

History, Implementation and Evolution of the Pharmaceutical Hazard Banding and Control System

John P. Farris, CIH
President and Managing Principal
SafeBridge Consultants, Inc.
Mountain View, CA
www.safebridge.com

In the Beginning...

- Concept evolved from an identified need in the pharmaceutical industry
- R&D scientists working with kilos of drug material
 - Novel compounds with little or no pharmacology and toxicology data
 - Several 'open' operations
 - Kilogram scale synthetic chemistry
 - Pilot scale process development
 - Formulation development/clinical manufacturing
 - Inability to set exposure limits
 - No target for air monitoring methods

What Should We Do?

- Issue arose at the 1988 Pharmaceutical Safety Group (PSG) meeting
 - Ad hoc gathering of 15 pharmaceutical safety directors
- Five companies volunteered to work on the issue
 - Syntex
 - Merck
 - Abbott
 - Lilly
 - Upjohn

Development of a Concept

- Quarterly working group sessions were held over the next two years
- Pharmaceutical approach based on the NIH/CDC Biosafety Level model
 - “Hand in glove” system
 - Linking pharmaceutical potency and toxicity to safe handling
 - Control recommendations were based on success with compounds having similar characteristics
 - Work environments, process controls, techniques, PPE
 - Air monitoring results to support control levels

Why Are There So Many Different Systems in the Pharma Industry?

- Tried to create a “one size fits all” system to take back to the other companies
 - Clearly the therapeutic substances were different in the five companies
 - The surprise was that the work environments and equipment was also different
- Conclusion was to develop company-specific systems based on the common theme
- Proper implementation depends on customization to match your needs

Where Are We Now?

- The idea of categorization or banding or PB-OELs is now standard in the pharmaceutical industry
 - Systems are protective when properly implemented
- Most systems are derivatives the Merck System (5 bands) or the SafeBridge System (4 bands)
 - Number of bands determined by number of different workplaces that can be described
- Systems evolve due to changes in manufacturing technology, containment options and therapies

Toxicity/Potency Categorization of Chemicals (SafeBridge System)

- **Category 1: Low Toxicity**
OEL $> 0.5 \text{ mg/m}^3$ (aspirin)
- **Category 2: Intermediate Toxicity**
OEL $10 \text{ } \mu\text{g/m}^3 - 0.5 \text{ mg/m}^3$ (insulin)
- **Category 3: Potent (default)**
OEL $30 \text{ ng/m}^3 - 10 \text{ } \mu\text{g/m}^3$
(estradiol 17- β , ganciclovir, paclitaxel)
- **Category 4: Highly potent**
OEL $\leq 30 \text{ ng/m}^3$ (nafarelin, leuprolide)

Implementation and Benefits of the System

- Initially thought to be slowly accepted
 - Within one year 15 operating sites at Syntex were speaking this language
 - Proactive training and planned 'roll out' essential
- Replaced cumbersome process
- Excellent risk communication tool
- Presents the 'default' concept for unknowns (the precautionary principle)
- Widely accepted to date
 - Over 2000 R&D scientists trained by SafeBridge alone

Limitations of the System

- Does not replace limit setting and air monitoring
- Does not demonstrate a health protective environment
- Placement of compounds is based on characteristics not exposure limits
- Compounds need to be reevaluated as new data become available
- Requires experienced toxicologists and industrial hygienists to get it right

Evolution and Spread of the Concept

- Merck published paper in AIHA Journal – January 1996
- Association of the British Pharmaceutical Industry (ABPI) picked up the idea
 - Published two technical guides in 1995
- UK Health and Safety Executive
 - COSHH Essentials developed in 1999
- New applications are being developed

More Information

- Naumann *et al*, "Performance-Based Exposure Control Limits for Pharmaceutical Active Ingredients", AIHA Journal, January 1996.
- Association of the British Pharmaceutical Industry
 - "Guidance on Setting In-House Occupational Exposure Limits for Airborne Therapeutic Substances and their Intermediates" – ABPI Publication, October 1995.
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- SafeBridge Consultants, Inc.
 - "Occupational Health Toxicity / Potency Categorization and Handling Practices" – SafeBridge, Fifth Revision – January 2002.

More Information (2)

- UK Health and Safety Executive
 - “Control of Substances Hazardous to Health Essentials”, HSE 1999, 2000.
- Wood *et al*, “Containment in the Pharmaceutical Industry”, Marcel Dekker, 2001.
 - Chapter 3, D. Heidel, “Industrial Hygiene Aspects of Pharmaceutical Manufacturing”.