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

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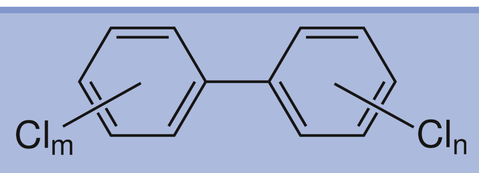
Question

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area derived 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, observing the BAT value does not exclude a risk to the developing foetus (Pregnancy Risk Group B). This led to the question at which internal concentration such a risk would not be expected, which would correspond to a classification of PCBs in Pregnancy Risk Group C.

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 included in the evaluation.



BAT (Biological Tolerance Value)

Σ PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, PCB 180 (Pregnancy Risk Group B)	***15 µg/l plasma***
Prerequisite for Pregnancy Risk Group C	***3.5 µg/l plasma***

BAR (Biological Reference Value)

≙ 95th percentile of background level in a reference population of persons of working age without regarding effects on health

PCB 28	***PCB 52***	***PCB 101***
0.02 µg/l plasma	***<0.01 µg/l plasma***	***<0.01 µg/l plasma***

General population *Σ PCB 138, PCB 153, PCB 180* *(95th percentile)*

18-25 years	***0.88 µg/l plasma***	
26-35 years	***1.14 µg/l plasma***	
36-45 years	***1.95 µg/l plasma***	***> 3.5 µg/l plasma: 0.5%***

(Schettgen et al. 2015)

Results

Human

Reduced Birth Weight

- Results of the birth weight studies are inconsistent.
- Negative association between PCBs and birth weights or postnatal weight development → causally related to PCBs?
- Two meta-analyses (*Casas et al. 2015*; *Iszatt et al. 2015*) → birth weight reduction of only 1% at 3.5 µg PCB/l maternal plasma.
- International subcohort → the average birth weight of 20486 newborns was 3.3 ± 0.5 kg (*Villar et al. 2014*).

Summary

The range of variation for lower than 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

- 15 published birth cohort studies (*HBM-Kommission 2012*)
- Investigation via neuropsychological and neuromotor test systems: age-related developmental deficits in newborns and toddlers
- Nine cohort studies → significant association between at least one specific effect parameter and the PCB burden
- Two other studies → in some cases weak associations
- Four studies → no associations

→ sufficient epidemiological evidence that PCBs induce developmental neurotoxicity → a NOAEC (concentration below which no neurotoxic effects were observed) was derived from the study of *Jacobson et al. (2002)* and was confirmed by the extensive review by *El Majidi et 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 (mainly di-, tri- and tetrachlorinated biphenyls)	8 µg/kg bw and day ≙ 12 ± 6 µg total PCB/l serum	30 µg/kg bw and day: birth weight ↓, behavioural and learning deficits ≙ 27 ± 8 µg total PCB/l serum
Aroclor 1254 (mainly tetra-, penta-, hexa- and heptachlorinated biphenyls)	5 µg/kg bw and day ≙ 20 µg total PCB/l plasma	25 µg/kg bw and day: birth weight ↓ ≙ 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, a level of internal exposure no higher than this concentration would be the prerequisite for an assignment to Pregnancy Risk Group C.

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HBM-Kommission (2012) Humanbiomonitoring-(HBM)-Werte für Polychlorierte Biphenyle (PCB) im Blut.

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