Karlsruhe Institute of Technology

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PCB – which internal exposure is safe for the developing foetus?

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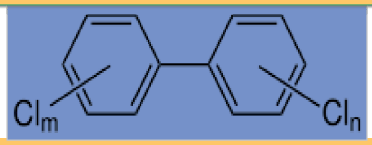
Question

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area evaluated a biological tolerance value (BAT value) for chlorinated biphenyls of 15 µg/L plasma for the sum of the indicator congeners PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, PCB 180. However, adhering the BAT value cannot exclude a risk to the developing foetus (Pregnancy Risk Group B). The question arose at which internal concentration such a risk is not to be expected and would correspond to Pregnancy Risk Group C for PCBs.

Methods

Numerous environmental epidemiological studies on developmental effects and birth weight, including extensive reviews of these studies, were taken into account and evaluated. Additionally studies on developmental toxicity in monkeys, the most sensitive species were also considered and evaluated.



Results

Human

Reduced Birth weight

- The results of the birth weight studies are inconsistent. Therefore it is questionable whether the negative association found in some studies between PCBs and birth weights or postnatal weight development can be causally related to PCBs.
- Even if the dose–response relationships established by the two recent and most comprehensive meta-analyses (*Casas et al. 2015*; *Iszatt et al. 2015*) could be causally related to PCBs, the birth weights would be reduced only by 1^% at a concentration of PCB indicator congeners of around 3.5^µg/l maternal plasma.
- In an international subcohort with a low risk for reduced birth weights, the average birth weight of 20^486 newborn babies was 3.3^±^0.5^kg (*Villar et al. 2014*).

Summary

The range of variation in below average birth weights is 15 times higher than the 1^% decrease in birth weight caused by a concentration of PCB indicator congeners of about 3.5^µg/l maternal plasma.

Developmental Neurotoxicity

- Findings on developmental neurotoxicity from 15 birth cohorts from 8 different countries had been published by the end of 2011 *(HBM-Kommission 2012)*.
- Different neuropsychological and neuromotor test systems were used to investigate age-related developmental deficits in newborn babies and toddlers.
- Nine cohort studies found a significant association between at least one specific effect parameter and the PCB burden.
- Two other studies reported only temporal (in some cases weak) associations.
- Four studies found no associations.

→ there is sufficient epidemiological evidence that PCBs induce neurotoxicity
→ a NOAEC (a concentration below which no neurotoxic effects were observed) was derived from the study of *Jacobson et al. (2002)* and is confirmed by the extensive review by *El Majidiet al. (2013)*.

Summary

A maternal concentration of total PCBs of 1^µg/g blood lipids was found to be the NOAEL for developmental neurotoxicity. This is equivalent to a concentration of PCB indicator congeners of 3.5^µg/l plasma.

Animal

Monkeys are the most sensitive species for developmental toxicity after oral treatment with PCB mixtures.

NOAEL and LOAEL for developmental toxicity and body burden in monkeys.

PCB mixture	NOAEL	LOAEL
Aroclor 1016	8^µg/kg body weight and day	30^µg/kg body weight and day birth weight ↓, behavioural and learning deficits
	PCB burden 12^±^6^µg total PCB/l serum	PCB burden 27^±^8^µg total PCB/l serum
Aroclor 1254	5^µg/kg body weight and day	25^µg/kg body weight and day birth weight ↓
	PCB burden 10^µg/l whole blood ≙^20^µg total PCB/l plasma	PCB burden about 40^µg/l whole blood (extrapolated) ≙^80^µg total PCB/l plasma

A NOAEL of 20 µg total PCB/l plasma which corresponds to a concentration for PCB indicator congeners of 10 µg/l plasma was derived from the studies in monkeys.

Conclusion

At a concentration of 3.5 µg/L plasma for the sum of the indicator congeners PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, PCB 180 damage to the embryo or foetus is not to be expected. Therefore, an internal exposure not higher than this concentration would be the prerequisite for an assignment to Pregnancy Risk Group C.

References: Casas M et al. (2015) Prenatal exposure to PCB-153, p,p'-DDE and birth outcomes in 9000 mother-child pairs: exposure-response relationship and effect modifiers. Environ Int 74: 23–31
El Majidi N et al. (2013) Systematic analysis of the relationship between standardized prenatal exposure to polychlorinated biphenyls and mental and motor development during follow-up of nine children cohorts. Regul Toxicol Pharmacol 66: 130–146
Iszatt N et al. (2015) Prenatal and Postnatal Exposure to Persistent Organic Pollutants and Infant Growth: A Pooled Analysis of Seven European Birth Cohorts. Environ Health Perspect 123: 730–736
Jacobson JL et al. (2002) A benchmark dose analysis of prenatal exposure to polychlorinated biphenyls. Environ Health Perspect 110: 393–398
Villar J et al. (2014) International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. Lancet 384: 857–868
HBM-Kommission (2012) Humanbiomonitoring-(HBM)-Werte für Polychlorierte Biphenyle (PCB) im Blut.

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