Health Hazard Banding = Occupational Exposure Banding

Susan D. Ripple, MS, CIH
Topics for Discussion

• Background and “big picture”
  – Value of occupational exposure bands (OEB)
  – OEB fit into the IH process

• OEB process for general chemicals
  – Framework and decision logic
  – Examples and exercises
Value of Health Hazard Banding?

• Health Hazard Banding provides a tool for hygienists to do exposure risk assessment and risk management in the workplace.

• By providing the relative hazard bands for the substances under review, HHB will serve the IH community in the qualitative aspects of risk management.
Exposure Risk Assessment Knowledge Gaps

HAZARD Assessment

<2000 OELs <2% REACH

Occupational Exposure Bands (OEBs) & Exposure Limits (OELs)

Exposure Risk Assessment (modeling, monitoring, analogy)

Occupational Health Hazard Criteria & Process

~21,000,000 commercial-available chemicals; >107,000 REACH

Exposure Management (Controls & Programs)

IH Expertise Understanding Exposure & Controls

"Exposure Gap"

Chemicals with OELs

Courtesy of Elizabeth Pullen and ERAM Working Group
Hierarchy of Exposure Limits

• (Traditional) Health-Based OELs
  – Key Feature - uses weight of evidence judgment about the point of departure and uncertainty factors using an adequate data

• Preliminary / Provisional OELs
  – Key Feature – includes weight of evidence judgment about the POD and uncertainty factors (UF), but using limited data

• Prescriptive or Process-based OELs (e.g., DNELs)
  – Key Feature - provides algorithm-based approach with heavy reliance on default decisions. Requires point of departure information.

• Occupational Exposure Band
  – Key Feature - enables use of hazard classification data to develop OEL ranges

Proposed by A. Maier, 2012
Hierarchy of OELs

As more toxicological and epidemiological data becomes available, we move up the hierarchy of OELs.

- **Health Based OELs**: Regulatory, Authoritative
  - Traditional (TLVs, MAKs, WEELs, PELs, MACs, RELs)

- **Working Provisional OELs**: (internal company, trade association, vendor limits)

- **Prescriptive Process Based OELs**: (REACH DNELs/DMELs)

- **Hazard Banding Strategies**
  - Pharmaceutical banding
  - Occupational exposure bands

Hazard Banding + Exposure Banding → Control Banding
NIOSH Project Plan

1. Establish minimum viable dataset, including data quality requirements
2. Establish process and decision logic
3. Validate data endpoints and band cut points, process, and decision logic
4. Identify data sources
5. Develop NIOSH guidance
6. Educate stakeholders
Hazard Banding (OEB) Criteria

• Criteria include qualitative, semi-quantitative, and quantitative data for each toxicological endpoint
  – Acute toxicity
  – Skin corrosion/irritation
  – Serious eye damage/eye irritation
  – Respiratory and skin sensitization
  – Germ cell mutagenicity
  – Carcinogenicity
  – Specific target organ toxicity, both single and repeated exposure
  – Reproductive toxicity
OSHA-GHS Link

• OEB toxicological endpoints are aligned with GHS classification and labeling system*

• Important goal is to relate potency of each toxicological hazard-banding endpoint to GHS hazard statements and categories, when possible

*CLP 2008 1272
## Qualitative Criteria and GHS Information

<table>
<thead>
<tr>
<th>Band</th>
<th>A</th>
<th>B</th>
<th>C (default)</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHS Signal Word</td>
<td>Warning</td>
<td>Warning</td>
<td>Danger</td>
<td>Danger</td>
<td>Danger</td>
</tr>
<tr>
<td>OEL (Control) Ranges</td>
<td>&gt; 1,000 µg/m³</td>
<td>&gt; 100 and &lt; 1,000 µg/m³</td>
<td>&gt; 10 and &lt; 100 µg/m³</td>
<td>&gt; 1 and &lt; 10 µg/m³</td>
<td>&lt; 1 µg/m³</td>
</tr>
<tr>
<td></td>
<td>&gt; 1000 ppm</td>
<td>&gt; 100 - &lt; 1000 ppm</td>
<td>&gt; 10 - &lt; 100 ppm</td>
<td>&gt; 1 - &lt; 10 ppm</td>
<td>&lt; 1 ppm</td>
</tr>
</tbody>
</table>

### Examples of Health Outcomes and Potency Considerations

- **Minor, reversible health effects occurring at high doses. Skin and eye irritation.**
- **Reversible organ toxicity, skin and eye corrosion (reversible), possible dermal sensitizer at high doses.**
- **Irreversible organ toxicity at high doses, irreversible skin and eye corrosion, dermal sensitizer at moderate doses.**
- **Irreversible organ toxicity at low doses, in vivo genotoxicity, dermal sensitizer at low doses, evidence of mutagenicity, potential developmental and reproductive toxicants.**
- **Human carcinogens at low doses, respiratory sensitization**

### Examples of GHS Hazard Statements and Hazard Categories

- **May cause drowsiness or dizziness**
- **Harmful if inhaled (4). Harmful in contact with skin (4).**
- **Toxic if inhaled (3). Toxic in contact with skin (3). Suspected of causing cancer (2). May cause damage to organs (2).**
- **Fatal if inhaled (2). Fatal in contact with skin (1). Causes damage to organs (1).**
- **May cause cancer (by route of exposure)—1A or B. Presumed or known human reproductive toxicant (1A or 1B). Causes damage to organs through prolonged or repeated exposure (1).**
- **Fatal if inhaled (1). Fatal in contact with skin (1). May cause cancer (by route of exposure)—1A. May cause allergy or asthma symptoms or breathing difficulties if inhaled (1A resp.). Known human repro toxicant (1A). Causes damage to organs through prolonged or repeated exposure (1).**
Framework for Decision Logic

• Tier 1 a & b: GHS hazard code or statement from SDS or the preferred GHS database (Annex VI, REACH, GESTIS, etc.). Hazard category will further define Bands D and E
  — **User**: H&S generalist; may overestimate risk
    *Warning* – negative results vs. absence of data

• Tier 2: quantitative data from authoritative sources
  — **User**: skilled industrial hygienist

• Tier 3: toxicological weight of evidence – determine the critical study from which a scientifically sound point of departure (POD) can be determined
  — **User**: toxicologist or experienced industrial hygienist
Overview of NIOSH Tier Approach to OEBs

<table>
<thead>
<tr>
<th>Tier 1a—Qualitative</th>
<th>Tier 1b—Semi-quantitative</th>
<th>Tier 2—Quantitative</th>
<th>Tier 3—Weight of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use GHS Hazard Statements to identify chemicals with potential for irreversible health effects at relatively low doses (Band D-E) or remain at default Band C</td>
<td>Use GHS Hazard Categories to assign chemicals into Bands D or E or remain at default Band C</td>
<td>Determine point of departure, factoring data availability, hierarchy, and quality to support assigning chemicals into Bands A, B, or C</td>
<td>Involves integration of all available data and determining the degree of conviction of the outcome.</td>
</tr>
</tbody>
</table>
Tier 1 - Minimum Data

**Tier 1a—Qualitative**
Use GHS Hazard Statements to identify chemicals with potential for irreversible health effects at relatively low doses (Band D-E) or remain at default Band C

**Tier 1b—Semi-quantitative**
Use GHS Hazard Categories to assign chemicals into Bands D or E or remain at default Band C

**User:** H&S generalist; may overestimate risk
Tier 2 – Requires More Data

User: skilled industrial hygienist

That’s You!
Tier 3 – Ideal Robust Data Set

User: toxicologist or experienced industrial hygienists

Tier 3—Weight of Evidence
Involves integration of all available data and determining the degree of conviction of the outcome.
Data relevance

• Tier 1
  – Relevance: any GHS criteria can determine “D” or “E” band
Data Quality

• Presence of GHS statements assumes data of adequate quality for classified endpoints

• Absence of GHS statements assumes either lack of adequate data or data quality
Where can I find Tier 1 data?

• GHS-compliant Safety Data Sheet or chemical label


“Default” Band “C”

• Tier 1 process begins by determining whether data exists to move a chemical from “default” band C (> 10 and < 100 µg/m³) to “D” or “E” band
Tier 1a and 1b
Goal: Identify Bands D-E from Default Band C

1. Chemical for OEB
   - Authoritative OEL available?
     - yes: No OEB necessary
     - no: Health statements available?
       - yes: Band C default assigned
         - yes: Tier 2 process to determine Band A or B
         - no: D or E statement?
           - yes: Band D-E assigned
           - no: Band C default assigned
             - yes: Tier 2 process to determine Band A or B
             - no: Band C default assigned
               - yes: Tier 2 process to determine Band A or B
               - no: Band D-E assigned
2. Need to define Band D vs. E?
   - yes: Review available H categories or go to Tier 2
     - yes: Assign Band E
     - no: Assign Band D
   - no: Remain at Band D-E

Tier 1 Bands ➔ D & E

Using GHS hazard statements or codes (qualitative hazard banding), for most criteria, cannot separate the “D” from the “E” bands

- Acute toxicity H codes: H300, H330, H310
- Sensitization H code: H334
- Germ cell mutagenicity: H340
- Carcinogenicity: H350
- Toxic to reproduction: H360f, H360d, or H360fd
- STOT(RE): H372

Using the GHS hazard category and/or a Tier II process will be required to separate D from E
## Acute Toxicity

<table>
<thead>
<tr>
<th>Band</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GHS Signal Word</strong></td>
<td>Precautionary</td>
<td>Warning</td>
<td>Danger</td>
<td>Danger</td>
<td>Danger</td>
</tr>
<tr>
<td><strong>GHS Hazard Category</strong></td>
<td>__</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>GHS Hazard Statements</strong></td>
<td>Harmful if swallowed. Harmful if inhaled. Harmful in contact with skin</td>
<td>Toxic if swallowed. Toxic if inhaled. Toxic in contact with skin.</td>
<td>Fatal if swallowed. Fatal if inhaled. Fatal in contact with skin.</td>
<td>Fatal if swallowed. Fatal if inhaled. Fatal in contact with skin.</td>
<td></td>
</tr>
<tr>
<td><strong>“H” Codes</strong></td>
<td>H302, H332, H312</td>
<td>H301, H331, H311</td>
<td>H300, H330, H310</td>
<td>H300, H330, H310</td>
<td></td>
</tr>
<tr>
<td><strong>Oral Toxicity LD₅₀ Technical Criteria (mg/kg bodyweight)</strong></td>
<td>&gt;2000</td>
<td>&gt;300 and ≤ 2000</td>
<td>&gt;50 and ≤ 300</td>
<td>&gt;5 and ≤ 50</td>
<td>≤ 5</td>
</tr>
<tr>
<td><strong>Inhalation Vapors (mg/l) LC₅₀ Technical Criteria (mg/kg bodyweight)</strong></td>
<td>&gt;10.0 and ≤ 20.0</td>
<td>&gt;2.0 and ≤ 10.0</td>
<td>&gt;0.5 and ≤ 2.0</td>
<td>≤ 0.5</td>
<td></td>
</tr>
</tbody>
</table>

### Example: Acetylene tetrabromide

- **H330** (fatal if inhaled) category 2 (LC50 inhalation rat: 0.549 mg/l/4 h)
- **H319** (causes serious eye irritation) category 2

**Band D (OSHA PEL: 1 ppm)**
# Sensitization Respiratory and Skin

<table>
<thead>
<tr>
<th>Band</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHS Signal Word</td>
<td>Warning</td>
<td>Warning</td>
<td>Danger</td>
<td>Danger</td>
<td>Consider “Ceiling” for respiratory sensitizers</td>
</tr>
<tr>
<td>GHS Hazard Category</td>
<td>1B (skin)</td>
<td>1A (skin)</td>
<td>1B (resp.)</td>
<td>1A (resp.)</td>
<td></td>
</tr>
<tr>
<td>GHS Respiratory and Skin Sensitization Hazard Statements</td>
<td>May cause an allergic skin reaction</td>
<td>May cause an allergic skin reaction</td>
<td>May cause allergy or asthma symptoms or breathing difficulties if inhaled</td>
<td>May cause allergy or asthma symptoms or breathing difficulties if inhaled</td>
<td></td>
</tr>
<tr>
<td>Respiratory and Skin Sensitization “H” Codes</td>
<td>H317</td>
<td>H317</td>
<td>H334</td>
<td>H334</td>
<td></td>
</tr>
</tbody>
</table>

**Example: Isopropyl Glycidyl Ether**
- H332 (harmful if inhaled) category 4
- H341 (suspected of causing genetic defects) category 2
- H317 (may cause allergic skin reaction) category 1
- H334 (may cause allergy or asthma symptoms...) category 1

Band D or E (NIOSH REL: 50 ppm C; IDLH 400 ppm)
# Carcinogenicity

<table>
<thead>
<tr>
<th>Band</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHS Signal Word</td>
<td>Warning</td>
<td>Warning</td>
<td>Danger</td>
<td>Danger</td>
<td></td>
</tr>
<tr>
<td>GHS Hazard Category</td>
<td>2</td>
<td>2</td>
<td>1B</td>
<td>1A</td>
<td></td>
</tr>
<tr>
<td>GHS Carcinogenicity Hazard statement</td>
<td>Suspected of causing cancer</td>
<td>Suspected of causing cancer</td>
<td>May cause cancer</td>
<td>May cause cancer</td>
<td></td>
</tr>
<tr>
<td>Carcinogenicity “H” Codes</td>
<td>H351</td>
<td>H351</td>
<td>H350</td>
<td>H350</td>
<td></td>
</tr>
</tbody>
</table>

**Example:** 4-Aminobiphenyl

H350 (may cause cancer) category 1A
H302 (harmful if swallowed) category 4 (oral)

**Band E (French OEL: 0.001 ppm or 7 µg/m3)**
Additional Tier 1 Examples

1-bromopropane

• TIER 1a
  – Signal word: danger
  – H360FD: May damage fertility or the unborn child
  – H373: May cause damage to organs through prolonged or repeated exposure (STOT-RE-2)
  – H319: Causes serious eye irritation
  – H335: May cause respiratory irritation
  – H315: Causes skin irritation
  – H336: May cause drowsiness or dizziness

TIER 1a outcome: Band D-E

• TIER 1b
  – Hazard Category Repro 1B

TIER 1b outcome: Band D: (1-10 ppm)

• TLV: 10 ppm
• OSHA-GHS: Presumed human reproductive toxicant

Cobalt Sulfate

• TIER 1a
  – Signal word: danger
  – H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled
  – STOT-RE 1
  – H350i: May cause cancer
  – H360F: May damage fertility
  – H341: Suspected of causing genetic defects
  – H302: Harmful if swallowed
  – H317: May cause allergic skin reaction

TIER 1a outcome: Band D-E

• TIER 1b
  – Germ cell mutagen category 2
  – Resp. Sens: 1
  – Carcinogen category 1B
  – Repro 1B

TIER 1b outcome: Band E: (< 1 µg/m³) or Band D: (1 – 10 µg/m³)

• TLV: 20 µg/m³
Tier 1 Summary

• All toxicological data relevant
  – Any toxicological outcome, assuming data is from an authoritative source, can result in band D or E
• Refer to GHS hazard category to better define “D” vs. “E”
• Tier 2 process is required to determine “A” and “B” bands
Tier 2 (Quantitative)

Goal: determine whether Bands A or B can be assigned

- OEB based on point of departure (POD) at which adverse effects are observed
  - NOAEL, BMDL or LOAEL for target organ systemic toxicity, developmental/reproductive toxicity;
  - CSFs, IUR, TD$_{05}$/TC$_{05}$, NSRLs (CalEPA Prop 65) of tumorigenic doses for carcinogenicity (still being investigated);
  - Skin and respiratory sensitization
  - LD50 (oral and dermal) or LC50 (inhalation) for acute toxicity data;
  - RD50 (in mice) for sensory irritation;
  - Irritation threshold (mice, rats or human volunteers) for irritation
Tier 2 Data Reliability

• Presence of authoritative assessment assumes data of adequate quality for classified endpoints

• Absent authoritative assessments, individual studies are evaluated
  – Consult toxicologist
Examples of reliable data sources

- IUCLID 5: [http://iuclid.eu/](http://iuclid.eu/)
## Tier 2 Data Weight

<table>
<thead>
<tr>
<th>Category</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinogenicity</td>
<td>15</td>
</tr>
<tr>
<td>Reproductive toxicity</td>
<td></td>
</tr>
<tr>
<td>Specific target organ toxicity repeated exposure</td>
<td></td>
</tr>
<tr>
<td>Specific target organ toxicity, single exposure</td>
<td>10</td>
</tr>
<tr>
<td>Germ cell mutagenicity <em>(in vivo)</em></td>
<td></td>
</tr>
<tr>
<td>Respiratory sensitization **</td>
<td></td>
</tr>
<tr>
<td>Acute toxicity</td>
<td>5</td>
</tr>
<tr>
<td>Skin corrosion/irritation</td>
<td></td>
</tr>
<tr>
<td>Serious eye damage/eye irritation</td>
<td></td>
</tr>
<tr>
<td>Germ cell mutagenicity <em>(in vitro)</em></td>
<td></td>
</tr>
<tr>
<td>Skin sensitization **</td>
<td></td>
</tr>
</tbody>
</table>

*use weight of evidence*
Tier 2
Can Band A or B be considered?

Tier 1 Process results in Band C

Identify points of departure

Score data relevance

Establish Total Determinant Score (TDS)

Does TDS exceed threshold for minimum, quality dataset?

yes

Establish OEB

no

Data insufficient for OEB, “C” default band

TDS reflects the availability of qualitative info and/or quantitative data for each endpoint under consideration. Endpoint scores include data relevance and quality factors. TDS is the sum of the endpoint scores.
## Total Determinant Score

<table>
<thead>
<tr>
<th>Category</th>
<th>Toxicological Endpoint</th>
<th>Assigned Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-systemic, POI, and/or immunological endpoints</td>
<td>Skin sensitization</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Skin/eye irritation</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Genotox/mutagen (in vitro)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Respiratory toxicity/asthma</td>
<td>5</td>
</tr>
<tr>
<td>Irreversible non-systemic</td>
<td>Skin/eye corrosion</td>
<td>5</td>
</tr>
<tr>
<td>Systemic endpoints</td>
<td>Acute toxicity/lethality</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Genotox/mutagen (in vivo)</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Target organ toxicity SE</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Target organ toxicity RE</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Reproductive toxicity</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Developmental toxicity</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Cancer</td>
<td>15</td>
</tr>
<tr>
<td>Data sufficiency threshold for TDS</td>
<td></td>
<td>20/50</td>
</tr>
</tbody>
</table>

POI = point of impact
Next Steps for NIOSH Matrix: Validate

- Criteria endpoints and band cut points
- Process
- Decision logic
- Modify based on validation results