Evidence on the Developmental and Reproductive Toxicity of Bisphenol A

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Chemical and physical characteristics of BPA

4,4'-dihydroxy-2,2-diphenyl propane
\((C_{15}H_{16}O_2)\)
Uses of BPA

• Produced in large quantities (2.3 billion pounds in 2004)
• Used primarily in the production of polycarbonate plastics and epoxy resins
  - Polycarbonate plastics used in:
    - food and drink packaging
      - water and infant bottles
    - compact discs
    - impact-resistant safety equipment
    - medical devices
  - Epoxy resins used as:
    - lacquers to coat metal products
      - food cans, bottle tops, and water supply pipes
    - dental sealants
Exposure to BPA

• The most common route of human BPA exposure is oral
  - BPA known to leach from:
    – dental composites
    – food containers (cans and polycarbonate plastic water bottles)
• Detectable levels of BPA in 92.6% of general population ≥ 6 years of age (0.4 μg/L to 149 μg/L, mean 2.6μg/L)
  – Child mean 4.5 μg/L
  – Adolescent mean 3.0 μg/L
  – Adult mean 2.6 μg/L
  - Neonates in intensive care 28.6 μg/L
General Toxicity of BPA

- **Oral LD$_{50}$**
  - $>2,000$ mg/kg in rat and mouse

- **Dermal LD$_{50}$**
  - $>2,000$ mg/kg in rabbit

- **Acute inhalation**
  - 6-hour exposure to $170$ mg/m$^3$ produced slight and transient slight nasal tract epithelial damage in rats
BPA Pharmacokinetics (PK)

- Absorption
- Metabolism
- Distribution
- Excretion
- Considerations for DART endpoints:
  - Routes of exposure
  - Age at exposure
BPA Pharmacokinetics (PK)

• **Absorption**
  - well absorbed by oral, i.p. or s.c. routes
  - less bioavailable from oral exposure than s.c. injection in rats and primates
  - similar bioavailability by oral and s.c. injection in neonatal mice at lower exposures
BPA Metabolism

Bisphenol A

BPA glucuronide

β-glucuronidase

glucuronyltransferase

sulfotransferase

BPA sulfate
BPA Pharmacokinetics (PK)

- Distribution
  - Widely distributed
  - Crosses placenta
  - Present in breast milk
BPA Pharmacokinetics (PK)

• Excretion
  - Rapidly excreted in urine
  - Undergoes enterohepatic recirculation in rodents
  - Higher levels of unconjugated BPA in rodents than humans
BPA Pharmacokinetics (PK)

- Considerations for DART endpoints:
  - Routes of exposure
  - Age at exposure
    - Maturation of glucuronidation and sulfation

Office of Environmental Health Hazard Assessment