

Comments on
EPA's 2010 Dioxin Reassessment:
*Presentation to the
EPA Science Advisory Board*

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Insufficient Evidence to Support a Nonlinear Dose-Response?

- Contrary to unanimous and clear conclusion of the NAS Panel reviewing 2003 document
- Contrary to EPA's own guidance for criteria for conducting nonlinear assessments
- Contrary to virtually all assessments in the rest of the world
- Quotes show that EPA guidance does NOT require linearity



MoA Not Understood?

- Not *Mechanism*, but MODE of Action
- MoA key features are established
- AhR-mediation
 - Acknowledged by EPA, indeed relied upon
 - Sufficient for HazID and TEFs but not dose-response?
- Receptor-mediated effects widely expected to have thresholds



EPA Guidance Permits and *Mandates* Nonlinear Assessment when MoA has “significant biological support”

- Quotes from several EPA guidance sources show mandate for forthright exploration of alternatives even if less-than-absolute support
- Show alternatives, strengths and weaknesses
- Choice is a RISK MANAGEMENT decision
- NAS, WHO show “scientific consensus” and “peer review” for MoA



Additivity to Preexisting AhR Binding?

- Novel and controversial principle:
 - Not justified in document
 - Has not been accepted as science policy
- Must assume a lot about MoA (elsewhere deemed too uncertain):
 - Preexisting binding sufficient for tumors in some
 - Endogenous ligands not competitors
 - Downstream processes equivalent and w/o thresholds
- *Bad precedent to accept without thorough debate*