

April 3, 2013

COMMENTS FOR THE 1ST MEETING OF THE EPA'S CHEMICAL ASSESSMENT ADVISORY COMMITTEE

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Oversimplification is Problematic

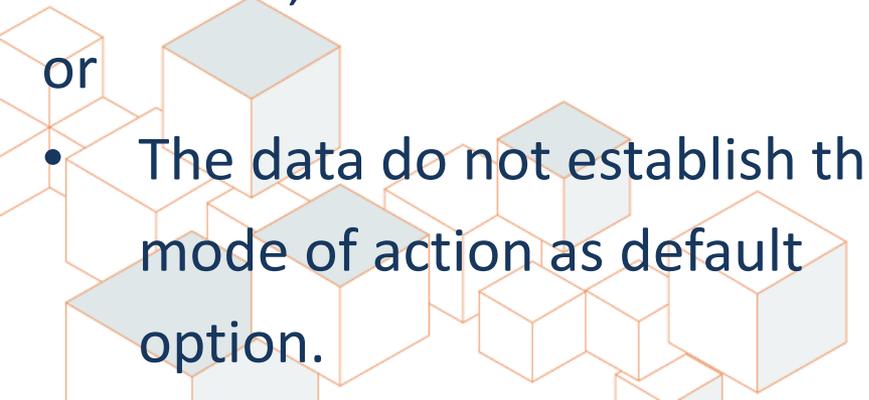
- ❑ The preamble offers an abbreviated view of EPA policies, guidance documents and standard practices.
 - ❑ It is not clear that this is what NAS asked for.
- ❑ In providing this abbreviated view, critical information is omitted and the preamble may unduly lead readers to incorrectly interpret EPA guidance.

EPA Approach Oversimplifies Complex Guidance

- ❑ EPA notes preamble distills 1600 pages of guidance into 20 pages. The preamble is not chemical specific.
- ❑ NAS 2011: *“Chapter 1 needs to be expanded to describe more fully the methods of the assessment, including a **description of search strategies used to identify studies with the exclusion and inclusion criteria articulated and a better description of the outcomes of the searches and clear descriptions of the weight-of-evidence approaches used for the various non-cancer outcomes.**”*
- ❑ *The committee emphasizes that it is not recommending the addition of long descriptions of EPA guidelines to the introduction, but rather clear concise statements of criteria used to exclude, include, and advance studies for derivation of the RfCs and unit risk estimates.”*

Transparency is in the Details: When to Conduct Linear Extrapolation

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slide 25:

- the agent has a mutagenic mode of action or acts through another mode of action expected to be linear at low doses,
or
 - The data do not establish the mode of action as default option.
- 

2005 Cancer guidelines:

Page 3-21 two prongs:

- “all available data are insufficient to establish the mode of action for a tumor site **AND**
- when scientifically plausible based on available data, linear extrapolation is used as a default..”.

Transparency is in the Details: When to Conduct Non-Linear Extrapolation

Science and Science Policy

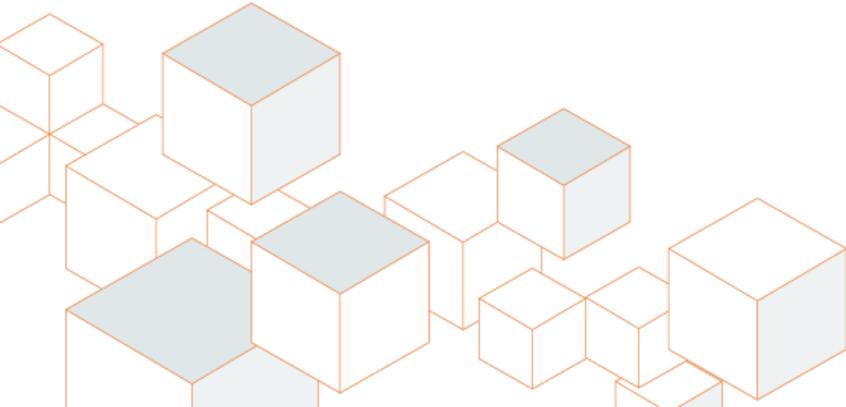
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slide 25:

- There is no evidence of linearity, and
- There is sufficient information to support a mode of action that is nonlinear at low doses.

2005 Cancer guidelines:

- Page 3-21 :
“Where alternative approaches with ***significant biological support*** are available for the same tumor response and no scientific consensus favors a single approach, an assessment may present results based on more than one approach.”



Transparency is in the Details: Nonlinear Extrapolation

Cancer Guidelines Page 3-23:

- “Nonlinear extrapolation having a *significant biological support* may be presented in addition to a linear approach when the available data and a weight of evidence evaluation support a nonlinear approach, but the data are not strong enough to ascertain the mode of action applying the Agency’s mode of action framework.”
- The cancer guidelines thus imply that a nonlinear mode of action is not necessary if there is significant biological support.



Transparency is in the Details: When to Conduct Nonlinear Extrapolation

Cancer Guidelines Page A-9:

- *“When the mode of action information indicates that the dose-response function may be adequately described by both a linear and a nonlinear approach, then the results of both the linear and the nonlinear analyses are presented. An assessment may use both linear and nonlinear approaches if different responses are thought to result from different modes of action or a response appears to be very different at high and low doses due to influence of separate modes of action.”*



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Thank You!



- Getting IRIS right is important.
 - IRIS is used by a wide variety of stakeholders, including the general public.
 - IRIS feeds directly into many important regulatory and non-regulatory decisions.
 - CAAC input on EPA guidance, handbook and developing approaches is essential.