



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

G. Scott Dotson, PhD, CIH  
CDC/NIOSH



## 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

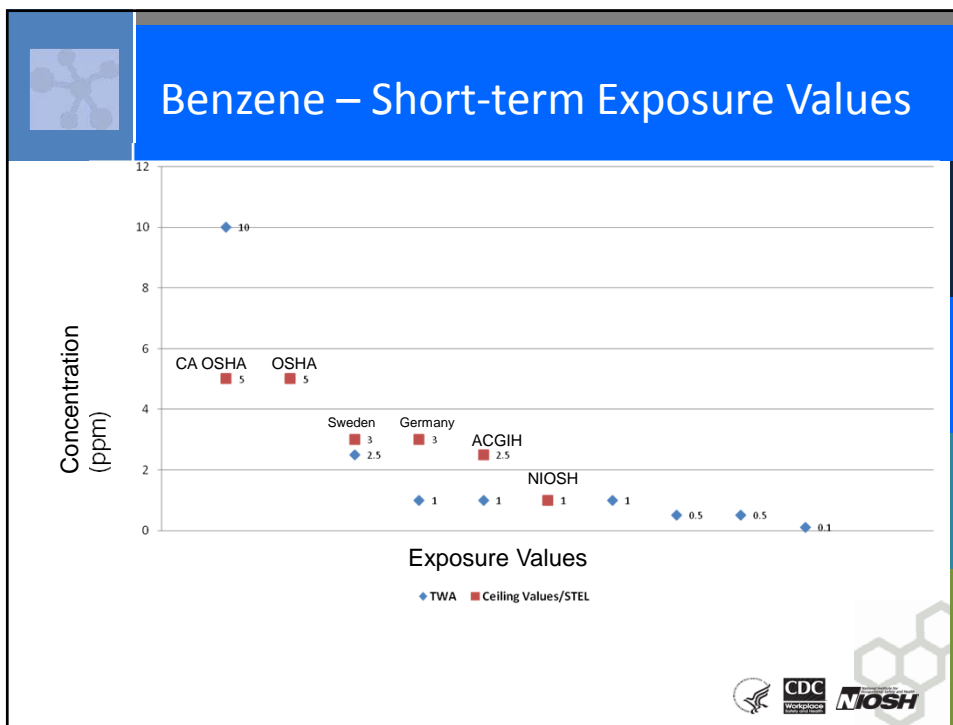
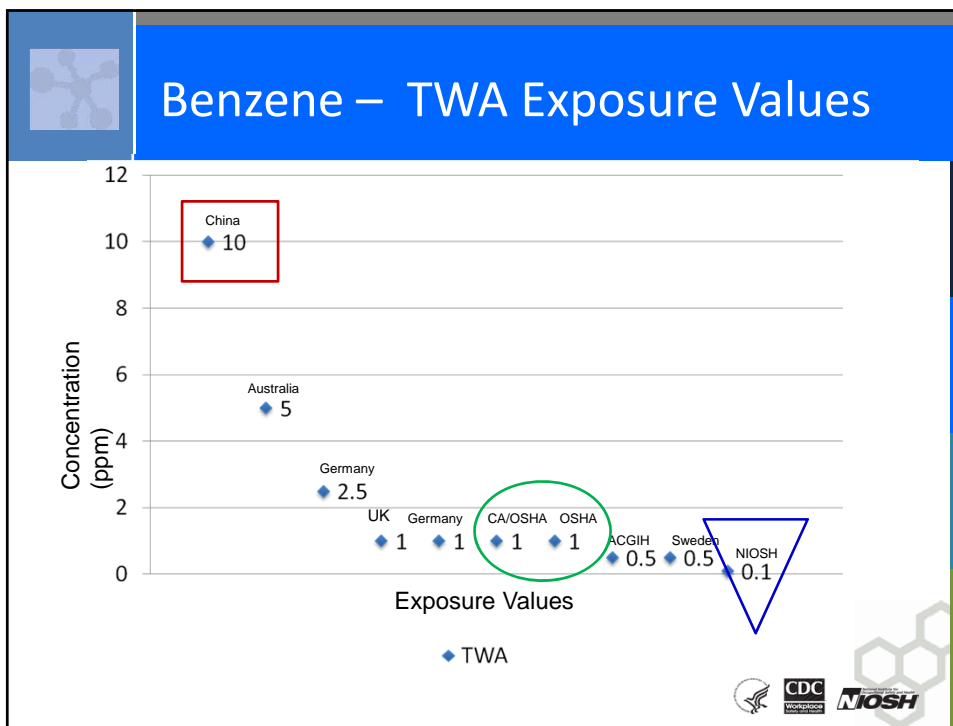
- Exposure recommendations and other health standards are important components of occupational health
  - What is a safe exposure?
  - What risks are represented by workplace conditions?
- Dozens of organizations and agencies develop occupational exposure recommendations worldwide
- Confusing landscape to navigate

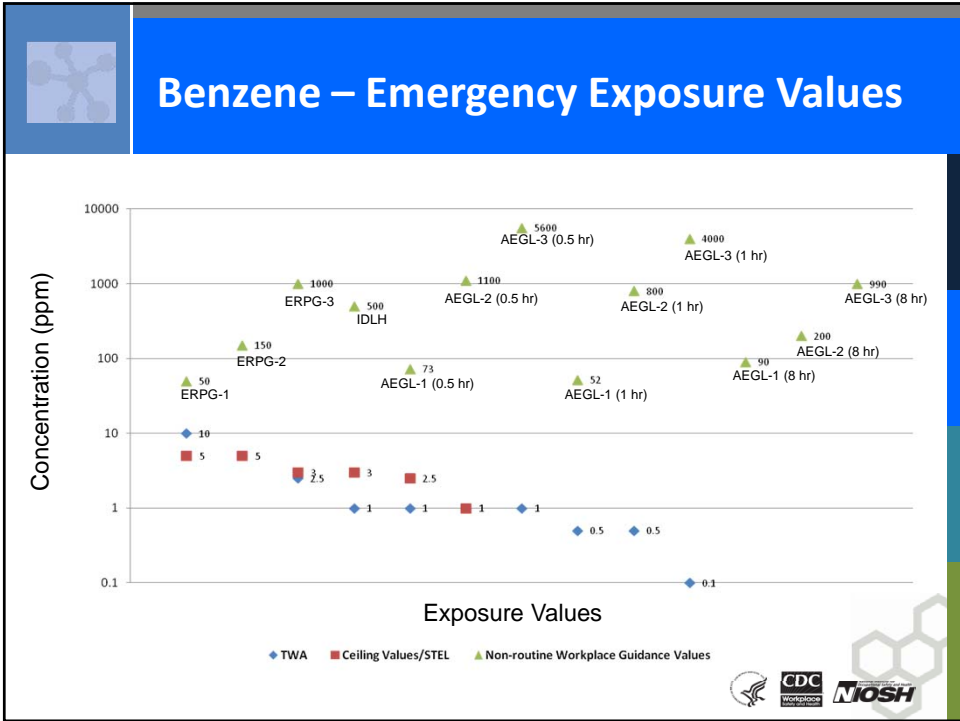


## Case Study 1 – Benzene

- 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?








- ## 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

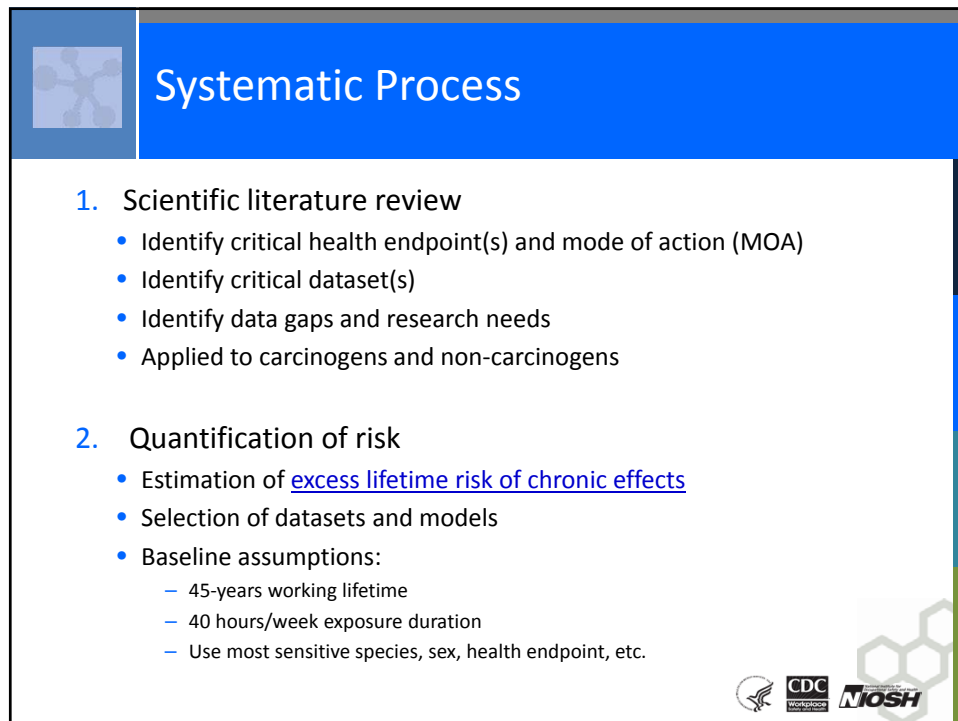
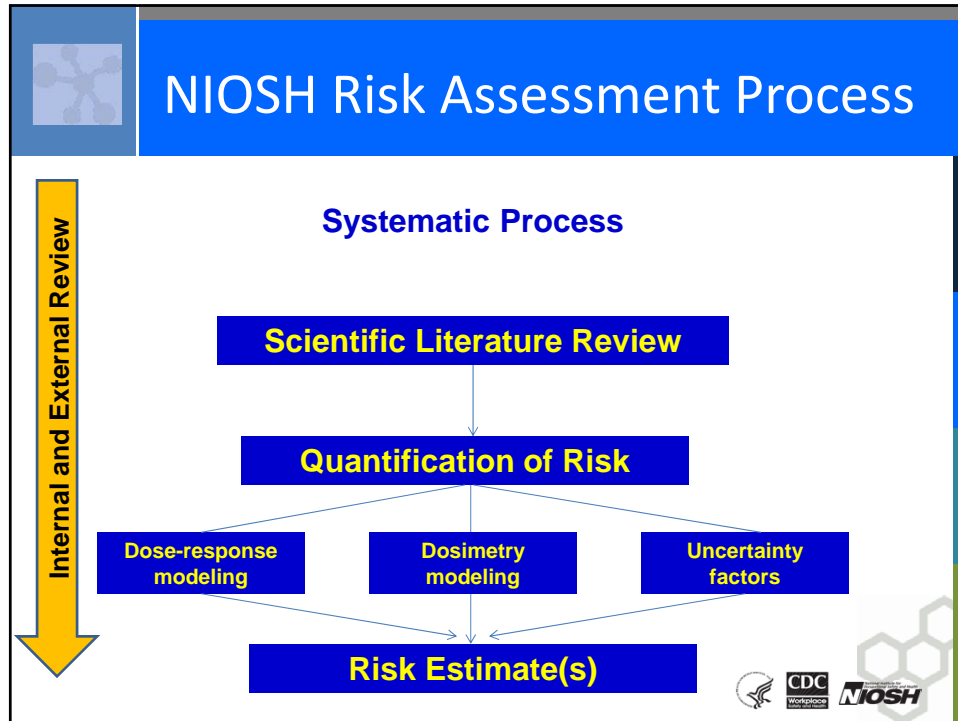
- NIOSH risk assessments are intended to:
  1. Generate new knowledge in the field of occupational safety and health and to transfer that knowledge into practice for the protection of workers
  2. Serve as the basis of authoritative recommendations
    - RELs
    - Scientific decision-making strategies
    - 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





## Critical considerations during REL development

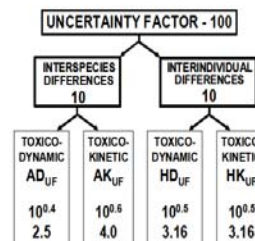
- Dose-response assessments and modeling
  - Foundation of OEL development
  - Facilitates the selection of point of departure (POD)
  - Non-linear (non-carcinogens) vs. Linear (carcinogens)
    - General rule
- Dosimetry methods and modeling
  - Estimation of internal dose
  - Link external exposure & 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)

Harmonization Project Document No. 2



AD<sub>UF</sub> = Uncertainty factor for animal to human differences in toxicodynamics  
 AK<sub>UF</sub> = Uncertainty factor for animal to human differences in toxicokinetics  
 HD<sub>UF</sub> = Uncertainty factor for human variability in toxicodynamics  
 HK<sub>UF</sub> = Uncertainty factor for human variability in toxicokinetics


- CSAF
  - Toxicodynamics
  - Toxicokinetics

Figure S-1. Subdivision of the usual uncertainty factor of 100 used in setting guidance values for the exposure of the general population, such as ADIs, TDIs or RfDs. Different numerical values could be derived if the usual total default uncertainty factor were not 100 — for example, in the risk assessment of occupational exposures (based on IPCS, 1994).

\*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)

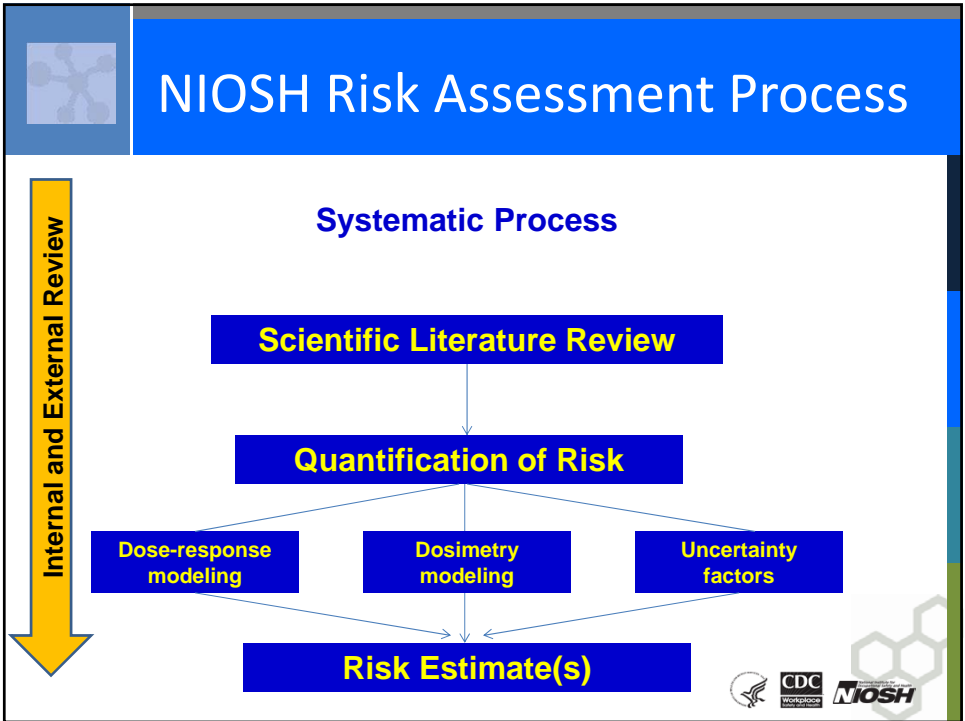
- Revised REL = 0.2 µg Cr(VI)/m<sup>3</sup>
  - Excess lifetime risk of lung cancer of ~1/1,000 workers
- Previous REL
  - 1.0 µg Cr(VI)/m<sup>3</sup>
  - Excess lifetime risk of lung cancer ~6/1,000 workers

Table 7-1. Cr(VI) exposure associated with various levels of excess risk of lung cancer after a 45-year working lifetime


Lifetime added risk* for a 45-year working lifetime exposure	Cr(VI) exposure µg/m <sup>3</sup> Cr	Cr(VI) exposure µg/m <sup>3</sup> CrO <sub>3</sub>
1 in 500	0.32	0.64
→ 1 in 1,000	0.16	0.32
1 in 2,000	0.08	0.16
1 in 5,000	0.032	0.064
1 in 10,000	0.016	0.032
1 in 100,000	0.0016	0.0032

\*Risk estimates from Park et al. [2004]












## 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]



## 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


\*NIOSH [2011]



## 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]



## Critical Questions

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





## Contact Information

G. Scott Dotson, PhD, CIH  
Industrial Hygienist  
CDC/NIOSH  
Cincinnati, Ohio  
[fya8@cdc.gov](mailto:fya8@cdc.gov)  
513.533.8540



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