

Evidence available for prioritization of *Bisphenol-A* (CAS # 80-05-7)

Marlissa Campbell, Ph.D., Staff Toxicologist

Bisphenol-A is used in:

polycarbonate products - eyeglass lenses, baby and water bottles, reusable food and drink containers

epoxy resins - dental composites, paints and adhesives, protective coatings in food and beverage containers



Bisphenol-A: Epidemiologic data

- 3 studies reporting increased risk of adverse developmental or reproductive outcomes
 - Blood levels: examined reproductive function and hormones
 - 2 of which were analytical studies of adequate quality
- 1 study reporting no increased risk of adverse developmental or reproductive outcomes
- 1 study whose outcome was unclear from the abstract
- 2 other related articles



Bisphenol-A: Animal data

- 63 animal studies reporting developmental or reproductive toxicity
 - estrogenic effects in males and females
- 13 meeting abstracts reporting developmental or reproductive toxicity
- 26 studies and 4 meeting abstracts that did not report developmental or reproductive toxicity
- 91 related articles and meeting abstracts
- 15 studies without abstracts identified by title only



Public Comments

Committee Discussion

Committee Recommendation

for bisphenol-A



Evidence available for prioritization of *Bromodichloromethane* (CAS # 75-27-4)

Ling-Hong Li, Ph.D., Staff Toxicologist

Major source in the environment:

One of the major trihalomethanes that are formed
as by-products during water chlorination



BDCM: Epidemiologic Data

- 4 studies reporting increased risk of adverse developmental or reproductive outcomes
 - BDCM levels in drinking water associated with: birth defects, stillbirth, spontaneous abortion, birth weights, etc.
 - Analytical studies of adequate quality
- 4 studies reporting no increased risk of adverse developmental or reproductive outcomes
- 2 related human studies:



BDCM: Animal Data

- 4 studies reporting developmental or reproductive toxicity
 - 3 developmental toxicity studies in rats: pregnancy loss, implantation resorption
 - 1 chronic study in rats: testicular histopathology, sperm parameters
- 6 studies reporting no developmental or reproductive toxicity
- 1 meeting abstract reporting development or reproductive toxicity
- 3 related studies in laboratory animals



Public Comments

Committee Discussion

Committee Recommendation

for BDCM



Evidence available for prioritization of *Caffeine* (CAS # 58-08-2)

Farla L. Kaufman, Ph.D., Staff Toxicologist

Caffeine is a psychoactive compound naturally occurring in or added to numerous products such as coffees, teas, chocolate, soft drinks and over-the-counter pharmaceuticals.

Consumption is widespread in California as well as in most parts of the U.S. and the world.



Caffeine: Epidemiologic data

(the past 10 years)

- **32 studies reporting increased risk of adverse developmental or reproductive outcomes**
 - caffeine intake: spontaneous abortion, fetal growth, birth weight, etc.
 - 30 of which were analytical studies of adequate quality
- **1 meeting abstract reporting increased risk**
- **18 studies reporting no increased risk**
- **2 studies with unclear findings and 3 related studies**



Caffeine: Animal data

- 52 studies reporting developmental or reproductive toxicity
 - effects on fertility, neural tube defects, decreased brain weight, ocular abnormalities, intrauterine growth retardation, skeletal and dental abnormalities, behavioral development
- 5 studies reporting no developmental or reproductive toxicity
- 12 studies with unclear outcomes
- 63 related articles and meeting abstracts



Public Comments

Committee Discussion

Committee Recommendation

for caffeine



Evidence available for prioritization of *Chlorpyrifos* (CAS # 2921-88-2)

Poorni Iyer, D.V.M., Ph.D., Staff Toxicologist

- Chlorpyrifos is a broad-spectrum organophosphate insecticide effective in controlling a variety of insects.
- It is used as an insecticide on grain, cotton; field, fruit, nut and vegetable crops, as well as on lawns and ornamental plants.
- Retail sale of chlorpyrifos for residential use was discontinued in the U.S. prior to 2002.



Chlorpyrifos: Epidemiologic data

- 9 epidemiologic studies of environmental exposure to chlorpyrifos reporting increased risk of adverse developmental or reproductive outcomes
 - Indoor residential studies: cognitive and motor development, fetal growth and semen quality
 - 6 of these were analytical studies of adequate quality
- 4 meeting abstracts reporting increased risk of adverse developmental or reproductive outcomes
- 1 epidemiologic study reporting no increased risk of adverse developmental or reproductive outcomes



Chlorpyrifos: Animal data

- 21 animal studies reporting developmental or reproductive toxicity
 - endpoints such as: resorptions, fetal weight and long-term effects on brain and behavior
- 1 meeting abstract reporting developmental or reproductive toxicity
- 3 animal studies that did not report developmental or reproductive toxicity
- 37 related articles



Public Comments

Committee Discussion

Committee Recommendation

for chlorpyrifos



Evidence available for prioritization of *Hexavalent Chromium* (chromium VI) (CAS # 18540-29-9)

Mari S. Golub, Ph.D., Staff Toxicologist

Chromium VI uses

dyes, paints, inks, anticorrosive agents, surface coatings,
electroplating baths

Occupational exposure

welding; chromium sulphate manufacture



Chromium VI: Epidemiologic data

- **5 studies reporting increased risk of adverse developmental or reproductive outcomes**
 - Occupational exposure of men: endpoints included sperm parameters, hormones, partner spontaneous abortion
 - All analytical studies of adequate quality
- **8 studies reporting no increased risk**



Chromium VI: Animal data

- **20 studies reporting developmental or reproductive toxicity**
 - Sperm/testes endpoints in rats, mice & monkeys
 - Developmental toxicity and other reproductive toxicity
- **3 abstracts of unpublished studies reporting developmental toxicity**
- **1 study that did not report developmental or reproductive toxicity**



Public Comments

Committee Discussion

Committee Recommendation

for hexavalent chromium



Evidence available for prioritization of *Dichlorodiphenyl-dichloroethylene (DDE)* (CAS # 72-55-9)

Farla L. Kaufman, Ph.D., Staff Toxicologist

- DDE is the initial and predominant environmental breakdown product of dichlorodiphenyl-trichloroethane (DDT)
- DDE is also a biological metabolite of DDT



DDE: Epidemiologic data

- 38 studies reporting increased risk of adverse developmental or reproductive outcomes
 - wide range of studies: wide range of outcomes
 - 17 of these were analytical studies of adequate quality
- 2 meeting abstracts reporting increased risk
- 33 studies reporting no increased risk
- 2 meeting abstracts reporting no increased risk
- 4 studies were unclear, 6 related studies, and 1 study without an abstract



DDE: Animal studies

- 4 studies reporting developmental or reproductive toxicity
 - effects on male reproductive tract development and sperm production
- 11 studies reporting no developmental or reproductive toxicity
- 22 related articles



Public Comments

Committee Discussion

Committee Recommendation

for DDE



Evidence available for prioritization of *Methylisocyanate* (CAS # 624-83-9)

Poorni Iyer, D.V.M., Ph.D., Staff Toxicologist

- Methylisocyanate is used in the production of pesticides and plastics
- Occupational exposure and exposure through environmental releases



Methylisocyanate: Epidemiologic data

- 7 epidemiologic studies of methylisocyanate reporting increased risk of adverse developmental or reproductive outcomes
 - Bhopal incident: pregnancy loss and neonatal and/or infant mortality
 - 2 of which were analytical studies of adequate quality
- 0 epidemiologic studies reporting no increased risk of adverse developmental or reproductive outcomes
- 2 related articles on the release of methylisocyanate in Bhopal, India



Methylisocyanate: Animal data

- 6 animal studies of methylisocyanate reporting developmental or reproductive toxicity
 - effects such as anomalies, implantation loss, fetal loss and disturbed estrous cycles
- 1 animal study that did not report developmental or reproductive toxicity



Public Comments

Committee Discussion

Committee Recommendation

for methylisocyanate



Evidence available for prioritization of *Sulfur dioxide* (CAS # 7446-09-5)

Francisco Moran Messen, Ph.D., Staff Toxicologist

Intermediate in the production of sulfuric acid

Fumigant, preservative, bleach and steeping agent for grain in food processing; catalyst or extraction solvent; flotation depressant for sulfide ores; intermediate for bleach production; reducing agent.

Ambient air exposure from activities such as the burning of coal and oil at power plants or from copper smelting



Sulfur Dioxide: Epidemiologic Data

- 18 epidemiologic studies reporting increased risk of adverse developmental or reproductive outcomes
 - air pollution studies: preterm delivery, low birth weight
 - 7 of which were analytical studies of adequate quality
- 1 meeting abstract reporting increased risk of adverse developmental or reproductive outcomes
- 1 epidemiologic study reporting no increased risk of adverse developmental or reproductive outcomes
- 1 related article



Sulfur Dioxide: Animal Data

- **6 animal studies reporting developmental or reproductive toxicity**
 - reproductive effects include biochemical parameters (glutathione oxidation-deoxidation system); disturbances in the estrous cycle; lower fertility
 - developmental effects include low birth weight; altered social/agonistic behavior
- **2 studies that did not report developmental or reproductive toxicity**
- **4 related articles**



Public Comments

Committee Discussion

Committee Recommendation

for sulfur dioxide

