

Health Hazard Banding = Occupational Exposure Banding

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Topics for Discussion

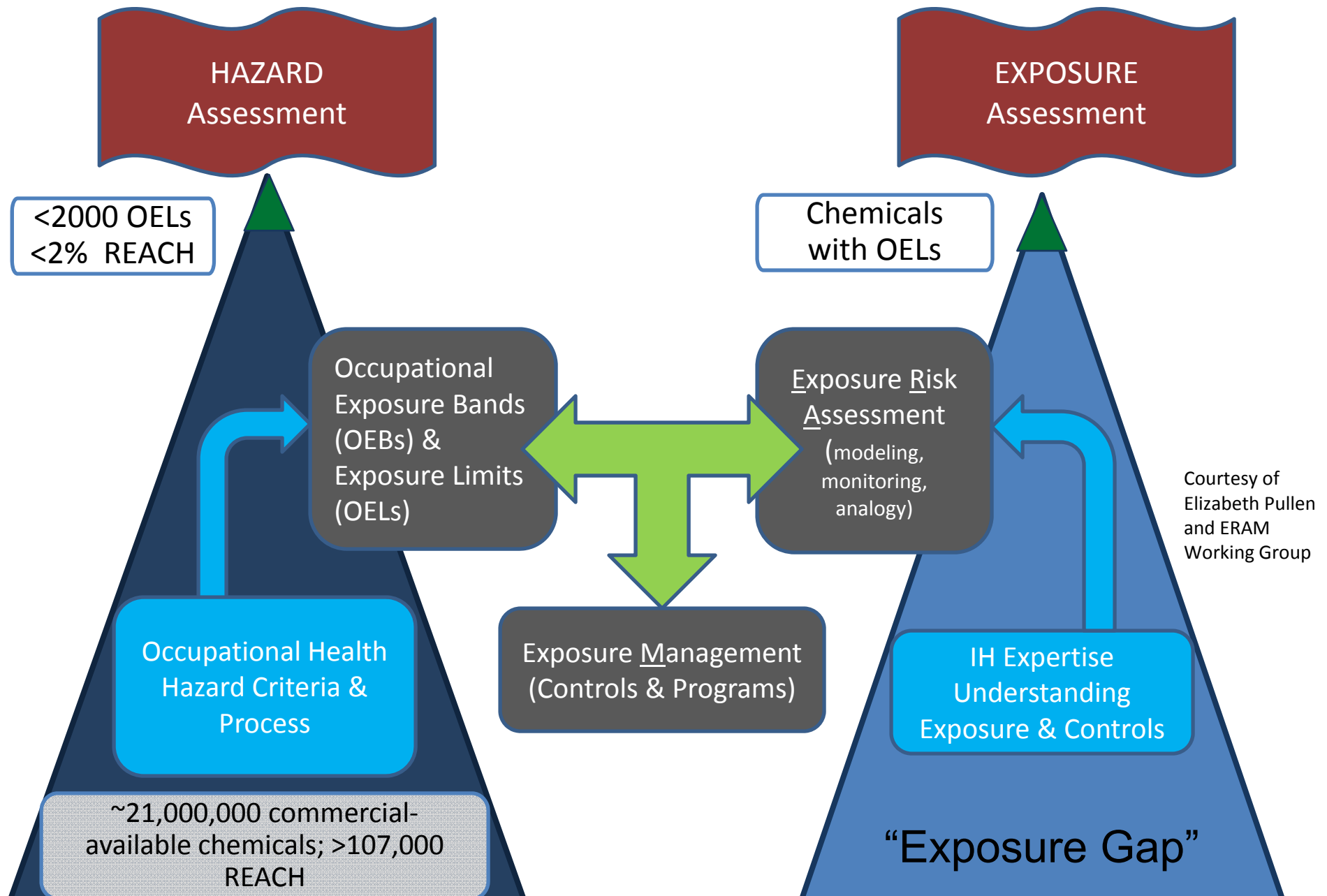
- Background and “big picture”
 - Value of occupational exposure bands (OEB)
 - OEB fit into the IH process
- OEB process for general chemicals
 - Framework and decision logic
 - Examples and exercises

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



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.

Quantitative
Health Based
OELs

Health Based OELs

- Regulatory, Authoritative
- Traditional

(TLVs, MAKs, WEELs, PELs, MACs, RELs)

Most Extensive Data Requirements

(human epidemiology studies)
> quality, > certainty

Working Provisional OELs

(internal company, trade association, vendor limits)

Moderate Data Requirements

(in vitro and animal studies and anecdotal reports of human health effects)
> quality, > certainty

Prescriptive Process Based OELs

(REACH DNELs/DMELs)

Least Data Requirements

(in vitro and animal studies)

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

Band	A	B	C (default)	D	E
GHS Signal Word	Warning	Warning	Danger	Danger	Danger
OEL (Control) Ranges	> 1,000 µg/m ³	> 100 and < 1,000 µg/m ³	> 10 and < 100 µg/m ³	> 1 and < 10 µg/m ³	< 1 µg/m ³
	> 1000 ppm	> 100 - < 1000 ppm	> 10 - < 100 ppm	> 1 - < 10 ppm	< 1 ppm
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, <i>in vivo</i> 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



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

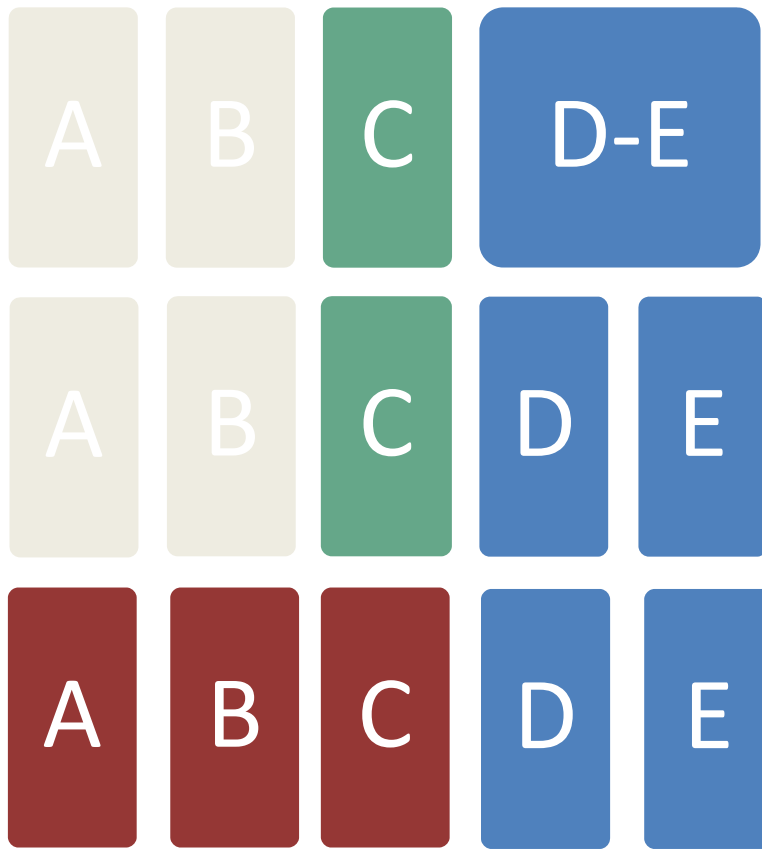
Tier 2—Quantitative

Determine point of departure, factoring data availability, hierarchy, and quality to support assigning chemicals into Bands A, B, or C

Tier 3—Weight of Evidence

Involves integration of all available data and determining the degree of conviction of the outcome.

Tier 1 - Minimum Data



Tier 1a—Qualitative

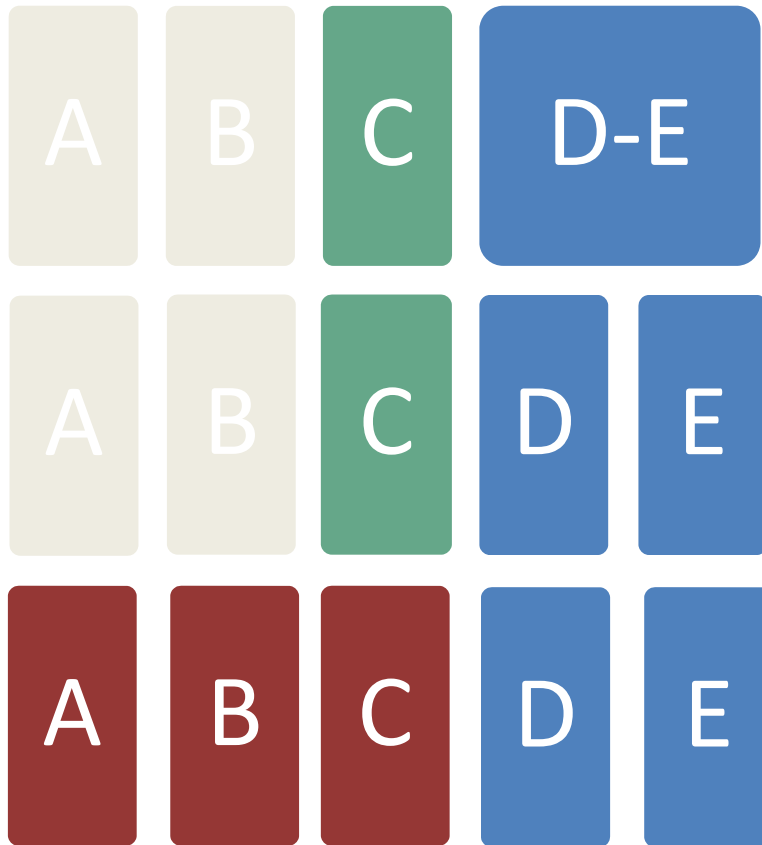
Use GHS Hazard Statements to identify chemicals with potential for irreversible health effects at relatively low doses (Band D-E) or remain at default Band C

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



Tier 2—Quantitative

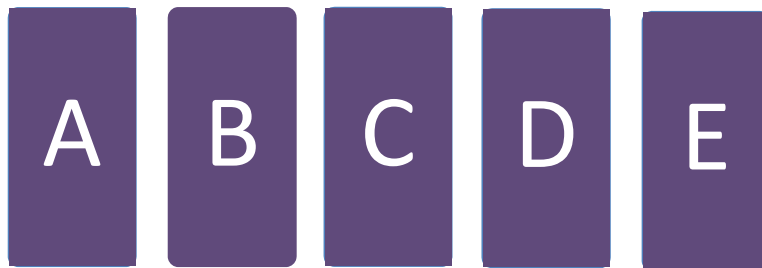
Determine point of departure, factoring data availability, hierarchy, and quality to support assigning chemicals into Bands A, B, or C

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

- OSHA HazCom 2012:

<http://www.osha.gov/dsg/hazcom/ghs-final-rule.html>

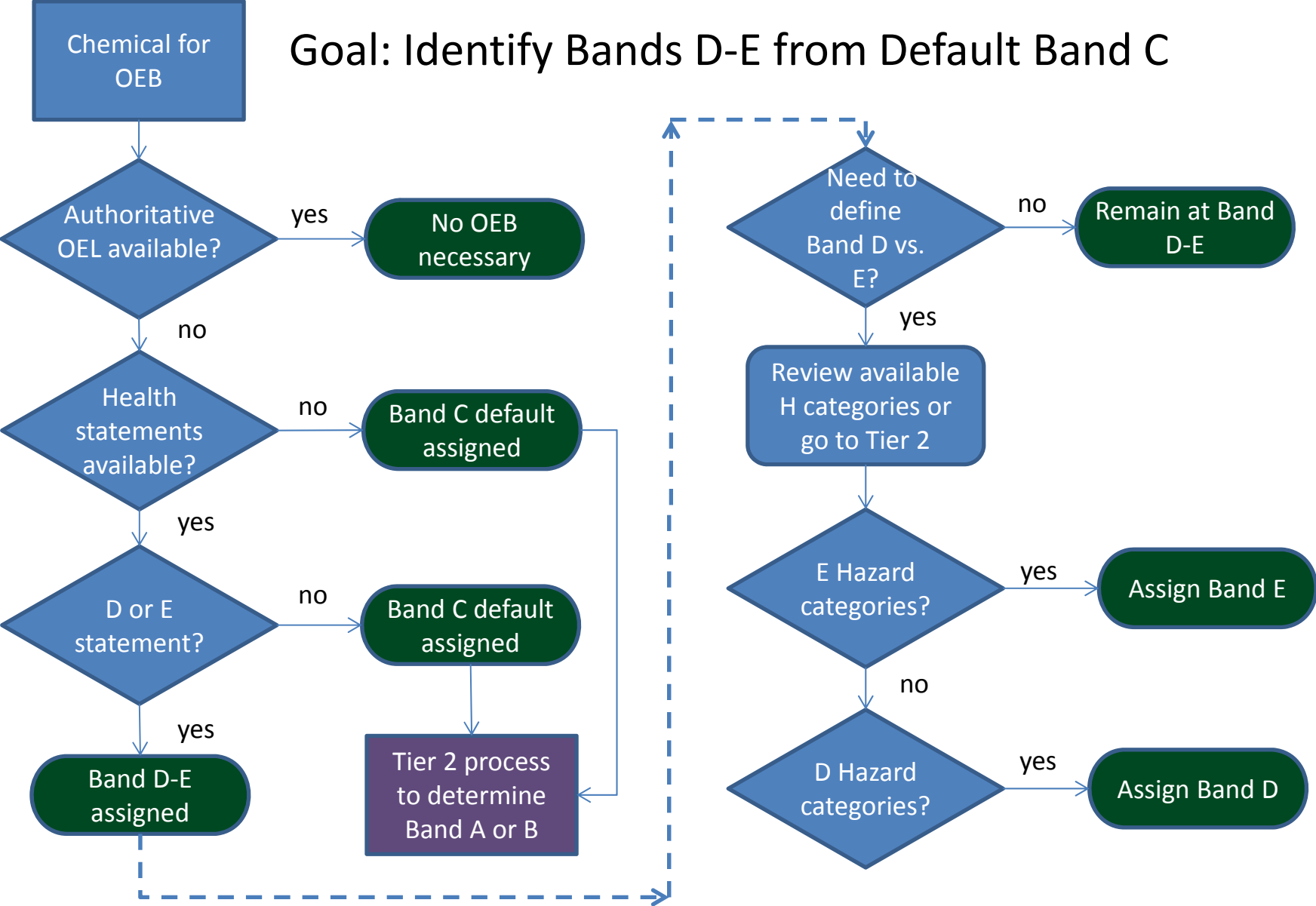
- ECHA classification and labeling inventory (includes Annex VI): <http://echa.europa.eu/regulations/clp/cl-inventory>

“Default” Band “C”

- Tier 1 process begins by determining whether data exists to move a chemical from “default” band C (> 10 and $< 100 \mu\text{g}/\text{m}^3$) to “D” or “E” band

Tier 1a and 1b

Goal: Identify Bands D-E from Default Band C



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

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

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

Band	A	B	C	D	E Consider "Ceiling" for respiratory sensitizers
GHS Signal Word		Warning	Warning	Danger	Danger
GHS Hazard Category		1B (skin)	1A (skin)	1B (resp.)	1A (resp.)
GHS Respiratory and Skin Sensitization Hazard Statements		May cause an allergic skin reaction	May cause an allergic skin reaction	May cause allergy or asthma symptoms or breathing difficulties if inhaled	May cause allergy or asthma symptoms or breathing difficulties if inhaled
Respiratory and Skin Sensitization "H" Codes		H317	H317	H334	H334

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

Band	A	B	C	D	E
GHS Signal Word		Warning	Warning	Danger	Danger
GHS Hazard Category		2	2	1B	1A
GHS Carcinogenicity Hazard statement		Suspected of causing cancer	Suspected of causing cancer	May cause cancer	May cause cancer
Carcinogenicity "H" Codes		H351	H351	H350	H350

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

- NIOSH Pocket Guide: <http://www.cdc.gov/niosh/npg/>
- IUCLID 5: <http://iuclid.eu/>
- OECD Chem Portal
http://www.echemportal.org/echemportal/index?pageID=0&request_locale=en
- National Library of Medicine ToxNet:
<http://toxnet.nlm.nih.gov/>
- ECHA registered substances database:
<http://echa.europa.eu/en/information-on-chemicals/registered-substances>
- GESTIS: <http://www.dguv.de/ifa/en/gestis/stoffdb/index.jsp>
- ATSDR: <http://www.atsdr.cdc.gov/mrls/mrllist.asp>

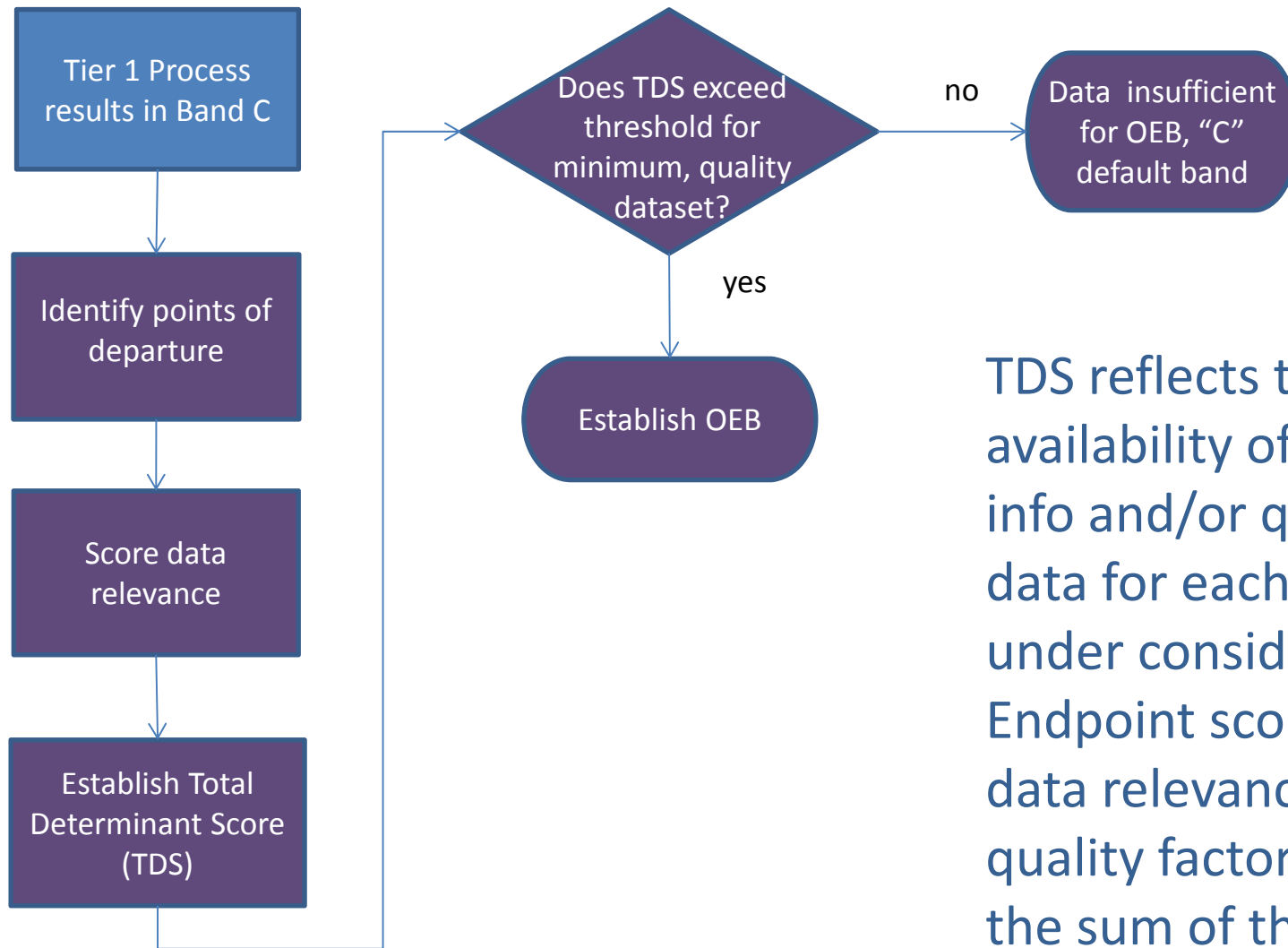
Tier 2 Data Weight

<ul style="list-style-type: none">• Carcinogenicity• Reproductive toxicity• Specific target organ toxicity repeated exposure	15
<ul style="list-style-type: none">• Specific target organ toxicity, single exposure• Germ cell mutagenicity (<i>in vivo</i>)*• Respiratory sensitization**	10
<ul style="list-style-type: none">• Acute toxicity• Skin corrosion/irritation• Serious eye damage/eye irritation• Germ cell mutagenicity (<i>in vitro</i>)*• Skin sensitization**	5

**use weight of evidence*

Tier 2

Can Band A or B be considered?



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

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

POI = point of impact

Next Steps for NIOSH Matrix: Validate

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