Occupational Exposure Banding 2.0: A Preliminary Case Study

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Occupational Exposure Banding Objective

To create a consistent and documented process to characterize chemical hazards so timely and well-informed risk management decisions can be made for chemicals lacking OELs.

What is Occupational Exposure Banding?

A mechanism to quickly and accurately assign chemicals into "categories" or "bands" based on their health outcomes and potency considerations

A	B	C	D	E

Higher Concentrations   Lower Concentrations

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NIOSH Occupational Exposure Bands

Occupational Exposure Band	Airborne Target Range	
	for Particulate Concentration (mg/m³)	for Gas or Vapor Concentration (ppm)
A	>10mg/m³	>100 ppm
B	>1 to 10 mg/m³	>10 to 100 ppm
C	>0.1 to 1 mg/m³	>1 to10 ppm
D	>0.01 to 0.1 mg/m³	>0.1 to 1 ppm
E	≤0.01 mg/m³	≤0.1 ppm

How is the Banding Process Organized?

Bands are assigned based on:
- acute toxicity
- skin corrosion and irritation
- serious eye damage and irritation
- respiratory sensitization
- skin sensitization
- genotoxicity
- carcinogenicity
- reproductive/developmental toxicity
- specific target organ toxicity resulting from repeated exposure

Tier 1 —GHS Hazard Codes

<u>User</u>: Health and safety generalist

A Tier 1 evaluation utilizes GHS Hazard Statements and Categories to identify chemicals that have the potential to cause irreversible health effects.

Tier 2— Secondary Data Sources

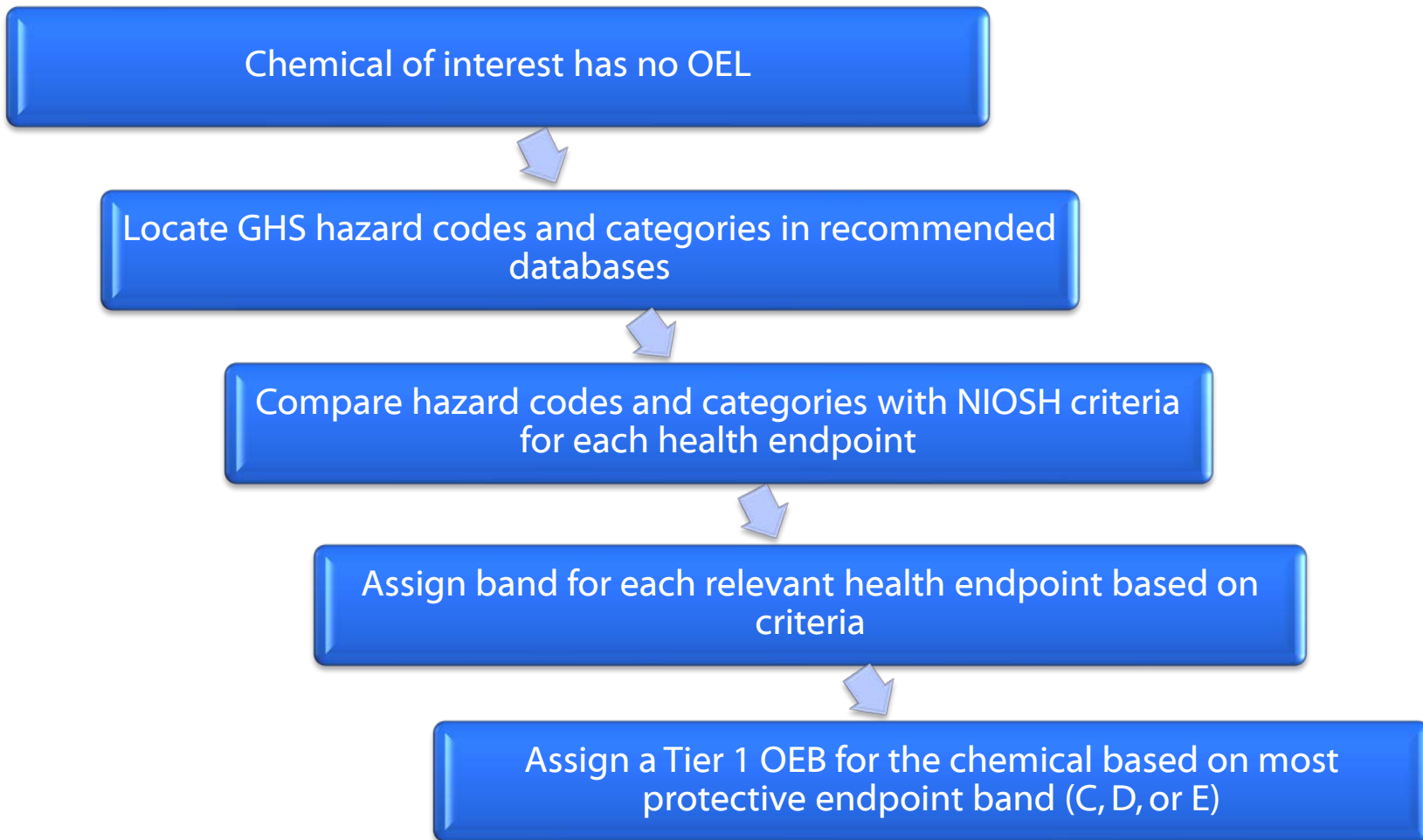<u>User</u>: Properly trained occupational hygienist

A Tier 2 evaluation produces a more refined OEB, based on point of departure data from reliable sources. Data availability and quality are considered.

Tier 3—Expert Judgement

<u>User</u>: Toxicologist or experienced occupational hygienist

Tier 3 involves the integration of all available data and determining the degree of conviction of the outcome.

TIER 1 OVERVIEW

Chemical of interest has no OEL

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Locate GHS hazard codes and categories in recommended databases

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Compare hazard codes and categories with NIOSH criteria for each health endpoint

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Assign band for each relevant health endpoint based on criteria

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Assign a Tier 1 OEB for the chemical based on most protective endpoint band (C, D, or E)

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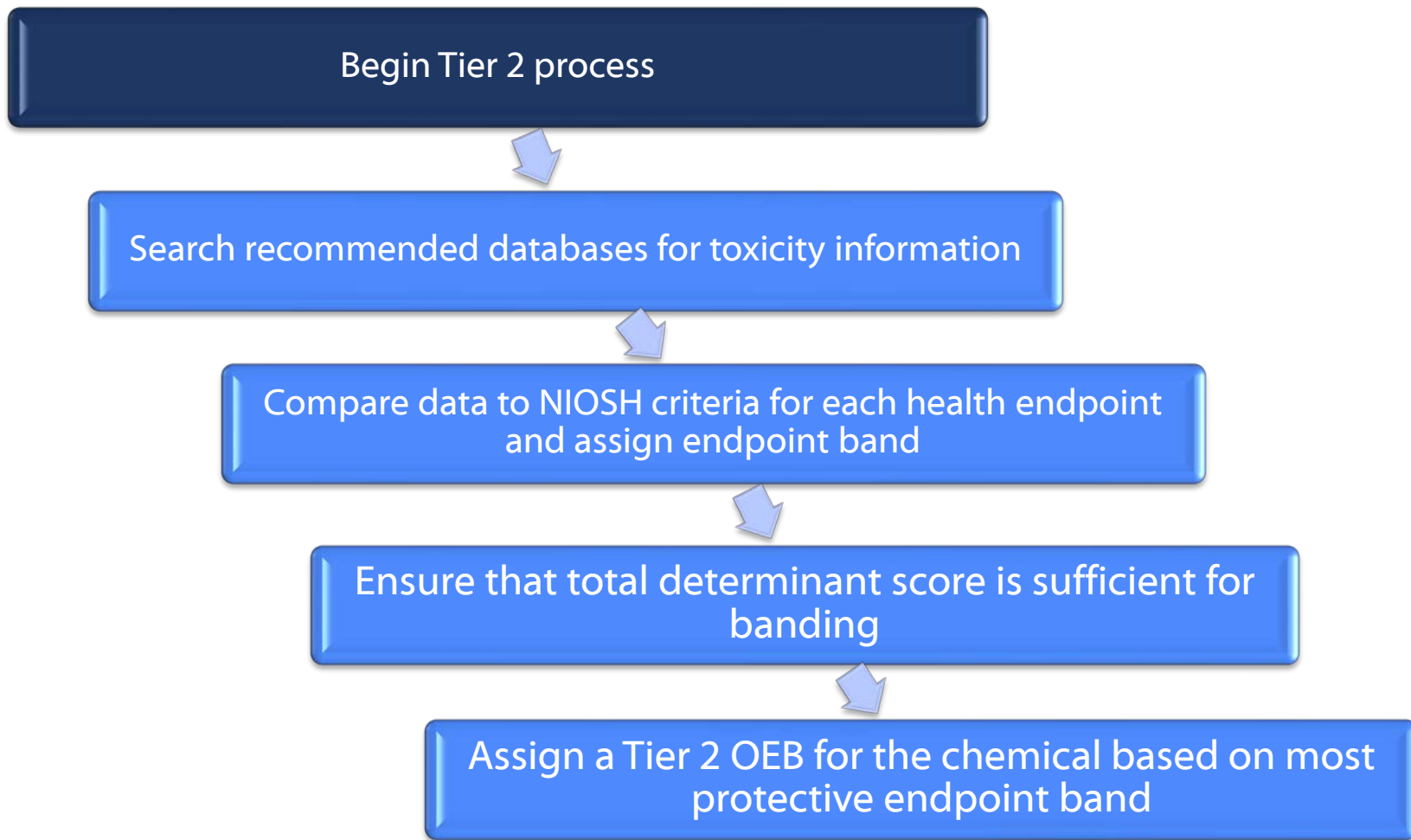| TIER 1 Criteria		C	D	E
OEL Ranges	**Particle**	> 0.1 to ≤ 1 mg per cubic meter of air (mg/m³)	> 0.01 to ≤ 0.1 mg/m³	≤ 0.01 mg/m³
	Vapor	> 1 to ≤ 10 parts per million (ppm)	> 0.1 to ≤ 1 ppm	≤ 0.1 ppm
Acute Toxicity		H301 Category 3 H302 Category 4 H331 Category 3 H332 Category 4 H311 Category 3 H312 Category 4	H300 Category 2 H330 Category 2 H310 Category 2	H300 Category 1 H330 Category 1 H310 Category 1
Skin Corrosion/ Irritation		H315 Category 2		H314 Category 1, 1A, 1B, or 1C
Serious Eye Damage/ Eye irritation		H319 Category 2, 2A or 2B		H318 Category 1
Respiratory and Skin Sensitization		H317 Category 1B	H317 Category 1 or 1A	
			H334 Category 1B	H334 Category 1 or 1A
Genotoxicity			H341 Category 2	H340 Category 1, 1A or 1B
Carcinogenicity				H350 Category 1, 1A, or 1B H351 Category 2
Toxic to Reproduction		H361 (including H361f, H361d, and H361fd) Category 2	H360 (including H360f, H360d, and H360fd) Category 1B	H360 (including H360f, H360d, and H360fd) Category 1 or 1A
Specific Target Organ Toxicity		H371 Category 2 H373 Category 2		H370 Category 1 H372 Category 1

Tier 2

Tier 2 is always recommended, but especially useful when:

- there are no GHS H codes
- the outcome of the Tier 1 analysis is incomplete, or an insufficient reflection of the health potency of the chemical

Tier 2

Tier 2 – Both Qualitative and Quantitative

- Some training in toxicology

- Based on readily available secondary data from authoritative sources (government, professional health agencies, authoritative toxicological benchmarks)

- Needs sufficient data to generate reliable OEB

- Prescriptive analytical strategy to ensure consistency

- Potential for chemicals to be moved from the Tier 1 OEB to a more or less protective OEB

TIER 2 OVERVIEW

Begin Tier 2 process

Search recommended databases for toxicity information

Compare data to NIOSH criteria for each health endpoint and assign endpoint band

Ensure that total determinant score is sufficient for banding

Assign a Tier 2 OEB for the chemical based on most protective endpoint band

Chemical Name: Rane Test 1
CAS Number: 1

Liquid/Vapor Range: <= 0.1 ppm
Particle Range: <= 0.01 mg/m³

Recommended Band			TDS=85	E
Endpoint	**Source**	**Data**	**EDS**	**Endpoint Band**
Carcinogenicity Quant	EPA IRIS Slope Factor	1 x 0.00001 (mg/kg-day)$^{-1}$	30	C
	California Slope Factor	1 x 0.000001 (mg/kg-day)$^{-1}$		C
Carcinogenicity WOE	U.S. EPA IRIS	Group C (possible human carcinogen)	20	D
Reproductive Toxicity				
Target-Organ Toxicity	U.S. EPA: IRIS	Rank 1; NOAEL; 90 hrs; 4.8 ppm	30	E
Genotoxicity Toxicity				
Respiratory Sensitization	WHO: International Programme on Chemical Safety	Rank: 1; Results: Mixed	10	C
Skin Sensitization				
Acute Toxicity	National Library of Medicine ChemID Plus	Rank: 1; Type: Oral LD50; Duration: 4.00 hrs; Input: 661	5	B
Skin Irritation	WHO: International Programme on Chemical Safety	Rank: 1; Results: Skin corrosion/irreversible effects	5	E
	Organization for Economic Co-operation and Development	Rank: 1; Results: Moderate to severe irritation		C
Eye Irritation	WHO: International Programme on Chemical Safety	Rank: 1; Results: Irreversible eye damage	5	E
Notes	**Carcinogenicity:** Cancer Test Information: https://ntp.niehs.nih.gov/pubhealth/roc/index.html			
	STOT: STOT Test Information: https://ntp.niehs.nih.gov/testing/types/heathandsafety/index.html			
	Acute Tox: Acute Toxicity Information: http://www.inchem.org/			

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Tier 2 Endpoints with Quantitative Criteria

- Carcinogenicity
  - Potency estimate (inhalation unit risk, slope factor)
  - *Qualitative assessment (Y/N in absence of potency determination)*
- Reproductive toxicity (includes developmental toxicity)
  - Potency based on NOAEL, BMDL, BMCL
- Specific target organ toxicity
  - Potency based on NOAEL, BMDL, BMCL
- Skin sensitization
  - Potency based on LLNA, GPMT, Beuhler
  - *Qualitative assessment (Y/N in absence of potency determination)*
- Acute toxicity
  - Potency based on LD_{50}, LC_{50}

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Tier 2 Endpoints with Qualitative Criteria

- Genotoxicity
  - Positive, mixed, negative results
- Respiratory Sensitization
  - Positive, mixed, negative results
- Skin Irritation or Corrosion
  - Non-irritating, mild to moderate, moderate to severe, irreversible
- Eye irritation or Damage
  - Non-irritating, mild to moderate, moderate to severe, irreversible

Tier 3 banding process

- Requires expert in toxicology
- Requires intensive review and evaluation of primary data
- Is required when insufficient data for Tier 2 banding
- No detailed guidance is available

Problem

- Many chemicals would not meet minimum data set requirement
  - What is the best way to consider chemicals with insufficient data?
- Are read-across or QSAR methods reliable enough to use?
- Are read-across or QSAR methods simple enough to use with a broad audience?
  - What are the uncertainties associated with these methods?
- How can these methods be reliably and reproducibly used to predict toxicity?

Potential Solution?

- **Read-across methods**
  - Strengths and weaknesses?
  - How much data is needed on other chemicals?
  - How are classes of chemicals defined reproducibly?
- **QSAR**
  - Expert- or data-driven?
  - What are the boundaries of the chemical structures that could be considered?
  - Strengths and weaknesses?

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Other Solutions?

- What other methods should NIOSH consider?
- Are there existing methods that would serve or could be adapted?
  - Strengths and weaknesses?
  - Reproducibility?
  - Reliability?

Let's Discuss!