

*39th Joint Meeting of the Chemicals Committee and the Working Party on Chemicals,  
Pesticides and Biotechnology  
15-17 February 2006*

**Focus Session: Experiences using integrated approaches to fulfil information requirements  
for Testing and Assessment**

**Contribution by BIAC  
(Perspectives on Integrated Testing)**

Slide 1

American Chemistry Council  
Good Chemistry  
Making it Possible

## BIAAC Perspectives on Integrated Testing

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February 2006

Slide 2

American Chemistry Council  
Good Chemistry  
Making it Possible


## Guiding Principles

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- Existing information (including comprehensive data searches) should be used as a starting point to inform data needs
- Tiered testing provides the most efficient mechanism to obtain needed data
- Any significant new chemical evaluation initiative should only be undertaken after evaluating other existing programs for possible alignment
- International harmonization of test guidelines, coordination of testing efforts, and sharing information helps to avoid country or company duplicate testing of the same chemicals

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## Guiding Principles (cont)

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- When conducting laboratory toxicity testing, the most likely and therefore relevant route of exposure should be utilized
- Both toxicological and exposure data should be used to set testing priorities and in decision making for consideration of additional testing
- When conducting initial hazard assessments, grouping chemicals with similar characteristics can reduce unnecessary testing and lead to more robust & efficient assessments
- A sound communications plan must be developed and utilized to ensure public understanding and use of testing data

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Slide 4



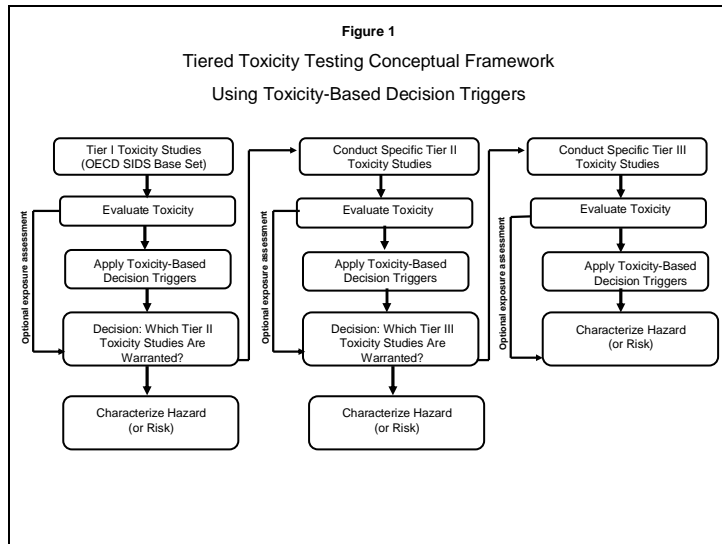
## Guiding Principles (cont)

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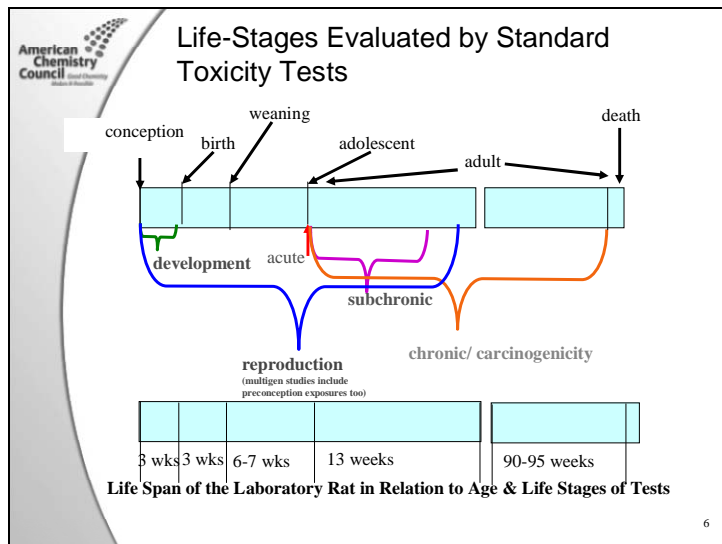
- Responsible use of animals in research and testing will continue to be required to protect human and animal health and to safeguard the environment.
- When animal testing is necessary, testing approaches should use animal models in the most humane ways possible and, when scientifically appropriate and valid, reduce the number of laboratory animals used
- Alternative methods need to be proven as suitable replacements for currently accepted methods. They need to provide an appropriate level of understanding to address concerns for human health and the environment with an adequate degree of scientific certainty.

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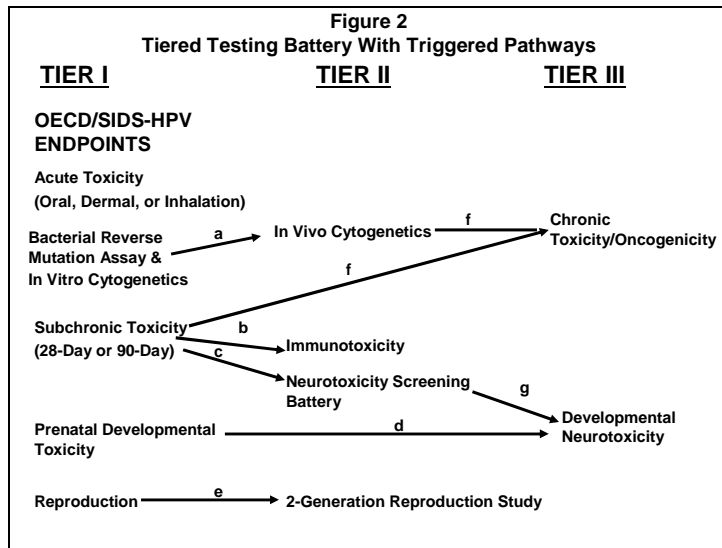
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Slide 6



Slide 7



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**TIERED TESTING: Toxicity-Based Triggers**

**FOOTNOTES:**

**a** - If in vitro study results are positive, taking into account the test system strengths and limitations, mechanism(s) of mutagenic activity, dose level and magnitude of the positive response.

**b** - Based on a weight of evidence determination, if the dose response data indicate non stress related primary effects on immune parameters (e.g. spleen weights, abnormal histopathology in the spleen, thymus and mesenteric/mandibular lymph nodes, and significant changes in white blood cell counts), at doses <1000 mg/kg/day.

**c** - If there are significant dose-related adverse behavioral effects, clinical signs suggestive of nervous system impairment, or brain and spinal cord histopathology observed in the subchronic study (in the absence of FOB/Motor activity assessment) at doses <1000 mg/kg/day. In addition, if a subchronic toxicity study has FOB/motor activity data available that indicates (based on a convergence/weight of evidence) adverse effects, then a Tier II neurotoxicity study may be triggered.

**d** - If neurotoxicity is observed during a prenatal developmental toxicity study (if adverse effects on the nervous system are detected - CNS malformations and/or other signs of nervous system involvement).

**e** - If Tier I reproduction data (from a subchronic toxicity study or a reproduction study) demonstrate adverse effects on reproductive parameters (conception index, gestation length, prenatal loss, etc.), pup indices (#live born, sex ratio, survival, body weight etc.), altered reproductive or accessory sex organ weights and histopathology at dose levels below those resulting in parental toxicity.

**f** - If there is positive mutagenic activity coupled with either indications of significant dose response target organ toxicity (histopathology) at dose levels <1000 mg/kg/day or pre-neoplastic changes, based upon a weight of evidence evaluation.

**g** - If the results of the Tier II Neurotoxicity Screening Battery confirm the results of the Tier I observations.