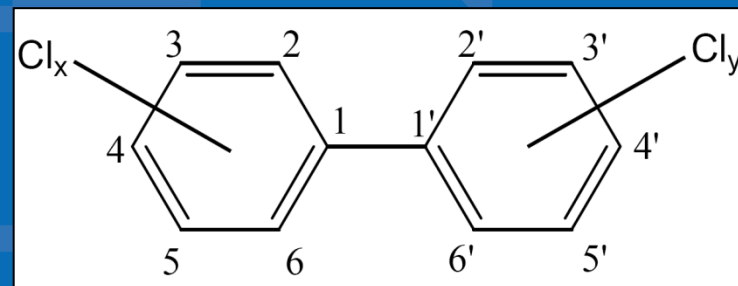


# Scoping and Problem Formulation for the IRIS Toxicological Review of Polychlorinated Biphenyls (PCBs): Effects Other Than Cancer

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# Key Science Topics

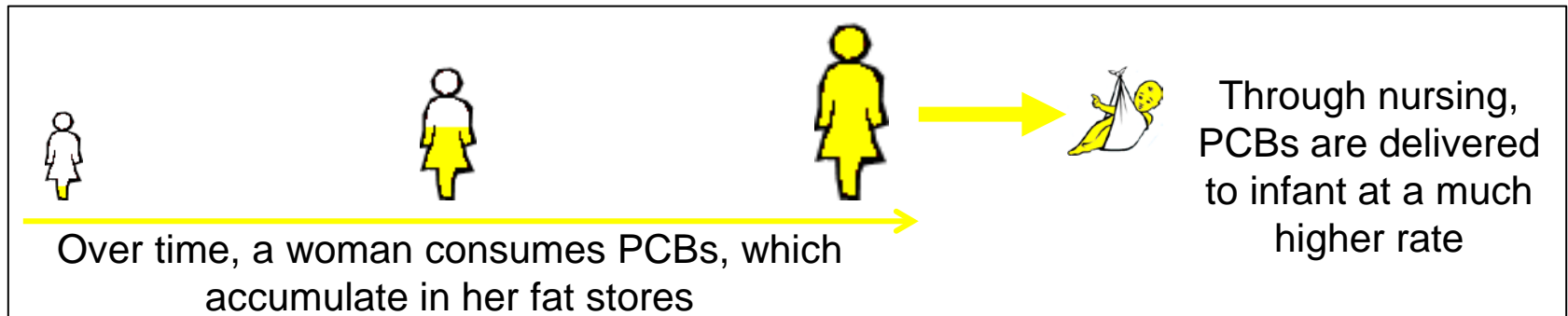
1. Impact of congener profile on the toxicity of PCB mixtures
2. Evaluation of epidemiological studies for PCB dose-response assessment
3. Potential for hazard identification and dose-response assessment for PCB exposure via inhalation
4. Suitability of available toxicokinetic models for reliable route-to-route, 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**

# Science Topic 7: Susceptibility

- EPA's reference values for non-cancer health effects:
  - estimates of exposure likely to be without health risk over a lifetime, even in susceptible subgroups
  - characteristics of susceptible subgroups: age, sex, genetic polymorphisms, socioeconomic status, etc.
- *Consider factors impacting susceptibility*
  - Infancy and childhood, including impacts of breastfeeding:
    - critical windows of exposure and development exist during infancy and childhood for the nervous, immune, reproductive and endocrine systems
    - relatively high exposure to PCBs occurs through ingestion of human milk

# Science Topic 5: Predicting Lactational Exposure

- Breastfed infants are exposed to relatively high levels of PCBs through ingestion of human milk



# Science Topic 5: Predicting Lactational Exposure

- Breastfed infants are exposed to relatively high levels of PCBs through ingestion of human milk
- *Gather information on the lactational transfer of PCBs and the relationship between long-term maternal PCB exposure and subsequent exposure in a breastfeeding infant*

# Science Topic 5: Predicting Lactational Exposure

	<u>Route</u>	<u>Species</u>	<u>PCBs</u>	<u>Compartments</u>
Verner et al. (2008)	oral	human	153, 180	brain, adipose, liver, richly perfused, poorly perfused, uterine, placenta, fetal, mammary
Verner et al. (2009)	oral	human	138, 153, 180	<b>Maternal:</b> brain, adipose, liver, richly perfused, poorly perfused, uterine, placenta, fetal, mammary <b>Infant:</b> brain, adipose, liver, richly perfused, poorly perfused
Verner et al. (2013)	oral	human	118, 153, 170, 180	maternal lipids, child lipids
Redding et al. (2008)	oral	human	153	blood, fat, liver, "other tissues", mammary

# Science Topic 5: Predicting Lactational Exposure

- Breastfed infants are exposed to relatively high levels of PCBs through ingestion of human milk
- *Gather information on the lactational transfer of PCBs and the relationship between long-term maternal PCB exposure and consequent exposure in a breastfeeding infant*
- ***Evaluate the potential for kinetic modeling approaches to be used to predict early-life exposure to PCBs via placental transfer and lactation based on long-term maternal PCB exposure***