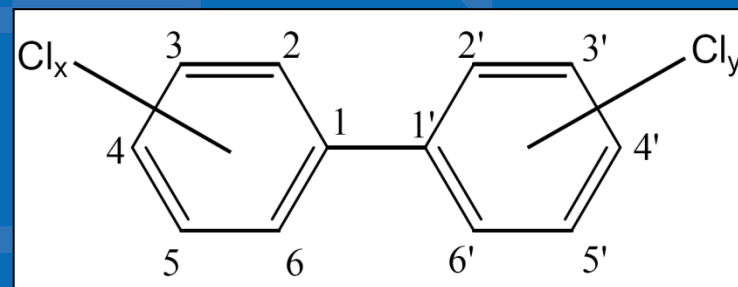


# Scoping and Problem Formulation for the IRIS Toxicological Review of Polychlorinated Biphenyls (PCBs): Effects Other Than Cancer

*Geniece M. Lehmann, PhD*  
*Assessment Manager*



# 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 4: Toxicokinetic Modeling

- A variety of toxicokinetic models are available for individual PCB congeners and PCB mixtures

# Science Topic 4: Toxicokinetic Modeling

	<u>Route</u>	<u>Species</u>	<u>PCBs</u>
Lutz et al. (1977, 1984); Tuey and Matthews (1980)	i.v.	rat; mouse; dog; monkey	3, 15, 101, 136, 153
Fisher et al. (1989)	dermal	rat	153
Lohitnavy et al. (2008); NTP (2006a, 2006b)	oral	rat	126, 153
Lee et al. (2002, 2007); NTP (2006c)	oral	mouse; rat	153 +/- 126
NTP (2006d)	oral	rat	118 + 126
Emond et al. (2005)	oral	rat	118 + 138 + 153 + 170 + 180 + 187
Maruyama et al. (2002)	oral	human	77 + 81 + 105 + 114 + 118 + 123 + 126 + 156 + 157 + 167 + 169 + 189

# Science Topic 4: Toxicokinetic Modeling

- A variety of toxicokinetic models are available for individual PCB congeners and PCB mixtures
- *Evaluate the potential for these models to be used to address route-to-route, interspecies, and intraspecies extrapolation of complex PCB mixtures*
- *Gather information on toxicokinetic differences*
  - *among PCB congeners and mixtures*
  - *between humans and laboratory animals*
  - *across life stages*

# Science Topic 4: Toxicokinetic Modeling

- Evaluate the potential for these models to be used to address route-to-route, interspecies, and intraspecies extrapolation of complex PCB mixtures
  - *Can existing models be used to support extrapolation from oral to inhalation routes of exposure?*
  - *Can existing models be used to reduce uncertainty in extrapolation of animal to human dose-response data?*