THE NIOSH CHEMICAL CARCINOGEN POLICY:
CLASSIFYING CHEMICAL CARCINOGENS AND ESTABLISHING A TARGET RISK LEVEL

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THE FINDINGS AND CONCLUSIONS IN THIS PRESENTATION HAVE NOT BEEN FORMALLY DISSEMINATED BY THE NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH AND SHOULD NOT BE CONSTRUED TO REPRESENT ANY AGENCY DETERMINATION OR POLICY.
CANCER POLICY: THREE POLICIES

- Carcinogen Classification
- Carcinogen Risk Management Limit
- Analytical feasibility
<table>
<thead>
<tr>
<th>CARCINOGEN CLASSIFICATION: AUTHORITATIVE CLASSIFICATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NTP</strong></td>
</tr>
<tr>
<td>• Known to be a human carcinogen</td>
</tr>
<tr>
<td>• Reasonably anticipated to be a human carcinogen</td>
</tr>
<tr>
<td><strong>EPA</strong></td>
</tr>
<tr>
<td>• Group A, Group B1, Group B2, Group C</td>
</tr>
<tr>
<td>• Carcinogenic to humans, Likely to be carcinogenic to humans, Suggestive evidence of carcinogenic potential</td>
</tr>
<tr>
<td><strong>IARC</strong></td>
</tr>
<tr>
<td>• Group 1, Group 2A, Group 2B</td>
</tr>
</tbody>
</table>
WHY DIDN’T NIOSH CONSTRUCT A CLASSIFICATION SCHEME?

- Many existing schemes to choose from (and all are similar in strategy)
- Risk management strategies do not change based on degree of certainty in classification
- In the event that NIOSH classifies a carcinogen, the Globally Harmonised System (GHS) scheme is appropriate
Initially, planned a retrospective adjustment of the chemical classifications in the *NIOSH Pocket Guide to Chemical Hazards*

This has proven not immediately feasible

Existing classifications remain [Ca] and the list of NIOSH carcinogens is not entirely consistent with EPA, IARC or NTP.
CARCINOGEN CLASSIFICATION: OCCUPATIONAL RELEVANCE

Industrial usage

- Worker exposures
- Current production/import/use

Science review

- Is evidence current?
- Do new sources of information cast doubt on classification?
IF NO AUTHORITATIVE CLASSIFICATION

NTP Review
- NIOSH can nominate to NTP for review of evidence

NIOSH Review
- If NTP declines, or chemical is of particular interest to NIOSH, NIOSH can review
- Criteria to be used are GHS Cancer Classification Criteria
Why? Concern that known human carcinogens, such as asbestos, benzene and cadmium, shouldn’t be characterized as “potential.”
No more RELs for Carcinogens!
RISK MANAGEMENT LIMITS FOR CARCINOGENS (RML-CA)

Acknowledges there is no known safe level for carcinogens

Provides a starting place for employers to control exposures to lower levels

When data permit, RML-CA is set at target risk level

May be set at limit of quantification when
  • LOQ > dose at target risk
  • No risk quantification possible
Currently, as we review individual chemicals, classifications are made consistent with the Carcinogen Policy.

Result: the Pocket Guide will go through an awkward stage where policies from different time periods apply to different chemicals.

Example: one chemical may have no numerical REL, but a Ca designation. Another chemical may be a NIOSH occupational carcinogen with a numerical RML-Ca.
### Analytical Feasibility

- If higher than risk estimate at 1/10,000, LOQ will drive the RML-CA
- If used for RML-CA, risk estimated at LOQ

### Engineering Achievability

- No longer considered in setting exposure limits
- Information on controlling exposures will continue to be provided
Quantitative exposure-response data are gathered

Statistical modeling of exposure-response data

Central tendency and lower confidence limit for a range of risks are estimated (1/100-1/1,000,000)

RML-CA is set at the lower confidence limit on the 1/10,000 risk (10X lower than previous practice) *(unless it is lower than LOQ)*
Target risk level needed to set RML-CA. Target risk level is defined as the lower 95% confidence limit on the concentration corresponding to a risk estimate of 1 excess cancer per 10,000 workers exposed for a 45-year working lifetime.
APPROACHING THE PROBLEM

NIOSH sought:
- Input of peer reviewers
- Stakeholders’ comments
- Other regulatory and recommending organizations’ comments
- Discussions with bioethicists
ISSUES IN DERIVING A TARGET RISK LEVEL FOR CANCER

- Revising the Carcinogen Policy gave us a chance to rethink target risk
  - Is cancer risk different from other chronic health endpoints?
  - Are occupational exposures “different” from environmental exposures?
  - What language is used to describe the risk level?
  - What level is the “right” level?
  - What evidence supports target risk level?
IS CANCER RISK DIFFERENT FROM OTHER CHRONIC HEALTH ENDPOINTS?

- Cancer as a health endpoint
  - Seriousness
  - Irreversibility
  - Dread

- Other health endpoints?
  - Lung disease (pneumoconiosis, COPD)
  - Neurological endpoints
  - Reproductive and/or developmental hazards
  - Chronic target organ toxicity (liver, kidney damage)
ARE OCCUPATIONAL EXPOSURES “DIFFERENT” FROM ENVIRONMENTAL EXPOSURES?

- Environmental organizations have considered environmental risks from 1/10,000 to 1/1,000,000 to support environmental regulations.
  - Should risks to workers be higher?
  - Should the benefits conferred from working be considered in setting a target risk?
WHAT LANGUAGE IS USED TO DESCRIBE THE RISK LEVEL?
More complex than it seems. Fraught with “loaded language”.

- Acceptable risk, minimal risk, negligible risk, target risk, maximum tolerated risk, just about tolerable risk . . .
Why “acceptable risk” is not always an “acceptable” term

Importance of risk communication
- Comparison of risks – advantages and pitfalls
- Ignoring the denominator issue
WHAT LEVEL IS THE “RIGHT” TARGET LEVEL OF RISK?

- Considerations in setting target level of risk
  - Whether it is explicit or not, there is always a risk/benefit
  - Under-protection leaves too many at risk
  - Over-protection may force substitution into riskier solutions, other hazards
  - Striving for “reasonableness” – but who determines what is reasonable?
WHAT EVIDENCE SUPPORTS TARGET RISK LEVEL?

- Scientific evidence versus policy determination
  - Societal decisions – whose values are represented?
  - The ever-present “reasonable” human
  - Factors of 10
  - Precedents
NIOSH HISTORY OF TARGET RISK

- 1970s: No acceptable exposures to carcinogens (the Delaney Clause)
- 1980: U.S. Supreme Court “Benzene Decision” characterized a range of acceptable risks between 1 in 1000 and 1 in a billion
  - Stated that 1 in 1000 could be considered a significant risk
    - How OSHA has interpreted 1 in 1000 (residual significant risk)
    - How NIOSH has interpreted 1 in 1000 (consistency with OSHA)
HISTORY OF USE OF 1 IN 1000 RISK LEVEL

- 1990 Benzene PEL (journal article, testimony to OSHA)
- 1990 Cadmium PEL (testimony to OSHA)
- 1991 1,3-Butadiene PEL (testimony to OSHA)
- 1995 Coal dust (REL) – NON-cancer
- 1998 Diesel exhaust (journal article)
- 2001 Silica (journal article)
2007 Manganese (journal article) – NON-cancer
2011 Titanium dioxide (RELs)
2012 Carbon nanotubes and nanofibers (REL) – NON-cancer
2013 Hexavalent chromium (REL)
2016 Diacetyl/2,3-Pentanedione (RELs) – NON-cancer
Surveyed other organizations that set target risk levels

Compared (when possible) to previous NIOSH position, noting rationale
### Table 1: Risk levels used for limiting exposure to carcinogenic compounds in the workplace and in the environment.

<table>
<thead>
<tr>
<th></th>
<th>Risk period</th>
<th>Exposure period</th>
<th>Risk level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Occupational Health and Safety</strong></td>
<td>Prohibitive risk</td>
<td>Life</td>
<td>Working life: $4 \times 10^{-3}$</td>
</tr>
<tr>
<td></td>
<td>Target risk</td>
<td>Life</td>
<td>Working life: $4 \times 10^{-5}$</td>
</tr>
<tr>
<td><strong>Environment</strong></td>
<td>Maximum tolerable risk</td>
<td>Life</td>
<td>Lifetime: $1 \times 10^{-4}$</td>
</tr>
<tr>
<td></td>
<td>Negligible risk</td>
<td>Life</td>
<td>Lifetime: $1 \times 10^{-6}$</td>
</tr>
</tbody>
</table>

*a For the calculation of the risk related to the exposure during a full (working) lifetime, a period of 40 years for workplace exposure and a period of 100 years for environmental exposure is taken into account.*
Acceptable risk (annual)

- 1 in 1000 per year as the ‘just about tolerable risk’ for any substantial category of workers for any large part of a working life.
- 1 in 10,000 as the ‘maximum tolerable risk’ for members of the public from any single non-nuclear plant.
- 1 in 100,000 as the ‘maximum tolerable risk’ for members of the public from any new nuclear power station.
- 1 in 1,000,000 as the level of ‘acceptable risk’ at which no further improvements in safety need to be made.
The **tolerable risk** defines the additional cancer risk of **4:1,000** that is tolerated, meaning that, statistically, 4 out of 1,000 persons exposed to the substance throughout their working life will develop cancer.

*This value corresponds to the lung cancer risk of a non-smoker who is not exposed to hazardous substances at work.*

The **acceptable risk** defines the additional cancer risk of **4:10,000** that is accepted during an initial phase ... this will be reduced to **4 out of 100,000 cases**.

*This value corresponds to the risk of cancer outside the workplace (“remaining general environmental risk”).*
Acceptable risk for genotoxic carcinogens of 1/100,000
- Acceptable risk = 1/10,000 (annual)
- “Career” deployments ~ 10 yrs = 1/1000 “working lifetime” risk.
SUMMARY

Relies on NTP, EPA and IARC for carcinogen classification

Sets new terminology (occupational carcinogen and RML-CA)

Changes our long-held policy on target risk to 1/10,000

When the LOQ > 1/10,000 risk level, LOQ = RML-CA
Questions?
NIOSH OCCUPATIONAL EXPOSURE BANDING PROCESS

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- Pranav Rane, M.P.H
- Melissa Seaton, M.S.,
- Christine Whittaker, Ph.D.
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.
An OEB is not meant to replace an OEL, rather it serves as a starting point to inform risk management decisions.
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.
### Proposed NIOSH Occupational Exposure Bands

<table>
<thead>
<tr>
<th>Occupational Exposure Band</th>
<th>Airborne Target Range for Particulate Concentration (mg/m³)</th>
<th>Airborne Target Range for Gas or Vapor Concentration (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>&gt;10 mg/m³</td>
<td>&gt;100 ppm</td>
</tr>
<tr>
<td>B</td>
<td>&gt;1 to 10 mg/m³</td>
<td>&gt;10 to 100 ppm</td>
</tr>
<tr>
<td>C</td>
<td>&gt;0.1 to 1 mg/m³</td>
<td>&gt;1 to 10 ppm</td>
</tr>
<tr>
<td>D</td>
<td>&gt;0.01 to 0.1 mg/m³</td>
<td>&gt;0.1 to 1 ppm</td>
</tr>
<tr>
<td>E</td>
<td>≤0.01 mg/m³</td>
<td>≤0.1 ppm</td>
</tr>
</tbody>
</table>
IS THIS THE SAME AS CONTROL BANDING? NO.

- **COSHH Essentials** is a control banding tool that helps small and medium-sized enterprises to do risk assessments for chemicals and mixtures of chemicals
  - identifies the control band (control approach),
  - produces advice on controlling risk from the chemical used in the specified task, and
  - provides written guidance and documentation as a result of the assessment
- NIOSH has reviewed control banding strategies previously
- NIOSH Occupational Exposure Banding is NOT Control Banding
HOW IS THE PROCESS ORGANIZED?

Bands are assigned based on the findings for nine standard toxicological endpoints:

- 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
User: 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
User: 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
User: Toxicologist or experienced occupational hygienist
Tier 3 involves the integration of all available data and determining the degree of conviction of the outcome.
Globally Harmonized System of Classification and Labeling of Chemicals

- GHS is a hazard classification system developed by the United Nations to standardize chemical regulations in different countries
  - Within GHS, each physical or health hazard is a hazard class (e.g., Carcinogenicity is a hazard class)
  - A hazard class may be sub-divided into several hazard categories based on the severity of the hazard
  - GHS uses alphanumeric hazard codes to represent these hazards
Chemical of interest has no OEL

Locate GHS hazard codes and categories in recommended databases

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

Assign band for each relevant health endpoint based on criteria

Assign a Tier 1 OEB for the chemical based on most protective endpoint band (C, D, or E)
<table>
<thead>
<tr>
<th>TIER 1 Criteria</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Particle</strong></td>
<td>&gt; 0.1 to ≤ 1 milligrams per cubic meter of air (mg/m³)</td>
<td>&gt; 0.01 to ≤ 0.1 mg/m³</td>
<td>≤ 0.01 mg/m³</td>
</tr>
<tr>
<td><strong>Vapor</strong></td>
<td>&gt; 1 to ≤ 10 parts per million (ppm)</td>
<td>&gt; 0.1 to ≤ 1 ppm</td>
<td>≤ 0.1 ppm</td>
</tr>
</tbody>
</table>

**Acute Toxicity**

- **H301** Category 3
- **H302** Category 4
- **H331** Category 3
- **H332** Category 4
- **H311** Category 3
- **H312** Category 4

**Skin Corrosion/ Irritation**

- **H315** Category 2

**Serious Eye Damage/ Eye irritation**

- **H319** Category 2, 2A or 2B

**Respiratory and Skin Sensitization**

- **H317** Category 1B
- **H334** Category 1B
- **H341** Category 2

**Genotoxicity**

- **H361** (including H361f, H361d, and H361d)

**Carcinogenicity**

- **H360** (including H360f, H360d, and H360d)

**Toxic to Reproduction**

- **H371** Category 2
- **H373** Category 2

**Specific Target Organ Toxicity**

- **H370** Category 1
- **H372** Category 1
RELIABLE SOURCES FOR TIER 1

- GESTIS SubstanceDatabase
  www.dguv.de/ifa/gestis-database

- ECHA Annex VI to CLP
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 — 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
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
TIER 2 BANDING PROCESS

- **Search authoritative databases for summary toxicity information:**
  For 9 specified health endpoints, search authoritative databases for summary toxicity information

- **Combine information through a weighted score:**
  Find the weighted score (Total Determinant Score) and calculate the Occupational Exposure Band (this is done automatically in the e-Tool)
**TOTAL DETERMINANT SCORE**

- **Endpoint determinant score (EDS)** = weighted score indicating the presence/absence of data for a specific health endpoint.

- **Total determinant score (TDS)** = sum of weighted scores for each health endpoint. Overall score gives an indication of sufficiency of data for banding. **TDS ≥ 30**: sufficient data for banding in Tier 2

**Example:** a cancer inhalation unit risk value tells us a lot about the hazardous nature of a chemical, so the presence of that information corresponds to a TDS of 30. However, an LD<sub>50</sub> value for the acute toxicity endpoint is only weighted as a TDS of 5.
<table>
<thead>
<tr>
<th>Health Endpoint</th>
<th>Endpoint Determinant Score (EDS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Irritation/Corrosion</td>
<td>5</td>
</tr>
<tr>
<td>Eye Irritation/Corrosion</td>
<td>5</td>
</tr>
<tr>
<td>Skin Sensitization</td>
<td>5</td>
</tr>
<tr>
<td>Acute Toxicity/Lethality ($LD_{50}$ or $LC_{50}$)</td>
<td>5</td>
</tr>
<tr>
<td>Genotoxicity</td>
<td>5</td>
</tr>
<tr>
<td>Respiratory Sensitization</td>
<td>10</td>
</tr>
<tr>
<td>Systemic Target Organ Toxicity (STOT-RE)</td>
<td>30</td>
</tr>
<tr>
<td>Reproductive and Developmental Toxicity</td>
<td>30</td>
</tr>
<tr>
<td>Cancer Weight of Evidence Descriptor</td>
<td>20 or 30</td>
</tr>
<tr>
<td>Cancer Quantitative Measures</td>
<td>30</td>
</tr>
<tr>
<td>Data Sufficiency/Total Determinant Score (TDS)</td>
<td>30/125</td>
</tr>
</tbody>
</table>
### Recommendation --- Rane Test 1(1)

**Chemical Name:** Rane Test 1  
**CAS Number:** 1  
**Liquid/Vapor Range:** <= 0.1 ppm  
**Particle Range:** <= 0.01 mg/m³

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Source</th>
<th>Data</th>
<th>TDS-85</th>
<th>E</th>
<th>Endpoint Band</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinogenicity Quant</td>
<td>EPA IRIS Slope Factor</td>
<td>1 x 0.00001 (mg/kg-day)¹</td>
<td>30</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td></td>
<td>California Slope Factor</td>
<td>1 x 0.000001 (mg/kg-day)¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinogenicity WOE</td>
<td>U.S. EPA IRIS</td>
<td>Group C (possible human carcinogen)</td>
<td>20</td>
<td>D</td>
<td></td>
</tr>
<tr>
<td>Reproductive Toxicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target-Organ Toxicity</td>
<td>U.S. EPA: IRIS</td>
<td>Rank 1; NOAEL; 90 hrs; 4.8 ppm</td>
<td>30</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td>Genotoxicity Toxicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory Sensitization</td>
<td>WHO: International Programme on Chemical Safety</td>
<td>Rank: 1; Results: Mixed</td>
<td>10</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Skin Sensitization</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute Toxicity</td>
<td>National Library of Medicine ChemID Plus</td>
<td>Rank: 1; Type: Oral LD50; Duration: 4.00 hrs; Input: 661</td>
<td>5</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>Skin Irritation</td>
<td>WHO: International Programme on Chemical Safety</td>
<td>Rank: 1; Results: Skin corrosion/irreversible effects</td>
<td>5</td>
<td>E</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Organization for Economic Co-operation and Development</td>
<td>Rank: 1; Results: Moderate to severe irritation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Irritation</td>
<td>WHO: International Programme on Chemical Safety</td>
<td>Rank: 1; Results: Irreversible eye damage</td>
<td>5</td>
<td>E</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:**  
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
TIER 1 EVALUATION: VAPORS

AGREEMENT BETWEEN OEL AND OEB: VAPORS

- OEB IS MORE PROTECTIVE THAN THE LOWEST OEL: 55.5% (227)
- OEB RANGE CONTAINS THE OEL: 35.2% (144)
- OEB IS 1 BAND LESS PROTECTIVE THAN LOWEST OEL: 7.8% (32)
- OEB IS 2 BANDS LESS PROTECTIVE THAN THE LOWEST OEL: 1.4% (6)
### TIER 1 EVALUATION: PARTICLES

**AGREEMENT BETWEEN OEL AND OEB: PARTICLES**

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>OEB is more protective than the lowest OEL</td>
<td>132</td>
<td>69.1%</td>
</tr>
<tr>
<td>OEB range contains the OEL</td>
<td>46</td>
<td>24.1%</td>
</tr>
<tr>
<td>OEB is 1 band less protective than lowest OEL</td>
<td>10</td>
<td>5.2%</td>
</tr>
<tr>
<td>OEB is 2 bands less protective than the lowest OEL</td>
<td>3</td>
<td>1.6%</td>
</tr>
</tbody>
</table>
Minimum OEL values banded vs. NIOSH Overall Tier 2 Band
(o = vapors, + = particles)
(n=46)
https://www.cdc.gov/niosh/topics/oeb/default.html
**CASE STUDY: BISPHENOL A**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Hazard Code</th>
<th>Hazard Category</th>
<th>Hazard Statement</th>
<th>Endpoint Band</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Toxicity</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin Corrosion/Irritation</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye Damage/Iritation</td>
<td>H318</td>
<td>1</td>
<td>Causes serious eye damage</td>
<td>E</td>
</tr>
<tr>
<td>Respiratory and Skin Sensitization</td>
<td>H317</td>
<td>1</td>
<td>May cause an allergic skin reaction</td>
<td>D</td>
</tr>
<tr>
<td>Germ Cell Mutagenicity</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive Toxicity</td>
<td>H360F</td>
<td>1B</td>
<td>Suspected of damaging fertility</td>
<td>D</td>
</tr>
<tr>
<td>Specific Target Organ Toxicity - Repeated Exposure</td>
<td>None</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Table 2. Tier 1: Occupational exposure banding results for BPA under Draft NIOSH Occupational Exposure Banding Process.*
# BISPHENOL A TIER 2 RESULTS

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Health Effect</th>
<th>Number of data points/study info</th>
<th>Endpoint Band</th>
<th>Endpoint Determinant Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute toxicity</td>
<td>LD$_{50}$</td>
<td>10; guinea pig, mouse, rabbit, rat; oral</td>
<td>A</td>
<td>5/5</td>
</tr>
<tr>
<td>Skin corrosion/irritation</td>
<td>Descriptor</td>
<td>2; dermal</td>
<td>A</td>
<td>5/5</td>
</tr>
<tr>
<td>Eye damage/irritation</td>
<td>Descriptor</td>
<td>1</td>
<td>E</td>
<td>5/5</td>
</tr>
<tr>
<td>Respiratory sensitization</td>
<td>No data</td>
<td></td>
<td></td>
<td>0/5</td>
</tr>
<tr>
<td>Skin sensitization</td>
<td>LLNA</td>
<td>2; 1 (case report)</td>
<td>A (E)</td>
<td>5/5</td>
</tr>
<tr>
<td>Genotoxicity</td>
<td>Descriptor</td>
<td>3</td>
<td>A</td>
<td>5/5</td>
</tr>
<tr>
<td>Carcinogenicity</td>
<td>No data</td>
<td></td>
<td></td>
<td>0/30</td>
</tr>
<tr>
<td>Reproductive toxicity</td>
<td>NOAEL</td>
<td>21 Rat, mouse; oral; multigen</td>
<td>C or E (A-E)</td>
<td>30/30</td>
</tr>
<tr>
<td>Specific target organ</td>
<td>NOAEL</td>
<td>3 Mouse, rat; oral, inhalation</td>
<td>D (B-D)</td>
<td>3030</td>
</tr>
</tbody>
</table>
THANK YOU!