NTP Activities on Bisphenols

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Bisphenol-A (BPA)

- Chemical widely used to make polycarbonate plastics and epoxy resins
- Widespread low exposure (<1 µg/kg body weight (bw)/day) from migration of small amounts into foods from food contact materials
- Considerable debate over risk posed by “low level” exposure
- Guideline studies conducted under Good Laboratory Practices (GLP) show no effects of concern at “low doses”
- Academic “investigative” studies report that BPA induces a variety of effects in a variety of model systems at low exposures
Historical NTP Context

• National Toxicology Program (NTP) Monograph (2008)
• Evaluated the available scientific literature about the possible effects of BPA on human development and reproduction
• Conclusions

![Diagram showing levels of concern for adverse effects: Serious Concern, Concern, Some Concern, Minimal Concern, Negligible Concern.]

- Developmental toxicity for fetuses, infants, and children (effects on the brain, behavior, and prostate gland)
- Developmental toxicity for fetuses, infants, and children (effects on the mammary gland and early puberty in females), and reproductive toxicity in workers
- Reproductive toxicity in adult men and women and malformations in newborns
Some Bisphenol Analogs/Derivatives

- Widespread exposure to a variety of chemicals with similarity to BPA
  - Detected in foodstuffs, house dust, river and lake sediment, personal care products, and thermal paper
  - Detected in human biological specimens
  - Several chlorinated and brominated derivatives of BPA are used as flame retardants
  - In contrast to BPA, most are poorly understood with respect to potential toxicity

<table>
<thead>
<tr>
<th>Structure</th>
<th>Abbreviation (CASRN)</th>
<th>Detection</th>
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<th>Abbreviation (CASRN)</th>
<th>Detection</th>
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Bisphenols are an exemplar for multiple issues being addressed by NTP and NIEHS

- What is “endocrine disruption”
- How do we effectively assess hazards posed by compounds that cause “endocrine disruption”
- What is low dose?
- Shape of the dose response and evidence for non-monotonicity of effects across the dose range
- How to integrate academic investigative research with regulatory guideline complaint research for decision making
- How to assess hazards for classes of structurally/functionally related compounds
- How to rapidly assess hazard of “replacements” for commodity chemicals that are shown to be toxic in model systems
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