Hazard Descriptors for Noncancer Outcomes in IRIS Assessments

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Issue: EPA has used cancer descriptors since 1986—is it time to do something similar for noncancer outcomes?

Why now?

- NRC reviews of IRIS, SAB/CAAC, HSST, Senate Appr C'tee
- Descriptors are a standard feature of systematic reviews
- Matter of style: consistency across assessments, outcomes

Goal for today: a path forward

- July 31: STPC/SSP to form an EPA-wide workgroup
- Sept 30: Workgroup to submit a plan for STPC approval
- Dec 15: STPC to approve the plan for implementation

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Some Hypothetical Examples of Hazard Descriptors

Chemical A is *known* to cause neurotoxicity in humans … The RfD is N x 10^{-M} mg/kg-d.

Chemical B is *likely* to cause respiratory toxicity in humans, based on *strong evidence* in experimental animals … The RfC is N x 10^{-M} mg/m^3.

Chemical C is *reasonably anticipated* to cause neurotoxicity in humans … The RfD is N x 10^{-M} mg/kg-d.

There is *strong evidence* that chemical D causes liver toxicity and kidney toxicity in experimental animals. The RfD is N x 10^{-M} mg/kg-d.

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We Already Use Hazard Descriptors for the Criteria Air Pollutants

ISA framework	**EPA's *Cancer Guidelines***
• *Causal relationship*	• *Carcinogenic to humans*
• *Likely to be a causal relationship*	• *Likely to be carcinogenic to humans*
• *Suggestive of a causal relationship*	• *Suggestive evidence of carcinogenic potential*
• *Inadequate to infer a causal relationship*	• *Inadequate information to assess carcinogenic potential*
• *Not likely to be a causal relationship*	• *Not likely to be carcinogenic to humans*

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We Already Stratify the Evidence That Supports RfDs and RfCs

***RfC Methods* (1994)**

- *High confidence:* reference value based on a comprehensive array of endpoints, not likely to change with more data
- *Medium confidence*
- *Low confidence:* reference value based on several extrapolations, may change with more data

***RfD/RfC Review* (2002):** A weight-of-evidence approach (such as for RfCs or for cancer) should be used in assessing the database

- *Minimal database*
- *Robust database*

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Many Other Public Agencies Use Hazard Descriptors

WHO/IARC

NTP *Report on Carcinogens*

CalEPA lists of carcinogens and reproductive toxicants

Institute of Medicine

Globally Harmonized System

- Developed by the UN (ILO, WHO) and OECD
- Adopted by the EU and a dozen other countries
- Adopted in the U.S. by OSHA and (proposed for) NIOSH

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Some Issues for Discussion

How can descriptors (e.g., *known*, *likely*, *suggestive*) support decision-making in our programs and regions?

- Rule-making
- Cleanups
- Other decisions
- Communication with the public

Can we develop hazard descriptors that both

- Support EPA's needs
- Advance the science of risk assessment

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Appendix

Examples of Pertinent Statements by Influential Organizations

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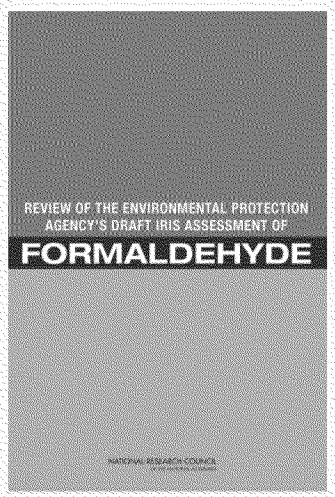
NRC and SAB Recommendations

State-of-the-art approaches have

- Standardized approach for grading the strength of evidence
- Clear and consistent summative language

– NRC 2011, *Formaldehyde*, p 157



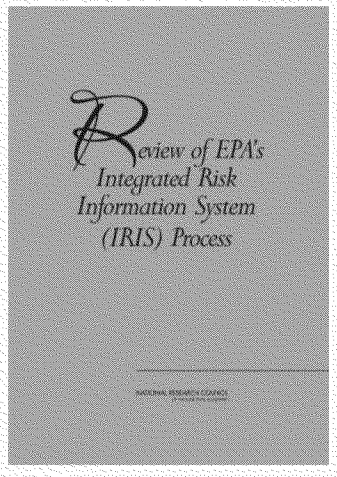
"Develop uniform language to describe the strength of evidence on noncancer effects"

– NRC 2011, *Formaldehyde*, p 165

NRC and SAB Recommendations

Options for moving forward

- Guided expert judgment (e.g., IARC)
- Structured (algorithmic) process (e.g., GRADE)
- Quantitative: meta-analysis, probabilistic bias analysis, Bayesian analysis
  - NRC 2014, *Review of IRIS Process*, pp 96-104



Include a statement about the confidence that the hazards have been adequately identified

– SAB 2015, Trimethylbenzenes, p 19

. . . and so on and so on . . .

"Despite NAS reiterating many of the same concerns in a 2014 report, IRIS has yet to implement all of those recommendations made by the NAS."

"The Committee is concerned that EPA is not taking the recommendations of GAO and NAS seriously."

– House Science, Space, and Technology Committee, May 10

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. . . and so on and so on . . .

"The Committee . . . remains concerned that the recommendations have not been fully implemented . . .

"The Committee directs the EPA to convene an interagency working group to be Co-Chaired with [OIRA] to review compliance with the NAS recommendations . . .

"The working group shall focus specifically on . . . the use of a transparent and reproducible weight-of-evidence process for applying scientific findings.

"The working group report shall also include a timetable for EPA's full implementation of the NAS recommendations for all IRIS assessments issued since the 2014 NAS report."

– Senate Appropriations Committee [draft], April 2016

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