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Scoping and Problem Formulation for the IRIS Toxicological Review of Polychlorinated Biphenyls (PCBs): Effects Other Than Cancer

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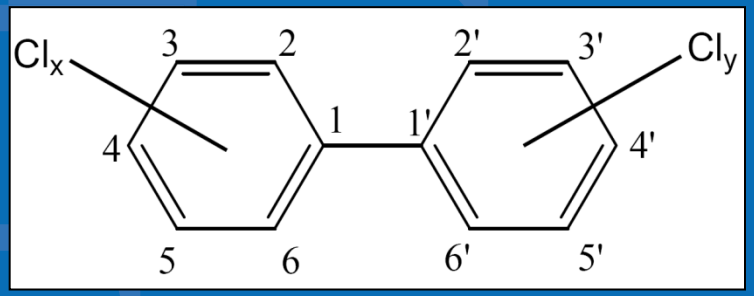

Office of Research and Development
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Key Science Topics

1. Impact of congener profile on the toxicity of PCB mixtures
2. Evaluation of epidemiological studies for PCB dose-response assessment
3. Potential for hazard identification and dose-response assessment for PCB exposure via inhalation
4. Suitability of available toxicokinetic models for reliable route-to-route, interspecies, and/or intraspecies extrapolation
5. Potential toxicokinetic models or methods to estimate the relationship between continuous daily maternal PCB intake and milk PCB concentrations in humans
6. Putative mechanisms of PCB toxicity
7. Factors influencing human susceptibility

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Science Topic 3: PCB Inhalation

- Humans are exposed to PCBs by inhalation.

Science Topic 3: PCB Inhalation

Fact Sheet for Schools: Caulk Containing PCBs May Be Present in Older Schools and Buildings

http://www.epa.gov/pcbsincaulk/pdf/caulkschools1.pdf
http://www.epa.gov/pcbsincaulk/pdf/caulkschools2.pdf

Science Topic 3: PCB Inhalation

- Proper Maintenance, Removal, and Disposal of PCB-Containing Fluorescent Light Ballasts (FLBs) in School Buildings: A Guide for School Administrators and Maintenance Personnel (http://www.epa.gov/epawaste/hazard/tsd/pcbs/pubs/ballasts.htm)
- How to Test for PCBs and Characterize Suspect Material (http://www.epa.gov/pcbsincaulk/guide/guide-sect3.htm)

Science Topic 3: PCB Inhalation

1. Characterize sources of PCBs in school buildings
2. Characterize levels of PCBs in exposure media and investigate relationships between these levels and PCB sources
3. Apply an exposure model for estimating children's exposure to PCBs in schools with PCB sources
4. Evaluate which routes of exposure (e.g., inhalation, contact with surfaces or dust) are likely to be most important
5. Provide information to inform risk management practices for reducing exposure to PCBs in schools

http://www.epa.gov/pcbsincaulk/pdf/pcb_EPA600R12051_final.pdf

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Science Topic 3: PCB Inhalation

- Inhalation is an important route of PCB exposure in humans.
- There are very few PCB inhalation studies.

PCB Inhalation Data - Animals

Treon et al. (1956). "The toxicity of the vapors of Aroclor 1242 and Aroclor 1254." *American Industrial Hygiene Association Quarterly* 17(2): 204-213.

Study Design

- Cats (n = 1), rabbits (n = 4), guinea pigs (n = 6), rats (n = 10) and mice (n = 10) exposed 7 hours/day, 5 days/week for 213 days
- 1.5 mg/m^3 Aroclor 1254
- Hepatotoxicity

Caveats

- Single PCB dose tested
- Some study animals died for reasons unrelated to treatment
- Uncertain exposure characterization

PCB Inhalation Data - Animals

Casey et al. (1999). "Aroclor 1242 inhalation and ingestion by Sprague-Dawley rats." *Journal of Toxicology and Environmental Health, Part A: Current Issues* 56(5): 311-342.

Study Design

- Rats exposed 23 hours/day for 30 days (n = 8)
- 0.0009 mg/m^3 Aroclor 1242
- histopathological changes in the thyroid, thymus, and urinary bladder
- increased serum thyroid hormone concentrations
- neurobehavioral changes

Caveats

- Single PCB dose tested
- Whole-body exposure
- Incomplete exposure information

PCB Inhalation Data - Animals

Hu et al. (2012). “Subchronic inhalation exposure study of an airborne polychlorinated biphenyl mixture resembling the Chicago ambient air congener profile." *Environmental Science and Technology* 46: 9653-9662.

Study Design

- Rats exposed 1.6 hours/day, 5 days/week for 4 weeks (n = 12)
- 0.52 mg/m^3 PCBs
- Investigated: pulmonary immune responses; histopathology (liver, lung, thymus, spleen, kidney, and thyroid); cytochrome P450 enzyme induction (liver and lung); redox status of glutathione (serum, liver and lung); and hematological parameters
- Observed: a shift to more oxidized glutathione in serum and elevated hematocrit

Caveats

- Single PCB dose tested
- Short exposure duration

PCB Inhalation Data - Animals

	Treon et al. (1956)	Casey et al. (1999)	Hu et al. (2012)
Exposure Duration	7 hours/day 5 days/week 213 days	23 hours/day 7 days/week 30 days	1.6 hours/day 5 days/week 28 days
Dose	1.5 mg/m^3 (Aroclor 1254)	0.0009 mg/m^3 (Aroclor 1242)	0.52 mg/m^3 (PCBs to mimic Chicago air)
Effects Observed	Hepatotoxicity	• Thyroid effects • Immunotoxicity • Neurotoxicity	Minimal toxicity
Notes on Exposure	Whole body exposure Uncertain exposure assessment	Whole body exposure Uncertain exposure assessment	Nose-only exposure

Science Topic 3: PCB Inhalation

- Inhalation is an important route of PCB exposure in humans.
- There are very few PCB inhalation studies.
- *Evaluate potential options for conducting a dose-response assessment for PCB inhalation exposure*
  - *use data from available inhalation studies*

Uncertainties in RfC Derivations Using Data from Available PCB Inhalation Studies

- **Human variation**
  - Susceptibility may vary across the human population, and the available data may not be representative of individuals who are most susceptible to the effect
- **Animal-to-human extrapolation**
  - Toxicokinetic differences between humans and animals may be addressed by standard dosimetric adjustment, but there may also be toxicodynamic differences to be addressed
- **Dose-response analysis based on a single dose**
  - Available studies were all single-dose, POD would be a LOAEL
  - One study identified a NOAEL, but did not assess the endpoints affected in the other two studies
- **Available studies were of subchronic or short-term duration**
- **Incomplete database**
  - A database is often considered to be incomplete if both a prenatal toxicity study and a two-generation reproduction study are missing

Science Topic 3: PCB Inhalation

- Inhalation is an important route of PCB exposure in humans.
- There are very few PCB inhalation studies.
- *Evaluate potential options for conducting a dose-response assessment for PCB inhalation exposure*
  - *use data from available inhalation studies*
  - *route-to-route extrapolation from oral PCB exposure data*
  - *additional options suggested by expert stakeholders*