The MAK Collection for Occupational Health and Safety

Addendum to Chlorinated biphenyls

Assessment Values in Biological Material – Translation of the German version from 2016

A. Rettenmeier[1], T. Kraus[2], H. Drexler[3,*], A. Hartwig[4,*], MAK Commission[5,*]

1 *Institute for Medical Informatics, Biometry and Epidemiology (IMIBE), University Essen, Hufelandstraße 55, 45122 Essen, Germany*

2 *Institute for Occupational and Social Medicine, RWTH Aachen University, Faculty of Medicine, Pauwelsstraße 30, 52074 Aachen, Germany*

3 *Head of the working group "Assessment Values in Biological Material" of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Friedrich-Alexander-Universität Erlangen-Nürnberg, Institute and Outpatient Clinic of Occupational, Social, and Environmental Medicine, Schillerstraße 25 and 29, 91054 Erlangen, Germany*

4 *Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany*

5 *Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany*

* *email: H. Drexler (hans.drexler@fau.de), A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)*

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Addendum to Chlorinated biphenyls

BAT Value Documentation

W. Rettenmeier[1], T. Kraus[2], H. Drexler[3, *], A. Hartwig[4, *], MAK Commission[5, *]

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Abstract

The German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area has evaluated chlorinated biphenyls and has derived a BAT value (biological tolerance value) for the combined plasma levels of the PCB congeners PCB 28, PCB 52, PCB 101, PCB 138, PCB 153 and PCB 180. Available publications are described in detail.
The evaluation of the BAT value was based on studies in rats and has therefore to be regarded as preliminary. In a 2-year NTP study of PCB 153 in female SD rats, a NOAEL of 10 µg/kg body weight was observed. Liver hypertrophy was the critical toxic effect. The mean blood concentration of PCB 153 was 17.4 µg/l. After extrapolation to humans and considering the non-dioxin-like indicator congeners, a BAT value for the combined plasma concentrations of PCB 28, 52, 101, 138, 153 and 180 of 15 µg/l was established. A specific sampling time is not required. The BAR („Biologische Arbeitsstoff-Referenzwerte") in plasma of 0.02 µg/l for PCB 28, <0.01 µg/l for PCB 52, and <0.01 µg/l for PCB 101 were reconfirmed. Exceeding the BAR indicates additional occupational exposure.

Keywords

chlorinated biphenyls; polychlorinated biphenyls; 2,4,4'-trichlorobiphenyl; 2,2',5,5'-tetrachlorobiphenyl; 2,2',4,5,5'-pentachlorobiphenyl; 2,2',3,4,4',5'-hexachlorobiphenyl; 2,2',4,4',5,5'-hexachlorobiphenyl; 2,2',3,4,4',5,5'-heptachlorobiphenyl; occupational exposure; biological tolerance value; BAT value; BAR; toxicity

Author Information

[1] Institute for Medical Informatics, Biometry and Epidemiology (IMIBE), University of Essen, Hufelandstraße 55, 45122 Essen, Germany
[2] Institute for Occupational and Social Medicine, RWTH Aachen University, Faculty of Medicine, Pauwelsstraße 30, 52074 Aachen, Germany
[3] Chair of the Working Group "Setting of Threshold Limit Values in Biological Materials", Deutsche Forschungsgemeinschaft, Institute and Outpatient Clinic of Occupational, Social and Environmental Medicine, Friedrich-Alexander University Erlangen-Nürnberg (FAU), Schillerstr. 25 and 29, 91054 Erlangen, Germany
[4] Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Department of Food Chemistry and Toxicology, Institute for Applied Biosciences, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Geb. 50.41, 76131 Karlsruhe, Germany
[5] Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany

[*] Email: H. Drexler (hans.drexler@fau.de), A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)

Addendum to Chlorinated Biphenyls

BAT (2015)	**∑ PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, PCB 180**	**15 µg/l plasma**
	Sampling time: not fixed	
BAR (2011)	**PCB 28**	**0.02 µg/l plasma**
	PCB 52	**<0.01 µg/l plasma**
	PCB 101	**<0.01 µg/l plasma**
	Sampling time: not fixed	
MAK value (2015)	**0.003 mg/m³ I**	
Absorption through the skin (1978)	H	
Carcinogenicity (2015)	Carcinogen Category 4	

	Chemical name	Formula	CAS number	Molecular weight [g/mol]
PCB	Polychlorinated biphenyls	$C_{12}H_{(10-n)}Cl_{(n)}$	1336-36-3	
Indicator congeners (non-dioxin-like PCBs)				
PCB 28	2,4,4′-Trichlorobiphenyl	$C_{12}H_7Cl_3$	7012-37-5	257.5
PCB 52	2,2′,5,5′-Tetrachlorobiphenyl	$C_{12}H_6Cl_4$	35693-99-3	292.0
PCB 101	2,2′,4,5,5′-Pentachlorobiphenyl	$C_{12}H_5Cl_5$	37680-73-2	326.4
PCB 138	2,2′,3,4,4′,5′-Hexachlorobiphenyl	$C_{12}H_4Cl_6$	35065-28-2	360.9
PCB 153	2,2′,4,4′,5,5′-Hexachlorobiphenyl	$C_{12}H_4Cl_6$	35065-27-1	360.9
PCB 180	2,2′,3,4,4′,5,5′-Heptachlorobiphenyl	$C_{12}H_3Cl_7$	35065-29-3	395.3

1 Re-evaluation

In 2011, a BAR ("Biologischer Arbeitsstoff-Referenzwert") was established for the PCB indicator congeners PCB 28, PCB 52 and PCB 101 (see BAT Documentation 2013). Owing to their comparatively high volatility these PCB congeners are prefer-

ably taken up at the workplace. Their concentrations in blood therefore reflect the exposure conditions at the workplace.

In 2012, a MAK value of 0.003 mg/m³ I was derived for the PCB congeners with four or more chlorine atoms. This derivation was based on the tolerated external exposure in addition to the background exposure which was determined in animal experiments using toxicity equivalents (TEQs) (Hartwig 2013). In 2015, this MAK value was adopted also for the congeners with one to three chlorine atoms (Hartwig 2016). The derivation of the MAK value using the TEQ approach is based on the consideration that the toxicity of the PCBs is determined decisively by the dioxin-like congeners.

For the derivation of the MAK value for the PCBs the reader is referred to the MAK Documentations (Hartwig 2013, 2016). Data on the metabolism and toxicokinetics of the PCBs, their toxicity, the analytical methods used and background exposure are also given in the BAR Documentations for PCB 28, PCB 52 and PCB 101 (see BAT Documentation 2013).

1.1 Selection of indicators

The changing composition of commercial PCB mixtures and the different physicochemical properties of the individual PCB congeners are reflected in the variable composition and concentration of the congeners measured in the plasma of persons exposed to PCBs. The more congeners are analysed the better the quantitative and above all the qualitative determination of the internal exposure. In the case of the non-dioxin-like congeners the six indicator congeners (PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, PCB 180) are determined by convention.

1.2 Derivation of a BAT value for the non-dioxin-like PCB congeners

There are no data available for relationships between internal exposure of persons exposed to PCBs and adverse effects on health from which a BAT value might be derived.

In an inhalation study in rats the only effects of PCB mixtures even at high proportions of low-chlorinated congeners (84% mono-, bi-, and trichlorinated congeners) were on the liver (Hu et al. 2012). The primary target organ of the toxic effects of the PCBs is thus the liver – also after inhalation exposure. For the non-dioxin-like PCB congeners a 2-year NTP study with PCB 153 revealed for female SD rats a lowest observed adverse effect level (LOAEL) (liver hypertrophy) of 10 µg/kg body weight and day (5 days a week) and – as this effect had not been observed until after 52 weeks – thus also a no observed adverse effect level (NOAEL) of the same level after 52-week exposure. The determined concentration of PCB 153 in blood, which was the result of the administered PCB 153 dose and the amount of PCB 153 additionally contained in the food, was 17.4 µg/l blood (NTP 2006). For simplification, it is assumed that, at a concentration of 17.4 µg/l blood, also no adverse effects on

human health occur also for the sum of all non-dioxin-like PCBs. From the fact that the PCB concentration in plasma is about twice as high as in whole blood, a limit value of 34.8 µg/l plasma is obtained.

As usually only the indicator congeners are determined and the plasma concentrations of PCB 28, PCB 52, PCB 101, PCB 138, PCB 152 and PCB 180 represent only about 50% of the total PCB concentration in plasma (e.g. Meyer et al. 2013), a **BAT value** of

15 µg Σ PCB 28, PCB 52, PCB 101, PCB 138, PCB 153, PCB 180/l plasma

is established for the non-dioxin-like congeners.

There is no fixed sampling time.

In this derivation it has been assumed for reasons of simplification that the other non-dioxin-like PCBs have the same mechanism of action and effect size as PCB 153 and have no non-Ah receptor-mediated effects exceeding those of PCB 153. In addition, it is taken into account that PCB 153 has probably the longest elimination half-life of these congeners (see Table 1). Additional protection is provided by the fact that the rat liver, the PCB-induced changes in which were the basis for this derivation, is more sensitive to PCB exposure than the human liver.

The derivation of the BAT value is based on animal data, taking the liver hypertrophy observed in rats as critical toxic effect. The BAT value is, therefore, to be regarded as provisional. Even if the BAT value for the non-dioxin-like PCBs is observed, there is the possibility of health risk by the dioxin-like PCB congeners, especially by PCB 126 (TEQ 0.1; van den Berg et al. 2006). According to data from analytical laboratories which determined PCBs in persons occupationally exposed to PCBs, the plasma concentrations of PCB 126 were, however, usually below or at most slightly above the quantification limit (0.01 µg/l) as long as the concentration of the indicator congeners did not exceed 15 µg/l.

The derivation of a BAT value using the TEQ approach, which, in principle, could be done by extrapolation of toxicity data from oral toxicity studies in animals to concentrations in human plasma, is here not possible because of the very different half-lives especially also of the dioxin-like PCB congeners (see Table 1) and their variable proportions in the total TEQ concentration in plasma. However, for the non-dioxin-like PCB congeners a BAT value can be derived because they have a critical toxic end point which is different from that of the dioxin-like PCBs and, for this end point, there are data available from an oral study in animals on the PCB concentration in blood.

The BARs for PCB 28 (three chlorine atoms) of 0.02 µg/l plasma as well as for PCB 52 and PCB 101 (four chlorine atoms) of <0.01 µg/l plasma each are retained because excursion of these values may be indicative of occupational exposure.

1.3 Interpretation of data

The BAT value of 15 µg/l established as sum value for the six non-dioxin-like PCB indicator congeners is markedly above the background exposure which increases

Table 1 Elimination half-lives of non-dioxin-like and dioxin-like PCB congeners

	Elimination half-life (years)	Source
Non-dioxin-like PCBs (indicator congeners)		
PCB 28	4.6 2.18 (mathematical model) 4.5 ± 0.9	Seegal et al. 2011 Broding et al. 2007 Schettgen et al. 2012
PCB 52	1.3 ± 0.1 3.95 (mathematical model) 0.3–5.5	Schettgen et al. 2012 Broding et al. 2007 Wolff and Schecter 1991; Wolff et al. 1992
PCB 101	0.02–0.04 2.8 ± 0.7	Luotamo et al. 1991 Schettgen et al. 2012
PCB 138	16.3 16.7 (8.4–40) 3.3–4.9 6–7 0.88	Yakushiji et al. 1984 Wolff et al. 1992 Ryan et al. 1993 Brown et al. 1989 Bühler et al. 1988
PCB 153	27.5 12.4 3.6–5.4 0.93	Yakushiji et al. 1984 Brown et al. 1989 Ryan et al. 1993 Bühler et al. 1988
PCB 180	0.34 3.7–5.7	Bühler et al. 1988 Ryan et al. 1993
Dioxin-like PCBs		
PCB 77	0.1–5.02	O'Grady Milbrath et al. 2009
PCB 81	0.7*	
PCB 105	0.51–7.0	
PCB 114	10	
PCB 118	0.77–17.6	
PCB 123	7.4–15.3	
PCB 126	1.6–11	
PCB 156	1.62–16	
PCB 157	18	
PCB 167	10*; 12	
PCB 169	7.3–10.4; 13*	
PCB 189	22	

* in adipose tissue

for all congeners with age. According to Schettgen et al. (2011), this increase is for the six indicator congeners from about 1.6 µg/l plasma in 20- to 29-year-old persons to about 5.5 µg/l in persons older than 60 years (95th percentile in each case).

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Authors: W. Rettenmeier, T. Kraus, H. Drexler (Chair of the Working Group "Setting of Threshold Limit Values in Biological Materials", Deutsche Forschungsgemeinschaft), A. Hartwig (Chair of the Permanent Senate Commission for the Investigation of Health Hazards in the Work Area, Deutsche Forschungsgemeinschaft), MAK Commission (Permanent Senate Commission for the Investigation of Health Hazards in the Work Area, Deutsche Forschungsgemeinschaft)
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