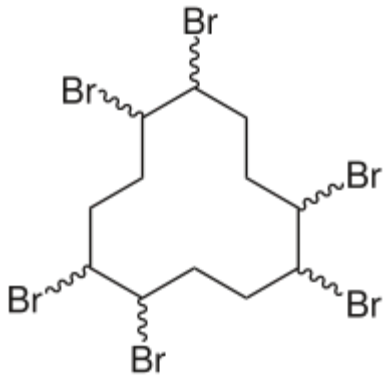
FACTSHEET **HBM value for** **HBCD**			
Substance	**1,2,5,6,9,10-Hexabromcyclododecan**		
Parameter	**Value / Descriptor**	**Dimension**	**Comments**
HBM Guide value			
Guide value II (HBM- II, Health hazard value)	n.a.		
Guide value I (HBM-I, Precautionary value)	0,3	µg/g lipid	plasma/ serum and breast milk lipid, adipose tissue
Year of issue	2015		
status	final		49. session of the HBM-commission
General Information			
CAS No	25637-99-4		3194-55-6 (unspec.) 25637-99-4 (isomere mixture) 134237-50-6 (α-HBCD) 134237-51-7 (β-HBCD) 134237-52-8 (γ-HBCD)
IUPAC name	Hexabromcyclododecane		
Molar mass	641,73	g/mol	$C_{12}H_{18}Br_6$
HBM-parameter	unchanged substance		concentration in lipid
Database			
Tolerable intake (TDI, RfD, DNEL)	0,1	mg/kg bw/d	DNEL (ECHA), value given for further information, not used by the HBM Commission
Key study / Author(s) (Year)	Eriksson et al. (2006)		used by HBM Commission
Species	mice		.
Route/type of study	oral		single oral dose on postnatal day 10
Study length	90 d		
Exposure	Single oral dose on postnatal day 10		
Critical endpoint/ effect	neurotoxicity		developmental neurotoxic effects
POD	BMDL	mg/kg bw	
POD Value	**0,93**	**mg/kg bw**	**BMDL10**
Assessment factors			**used by HBM Commission**
Dose-response assessment factor	n.a.		
Severity of effect	-		
Adjusted exposure duration factor (time scaling)	n.a.		Oral study
Adjusted study length factor	n.a.		
Route-to-route extrapolation factor	n. a.		
Interspecies factor	_		kinetic

	2.5		dynamic
Intraspecies factor	-		kinetic
	3.16		dynamic
Sensitive population factor	1		included in study design
Other adjustment factors Quality of whole database	-		Klimisch (reliable)
Total assessment factor (TAF)	**8**		
Kinetik terms			
absorption factor	0,85		
absorbed dose (internal POD)	0,79	mg/kg bw	0,93 x 0,85
percentage of fatty tissue (women)	32	%	lipid compartment (women)
Result (Calculation)			
Internal POD/TAF	0,099	mg/kg bw	0,79 / 8; absorbed single dose
Kinetic extrapolation Body burden (fatty tissue, lipid) and calculated HBM values	0,099 / 0,32 = 0,31	mg/kg lipid	Rounded guide value : 0,3 µg/g lipid equivalent to 1,6 µg/l plasma

Rationale

HBM Commission deliberated the HBM value for HBCD on the basis of a dossier prepared by the Fraunhofer Institute (FhG, O. Licht and I. Mangelsdorf) on behalf of the Federal Environment Agency

ECHA has used a NOAEC of 10 mg/kg bw/d from the 2 generation oral feeding study by Ema et al 2008 and derived a DNEL of 0.1 mg/kg bw/d by using a default UF of 100 (10 x 10). Aylward and Hays (2011) estimated lipid-adjusted tissue concentrations in the laboratory animals at this point of departure in the range of 120,000 ng/g lipid. A provisional BE value of approximately 10,000 ng/g lipid was estimated correspondingly.

EFSA (2011) identified neurodevelopmental effects on behaviour as the critical endpoint, and derived a benchmark dose lower confidence limit for a benchmark response of 10 % (BMDL10) of 0.93 mg/kg body weight.

In accordance with the EFSA Panel on Contaminants in the Food Chain (2011) the HBM Commission considered the study of Eriksson et al. 2006 as key study and the resulting BMDL10 as POD for the derivation of the HBM value and followed the EFSA Panel procedure.

The available toxicokinetic data suggest that orally administered HBCD is easily absorbed and accumulates in lipid tissue. Because elimination kinetics of HBCD in rodents and humans differ, external dose levels of HBCD associated with toxic effects in animals cannot be simply extrapolated for the risk assessment in humans. Instead, the internal dose or body burden provides a more appropriate dose metric for a direct comparison of effects in animals and humans. Based on the calculated BMDL10 value of 0.93 mg/kg bw as derived from the Eriksson et al. study using a single oral administration, and considering an oral absorption in rodents of 85 %, a body burden at the BMDL10 of 0.79 mg/kg bw was derived.

Standard assessment factors (AFs) for differences in toxicodynamics (interspecies = 2.5 and intraspecies = $\sqrt{10}$) were applied, resulting in a total assessment factor (TAF) of 8.

With reference to a proportion of 32% fatty tissue (women) a factor of 0,32 has to be applied to relate the internal dose to the lipid compartment of the body.

The rounded HBM value is set at 0,3 µg/g lipid.

Concentrations in adipose tissue of the general population range from < 0,08 to 10 ng/g lipid (median), which is clearly below the HBM-I value.

Literature

Aylward LL, Hays SM (2011) Biomonitoring-based risk assessment for hexabromocyclododecane (HBCD). Int J Hyg Environ Health. 214(3), 179-187

EFSA Panel on Contaminants in the Food Chain (CONTAM); Scientific Opinion on Hexabromocyclododecanes (HBCDDs) in Food. EFSA Journal 2011;9(7):2296. [118 pp.] doi:10.2903/j.efsa.2011.2296. Available online: www.efsa.europa.eu/efsajournal

Ema M, Fujii S, Hirata-Koizumi M, Matsumoto M (2008)Two-generation reproductive toxicity study of the flame retardant hexabromocyclododecane in rats. Reprod Toxicol. 25(3):335-351 http://www.ncbi.nlm.nih.gov/pubmed/18262388

Eriksson P, Fischer C, Wallin M, Jakobsson E, Fredriksson A. Impaired behaviour, learning and memory, in adult mice neonatally exposed to hexabromocyclododecane (HBCDD). Environ Toxicol Pharmacol. 2006 May;21(3):317-22.

Kommission Human-Biomonitoring des Umweltbundesamtes (2014):Grundsatzpapier zur Ableitung von HBM-Werten. Stellungnahme der Kommission Human-Biomonitoring des Umweltbundesamtes. Bundesgesundheitsbl Gesundheitsforsch Gesundheitsschutz 57(1):138-147 http://link.springer.com/article/10.1007/s00103-013-1867-2