Assessing Tolerable Risks for Carcinogens and other Toxics Substances: 
*NIOSH Risk Assessment Activities*

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Disclaimer

- The findings and conclusions in this presentation have not been formally disseminated by the National Institute for Occupational Safety and Health (NIOSH) and should not be construed to represent any agency determination or policy.
Confusing Landscape

- Exposure recommendations and other health standards are important components of occupational health
  - What is a safe exposure?
  - What risks are represented by workplace conditions?

- Dozens of organizations and agencies develop occupational exposure recommendations worldwide

- Confusing landscape to navigate

Case Study 1 – Benzene

- Recognized human carcinogen

- How many occupational exposure limits (OELs) or other guidance values are available for benzene?
  1. Which value is the “best”? 
  2. What is the science behind the OEL?
  3. What is the basis of the OEL?
     - Health- or risk-based approaches
     - Technical achievability or analytical feasibility
     - Other
  4. Key assumptions?
  5. Uncertainties?
  6. Limitations?
Benzene – TWA Exposure Values

Benzene – Short-term Exposure Values
Benzene – Emergency Exposure Values

Overcoming the confusion

- Case study could be replicated for:
  - Cancer designations
  - Skin notations
  - Other exposure recommendations or health standards

- Increased transparency of the scientific principles and assumptions used in the underlying methodologies is critical
  - Increased understanding of the science
  - Increased communication of the strengths and weaknesses
  - Increased harmonization between organizations
Purpose

- Highlight on-going NIOSH risk-related activities
  - Quantitative Risk Assessments & Recommended Exposure Limit (REL) development
  - Carcinogen Policy Update

- Highlight underlying risk assessment processes and scientific principles

Why NIOSH conducts risk assessments

- NIOSH Mandate
  - OSH Act, Section 20 (a)(3)
    - “...develop criteria dealing with toxic materials and harmful physical agents and substances which will describe exposure levels that are safe for various periods of employment, including but not limited to exposure levels at which no employee will suffer impaired health or functional capacities or diminished life expectancy as a result of his work experience.”
Authoritative Recommendations

• NIOSH risk assessments are intended to:
  1. *Generate new knowledge* in the field of occupational safety and health and to *transfer that knowledge into practice* for the protection of workers

  2. Serve as the basis of authoritative recommendations
     - RELs
     - *Scientific decision-making strategies*
     - Skin notations
     - Immediately dangerous to life or health values

NIOSH Quantitative Risk Assessment

• NIOSH has conducted quantitative risk assessment and risk assessment methods research since 1986.

• Outputs include:
  - NIOSH RELs
  - Risk assessment journal articles
  - Conference presentations & workshops
NIOSH Risk Assessment Process

Systematic Process

Scientific Literature Review

Quantification of Risk

- Dose-response modeling
- Dosimetry modeling
- Uncertainty factors

Risk Estimate(s)

1. Scientific literature review
   - Identify critical health endpoint(s) and mode of action (MOA)
   - Identify critical dataset(s)
   - Identify data gaps and research needs
   - Applied to carcinogens and non-carcinogens

2. Quantification of risk
   - Estimation of excess lifetime risk of chronic effects
   - Selection of datasets and models
   - Baseline assumptions:
     - 45-years working lifetime
     - 40 hours/week exposure duration
     - Use most sensitive species, sex, health endpoint, etc.
Critical considerations during REL development

• Dose-response assessments and modeling
  – Foundation of OEL development
  – Facilitates the selection of point of departure (POD)
  – Non-linear (non-carcinogens) vs. Linear (carcinogens)
    • General rule

• Dosimetry methods and modeling
  – Estimation of internal dose
  – Link external exposure & biological response
  – Toxicokinetics & toxicodynamics

Critical considerations during REL development

• Uncertainty and modifying factors
  – Key component of human health risk assessment
  – Default uncertainty factors vs. Chemical-specific adjustment factors (CSAF)

• CSAF
  – Toxicodynamics
  – Toxicokinetics

*IPCS (2005)
Case Study 2 - Hexavalent Chromium [Cr(VI)]

- Systematic review
  - Critical health endpoint: Lung cancer
  - Epidemiological data:
    - Ohio chromate production facility
    - Maryland chromate production facility

- Quantification of risk
  - Estimated the excess lifetime risk of lung cancer deaths associated with Cr(VI) exposure
  - Exposure-response modeling (Park et al., 2004) based on Maryland chromate production facility (Gibbs et al. 2000)

Case Study 2 – Cr(VI)

- Considerations/assumptions
  - Epidemiological data suitable for extrapolating exposure-response
  - REL is intended to reduce workers’ lung cancer risk over a 45-year working lifetime
  - Risk estimates calculated from 1/500 to 1/100,000
  - Data supports the inclusion of workers exposed to all forms of Cr(VI)
  - Limited or no dosimetric adjustments needed
  - Analytical feasibility and technical achievability
Case Study 2 – Cr(VI)

- Revised REL = 0.2 µg Cr(VI)/m³
  - Excess lifetime risk of lung cancer of ~1/1,000 workers
- Previous REL
  - 1.0 µg Cr(VI)/m³
  - Excess lifetime risk of lung cancer ~6/1,000 workers

<table>
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<tr>
<th>Lifetime added risk* for a 45-year working lifetime</th>
<th>Cr(VI) exposure µg/m³ Cr</th>
<th>Cr(VI) exposure µg/m³ CrO₃</th>
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<tr>
<td>1 in 500</td>
<td>0.32</td>
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<td>1 in 1,000</td>
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<td>1 in 2,000</td>
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<tr>
<td>1 in 100,000</td>
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</table>

*Risk estimates from Park et al. [2004]

NIOSH Risk Assessment Process

-systematic process
- scientific literature review
- quantification of risk
  - dose-response modeling
  - dosimetry modeling
  - uncertainty factors
- risk estimate(s)

Internal and External Review
Dissemination

- NIOSH Numbered Publications
  - Criteria Document
  - Current Intelligence Bulletins
  - Hazard Reviews or Technical Reports

- Peer reviewed journal articles

NIOSH Carcinogen Policy

- **Potential Occupational Carcinogen (1978)**

- The NIOSH Pocket Guide lists 135 substances as carcinogens
  - Designation: Ca

- And NIOSH has developed RELs for most of these
NIOSH Carcinogen Policy

Key Milestones

- 1976: “No detectable exposure levels for proven carcinogenic substances”
  - Lowest feasible concentration

- 1978: Testimony on the OSHA Notice of Proposed Rulemaking on the Identification, Classification, and Regulation of Toxic Substances Posing a Potential Occupational Carcinogenic Risk
  - OSHA Carcinogen Policy

*NIOSH [2011]

NIOSH Carcinogen Policy

Key Milestones

- 1978: First use of the term “potential occupational carcinogen” in NIOSH Criteria Documents

- 1988: Testimony on the OSHA Proposed Rule on Air Contaminants which includes proposed updates on many OSHA Permissible Exposure Limits (PELs).
  - NIOSH reaffirms its policy that carcinogens should be restricted to the lowest feasible level.

*NIOSH [2011]
NIOSH Carcinogen Policy

- **Key Milestones**
  - 1995: NIOSH adopted a more inclusive policy due to advances in science, risk assessment and risk management
  
  - NIOSH REL Policy stated, “[RELs] will be based on risk evaluations using human or animal health effects data, and on an assessment of what levels can be feasibly achieved by engineering controls and measured by analytical techniques. To the extent feasible, NIOSH will project not only a no-effect exposure, but also exposure levels at which there may be residual risks. This policy applies to all workplace hazards, including carcinogens...”
  
  - Shift away from lowest feasible concentration

*NIOSH [2011]*

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NIOSH Carcinogen Policy Update

- In August 2011, NIOSH announced in the Federal Register (76 FR 52664) its intention to

  “review its approach to classifying carcinogens and establishing recommended exposure limits (RELs) for occupational exposures to hazards associated with cancer.”

- In short, concerns raised by NIOSH and stakeholders identified potential challenges in NIOSH’s carcinogen policy

- Currently, under review to ensure that it reflects current scientific and risk management practices

*NIOSH [2011]*
Challenges

• Use of the term “potential occupational carcinogen”
  – Conveys uncertainty about many known carcinogens (e.g. asbestos, benzene, and vinyl chloride)
  – How to incorporate levels of uncertainty in the policy

• Technical questions on developing RELs
  – Levels of residual risk
  – Meaning of the phrase “to the extent feasible”
  – Utility of the “action level” concept in RELs
  – How to incorporate advances in cancer science

Advances in Cancer Science*

• New understanding of mechanisms of chemical carcinogenesis

• Ability to screen large numbers of chemicals with high throughput technologies

• Ability to identify subgroups at high risk of cancer based on genetic or epigenetic data

• Ability to develop hazard and control bands for groups of chemicals based on available health effects data and exposure characteristics

*NIOSH [2011]
Critical Questions

1. Should there explicitly be a carcinogen policy as opposed to a broader policy on toxicant identification and classification (e.g. carcinogens, reproductive hazards, neurotoxic agents)?

   a) Carcinogens vs. Broader classification scheme
      • Prop 65 (California)

   *NIOSH [2011]

Critical Questions

2. What evidence should form the basis for determining that substances are carcinogens?
   – How should these criteria correspond to nomenclature and categorizations (e.g., known, reasonably anticipated, etc.)?

   a) Scientific basis of classification
   b) Linkage to the categories

   *NIOSH [2011]
Critical Questions

3. Should 1 in 1000 working lifetime risk (for persons occupationally exposed) be the target level for a recommended exposure limit (REL) for carcinogens or should lower targets be considered?

   - Residual risk at the REL (?)
     • 1/1,000
     • 1/10,000
     • 1/100,000
     • 1/1,000,000

*NIOSH [2011]

4. In establishing NIOSH RELs, how should the phrase “to the extent feasible” (defined in the 1995 NIOSH Recommended Exposure Limit Policy) be interpreted and applied?

*NIOSH [2011]
Critical Questions

5. In the absence of data, what uncertainties or assumptions are appropriate for use in the development of RELs?

- What is the utility of a standard “action level” (i.e., an exposure limit set below the REL typically used to trigger risk management actions) and how should it be set?

- How should NIOSH address worker exposure to complex mixtures?

*NIOSH [2011]

Wrap-up

- Quantitative Risk Assessment & REL Development
  - Reflect current understanding in science and risk assessment

- Update of Carcinogen Policy
  - Moving beyond potential occupational carcinogen
  - Reflect current scientific understanding
  - Harmonize with other agencies

- Future risk-related efforts
  - Hazard banding
  - Cumulative risk assessment
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References