bulb-Globe Temperature Index*. Research Report No. 7, Contract No. MR 005.01-0001.01, Naval Medical Research Institute, Bethesda, MD (March 12, 1964).
5. **Astrand, Per-Dlof and Kaare Rodahl:** *Textbook of Work Physiology*. McGraw-Hill Book Co., New York, San Francisco (1970).
6. Ergonomics Guide to Assessment of Metabolic and Cardiac Costs of Physical Work. *Am. Ind. Hyg. Assoc. J. 32*:560 (1971).
7. *Energy Requirements for Physical Work*. Research Progress Report No. 30. Purdue Farm Cardiac Project, Agricultural Experiment Station, West Lafayette, IN (1961).
8. **Durnin, J. V. G. A. and R. Passmore:** *Energy, Work and Leisure*. Heinemann Educational Books, Ltd., London (1967).
9. **Lehmann, G. E., A. Muller and H. Spitzer:** Der Kalorienbedarf bie Gewerblicher Arbeit. *Arbeitsphysiol. 14*:166 (1950).

IONIZING RADIATION

The Committee accepts the philosophy and recommendations of the National Council on Radiation Protection and Measurements (NCRP) for the ionizing radiation TLV. The NCRP is charted by Congress to, in part, collect, analyze, develop and disseminate information and recommendations

about protection against radiation and about radiation measurements, quantities and units, including development of basic concepts in these areas. NCRP Report No. 39 provides basic philosophy and concepts leading to protection criteria established in the same report.[1] Other NCRP reports address specific areas of radiation protection and, collectively, provide an excellent basis for establishing a sound program for radiation control. The Committee recommends the listed references as substantative documentation of a sound basis for ionizing radiation protection. The committee also strongly recommends that all exposures to ionizing radiations be kept as low as reasonably achievable within the stated guidance.

References:

1. *Basic Radiation Protection Criteria*. NCRP Report No. 39 (January 15, 1971).
2. *Maximum Permissible Body Burdens and Maximum Permissible Concentrations of Radionuclides in Air and in Water for Occupational Exposure*. National Bureau of Standards Handbook 69, (June 5, 1959), with *Addendum 1* (August 1963). Available as NCRP Report No. 22.

The above documents, as well as information on numerous other NCRP Reports addressing specific subjects in ionizing radiation protection are available from: NCRP Publications, PO Box 30175, Washington, DC 20014.

LASERS

The threshold limit values are for exposure to laser radiation under conditions to which nearly all workers may be exposed without adverse effects. The values should be used as guides in the control of exposures and should not be regarded as fine lines between safe and dangerous levels. They are based on the best available information from experimental studies.

Limiting Apertures

The TLVs expressed as radiant exposure or irradiance in this section may be averaged over an aperture of 1 mm except for TLVs for the eye in the spectral range of 400–1400 nm, which should be averaged over a 7 mm limiting aperture (pupil); and except for all TLVs for wavelengths between 0.1–1 mm where the limiting aperture is 10 mm. No modification of the TLVs is permitted for pupil sizes less than 7 mm.

The TLVs for "extended sources" apply to sources which subtend an angle greater than α (Table 7) which varies with exposure time. This angle is *not* the beam divergence of the source.

Correction Factors A and B (C_A and C_B)

The TLVs for ocular exposure in Tables 4 and 5 are to be used as given for all wavelength ranges. The TLVs for wavelengths between 700 nm and 1049 nm are to be increased by a uniformly extrapolated factor (C_A) as shown in Figure 2. Between 1049 nm and 1400 nm, the TLV has been increased by a factor (C_A) of five. For certain exposure times at wavelengths between 550 nm and 700 nm, correction factor (C_B) must be applied.

The TLVs for skin exposure are given in Table 6. The TLVs are to be increased by a factor (C_A) as shown in Figure 2 for wavelengths between 700 nm and 1400 nm. To aid in the determination of TLVs for exposure durations requiring calculations of fractional powers Figures 3, 4, 5 and 6 may be used.

Repetitively Pulsed Lasers

Since there are few experimental data for multiple pulses, caution must be used in the evaluation of such exposures. The protection standards for irradiance or radiant exposure in multiple pulse trains have the following limitations:

(1) The exposure from any single pulse in the train is limited to the protection standard for a single comparable pulse.

(2) The average irradiance for a group of pulses is limited to the protection standard as given in Tables 4, 5, or 7 of a single pulse of the same duration as the entire pulse group.

(3) When the Instantaneous Pulse Repetition Frequency (PRF) of any pulses within a train exceeds one, the protection standard applicable to each pulse is reduced as shown in Figure 6 for pulse durations less than 10^{-5} second. For pulses of greater duration, the following formula should be followed:

$$\text{Standard}\left(\begin{matrix}\text{single pulse}\\ \text{in train}\end{matrix}\right) = \frac{\text{Standard (pulse } n\tau)}{n}$$

where:

n = number of pulses in train
τ = duration of a single pulse in the train
Standard ($n\tau$) = protection standard of one pulse having a duration equal to $n\tau$ seconds.

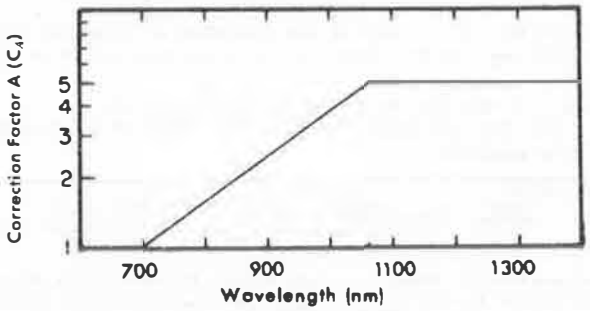

Figure 2 — TLV correction factor for $\lambda = 700 - 1400$ nm*

*For $\lambda = 700 - 1049$ nm, $C_A = 10^{[0.002(\lambda - 700)]}$
For $\lambda = 1050 - 1400$ nm, $C_A = 5$

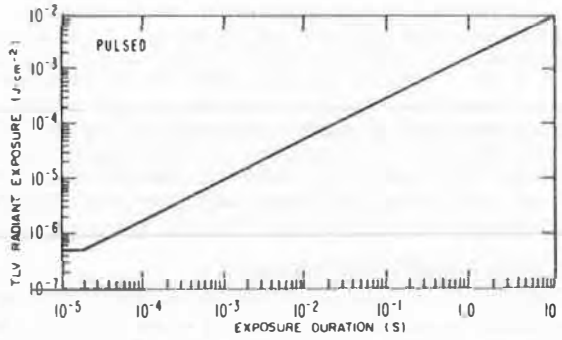

Figure 3a — TLV for intrabeam (direct) viewing of laser beam (400–700 nm).

TABLE 4

Threshold Limit Value for Direct Ocular Exposures
(Intrabeam Viewing) from a Laser Beam

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV	
† UVC	200 nm to 280 nm	10^{-9} to 3×10^{4}	3 mJ • cm^{-2}	
UVB	280 nm to 302 nm	"	3 "	
	303 nm	"	4 "	
	304 nm	"	6 "	
	305 nm	"	10 "	
	306 nm	"	16 "	
	307 nm	"	25 "	*not to exceed $0.56\ t^{1/4}$ J • cm^{-2} for t ≦ 10 s.
	308 nm	"	40 "	
	309 nm	"	63 "	
	310 nm	"	100 "	
	311 nm	"	160 "	
	312 nm	"	250 "	
	313 nm	"	400 "	
	314 nm	"	630 "	
UVA	315 nm to 400 nm	10^{-9} to 10	$.56\ t^{1/4}$ J • cm^{-2}	
	" "	10 to 10^{3}	1.0 J • cm^{-2}	
	" "	10^{3} to 3×10^{4}	1.0 mW • cm^{-2}	
Light	400 nm to 700 nm	10^{-9} to 1.8×10^{-5}	5×10^{-7} J • cm^{-2}	
	400 nm to 700 nm	1.8×10^{-5} to 10	$1.8\ (t/\sqrt[4]{t})$ mJ • cm^{-2}	
	400 nm to 549 nm	10 to 10^{4}	10 mJ • cm^{-2}	
	550 nm to 700 nm	10 to T_1	$1.8\ (t/\sqrt[4]{t})$ mJ • cm^{-2}	
	550 nm to 700 nm	T_1 to 10^{4}	10 C_B mJ • cm^{-2}	
	400 nm to 700 nm	10^{4} to 3×10^{4}	C_B μW • cm^{-2}	
IR-A	700 nm to 1049 nm	10^{-9} to 1.8×10^{-5}	5 $C_A \times 10^{-7}$ J • cm^{-2}	
	700 nm to 1049 nm	1.8×10^{-5} to 10^{3}	$1.8\ C_A\ (t/\sqrt[4]{t})$ mJ • cm^{-2}	
	1050 nm to 1400 nm	10^{-9} to 10^{-4}	5×10^{-6} J • cm^{-2}	
	1050 nm to 1400 nm	10^{-4} to 10^{3}	$9(t/\sqrt[4]{t})$ mJ • cm^{-2}	
	700 nm to 1400 nm	10^{3} to 3×10^{4}	320 C_A μW • cm^{-2}	
IR-B & C	1.4 μm to 10^{3} μm	10^{-9} to 10^{-7}	10^{-2} J • cm^{2}	
	" "	10^{-7} to 10	$0.56\sqrt[4]{t}$ J • cm^{-2}	
	" "	10 to 3×10^{4}	0.1 W • cm^{-2}	

C_1 – See Fig. 2.
$C_B = 1$ for λ = 400 to 549 nm; $C_B = 10^{[0.015\ (\lambda\ -\ 550)]}$ for λ = 550 to 700 nm.
$T_1 = 10$ s for λ = 400 to 549 nm; $T_1 = 10 \times 10^{[0.02\ (\lambda\ -\ 550)]}$ for λ = 550 to 700 n.
† 1981 Addition.

TABLE 5

Threshold Limit Values for Viewing a Diffuse Reflection
of a Laser Beam or an Extended Source Laser

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
† UV	200 nm to 400 nm	10^{-9} to 3×10^{4}	Same as Table 4
Light	400 nm to 700 nm	10^{-9} to 10	$10\sqrt[4]{t}$ J • cm^{-2} • sr^{-1}
	400 nm to 549 nm	10 to 10^{4}	21 J • cm^{-2} • sr^{-1}
	550 nm to 700 nm	10 to T_1	$3.83\ (t/\sqrt[4]{t})$ J • cm^{-2} • sr^{-1}
	550 nm to 700 nm	T_1 to 10^{4}	21 C_B J • cm^{-2} • sr^{-1}
	400 nm to 700 nm	10^{4} to 3×10^{4}	2.1 $C_B t \times 10^{-3}$ W • cm^{-2} • sr^{-1}
IR-A	700 nm to 1400 nm	10^{-9} to 10	$10\ C_A\sqrt[4]{t}$ J • cm^{-2} • sr^{-1}
	700 nm to 1400 nm	10 to 10^{3}	$3.83\ C_A\ (t/\sqrt[4]{t})$ J • cm^{-2} • sr^{-1}
	700 nm to 1400 nm	10^{3} to 3×10^{4}	0.64 C_A W • cm^{-2} • sr^{-1}
IR-B & C	1.4 μm to 10^{3} μm	10^{-9} to 3×10^{4}	Same as Table 4

C_A, C_B, and T_1 are the same as in footnote to Table 4.
† 1981 Addition.

TABLE 6

Threshold Limit Value for Skin Exposure from a Laser Beam

Spectral Region	Wave Length	Exposure Time, (t) Seconds	TLV
† UV	200 nm to 400 nm	10^{-9} to 3×10^{4}	Same as Table 4
Light &	400 nm to 1400 nm	10^{-9} to 10^{-7}	$2\ C_A \times 10^{-2}$ J • cm^{-2}
IR-A	" "	10^{-7} to 10	$1.1\ C_A \sqrt{t}$ J • cm^{-2}
IR-A	" "	10 to 3×10^{4}	$0.2\ C_A$ W • cm^{-2}
IR-B & C	1.4 μm to 10^{3} μm	10^{-9} to 3×10^{4}	Same as Table 4

C_A = 1.0 for λ = 400–700 nm; see Figure 2 for λ = 700 to 1400 nm.
† 1981 Addition.

TABLE 7

Limiting Angle to Extended Source
Which May Be Used for Applying Extended Source TLVs

Exposure Duration(s)	Angle α (mrad)	Exposure Duration(s)	Angle α (mrad)
10^{-9}	8.0	10^{-2}	5.7
10^{-8}	5.4	10^{-1}	9.2
10^{-7}	3.7	1.0	15
10^{-6}	2.5	10	24
10^{-5}	1.7	10^{2}	24
10^{-4}	2.2	10^{3}	24
10^{-3}	3.6	10^{4}	24

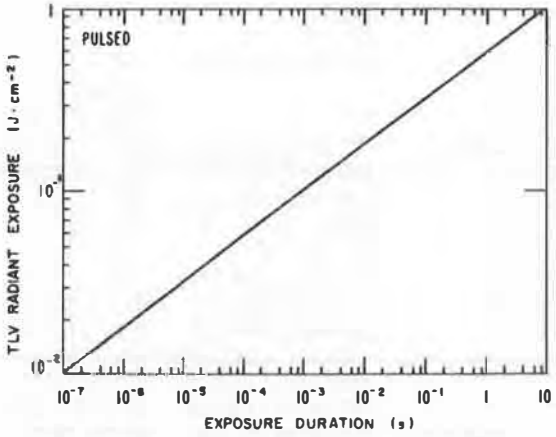

Figure 4a — TLV for laser exposure of skin and eyes for far-infrared radiation (wave-lengths greater than 1.4 μm).

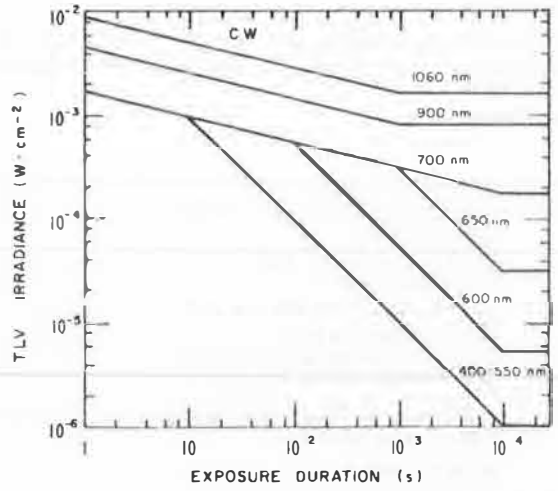

Figure 3b — TLV for intrabeam (direct) viewing of CW laser beam (400–1400 nm)

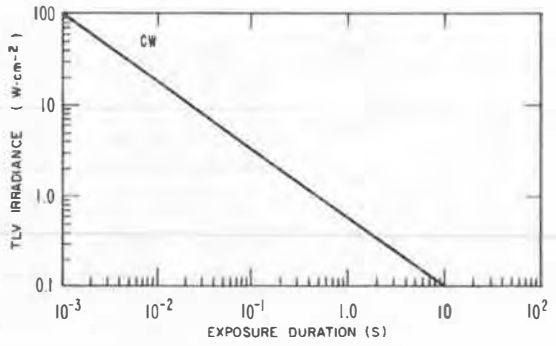

Figure 4b — TLV for CW laser exposure of skin and eyes for far-infrared radiation (wave-lengths greater than 1.4 μm).

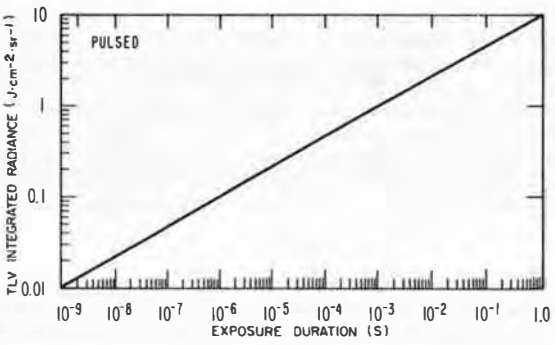

Figure 5a — TLV for extended sources or diffuse reflections of laser radiation (400–700 nm).

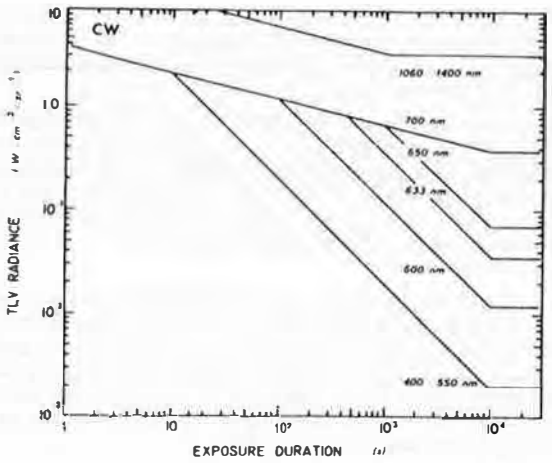

Figure 5b — TLV for extended sources or diffuse reflections of laser radiation (400–1400 nm).

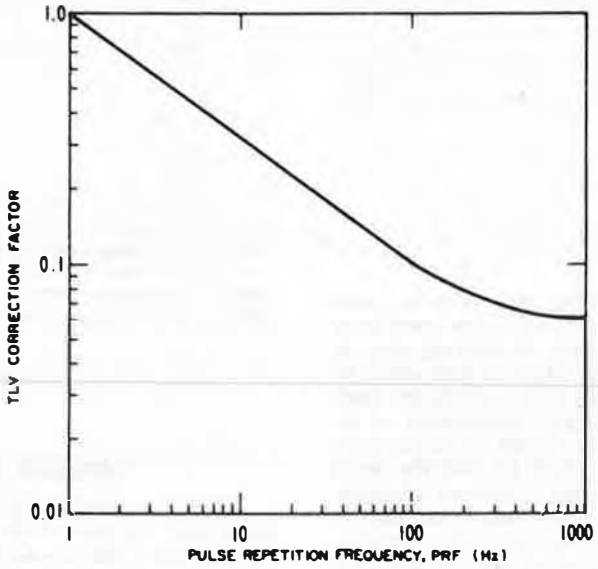

Figure 6 — Multiplicative correction factor for repetitively pulsed lasers having pulse durations less than 10^{-5} second. TLV for a single pulse of the pulse train is multiplied by the above correction factor. Correction factor for PRF greater than 1000 Hz is 0.06.

**MICROWAVES

These Threshold Limit Values refer to microwave energy in the frequency range of 300 MHz to 300 GHz and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect.

Under conditions of moderate to severe heat stress, the recommended values may need to be reduced.[1] Therefore, these values should be used as guides in the control of exposure to microwave energy and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The Threshold Limit Value for occupational exposure to microwave energy, where power density or field intensity is known and exposure time is controlled, is as follows:

1. For exposure to continuous wave (CW) sources, the power density level shall not exceed 10 milliwatts per square centimeter (mW/cm^2) for continuous exposure, and the total exposure time shall be limited to an 8-hour

**See Notice of Intended Changes.

workday. This power density is approximately equivalent to a free-space electric field strength of 200 volts-per-meter rms (V/m) and a free-space magnetic field strength of 0.5 ampere-per-meter rms (A/m).

2. Exposures to CW power density levels greater than 10 mW/cm^2 are permissible up to a maximum of 25 mW/cm^2 based upon an average energy density of 1 milliwatt-hour per square centimeter (mWh/cm^2) averaged over any 0.1 hour period. For example, at 25 mW/cm^2, the permissible exposure duration is approximately 2.4 minutes in any 0.1 hour period.
3. For repetitively pulsed microwave sources, the average field strength or power density is calculated by multiplying the peak-pulse value by the duty cycle. The duty cycle is equal to the pulse duration in seconds times the pulse repetition rate in Hertz. Exposure during an 8-hour workday shall not exceed the following values which are averaged over any 0.1 hour period:

Power Density	10 mW/cm^2
Energy Density	1 mWh/cm^2
Mean Squared Electric Field Strength	40,000 V^2/m^2
Mean Squared Magnetic Field Strength	0.25 A^2/m^2

4. Exposure is not permissible in CW or repetitively pulsed fields with an average power density in excess of 25 mW/cm^2 or approximate equivalent free-space field strengths of 300 V/m or 0.75 A/m.

Reference:

1. **Mumford, W. W.:** Heat Stress Due to R. F. Radiation. *Proceedings of IEEE 57(2):* 171–178 (Feb. 1969).

NOISE

These threshold limit values refer to sound pressure levels and durations of exposure that represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect on their ability to hear and understand normal speech. Prior to 1979, the medical profession had defined hearing impairment as an average hearing threshold level in excess of 25 decibels (ANSI-S3.6-1969) at 500, 1000, and 2000 Hz, and the limits which are given have been established to prevent a hearing loss in excess of this level.[a] The values should be used as guides in the control of noise exposure and, due to individual susceptibility, should not be regarded as fine lines between safe and dangerous levels.

It should be recognized that the application of the TLV for noise will not protect all workers from the adverse effects of noise exposure. A hearing conservation program with audiometric testing is necessary when workers are exposed to noise at or above the TLV levels.

Continuous or Intermittent

The sound level shall be determined by a sound level meter, conforming as a minimum to the requirements of the American National Standard Specification for Sound Level Meters, S1.4 (1971) Type S2A, and set to use the A-weighted network with slow meter response. Duration of exposure shall not exceed that shown in Table 8.

These values apply to total duration of exposure per working day regardless of whether this is one continuous exposure or a number of short-term exposures and does include the impact and impulsive type of noise that contributes to the sound level meter reading at slow response.

When the daily noise exposure is composed of two or more periods of noise exposure of different levels, their combined effect should be considered, rather than the individual effect of each. If the sum of the following fractions:

$$\frac{C_1}{T_1} + \frac{C_2}{T_2} + \ldots \frac{C_n}{T_n}$$

exceeds unity, then, the mixed exposure should be considered to exceed the threshold limit value, C_1 indicates the total duration of exposure at a specific noise level, and T_1 indicates the total duration of exposure permitted at that level. All on-the-job noise exposures of 80 dBA or greater shall be used in the above calculations.

Table 8
Threshold Limit Values

Duration per Day Hours	Sound Level dBA†
16	80
8	85
4	90
2	95
1	100
1/2	105
1/4	110
1/8	115*

†Sound level in decibels are measured on a sound level meter, conforming as a minimum to the requirements of the American National Standard Specification for Sound Level Meters, S1.4 (1971) Type S2A, and set to use the A-weighted network with slow meter response.

*No exposure to continuous or intermittent in excess of 115 dBA

IMPULSIVE OR IMPACT NOISE

It is recommended that exposure to impulsive or impact noise shall not exceed the limits listed in Table 9 or taken from Figure 7. No exposures in excess of 140 decibels peak sound pressure level are permitted. Impulsive or impact noise is considered to be those variations in noise levels that involve maxima at intervals of greater than one per second. Where the intervals are less than one second, it should be considered continuous.

Table 9
Threshold Limit Values Impulsive or Impact Noise

Sound Level dB**	Permitted Number of Impulses or Impacts per day
140	100
130	1000
120	10,000

[a] In 1979, the American Academy of Ophthalmology and Otolargyngology (AAOO) included 3000 Hz in their hearing impairment formula.

**Decibels peak sound pressure level. re 20 μPa

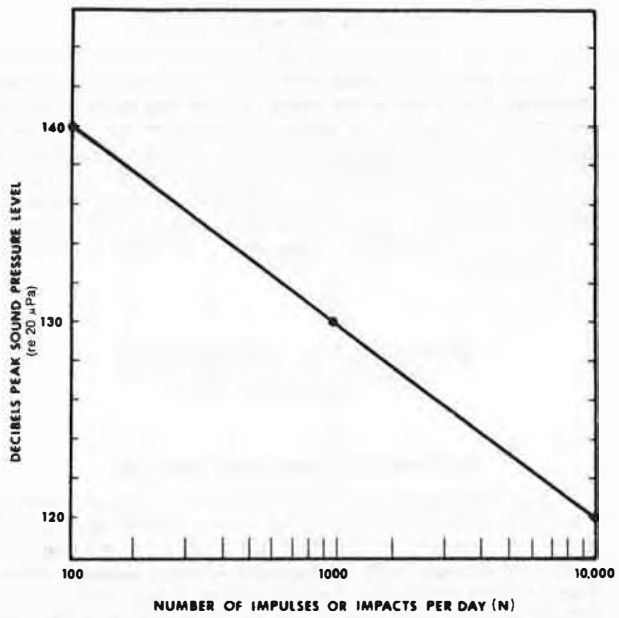

Figure 7 — Threshold Limit Values for Impulse/Impact Noise.

ULTRAVIOLET RADIATION*

These threshold limit values refer to ultraviolet radiation in the spectral region between 200 and 400 nm and represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect. These values for exposure of the eye or the skin apply to ultraviolet radiation from arcs, gas, and vapor discharges, fluorescent, and incandescent sources, and solar radiation, but do not apply to ultraviolet lasers.* These values do not apply to ultraviolet radiation exposure of photosensitive individuals or of individuals concomitantly exposed to photosensitizing agents.[1] These values should be used as guides in the control of exposure to continuous sources where the exposure duration shall not be less than 0.1 sec.

These values should be used as guides in the control of exposure to ultraviolet sources and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The threshold limit value for occupational exposure to ultraviolet radiation incident upon skin or eye where irradiance values are known and exposure time is controlled are as follows:

1. For the near ultraviolet spectral region (320 to 400 nm) total irradiance incident upon the unprotected skin or eye should not exceed 1 mW/cm² for periods greater than 10^3 seconds (approximately 16 minutes) and for exposure times less than 10^3 seconds should not exceed one J/cm².
2. For the actinic ultraviolet spectral region (200 — 315 nm), radiant exposure incident upon the unprotected skin or eye should not exceed the values given in Table 11 within an 8-hour period.
3. To determine the effective irradiance of a broadband source weighted against the peak of the spectral effectiveness curve (270 nm), the following weighting formula should be used:

$$E_{eff} = \sum E_\lambda S_\lambda \Delta\lambda$$

where:

E_{eff} = effective irradiance relative to a monochromatic source at 270 nm in W/cm² (J/s/cm²)

E_λ = spectral irradiance in W/cm²/nm

S_λ = relative spectral effectiveness (unitless)

$\Delta\lambda$ = band width in nanometers

4. Permissible exposure time in seconds for exposure to actinic ultraviolet radiation incident upon the unprotected skin or eye may be computed by dividing 0.003 J/cm² by E_{eff} in W/cm². The exposure time may also be determined using Table 12 which provides exposure times corresponding to effective irradiances in μW/cm².
5. All the preceding TLVs for ultraviolet energy apply to sources which subtend an angle less than 80°. Sources which subtend a greater angle need to be measured only over an angle of 80°.

TABLE 11

Relative Spectral Effectiveness by Wavelength*

Wavelength (nm)	TLV (mJ/cm²)	Relative Spectral Effectiveness S_λ
200	100	0.03
210	40	0.075
220	25	0.12
230	16	0.19
240	10	0.30
250	7.0	0.43
254	6.0	0.5
260	4.6	0.65
270	3.0	1.0
280	3.4	0.88
290	4.7	0.64
300	10	0.30
305	50	0.06
310	200	0.015
315	1000	0.003

*See Laser TLVs.

TABLE 12

Permissible Ultraviolet Exposures

Duration of Exposure Per Day	Effective Irradiance, E_{eff} (μW/cm^2)
8 hrs	0.1
4 hrs	0.2
2 hrs	0.4
1 hr	0.8
30 min	1.7
15 min	3.3
10 min	5
5 min	10
1 min	50
30 sec	100
10 sec	300
1 sec	3,000
0.5 sec	6,000
0.1 sec	30,000

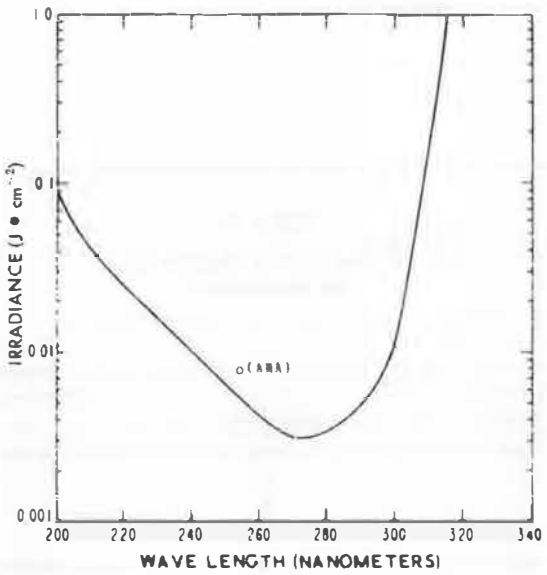

Figure 9 — Threshold Limit Values for Ultraviolet Radiation

Conditioned (tanned) individuals can tolerate skin exposure in excess of the TLV without erythemal effects. However, such conditioning may not protect persons against skin cancer.

Reference:

1. *Sunlight and Man*. Fitzpatrick *et al*, Eds. Univ. of Tokyo Press, Tokyo, Japan (1974).

NOTICE OF INTENDED CHANGES (1981)

These physical agents, with their corresponding values, comprise those for which either a limit has been proposed for the first time, or for which a change in the "Adopted" listing has been proposed. In both cases, the proposed limits should be considered trial limits that will remain in the listing for a period of at least one year. If after one year no evidence comes to light that questions the appropriateness of the values herein the values will be reconsidered for the "Adopted" list.

NOTICE OF INTENT TO ESTABLISH THRESHOLD LIMIT VALUES

LIGHT AND NEAR-INFRARED RADIATION

These Threshold Limit Values refer to visible and near-infrared radiation in the wavelength range of 400 nm to 1400 nm and represent conditions under which it is believed that nearly all workers may be exposed without adverse effect. These values should be used as guides in the control of exposure to light and should not be regarded as a fine line between safe and dangerous levels.

Recommended Values:

The Threshold Limit Value for occupational exposure to broad-band light and near-infrared radiation for the eye apply to exposure in any eight-hour workday and require knowledge of the spectral radiance (L_λ) and total irradiance (E) of the source as measured at the position(s) of the eye of the worker. Such detailed spectral data of a white light source is generally only required if the luminance of the source exceeds 1 cd cm^{-2}. At luminances less than this value the TLV would not be exceeded.

The TLV's are:

1. To protect against retinal thermal injury, the spectral radiance of the lamp weighted against the function R (Table 13) should not exceed:

$$\sum_{400}^{1400} L_\lambda R_\lambda \Delta\lambda \leqq 1/\alpha t^{1/2} \qquad (1)^*$$

where L_λ is in W cm^{-2} sr^{-1} nm^{-1} and t is the viewing duration (or pulse duration if the lamp is pulsed) limited to 1 μs to 10 s, and α is the angular subtense of the source in radians. If the lamp is oblong, α refers to the longest dimension that can be viewed. For instance, at a viewing distance r = 100 cm from a tubular lamp of length l = 50 cm, the viewing angle is:

$$\alpha = l/r = 50/100 = 0.5 \text{ rad} \qquad (2)$$

2. To protect against retinal photochemical injury from chronic blue-light exposure the integrated spectral radiance of a light source weighted against the blue-light hazard function B_λ (Table 13) should not exceed:

$$\sum_{400}^{1400} L_\lambda t B_\lambda \Delta\lambda \leqq 100 \text{ Jcm}^{-2} \text{ sr}^{-1} \ (t \leqq 10^4 \text{s}) \qquad (3a)$$

$$\sum_{400}^{1400} L_\lambda B_\lambda \Delta\lambda \leqq 10^{-2} \text{ Wcm}^{-2} \text{ sr}^{-1} \ (t > 10^4 \text{s}) \qquad (3b)$$

For a source radiance L which exceeds 10 mW•cm^{-2}•sr^{-1} in the blue spectral region, the permissible exposure duration t_{max} in seconds is simply:

$$t_{max} = 100 \text{ J cm}^{-2} \text{ sr}^{-1}/L \text{ (blue)} \quad (4)$$

The latter limits are greater than the maximum permissible exposure limits for 440 nm laser radiation (see Laser TLV) because a 2–3 mm pupil is assumed rather than a 7 mm pupil for the Laser TLV.

For a light source subtending an angle α less than 11 mrd (0.011 radian) the above limits are relaxed such that the spectral irradiance weighted against the blue-light hazard function B_λ [E(blue)] should not exceed:

$$\sum_{400}^{1400} E_\lambda \bullet t \bullet B_\lambda \bullet \Delta\lambda \leqq 10 \text{ mJ} \bullet \text{cm}^{-2} \; (t \leqq 10^4 \text{ s}) \quad (5a)$$

$$\sum_{400}^{1400} E_\lambda \bullet B_\lambda \bullet \Delta\lambda \leqq 1 \mu\text{W} \bullet \text{cm}^2 \; (t \geqq 10^4 \text{ s}) \quad (5b)$$

For a source where the blue light weighted irradiance E(blue) exceeds 1 μW • cm^{-2} is the maximum permissible exposure duration t_{max} in seconds is:

$$t_{max} = 10 \text{ mJ} \bullet \text{cm}^{-2} \text{ E (blue)} \quad (6)$$

3. *Infrared Radiation:* To avoid possible delayed effects upon the lens of the eye (cataractogenesis), the infrared radiation ($\lambda > 770$ nm) should be limited to 10 mWcm^{-2}. For an infrared heat lamp or any near-infrared source where a strong visual stimulus is absent, the near infrared (770–1400 nm) radiance as viewed by the eye should be limited to:

TABLE 13

Spectral Weighting Functions for Assessing Retinal Hazards from Broad-Band Optical Sources

Wavelength (nm)	Blue-Light Hazard Function B_λ	Burn Hazard Function R_λ
400	0.10	1.0
405	0.20	2.0
410	0.40	4.0
415	0.80	8.0
420	0.90	9.0
425	0.95	9.5
430	0.98	9.8
435	1.0	10.0
440	1.0	10.0
445	0.97	9.7
450	0.94	9.4
455	0.90	9.0
460	0.80	8.0
465	0.70	7.0
470	0.62	6.2
475	0.55	5.5
480	0.45	4.5
485	0.40	4.0
490	0.22	2.2
495	0.16	1.6
500–600	$10^{[(450-\lambda)/50]}$	1.0
600–700	0.001	1.0
700–1049	0.001	$10^{[(700-\lambda)/505]}$
1050–1400	0.001	0.2

$$\sum_{770}^{1400} L_\lambda \Delta\lambda \leqq 0.6/\alpha \quad (7)^*$$

for extended duration viewing conditions. This limit is based upon a 7 mm pupil diameter.

*Formulae (1) and (7) are empirical and are not, strictly speaking, dimensionally correct. To make the formulae dimensionally correct, one would have to insert a dimensional correction factor k in the right hand numerator in each formula. For formula (1) this would be k_1 = 1 W • rad • s½/(cm² • sr), and for formula (7) k_2 = 1 W • rad/(cm² • sr).

AIRBORNE UPPER SONIC AND ULTRASONIC ACOUSTIC RADIATION

These threshold limit values refer to sound pressure levels that represent conditions under which it is believed that nearly all workers may be repeatedly exposed without adverse effect. The values listed in Table 14 should be used as guides in the control of noise exposure and, due to individual susceptibility, should not be regarded as fine lines between safe and dangerous levels. The levels for the third octave bands centered below 20 kHz are below those which cause subjective effects. Those levels for 1/3 octaves above 20 kHz are for prevention of possible hearing losses from subharmonics of these frequencies.

TABLE 14

Permissible Ultrasound Exposure Levels

Mid-Frequency of Third-Octave Band kHz	One-Third Octave — Band Level in dB re 20 μPa
10	80
12.5	80
16	80
20	105
25	110
31.5	115
40	115
50	115

RADIOFREQUENCY/MICROWAVE RADIATION

These Threshold Limit Values (TLVs) refer to radiofrequency (RF) and microwave radiation in the frequency range from 0.01 MHz to 300 GHz, and represent conditions under which it is believed workers may be repeatedly exposed without adverse health effects. The TLVs shown in Table 10 are selected to limit the average whole body specific absorption rate (SAR) to 0.4 W/kg in any six minutes (0.1 hr.) period for 3 MHz to 300 GHz, see Figure 8.

Since it is usually impractical to measure the SAR, the TLVs are expressed in units that are measurable, viz, squares of the electric and magnetic field strengths, averaged over any 0.1 hour and this can be expressed in units of equivalent plane wave power density for convenience. The squared electric field (E), magnetic field (H) strength values, and power density (PD) values are shown in Table 10. For near field exposures PD cannot be measured directly, but equivalent plane wave power density can be calculated from the field strength measurement data as follows:

$$\text{PD in mW/cm}^2 = \frac{E^2}{3770}$$

where:

E^2 is in volts squared (V^2) per meter squared (m^2).

$$\text{PD in mW/cm}^2 = 37.7\ H^2$$

where:

H^2 is in amperes squared (A^2) per meter squared (m^2).

These values should be used as guides in the evaluation and control of exposure to radiofrequency/microwave radiation, and should not be regarded as a fine line between safe and dangerous levels.

Notes:

1. All Radiofrequency Radiation (RFR) exposures should be kept as low as reasonably possible given the current state of knowledge on human effects, particularly non-thermal effects.
2. For fields consisting of a number of frequencies, the fraction of the protection guide incurred within each frequency level should be determined and the sum of all fractions should not exceed unity.
3. For pulsed and continuous wave fields, the power density is averaged over the six minute period, and should not exceed the values in Table 10, except as rated for partial body exposure.
4. For partial body exposures at frequencies between 0.01 MHz and 1.0 GHz, the protection guides in Table 10 may be exceeded if the output power of a radiating device is 7 watts or less. For example, if a hand held transmitter operating at 27 MHz has a maximum output of 5 watts, it would be excluded from any further field measurements.
5. No measurement should be made within 5 cm of any object.
6. All exposures should be limited to a maximum (peak) electric field intensity of 10 kV/m.

TABLE 10

RADIOFREQUENCY/MICROWAVE THRESHOLD LIMIT VALUES

Frequency		Power Density (mW/cm^2)†	Electric Field Strength Squared (V^2/m^2)	Magnetic Field Strength Squared (A^2/m^2)
10 kHz to	3 MHz	100	377,000	2.65
3 MHz to	30 MHz	$900/f^{2*}$	$3770 \times 900/f^{2*}$	$900/37.7 \times f^{2*}$
30 MHz to	100 MHz	1	3770	0.027
100 MHz to	1000 MHz	$f^*/100$	$3770 \times f^*/100$	$f^*/37.7 \times 100$
1 GHz to	300 GHz	10	37,700	0.265

†mW/cm^2 = milliwatts per centimeter squared
*f = frequency in MHz

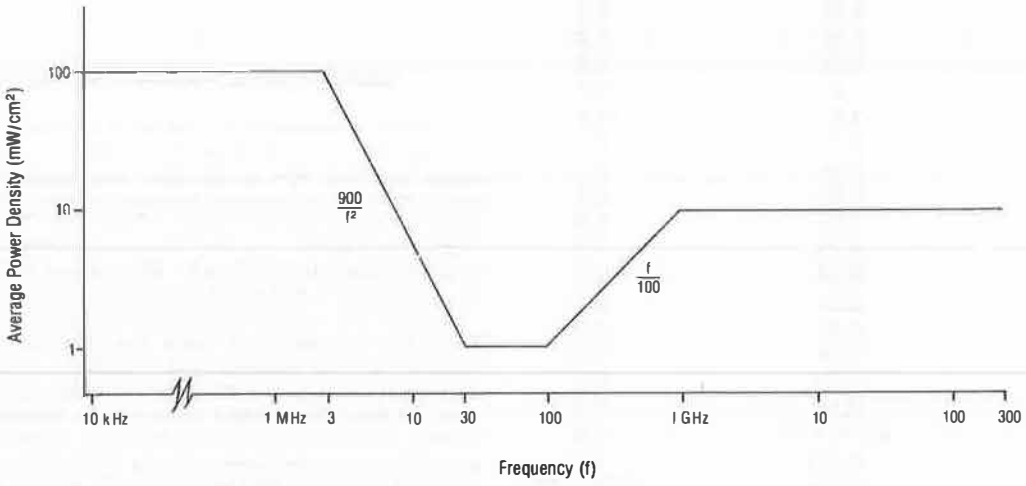

Figure 8 — Threshold Limit Values (TLV) for Radiofrequency/Microwave Radiation in Workplace (Whole Body SAR Less Than 0.4 W/kg).

PHYSICAL AGENTS UNDER STUDY

The Physical Agents Committee of ACGIH has examined the current literature and has not found sufficient information to propose a TLV. However, these agents will remain under study during the coming year to examine new evidence indicating the need and feasibility for establishing a proposed TLV. Comments and suggestions, accompanied by substantive documentation are solicited and should be forwarded to the Executive Secretary, ACGIH, Documentation summarizing the current status of the biological effects literature is available on those agents preceded by an asterisk (*).

1. **Extremely Low Frequency (ELF) Radiation*. Specifically, that portion of the spectrum from 0 to 300 Hz.
2. *Magnetic Fields*. Both pulsed and *continuous.
3. *Laser Radiation*. Specifically laser exposures of less than one (1) nanosecond.
4. *Vibration*. Segmental and whole-body.
5. *Cold Stress*.
6. *Pressure Variations*.

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APPENDICES

The third annual meeting of the National Conference of Governmental Industrial Hygienist held in Bethesda, Maryland, April 30 through May 2, 1940 provided the forum or set the stage for the beginning of Threshold Limit Values Committee as it is now known. History informs us that at this meeting a sub-committee was established for this purpose as a part of the Committee on Technical Standards. Discussions were held as to whether or not these values should be considered as "regulations passed upon by a national organization." No decision was reached at that time.

At the next meeting held in Washington D.C. in February 1941, the Subcommittee on Threshold Limits had not yet begun to function. The committee was charged with the task of digesting all of the information currently available and reporting to the conference at the annual meeting in 1942. The report presented follows.

APPENDIX A

Report of the subcommittee on threshold limits*

The Subcommittee on Threshold Limits presents the attached table (Table I) of maximum allowable concentrations of atmospheric contaminants as its first report to the Conference. The table was prepared from lists furnished by various State units. It is not necessarily complete because some States did not reply. Others indicated that they used a list furnished by the U.S. Public Health Service. Inquiry revealed that the U.S. Public Health Service now considers that list not "applicable in the light of present knowledge."

The table is not to be construed as recommended safe concentrations. The material is presented without comment.

Supplementary to the table of concentrations is a summary of the activities of the American Standards Association (Table II) and a list of maximum allowable concentrations of various substances as proposed by various authorities (Table III).

* Published in *Trans. of Fifth Annual Meeting of the National Conference of Governmental Industrial Hygienists,* pp. 163-170 (1942). A joint meeting with the Subcommittee on Industrial Health and Medicine, Health and Medical Committee, Federal Security Agency, April 9-10, 1942, Washington, DC.

TABLE I
Maximum Permissible Concentrations of Atmospheric Contaminants as Recommended by Various State Industrial Hygiene Units
(Expressed in ppm, except for those with an asterisk, indicating mg/m^3)

Substance	Concentration	States
Acetone	200	Calif., Colo.
Aliphatic acetates	500	Mich.
Ammonia	100	Calif., Colo., Kans., Mass., Mich., Minn., Okla. Wis.
Amyl acetate (n)	500	Mich.
	400	Calif., Colo., Kans., Ky., Mass., Minn., Okla., Wis.
Aniline	5	Calif., Colo., Kans., Mass., Minn., Wis.
Arsenic trioxide	0.5*	Okla.
Arsine	1	Calif., Colo., Kans., Mass., Minn., Okla., Wis.
Benzene	100	Calif., Colo., Conn., Pa., S.C.
	75-100	Kans.
	75	Ky., Md., Mass., Mich., Minn., Ohio, Okla., Wis.
Bromine	1	Mich.
Butanol	100	Calif., Colo., Kans., Okla.
Butyl acetate	500	Mich.
	400	Calif., Colo., Kans., Ky., Mass., Minn., Okla., Pa., Wis.
Cadmium	0.1*	Calif., Colo., Kans., Ky., Mass., Minn., Okla., Pa., Wis.

Substance	Concentration	States
Carbon dioxide	5500	Calif., Colo.
Carbon disulfide	20	Conn., Ky., Mich., Pa.
	15	Calif., Colo., Kans., Mass., Minn., Okla., Wis.
Carbon monoxide	100	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Ohio, Okla., Pa., S.C., Wis.
Carbon tetrachloride	100	Calif., Colo., Conn., Kans., Ky., M.D., Mass., Miss., Ohio, Okla., Pa., S.C., Wis.
	75	Mich.
Chlorine	1	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Okla., S.C., Wis.
Chlorodiphenl	1*	Calif., Colo., Kans., Mass., Minn., Okla., Pa., Wis.
Chloroform	100	Calif., Colo.
Chloronaphthalenes	1-5*	Kans., Mass., Minn., Pa., Wis.
Chloronaphthalenes (above "tri")	1*	Okla.
Chloronaphthalenes "tri"	5*	Calif., Colo., Okla.
Chloronaphthalenes "penta"	0.5*	Calif., Colo.
Chromium — hexavalent (chromic acid)	0.1*	Calif., Colo., Conn., Kans., Ky., Mass., Mich., Minn., Ohio, Okla., Pa., Wis.
	0.1*	Md. (for electroplating only)
Dichlorbenzene	75	Calif., Colo., Kans., Mass., Minn., Okla. Wis.
Dichlorethylene (trans)	100	Ky.
Dichlorethyl ether	15	Calif., Colo., Kans., Ky., Mass., Minn., Okla., Wis.
Ethanol	250	Calif., Colo.
Ethyl chloride	2000	Calif., Colo.
Ethyl bromide	1700	Calif., Colo.
Ethyl ether	400	Calif., Colo., Kans., Mass., Minn., Okla., Wis.
Ethylene dichloride	100	Calif., Colo., Kans., Mass., Mich., Minn., Okla., Wis.
Formaldehyde	20	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Okla., Pa., S.C., Wis.
Gasoline	1000	Calif., Colo., Conn., Kans., Ky., Md., Mass., Minn., Okla., S.C., Wis.
Hydrogen chloride	10	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Okla., S.C., Wis.
Hydrogen cyanide	20	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Okla., S.C., Wis.
Hydrogen fluoride	3	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Okla., S.C., Wis.
Hydrogen sulfide	50	S.C.
	20	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Okla., Pa., Wis.
Iron oxide fume (Fe_2O_3)	15*	Mich.
Lead	0.15*	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Ohio, Okla, Pa., S.C., Wis.
Magnesium oxide fume	15*	Mich.
Manganese	50*	Calif., Colo.
	6*	Kans., Okla.
	5*	Ky.
Mercury	0.1-0.2*	Calif., Colo.
	0.15*	Okla.
	0.1*	Conn., Kans., Ky., Mass., Mich., Minn., Ohio, Wis.
Methanol	200	Kans., Mass., Mich., Minn., Okla., Wis.
	100	Calif., Colo., Conn., Ky., Md., S.C.
Methyl bromide	50	Calif., Colo.
Methyl chloride	500	Calif., Colo.
Monochlorbenzene	75	Calif., Colo., Kans., Mass., Minn., Okla., Wis.
Naphtha	5000	Calif., Colo.

Appendix A

Substance	Concentration	States
Nitrobenzene	5	Kans., Mass., Minn., Okla., Wis.
	1	Calif., Colo.
Nitrogen oxides	29-70	Kans.
	40	Conn., Ky., Okla., S.C.
	10	Calif., Colo., Md., Mass., Mich., Minn., Minn., Wis.
Ozone	1	Calif., Colo., Kans., Mass., Minn., Okla., Wis.
	0.1	Mich.
Petroleum vapors	1000	Mich.
Phosgene	1	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Okla., S.C., Wis.
Phosphine	2	Calif., Colo., Kans., Mass., Minn., Okla., Wis.
Phosphorus trichloride	0.7	Calif., Colo.
Sulfur dioxide	10	Calif., Colo., Conn., Kans., Ky., Md., Mass., Mich., Minn., Okla., Pa., S.C., Wis.
Tetrachloroethane	10	Calif., Colo., Kans., Ky., Mass., Minn., Okla., Wis.
Tetrachloroethylene	200	Calif., Colo., Kans., Ky., Mass., Minn., Okla., Wis.
Tetrachloroethylene (perchloroethylene)	100	Mich.
Toluene	200	Kans., Ky., Mass., Mich., Minn., Okla., Wis.
	100	Calif., Colo.
Trichloroethylene	200	Calif., Colo., Kans., Mass., Minn., Okla., Wis.
	100	Mich.
Turpentine	700	Calif., Colo., Conn., Ky., S.C.,
	200	Kans., Mass., Mich., Minn., Okla., Wis.
Xylene	200	Kans., Ky., Mass., Mich., Minn., Okla., Wis.
	100	Calif., Colo.
Zinc oxide fume	15*	Calif., Colo., Kans., Ky., Mass, Mich., Minn, Okla., Pa., Wis.

Dusts
(Millions of particles per cubic foot of air – light field count)

Substance	Concentration	States
Alundum	15	Okla.
Asbestos	15	S.C.
	5	Calif., Colo., Mass., Mich., N.C., Okla., Pa.
Carborundum	15	Okla.
Cement	50	Calif.
Feldspar	10	N.C.
Foundry	25	Mass.
	20	N.C. (cleaning castings)
	15	Minn.
	12	N.C. (molding)
Granite	25	N.C.
	10	Mass., Vt.
Mica	50	Mich.
	10	N.C.
Nuisance	50	Mass., Mich.
Pottery	4	Calif., Colo.
Organic	50	Calif., Colo., Mass.
Pyrophyllite talc	25	N.C. (milling)
	10	N.C. (mining)
Silica (based on percentage of free silica in the dust)		
Count x%	5	Kans., Minn., Okla., Wis.
10%	50	Idaho

Substance	Concentration	States
("low")	50	Mass., Mich.
10%	10	Idaho
23-35%	10	Calif., Colo.
"medium"	20	Mass., Mich.
"high"	5	Mass., Mich., Ohio
over 75%	5	Calif., Colo.
over 90%	5	Conn.
Silicates	15	Okla.
Slate	50	Mich.
	15	Calif., Colo.
Soapstone	50	Mich.
Talc	50	Mich.
	15	Calif., Colo.
Total dust	50	Mass., Okla.

TABLE II
Activities of American Standards Association

American Standards completed:

Carbon monoxide	100 ppm	Z.37-1, 1941
Hydrogen sulfide	20 ppm	Z.37-2, 1941
Carbon disulfide	20 ppm	Z.37-3, 1941
Benzene	100 ppm	Z.37-4, 1941

American Standards in development:

Nitrous gases
Carbon tetrachloride
Mercury
Chromic acid and chromates
Lead
Formaldehyde
Toluol

Emergency Standards completed:

Cadmium	0.1 mg/m^3	Z.35-5, 1941

Emergency Standards proposed:

Manganese
Ether (diethyl ether)
Arsenic
Antimony
Zinc
Xylol

Appendix A

TABLE III
Additional Maximum Permissible Concentrations as Proposed by Various Authorities

Substance	Concentration	Source
Acrolein	3.3 ppm 1 ppm	Int. Crit. Tables 2:318, 1927 Los Angeles Department of Health (suggested)
Iodine	0.5-1.0 ppm 0.1 ppm	Int. Crit. Tables 2:320, 1927 Matt in Flury & Zernik, Berlin, 1931
Sulfur trioxide (as SO_3)	2 ppm	Int. Crit. Tables 2:320, 1927
Nicotine (tobacco dust)	5 mg/m^3 30 mg/m^3	Soviet Industrial Stnd. (U.S.S.R.) States Sci. Inst. (U.S.S.R.)
Toluidine (o-m-p)	1.0-2.5 ppm 6-23 ppm	Int. Crit. Tables 2:320, 1927 Henderson & Haggard, Noxious Gases, New York, 1927
X-ray radiation	1×10^{-5} roentgen units per sec. (200 work hrs. per month)	Mutscheller, Am. J. Roentgen. 13:65 1925
Radium	0.1 micrograms (by expired air test)	Handbook H-27, U.S. Bur. Stands., May 2, 1941
Radon	10^{-11} curies per liter	Handbook H-27, U.S. Bur. Stands., May 2, 1941
Gamma radiation	0.1 roentgen units per work day. When in combination, lower values for each.	Handbook H-27, U.S. Bur. Stands., May 2, 1941

APPENDIX B

During World War II an Office of Defense, Health and Welfare Services was created by Executive Order. A subcommittee on Industrial Health and Medicine was appointed to advise on the industrial health and medical aspects of the war effort. "This committee requested the Division of Industrial Hygiene of the National Institute of Health to assume leadership in achieving certain objectives." The following table was developed by the Division of Industrial Hygiene and published in a *Manual of Industrial Hygiene,* Chapter 11, page 264 (W. B. Sanders Company, Philadelphia, April 1943.) It is interesting to note that J.J. Bloomfield was with that division at that time.

Toxic Limits of Various Substances

Substance	Maximum Allowable Concentration*
Acrolein	1 ppm
Acrylonitrile	20 ppm†
Ammonia	100 ppm
Amyl acetate	400 ppm†
Aniline	5 ppm
Arsine	1 ppm
Benzene (Benzol)	100 ppm
Butyl acetate	400 ppm†
Butyl alcohol	200 ppm†
Carbon dioxide	5000 ppm
Carbon disulfide	20 ppm
Carbon monoxide	100 ppm
Carbon tetrachloride	100 ppm
Dichlorobenzene	75 ppm
Dimethylaniline	similar to aniline
Ethylene dichloride	100 ppm
Gasoline (Petroleum)	1000 ppm
Hydrogen chloride	10 ppm
Hydrogen cyanide	20 ppm
Hydrogen fluoride	3 ppm
Hydrogen sulfide	20 ppm
Methyl alcohol	200 ppm
Monochlorobenzene	75 ppm
Mononitrotoluene	similar to nitrobenzene
Nitrobenzene	5 ppm
Nitrogen oxides	40 ppm
Petroleum naphthas	1000 ppm
Phosgene	1 ppm
Phosphine	1 ppm
Sulfur dioxide	10 ppm
Tetrachloroethane	10 ppm
Tetrachloroethylene	200 ppm
Toluene (Toluol)	200 ppm
Trichlorethylene	200 ppm
Turpentine	200 ppm
Xylene (Xylol)	200 ppm
Barium peroxide	0.5 mg/m^3§
Cadmium	0.1 mg/m^3
Chromic acid	0.1 mg/m^3
Lead	0.15 mg/m^3
Mercury	0.1 mg/m^3
Dinitrotoluene	similar to TNT
Tetryl	1.5 mg/m^3§
TNT	1.5 mg/m^3
Zinc oxides	15.0 mg/m^3
Silica (SiO_2) (free or uncombined)	5 mppcf

* The maximum allowable concentration for the various substances listed are the values most widely accepted today and are based on an eight-hour daily exposure.

† These values have not been definitely established but are included to serve as a guide.

§ No specific information available, but believed to present no health hazards at this concentration.

Note:

ppm = Parts of substances per million parts of air by volume.

mg/m^3 = Milligrams of substance per cubic meter of air.

mppcf = Millions of particules of substances per cubic foot of air.

APPENDIX C

Maximum allowable concentrations of industrial atmospheric contaminants*

WARREN A. COOK
Director, Division of Industrial Hygiene and Engineering Research, Zurich Insurance Companies

The following table presents a list of maximum allowable concentrations of industrial atmospheric contaminants as set up by a number of states, and includes the values recommended by the U.S. Public Health Service and the American Standards for substances so far promulgated by the American Standards Association. A list of accepted and tentative values is also presented for practical use in the control of occupational disease and for the provision of both healthful and comfortable working conditions where toxic or obnoxious materials may be present. A number of these values are soundly founded on a combination of animal experimentation and experience with workers under actual industrial conditions. Others of these values have a basis only in animal experimentation, some of which is so limited as merely to give an indication of the approximate concentrations which should be permitted. Still others of these values are based on judgment which has its foundation in sensory response of persons to known concentrations of the atmospheric contaminant or in human experience under occupational conditions of insufficient extent to be truly significant.

The final column of accepted and tentative values is offered with the hope that further work both in the experimental laboratory and under industrial conditons may be stimultated. Already correlation of medical findings, both clinical and laboratory, with the results of determinations of concentrations of atmospheric contaminants have given us much information. Only through further correlated activity of this type can we arrive at more complete dependable information on these maximum allowable concentrations. It is advised that there be medical observation of workers whose exposure to an atmospheric contaminant may be close to the allowable concentration especially where it may be one of those values based on such limited data as to be of questionable reliablility.

More complete discussions of the use and limitations of maximum allowable concentrations are given by J.H. Sterner in *Industrial Medicine 12*:514-518 (August 1943), "Determining Margins of Safety — Criteria for Defining a 'Harmful' Substance;" by Ludwig Teleky in *Industrial Hygiene Supplement* of *Industrial Medicine 9*:63-71 (October 1940), "Toxic Limits"; and in an editorial on pages 53, 54 of this latter issue. It is advised that these be carefully read as a background to the application of maximum allowable concentrations.

It is to be emphasized that the intent in presenting these maximum allowable concentrations is to provide a handy yardstick to be used as guidance for the routine industrial control of these health hazards — not that compliance with the figures listed would guarantee protection against ill health on the part of exposed workers, nor should the maintenance of the suggested concentrations be considered a substitute for medical control.

In every case, the concentrations given are considered allowable for prolonged exposures, usually assuming a 40-hour week.

The several lists in the table refer to the following sources:

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* From the Appendix of *Job Placement of Physically Handicapped,* by Clark D. Bridges, McGraw-Hill Book Company (1946), prepublication release in *Ind. Med. 14(11)*:936-946 (November 1945). Reprinted by permission of the American Industrial Hygiene Association.

A. California Industrial Accident Commission (September 1945).

B. Connecticut State Department of Health, Bureau of Industrial Hygiene, Regulation 281 of the Sanitary Code (September 1945).

C. Massachusetts Department of Labor and Industires. Not official, but used by the Divison of Occupational Hygiene as a guide (September 1945).

D. New York State Department of Labor. Not official, but used by the Division of Industrial Hygiene as a guide (June 1945).

E. Oregon State Board of Health. Rules and Regulations for the Prevention of Occupational Diseases (August 1945).

F. Utah Department of Health. Compiled by the Industrial Hygiene Division as part of a booklet on *Useful Criteria in the Identification of Certain Occupational Health Hazards* (1945).

G. United States Public Health Service. Presented as a guide for occupational disease control, as published in *Manual of Industrial Hygiene* (W.B. Saunders Company, Philadelphia, 1943), with revisions here to show U.S. Public Health Service opinion as of September 1945.

H. American Standards promulgated by the American Standard Association up to September 1945. Parentheses indicate value is an "American War Standard" only.

I. Accepted and tentative valued based on industrial experience, animal experimentation, sensory responses of persons, or a combination of these.

Following the table is an indication of the basis and reliability of each of the values given in Columnn I. Since there is no fine line of demarcation between physiological response to small differences in concentrations of any of these atmospheric contaminants round numbers are used in most instances. For example, if 1000 parts per million of a contaminant such as gasoline vapor cause irritation but somewhat lesser concentration — perhaps 750 or 825 parts per million — do not cause irrition of some group of persons under observation, the allowable concentration is given as 500 parts per million rather than an intermediate value.

TABLE I

Maximum Allowable Concentrations of Industrial Atmospheric Contaminants

In all columns except I, the figures in this table refer to parts of gas or vapor per million parts of air [abbreviated in the discussion of which follows as ppm] with the exception the figures for dusts, fumes and mists which are expressed as milligrams of the substance per cubic meter of air [abbreviated as mg./m^3] in columns A though H are designated with an asterisk.

Under I, the first column includes values normally expressed as parts per million. The second column gives round number equivalents in milligrams per cubic meter so that there may be a comparison between the toxicities of the various substances on the basis of mass per unit volume.

	A	B	C	D	E	F	G	H	I	
									ppm	mg/m^3
Acetaldehyde									200	400
Acetic acid				10					10	25
Acetone	500		500	1000	500	200			500	1000
Acetylene tetrachloride (See 1, 1, 2, 2-Tetrachloroethane)										
Acrolein	1				1	3.3	1		0.5	1
Acrylonitrile	20			20	20		20		20	50
Ammonia	100		100	100	100	100	100		100	50
Amyl acetate	400		200	400	400	400	400		200	1000
iso-Amyl alcohol	200			200		55.6			100	400
Aniline	5		5	5	5	5-7	5		5	20
Arsenic		0.15*	0.15*	0.15*	0.15*	0.5*		(.15*)		0.15
Arsine	1		0.05	1	0.5	1	1		1	2
Barium peroxide (as Ba)				0.5*			0.5*			0.5
Benzene (Benzol)	100	100	75	50	75	75-100	100	100	100	200
Benzine (Gasoline)	1000	1000	1000	1000		1000	1000		500	2000
Bromine	1			1		1			1	5

Appendix C

	A	B	C	D	E	F	G	H	I	
									ppm	mg/m³
1, 3-Butadiene									5000	10000
n-Butanol (Butyl alcohol)	200		50	200		100	100		50	200
2-Butanone	500		300						200	500
n-Butyl acetate	400		200	400	400	400	400		200	1000
Butyl cellosolve	50								200	1000
Cadmium	0.1*	0.1*	0.1*	0.1*	0.1*	0.1*	0.1*	(0.1*)		0.1
Carbon dioxide	5000			5000	5000	5550	5000		5000	10000
Carbon disulfide	20	20	20	20	20	20	20	20	20	50
Carbon monoxide	100	100	100	100	100	100	100	100	100	100
Carbon tetrachloride	100	100	50	75	50	100	100		100	500
Carrene No. 2 (See Monofluorotrichloromethane)										
Cellosolve	500					500			200	1000
Cellosolve acetate									100	500
Chlorine	1	1	1	1	1	1		2	5	10
2-Chlorobutadiene (Chloroprene)						83			25	100
Chlorodiphenyl	1*		5*	1*	0.3*	1*				1
Chloroform	100			100		100			100	500
Chloronaphthalenes (See Penta and trichloronaphthalenes)			1-5							
1-Chloro-1-nitropropane									20	100
Chromic acid	0.1*	0.1	0.1*	0.1*	0.1*	0.1*	0.1*	0.1*		0.1
Cyclohexane									400	1000
Cyclohexanol									100	400
Cyclohexanone									100	400
Cyclohexene									400	1000
o-Dichlorobenzene	75		75	75	75		75		75	500
Dichlorodifluoromethane (Freon-12)									100000	500000
1.1-Dichloroethane (ethylidine chloride)									100	400
1, 2-Dichloroethane (ethylene dichloride)	100		75	100	100	100	100		100	400
1, 2-Dichloroethylene	200					100			100	400
Dichloroethyl ether	15		15	15		15			15	100
Dichloromethane	200			500					500	2000
Dichloromonofluoromethane (Freon-21)									5000	20000
1, 1-Dichloro-1-nitroethane									10	50
Dichlorotetrafluoroethane (Freon-114)									10000	50000
Difluoromonochloromethane (Freon-22)									20000	50000
Dimethylaniline	5			5	5		5		5	25
Dimethylsulfate									1	5
Dinitrotoluene				1.5*			1.5*			1.5
Dioxane						1000			500	2000
Ethyl acetate			400						400	1000
Ethyl alcohol	1000			1000					1000	2000
Ethyl benzene						<1000			200	1000
Ethyl bromide	1700					1700			400	2000
Ethyl chloride	20000					20000			5000	10000
Ethylene chlorhydrin									10	25
Ethylene dichloride (Commercial name for 1; 2-Dichloroethane)										
Ethylene oxide						<250			100	200
Ethyl ether	400		400	400	400	400			500	2000
Ethyl formate									200	500
Ethyl silicate						<500			100	2000
Fluoride dusts, smokes			1*		2*					
Formaldehyde	10	10	10	5	10	20		10	10	10

	A	B	C	D	E	F	G	H	I	
									ppm	mg/m³
Freon (See respective Dichloro, Difluoro and Monofluoro Compounds)										
Furfural									See note	
Gasoline	1000	1000	1000	1000	500	1000	1000		500	2000
Heptane									500	2000
Hexane									1000	4000
Hexanone (See methyl butanone)										
Hexone (See methyl iso-butanone)										
Hydrochloric acid (hydrogen chloride)	10	10	10	10	10	10	10		10	10
Hydrogen cyanide	20	20	20	20	20	20	20		20	20
Hydrogen fluoride	3	3	1.5	3	3	3	3		3	2
Hydrogen selenide									0.1	.2
Hydrogen sulfide	20	20	20	20	20	20	20	20	20	20
Iodine				1	.05-1.0				0.1	1
Iron oxide				30*						30
Isophorone									25	100
Lead	0.15*	0.15*	0.15*	0.15*	0.15*	0.15*	0.15*	0.15*		0.15
Magnesium						15*				15
Manganese	6*	6*	6*	6*	6*	5-50*		(6*)		6
Mercury	0.1*	0.1*	0.1*	0.1*	0.1*	0.1-0.2*	0.1*	0.1*		0.1
Mesityl oxide									50	200
Methanol (methyl alcohol)	200	200	200	200	100	100-200	200	200	200	200
Methyl acetate	400								100	200
Methyl bromide	500			35	35	50-100			20	50
Methyl butanone						<1500			200	500
Methyl cellosolve						<25			100	1000
Methyl cellosolve acetate									100	500
Methyl chloride	500				100	500			200	400
Methylcyclohexane									1000	4000
Methyl cyclohexanol									100	500
Methylcyclohexanone									100	500
Methyl ethyl ketone (See 2-Butanone)										
Methyl formate						<1500			400	1000
Methyl iso-butanone						1000			200	500
Monochlorobenzene	75		75	75		75	75		75	400
Monofluorotrichloromethane (Freon-11—Carrene ν2)									10000	50000
Mononitrotoluene				5			5		5	25
Naphtha (Coal tar)	100		200		200				100-200	200-500
Naphtha (Petroleum)					500	5000			500	2000
Nitrobenzene	5		5	5	5	1-5	5		5	25
Nitroethane									200	500
Nitrogen dioxide			10							
Nitrogen oxides	25	25		40	25	10-40	25	25	25	100
Nitroglycerine						10-40	0.5		0.5	5
Nitromethane									200	500
Octane									500	2000
Ozone	1		1	1	0.5	1			1	2
Pentachloronaphthalene	1.0*			0.5*	0.5*	0.5*				0.5
Pentane									5000	10000
Pentanone (methyl propanone)	500					1500			400	1000
Perchlorethylene (Commercial name for tetrachloroethylene)										
Phosgene	1	1		1	1	1	1		1	5
Phosphine	1		1	1	1	2	1		1	1
Phosphorus trichloride	1					0.7			0.5	4
iso-Propanol (iso-Propyl alcohol)									400	1000
Propyl acetate									200	1000
iso-Propyl ether									500	2000

	A	B	C	D	E	F	G	H	I	
									ppm	mg/m³
Radon (radium emanation)									10^{-11}	curie/l
Stibine									10	50
Stoddard solvent				750					500	2000
Styrene monomer	400	400	400	400	400			(400)	400	1000
Sulphur chloride									1	5
Sulphur dioxide	10	10	10	10	10	10	10		10	25
Sulphuric acid				5*		2*				5
Tellurium										0.01
1, 1, 2, 2-Tetrachlorethane	10		5	10	10	10	10		10	50
Tetrachloroethylene	200		200	200	200	200	200		200	1000
Tetryl	1.5*					1.5*				1.5
Toluene (Toluol)	200	200	200	200	200	200	200	200	200	500
Toluidine									5	20
Trichloroethylene	200	200	200	200	200	200	200		200	1000
Trichloronaphthalene	10*		5*	5*	5*	5*				5
Trinitrotoluene (TNT)	1.5*		2*	1.5*		1.5*				1.5
Turpentine	200	700	200	200	200	200-700	200		100	500
Vinyl chloride						500			1000	1000
Vinyl cyanide (See acrylonitrile)										
X-Ray								(0.1r)	0.1 roentgen	
Xylene (Xylol)	200	200	200	200	200	200	200	(200)	200	500
Zinc oxide	15*		15*	15*		15*	15*			15

NOTE: A number of gases, such as acetylene, butane, ethane, ethylene, hydrogen, methane, propane, helium and nitrogen, are considered to be essentially non-toxic but act as simple asphyxiants at high concentrations.

Basis of values in column I

Acetaldehyde: Iwanoff, in *Arch f. Hyg.* 73:32 (1911), reported that cats showed no noticeable effects on seven hours exposure to 280 parts per million. The value of 200 ppm is based on this brief exposure since the immediate irritative effect of low concentrations appears to be more prominent than systemic effects.

Acetic acid: 10 ppm is based on sensory response to this irritant.

Acetone: This substance is one of the least toxic of the commercially used solvents as has been shown both by industrial exposures involving many hundreds of persons and also through animal experimentation. From the point of view of toxicity, an allowable concentration of even 2000 or 3000 ppm may be lower than necessary. H. Specht, J.W. Miller and P.J. Valaer, in Reprint No. 2076, *Pub. Health Repts.* 54:944-955 (June 2, 1939), "Acute Response of Guinea Pigs to the Inhalation of Dimethyl Ketone (Acetone) Vapor in Air," reported that 1% acetone vapor in air for approximately 48 hours caused systemic injury to experimental animals. The tentative value of 500 ppm is based on sensory response to acetone vapor which caused irritation of the eyes, nose and throat of a group of human subjects at concentrations of 500 ppm as reported by K.W. Nelson, J.F. Ege, Jr., Morwick Ross, L.E. Woodman, and Leslie Silverman, in *J. Ind. Hyg. & Tox.* 25:282-285 (September 1943), "Sensory Response to Certain Industrial Solvent Vapors." Although the exposed group estimated 200 ppm as the highest satisfactory exposure for eight hours, it is felt that some habituation usually develops on daily exposure to moderately irritative atmospheres. In war industries where hundreds of workers were exposed to acetone, it was found necessary to maintain vapor concentrations below 700 ppm to avoid irritation. A number of state departments have found it necessary to require limitation of acetone vapor to 500 ppm to avoid irritation. There is no published evidence that concentrations of 1000 ppm are regularly tolerated without irritation, though in some large industries such concentrations are said to exist with no complaints by those exposed. Where irritative qualities of a substance are the deciding factor in recommending a concentration which may be appreciably lower than the toxic limit, this fact should be fully recognized in the application of the suggested value.

Acrolein: Since a concentration of 1 ppm of acrolein produces marked irritation of eyes and nose in five minutes or less, as shown by W.P Yant, H.H. Schrenk, F.A. Patty, and R.R. Sayers, in U.S. Bureau of Mines Report of Investigations No. 3027 (1939), *Acrolein as a Warning Agent for Detecting Leakage of Methyl Chloride from Refrigerators,* a concentration of half this value is tentatively suggested for prolonged exposure.

Acrylonitrile: The U.S. Public Health Service suggests 20 ppm as not definitely established but to serve as a guide following animal experimentations published under the general title *Toxicology of Acrylonitrile (Vinyl Cyanide)* as follows: H.C. Dudley and P.A. Neal, "(I) A Study of the Acute Toxicity," *J. Ind. Hyg. & Tox. 24*:27-36 (February 1942); H.C. Dudley, T.R. Sweeney and J.W. Miller, "(II) Studies of Effects of Daily Inhalation," *J. Ind. Hyg. & Tox. 24*:255-258 (November 1942); A.H. Lawton, T.R. Sweeney and H.C. Dudley, "(III) Determination of Thiocyanates in Blood and Urine," *J. Ind. Hyg. & Tox. 25*:13-19 (January 1943).

Ammonia: The authority for 100 ppm goes back to K.B. Lehmann, in *Arch. f. Hyg. 5*:68 (1886). This concentration is generally accepted today.

Amyl acetate: The value of 200 ppm is based on irritative effects as reported by Nelson *et al* in the "Sensory Response" paper, *J. Ind. Hyg. & Tox. 25*:282-285 (September 1943).

Amyl alcohol: The value of 100 ppm is based on irritative effects as shown by Nelson *et al, J. Ind. Hyg. & Tox. 25*:282 (September 1943).

Aniline: W.F. von Oettingen, in *Pub. Health Bull. 271*(1941), "The Aromatic Amino and Nitro Compounds, their Toxicity and Potential Dangers — A Review of the Literature," stated that the available literature is not sufficent to allow the establishment of definite standards, but quoted the table from Henderson and Haggard, *Noxious Gases,* 1927, in which 7.0 to 25.0 ppm are described as giving slight symptoms after several hours. Workers exposed to concentrations approaching the suggested value of 5 ppm should be under medical observation — particularly as aniline is readily absorbed through the skin.

Arsenic and Arsenic trioxide: The allowable concentration of 0.15 mgs. per cubic meter for metallic arsenic and arsenic trioxide was based on analogy with other metals such as cadmium and lead in setting up the American War Standard by the American Standards Association. On the basis of long experience involving many occupational exposures, at least one large concern considers it permissible to increase this limit to 5 mg. per cubic meter. R.M. Watrous, M.D., and M.B. McCaughey, in *Industrial Medicine 14*:639-646 (August 1945) "Occupational Exposure to Arsenic — In the Manufacture of Arsphenamine and Related Compounds — " reported that exposures in manufacturing operations ranging from 0.007 to 0.60 milligrams per cubic meter as As_2O_3 resulted in no clinical symptoms attributable to arsenic except in a few isolated workers during a short period of unusually heavy exposure.

Arsine: The value of 1 ppm is suggested as a guide by the U.S. Public Health Service. Flury and Zernik in *Schadliche Gase,* 1931, stated in an unidentified reference to K.B. Lehmann that 3.1 ppm is tolerable for six hours without apparent symptoms.

Barium peroxide: The maximum allowable concentration of 0.5 mgs. per cubic meter (as barium) has been suggested by the U.S. Public Health Service as a guide. Where workers are exposed to concentrations approaching this value they should be placed under medical observation.

***Benzene** (Benzol):* Though 100 ppm has been adopted as the American Standard, there is no evidence that poisoning has occurred at less than 100 ppm. The National Safety Council Study of Benzol Poisoning, as summarized by C-E. A. Winslow in *J. Ind. Hyg. & Tox. 9*:61 (1927), the technical data of which was published by L. Greenburg, in Reprint No. 1096, *Pub. Health Repts. 41*:1367, 1410, 1519 (1926), concluded that a substantial hazard is involved even where the average exposure is below 100 ppm. M. Bowditch and H.B. Elkins, in *J. Ind. Hyg & Tox. 21*:321-330 (October 1939), "Chronic Exposures to Benzene (Benzol). I. The Industrial Aspects," suggested 75 ppm as a maximum allowable concentration but cited two cases of poisoning where they believed the average exposure was below this concentration. It is accordingly suggested that exposures be kept below 50 ppm until further experience either substantiates the suggested limit of 100 ppm as safe or causes it to be decreased.

Benzine: This term is applied to petroleum distillates such as gasoline. See "Gasoline" for discussion.

Bromine: Zederbaum, in *Gig. Truda*, page 68 (1927), referred to by Koelsch in *Munch. med. Wochschr.*, No. 33 (1928), found 4 ppm in a workroom to be productive of no noteworthy injury. An unidentified reference to K.B. Lehmann by Flury and Zernik in *Schadliche Gase,* 1931, stated six hours' exposure to bromine was without noticeable symptoms at a concentration of 0.75 parts per million. The value of 1 ppm should receive further substantiation.

Butadiene: C.P. Carpenter, C.B Shaffer, C.S. Weil and H.F. Smyth, Jr., in *J. Ind. Hyg. & Tox. 26*:69-78 (March 1944) "Studies on the Inhalation of 1,3-Butadiene," concluded that concentrations of 600, 2300, and 6700 ppm caused no significant progressive injury to small animals during an eight months' exposure, although the highest concentration retarded slightly and caused light cloudy swelling in some livers.

n-Butanol: H.F. Smyth and H.F. Smyth, Jr., in *J. Ind. Hyg. 10*:261-271 (October 1928), "Inhalation Experiments with Certain Lacquer Solvents," reported development of pathology on animal experimentation with exposures at 100 ppm. I.R. Tabershaw, J.P. Fahy, and J.B. Skinner, *J. Ind. Hyg. & Tox. 26*:328-330 (December 1944) "Industrial Exposure to Butanol," found that eye inflammation will result when atmospheric concentrations exceed 50 ppm and that no systemic effects may be expected below 100 parts per million.

2-Butanone: Although the acute response of guinea pigs to butanone, as observed by F.A. Patty, H.H. Schrenk and W.P. Yant, in Reprint No. 1702 from *Pub. Health Repts. 50*:1217-1228 (September 6, 1935), showed that 3000 parts per million could be tolerated by animals for several hours without serious disturbance, Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282 (1943), demonstrated sufficient irritation to humans at concentrations of 350 ppm to recommend 200 ppm as a practical limit.

n-Butyl acetate: The acute response of guinea pigs to normal butyl acetate, as shown by R.R. Sayers, H.H. Schrenk, and F.A. Patty in Reprint No. 1769 from *Pub. Health Repts. 51*:1229-1236 (September 4, 1936), indicated the maximum exposure for several hours with slight or no symptoms to be 3300 ppm. Sensory response to this vapor, as shown by Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282 (1943), was severe throat irritation of which all subjects complained at a concentration of 300 ppm. Though 100 ppm was recommended by the exposed persons, a concentration of 200 ppm is being suggested, as this group was not accustomed to occupational exposure to the material.

Butyl Cellosolve: H.W. Werner, C.W. Nawrocki, J.L. Mitchell, J.W. Miller, and W.F. von Oettingen, in *J. Ind. Hyg. & Tox. 25*:374-379 (October 1943), "Effects of Repeated Exposures of Rats to Vapors of Monoalkyl Ethylene Glycol Ethers," found that exposures of rats to a range of 300 to 400 ppm of n-butyl glycol ether produced small but measurable toxicological effects on daily exposure of seven hours, five days a week for five weeks.

Cadmium: L. Prodan, in *J. Ind. Hyg. 14*:174-196 (May 1932), "Cadium Poisoning. II. Experimental Cadmium Poisoning," reported on extensive animal experimentation including inhalation. Although the lowest concentrations used were much in excess of those considered poisonous for continued exposure, it is to be concluded from Prodan's work that cadmium is as poisonous as lead or somewhat more so. In view of the rapidity with which excessive cadmium exposures can cause serious pulmonary edema and death, as shown by L.W. Spolyar, J.F. Keppler, and H.G. Porter in *J. Ind. Hyg. & Tox. 26*:232-240 (September 1944), "Cadmium Poisoning in Industry: Report of Five Cases, Including One Death," any new exposure to cadmium dust or vapor should be carefully watched. Determination of concentrations to which workers are exposed together with medical observation of the workers are important both for avoiding serious injury and to gain more reliable information concerning the maximum allowable concentration.

Carbon dioxide: Flury and Zernik, *Schadliche Gase,* 1931, refer to Lehmann-Hess as authority that six hours' exposure to 5550 ppm carbon dioxide caused no noticeable symptoms.

Carbon disulfide: F.H. Wiley, W.C. Kueper, W.S. von Oettingen, in *J. Ind. Hyg. & Tox. 18*:733-740, (1936), "On the Toxic Effects of Low Concentration of Carbon Disulfide," reported that animals exposed to concentrations of 30 ppm over a long term showed no significant toxic effects. N.L. Barthelemy, in *J. Ind. Hyg. & Tox. 21*:141-151 (1939), "Ten Years Experience with Industrial

Hygiene in Connection with the Manufacture of Viscose Rayon," reported that no trouble whatever was experienced where carbon disulfide exposures were kept in less than 30 ppm.

Carbon monoxide: Y. Henderson, H.W. Haggard, M.C. Teague, A.L. Prince, and R.M. Wunderlich, in *J. Ind. Hyg. & Tox. 3*:79-137 (1921), "Physiological Effects of Automobile Exhaust Gas and Standards of Ventilation for Brief Exposure," showed that 100 ppm could be considered allowable for an exposure of several hours. R.R. Sayers, W.P. Yant, E. Levy, and W.B. Fulton, in Public Health Bulletin No. 186 (1929), *Effects of Repeated Daily Exposure of Several Hours to Small Amounts of Automobile Exhaust Gas*, reported that the daily exposure of six men over a period of 68 days to 200 ppm of carbon monoxide caused some of the more susceptible persons to develop slight but not discomforting symptoms after two hours. R.F. Sievers, T.I. Edwards, A.L. Murray, and H.H. Schrenk, in *J.A.M.A. 188*:585-588 (February 21, 1942), "Effect of Exposure to Known Concentrations of CO," reported that a group of 156 Holland Tunnel traffic officers exposed over a 13 year period to an average of 70 parts per million of carbon monoxide did not reveal any evidence of injury to health attributable to the exposure.

Carbon tetrachloride: H.F. Smyth, H.F. Smyth, Jr., and C.P. Carpenter, in *J. Ind. Hyg. & Tox. 18*:277-298 (1936), "The Chronic Toxicity of Carbon Tetrachloride: Animal Exposures and Field Studies," concluded on the basis of animal experiments over a period of 10.5 months that 100 ppm is safe for continuous exposure of workmen throughout the day, and day after day. There has been an increasing amount of evidence since the date of that publication that concentrations less than 100 ppm may cause injury to health. As in the case of benzol, it is recommended that exposures be kept at less than half the maximum allowable limit for carbon tetrachloride until such time as further experience either provides justification of the present suggested limit or causes it to be revised downward.

Cellosolve: H.W. Werner, C.W. Nawrocki, J.L. Mitchell, J.W. Miller, and W.F. von Oettingen, in *J. Ind. Hyg. & Tox. 25*:374-379 (October 1943), "Effects of Repeated Exposures of Rats to Vapors of Monoalkyl Ethylene Glycol Ethers," found that exposures of rats to a range of 300 to 400 ppm of ethyl glycol ether (cellosolve) produced small but measurable toxicological effects on daily exposures of seven hours five days a week for five weeks.

Cellosolve acetate: The maximum allowable concentration of 100 ppm is based on an unpublished report of tests made by the Chemical Hygiene Fellowship at Mellon Institute, reported in July 1945.

Chlorine: Early work has indicated that 1 ppm should be taken as the maximum allowable concentration and this has been generally followed. Ronzani, *Arch. f. Hyglene 67*:285 (1909), showed that 1.7 ppm caused impaired nutrition and blood changes in animals, but that 0.7 ppm caused no disturbances. K.B. Lehmann listed in a table in 1912, quoted in U.S. Bureau of Mines Tech. Paper 248 (1921), that 1 ppm causes slight symptoms after several hours and 4 ppm is the maximum concentration without symptoms for one hour exposure. As long ago as 1899, Lehmann observed that an increase in resistance occurs on acclimatization (*Arch. f. Hyg. 34*:302). Capable research of more recent date in this country conducted by the American University Experiment Station of the Chemical Warfare Service, referred to in U.S. Bureau of Mines Tech. Paper 248 (1921), showed the least concentration to give detectable odor was 3.5 ppm; to cause throat irritation, 15.1 ppm; and to cause coughing, 30.2 ppm. On the basis of these data, it is considered in order to suggest 5 ppm rather than 1 ppm as the allowable concentration.

Chloro-butadiene (Chloroprene): W.F. von Oettingen, W.C. Hueper, W. Deichmann-Gruebler, and F.H. Wiley, in *J. Ind. Hyg. & Tox. 18*:240 (1936), "2-Chlorobutadiene (Chloroprene): Its Toxicity and Pathology and Mechanism of its Action," reported that animal experimentation indicates that continued exposure to 0.3 mgs. per liter (83 ppm) and even less may cause toxic effects. It is consequently considered desirable to suggest 25 ppm until further data are available as to effects on man on prolonged exposure.

Chlorodiphenyl: C.K. Drinker, in *J. Ind. Hyg. & Tox. 21*:155-159 (May 1939), "Further Observations on Possible Systemic Toxicity of Certain of the Chlorinated Hydrocarbons with Suggestions for Permissible Concentrations in the Air of Workrooms," lists a table of 14 chlorinated hydrocarbons with permissible limits. Exposure of rats to 0.5 mgs./m^3 in one test and 10.0 mgs./m^3 in

another was found to cause no injury. A maximum allowable concentration of 1 mg./m^3 is suggested, though it is very possible that exposure to this substance may extend to 5 mgs./m^3 without injury to health.

Chloroform: Since there is no published work on prolonged exposures of animals under experimental conditions or of humans in industrial occupations to known low concentrations of chloroform, a value of 100 ppm is generally accepted on the basis of analogy with carbon tetrachloride. The value as given should be further substantiated and there should be close medical observation of any group of workers exposed to chloroform concentrations approximating 100 ppm. As is the case with carbon tetrachloride, it would be wise to retain exposures to less than 50 ppm until more data are available.

Chloronaphthalenes: Results of animal experiments with chloronaphthalenes are given in the reference cited under "Chlorodiphenyl." Inhalation of a concentration of 10 mgs./m^3 of trichloronaphthalene by rats caused no pathology. In view of the fact that industrial experience has indicated that there is an unusually marked difference in susceptibility, 5 mgs./m^3 is generally accepted as the allowable concentration. As the chlorine content of the compound increases, a lower allowable limit is necessary to avoid poisoning. For a combination of tetra and penta chloronaphthalenes, a limit of 1 mg./m^3 was suggested; for a mixture of penta and hexachlorohaphthalenes, a limit of 0.5 mgs./m^3.

1-Chloro-1-nitropropane: Willard Machle, E.W. Scott, J.F. Treon, F.F. Heyroth, and J.V. Kitzmiller, in *J. Ind. Hyg. & Tox.* 27:95-102 (April 1945), "The Physiological Response of Animals to Certain Chlorinated Mononitroparaffins," showed by animal experiment that this substance is considerably less toxic than 1,1-dichloro-1-nitroethane. The longest exposure to the propane derivative was for two hours only. The allowable concentration of 20 ppm for long exposures is based on a comparison with that of the ethane derivative on which more extensive research was done. Longer animal experimentation or human experience under medical observation may indicate that a somewhat higher concentration is not injurious.

Cyclohexane: J.F. Treon, W.E. Crutchfield, J., and K.V. Kitzmiller, in *J. Ind. Hyg. & Tox.* 25:323-347 (October 1943), "The Physiological Response of Animals to Cyclohexane, Methycyclohexane, and Cetain Derivatives of these Compounds," reported that animal experimentation of 50 periods of exposure of six hours each showed barely demonstratable microscopic changes in the liver and kidneys of rabbits that had been exposed to 786 ppm and no toxic changes after similar periods of exposure to 434 ppm. As the pathological effects of the higher exposures were so slight, it is considered permissible to set the allowable concentration at 400 ppm.

Cyclohexanol: The reference quoted under "Cyclohexane" includes similar data on cyclohexanol. These authors showed that 693 ppm caused barely demonstrable pathological changes on a monkey and that 145 ppm caused scanty but definite changes in the liver and kidneys of rabbits, with the conclusion that this latter exposure is very near to the maximum safe level for rabbits. One hundred ppm is being suggested as the maximum allowable concentration but, until there is more experience with human exposure, there should be medical observation of workers exposed to these compounds where concentrations approach the allowable limits.

Cyclohexanone: In the preceding reference these authors reported the maximum allowable concentration for cyclohexanone is slightly below 190 ppm. A maximum allowable limit of 100 ppm is suggested for this compound. In the experimental human exposures to cyclohexanone carried on by Nelson *et al,* and described in *J. Ind. Hyg. & Tox. 25*:282 (September 1943), irritation was experienced at 75 ppm. If actual industrial exposures show similar irritation to workmen, the permissible exposure should be adjusted downward.

Cyclohexene: The only quantititive toxicological work conducted on this compound is that on acute exposures which N.W. Lazarew reported in *Arch. exptl. Path. Pharmakol. 143*:223 (1929), "On the Toxicity of Vapors of Different Hydrocarbons," showing that 9000 ppm caused experimental animals to assume "sidepositlon," indicating mild narcosis. On analogy to the toxicity of cyclohexane which it closely resembles structurally, though introduction of double bond may increase its toxicity somewhat, the maximum allowable concentration of 400 ppm is suggested. With this inadequate basis for setting an allowable concen-

tration, medical observation should be afforded workers who may be exposed to concentrations approaching this value.

o-Dichlorobenzene: A value of 75 ppm is recommended by the U.S. Public Health Service as a guide.

Dichlorodifluoromethane (Freon-12): R.R. Sayers, W.P. Yant, John Chornyak, and H.W. Shoaf stated in U.S. Bureau of Mines Report of Investigations No. 3013, *Toxicity of Dichlorodifluoromethane: A New Refrigerant*, (May 1930), that a 12 week daily exposure of animals to 20% by volume of this vapor caused no gross pathology attributable to the exposure. Since generalized tremor and a gait simulating alcoholic ataxis were observed in some of the animals, it is recommended that the maximum exposure be no more than 10% or 100,000 ppm.

1,1-Dichloroethane (Ethylidine chloride): The value of 100 ppm is set up for this compound as its action is considered by Flury and Zernik, *Schadliche Gase*, 1931, to be analogous to chloroform though less severe. The only reported animal experimentations are those by Lazarew and Mueller, who determined narcotic action of concentrations only as low as 7400 ppm and 4400 ppm, respectively. Their work is reported in *Arch. exptl. Pathl. Pharmakol. 141*:19 (1924), and *109*:276 (1925), respectively.

1,2-Dichloroethane (Ethylene dichloride): The value of 100 ppm is recommended by the U.S. Public Health Service as a guide and is generally accepted though there is some indication that somewhat lower concentrations should be used as the maximum allowable limit. Where exposures approach this value, medical observation of workers is recommended.

Dichloroethylene: The value of 100 ppm is suggested as a tentative value but no specific work has been done on prolonged exposure to known concentrations of this material. There has been some suggestion that the unsaturated chlorinated hydrocarbons do not cause liver damage at as low concentrations as do the saturated compounds, but specific information should be developed on this particular unsaturated chlorinated hydrocarbon before the suggested value is increased to possibly 200 ppm.

Dichloroethyl ether: H.H. Schrenk, F.A. Patty, and W.P. Yant, in Reprint No. 1602 from *Public Health Repts. 48*:1389-1398 (November 17, 1933) "Acute Response of Guinea Pigs to Vapors of Dichloroethyl Ether," reported that slight nasal irritation was noted among experimental animals at 35 ppm. It has been generally accepted that where prolonged exposures are contemplated, the exposure should not exceed 15 ppm.

Dichloromethane: L.A. Heppel, P.A. Neal, L.T. Perrin, M.L. Orr, and V.T. Porterfield, in *J. Ind. Hyg. & Tox. 26*:8-16 (January 1944), "Toxicology of Dichloromethane (Methylene Chloride)," concluded that on the basis of animal experimentation the maximum allowable limit be tentatively set at 500 ppm for eight hours daily exposure. Although Henderson and Haggard, in *Noxious Gases*, 1943, quote F. Flury in Lehmann and Flury, *Toxicology and Hygiene of Industrial Solvents*, (Williams & Wilkins, 1943) that 290 ppm should be a maximum allowable concentration, it is to be noted that the animal experimentation by Heppel *et al* of the U.S. Public Health Service, cited above, showed that even at 5000 parts per million, repeated seven hours exposures, five days a week for six months, caused no evidence of toxic action by rats, rabbits or dogs.

Dichloromonofluoromethane (Freon 21): Shown by the *Underwriters' Laboratories Report MH-2630* (1935) and *U.S. Bureau of Mines Report R.I. 3125* (1933) to be somewhat more toxic than monofluorotrichloromethane (Freon 11) for which the value of 10,000 ppm is suggested.

1,1-Dichloro-1-nitroethane: Willard Machle, E.W. Scott, J.F. Treon, F.F. Heyroth, and K.V. Kitzmiller, in *J. Ind. Hyg. & Tox. 27*:95-102 (April 1945), "The Physiological Response of Animals to certain Chlorinated Mononitroparaffins," reported that exposure of animals to 25 ppm was without lethal effect for 204 hours. They observed that the irritation on exposure to this compound was greater than that caused by equivalent concentrations of diethyl ether but definitely less than that resulting from equivalent exposure to acid gases.

Dichlorotetrafluoroethane (Freon 114): A.H. Nuckolls, in *Underwriters' Laboratories Report MH-2375* (November 1923), reported that animals showed occasional retching movements from which they recovered quickly after two hours' exposure to 2.5% of this material, though no

pathological conditions were found on autopsy after the two hours' exposure. There has been no published work on prolonged exposure.

Dimethylsulfate: Flury and Zernik, *Schadliche Gase*, 1931, reported without giving specific reference to original work, that 20 ppm killed cats in 11 minutes and that 13 ppm caused severe poisoning on 20 minutes' exposure. On the basis of these animal experiments, a value of 1 ppm is suggested as the maximum allowable concentration. However, there should by all means be close medical supervison whenever there may be exposure to this dangerous substance.

Difluqromonochloromethane (Freon 22): Underwriters' Laboratories Report MH-3134 (1940) concluded that this substance is less toxic than Freon 11 and than carbon dioxide but more toxic than Freon 12.

Dimethylaniline: The U.S. Public Health Service suggests that this compound is similar to anailine in its toxicity.

Dinitrotoluene: The toxicity of dinitrotoluene is considered similar to that of TNT for which the U.S. Public Health Service suggests 1.5 mgs. per cubic meter as a guide.

Dioxane: A. Fairley, E.C. Linton, and A.H. Ford-Moore, in *J. Hyg. 34*:486 (1934), "The Toxicitiy to Animals of 1,4-Dioxan," report kidney and liver damage to animals on exposures to 100 ppm over periods for the most part of 100 to 200 hours' duration. Persons who are exposed to dioxane at concentrations approaching that considered allowable should be under medical observation until more data are available concerning effects of known concentrations.

Ethyl acetate: This material is among the lesser toxic of organic solvents but causes irritation of eyes, nose and throat to experimental human subjects at 400 ppm according to Nelson *et al* in *J. Ind. Hyg. & Tox. 25*:282 (September 1943). Attention should be given to complaints at exposures even less than this concentration as experimental subjects estimated that the concentration would have to be reduced to 100 ppm to be considered satisfactory for eight hours' exposure.

Ethyl alcohol: Although as reliable an authority as Lehmann and Flury, *Toxicology and Hygiene of Industrial Solvents*, (Williams & Wilkins, 1943) observed, without specific reference, that 1000 ppm in the air is considered a dangerous concentration, large numbers of workers in this country have been exposed over long periods of time to concentrations of 1000 ppm with no demonstrable injury to health and with no increase in accident frequency. There is an occasional initial complaint of eye irritation but this is only on very first introduction to the exposure.

Ethyl benzene: W.P. Yant, H.H. Schrenk, C.P. Waite, and F.A. Patty, in Reprint No. 1379 from *Public Health Repts. 45*:1241-1250 (May 30, 1930) "Acute Response of Guinea Pigs to Ethyl Benzene," found no symptoms other than eye and nose irritation on exposures of 1000 ppm for as long as 480 minutes. N.W. Lazarew, in *Arch. exptl. Path. Parmakol. 143*:223 (1929), "On the Toxicity of Vapors of Different Hydrocarbons," reported that ethyl benzene has greater narcotic action than benzene. Ethyl benzene thus compares with toluene in its relation to benzene on high exposure and, from its structural formula, can be expected to correspond to toluene on extended exposure to lower concentrations. A value of 200 ppm is accordingly suggested. Where exposures approach this concentration, there should be medical observation of persons exposed in view of the lack of specific data supporting this value.

Ethyl bromide: R.R. Sayers, W.P. Yant, B.H.G. Thomas, and L.B. Berger, in Public Health Bulletin No. 185 (March 1929), *Physiological Response Attending Exposure to Vapors of Methyl Bromide, Methyl Chloride, Ethyl Bromide and Ethyl Chloride*, observed that exposures of animals to 1700 ppm for 540 minutes caused no symptoms. In view of the lack of experimental data covering exposure over prolonged periods or quantitative information exposure of workers, a value of approximately one-quarter of the above concentration or 400 ppm is arbitrarily suggested as a tentative allowable concentration. Where workers may be exposed to concentrations approaching this value, they should be under medical observation.

Ethyl chloride: Public Health Bulletin No. 185 (March 1929), cited as reference for "Ethyl Bromide," recommended 20,000 ppm as the maximum amount for long exposures. Following the same arbitrary rule as for ethyl bromide, 5000 ppm is suggested for ethyl chloride. Here again persons who may be regularly exposed to concen-

trations approaching this value should be under medical observation.

Ethlene chlorohydrin: Hugh Dierker and Paul G. Brown, in *J. Ind. Hyg. & Tox. 26*:277-279 (October 1944), "Study of a Fatal Case of Ethylene Chlorohydrin Poisoning," found that the victim had been exposed to a concentration of 305 ppm for only two hours. Animal exposure to a concentration of 365 for two hours caused pathological conditions to develop. Until further data on effects of prolonged exposures are available, it is recommended that concentrations not exceed 10 ppm. Particularly in view of the considerable skin absorption of ethylene chlorohydrin, as observed by H.F. Smyth, Jr., and C.P. Carpenter, in *J. Ind. Hyg. & Tox. 27*:93 (March 1945), "Note upon the Toxicity of Ethylene Chlorohydrin by Skin Absorption," workers exposed to this solvent should be under medical observation.

Ethylene oxide: C.P. Waite, F.A. Patty, and W.P. Yant, in Rept. No. 1401, *Pub. Health Repts. 45*:1832-1843 (August 1930), "Acute Response of Guinea Pigs to Ethylene Oxide," found that 250 ppm caused no symptoms on exposure of animals for 480 minutes. With lack of long-time animal experiments and no published data on prolonged exposures of the workers at known concentrations, a value of 100 ppm is arbitrarily suggested. Where workers are exposed to concentrations in the vicinity of this value, they should be under medical observation.

Ethyl ether: In this country, large numbers of persons are at work in operations involving exposures of 500 to 1000 ppm and as high as 2000-3000 ppm without demonstrable effect on health. Unfortunately there has been no publication correlating prolonged exposures to these concentrations with medical findings — or lack of them. Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282 (1943), reported nasal irritation at 20 ppm to persons under experimental conditions who considered that 300 ppm would be objectionable as a working atmosphere. However, this experimental group has no opportunity for occupational acclimatization. The concentration of 500 ppm is suggested as the maximum allowable, not that appreciably more than this concentration cannot be regularly tolerated without injury to health, but to avoid irritation and complaint.

Ethyl formate: Flury and Zernik in *Schadliche Gase*, 1931, reported that 330 ppm causes slight irritation of the eyes and rapidly increasing nasal irritation. In view of the inadequate data available concerning exposure to this material, there should be medical observation of workers who may be exposed to concentrations in the vicinity of the suggested limit of 200 ppm.

Ethyl silicate (Tetraethyl ortho-silicate): J.A. Kasper, C.P. McCord, and W.G. Fredrick, *Industrial Medicine 6*:660-664 (1937), "The Toxicity of Organic Silicon Compounds. I. Tetraethyl ortho-Silicate," reported that animals exposed to 164 ppm, eight hours a day for 17 days did not shown weight increases equal to the controls, but mentioned no other indications of injury from this exposure. H.F. Symth, Jr., and J. Seaton, in *J. Ind. Hyg. & Tox. 22*:288-296 (September 1940) "Acute Response of Guinea Pigs and Rats to Inhalation of the Vapors of Tetraethyl Ortho-silicate (Ethyl Silicate)," found that concentrations as low as 245 ppm gave rise to some pathology in animals after several hours exposure. An allowable limit of 100 ppm is suggested for prolonged exposure, but with the lack of industrial experience at known concentrations, any workers subjected to an exposure approaching 100 ppm should be under medical observation.

Formaldehyde: The principle effect of exposure to low concentrations of formaldehyde is irritation, expecially in the nose and eyes with lachrymation. E.C. Barnes and H.W. Speicher, in *J. Ind. Hyg. & Tox. 24*:10-17 (January 1942) "The Determination of Formaldehyde in Air," stated that they exposed themselves to 20 ppm for a short length of time. From the discomfort and lachrymation produced, it was their opinion that somewhat lower concentrations would be desirable for continued exposure. It is generally accepted that exposures should not exceed 10 ppm.

Furfural: According to the producer, with reasonably good ventilation, the health hazard presented by the use of furfural is slight under practically all industrial conditions. Over the 20 years of its industrial use, there has not been a single case of injury to health from industrial exposures, its low vapor pressure presumably maintaining atmospheric concentrations at less than injurious levels under normal industrial conditions.

Gasoline: Philip Drinker, C.P. Yaglou, and M.F. Warren, *J. Ind. Hyg. & Tox. 25*:225-232 (June 1943), "The Threshold Toxicity of Gasoline Vapor," concluded "that 0.1 per cent gave the beginning of real effects in our group." The human subjects used in these experiments complained only of subjective symptoms such as irritation or headache. R.R. Sayers, A.C. Fieldner, W.P. Yant, and B.G.H. Thomas, in "Experimental Studies on the Effect of Ethyl Gasoline," Rept. of the U.S. Bureau of Mines (1927), reported that 0.07 to 0.28% gasoline vapor caused dizziness. The concentration of 500 ppm is suggested as the maximum so that these subjective symptoms may be avoided. Furthermore, present-day gasoline contains varying amounts of aromatic hydrocarbons which tend to increase its toxicity.

Heptane: Since 1000 ppm was shown to cause slight dizziness in experimentation carried on by the U.S. Bureau of Mines as given in the Report of Investigations No. 2979 (1929), an allowable limit of 500 ppm is suggested. However, exposures somewhat in excess of this concentration are not considered toxic.

Hexane: Philip Drinker, C.P. Yaglou, and M.F. Warren, in *J. Ind. Hyg. & Tox. 25*:225-232 (June 1943) "The Threshold Toxicity of Gasoline Vapor," reported on exposure to a petroleum distillate, 90% of which boiled between 107°F and 260°F, thus including the hexane range. Two groups of persons were exposed to concentrations in one case of 1500 ppm and in the other 1400 ppm. Sickness at the stomach, headache, throat irritation and eye irritation were complained of, but no one considered the exposure disagreeable or felt unwilling to work in such atmosphere. Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282 (1943), exposed a group of persons to 500 ppm of hexane which proved to be quite innocuous. Though higher concentrations were not used, the opinion was that much greater amounts could be tolerated. A maximum allowable concentration of 1000 ppm is accordingly suggested.

Hydrochloric acid (Hydrogen chloride): Willard Machle, K.V. Kitzmiller, E.W. Scott, and J.F. Treon, in *J. Ind. Hyg. & Tox. 24*:222-225 (October 1942), "The Effect of the Inhalation of Hydrogen Chloride," concluded on exposure of animals six hours a day, five days a week for four weeks that the upper limit of safety is about 30 ppm though it is possible that even this concentration would be harmful if daily exposures were continued for periods longer than a month. The maximum allowable concentration of 10 ppm is generally accepted.

Hydrogen cyanide: Reference is made by Flury and Zernik in *Schadliche Gase*, 1931, to Lehmann-Hess that 18 to 36 ppm could be tolerated over a six hour period without apparent symptoms. A value of 20 ppm is generally accepted as the maximum allowable contentration.

Hydrogen fluoride: E. Ronzani, in *Arch f. Hygiene 70*:217-269 (1909), found no injurious action on animals exposed for 30 days to 3 ppm. K. Roholm, in *Fluorine Intoxication. A Clinical, Hygiene Study* (Lewis & Company, London, 1937), and *Fluoride Compounds* Occupational and Health Supplement, International Labor Office (September 1938), reported that fluorosis of the bones occurred among cryolite workers after prolonged exposure to 2 to 3 ppm. Three ppm has been generally accepted as a maximum allowable concentration.

Hydrogen selenide: H.C. Dudley and J.W. Miller, in Reprint No. 1855, from *Publ. Health Repts. 52*:1217 (1937), found that animals exposed to six parts per million for 60 minutes all died within 24 days. These workers, in a subsequent study in *J. Ind. Hyg. & Tox. 23*:470-477 (1941), "Toxicology of Selenium. VI. Effects of Subacute Expousres to Hydrogen Selenide," reported that death occurred in 50% of animals exposed for eight hours to a concentration of from 0.3 to 1.2 ppm. A concentration of 1.5 ppm was intolerable to man, producing eye and nasal irritation, but 0.3 ppm caused no such irritation. In view of the great toxicity of this gas, the allowable concentration of 0.1 ppm is suggested with the recommendation that wherever men may be exposed they be under medical observation and information be maintained concerning exposures.

Hydrogen sulfide: H.L. Barthelemy, in *J. Ind. Hyg. & Tox. 21*:141-151 (April 1939), "Ten Years' Experience with Industrial Hygiene in Connection with the Manufacture of Viscose Rayon," concluded that with hydrogen sulfide at less than 20 ppm no trouble whatsoever was experienced. This value is generally accepted as causing neither poisoning or eye irritation.

Iodine: Henderson and Haggard, *Noxious Gases*, 1943, and Flury and Zernik, *Schadliche Gase*,

1931, both quote Matt, Dissertation at Wurzburg, 1889, as authority for 0.1 ppm being the concentration at which "work is not disturbed." The infrequent exposure of iodine vapor hardly justifies much research on this material but added data are needed to substantiate this tentative value of 0.1.

Iron oxide: It has been shown through determination of iron oxide concentrations at many welding operations that the condition is satisfactory where the iron oxide fume is kept below 30 mgs. per cubic meter. Although exposure to iron oxide in excess of this value will not cause poisoning, continued exposure to higher concentrations may produce a chronic bronchitis. This suggested allowable concentration is given by Philip Drinker and A.G. Cranch in *Control of Welding Hazards In Defense Industries*, Special Bulletin No. 5, U.S. Division of Labor Standards (1942).

Isophorone: H.F. Smyth, Jr., J. Seaton, and L. Fischer, in *J. Ind. Hyg. & Tox. 24*:46-50 (March 1942), "Response of Guinea Pigs and Rats to Repeated Inhalation of Vapors of Mesityl Oxide and Isophorone," concluded on the basis of animal experimentation of 30 eight-hour exposures that no effect whatever results from exposure of 25 ppm of isophorone.

Lead: The American Public Health Association Committee on Lead Poisoning — R.A. Kehoe, Chairman, J.C. Aub, E.L. Belknap, W.C. Dreessen, G.H. Gehrman, M.H. Kronenberg, May R. Mayers, and W.P. Yant — in the 1943 Committee Report "Occupational Lead Exposure and Lead Poisoning" stated that, when the air of workrooms regularly contain no more than 0.15 mgs. per cubic meter, cases of disabling lead intoxication do not occur and cases of questionable or mild intoxication are rare. This conclusion is based on such extensive studies as those by the U.S. Public Health Service in storage battery plants as reported by A.E. Russell, R.R. Jones, J.J. Bloomfield, R.H. Britten, and L.R. Thompson in Public Health Bulletin No. 205 (1933), and by W.C. Dreessen, T.I. Edwards, W.H. Reinhart, R.T. Page, S.H. Webster, D.W. Armstrong and R.R. Sayers, Public Health Bulletin No. 262 (1941).

Manganese: R.H. Flinn, P.A. Neal, W.H. Reinhart, J.M. Dallavalle, W.B. Fulton, and A.E. Dooley, in Pulic Health Bulletin No. 247 (1940) *Chronic Manganese Poisoning in an Ore-Crushing Mill*, showed that workers exposed to less than 30 mgs. per cubic meter of manganese developed no symptoms of poisoning but that workers exposed to more that 90 mgs. per cubic meter were found to have the disease. Since only a small number of men with limited exposure were included in the study, and as the exposure could be readily reduced to 6 mgs. per cubic meter, the U.S. Public Health Service has recommended, in National Institute of Health Bulletin No. 182 (1943), *Industrial Manganese Poisoning* by L.T. Fairhall and P.A. Neal, that the maximum allowable concentration be tentatively placed at 6 mgs. per cubic meter.

Magnesium: Philip Drinker, R.M. Thomson, and J.L. Flinn, in *J. Ind. Hyg. 9*:187 (1927), "Metal Fume Fever. III. The Effects of Inhaling Magnesium Oxide Fume," reported on experimental production of metal fume fever from excessive inhalation of this fume. It was considered that exposure to less than 16 mgs. per cubic meter will cause no such manifestation.

Mercury: P.A. Neal, R.H. Flinn, T.I. Edwards, W.H. Reinhart, J.W. Hough, J.M. Dallavalle, H. Goldman, W. Armstrong, A.S. Gray, A.L. Coleman, B.F. Postman, Pub. Health Bull. No. 263 (1941), *Mercurialism and Its Control in the Felt Hat Industry*, found on the basis of examination of 534 hatters in five representative felt hat factories that no injury to health occurred where the exposure was less than 0.1 mg. per cubic meter.

Mesityl oxide: H.F. Smyth, Jr., J. Seaton and L. Fisher, in *J. Ind. Hyg. & Tox. 24*:46-50 (March 1942), "Response of Guinea Pigs and Rats to Repeated Inhalation of Vapors of Mesityl Oxide and Isophorone," report that no effect whatever was found from 50 ppm of mesityl oxide after 30 eight-hour exposures of all animals.

Methanol: R.R. Sayers, W.P. Yant, H.H. Schrenk, J. Chornyak, S.J. Pearce, F.A. Patty, and J.G. Linn, in U.S. Bureau of Mines Report of Investigation No. 3617 (1942), *Methanol Poisoning*. "I. Exposure of Dogs to 450-500 ppm Methanol Vapor in Air," observed no symptoms or unusual behavior among dogs exposed eight hours daily seven days a week for 379 days to 450-500 ppm. It is accordingly considered that 200 ppm can be accepted as a maximum allowable concentration.

Methyl acetate: Although no animal experimentation work has been reported on low concentrations of this solvent, work done by Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282 (1943), on ethyl, butyl

and amyl acetate indicates that 100 ppm is the highest concentration which would be satisfactory for eight hour exposure from the point of view of sensory response to the vapor. In view of the possibility of poisoning through hydrolysis of this ester within the body and the consequent production of methanol workers exposed to concentrations exceeding the suggested limit should be under medical observation.

Methyl bromide: D.D. Irish, E.M. Adams, H.C. Spencer, and V.K. Rowe, in *J. Ind. Hyg. & Tox. 22*:218-230 (June 30, 1940), "The Response Attending Exposure of Laboratory Animals to Vapors of Methyl Bromide," reported that six months' exposure of rats, guinea pigs and monkeys to 33 ppm was without gross symptoms or histopathological changes. However, the rabbits developed paralysis on repeated exposures. With concentrations dropped to 17 ppm, no abnormal conditions were noted. R.M. Watrous, in *Industrial Medicine 11*:575-579 (December 1942), "Methyl Bromide — Local and Mild Systemic Toxic Effects," discusses an industrial exposure where 90 persons were at work at concentrations generally less than 35 ppm and mild systemic symptoms occured in 33 of these workers. A maximum allowable limit of 20 ppm is suggested. Workers exposed to or working with methyl bromide should be under medical observation and exposures checked quantitatively.

Methyl butanone: H.H. Schrenk, W.P. Yant, and F.A. Patty, in Reprint No. 1747 from *Pub. Health Repts. 51*:624-631 (May 15, 1936), "Acute Response of Guinea Pigs to Vapors of Hexanone (Methyl Butyl Ketone)," found that animals exposed to 1000 ppm for 810 minutes showed but slight or no symptoms although human beings noted a strong odor and developed moderate eye and nasal irritation at this exposure. Arbitrarily placing the maximum allowable limit for prolonged exposure at less than quarter of the amount suggested for acute response, the maximum allowable concentation of 200 ppm is suggested. Medical observation of workers exposed to vapors at this concentration may result in a more liberal limit.

Methyl Cellosolve: H.W. Werner, J.L. Mitchell, J.W. Miller, and W.F. von Oettingen, in *J. Ind. Hyg. & Tox. 25*:409-414 (November 19, 1943), "Effects of Repeated Exposure of Dogs to Monoalkyl Ethylene Glycol Ether Vapors," reported on findings after exposure of seven hours daily, five days week for 12 weeks to a concentration of 800 parts per million of ethyl cellosolve. Blood changes are recorded at this concentration. L. Greenburg, M.R. Mayers, L.J. Goldwater, W.J. Burke, and S. Moskowitz, in *J. Ind. Hyg. & Tox. 20*:134-147 (February 1938), "Health Hazards in the Manufacture of 'Fused Collars.' I. Exposure to Ethylene Glycol Monomethyl Ether," reported on workrooms concentrations where poisoning occurred. The ventilation was functioning ineffectively following the poisoning cases but was placed in proper condition when atmospheric analyses were made. The methyl cellosolve portion of the combined solvent concentration was then found to be 25 ppm with all windows wide open and 76 ppm with windows partly closed to represent conditions in cold weather. Though it was concluded by these investigations that the concentrations should be kept below 25 ppm, it would seem, in view of the more favorable conditions under which the analyses were made, that the maximum allowable concentration of 100 ppm should be permissible. This suggested limit is supported by an unpublished report of tests made by the Chemical Hygiene Fellowship at Mellon Institute, reported in July 1945.

Methyl Cellosolve acetate: The maximum allowable concentation of 100 ppm is suggested on the basis of an unpublished report of tests made by the Chemical Hygiene Fellowship at Mellon Institute, reported in July 1945.

Methyl chloride: R.R. Sayers, W.P. Yant, B.G.H. Thomas, L.B. Berger, in Pub. Health Bull. No. 185 (1929), *Physiological Response Attending Exposure to Vapors of Methyl Bromide, Methyl Chloride, Ethyl Bromide and Ethyl Chloride*, found on exposing animals for a period of 800 minutes that from 500 to 1000 ppm caused slight symptoms after several hours exposure. Arbitrarily taking one-fourth of this value for continued exposure, a maximum allowable concentration of 200 ppm is suggested. Workers exposed to concentrations in this vicinity should be under medical observation.

Methylcyclohexane: J.F. Treon, W.E. Crutchfield, Jr., and K.V. Kitzmiller, in *J. Ind. Hyg. & Tox. 25*:323-347 (October 1943), "The Physiological Response of Animals to Cyclohexane, Methylcyclohexane, and Certain Derivatives of these Compounds," concluded that a maximum safe concentration for prolonged exposure of rabbits lies between 1162 and 2886 ppm. A concentration of

1000 ppm is suggested as a maximum allowable limit but if workers are exposed to such a concentration, medical observation is recommended until data are obtained on effects of human exposure within this range.

Methylcyclohexanol: In the reference cited above for methylcyclohexane, the maximum safe concentration for prolonged exposure of rabbits to methylcyclohexanol was found to be slightly below 145 ppm. One hundred ppm is suggested as allowable, but workers exposed to such a concentration should be under medical observation.

Methylcyclohexanone: The foregoing reference cited for methylcyclohexane is authority for the conclusion that the maximum safe concentration for prolonged exposure of rabbits to methylcyclohexanone lies between 182 and 514 ppm. A maximum allowable concentration of 100 ppm is suggested but here again medical observation is recommended where exposures are of this order.

Methyl formate: H.H. Schrenk, W.P. Yant, John Chornyak, and F.A. Patty, in Reprint No. 1773 from *Publ. Health Reports 51*:1329-1337 (September 25, 1926), "Acute Response of Guinea Pigs to Vapors of Methyl Formate," concluded that the maximum exposure for several hours without serious disturbance lies between 1500 and 2000 ppm. Reducing this concentration for acute exposure arbitrarily to one-fourth the value, a maximum allowable concentration of 400 ppm is suggested for prolonged exposure. Until information is obtained on response of humans to exposures of this order, workers, exposed to such concentrations should be under medical observations.

Methyl iso-butanone *(Hexone):* H. Specht, in Reprint No. 1911 of *Pub. Health Reports 53*:292-300 (February 1938) "Acute Response of Guinea Pigs to Inhalation of Methyl Iso-butal Ketone," concluded that a concentration below 1000 parts per million is well tolerated by guinea pigs but causes eye and nose irritation in man. Applying the arbitrary rule of reducing this concentration to one-fourth where there is prolonged exposure to the vapor, the maximum allowable limit of 200 ppm is suggested. Until further data are obtained on human response, medical observation is recommended where exposures may be of this order.

Monochlorobenzene: The maximum allowable concentration of 75 ppm is suggested by the U.S. Public Health Service as a guide.

Monofluorotrichloromethane *(Freon 11 — Carrene No. 2):* A.H. Nuckolls, in *Underwriters' Laboratories Miscellaneous Hazards Report No. 2375* (November 1933), found that animals have occasional tremors and retching movements upon two hours' exposure to 2.2 to 2.5% in air. Consequently, a maximum allowable limit of 10,000 ppm is suggested for prolonged exposure. In view of the lack of information on prolonged exposures on humans to this refrigerant, there should be medical observation if exposures approach this value.

Mononitrotoluene: The maximum allowable concentration for this compound is considered by the U.S. Public Health Service to be similar to that of nitrobenzene for which a value of 5 ppm is suggested as a guide.

Naphtha *(Coal tar):* A maximum allowable concentration of 100 to 200 ppm is suggested, dependent upon the relative proportions of benzene, toluene and xylene present. If the boiling point range of a solvent naphtha obtained from coal tar or from by-product coke distillation includes any appreciable percentage between the boiling point of benzene and toluene, no more than 100 ppm should be permitted; but if the boiling point of the major portion of this naphtha is above that of toluene, then 200 ppm may be considered allowable. References are given under the respective chemical compounds.

Naphtha *(Petroleum):* A concentration of 500 ppm is suggested on the basis of the discussion and references included under gasoline.

Nitrobenzene: The U.S. Public Health Service suggests a maximum allowable concentration of 5 ppm to serve as a guide. A value of 1 ppm has been used in the past, based presumably on this value as listed without specific reference in Henderson and Haggard, *Noxious Gases*, 1927, as a maximum amount that can be inhaled for one hour without serious disturbance.

Nitroethane: Willard Machle, E.W. Scott, and Joseph Treon, *J. Ind. Hyg. & Tox. 22*:315-332 (October 1940), "The Physiological Response of Animals to Some Simple Mononitroparaffins and to Certain Derivatives of These Compounds," exposed animals to concentrations of as low as 1000 ppm and 500 ppm. At the former concentration, death resulted in some of the animals and no

fatalities at the latter concentration. Since no data are given as to the possibility of symptoms or of pathology on long exposure of these animals to 500 ppm, a tentative allowable concentration of 200 ppm is suggested. In view of the lack of quantative data on experience with persons where nitroethane may be present in industrial atmospheres, there should be medical observation of workers exposed to such concentrations.

Nitrogen oxide: L.W. LaTowsky, E.L. MacQuiddy, and J.P. Tollman, in *J. Ind. Hyg. & Tox. 23*:129-133 (April 1941), "Toxicology of Oxides of Nitrogen. I. Toxic Concentrations," concluded on animal experimentation that the concentration of 30 ppm of NO_2 on three hour exposure produces no immediate or delayed harmful effects on guinea pigs and that a concentration of 55 ppm on two to three hour exposure may or may not produce harmful effects on rats and mice but no effect on rabbits, cats and guinea pigs. This and other recent data support the American Standard of 25 ppm.

Nitroglycerine: The U.S. Public Health Service have found no systemic effects occur even at exposures of 10 ppm, but after absence of exposure for as little as a 40 hour period over a weekend, severe headaches occur on being first exposed as to as little as 0.5 ppm for a brief period. Skin absorption is a major source of intake where there is contact with nitroglycerine.

Nitromethane: In the reference quoted for "Nitroethane," Willard Machle, E.W. Scott, and Joseph Treon found that no deaths have occurred on daily six hour exposure for a total of 140 hours to 500 ppm. A maximum allowable concentration of 200 pmm is suggested in view of lack of specific data of effect on nitromethane of persons under industrial exposures. Where exposures approach the suggested allowable concentration, there should be medical observation of such exposed persons.

Octane: A suggested allowable limit of 500 ppm is based on the U.S. Bureau of Mines Report of Investigations No. 2979 (1929), in which it was stated that 1000 ppm of heptane cause slight dizziness. Octane is considered to be somewhat more narcotic than heptane but to cause substantially the same physiological reaction.

Ozone: C.E. Thorp, in *News Edition, American Chemical Society 19*:686-689 (June 25, 1941), "Influence of Nitrogen Oxides on the Toxicity of Ozone," reported that 1 ppm of pure ozone becoming annoying to 25% of exposed persons but even at seven hours a day for five days did not cause irritation of nose or throat. Thorp refers to earlier work in which oxides of nitrogen are presumably contaminating the ozone and headaches and sore throats are produced in two hours to three hours at concentrations of 1.0 ppm.

Petachloronaphthalene: References on these compounds are given under the heading, "Chloronaphthalenes."

Pentane: U.S. Bureau of Mines Reports of Investigations No. 2979 (1929) reports that 5000 ppm produced no effect after 10 minutes' exposure. Since the allowable concentration of this almost non-toxic hydrocarbon is properly to be based more on sensory response rather than on systemic poisoning, this concentration of 5000 ppm is tentatively suggested as allowable.

Pentanone (Methyl propanone): W.P. Yant, F.A. Patty, H.H. Schrenk, in Reprint No. 1739, *Pub. Health Reports 51*:392-399 (April 3, 1936), "Acute Response of Guinea Pigs to Vapors of Pentanone (Methylpropylketone)," concluded on exposure of animals for 810 minutes that the maximum amount for several hours with slight or no symptoms is 1500 ppm. This concentration was found to be very irritating to men even for short exposures. A maximum allowable concentration of 400 ppm for prolonged exposure is arbitrarily taken at one-fourth of the suggested limit for several hours exposure. With lack of quantitative information on human subjects at these concentrations, there should be medical observation of workers exposed to vapor in the vicinity of this limit.

Phosgene: U.S. Bureau of Mines, Technical Paper No. 248 (1921), *Gas Masks for Gases Met in Fighting Fires*, by A.C. Fieldner, S. H. Katz, and S.P. Kinne, referred to the work of the American College Experiment Station, Chemical Warfare Service, as authority for considering 1 ppm as the maximum concentration allowable for prolonged exposure. Flury and Zernik, *Schadliche Gase*, 1931, gave in a table without specific reference to original work that the perceptible concentration was between 1.4 and 2.8 ppm.

Phosporus trichloride: Butjag, in *Arch. f. Hyg. 49*:307 (1904), reported on the basis of animal experimentation that 0.7 ppm caused only slight irritation.

***iso-Propanol** (Iso-Propyl alcohol):* Although brief exposures to animals have been conducted at high concentrations, there has been no toxicological work done on low exposures over prolonged periods of time. Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282, (September 1943), reported that mild irritation of the eyes, nose and throat was caused at 400 ppm among human subjects experimentally but that even at 800 ppm the effects were not severe though the majority declare the atmosphere unsuitable. Iso-propyl alcohol is somewhat more toxic than ethyl alcohol, but it is believed that no difficulty would be experienced at concentrations of 400 ppm. Workers exposed to concentrations approaching this value should be under medical observation.

Propyl acetate: A maximum allowable concentration of 200 ppm is suggested, not that somewhat higher exposures are toxic but to avoid irritation. Although Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282 (1943), did not include this ester among the solvents on which sensory responses were obtained, on analogy with ethyl and butyl acetates, it is considered that the suggested limit is in order.

iso-Propyl ether: Willard Machle, E.W. Scott, and Joseph Treon, in *J. Ind. Hyg. & Tox. 21*:72-95 (March 1939), "The Physiological Response to Isopropyl Ether and to a Mixture of Isopropyl Ether and Gasoline," reported on exposure of animals for 20 two-hour and three-hour periods to concentrations down to 3000 ppm and 4000 ppm. No noticeable effect followed this exposure. The toxicity of isopropyl ether and gasoline were considered to be closely parallel on the basis of these animal experimentations. Although it appears possible that exposures may be appreciably greater than the suggested limit before toxic action occurs, any increase in this value should be based on quantitative results of exposures to workers.

***Radon** (Radium emanation):* An advisory committee to the National Bureau of Standards, composed of L.F. Curtiss, R.D. Evans, G. Failla, Frederick B. Flinn, Harrison S. Martland, J.E. Paul, J.S. Rogers, C.S. Stephenson and G.T. Taylor, recommended in National Bur. of Stand. Handbook H 27, *Safe Handling of Radioactive Luminous Compounds*, 1941, that the radon concentration in the atmosphere of workrooms should not exceed 10^{-11} curie per liter, and that the whole-body exposure of the worker to gamma radiation should not exceed 0.1 roentgen per working day. These figures, noted as being "according to present knowledge" in 1941, continue to be accepted in 1945.

***Stibine** (Hydrogen antimonide):* Stock, Guttmann, and Gergell, *Ber. Dtsch. Chem. Ges. 37*:893 (1904), reported that 100 parts per million on exposure for 20 minutes causes death after a few days. The maximum allowable concentration of 10 ppm is tentatively suggested. Wherever there may be possibility of exposure to stibine, workers should be under medical observation.

Stoddard solvent: A maximum allowable concentration of 500 ppm is suggested on the basis of the discussion on gasoline. Although the higher boiling constituents which are included in Stoddard Solvent are somewhat more toxic than those included in gasoline, it is believed that exposures could be considerably greater than the suggested concentration without causing toxic effect. The limit is set up largely to avoid subjective symptoms. Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282 (1943), report that experimental human subjects complain of no marked effects of Stoddard Solvent vapor up to 400 ppm and conclude that the exposure can exceed this amount somewhat and still be considered a satisfactory atmosphere.

Styrene monomer: H.C. Spencer, D.D. Irish, E.M. Adams, and V.K. Rowe, in *J. Ind. Hyg. & Tox. 24*:295-301 (1942), "The Response of Laboratory Animals to Monomeric Styrene," concluded on the basis of lack of effect on animals exposed for seven hours a day over a period of six months to 650 ppm that this concentration would probably produce no serious disturbances in man but is definitely irritating to the eyes and nose. It was considered that 400 ppm which Spencer *et al* considered as giving a disagreeable odor but not producing appreciable eye or nose irritation, could be suggested tentatively as a permissible limit for repeated exposures. This has been accepted as an "American War Standard." Experience has already indicated that this concentration causes sufficient irritation under actual working conditions to revise this Standard downward. Until broader experience is available, it is suggested that concentrations be not allowed to exceed half the tentative value of 400 ppm.

Sulfur chloride: Adler-Herzmark, in *Zentr. Gewerbehyg. u. Unfallverhut. 6*:97 (1929), reported that cats tolerated 12 parts per million for 15 minutes without death. At 48 ppm for 15 minutes, death occurred after several days. A maximum allowable concentration of 1 ppm is suggested as a tentative limit.

Sulfur dioxide: Fieldner and Katz, in *Eng. & Mining J. 107*:693 (1909), considered 10 ppm as the highest concentration tolerable for prolonged exposure. Flury and Zernik in *Schadliche Gase*, 1931, include an unidentified reference to Lehmann-Hess in which a concentration of 8 to 12 ppm is suggested as permissible for several hours' exposure.

Sulfuric acid: The individual susceptibility to irritaiton by sulfuric acid differs widely among individuals, much higher concentrations being tolerated by workers habitually exposed. Flury and Zernik, *Schadliche Gase*, 1931, includes one reference indicating 40 milligrams per cubic meter and even two to three times this concentration as being non-injurious or hardly injurious and another reference indicating that 0.5 to 2 milligrams per cubic meter caused slight trouble with 3 to 4 milligrams per cubic meter causing definite trouble. J.H. Sterner, in *Industrial Medicine 12*:514-518 (August 1943), "Determining Margins of Safety — Criteria for Defining a 'Harmful' Exposure," lists 5.0 milligrams per cubic meter in his well considered table of maximum allowable concentrations.

1,1,2,2-Tetrachloroethane: On the basis of severe poisoning of workers in industry resulting in a number of deaths together with animal experimentation showing it to cause narcosis with smaller amounts than are necessary for carbon tetrachloride, a maximum allowable concentration of 10 ppm has been suggested for tetrachloroethane. Such cases are cited by A. Hamilton in *Industrial Toxicology*, pp. 212, *et seq.* (Harper and Co., 1934), and more recently by H.A. Coyer in *Industrial Medicine 12*:230-233 (March 1944). Medical observation of persons exposed to known concentrations of tetrachloroethane under industrial conditions are necessary to substantiate this tentative maximum allowable concentration.

Tetrachloroethylene: C.P. Carpenter, in *J. Ind. Hyg. & Tox. 19*:323-336 (September 1937), "The Chronic Toxicity of Tetrachloroethylene," reported on animal exposure to low concentrations for periods up to 1200 hours and on exposures of humans to concentrations of 500 ppm and above. No injurious exposure was observed at 70 ppm but at 230 ppm some of the animals showed effects of the solvent on kidneys, spleen and liver though there were no signs of progressive injury to the liver. This author concluded that on the basis of the findings, a concentration somewhere between 100 and 500 ppm is considered safe for daily exposure not in excess of 40 hours a week. Until more evidence is available on human exposures under industrial conditions, workers exposed to concentrations in the vicinity of the suggested allowable limit of 200 ppm should be under medical observation.

Tellurium: H.H. Steinberg, S.C. Massari, A.C. Miner, and R. Rink, in *J. Ind. Hyg. & Tox. 24*:183-192 (September 1942), "Industrial Exposure to Tellurium: Atmospheric Studies and Clinical Evaluation," reported on industrial exposure of workers to tellurium and tellurium oxide fume together with clinical and laboratory findings. At exposures ranging for the most part from 0.01 to 0.1 milligrams per cubic meter, no evidence of tellurium as such was found but a social stigma resulted from the presence of garlic odor of the breath and of the sweat. On the basis of these findings, the maximum allowable concentration of 0.01 milligrams per cubic meter is suggested, not that concentrations 10 times this limit will cause poisoning but to avoid the development of the exceedingly distasteful garlic odor eminated by the exposed person.

Tetryl: The U.S. Public Health Service states, in *Manual of Industrial Hygiene* (W.B. Saunders Company, 1943), that "no specific information is available but 1.5 milligrams per cubic meter is believed to present no health hazard."

Toluene (Toluol): W.F. Von Oettingen, P.A. Neal, D.D. Donahue, J.L. Svirbely, H.D. Baernstein, A.R. Monaco, P.J. Valaer, and J.L. Mitchell, in Pub. Health Bull. No. 279, *The Toxicity and Potential Dangers of Toluene, with Special Reference to Its Maximal Permissible Concentration*, 1942, concluded that it appears, as far as toxicity is concerned, the maximal permissible concentration for toluene in air for eight hours exposure daily is 200 ppm. Since the exposure causes slight but definite impairment of coordination and reaction time, it was suggested that where the occupation may cause

specific accident hazards, this concentration might prove to be too high.

Trichloroethylene: Joseph Seifter, in *J. Ind. Hyg. & Tox. 25*:250-252 (September 1944), "Liver Injury in Dogs Exposed to Trichloroethylene," reported that an exposure of 500 to 750 ppm four to six hours daily, five days a week for eight weeks resulted in liver injury to experimental dogs. There is no published animal experimentation at concentrations lower than this value. It has been rather generally accepted that a concentration of 200 ppm can be tolerated without injury to health. K.M. Morse and Louis Goldberg, in Indust. Hyg. Supplement, *Industrial Medicine 12*:706-713 (October 1943), "Chlorinated Solvent Exposures at Degreasing Operations," reported that 18% of some 336 vapor degreasing tanks provided with condensers exposed the operators to more than 200 ppm. Although this paper does not include clinical findings on exposed workers, the fact that no reference is made to cases of poisoning among operators of these tanks would indicate that 200 ppm is not greatly out of line as the maximum allowable concentration. There is evidence, however, that a concentration of this order may cause difficulty among a sufficient number of operators to require that it be reduced. Morse and Goldberg, cited above, report that some men will complain of headaches, nausea and dizziness even at concentrations of 100 ppm. Consequently, it is recommended that, until further clinical evidence is available concerning possible injury at concentrations lower than 200 ppm exposures be not allowed to exceed half the value suggested as the maximum allowable concentration.

Trichloronaphthalene: This compound was discussed under the heading "Chloronaphthalene."

Trinitrotoluene (TNT): The U.S. Public Health Service recommends that 1.5 milligrams per cubic meter be used as a guide. W.F. von Oettingen, D.D. Donahue, R.K. Snyder, and A.R. Monaco in Public Health Bull. No. 285 *Experimental Studies on the Toxicity and Potential Dangers of Trinitrotoluene (TNT)*, 1944, "IV. Toxicity of TNT for Dogs with Inhalation of Its Fumes," stated that an attempt was made to determine the effect of various concentrations of TNT vapor on dogs but it was found very difficult if not impossible to volatilize TNT in sufficient quantities to produce definite systemic and toxic effects on them. Experience has shown that where there is exposure to TNT dust, fume or vapor, workers should be under medical observation.

Toluidine: Henderson and Haggard, *Noxious Gases*, 1927, include a table, without specific reference to original work, which states that slight symptoms after several hours exposure are caused by concentrations in the range of 7 to 26 ppm. This same table refers to similar response being caused by a range of 7 to 53 parts per million of aniline. Since a broader experience with aniline indicates that 5 ppm can be considered as a maximum allowable limit, a similar concentration is suggested for toluidine. In view of the lack of specific data on prolonged exposure, persons subjected to toluidine should be under medical observation.

Turpentine: H.F. Smyth and H.F. Smyth, Jr., in *J. Ind. Hyg. 10*:261 (1928), "Inhalation Experiments with Lacquer Solvents," found that continued inhalation of 750 ppm caused no injury to experimental animals. K.B. Lehmann, in *Arch. f. Hyg. 83*:239 (1914), "Comparative Research on the Toxicity of Turpentine," reported that inhalation by himself and his assistant of concentrations of 750 to 1000 ppm for several hours caused eye irritation, headache, dizziness and nausea. Nelson *et al*, in *J. Ind. Hyg. & Tox. 25*:282 (1943), found eye and nose irritations at 175 ppm and throat irritation at 125 ppm. A maximum allowable concentration of 100 ppm has been suggested not that an appreciably higher concentration will cause poisoning but to avoid irritation.

Vinyl chloride: F.A. Patty, W.P. Yant, and C.P. Waite, in Reprint No. 1405 from *Pub. Health Repts. 45*:1963-1971 (August 22, 1930), "Acute Response of Guinea Pigs to Vapor of Vinyl Chloride," found on exposure of animals to periods as long as 500 minutes that the maximum amount for several hours without serious disturbance was 5000 ppm. Arbitrarily using approximately a fourth of this value as the maximum allowable concentration for prolonged exposure, a value of 100 ppm has been suggested. In view of the lack of animal experimentation over a long period and of industrial exposure to known concentrations, there should be medical observation of exposed workers where concentrationsd may be in the vicinity of the suggested limit.

X-ray: Although the International X-ray and Radium Protection Commission recommended in

1937 that about 0.2 roentgen per day or one roentgen per week could be tolerated by a person in normal health as published in *Radiology 30*:511 (April 1938), an able and representative committee under the chairmanship of George Singer, National Bureau of Standards, set up the American War Standard of 0.1 roentgen as the permissible daily dose under the American Standards Association procedure, May 1945. This maximum allowable limit is now generally accepted.

Xylene (Xylol): On the basis of analogy of the action of xylene with that of toluene, a maximum allowable concentration of 200 ppm is suggested. Xylene vapor is somethat more irritating to the eyes than that of toluene and it is probable that a somewhat lower limit of exposures may be required to permit comfort of the worker.

Zinc: Philip Drinker, R.M. Thomson, and J.L. Finn, in *J. Ind. Hyg. & Tox. 9*:331-345 (August 1927), "Metal Fume Fever: IV. Threshold Doses of Zinc Oxide," found that concentrations of 14 milligrams of zinc oxide per cubic meter (measured as zinc) produced no reaction on the average subject after an exposure of eight hours. They add that if the dosage of zinc oxide is insufficient to cause fever, there is no evidence that daily inhalation of the fumes does chronic damage. D. Mark Hegsted, J.M. McKibbin, and C.K. Drinker, in Supplement No. 179 to *Pub. Health Repts.* (1945), "The Biological, Hygienic, and Medical Properties of Zinc and Zinc Compounds," include the statement that "15 mg. zinc oxide per cubic meter of air are considered as representing a safe maximum, there being no possibility of harm from prolonged exposure at this level of concentration in the air breathed."

APPENDIX D

Additional reading

Mercurial Poisoning
J.A. Turner
Public Health Rep. 39:329-341 (1924)

Further Observations on Possible Systemic Toxicity of Certain of the Chlorinated Hydrocarbons with Suggestions for Permissible Concentration in the Air of Workrooms
C.K. Drinker
J. Ind. Hyg. & Tox. 21:155-159 (1939)

Noxious Gases and the Principles of Respiration Influencing their Action, 2nd (Rev. ed.)
Y. Henderson and H. Haggard
Reinhold Publishing Corp., New York (1943)

Transactions of the Annual Meeting of the ACGIH
Am. Conf of Govt. Ind. Hyg., Cincinnati, OH (1946-1984)

Forty Years in the Poisonous Trades
A. Hamilton
Ind. Hyg. Assoc. Q. 9:5-17 (1948)

Toxicology of Gases and Vapors: International Critical Tables of Numerous Data
R.R. Sayers
Physics, Chemistry, and Technology, Vol. 2, pp. 318-321. New York

Symposium on Threshold Limits, Present Trends in MACs
W.A. Cook
Ind. Hyg. Q. 17:273-275 (1956)

The Need for Threshold Limits
M. Sacks
Ind. Hyg. Q. 17:274-278 (1956)

Prepared Discussion
H.F. Smyth
Ind. Hyg. Q. 17:279 (1956)

Recent Developments in the Field of Industrial Toxicology
H.E. Stokinger
Ind. Hyg. Q. 17:340-344 (1956)

Nuclear Insurance and Standards
R.G. McAllister
Am. Ind. Hyg. Assoc. Q. 19:345-348 (1958)

Brief History of the National Committee on Radiation Protection Measurements (NCRP) Covering the Period 1929-1946
L.S. Taylor
Health Physics 1:30-10 (1958)

History of the International Commission on Radiological Protection (ICRP)
L.S. Taylor
Health Physics 1:97-104 (1958)

Scientific Principles for the Establishment of the Maximum Allowable Concentrations of Toxic Substances in the U.S.S.R.
A.A. Letavet
Proceedings 13th International Congress of Occupational Health (1960)

Early X-ray Protection in the United States
R.L. Kathren
Health Physics 8:503-511 (1962)

Basis for Establishing Emergency Inhalation Exposure Limits Applicable to Military and Space Chemicals
Prepared by the Ad Hoc Committee
Henry F. Smyth, *Chairman;* Theodore F. Hatch; Keith H. Jacobson; Moreno L. Keplinger; and Frank Princi
Revised and approved by the Committee on Toxicology
Arnold J. Lehman, *Chairman;* William G. Fredrick; Horace W. Gerarde; Herbert E. Stokinger; and John A. Zapp, Jr.
National Academy of Sciences-National Research Council, Washington, DC (1964)

Concepts of Standards
D.D. Irish
Arch. Env. Health 10:546-549 (1965)

Threshold Limit Values Report to Medical Directors
Forum June 28, 1967
Unpublished report

Testing Compliance with Threshold Limit Values for Respirable Dust.
S.A. Roach, E.J. Baier, H.E. Ayers and R.L. Harris
Am. Ind. Hyg. Assoc. J. 28:543-550 (Nov./Dec. 1967)

The Spectre of Today's Environmental Pollution — USA Brand: New Perspectives from an Old Scout
H.E. Stokinger
Am. Ind. Hyg. Assoc. J. 30:195-216 (May/June 1969)

Occupational Safety and Health Act of 1970
U.S. 91st Congress
Public Law 91-596

The Concept of Maximum Permissible Concentration of Chemical Substances in the Working Environment
L. Ulrich and L. Rosival
Bratislavske Lekarske Listy 58:366-373 (1972)

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Federal Register, Vol. 39, No. 119, Part II (June 19, 1974)

Construction Safety and Health Standards
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Federal Register, Vol. 39, No. 122, Part II (June 27, 1974)

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T. Hatch
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Non-Ionizing Radiation
Proceedings of a topical symposium, 276 pp.
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Protection of the Sensitive Individual
W.D. Kelley, Ed.
Ann. of Am. Conf. Govt. Ind. Hyg., Vol. 3, 187 pp. (1982)

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Michael L. Dourson and Jerry F. Stara
Regulatory Toxicology and Pharmacol. 3:224-238 (1983)

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C.D. Yaffe, Ed.
Ann. of Am. Conf. Govt. Ind. Hyg., Vol. 7, 137 pp. (1984)

The Origin and Basis of Threshold Limit Values
Jeffery M. Paull
Am. J. Ind. Med. 5:227-238 (1984)

Yearly index of action on TLV substances

Dust and salts (as Cd), 1976
Cadmium oxide fume, 1956, 1968, 1970, 1973, 1974, 1976, 1977, 1978
Calcite, 1960
Calcium arsenate, 1957, 1962, 1976, 1977, 1980
Calcium carbonate, 1965, 1972, 1978 calcium carbonate/marble, 1981
Calcium cyanamide, 1976
Calcium hydroxide, 1977, 1978
Calcium oxide, 1965, 1976, 1978
Camphor, 1964, 1969, 1971, 1972
Caprolactam
Dust, 1974
Vapor, 1974
Captafol (Difolatan®), 1977
Captan, 1976
Catechol (Pyrocatechol), 1977
Carbaryl (Sevin), 1966
Carbofuran (Furadan), 1976, 1977
Carbon black, 1967
Carbon dioxide, 1946, 1973
Carbon disulfide (see Carbon bisulfide), 1946, 1961, 1978, 1980
Carbon monoxide, 1946, 1965, 1967
Carbon tetrabromide, 1975
Carbon tetrachloride, 1946, 1953, 1961, 1962, 1978, 1979, 1981
Carbonyl chloride (see Phosgene)
Carbonyl fluoride, 1978, 1979, 1981
Carborundum, 1946
Cellosolve (2-Ethoxyethanol), 1946
Cellosolve acetate (see 2-Ethoxyethyl acetate), 1946
Cellulose paper fiber, 1965, 1972, 1981
Cement, 1954
Cesium hydroxide, 1975, 1976, 1977
Chlordane (1,2,4,5,6,7,8,8 octa-chloro-3a,4,7,7a-tetrahydro-4,7-methanoindane), 1956, 1962
Chlorinated camphene, 1957
Chlorinated diphenyl oxide, 1956
Chlorine, 1946, 1948, 1965, 1967, 1969, 1970
Chlorine dioxide, 1960
Chlorine trifluoride, 1956, 1963, 1976, 1977
Chloroacetaldehyde, 1962, 1963, 1976, 1977
α-Chloroacetophenone (phenacylchloride), 1968, 1976, 1977
Chloroacetyl chloride, 1980
Chlorobenzene (Monochlorobenzene), 1950, 1976, 1977
o-Chlorobenzylidene malononitrile (OCBM), 1967, 1976, 1977, 1980
2-Chlorobutadiene (Chloroprene), 1946, 1957
2-Chloro-1,3-butadiene, 1957, 1976
β-Chloroprene, 1978, 1980
Chlorodifluoromethane, 1975 (see Difluoromonochloromethane)
Chlorodiphenyl, 1946, 1957, 1961
(42% chlorine), 1961, 1976, 1977, 1978
(54% chlorine), 1961, 1976, 1977
2-Chloroethanol (Ethylene chlorohydrin), 1976, 1977
Chloroethylene (see Vinyl chloride), 1976
Chloroform (Trichloromethane), 1946, 1959, 1963, 1971, 1974, 1976, 1978, 1980, 1981
Chloropentafluoroethane, 1981
β-Chloroprene (see 2-Chloro-1,3-butadiene), 1978
Chloropicrin, 1957, 1976, 1977, 1978
Chlorpyrifes (Dursban®), 1975
bis-Chloromethyl ether, 1974, 1976, 1977, 1981
1-Chloro-1-nitropropane, 1946, 1976, 1977, 1979, 1981
o-Chlorostyrene, 1975
2-Chloro-6-(trichloromethyl) pyridine (N-Serve®), 1975
o-Chlorotoluene, 1974
Chromates certain insoluble forms, 1974, 1976, 1977, 1979, 1981
Chromic acid and chromates (as Cr_2O_3), 1946, 1979, 1981
Chromite ore processing (Chromate) (as Cr), 1978, 1981
Chromium
Soluble chromic, chromous salts (as Cr), 1968, 1976, 1977, 1981
Metals and insoluble salts, 1968, 1974, 1981
Chrysene, 1981
Clopidol (Coyden®), 1975
Coal dust, 1973
Coal tar pitch volatiles (benzene soluble fractions) (anthracene BaP, Phenanthrene, acridene chrysene, pyrene), 1967, 1975 change to:
Particulate polycyclic organic matter (PPOM) as benzene solubles, 1981
Cobalt, 1963, 1966
Metal fume and dust, 1968, 1975
Copper fume, 1965, 1973, 1975, 1976, 1977
Corundum (Al_2O_3), 1965, 1972, 1980, called Aluminum oxide
Cotton dust, (raw), 1966, 1974
Crag herbicide (sodium 2-[2,4-dichloro-phenoxy] ethanol hydrogen sulfate), 1956, 1971
Cresol, 1952, 1961, 1976, 1977
Crotonaldehyde, 1967
Crufomate (Ruelene®), 1975, 1976
Cumene, 1967
Cyanamide, 1977
Cyanide (as CN), 1947
Cyanogen, 1969, 1975, 1976, 1977
Cyanogen chloride, 1980
Cyclohexylamine, 1974, 1976, 1977
Cyclohexane, 1946, 1965, 1967
Cyclohexanol, 1946, 1961, 1976, 1977
Cyclohexanone, 1946, 1961, 1976, 1977, 1979, 1981
Cyclohexene, 1946, 1965, 1967, 1976, 1977
Cyclonite, 1980
Cyclopentadiene, 1966
Cyclopentane, 1981
Cyclopropane (propene), 1947

2,4-D (2,4-dichlorophenoxyacetic acid), 1956
DDT (2,2-bis[p-chlorophenyl]-1,1,1-trichloroethane), 1957, 1962
DDVP (o,o-Dimethyl-2,2-dichloro-vinyl phosphate) (see Dichlorvos), 1964, 1970, 1976
Decaborane, 1957, 1961
Demeton (Systox), 1965, 1966, 1973
1,2-Diaminoethane (see Ethylenediamine), 1976, 1977
2-N-Dibutlyaminoethanol, 1972
Dibutyl phosphate, 1968
Dibutyphthalate, 1968
Diacetone alcohol (4-hydroxy-4-methyl-2-pentanone), 1956

Ethylidene norborene, 1974, 1976, 1977
Ethyl mercaptan, 1962, 1963, 1965, 1967, 1968, 1970, 1976, 1977, 1978
N-Ethylmorpholine, 1967, 1976, 1977, 1980
Ethyl silicate, 1946, 1976, 1977, 1979

Fensulfothion (Dasanit), 1976, 1977
Fenthion, 1980, 1981
Ferbam (ferric dimethyl dithiocarbamate), 1957, 1971
Ferrovanadium, 1956
Fluoride dust, smokes, 1946, 1975, 1976
Fluorine (gas), 1953, 1971, 1973
Fluorotrichloromethane 1950, 1980
Formaldehyde, 1946, 1948, 1963, 1970, 1972, 1976, 1977, 1981
Formamide, 1975
Formic acid, 1967, 1976, 1977
Freon (see Respective Dichloro, Difluoro and Monofloro compounds)
Furfural, 1957, 1979, 1981
Furfural alcohol, 1960, 1971, 1973, 1974, 1980, 1981

Gamma radiation, 1947, 1950
Gasoline, 1946, 1966, 1969, 1972, 1980
Germanium tetrahydride, 1973
Glass, fibrous or dust, 1971, 1972, 1978
Glutaraldehyde, 1979
Glycerine mist, 1965, 1972, 1981
Glycidol (2,3-epoxy-1-propanol), 1962, 1979, 1981
Graphite, 1965, 1972, 1981
Gypsum, 1965, 1972, 1981

Hafnium, 1965
Heat stress, 1973
Helium, 1965, 1972, 1981
Heptane, 1946, 1974, 1976
Heptachlor (1,4,5,6,7,8,8a-heptachloro-3a,4,7,7a-tetrahydro-4,7-methane indane), 1964
HETP (hexaethyl tetraphosphate), 1957
Hexachloroethane, 1966, 1980
Hexachloronaphthalene, 1968
Hexafluoroacetone, 1973
Hexamethylphosphoramide, 1978
Hexane, 1946, 1974, 1976, 1979
Hexanone (see Methyl butanone) (methyl butyl ketone), 1954, 1966 change to:
2-Hexanone, 1975, 1976, 1979, 1981
Hexone (see Methyl iso-butanone)
sec-Hexyl acetate, 1962, 1963, 1967, 1976, 1977
Hexylene glycol, 1977
Hydrazine, 1956, 1961, 1963, 1964, 1975, 1977, 1978
Hyrogen, 1965, 1972, 1981
Hydrogenated terphenyls, 1976, 1977
Hydrogen bromide, 1956, 1961, 1976, 1977
Hydrogen chloride (see Hydrochloric acid), 1946, 1948, 1976, 1977
Hydrogen cyanide, 1946, 1948, 1961, 1978, 1980
Hydrogen fluoride, 1946, 1976, 1977, 1980
Hydrogen peroxide, 1956
Hydrogen selenide, 1946, 1948, 1976, 1977
Hydrogen sulfide, 1946, 1963, 1964, 1966

2-Hydroxypropyl acrylate, 1980
Hydroquinone, 1956

Indene, 1970, 1978
Indium and compounds, as In, 1969
Inert dusts, 1961, 1964
Iodine, 1946, 1948, 1956, 1963, 1976, 1977
Iodoform, 1976, 1978
Iron oxide fume (Fe_2O_3), 1946, 1965, 1967, 1973, 1975, 1977
Iron penta carbonyl, 1972, 1976, 1977, 1980
Iron salts soluble, as Fe, 1969, 1976
Isoamyl acetate, 1967
Isobutyl acetate, 1967
Isophorone, 1946, 1971, 1976, 1977
Isophorone diisocyanate, 1977
Isopropoxy ethane, 1981
Isopropyl acetate, 1967
Isopropyl alcohol (iso-Propanol), 1946, 1966
Isopropylamine, 1956
N-Isopropylaniline, 1980
Isopropyl ether, 1946, 1948, 1971, 1973
Isopropyl glycidyl ether, 1962

Kaolin, 1970, 1972, 1981
Ketene, 1963

Lasers, 1969, 1973
Lead, 1946, 1957, 1971, 1973
Lead arsenate, 1957, 1980
Lead chromate (as Cr), 1977
Limestone, 1960, 1965, 1972, 1981
Lindane (hexachlorocyclohexane, gamma isomer), 1956
Lithium hydride, 1960, 1976, 1977
LPG Liquified petroleum gas), 1966

Magnesite, 1965, 1972, 1981
Magnesium oxide fume, 1946, 1971, 1976, 1977
Malathion (o,o-dimethyl dithio-phosphate of dimethyl mercapto succinate), 1956, 1961, 1971, 1976, 1977
Maleic anhydride, 1968, 1976, 1977
Manganese, 1946, 1960, 1963, 1976, 1977, 1979
Manganese cyclopentadienyl tricarbonyl (as Mn), 1974
Manganese tetroxide, 1978
Marble, 1943, 1960, 1965, 1972, 1981
Mercury, 1946, 1971, 1980
Organic compounds, 1956, 1961, 1971
Alkyl compounds, 1973, 1980
Mesityl oxide, 1946, 1958, 1976, 1977, 1979, 1981
Methacrylic acid, 1981
Methane, 1965, 1972, 1981
Methanethiol (see Methyl mercaptan)
Methanol (see Methyl alcohol), 1946
Methomyl (Lannate®), 1977
Methoxychlor (2,2-di-p-methoxy-phenyl-1,1,1-trichloroethane), 1956, 1971, 1976, 1977
2-Methoxyethanol (Methyl cellosolve), 1971
Methyl acetate, 1946
Methyl acetylene (propyne), 1956, 1976
Methyl acetylene-propadiene mixture (MAPP), 1966
Methyl acrylate, 1957, 1961, 1976, 1977

Petroleum distillates (naptha), 1967, 1970, 1971, 1972, 1977
Phenol, 1952, 1961
Phenothiazine, 1971
p-Phenylene diamine, 1966, 1976, 1977
Phenyl ether, 1967
Phenyl ether-biphenyl mixture (vapor), 1967, 1971 Diphenyl mixture, 1979
Phenyl glycidyl ether, 1962, 1968, 1980
Phenylhydrazine, 1956, 1961, 1981
Phenyl mercaptan, 1978
n-Phenyl-beta-naphthylamine, 1979
Phenylphosphine, 1973, 1976, 1977
Phorate (Thimet®), 1974
Phosdrin (Mevinphos®), 1963, 1973
Phosgene (carbonyl chloride), 1946, 1964, 1966, 1974, 1976, 1977, 1978
Phosphine, 1946, 1963
Phosphoric acid, 1960
Phosphorus (yellow), 1947
Phosphorus pentachloride, 1947, 1978, 1980
Phorphorus pentasulfide, 1947
Phosphorus trichloride, 1946, 1976, 1977, 1980
Phthalic anhydride, 1966, 1975, 1976
m-Phthalodinitrile, 1977
Picloram (Tordon®), 1975
Picric acid, 1956, 1961
Pival (2-Pivalyl-1,3-indandione), 1967
Plaster of Paris, 1965, 1972, 1981
Platinum
  Soluble salts, 1963, 1976, 1977, 1981
  Metal, 1981
Polonium 210 (microcuries per cubic meter), 1951
Polytetrafluoroethylene (decomposition products), 1965, 1969, 1972
Portland cement, 1946, 1965, 1972
Potassium hydroxide, 1974, 1976, 1977
Propane, 1966, 1970, 1972, 1981
Propane sultone, 1977
iso-Propanol (isopropyl alcohol), 1946, 1966
Propargyl alcohol, 1969, 1973
β-Propiolactone, 1963, 1965, 1969, 1972, 1979, 1981
Propionic acid, 1980
n-Propyl acetate, 1946
Propyl alcohol, 1968, 1974
Propylene glycol dinitrate, 1978, 1979
Propylene imine, 1956, 1961, 1965, 1967, 1976, 1977, 1980
Propylene glycol monomethyl ether, 1971
Propylene oxide, 1959, 1969, 1981
iso-Propyl ether, 1945, 1948, 1963
n-Propyl nitrate, 1962, 1978
Propyne (see Methyl acetylene)
Pyrethrum, 1957, 1962
Pyridine, 1956, 1961

Quinone, 1981

Radium 226 (microcuries per cubic meter), 1951
Radon or thoron gas, 1946
RDX, 1969
Resorcinol, 1976
Rhodium
  Metal fume and dusts, 1967, 1980
  Soluble salts, 1967
Roentgen ray (roentgens per week), 1950
Ronnel, 1968, 1976, 1977
Rosin core solder pyrolysis products (as formaldehyde), 1971
Rotenone, 1957
Rouge, 1965, 1972, 1981
Rubber solvent, 1977

Selenium compounds (as Se), 1947, 1954, 1964, 1966, 1976, 1977
Selenium hexafluoride, 1967, 1976, 1979
Silane (see Silicon tetra hydride), 1974, 1980
Silica, 1946, 1962, 1970
Silica, amorphous, 1961
Silica, crystabolite, 1960, 1970, 1972
Silica, fused, 1973
Silica, tridymite, 1972
Silica, quartz, 1970, 1972
Silicon, 1973, 1974, 1981
Silicon carbide, 1960, 1972, 1981
Silicon tetrahydride, 1974, 1980
Silicates (< 1% quartz)
  Asbestos, 1974
  Mineral wool fiber, 1974
  Tripoli, 1974
Silver
  Metal and soluble compounds, 1966, 1978, 1980, 1981
  Metal, 1980
  Soluble compounds (as Ag), 1981
Slate (below 5% free SiO_2), 1946
Soapstone (below 5% free SiO_2), 1946, 1948, 1962 (less than 1% crystalline silica)
Sodium azide, 1976, 1977
Sodium bisulfite, 1980
Sodium 2,4-dichloro phenoxy ethyl sulfate, 1980
Sodium fluoroacetate (1080), 1957, 1961, 1962
Sodium hydroxide, 1956, 1973, 1975, 1976, 1977
Sodium meta bisulfite, 1980
Starch, 1965, 1972, 1981
Stibine, 1946
Stoddard solvent, 1946, 1970, 1974, 1976, 1980
Styrchnine, 1957
Styrene monomer (phenylethylene), 1946, 1957, 1964, 1971, 1979, 1980, 1981
Subtilisin (Proteolytic enzymes as 100% pure crystalline enzymes), 1975, 1976, 1977
Sucrose, 1965, 1972
Sulfur chloride, 1946
Sulfur dioxide, 1946, 1957, 1976, 1977, 1978, 1980
Sulfur hexafluoride, 1956
Sulfur pentafluoride, 1956, 1969
Sulfur tetrafluoride, 1973
Sulfuric acid, 1946, 1948, 1976, 1977

2,4,5-T (2,4,5-Trichlorophenoxy-acetic acid), 1963
Talc, 1946, 1970, 1978
Tantalum, 1965
TEDP (tetraethyl dithionopyro-phosphate), 1956, 1961
Teflon® decomposition products, 1963, 1970, 1972