Update on EPA's Dioxin Reassessment

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GREAT LAKES BINATIONAL TOXICS STRATEGY MEETING

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A Short History

- 2003 – EPA releases the most recent version of the draft dioxin reassessment
- EPA request review by the National Academy of Science (NAS).
- 2006 - NAS completes review
- 2009 – EPA Administrator Lisa Jackson commits to completing the Dioxin Reassessment
- May 2010 – EPA releases the Draft Dioxin Report that addresses NAS comments

What Does the Report Address?

- The report addresses the three main areas of critique by the NAS related to EPA's characterization of human risk from TCDD:
  - Provide improved transparency and clarity in the selection of key data sets for dose-response analysis
  - Provide further justification of the approaches to dose-response modeling for cancer and noncancer endpoints
  - Improve transparency, thoroughness, and clarity in quantitative uncertainty analysis.

- *"While indicating that distinction between the categories of "carcinogenic to humans" and "likely to be carcinogenic to humans" is "…based more on semantics than on science…" (NAS, 2006, 14 198441, p. 141)*

How Did EPA Address These Concerns?

- Conducted an updated literature search and external partner workshop
- Developed inclusion criteria for key studies
- Conducted kinetic and dose-response modeling
- Provided uncertainty analysis
- Calculated a Reference Dose (RfD)
- Revised the Oral Slope Factor (OSF)

Noncancer Risk

- Oral reference doses and inhalation reference concentrations (RfDs and RfCs, respectively) for effects known or assumed to be produced through a nonlinear mode of action. In most instances, RfDs and RfCs are developed for the noncarcinogenic effects of substances.
  - EPA did not develop an RfD in the last version because it would have been below background.
  - The new RfD for TCDD is 7×10^{-10} mg/kg-day
  - This number is just slightly above background levels.

Cancer Risk

- **Cancer effects:** Descriptors that characterize the weight of evidence for human carcinogenicity, oral slope factors, and oral and inhalation unit risks for carcinogenic effects.
- Cancer mortality risk is strictly linear only with TCDD blood concentration, such that a single OSF cannot represent the entire range of risks for oral ingestion.

Cancer Risk

- The U.S. EPA's **previous** draft dioxin reassessment efforts produced two upper bound slope factors for estimating human cancer risk from exposure to dioxins.
- The actual shape of the low-dose exposure-response relation for animals or humans could not be determined from the available data. For this reason EPA utilized a linear dose extrapolation model. EPA surmised the true risk was likely to be lower.

Cancer Risk

- New assessment also considered Weight of Evidence (WOE) and many new studies.
  - **Temporality**
  - **Strength of Association**
  - **Consistency**
  - **Biological Gradient**
  - **Biological Plausibility**
  - **Specificity**
- Additionally, new studies and research were thoroughly investigated.

Cancer Risk

- EPA continues to classify TCDD as a carcinogen.
- The OSF developed is almost identical to the 2003 version.
- EPA recommends the use of an OSF of 1×10^{6} (mg/kg-day) when the target risk range is 10^{-5} to 10^{-7}.