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Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

Conference of the Parties to the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade
Ninth meeting
Geneva, 29 April–10 May 2019
Item 5 (b) of the provisional agenda*

Matters related to the implementation of the Convention: listing of chemicals in Annex III to the Convention

Comments and further information related to the draft decision guidance document for hexabromocyclododecane

Note by the Secretariat

1. At its fourteenth meeting, the Chemical Review Committee finalized the text of the draft decision guidance document for hexabromocyclododecane, as set out in the annex to document UNEP/FAO/RC/COP.9/7/Add.1, and agreed to forward it, together with the related tabular summary of comments received and how they were taken into account in the preparation of the draft decision guidance document, to the Conference of the Parties for its consideration.

2. The tabular summary of comments is set out in the annex to the present note. The present note, including its annex, has not been formally edited.

* UNEP/FAO/RC/COP.9/1.

Annex

Comments and further information related to the draft decision guidance document for hexabromocyclododecane

Source	Section	Comment and further information related to the draft decision guidance document for hexabromocyclododecane	Response
Canada	Throughout	Editorial.	Accepted.
European Union	Throughout	Editorial.	Accepted.
Japan	1 (Identification and uses)	"Japan replies that the risk assessment on FRA in Japan covered all 5 CAS numbers."	Confirmation received. All 5 CAS numbers now reflected in the draft DGD.
USA	Throughout	Editorial.	Accepted.
	Footer	"Revised 4 April 2012" changed to "Revised February 2018"	Rejected. The footer links to the version of the template used for the draft DGD and is ultimately removed when the draft is forwarded for consideration by the CRC as a meeting document.
	Set of abbreviations	Added: "NES – no effects at saturation"	Accepted.
	2.2 (Risk Evaluation)	Hazard endpoints are provided in the supporting information from Norway, originating from the United States Environmental Protection Agency 2014 report, *Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)* ~~on flame retardant alternatives~~.	Accepted.
	3.3 (Alternatives)	This additional background information from the report should be included for context: The report provides information on hexabromocyclododecane used as a flame retardant in polystyrene building insulation, possible substitutes, and alternative materials. The report was developed by the U.S. Environmental Protection Agency with input from a partnership of stakeholders from business, government, academia, and environmental organizations. According to technical experts on the Partnership, between 2011 and 2014 there were only three viable flame-retardant alternatives to HBCD for use in expanded and extruded polystyrene foam (EPS and XPS) insulation under current manufacturing processes. Alternative materials are also available as substitutes to HBCD-containing insulation. These alternatives may require additive flame retardants or other treatment to meet fire safety requirements.	Accepted.
	3.3 (Alternatives)	Add text: Figure ES-1 summarizes the hazard information for hexabromocyclododecane and the three alternatives assessed. (Figure ES-1 indicates whether endpoints were	Accepted and inserted figure ES-1 into the DGD.

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		assigned based on empirical data or using values from predictive models and/or professional judgment. The caveats listed in Figure ES-1 must also be taken into account when interpreting the information in the table.)	
	Annex 1: 2.1.3 (Absorption, distribution, excretion and metabolism in mammals) Under "Absorption" heading.	Additional information from the report about the studies should also be included here. Please also cite the sources referenced in the report and include notes from the report regarding data quality. See below. Rats (2 males, 8 females) administered a single oral dose of 1.93 mg radiolabeled HBCD eliminated 86% of the dose within 72 hours (70% in feces and 16% in urine). Absorption is quick from the gastrointestinal tract with a half-life of 2 hours (absorbed fraction not reported); elimination is slower in adipose tissue as opposed to non-adipose tissue. (EPA, 2005; NICNAS, 2012; reported in a secondary source. Authors state that caution is urged in interpreting the data due to the small sample size and the brief nature of the final report.) In rodents, HBCD is readily absorbed through the gastrointestinal tract with highest concentrations in adipose tissue and muscle, followed by the liver; it has been found in much lower concentrations in the lungs, kidneys, blood and brain. Oral absorption estimated to be 50-100%; accumulation of α-diastereomer is much higher than other diastereomers. EU risk assessment concluded 4% dermal absorption for fine particles and 2% for granular particles. (ECHA, 2008; reported in a secondary source with limited study details.)	The suggested modifications are all valid and found in the supporting documentation. However, this text has been removed from the DGD to reduce the overall length of the document and repetition/duplication.
	Annex 1: 2.1.3 (Absorption, distribution, excretion and metabolism in mammals) Under "Absorption" heading	Add reference and statement on data quality: (Marvin et al., 2011; reported in a secondary source with limited study details.)	Accepted.
	Annex 1: 2.1.3 (Absorption, distribution, excretion and metabolism in mammals) Under "Distribution" heading	Add reference and statement on data quality: (ECHA, 2008; reported in a secondary source with limited study details.)	Accepted.
	Annex 1: 2.1.3 (Absorption, distribution, excretion and metabolism in mammals)	Add text, reference and statement on data quality: 90-Day gavage study in Crl:CD(SD)IGS BR rats (20/sex) Doses: 0 and 1,000 mg technical-grade HBCD/kg/day at a dosage volume of 5 mL/kg for 90 days (Measured) The relative bioaccumulation factor for mammals is 99:11:1 for α–, β– and γ– hexabromocyclododecane.	The suggested modifications are all valid and found in the supporting documentation. However, this text has been removed from the DGD to

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	Under "Bioaccumulation and metabolism" heading	(EINECS, 2008; values were obtained from a secondary source provide supporting information concerning the isomer profile of HBCD bioaccumulation.)	reduce the overall length of the document and repetition/duplication.
	Annex 1: 2.1.3 (Absorption, distribution, excretion and metabolism in mammals) Under "Excretion" heading	Add references and statements on data quality as follows: Rats (2 males, 8 females) administered a single oral dose of 1.93 mg radiolabeled hexabromocyclododecane eliminated 86% of the dose within 72 hours (70% in feces and 16% in urine). (EPA, 2005; NICNAS, 2012; reported in a secondary source. Authors state that caution is urged in interpreting the data due to the small sample size and the brief nature of the final report.) Four male Wistar rats orally administered 500 mg/kg-day hexabromocyclododecane in olive oil for 5 days Average daily rate of excretion in the feces was 29-37% of the dose; the cumulative excretion was constant at 32-35%; urinary excretion was not observed; metabolites were not detected in the urine or feces; hexabromocyclododecane was detected only in adipose tissue (0.3-0.7 mg/g fat). (EPA, 2005; NICNAS, 2012, reported in a secondary source.)	Accepted.
	Annex 1: 2.2.1 (Acute toxicity)	Add references and statements on data quality as follows: Oral: Rat LD50 > 10,000 mg/kg (EPA, 2005; NICNAS, 2012; reported in a secondary source with limited study details.) Rat LD50 > 6,400 mg/kg (EINECS, 2008; reported in a secondary source. Non-guideline study. Dose and particle size not reported; 7-day observation period.) Dermal: Rabbit LD50 > 8,000 mg/kg (EPA, 2005; NICNAS, 2012; reported in a secondary source with limited study details) Rabbit LD50 > 20,000 mg/kg (EINECS, 2008; NICNAS, 2012; non-guideline study. Too few animals were used; clinical signs not reported.) Inhalation: Rat LC50 > 200 mg/L (EPA, 2005; NICNAS, 2012; reported in a secondary source with limited study details.)	Accepted.
	Annex 1: 2.2.3 (Genotoxicity (including mutagenicity))	Add references and statements on data quality as follows: Gene mutation in vitro: Negative in Salmonella typhimurium (strains not specified) in the presence and absence of metabolic activation. (EPA, 2005; NICNAS, 2012; reported in a secondary source with limited study details.) Chromosomal aberrations in vitro:	Accepted.

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		Negative, mammalian chromosomal aberration test with human peripheral blood lymphocytes in the presence and absence of metabolic activation Doses: 10, 19, 38, 75, 150, 300 and 600 µg/mL. (EPA, 2005; NICNAS, 2012; reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines, and GLP.) Other in vitro: Positive, intragenic recombination test in Sp5/V79 and SPD8 hamster cells; cell lines developed by study authors. Doses: 2-20 µg/mL. (EPA, 2005; NICNAS, 2012; reported in a secondary source. Non-guideline study. Not a standard test used by regulatory agencies to assess genotoxicity. Reliability and predictive ability is unknown.) Negative, mouse micronucleus test. Doses: 0, 500, 1,000 or 2,000 mg/kg in dimethyl sulfoxide. (EPA, 2005; reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.)	
	Annex 1: 2.2.4 (Long term toxicity and carcinogenicity)	Add references and statements on data quality as follows: (Kurokawa et al., 1984; EINECS, 2008; EPA, 2005; NICNAS, 2012; Study not conducted according to OECD guidelines; this study is not adequate to determine a hazard designation for the carcinogenicity endpoint.) Hexabromocyclododecane does not meet criteria (NOHSC, 2004) for classification as a carcinogen (R45, R49, R40). (NICNAS, 2012; reported in a secondary source.)	The suggested modifications are all valid and found in the supporting documentation. However, this text has been removed from the DGD to reduce the overall length of the document and repetition/duplication.
	Annex 1: 2.2.5 (Effects on reproduction)	Add references and statements on data quality as follows: (Ema et al., 2008 (as cited in EINECS, 2008; NICNAS, 2012); reported in a secondary source. Guideline study. Performed according to current EPA, OECD 416 guidelines and GLP. HBCD particles were mixed with ground dry feed at the reported concentrations; bioavailability may be dependent on particle size and dose. Study does not consider litter effects; It is noted that the number of primordial cells in background control data was 189.5 – 353.4 (mean = 295.6) in 4 studies (10 females/study) in studies conducted in 2005-2006. While the number of primordial cells was variable within these studies, the 30% treatment-related decrease at the 138 mg/kg-day dose level compared to controls in this study, is a significant decrease; in addition, the decrease at 198 mg/kg dose suggests a dose-response.) (Zeller and Kirsch, 1969 (as cited in EINECS, 2008; EPA, 2005; NICNAS, 2012; unpublished laboratory report, described in a secondary source. Non-guideline	The suggested modifications are all valid and found in the supporting documentation. However, this text has been removed from the DGD to reduce the overall length of the document and repetition/duplication.

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		study; EINECS (2008) states that this study was not carried out in accordance with present standards.) (Chengelis, 2001 (as cited in EPA, 2005; NICNAS, 2012; unpublished laboratory report, described in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.)	
	Annex 1: 2.2.6 (Neurotoxicity/ delayed neurotoxicity, Special studies where available)	Add references and statements on data quality as follows: (Chengelis, 2001 (as cited in EPA, 2005; NICNAS, 2012); reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP.) (Mariussen and Fonnum, 2003 (as cited in EINECS, 2008; NICNAS, 2012); study reported in a secondary source.) (Lilienthal et al., 2006, 2009 (as cited in EINECS, 2008; NICNAS, 2012) Guideline study. Conducted according to current EPA, OECD Guideline 415. BMD doses were calculated by the authors using a biologically relevant benchmark response of 5% deviation change from control. Rats were tested at 110 and 140 days old for the cataleptic and hearing impairment tests, respectively. It is difficult to determine, however, if the effect is due to developmental exposure to HBCD, a result of repeated-dose exposure, or a combination of the two. Due to this uncertainty, this study was not used to determine the hazard designation; however, the results of this study suggest that there is potential for neurotoxic effects.)	The suggested modifications are all valid and found in the supporting documentation. However, this text has been removed from the DGD to reduce the overall length of the document and repetition/duplication.
	Annex 1: 4.1.4 (Bioaccumulation)	Editorial – adjusted formatting and added headings to separate the studies.	Accepted.
	Annex 1: 4.1.4 (Bioaccumulation)	Add references and statements on data quality as follows: (Drottar and Kruger, 2000; EINECS, 2008; EPA, 2005; NICNAS, 2012; Guideline study performed according to current EPA, OECD guidelines and GLP.) (EINECS, 2008; Veith et al., 1979; Non-guideline study that was conducted before the implementation of standardized test procedures for BCF.) (EPI Suite; These estimated results are from the BCFBAF v3.01 Arnot-Gobas method, reporting the upper trophic value with an entered measured Log KOW value of 5.6.) (Law, 2006; NICNAS, 2012; The secondary source reported these calculated results as BAF values; however, the original source refers to these as BMF values. Despite the difference in nomenclature, these values from non-guideline studies demonstrate that HBCD isomers bioaccumulate in fish through dietary exposure.) (EINECS, 2008; Values were obtained from a secondary source provide supporting information	The suggested modifications are all valid and found in the supporting documentation. However, this text has been removed from the DGD to reduce the overall length of the document and repetition/duplication.

Source	Section	Comment and further information related to the draft decision guidance document for hexabromocyclododecane	Response
		concerning the isomer profile of HBCD bioaccumulation.)	
	Annex 1: 4.2.1 (Terrestrial vertebrates)	Add references and statements on data quality as follows: (MOEJ, 2009; Limited study details; only abstract is available.) (Fernie et al., 2009; Exposure was to a mixture of HBCD and PBDE. There are currently no DfE criteria to determine a hazard designation for this endpoint.)	The suggested modifications are all valid and found in the supporting documentation. However, this text has been removed from the DGD to reduce the overall length of the document and repetition/duplication.
	Annex 1: 4.2.2 (Aquatic species)	Editorial – adjusted formatting and added headings to separate the studies.	Accepted.
	Annex 1: 4.2.2 (Aquatic species)	Add references and statements on data quality as follows: (EPA, 2005; NICNAS, 2012; Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility.) (EPA, 2005; Reported in a secondary source with limited study details. Value exceeds water solubility.) (EPA, 2005; Reported in a secondary source with limited study details. Value exceeds water solubility.) (ECOSAR v1.10; No effects at saturation (NES): The log Kow of 5.6 for this chemical exceeds the SAR limitation for the log Kow of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.) (Deng et al., 2009; Guideline study. Study details taken from abstract. This study is for a nontraditional endpoint for determining hazard designation. In addition, NOEC and LOEC values are above the limit of water solubility and will not be used to determine a hazard designation. No effects at saturation (NES) are predicted.) (EPA, 2005; NICNAS, 2012; Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility; NES.) (EINECS, 2008; Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Value exceeds water solubility.) (ECOSAR v 1.10; NES: The log Kow of 5.6 for this chemical exceeds the SAR limitation for the log K Kow of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR	Accepted with removal of typo noted.

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		classes that have a more specific mode of action relative to narcosis.) (Desjardins et al., 2005; ECHA, 2008; Reported in a secondary source with limited study details.) (EPA, 2005; NICNAS, 2012; Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility; NES.) (EPA, 2005; NICNAS, 2012; Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility; NES.) (EPA, 2005; NICNAS, 2012; Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility; NES.) (ECHA, 2008; Reported in a secondary source with limited study details. The test substance was made up of a composite of HBCD samples from three manufacturers containing 6.0% α-, 8.5% β- and 79.1% γ-diastereomers; total HBCD was 93.6% of test substance. There were no effects at the highest concentration tested.) (Desjardins et al., 2004 (as cited in ECHA, 2008; NICNAS, 2012); Reported in a secondary source with limited study details; LOECs were not identified. One test concentration at the limit of water solubility; NES.) (Walsh et al., 1987 (as cited in EPA, 2005; NICNAS); Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility.) (Siebel-Sauer and Bias, 1987 (as cited in EINECS, 2008); Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Value exceeds water solubility.) (ECOSAR v. 1.10; The estimated effect exceeds the water solubility of 0.66 mg/L, but not by 10x as required to be considered NES by ECOSAR. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.) (Drotter et al., 2001; EPA, 2005; Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP; LOEC and MATC could not be determined due to absence of toxicity, but were considered >0.0037 or 0.0068 mg/L (more than twice γ-HBCD's water solubility). HBCD was not chronically toxic to rainbow trout at concentrations at or above its limit of solubility.) (ECOSAR v. 1.10; Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.)	

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		(Zhang et al., 2008; Study details reported in abstract. Values exceed water solubility. This study is for a non-traditional endpoint for determining hazard designation. In addition, LOEC values are above the limit of water solubility and will not be used to determine a hazard designation. A NOEC was not identified.) (Drotter and Kruger, 1998 (as cited in EINECS, 2008; EPA, 2005; NICNAS, 2012); Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Within the range of water solubility. The test substance was made up of a composite of HBCD samples from three manufacturers containing 6.0% α-, 8.5% β- and 79.1% γ-diastereomers; total HBCD was 93.6% of test substance. Reduced lengths, dry weight and fewer young observed in daphnia exposed to 0.011 mg/L.) (ECOSAR v. 1.10; Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.) (ECOSAR v. 1.10; The effect level exceeds the water solubility of 0.66 mg/L, but not by 10x as required to be considered NES by ECOSAR. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.) (EINECS, 2008; Oetken et al., 2001; Performed in contrast with OECD Draft Guideline 218, artificial sediment with a coarse grain size (100-2,000 µm) and other carbon sources (stinging-nettle and leaves of alder). EINECS states that the results for total emergence and emergence rate were not considered valid for the purpose of risk assessment due to the large variations in solvent control.)	
	Annex 1: 4.1 (Risk evaluation)	Adjust paragraph as follows: Hazard endpoints identified in the United States Environmental Protection Agency 2014 report, *Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)* are also provided in the supporting information from Norway ~~as part of the United States Environmental Protection Agency report on flame retardant alternatives~~. High or very high hazards are noted for developmental effects, acute aquatic toxicity, and chronic aquatic toxicity. Hexabromocyclododecane is highly persistent and has very high bioaccumulation. (UNEP/FAO/RC/CRC.13/INF/18)	Accepted.