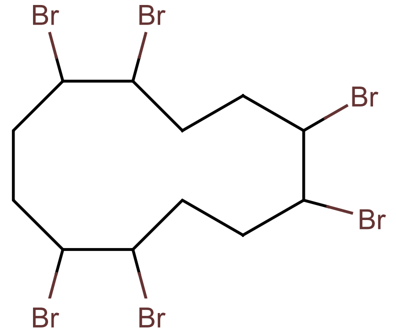
HEXABROMOCYCLODODECANE

This EQS dossier was prepared by the Sub-Group on Review of the Priority Substances List (under Working Group E of the Common Implementation Strategy for the Water Framework Directive).

The dossier was reviewed by the Scientific Committee on Health and Environmental Risks (SCHER), which commented that it did not agree with the generic use of an additional assessment factor of 10 for the marine AA-QS or MAC-QS, nor with the additional assessment factor of 5 for the marine sediment EQS. The basis for the use of the additional factors in these cases has been explained in more detail with reference to the Technical Guidance for Deriving EQS (European Commission, 2011). The SCHER also commented that it did not agree with the NOAEL selected for human health. Further explanation has been included in the dossier. Some statements in sections 4.2 and 6.1 regarding emissions and concentrations have also been qualified in response to the SCHER's comments.

1 CHEMICAL IDENTITY

Common name	Hexabromocyclododecane
Chemical name (IUPAC)	Hexabromocyclododecane
Synonym(s)	Cyclododecane, hexabromo- HBCDD HBCD
Chemical class (when available/relevant)	
CAS numbers	25637-99-4 (1,3,5,7,9,11-Hexabromocyclododecane) 3194-55-6 (1,2,5,6,9,10- Hexabromocyclododecane) 134237-50-6 (α-Hexabromocyclododecane) 134237-51-7 (β-Hexabromocyclododecane) 134237-52-8 (γ- Hexabromocyclododecane)
EU number	247-148-4 221-69-59
Molecular formula	$C_{12}H_{18}Br_6$
Molecular structure	
Molecular weight (g.mol^{-1})	641.7

2 EXISTING EVALUATIONS AND REGULATORY INFORMATION

Annex III EQS Dir. (2008/105/EC)	Not Included
Existing Substances Reg. (793/93/EC)	Priority List No 2, ECB # 044
Pesticides (91/414/EEC)	Not included in Annex I
Biocides (98/8/EC)	Not included in Annex I
PBT substances	Fulfilling PBT criteria
Substances of Very High Concern (1907/2006/EC)	Yes (on the candidate list for authorisation)
POPs (Stockholm convention)	Under evaluation*
Other relevant chemical regulation (veterinary products, medicament, ...)	No
Endocrine disruptor	Effects of HBCDD on the thyroid system in mammals has been shown in some studies (see *e.g.* Ema *et al.* 2008; Saegusa *et al.* 2009; van der Ven *et al.* 2009; Lilienthal *et al.* 2009, evaluated in EU-RAR (2008) and CHL Report for hexabromocyclododecane (2009). Effects on the thyroid system in fish has also been seen in some studies (*e.g.* Palace *et al.,* 2008). See sections 6.3 and 6.4 below. However, no evaluation specifically addressing endocrine disruptive properties has been undertaken.

* HBCDD is a candidate substance under evaluation by the Persistent Organic Pollutants Review Committee, see http://chm.pops.int/Default.aspx (accessed 2010-02-12).

3 PROPOSED QUALITY STANDARDS (QS)

3.1 ENVIRONMENTAL QUALITY STANDARD (EQS)

QS for secondary poisoning is the “critical QS” for derivation of an Environmental Quality Standard.

The technical HBCDD products consist primarily of the γ-stereoisomer and with some α- and β-HBCDD. The stereoisomers have different chemical and physical properties. However, in most toxicity studies commercial products containing all stereoisomers have been used. It is thus not possible to derive QSs for the stereoisomers separately. Further, there is evidence for both abiotic and biotic isomerization between diastereoisomers. The composition in environmental compartments therefore differs from the technical products and it can also shift within food webs. The QSs and EQS are derived for the sum of stereoisomers.

	Value	Comments
Proposed AA-EQS for [biota] [μg.kg^{-1}$_{biota\ ww}$] Corresponding AA-EQS in [water] [μg.L^{-1}]	**167** 0.0016 (freshwater), 0.00080 (marine water)	**Critical QS is QS$_{biota, sec\ pois}$** **See section 7.2**
Proposed MAC-EQS for [freshwater] [μg.L^{-1}] **Proposed MAC-EQS for [marine waters] [μg.L^{-1}]**		**See section 7.1**

3.2 SPECIFIC QUALITY STANDARD (QS)

Protection objective*	Unit	Value	Comments
Pelagic community (freshwater)	[μg.l^{-1}]	0.31	See section 7.1
Pelagic community (marine water)	[μg.l^{-1}]	0.031	
Benthic community (freshwater)	[μg.kg^{-1} $_{dw}$]	860	See section 7.1
	[μg.l^{-1}]		
Benthic community (marine)	[μg.kg^{-1} $_{dw}$]	170	
	[μg.l^{-1}]		
Predators (secondary poisoning)	[μg.kg^{-1}$_{biota\ ww}$]	167	See section 7.2
	[μg.l^{-1}]	0.0016 (freshwaters) 0.00080 (marine waters)	
Human health via consumption of fishery products	[μg.kg^{-1}$_{biota\ ww}$]	6100	See section 7.3
	[μg.l^{-1}]	0.058 (fresh and marine waters)	
Human health via consumption of water	[μg.l^{-1}]		

* Please note that as recommended in the Technical Guidance for deriving EQS (draft version), “EQSs […] are not reported for ‘transitional and marine waters’, but either for freshwater or marine waters”. If justified by substance properties or data available, QS for the different protection objectives are given independently for transitional waters or coastal and territorial waters.

4 MAJOR USES AND ENVIRONMENTAL EMISSIONS

4.1 USES AND QUANTITIES

HBCDD is a high production volume (HPV) chemical with four producers/importers listed in ESIS (http://ecb.jrc.ec.europa.eu/esis/). According to the risk assessment (EU-RAR, 2008) HBCDD is only produced at one site in EU (EU 15). This site is located in the Netherlands and had an assumed production volume of 6000 tonnes in the year 2005. Two other European factories were closed down in 1997 and 2003, respectively. The global production in 2008 was around 13,400 tonnes annually.

HBCDD is used as a flame retardant, mainly within the polymer and textile industry (EU-RAR, 2008). According to Frölich (2002, quoted in EU-RAR, 2008) 90 % of the HBCDD is used in polystyrene and the major use of this material is in rigid insulation panels/boards (EPS and XPS) that are used in building constructions.

HBCDD is covered by the industrial voluntary control programs VECAP[†] and SECURE[‡]. According to the VECAP annual report (VECAP, 2009) total sold amount of HBCDD in the EU was 10897 tonnes in 2007 and 8913 tonnes in 2008. These numbers are based on a survey conducted amongst 135 user's sites and 93 % of the HBCDD volume consumption sold by EBFRIP[§] members sold was covered in 2007 (60 out of 73 sites).

[†] VECAP is a voluntary initiative of the European Brominated Flame Retardant Industry Panel – EBFRIP together with the industry's global organisation, the Bromine Science and Environmental Forum – BSEF

[‡] Self Enforced Control of Use to Reduce Emissions (SECURE), a programme operated by PlasticsEurope and EXIBA.

[§] The European Brominated Flame Retardant Industry Panel (EBFRIP) www.ebfrip.org

4.2 ESTIMATED ENVIRONMENTAL EMISSIONS

Emissions of HBCDD as estimated in the EU-RAR (2008) are presented in the summary table below. Direct releases to soil were not considered a relevant route within the EU-RAR (2008). The largest estimated emissions were related to textile uses. More updated estimates on total emissions from production, warehouses and first line direct users have been done by surveys conducted by the European Brominated Flame Retardant Industry Panel (VECAP, 2009). These surveys do not cover back coating of textiles. The 2008 survey resulted in a total potential emission of 2017 kg/year, whereas the 2009 survey resulted in a decrease to 309 kg/year (VECAP, 2009). The reduction for the 2009 survey was achieved by the implementation of the VECAP best practices for controlling emissions, but also partially explained by refinements of the estimation methodology due to better information on packaging waste disposal.

Table 3.34 Summary of releases from the EU-RAR (2008)

	Total (kg/year)			Continental (kg/year)			Regional (kg/year)		
Life-cycle stage	**Air**	**Waste-water**	**Surface-water**	**Air**	**Waste-water**	**Surface-water**	**Air**	**Waste-water**	**Surface-water**
Production	2.0	0.73	0	0	0	0	2.0	0.73	0
Micronising	0.3	0	0	0	0	0	0.3	0	0
Formulation EPS and HIPS	19.5	48	212	19.1	48	99	0.4	0	113.4
Formulation XPS	11.3	71.2	8.5	5.7	35.6	4.3	5.7	35.6	4.3
Formulation polymer dispersion (for textiles)	6.8	220	55	4.5	146	37	2.3	74	18
Industrial use EPS	102	82	20.4	92	74	18	10.2	8.2	2
Industrial use HIPS	6.3	5.0	1.3	5.7	4.5	1.2	0.63	0.5	0.13
Industrial use XPS (compound)	100	27	7	80	21.6	5.6	20	5.4	1.4
Industrial use XPS (powder)	23.6	26.4	6.6	21.5	9.5	2.4	2.1	16.9	4.2
Industrial use textile (backcoating)	0.64	5653	1413	0.32	2826	706	0.32	2826	706
Professional use insulation boards (at building sites)	182	0	182	164	0	164	18	0	18
Service Life Textiles (washing)	0	10.5	0	0	7.9	0	0	2.6	0
Service Life Textiles (wear)	0	107	27	0	80	20	0	27	7
Service Life EPS&XPS	54	0	0	48.6	0	0	5.4	0	0
Total emissions	508	6251	1933	441	3253	1058	67.4	2997	874
kg/day*	1.39	17.1	5.29	1.21	8.9	2.89	0.18	8.21	2.39

*These emissions are used in the EUSES model for the estimation of the regional and continental background

5 ENVIRONMENTAL BEHAVIOUR

5.1 ENVIRONMENTAL DISTRIBUTION

		Master reference
Water solubility ($mg.l^{-1}$)	0.066 at 20°C (sum of α-, β-, γ-HBCDD) 0.0488 (α-HBCDD) 0.0147 (β-HBCDD) 0.0021 (γ-HBCDD)	MacGregor and Nixon (2004) Cited in EU-RAR (2008)
Volatilisation		
Vapour pressure (Pa)	$6.3*10^{-5}$ Pa at 21°C	Stenzel and Nixon (1997) Cited in EU-RAR (2008)
Henry's Law constant ($Pa.m^{3}.mol^{-1}$)	0.75 (calculated from vapour pressure and water solubility)	EU-RAR (2008)
Adsorption	**The Koc value 45709 is used for derivation of quality standards.**	
Organic carbon – water partition coefficient (K_{OC})	K_{OC} = 45709 (Log K_{oc}= 4.66, QSAR equation Log K_{oc}= 0.81 Log K_{ow} + 0.10)	EU-RAR (2008)
Suspended matter – water partition coefficient ($K_{sed\text{-}water}$)	1143.7	Calculated from the Koc according to the methodology described in the TGD for deriving EQS (2010)
Bioaccumulation	**The BCF value 18100 for fish is used for derivation of quality standards.**	
Octanol-water partition coefficient (Log Kow)	5.62 (technical product)	MacGregor and Nixon (1997) Cited in EU-RAR (2008)
	5.07±0.06 α-HBCDD 5.12±0.09 β-HBCDD 5.47±0.10 γ-HBCDD	Hayward *et al.* (2006) Cited in EU-RAR (2008)
BCF (measured)	18100 (*Pimephales promelas*, steady state) 8974-21940 (*Oncorhynchus mykiss*, whole fish, BCF differ depending on exposure concentration and calculation method)	Veit *et al.* (1979) and Drottar and Krueger (2000) Evaluated in EU-RAR (2008)
	BAFs, various fish species: 310-6000 ΣHBCDD 1200-23000 α-HBCDD 250-3500 β-HBCDD 110-3200 γ-HBCDD (L/ng lw)	Harrad *et al.* (2009a) Harrad *et al.* errata (2010)

	105000 ΣHBCDD (average) (L/kg fw)	
	Only α-HBCDD found in eggs of guillemot, white-tailed sea eagle and peregrine falcon, whereas γ-HBCDD made up 25-33% of total HBCDD in herring. Highest concentrations were found in eggs of the two top-predators.	Janak *et al.* (2008)
	BMF of α-HBCDD, ringed seal (blubber) to polar bear (adipose tissue: 1.7	Letcher *et al.* (2009)
	Arctic marine food web (beluga whale, narwhal, walrus, cod, shrimp, clams, deepwater redfish and zooplankton), eastern Canada. Trophic magnification factor (TMF) of 2.1 for α-HBCDD. Dilution of γ-HBCDD with trophic level. Determined using stable N-isotopes.	Tomy *et al.* (2008)
	Fresh water food web (snail, prawn, carps, snakehead, water snake), southern China. TMF of 1.8 and 2.2 (ΣHBCDD and α-HBCDD, respectively)	Wu *et al.* (2010)
	BMFs for *Oncorhynchus mykiss* fed fortified food. 9.2 (α-HBCDD) 4.3 (β-HBCDD) 7.2 (γ-HBCDD)	Law *et al.* (2006a)
	Fresh water food web (zooplankton, mussels and various fish species), Lake Winnipeg, Canada. TMF of 1.8 (ΣHBCDD) BMFs (predator/prey): 0.1-8.2 (α-HBCDD) 0.3-5.0 (β-HBCDD) 0.3-6.3 (γ-HBCDD)	Law *et al.* (2006b) Law *et al.* (2007)
	Fresh water food web (plankton, various invertebrates and fish species), Lake Ontario, Canada. TMF of 6.3 (ΣHBCDD) BMFs (predator/prey): 0.4-10.8 (α-HBCDD) 0.2-9.9 (β-HBCDD)	Tomy *et al.* (2004)
	Arctic marine food web (beluga, ringed seal, cod, herring, cisco), western Canada No significant TMF found BMFs (predator/prey): 0.1-1.7 (α-HBCDD) Results suggest accumulation in lower TL animals, but metabolic depletion in higher	Tomy *et al.* (2009)

	TL animals.	
	Food chain scenarios based on median concentrations of monitoring data (marine mammals/fish). Baltic Sea: 61 and 5.8 Western Scheldt: 187 and 11 UK Harbour porpoise: 1859 and 44 (wet weight basis and lipid weight basis respectively)	EU-RAR (2008)

5.2 ABIOTIC AND BIOTIC DEGRADATIONS

		Master reference
Hydrolysis	Hydrolysis considered to be of low significance	EU-RAR (2008)
Photolysis		
	Shift in diastereomer composition caused by exposure to light, predominantly from γ to α. Estimated half-life in indoor dust: 12.2 weeks in presence of light, 26 weeks in absence of light.	Harrad *et al.* (2009b)
Biodegradation	Degradation half-lives based on 2 simulation studies Aer. fresh. sed: 11 & 101 days (20˚C), 21 & 191 days (12˚C) Anaer. fresh. sed: 1.5 & 66 days (20˚C), 2.8 & 125 days (12˚C) Method of scaling measured half-lives from 20˚C to 12˚C questioned by Arnot *et al.* (2009)	EU-RAR (2008) Arnot *et al.* (2009)

6 AQUATIC ENVIRONMENTAL CONCENTRATIONS

6.1 ESTIMATED CONCENTRATIONS

Compartment	Predicted environmental concentration (PEC)	Master reference
Freshwater	0.028-170 µg/l (local, annual average) 0.028 µg/l (regional) 0.0005 µg/l (continental) Calculated with EUSES	EU-RAR (2008)
Marine waters (coastal and/or transitional)	0.0028-17 µg/l (local, annual average) 0.0028 µg/l (regional) 0.000010 µg/l (continental) Calculated with EUSES	EU-RAR (2008)
Sediment	Fresh water sediment: 130-1700000 µg/kg dw (local) 81 µg/kg dw (regional) 1.4 µg/kg dw (continental) Marine sediment: 13-170000 µg/kg dw (local) 3.5 µg/kg dw (regional) 0.013 µg/kg dw (continental) Calculated with EUSES	EU-RAR (2008)
Biota (freshwater)	5430-4799215 µg/kg ww Modified based on measured values: 20-6000000 µg/kg ww Calculated with EUSES	EU-RAR (2008)
Biota (marine)	543-1719772 µg/kg ww Modified based on measured values: 1.8-1600000 µg/kg ww Calculated with EUSES	EU-RAR (2008)
Biota (marine predators)	5430-3443887 µg/kg ww Modified based on measured values: 336-3100000 µg/kg ww Calculated with EUSES	EU-RAR (2008)

In the EU-RAR (2008), the local, regional, and continental predicted environmental concentrations (PECs) have been calculated with EUSES 2.0.3. Local PECs have been determined both for sites with site-specific data provided by industry, and as generic local PECs. For sediments, the highest local PECs represents intermittent releases. In the EU-RAR, PECs for biota have been calculated according to the following formulas:

$PEC_{oral,\ predator} = (PEClocal_{freshwater} + PECregional_{freshwater}) * 0.5\ BCF_{fish} * BMF_1$

$PEC_{oral,\ predator} = (PEClocal_{seawater} + PECregional_{seawater}) * 0.5\ BCF_{fish} * BMF_1$

$PEC_{oral,\ toppredator} = (0.1 * PEClocal_{seawater} + 0.9 * PECregional_{seawater}) * BCF_{fish} * BMF_1 * BMF_2$

with

BCF_{fish}: 18100

BMF_1: 10

BMF_2: 10

For biota, PECs modified based on measured concentrations are also presented. Comparisons of calculated biota PECs and measured concentrations indicate possible overestimations by the model. For the risk characterization in the EU-RAR (2008), the values for $PECregional_{freshwater}$ and $PECregional_{seawater}$ where thus modified so that the resulting regional parts of the biota PECs became equal to median measured values selected to represent regional concentrations in freshwater fish, marine fish and marine mammals. The calculations of modified PECs are presented in detail in the EU-RAR (2008).

6.2 MEASURED CONCENTRATIONS

Compartment	**Measured environmental concentration (MEC)**	**Master reference**
Freshwater	<0.05-1.52 and <0.05-1.31 µg/l (UK rivers 2002, filtrated water and associated with suspended solids respectively) < 0.4-0.88 µg/l (UK rivers 2005, total concentrations)	Deuchar (2002) and UK Environment Agency (2006) Cited in EU-RAR (2008)
	Recipient river Viskan, Sweden, 2008 Below the reporting limits 0.1 and 0.05 ng/l (n=6, unfiltered samples)	Lilja *et al.* (2010)
	Nine English freshwater lakes, sampled 2008-2009 0.080-0.270 ng/l (sum of particulate and dissolved phases)	Harrad *et al.* (2009a)

Marine waters (coastal and/or transitional)	74 µg/kg dw (Western Scheldt, suspended particles) 472 µg/kg dw (Gent, Tern Canal, suspended particles)	Bouma *et al.* (2000) Cited in EU-RAR (2008)
WWTP effluent	Swedish municipal WWTPs, 2008 0.05-0.25 ng/l (n=7, unfiltered samples)	Lilja *et al.* (2010)
Sediment	Concentrations in freshwater sediments measured in Belgium, Swizerland, Spain, Ireland, Norway, Sweden and UK: <0.1-33500 µg/kg dw mean: 338±2690 µg/kg dw median: 1.6 µg/kg dw (n=183) <0.1-511 µg/kg dw mean: 31±78 µg/kg dw median:1.5 µg/kg dw (samples considered affected by local point sources excluded, n=162)	EU-RAR (2008)
	Nine English freshwater lakes, sampled 2008-2009 0.880-4.80 µg/kg dw	Harrad *et al.* (2009a)
	Concentrations in estuarine/brackish/marine sediments measured in Ireland, the Netherlands and Norway: <0.5-8024 µg/kg dw, mean: 174±1100 µg/kg dw median: 4.2 µg/kg dw (n=53) <0.5-128 µg/kg dw, mean: 11±26 µg/kg dw median: 2.8 µg/kg dw (samples considered affected by local point sources excluded, n=45)	EU-RAR (2008)

Biota	Lake Geneva, Switzerland Lake trout 49-324 ng g^{-1} l.w.	Cheaib *et al.* (2009)
	Sweden, several sampling sites along the west and east coasts Herring (muscle) 1.5-185 ng g^{-1} l.w. (decreasing concentrations at three out of six sampling stations)	Bignert *et al.* (2009)
	Dutch freshwaters Eel <0.1-230 Pike-perch <0.1 (ng g^{-1} w.w.)	Van Leeuwen and de Boer (2008)
	Nine English freshwater lakes, various species sampled 2008 14-290 ng g^{-1} l.w.	Harrad *et al.* (2009a)
	Freshwater fish, EU and Norway 0.005-9432 ng g^{-1} w.w. 0.52-160905 ng g^{-1} l.w.	EU-RAR (2008)
Biota (marine predators)	Sweden, Baltic Sea, Stora Karlsö, 2007 Guillemot eggs 140-210 ng g^{-1} l.w., increasing trend (3% $year^{-1}$)	Bignert *et al.* (2009)
	Northern and southwestern Sweden Peregrine falcon eggs < 8.9-1900 ng g^{-1} l.w.	Johansson *et al.* (2009)
	Northern Norway Increasing concentration in seabird eggs 1983-2003 Herring gulls, 16-108 (1983-2003) Kittiwake, 30-142 (1983-2003) Atlantic puffin 12-58 (1983-2003) ng g^{-1} l.w.	Helgason *et al.* (2009)
	UK coasts Harbour porpoises	Law *et al.* (2008)

	stranded or by-caught, 1994-2006, blubber Yearly mean: 30-5450 ng g^{-1} l.w., Range of individual measurements: < 10-21400 ng g^{-1} l.w., Significant increase 2000-2001, decrease 2003-2004.	

7. EFFECTS AND QUALITY STANDARDS

7.1 ACUTE AND CHRONIC AQUATIC ECOTOXICITY

ACUTE EFFECTS			Val. score[**]/Comments given in EU-RAR	Master reference
Algae & aquatic plants ($mg.l^{-1}$)	**Freshwater**	*Selenastrum capricornutum* / 72 h EC_{50} : > 0.0025 (measured highest tested concentration)	Considered valid.	Roberts and Swigert (1997) Evaluated in EU-RAR (2008)
	Marine	*Chlorella sp.*/ 96 h EC_{50} : > above water solubility	Study not performed according to guideline. Results used as supportive data in EU-RAR	Walsh *et al.* (1987) Evaluated in EU-RAR (2008)
		Thallassiosira pseudonana / 72 h EC_{50} : 0.040		
		Skeletonema costatum / 72 h EC_{50} : 0.009		
		Skeletonema costatum / 72 h EC_{50} : 0.052	Considered valid	Desjardins *et al.* (2005) Evaluated in EU-RAR (2008)
Invertebrates ($mg.l^{-1}$)	**Freshwater**	*Daphnia magna* / 48 h EC_{50} : > 0.0032 (mean of measured values at the highest tested concentration)	Considered valid	Graves and Swigert (1997a) Evaluated in EU-RAR (2008)
	Marine	*Gender species* / d or h EC_{50} : No data available		
	Sediment	*Gender species* / d or h EC_{50} : No data available		
Fish ($mg.l^{-1}$)	**Freshwater**	*Oncorhynchus mykiss* / 96 h EC_{50} : > 0.0068 (no effects observed at highest tested concentration, with a mean measured value of 0.0025 mg/l)	Considered valid	Graves and Swigert (1997b) Evaluated in EU-RAR (2008)
		Leuciscus idus / 96 h EC_{50} : > 10000 (no effects observed at any tested concentartion)	Considered to be of low reliability	Kirsch and Munk (1988) Evaluated in EU-RAR (2008)

[**] Klimisch, H. J., M. Andreae, et al. (1997). "A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data." Regulatory Toxicology and Pharmacology **25**: 1-5.

		Lepomis macrochirus / 96 h EC_{50} : > 100 (no effects observed at any tested concentration)	Considered to be of low reliability	Calmbacher (1978) Evaluated in EU-RAR (2008)
		Danio rerio / 96 hpf Effects on survival rate and heart rate at 0.05 mg/l. Effects on malformation rate, body length, apoptotic cells and ROS formation at 0.1 mg/l	2	Deng *et al.* (2009)
	Marine	*Gender species* / d or h EC_{50} : No data available		
	Sediment	*Gender species* / d or h EC_{50} : No data available		
Other taxonomic groups		*Gender species* / d or h EC_{50} : No data available		

CHRONIC EFFECTS			Val. score/Comments given in EU-RAR	Master reference
Algae & aquatic plants (mg.l^{-1})	**Freshwater**	*Selenastrum capricornutum* / 72 h NOEC : > 0.0025 (measured highest tested concentration)	Considered valid	Roberts and Swigert (1997) Evaluated in EU-RAR (2008)
	Marine	*Sceletonema costatum* / 72 h NOEC : > 0.010	Considered valid	Desjardins *et al.* (2005) Evaluated in EU-RAR (2008)
		Sceletonema costatum / 72 h NOEC : ≤ 0.040	Considered valid	Desjardins *et al.* (2004) Evaluated in EU-RAR (2008)
Inver tebrates (mg.l^{-1})	**Freshwater**	*Daphnia magna* / 21 d NOEC : 0.0031	Considered valid	Drottar and Krueger (1998) Evaluated in EU-RAR (2008)
	Marine	*Macoma baltica* / 50 d / nuclear and nucleolar abnormalities NOEC : < 0.1 (static experiment, nominal water concentration, exposure also through food)	2	Smolarz and Berger (2009)
	Sediment	*Hyalella azteca* / 28 d NOEC : ≥ 1000 mg/kg dw (2% and 5% organic carbon)	Considered valid	Thomas *et al.* (2003a) and Thomas *et al.* (2003b) Evaluated in EU-RAR (2008)
		Lumbriculus variegatus / 28 d NOEC : 8.6 mg/kg dw (total number of worms, normalised to 5% organic carbon)	Considered valid	Oetken *et al.* (2001) Evaluated in EU-RAR (2008)
		Chironomus riparius / 28 d NOEC : 37.8 mg/kg dw (number of eggs from F1 generation, normalised to 5% organic carbon)	Considered valid	Oetken *et al.* (2001) Evaluated in EU-RAR (2008)
Fish (mg.l^{-1})	**Freshwater**	*Oncorhynchus mykiss* / 88 d (27 d hatching, 61 d post-hatch) NOEC : > 0.0037 (no effects on hatching success, time to swim-up, larvae and fry survival or growth, at highest measured tested concentration)	Considered valid	Drottar *et al.* (2001) Evaluated in EU-RAR (2008)

		Gobiocypris rarus / 42 d SOD activity, ROS and protein carbonyl formation in brain, DNA damage (Oliver tail movement) in erythrocytes. NOEC: 0.001 EROD and PROD activity in liver, lipid peroxidation (TBARS) in brain. NOEC: 0.01	2	Zhang *et al.* (2008)
		Salmo salar / 30 d, peak smoltification period / decreased olfactory sensitivity, effects on thyroid hormone levels Exposure conc: 0.000011	3	Lower and Moore (2007)
		Oncorhynchus mykiss / 56 d / altered thyroid hormone levels and deiodinase activity. Exposure to α-, β- & γ-HBCDD separately through fortified food. Exposure concentrations were 29, 11, and 23 ng/g lw, respectively.	2	Palace *et al.* (2008)
	Marine			
	Sediment	*Platichthys flesus* / 78 d / thyroid hormones, histology, enzyme activities. No effects seen at the highest tested doses; 800 µg/g TOC (0.24 mg/kg dw) + 300 µg/g lipid in food, or 8000 µg/g TOC (2.4 mg/kg dw)	2	Kuiper *et al.* (2007)
Other taxonomic groups		*Gender species* / d NOEC : No data available		

There are acute toxicity data for nine species representing algae, crustaceans and fish. Chronic toxicity data are available for 11 species representing algae, crustaceans, molluscs, annelids and fish.

Most of the studies have been evaluated in the EU-RAR (2008), but in the EU-RAR no Klimisch codes are presented. For these studies, it is indicated if they are considered valid in the EU-RAR.

The tentative AA-QSs for fresh and marine water for direct ecotoxicity were calculated from the chronic toxicity NOEC of 0.0031 $mg.l^{-1}$ derived from a 21-day study with *Daphnia magna*, and the assessment factors 10 and 100, in accordance with the TGD for deriving EQS (2010). There are two studies available reporting lower effect concentrations (Zhang *et al.*, 2008; Lower and Moore, 2007). However, the relevance of the endpoints used in these studies is not easily assessed. Further, the study by Lower and Moore (2007) is considered to be of low reliability due to the lack of true replicates and only one exposure concentration. For the tentative MAC-QSs for direct ecotoxicity, the EC_{50} value derived from a toxicity study with *Sceletonema costatum* is used and assessment factors of 100 and 1000 are applied for freshwater and marine waters, respectively. The limited acute and chronic toxicity data do not provide convincing evidence that the sensitivity of marine organisms is covered by the sensitivity of freshwater species. Thus, in accordance with the TGD for deriving EQS (European Commission 2011) larger assessment factors are applied to derive the marine QSs.

Tentative QSs for sediment were calculated from the lowest chronic NOEC of three, from studies with sediment dwelling species with different feeding regimes. No marine benthic toxicity data on relevant endpoints has been identified. In accordance with chapter 5.2 of the TGD for deriving EQS (European Commission 2011), an assessment factor of 10 was used for the $QS_{freshwater, sed.}$, whereas for the $QS_{marine water, sed.}$ the assessment factor was 50.

The TGD for deriving EQS (2011) recommend the adoption of PNECs derived in risk assessments under Regulation (EC) No. 793/93 as QSs, if new data do not alter the evaluation undertaken. The resulting tentative QSs are the same as the PNECs derived in the EU-RAR (2008).

Tentative QS_{water}	**Relevant study for derivation of QS**	**Assessment factor**	**Tentative QS**
$MAC_{freshwater, eco}$	*Sceletonema costatum* / 72 h EC_{50} : 0.052 $mg.l^{-1}$	100	0.52 $µg.l^{-1}$
$MAC_{marine water, eco}$		1000	0.052 $µg.l^{-1}$
$AA\text{-}QS_{freshwater, eco}$	*Daphnia magna* / 21d NOEC : 0.0031 $mg.l^{-1}$	10	0.31 $µg.l^{-1}$
$AA\text{-}QS_{marine water, eco}$		100	0.031 $µg.l^{-1}$
$AA\text{-}QS_{freshwater, sed.}$	*Lumbriculus variegatus* / 28 d NOEC : 8.6 mg/kg dw (total number of worms, 5% organic carbon)	10	0.86 mg/kg dw
$AA\text{-}QS_{marine water, sed.}$	*Lumbriculus variegatus* / 28 d NOEC : 8.6 mg/kg dw (total number of worms, 5% organic carbon)	50	0.17 mg/kg dw

7.2 SECONDARY POISONING

Secondary poisoning of top predators		Master reference
Mammalian oral toxicity	Rat / Oral / 28 days / liver weight NOAEL : 22.9 $mg.kg^{-1}_{bw}.d^{-1}$ NOEC : 229 $mg.kg^{-1}_{feed}$ (CF= 10)	van der Ven *et al.* (2006) Evaluated in EU-RAR (2008)
	Rat / Oral / 2-generation / decrease in fertility-index and reduced number of primordial follicles, increased pup mortality during lactation in F2. NOAEL : 10 $mg.kg^{-1}_{bw}.d^{-1}$ NOEC : 150 $mg.kg^{-1}_{feed}$	Ema *et al.* (2008) Evaluated in EU-RAR (2008)
	Mouse / Oral / single dose postnatal day 10 / spontaneous behaviour, learning and memory LOAEL: 0.9 $mg.kg^{-1}_{bw}.d^{-1}$ (indicative, results need to be confirmed)	Eriksson *et al.* (2006) Evaluated in EU-RAR (2008)
	Rat / Oral / 1-generation / thyroid related parameters and brain morphometry in offspring NOAEL: 8-21 $mg.kg^{-1}_{bw}.d^{-1}$ NOEC: 100 $mg.kg^{-1}_{feed}$	Saegusa *et al.* (2009) Evaluated in CHL Report for hexabromocyclododecane (2009)
	Rat / Oral / 1-generation / various endocrine and immunological endpoints BMDLs : 0.056-8.6 $mg.kg^{-1}_{bw}.d^{-1}$ NOEC: 0.56-86 $mg.kg^{-1}_{feed}$ (CF= 10, CF in the study varied from 8 to 15)	van der Ven *et al.* (2009) Evaluated in CHL Report for hexabromocyclododecane (2009)
	Rat / Oral / 1-generation / cataleptic behaviour and BAEP BMDLs : 0.6-6 $mg.kg^{-1}_{bw}.d^{-1}$ NOEC : 6-60 $mg.kg^{-1}_{feed}$ (CF= 10, same study as by van der Ven *et al.* (2009))	Lilienthal *et al.* (2009) Evaluated in CHL Report for hexabromocyclododecane (2009)
Avian oral toxicity	*Coturnix coturnix japonica* (Japanese quail) / Oral / 6 weeks / survival of hatched chicks NOAEL : 0.7 $mg.kg^{-1}_{bw}.d^{-1}$ NOEC : 5 $mg.kg^{-1}_{feed}$	MOEJ (2009)
	Falco sparverius / Oral / 3 wks prior pairing until 2 days before hatching LOAEL: 0.8 $mg.kg^{-1}_{bw}.d^{-1}$ Reduced weight and growth rate of nestlings	Marteinson *et al.* (2009)

In the EU-RAR on HBCDD, there are mainly three studies considered for the risk characterization. From an oral 28-days study on rats, conducted by van der Ven *et al.* (2006), a NOAEL of 22.9 $mg.kg^{-1}_{bw}.d^{-1}$ has been derived. The study found increased liver, thyroid, and pituitary weights. A 2-generation rat study conducted by Ema *et al.* (2008) resulted in a NOAEL of 10 $mg.kg^{-1}_{bw}.d^{-1}$, effects found included a decrease in fertility-index, a reduced number of primordial follicles, and an increased pup mortality during lactation in F2. There is also a study on developmental neurotoxicity effects (seen as changes in spontaneous behaviour, learning and memory defects) conducted by Eriksson *et al.* (2006). It resulted in an indicative LOAEL of 0.9 $mg.kg^{-1}_{bw}.d^{-1}$. In the EU-RAR it is concluded that the study by Eriksson *et al.* (2006) is well performed, but the results need to be confirmed by other laboratories.

Since the EU-RAR on HBCDD was finalised in 2008, some new toxicity studies of relevance for the derivation of QS_{biota} have been published. Two studies not included in the EU-RAR are reviewed in the ongoing European Chemicals Agency (ECHA) evaluation for harmonisation of classification and labelling (CHL Report for hexabromocyclododecane, 2009). A rat 1-generation study performed by Saegusa *et al.* (2009) found effects on the thyroid system (thyroid weight, T3 and TSH levels), the liver (weight), and also brain morphometry (impaired oligodendroglial development) in offspring, resulting in a of NOAEL of 8-21 $mg.kg^{-1}{}_{bw}.d^{-1}$. The study was not conducted according to any guideline. The ECHA-evaluation also presents the study presented by van der Ven *et al.* (2009) and by Lilienthal *et al.* (2009). The experimental set up was based on the OECD415 guideline, but modified to fit a Benchmark Design. In addition, it was enhanced according to the OECD407 guideline for endocrine and immunological endpoints (results reported in van der Ven *et al.*, 2009), and also for assessments on cataleptic behaviour and brainstem auditory evoked potentials (BAEP) (reported in Lilienthal *et al.*, 2009). The results are reported as benchmark dose lower bounds (BMDLs). Reported BMDLs for several parameters are low, in the same range as the indicative LOAEL presented by Eriksson *et al.* (2006). The lowest value, 0.056 $mg.kg^{-1}{}_{bw}.d^{-1}$, is for trabecular bone mineral density. In the ECHA-evaluation it is however stated that the BMDLs derived in the articles by Lilienthal *et al.* (2009) and van der Ven *et al.* (2009) should be viewed with caution.

There are also two recent avian toxicity studies available. An avian reproduction study on Japanese quail, sponsored by the Japan Ministry of the Environment, has been performed by the Research Institute for Animal Science in Biochemistry & Toxicology (MOEJ, 2009). Statistically significant effects on young bird survival and reproductive ability index were seen in the 15 ppm and higher exposure groups. The study reports a NOEC of 5 ppm (0.7 mg/kg/day). These low effect concentrations are supported by a study conducted by Marteinson *et al.* (2009) presented as an abstract. Marteinson *et al.* (2009) exposed American kestrels (*Falco sparverius*) to HBCDD (0.8 mg/kg/day) for three weeks prior pairing until two days before hatching. Reduced weight and growth rates of nestlings were observed.

The tentative QS_{biota} was derived based on the results from the Quail study, using the reported NOEC 5 mg/kg food and an assessment factor of 30. It should be noted that some studies have reported effects at exposure levels lower or in the same range as this NOEC, see above.

The corresponding tentative QS for freshwater and marine waters were calculated with the following formulas according to the TGD for deriving EQS (2010):

$$QS_{freshwater}\ (\mu g/l) = QS_{biota}\ ((\mu g/kg) / BCF\ (l/kg) * BMF_1)$$

$$QS_{marine\ waters}\ (\mu g/l) = QS_{biota}\ ((\mu g/kg) / BCF\ (l/kg) * BMF_1 * BMF_2)$$

For the calculation, the BCF 18100 was used, see Chapter 5.1. Based on the results from a dietary accumulation study, studies on food chains and food chain scenarios based on monitoring data, the EU-RAR (2008) concluded that HBCDD biomagnifies with a $BMF_1 > 1$ and $BMF_2 > 10$. However, no definite BMFs could be determined and the default values for substances with BCF>5000 (BMF_1: 10, BMF_2: 10) were used in the risk assessment.

Since the EU-RAR, some new studies presenting BMFs and TMFs have been published, see section 5.1.

The available BMFs vary between 0.1 and 10.8, whereas the TMFs are in the range 1.8-6.3, most values approximately 2. For the food chain scenarios based on monitoring data given in the EU-RAR, ratios between marine mammals and fish in the range 61-1859 based of fresh weight and 5.8-44 based lipid weight are presented. Thus, for the extrapolation between the tentative QS_{biota} and water concentrations, most of the avaliable TMFs indicate that a factor of 2 for BMF_1 and BMF_2 could be used, whereas some of the BMFs and also the food chain scenarios based on monitoring data indicate a higher biomagnification potential. There are however drawbacks to the use of both the TMF studies and the food chain scenarios presented in the EU-RAR in setting definitive BMFs. Drawbacks include e.g. sampling over several years, lack of TMFs for ΣHBCDD, and the use of trophic levels assigned based on previous studies. Further, for BMF_1 the inclusion of higher trophic level animals potentially metabolising HBCDD may result in TMFs that underestimate the biomagnification potential in fish.

BMF_1 can also be estimated by triangulation with BAFs. In the study by Harrad *et al.* (2009) BAFs expressed on a lipid weight basis are presented. However, in an errata Harrad *et al.* (2010) estimate an average BAF (30 samples, several species) for ΣHBCDD of 105000 L/kg fw assuming a total body lipid content of 5 % to derive the average BMF based on fresh weight. The range for individual data would be 15500-300000 L/kg fw (using same assumptions regarding lipid content as in the errata). By triangulation with the BCF 18100, this result in an average BMF of 5.8, range 0.86-17. BAFs can also be derived from reported concentrations in water and fish in the study by Wu *et al.* (2010). This data results in BAFs (L/kg fw) of 78045, 415139 and 46438, for carp, mud carp and northern snakehead. By triangulation with the BCF 18100, these values result in BMFs of 4.3, 29 and 2.6, respectively.

For BMF_1 the average value of 5.8 derived by triangulation with the BAF presented by Harrad *et al.* (2010) is used.

To illustrate the higher metabolism of HBCDD in higher trophic level animals suggested by several studies (see e.g. Letcher *et al.,* 2009 and Tomy *et al.,* 2009), a BMF_2 of 2 is used for the calculation of corresponding water concentrations.

Tentative QS_{biota}	**Relevant study for derivation of QS**	**Assessment factor**	**Tentative QS**
Biota	NOEC : 5 $mg.kg^{-1}_{feed}$	30	167 $\mu g.kg^{-1}_{biota\ ww}$ corresponding to 0.0016 $\mu g.L^{-1}$ (freshwater) 0.00080 $\mu g.L^{-1}$ (marine waters)

7.3 HUMAN HEALTH

Human health via consumption of fishery products		**Master reference**
Mammalian oral toxicity	Rat / Oral / 28 days / liver weight NOAEL : 22.9 $mg.kg^{-1}_{bw}.d^{-1}$	van der Ven *et al.* (2006) Evaluated in EU-RAR (2008)
	Rat / Oral / 2-generation / decrease in fertility-index and reduced number of primordial follicles, increased pup mortality during lactation in F2 NOAEL : 10 $mg.kg^{-1}_{bw}.d^{-1}$	Ema *et al.* (2008) Evaluated in EU-RAR (2008)

	Mouse / Oral / single dose postnatal day 10 / spontaneous behaviour, learning and memory Indicative LOAEL: 0.9 $mg.kg^{-1}{}_{bw}.d^{-1}$	Eriksson *et al.* (2006) Evaluated in EU-RAR (2008)
	Rat / Oral / 1-generation / thyroid related parameters and brain morphometry in offspring NOAEL: 8-21 $mg.kg^{-1}{}_{bw}.d^{-1}$	Saegusa *et al.* (2009) Evaluated in CHL Report for hexabromocyclododecane (2009)
	Rat / Oral / 1-generation / various endocrine and immunological endpoints BMDLs : 0.056-8.6 $mg.kg^{-1}{}_{bw}.d^{-1}$	van der Ven *et al.* (2009) Evaluated in CHL Report for hexabromocyclododecane (2009)
	Rat / Oral / 1-generation / cataleptic behaviour and BAEP BMDLs : 0.6-6 $mg.kg^{-1}{}_{bw}.d^{-1}$	Lilienthal *et al.* (2009) Evaluated in CHL Report for hexabromocyclododecane (2009)
CMR	HBCDD is possibly toxic to reproduction, proposed classification based on Directive 67/548/EEC Criteria : R62 – Possible risk of impaired fertility R63 – Possible risk of harm to the unborn child R64 – May cause harm to breastfed babies	CHL Report for hexabromocyclododecane (2009)

The NOAEL 10 $mg.kg^{-1}{}_{bw}.d^{-1}$ from the 2-generation is used to calculate the $QS_{biota,hh}$ using the formula given below according to the TGD for deriving EQS (2010). The threshold level (TL) was calculated from the NOAEL divided by an assessment factor of 100. This assessment factor is equivalent to the minimal margin of safety (MOS) for reproductive toxicity/fertility used in the risk characterisation for man exposed indirectly via the environment in the EU-RAR (2008).

It should be noted that effect values for mammals lower compared to this NOAEL have been reported (Eriksson *et al.*, 2006; van der Ven *et al.*, 2009; Lilienthal *et al.*, 2009). These values have however been considered not suitable for the calculation of $QS_{biota,\ hh}$. The lowest BMDL reported by van der Ven *et al*. (2009) is for increased trabecular bone mineral density. For this endpoint the ECHA-evaluation (CHL-Report for hexabromocyclododecane, 2009) states that *“Bone mineral density is not normally studied, and whereas a previous 28 days study in adult rats suggested an increased density, this one-generation study shows a decreased bone density in the offspring. Potential effects of HBCDD on bone density are, thus, indicated, but needs verification in further studies.”* Low BMDLs are also reported for effects on the immune system. The ECHA-evaluation however considers that “*the data are difficult to evaluate*” and make the following statement: *“As to the effect levels, the setting of conventional LOEALs/NOAELs are hampered by the chosen benchmark study design. It is also noted that there is still limited regulatory experience in assessing and handling benchmark studies. The benchmark dose modeling in this study follows standard procedures, with a default critical effect size of 10 %. The calculated BMDLs are very much dependent on the size of the chosen critical effect size, and it is noted that also individual control animals usually fall below/over the chosen critical effect sizes. For some effects, the normal variation is so high (e.g., mean±S.D. = 0.18±0.12 for IgG response after immunization with sheep red blood cells) that the chosen 20 % critical effect size becomes meaningless. We are therefore of the opinion that the BMDLs calculated in this study should be viewed with caution.”*

Regarding the endpoints reported by Lilienthal *et al.* (2009) it is stated that *“The parameters investigated are not part of any test guidelines, and it is therefore difficult to assess the robustness of these assays and the degree of adversity of the effects. However, the main author has been consulted, and provided further interpretation of the data. Thus, the increased hearing threshold by 5-9 dB can be translated into requiring a (4-8)-fold increase in sound intensity to pass the hearing threshold in the lower frequency range, or into requiring a (1.5-3)-fold increase in loudness to pass the threshold. Considering the importance of hearing, the effects observed at the top dose in this study on hearing have to be viewed as adverse effects.”*

Also avian reproductive toxicity has been shown at lower concentrations (MOEJ, 2009). See section 6.4 for details.

$$QS_{biota,hh} = \frac{0.1 \cdot TL(NOAEL/AF) \cdot 70}{0.115} = \frac{0.1 \cdot (10/100) \cdot 70}{0.115}$$

The corresponding range in QS_{water} was calculated according to the formula below, employing the same BCF and BMF_1 as presented under section 7.2.

Tentative $QS_{biota, hh}$	Relevant study for derivation of $QS_{biota, hh}$	Assessment Factor	Tentative $QS_{biota, hh}$
Human health	NOAEL : 10 mg.kg$^{-1}{}_{bw}$.d^{-1}	100	6100 µg.kg$^{-1}{}_{biota\ ww}$ (0.058 µg.L^{-1}, freshwater and marine water)

Since no EU or WHO drinking water standard is available, a provisional drinking water standard is calculated in accordance with section 3.9.2 of the EQS-TGD [2]. Since no ADI or TDI is available, TL_{hh} is estimated from the mammalian NOAEL value 10 mg.kg$^{-1}{}_{bw}$.d^{-1} divided by 100 according to equation C in section 3.9.2 of the EQS-TGD.

This is done according to the formula below:

$$MPC_{\mathrm{dw,\,hh}} = \frac{0.1 \cdot TL_{\mathrm{hh}} \cdot bw}{uptake_{\mathrm{dw}}} = \frac{0.1 \cdot NOAEL/100 \cdot 70}{2} = 0.35 \text{ mg/l}$$

The resulting provisional water standard is above water solubility of HBCDD

Human health via consumption of drinking water		**Master reference**
Existing drinking water standard(s)	Not available	Directive 98/83/EC
Any guideline		

8 BIBLIOGRAPHY, SOURCES AND SUPPORTIVE INFORMATION

Arnot, J., McCarty, L., Armitage, J., Toose-Reid, L., Wania, F., Cousins, I. (2009) An evaluation of hexabromocyclododecane (HBCD) for persistent organic pollutant (POP) properties and the potential for adverse effects in the environment. European Brominated Flame Retardant Industry Panel (EBFRIP). May 26, 2009.

Bignert, A., Danielsson, S., Nyberg, E., Asplund, L., Eriksson, U., Berger, U., Haglund, P. (2009) Comments Concerning the National Swedish Contaminant Monitoring Programme in Marine Biota, 2009. Sakrapport Övervakning av metaller och organiska miljögifter i marin biota, 2009. Swedish Museum of Natural History. http://www.nrm.se/download/18.6321786f122df65955f80002587/Marina+programmet+2009.pdf

Bouma, S., Vethaak, D., Meininger, P., Holland, A. (2000) De visdiefkolonie (*Sterna hirundo*) bij Terneuzen: blijven er problemen? De resultaten van een vervolgonderzoek in 2000. RIKZ-2000.45. Rijksinstitut voor Kust en Zee/RIKS, Middelburg, The Netherlands.

Calmbacher, C.W. (1978) The acute toxicity of HBCDD lot 990- 17 to the bluegill sunfish *Lepomis macrochirus* Rafinisque with test data and cover letter. UCES proj. No. 11506-06- . Union Carbide Corporation, Tarrytown, New York.

Cheaib, Z., Grandjean, D., Kupper, T., Alencastro, L.F. (2009) Brominated flame retardants in fish of Lake Geneva (Switzerland). Bull. Environ. Contam. Toxicol. 82:522–527.

CHL Report for hexabromocyclododecane (2009) Proposal for Harmonised Classification and Labelling. Version Number : 2. September 2009.
http://echa.europa.eu/consultations/harmonised_cl/harmon_cl_prev_cons_en.asp

Deng, J., Yu, L., Liu, C., Yu, K., Shi, X., Yeung, L.W.Y., Lam, P.K.S., Wu, R.S.S., Zhou, B. (2009) Hexabromocyclododecane-induced developmental toxicity and apoptosis in zebrafish embryos. Aquat. Toxicol. 93 : 29-36.

Desjardins, D., MacGregor, J.A., Krueger, H.O. (2004) Hexabromocyclododecane (HBCD): A 72-hour toxicity test with the marine diatom (*Skeletonema costatum*) Final report. Wildlife International Ltd, Easton, Maryland, USA.

Desjardins, D., MacGregor, J.A., Krueger, H.O. (2005) Chapter 1, Hexabromocyclododecane (HBCD): A 72-hour toxicity test with the marine diatom (*Skeletonema costatum*) using a co-solvent. Chapter 2, Hexabromocyclododecane (HBCD): A 72-hour toxicity test with the marine diatom (*Skeletonema costatum*) using generator column saturated media. Final report. Wildlife International Ltd, Easton, Maryland, USA.

Drottar, K.R., Krueger, H.O. (1998) Hexabromocyclododecane (HBCD): A flow-through life cycle toxicity test with the cladoceran (*Daphnia magna*). Final report.439A-108. Wildlife International Ltd, Easton, Maryland, USA.

Drottar, K.R., Krueger, H.O. (2000) Hexabromocyclododecane (HBCD): A flow-through bioconcentration test with the rainbow trout (*Onchorhynchus mykiss*). Final report. 439A-111. Wildlife International Ltd, Easton, Maryland, USA.

Drottar, K.R., MacGregor, J.A., Krueger, H.O. (2001) Hexabromocyclododecane (HBCD): An early life-stage toxicity test with the rainbow trout (*Onchorhynchus mykiss*). Final report. Wildlife International Ltd, Easton, Maryland, USA.

Deuchar, J. (2002) Draft. Environment Agency, National Laboratory Service, Nottingham, UK.

Ema, M., Fujii, S., Hirata-Koizumi, M., Matsumoto, M. (2008) Two-generation reproductive toxicity of the flame retardant hexabromocyclododecane in rats. Reprod. Toxicol. 25 :335-351.

Eriksson, P., Fisher, C., Wallin, M., Jakobsson, E., Fredriksson, A. (2006) Impaired behaviour, learning and memory, in adult mice neonatally exposed to hexabromocyclododecane (HBCDD). Environ. Toxicol. Pharmacol. 21 : 317-322.

EU-RAR (2008) European Union Risk Assessment Report: Hexabromocyclododecane - CAS No: 25637-99-4 EINECS No: 247-148-4 Series: 2nd Priority List, Volume: 44. European Commission - Joint Research Centre, Institute for Health and Consumer Production, European Chemicals Bureau (ECB). European Communities, 2008. The final report is available at the internet site of the European Chemicals Bureau: http://ecb.jrc.ec.europa.eu/ tick ESIS button, then enter CAS or EINECS number of substance.

European Commission (2011). TGD-EQS: Technical Guidance for deriving Environmental Quality Standards. Common Implementation Strategy for the Water Framework Directive Guidance Document No 27.

Frölich, J. HBCD Emissions from polystyrene compounding production in europe. Survey plan dated 27 March 2002 draft. E-mail to KemI 6 april. 2002; quoted in ECB European Chemicals Bureau 2008. Risk Assessment Hexabromocyclododecane. May 2008

Graves, W.C., Swigert, J.P. (1997a) Hexabromocyclododecane (HBCD): A 48-hour flow-through acute toxicity test with the Cladoceran (Daphnia magna). Final report. 439A-102. Wildlife International Ltd, Easton, Maryland, USA.

Graves, W.C., Swigert, J.P. (1997b) Hexabromocyclododecane (HBCD): A 96-hour flow-through acute toxicity test with the rainbow trout (*Onchorhynchus mykiss*). Final report. 439A-102. Wildlife International Ltd, Easton, Maryland, USA.

Harrad, S., Abdallah, M.A-E., Rose, N.L., Turner, S.D., Davidson, T.A. (2009a) Current-use brominated flame retardants in water, sediment, and fish from English Lakes. Environ. Sci. Technol. 43: 9077-9083

Harrad, S., Abdallah, M.A-E., Covaci, A. (2009b) Causes of variability in concentrations and diastereomer patterns of hexabromocyclododecanes in indoor dust. Environ. Int. 35 : 573-579.

Harrad, S., Abdallah, M.A-E., Rose, N.L., Turner, S.D., Davidson, T.A. (2010) Additions and Corrections. Current-use brominated flame retardants in water, sediment, and fish from English Lakes. Environ. Sci. Technol. 44: 5318.

Hayward, S., Lei, Y., Wania, F. (2006) Comparative evaluation of three high-performance liquid chromatography-based Kow estimation methods for highly hydrophobic organic compounds : polybrominated diphenyl ethers and hexabromocyclododecane. Environ. Toxicol. Chem. 25: 2018-2027.

Helgason, L.B., Polder, A., Føreid, S., Bæk, K., Lie, E., Gabrielsen, G.W., Barrett, R.T., Skaare, J.U. (2009) Levels and temporal trends (1983-2003) of polybrominated diphenyl ethers and hexabromocyclododecanes in seabird eggs from north Norway. Environ. Toxicol. Chem. 28: 1096-1103.

Janák, K., Sellström, U., Johansson, A-K., Becher, G., de Wit, C.A., Lindberg, P., Helander, B. (2008) Enantiomer-specific accumulation of hexabromocyclododecanes in eggs of predatory birds. Chemosphere, 73: S193–S200.

Johansson, A-K., Sellström, U., Lindberg, P., Bignert, A., De Wit, C. (2009). Polybrominated diphenyl ether congener patterns, hexabromocyclododecane, and brominated biphenyl 153 in eggs of peregrine falcon (*Falco peregrinus*) breeding in Sweden. Environ. Toxicol. Chem. 28 : 9-17.

Kirsch, P., Munk, R. (1988) Report on the study of acute toxicity of Hexabromin S to Golden Orfe (*Leuciscus idus* L, golden variety). 10F0678/875011, BASF.

Law, K., Palace, V.C., Halldorson, T., Danell, R., Wautier, K., Evans, B., Alaee, M., Marvin, C., Tomy, G.T. (2006a) Dietary accumulation of hexabromocyclododecane diasteroisomers in juvenile rainbow trout (Oncorhynchus mykiss) I: Bioaccumulation parameters and evidence of bioisomerization. Environ. Toxicol. Chem. 25: 1757-1761.

Law, K., Halldorson, T., Danell, R., Stern, G., Gewurtz, S., Alaee, M., Marwin, C., Whittle, M., Tomy, G. (2006b) Bioaccumulation and throphic transfer of some brominated flame retardants in a Lake Winnipeg (Canada) food web. Environ. Toxicol. Chem. 25: 2177-2186.

Law, K. (2007) ERRATUM. Environ. Toxicol. Chem. 26: pp 190-.

Law, R.J., Bersuder, P., Barry, J., Wilford, B.H., Allchin, C.R., Jepson, P.D. (2008) A significant downturn in levels of hexabromocyclododecane in the blubber of harbor porpoises (*Phocoena phocoena*) stranded or bycaught in the UK: an update to 2006. Environ. Sci. Technol. 42: 9104–9109.

Letcher, R.J., Gebbink, W.A., Sonne, C, Born, E.W., McKinney, M., Dietz, R. (2009) Bioaccumulation and biotransformation of brominated and chlorinated contaminants and their metabolites in ringed seals (*Pusa hispida*) and polar bears (*Ursus maritimus*) from East Greenland. Environ. Int. 35: 1118–1124.

Lilja K., Remberger M., Kaj K., Allard A-S., Andersson H. and Brorström-Lundén E. 2010. Chemical and biological monitoring of sewage effluent water. IVL Report B1897.

Lilienthal, H., van der Ven, L.T.M., Piersma, A.H., Vos, J.G. (2009) Effects of the brominated flame retardant hexabromocyclododecane (HBCD) on dopamnie-dependent behaviour and brainstem auditory evoked potentials in a one-generation reproduction study in Wistar rats. Toxicol. Lett. 185 : 63-72.

Lower N, Moore A. The impact of a brominated flame retardant on smoltification and olfactory function in Atlantic salmon (*Salmo salar* L.) smolts. Mar. Freshw. Behav. Physiol. 2007;40:267-284.

MacGregor, J.A., Nixon, W.B. (1997) Hexabromocyclododecane (HBCD): Determination of n-octanol/water partition coefficient. 439C- 104. Wildlife International Ltd, Easton, Maryland, USA.

MacGregor, J.A., Nixon, W.B. (2004) Determination of water solubility of hexabromocyclododecane (HBCD) using a generator column method. Wildlife International Ltd, Easton, Maryland, USA.

Marteinson et al, Behavioural and reproductive changes in American kestrel (*Falco sparverius*) exposed to technical hexabromocyclododecane (HBCD) at environmentally relevant concentrations. Abstract, BFR2009 Workshop, Ottawa, Canada, May19-20, 2009.

MOEJ (2009) Ministry of the Environment, Japan; 6-Week Administration Study of 1,2,5,6,9,10-Hexabromocyclododecane for Avian Reproduction Toxicity under Long-day Conditions using Japanese Quail – Supplemental study. Study No: 08-016. Study Report (II). Research Institute for Animal Science in Biochemistry & Toxicology, 2009

Oetken, M., Ludwichowski K-U., Nagel, R. (2001) Validation of the preliminary EU-concept of assessing the impact of chemicals to organisms in sediment by using selected substances. UBA-FB 299 67 411. Institute of Hydrobiology, Dresden University of Technology, Dresden, Germany.

Roberts, C.A., Swigert, J.P. (1997) Hexabromocyclododecane (HBCD): A 96-hour toxicity test with the freshwater alga (*Selenastrum capricornutum*). Final report. 439A-103, Wildlife International Ltd, Easton, Maryland, USA.

Saegusa, Y., Fujimoto, H., Woo, G-H., Inoue, K., Takahashi, M., Mitsumori, K., Hirose, M., Nishikawa, A., Shibutani, M. (2009) Developmental toxicity of brominated flame retardants, tetrabromobisphenol A and 1,2,5,6,9,10-hexabromocyclododecane, in rat offspring after maternal exposure from mid-gestation through lactation. Reprod. Toxicol. 28 : 456-467.

Smolarz, K., Berger, A. (2009). Long-term toxicity of hexabromocyclododecane (HBCDD) to the benthic clam *Macoma baltica* (L.) from the Baltic Sea. Aquat. Toxicol. 95 : 239-247.

Stenzel, J.I., Nixon, W.B. (1997) Hexabromocyclododecane (HBCD): Determination of the vapour pressure using a spinning rotor gauge. 439C-105. Wildlife International Ltd, Easton, Maryland, USA.

Thomas, S., Kreuger, H.O., Kendall, T.Z. (2003a) Hexabromocyclododecane (HBCD): a prolonged sediment toxicity test with *Hyalella azteca* using spiked sediment with 2% total organic carbon. Final report. 439A-119B. Wildlife International Ltd, Easton, Maryland, USA.

Thomas *et al.* (2003b) Full reference missing in the EU-RAR

Tomy, G.T., Budakowski, W., Halldorson, T., Whittle, D.M., Keir, M.J., Marvin, C., Macinnis, G., Alaee, M. (2004) Biomagnification of α- and γ-hexabromocyclododecane isomers in a Lake Ontario food web. Environ. Sci. Technol. 38 : 2298-2303.

Tomy, G.T., Pleskach, K., Oswald, T., Halldorson, T., Helm, P.A., Macinnis, G., Marvin, C.H. (2008) Enantioselective bioaccumulation of hexabromocyclododecane and congener-specific accumulation of brominated diphenyl ethers in an eastern Canadian arctic marine food web. Environ. Sci. Technol. 42 : 3634-3639.

Tomy, G.T., Pleskach, K., Ferguson, S.H., Hare, J., Marvin, C.H., Loseto, L. (2009) Trophodynamics of some PFCs and BFRs in a western Canadian arctic marine food web. Environ. Sci. Technol. 43 : 4076-4081.

UK Environment Agency (2006) Review of 2005 UK Monitoring Data for HBCD.

van der Ven, L.T.M., Verhoef, A., van de Kuil, T., Slob, W., Leonards, P.E.G., Visser, T.J., Hamers, T., Herlin, M., Håkansson, H., Olausson, H., Piersma, A.H., Vos, J.P. (2006) A 28-day oral dose toxicity study enhanced to detect endocrine effects of hexabromocyclododecane in Wistar rats. Toxicol. Sci. 94 : 281-292.

van der Ven, L.T.M., van de Kuil, T., Leonards, P.E.G., Slob, W., Lilienthal, H., Litens, S., Herlin, M., Håkansson, H., Cantón, R.F., van den Berg, M., Visser, T.J., van Loveren, H., Vos, J.G., Piersma, A.H. (2009) Endocrine effects of hexabromocyclododecane (HBCD) in a one-generation reproduction study in Wistar rats. Toxicol. Lett. 185 : 51-62.

van Leeuwen, S.P.J., de Boer, J. (2008) Brominated flame retardants in fish and shellfish – levels and contribution of fish consumption to dietary exposure of Dutch citizens to HBCD. Mol. Nutr. Food Res. 52: 194-203.

VECAP (2009) The Volontary Emissions Control Action Programme. Measurable Achievements. Annual progress Report 2009. Available at : http://www.vecap.info/flipbook/ 2010-03-05

Veit, G.D., Defoe, D.L., Bergstedt, B.V. (1979) Measuring and estimating the the bioconcentration factor of chemicals in fish. J. Fish Res. Board Can. 36: 1040-1048.

Walsh, G.E., Yoder, M.J., McLaughlin, L.L., Lores, E.M. (1987) Responses of marine unicellular algae to brominated organic compounds in six growth media. Ecotoxicol. Environ. Safety, 14: 215-222.

Wu, J-P., Guan, Y-T., Zhang, Y., Luo, X-J., Zhi, H., Chen, S-J., Mai, B-X (2010) Trophodynamics of hexabromocyclododecanes and several other non-PBDE brominated flame retardants in a freshwater food web. Environ. Sci. Technol. 44: 5490-5495.

Zhang, X., Yang, F., Zhang, X., Xu, Y., Liao, T., Song, S., Wang, J. (2008) Induction of hepatic enzymes and oxidative stress in Chinese rare minnow (*Gobicypris rarus*) exposed to waterborne hexabromocyclododecane (HBCDD). Aquat. Toxicol. 86: 4-11.