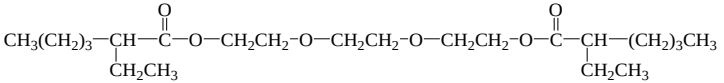
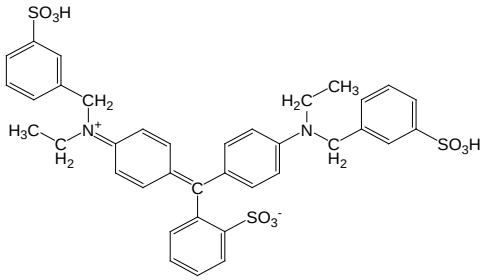
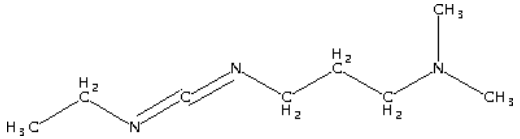
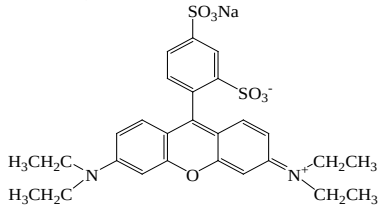
平成２０年１２月　既存化学物質点検（分解・蓄積）結果資料　〈第81回審査部会〉

資料1－1

K番号	物質名 (CAS No.) [PRTR番号] 官報公示整理番号	分解度(%)	分配係数 (log Pow)	濃縮倍率	判定結果 ()内は既判定	後続の試験案 (試験の種類， 試験物質)	頁
1831	３，６－ジオキサオクタン－１，８－ジイル＝ビス（２－エチルヘキサノアート） (94-28-0) 7-88 	BOD ：　92，92，91　(92) HPLC：　99,100,100　(100)	－	－	**良分解性**	なし	1
1822	２－（｛４－［*N*－エチル－*N*－（３－スルホベンジル）アミノ］フェニル｝｛４－［*N*－エチル－*N*－（３－スルホベンジル）アザニウミリデン］シクロヘキサー２，５－ジエン－１－イリデン｝メチル）ベンゼンスルホナート 5-1632 	BOD ：　5，　1，　1　(2) TOC ：　-1，　1，　1　(0) HPLC：　-1，　0，-1　(0)*1 Na塩(3844-45-9)にて試験実施	-0.32*2	－	**難分解性**	濃縮度試験	4
1829	*N*－［（エチルイミノ）メチリデン］－*N*’，*N*’－ジメチルプロパン－１，３－ジイルジアミン (1892-57-5) 2-1696 	BOD ：　-3，-4，-5　(0)*1 TOC ：　4，　5，　3　(4) HPLC：　0，　0，　1　(0) 塩酸塩(25952-53-8)にて試験実施	0.21*2	－	**難分解性**	濃縮度試験	8
1830	ナトリウム＝４－［６－（*N*，*N*－ジエチルアミノ）－３－（*N*，*N*－ジエチルアザニウミリデン）－３*H*－キサンテン－９－イル］ベンゼン－１，３－ジスルホナート (3520-42-1) 5-1504 	BOD ：　8，　5，　5　(6) TOC ：　0，　1，　0　(0) HPLC：　-3，-2，-2　(0)*1	-6.15*2	－	**難分解性**	濃縮度試験	11

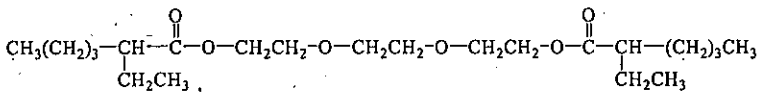
*1　分解度の平均値が負の値に算出されたため、0と表記した。

*2　Kowwin v1.67 SRC-LOGKOW for Microsoft Windowsによる計算値。

整理番号　K－１８３１　　（７－８８）

３，６－ジオキサオクタン－１，８－ジイル＝ビス（２－エチルヘキサノアート）
(94-28-0)

構造式（示性式）・物理化学的性状



分子式　$C_{22}H_{42}O_6$　　分子量　４０２．５７

純　度*1　99.5%	外　観　無色透明液体
不純物　（物質名，含有率） 2-エチルヘキサン酸　0.0022% 残り 0.9978%は不明	溶解度（対水，その他） 対水　1.74 mg/L (20℃) 対酢酸エチル　10 g/L 以上 対アセトニトリル　10 g/L 以上
融　点　融点は測定範囲 (-100～25℃) に存在しない	１－オクタノール／水分配係数 log Pow = 6.4 (HPLC 法) *2
沸　点　342.8℃	
蒸気圧　3.59×10^{-6} Pa (25℃)	加水分解性 pH4, 7, 9　加水分解性なし
密　度	
LD50	解離定数 －
ＩＲチャートの有無　(有)・無	

用　途*3　中間物、添加剤（繊維用、樹脂用）洗剤用等

生産量*3（16 年）製造及び輸入：7-88 として 10,000～100,000 t 未満

試　料　購入先　Sigma-Aldrich

経済産業公報発表年月日　　年　月　日

分解度試験	分解度試験	分解度試験
事業対象年度　平成１９年度	契　約　年　月　日	契　約　年　月　日
試験期間　20. 1. 16～20. 2. 29	試験期間　. . ～ . .	試験期間　. . ～ . .
試験装置　(標)・揮	試験装置　標・揮	試験装置　標・揮
試験濃度	試験濃度	試験濃度
被験物質　100 mg/L	被験物質　mg/L	被験物質　mg/L
汚　泥　30 mg/L	汚　泥　mg/L	汚　泥　mg/L
本試験期間　4　週間	本試験期間　週間	本試験期間　週間
試験結果 間接 BOD　92, 92, 91 (92) %	試験結果 間接	試験結果 間接
試験結果 直接 HPLC　99, 100, 100 (100) %	試験結果 直接	試験結果 直接
審査部会　第８１回 ２０年１２月１９日開催	審査部会　第　回 年　月　日開催	審査部会　第　回 年　月　日開催
判　定	判　定	判　定

備　考

1. 回収率※
（水＋被験物質）系　99.4%
（汚泥＋被験物質）系　96.9%

・生成が予想された２－エチルヘキサン酸及びトリエチレングリコールは検出されなかった。

2. 実施機関
・財団法人 化学物質評価研究機構

3. 特記事項
・DOC 検出率（%）

(水＋被験物質) 系	(汚泥＋被験物質) 系		
	1	2	3
0	7	5	4

備　考

*1　Sigma-Aldrich 添付資料による。　　*2　溶離液：メタノール／精製水（75/25 v/v）　　*3　化学物質の製造・輸入量に関する実態調査による。

Study No. 205156 (Test item K-1831)
Cultivating conditions:
Concentration
Test item ..... 100 (mg/L)
Reference item (aniline) ..... 100 (mg/L)
Activated sludge ..... 30 (mg/L)
Temperature ..... 25 ± 1 ℃
Duration ..... 28 days (Jan.17,2008 - Feb.14,2008)
Note: –

Vessel No.	Sample Description	BOD (mg)			
		7th day	14th day	21st day	28th day
[1]	Water + test item	0.0	0.0	0.4	0.7
[2]	Sludge + test item	31.7	51.5	68.1	72.6
[3]	Sludge + test item	31.0	50.9	68.9	72.3
[4]	Sludge + test item	28.8	52.3	67.9	71.7
[5]	Sludge + aniline	60.8	73.0	74.8	76.0
[6]	Control blank [B]	3.8	5.6	6.6	7.8

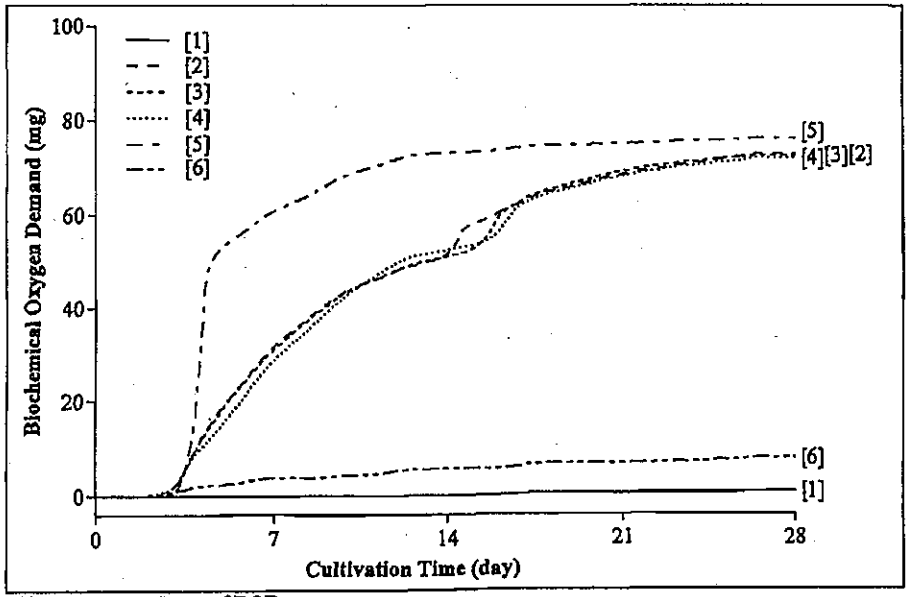


Fig. 1 Chart of BOD.

Feb.14,2008 Name _____

試験液の分析結果

28 日後の分析結果は下記のとおりであった。

		(水+被験物質)系	(汚泥＋被験物質) 系			理論量
		[1]	[2]	[3]	[4]	
BOD*1	mg	0.7	64.8	64.5	63.9	70.2
DOC 検出量及び検出率	mgC	0	1.4	1.1	0.8	19.7
	%	0	7	5	4	–
被験物質残留量及び残留率 (HPLC) *1	mg	31.6	0.2	0.1	0.1	30.0
	%	105	1	0	0	–
2-エチルヘキサン酸生成量及び生成率 (HPLC)	mg	0	0	0	0	21.5
	%	0	0	0	0	–
トリエチレングリコール生成量及び生成率 (GC)	mg	0	0	0	0	11.2
	%	0	0	0	0	–

*1 (汚泥＋被験物質) 系は、汚泥ブランク系の値を差し引いて表示した。

分 解 度

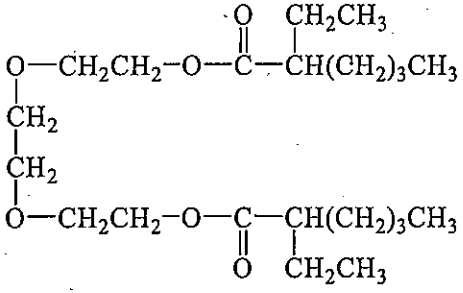
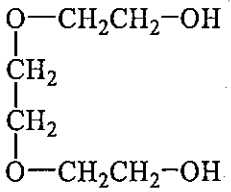
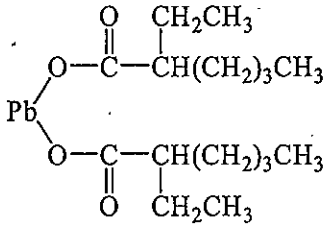
28 日後の分解度は下記のとおりであった。

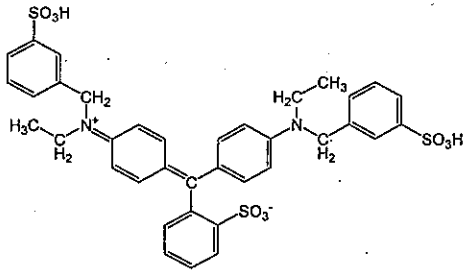
		(汚泥＋被験物質) 系			
		[2]	[3]	[4]	平 均
BOD 分解度	%	92	92	91	92
被験物質分解度 (HPLC)	%	99	100	100	100

結 論

本試験条件下において、被験物質は微生物により分解された。

K－１８３１の類似物質表

化合物名 (CAS番号)	構造式	官報公示整理番号 (K-番号)	分解度(%)	分解判定 (年)	分配係数 (log Pow)	LC50 mg/L (ヒメダカ)	濃縮倍率	濃縮判定 (年)
3，6－ジオキサオクタン－1，8－ジイル＝ビス(2－エチルヘキサノアート) (94-28-0)		7-88 (K-1831)	標準(4W) 2008年実施 BOD 92, 92, 91 (92) HPLC 99, 100, 100 (100)					
トリエチレングリコール (112-27-6)		2-0429 (K-915)	標準(4W) 1989年実施 BOD 92, 25, 64 (60) TOC 97, 53, 66 (72) G C 98, 39, 66 (68)	良分解性 (1989)				
2－エチルヘキサン酸鉛塩 (301-08-6)		2-0615 (K-1807)	標準(4W) 2007年実施 BOD 102, 101, 94 (99) 水中で速やかに変化し、2-エチルヘキサン酸及び不溶性鉛(水にも有機溶媒にも溶解しない無機の鉛)が生成した。2-エチルヘキサン酸は微生物により分解され、不溶性鉛は試験液中に残留した。	難分解性 (2007)				

整理番号　K－１８２２　（５－１６３２）	分解度試験	分解度試験	分解度試験
２－（｛４－［*N*－エチル－*N*－（３－スルホベンジル）アミノ］フェニル｝｛４－［*N*－エチル－*N*－（３－スルホベンジル）アザニウミリデン］シクロヘキサ－２，５－ジエン－１－イリデン｝メチル）ベンゼンスルホナート	事業対象年度　平成１９年度	契約　年　月　日	契約　年　月　日
	試験期間　19. 9.11～19.12.10	試験期間　. . ～ . .	試験期間　. . ～ . .
構造式（示性式）・物理化学的性状	試験装置　㊞・揮	試験装置　標・揮	試験装置　標・揮
	試験濃度	試験濃度	試験濃度
	被験物質　100 mg/L	被験物質　mg/L	被験物質　mg/L
	汚泥　30 mg/L	汚泥　mg/L	汚泥　mg/L
分子式　$C_{37}H_{36}N_2O_9S_3$　　分子量　７４８.１６	本試験期間　4　週間	本試験期間　週間	本試験期間　週間
	試験結果 間接 BOD　5, 1, 1 (2) %	試験結果 間接	試験結果 間接
	試験結果 直接 TOC　-1, 1, 1 (0) %	試験結果 直接	試験結果 直接
	試験結果 直接 HPLC　-1, 0, -1 (0) %	試験結果 直接	試験結果 直接
	審査部会　第８１回 ２０年１２月１９日開催	審査部会　第　回 年　月　日開催	審査部会　第　回 年　月　日開催
	判定	判定	判定
	備考 1. 回収率※ （水＋被験物質）系　100% （汚泥＋被験物質）系　100% ※試験液を直接分析機器に導入。 2. 実施機関 ・財団法人 化学物質評価研究機構 3. 特記事項 ・試験サンプルはNa塩を用い、物性値はNa塩の値である。 ・分解度の平均値が負の値に算出されたため、0と表記した。	備考	備考

純　度*1	96.5%（異性体混合物）	外　観	赤紫色粉末
不純物*1（物質名，含有率）	複数の不明成分　3.5%	溶解度（対水，その他）	対水　300 g/L 以上（20℃） 対メタノール　10 g/L 以上
融　点	測定不可 （270℃以上で変化する）	1－オクタノール／水分配係数	0.32*3
沸　点	測定不可 （270℃以上で変化する）		
蒸気圧	3.66×10^{-6} Pa 以下 （測定温度 80℃）	加水分解性	pH4, 7, 9　加水分解性なし
密　度			
LD_{50}		解離定数	－
ＩＲチャートの有無	㊒・無		
用　途*2	接着剤、殺虫剤･殺菌剤等、色素（塗料、顔料）		
生産量*2（16 年）製造及び輸入：5-1632 として 10,000～100,000 t 未満			
試　料	購入先　和光純薬工業　和光一級		
経済産業公報発表年月日	年　月　日		

*1　HPLC（面積比）による。　　*2　化学物質の製造・輸入量に関する実態調査による。　*3 Kowwin v1.67 SRC-LOGKOW for Microsoft Windows による計算値。

Study No. 205147 (Test item K-1822)
Cultivating conditions:
Concentration
Test item ..... 100 (mg/L)
Reference item (aniline) ..... 100 (mg/L)
Activated sludge ..... 30 (mg/L)
Temperature ..... 25 ± 1 ℃
Duration ..... 28 days (Sep.13,2007 - Oct.11,2007)
Note: —

Vessel No.	Sample Description	BOD (mg)			
		7th day	14th day	21st day	28th day
[1]	Water + test item	0.5	0.5	0.5	0.5
[2]	Sludge + test item	4.8	6.6	7.5	8.8
[3]	Sludge + test item	3.5	5.1	5.8	7.0
[4]	Sludge + test item	3.8	5.0	5.6	7.0
[5]	Control blank [B]	3.0	4.2	5.1	6.2
[6]	Sludge + aniline	53.7	69.6	72.3	74.5

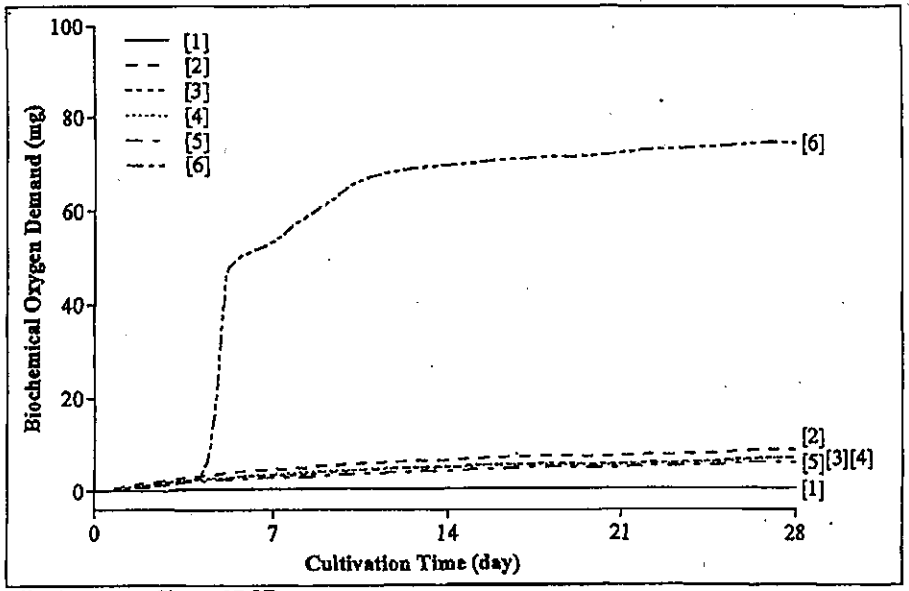


Fig. 1 Chart of BOD.

Oct.11,2007 Name _____

試験液の分析結果

28 日後の分析結果は下記のとおりであった。

なお、(水＋被験物質) 系、(汚泥＋被験物質) 系共に被験物質はほぼ理論量残留し、HPLC クロマトグラム上に被験物質以外のピークは認められなかった。

		(水+被験物質)系	(汚泥＋被験物質)系			理論量
		[1]	[2]	[3]	[4]	
BOD*1	mg	0.5	2.6	0.8	0.8	56.4
DOC 残留量及び残留率	mgC	16.3	16.5	16.2	16.1	16.8
	%	97	98	97	96	-
被験物質残留量及び残留率 (HPLC)*2	mg	30.2	30.5	30.2	30.4	30.0
	%	101	102	101	101	-

*1 (汚泥＋被験物質) 系は、汚泥ブランク系の値を差し引いて表示した。

*2 クロマトグラム上のピークの総面積を用いて算出した。

分 解 度

28 日後の分解度は下記のとおりであった。

		(汚泥＋被験物質) 系			
		[2]	[3]	[4]	平 均
BOD 分解度	%	5	1	1	2
DOC 分解度	%	-1	1	1	0
被験物質分解度 (HPLC)	%	-1	0	-1	0 (-1)*3

*3 分解度の平均値が負の値に算出されたため、平均値を 0 としカッコ内にその計算値を示した。

考　察

HPLC分析において、被験物質はクロマトグラム上に3本のピークとして検出された。そこで、ピーク毎の分解度を算出したところ、いずれのピークについても分解度は-1～0%であった（下表参照）。よって、本試験条件下において、被験物質の全成分が微生物により分解されなかったと考えられる。

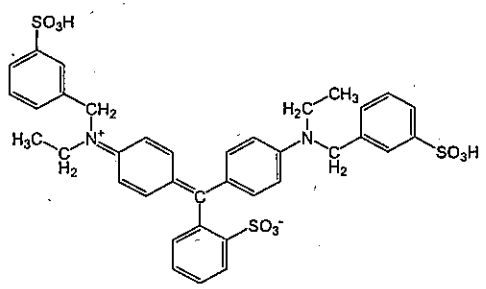
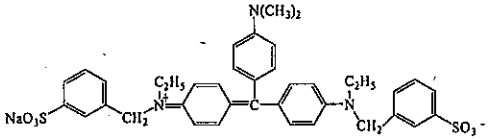
被験物質のピーク毎の分解度

		(汚泥＋被験物質) 系			
		[2]	[3]	[4]	平　均
ピーク 1	%	-1	0	0	0(-1)*3
ピーク 2	%	-1	0	-1	0(-1)*3
ピーク 3	%	-1	0	-1	0(-1)*3

結　論

本試験条件下において、被験物質は微生物により分解されなかった。

K－１８２２の類似物質表

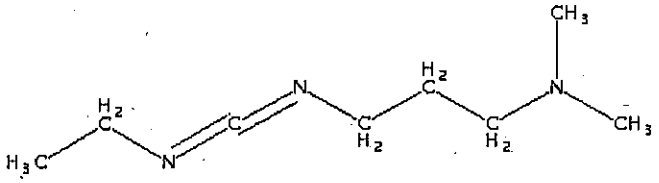
化合物名 (CAS 番号)	構造式	官報公示 整理番号 (K- 番号)	分解度 (%)	分解 判定 (年)	分配係数 (log Pow)	LC_{50} mg/L (ヒメダカ)	濃縮倍率	濃縮 判定 (年)
2－({4－[*N*－エチル－*N*－(3－スルホベンジル) アミノ] フェニル}{4－[*N*－エチル－*N*－(3－スルホベンジル) アザニウミリデン] シクロヘキサ－2，5－ジエン－1－イリデン} メチル) ベンゼンスルホナート		5-1632 (K-1822)	標準 (4 W) 2007年実施 BOD　5,　1,　1　(2) TOC　-1,　1,　1　(0) HPLC　-1,　0,　-1　(0) * (試験はNa塩で実施)					
ナトリウム＝3－(*N*－(4－((4－(ジメチルアミノ) フェニル) (4－(エチル((3－スルホナトフェニル) メチル) アミノ) フェニル) メチレン) －2，5－シクロヘキサジエン－1－イリデン) －*N*－エチルアンモニオメチル) ベンゼンスルホナート (1694-09-3)		5-1611 (K-1571)	標準 (4 W) 2001年実施 BOD　1,　1,　1　(1) TOC　6,　3,　3　(4) HPLC　0,　0,　0　(0)	難分解性 (2002)		>50 (96 hr)	2001 年実施 定常状態における濃縮倍率 1 区 (0.50 mg/L) :　0.9 2 区 (0.050 mg/L) :＜8.4 脂質含有率　開始前　3.0% 終了後　3.2%	高濃縮性ではない (2002)

＊　分解度の平均値が負の値に算出されたため、0 と表記した。

整理番号　K－１８２９　　（２－１６９６）

N－［（エチルイミノ）メチリデン］－*N*’，*N*’－ジメチルプロパン－１，３－ジイルジアミン
(1892-57-5)

構造式（示性式）・物理化学的性状



分子式　$C_8H_{17}N_3$　　分子量　１５５．２４

純　度*1　99.7%	外　観　白色粉末
不純物*1（物質名，含有率） 水分　0.08% 残り 0.22%は不明	溶解度（対水，その他） 対水　300 g/L 以上（目視による） (20℃) 対アセトニトリル　10 g/L 以上
融　点*1　111.7～112.8℃	1－オクタノール／水分配係数 -0.21*3
沸　点　測定不可 (160℃以上で分解)	
蒸気圧　5.06×10² Pa (25℃)	加水分解性 pH4, 7, 9　加水分解性なし
密　度	
LD50	解離定数 －
ＩＲチャートの有無　(有)・無	
用　途*2　中間物、脱水剤、乾燥剤	
生産量（16 年）　製造及び輸入　10,000～100,000 t 未満	
試　料　購入先　東京化成工業	
経済産業公報発表年月日　年　月　日	

分解度試験	分解度試験	分解度試験
事業対象年度　平成１９年度	契　約　年　月　日	契　約　年　月　日
試験期間　19. 10. 1～20. 2. 1	試験期間　. . ～ . .	試験期間　. . ～ . .
試験装置　(標)・揮	試験装置　標・揮	試験装置　標・揮
試　験　濃　度	試　験　濃　度	試　験　濃　度
被験物質　100 mg/L	被験物質　mg/L	被験物質　mg/L
汚　泥　30 mg/L	汚　泥　mg/L	汚　泥　mg/L
本試験期間　4　週間	本試験期間　週間	本試験期間　週間
試験結果 間接 BOD　-3, -4, -5　(0) %	試験結果 間接	試験結果 間接
試験結果 直接 TOC　4, 5, 3　(4) %	試験結果 直接	試験結果 直接
試験結果 直接 HPLC　0, 0, 1　(0) %		
審査部会　第８１回 ２０年１２月１９日開催	審査部会　第　回 年　月　日開催	審査部会　第　回 年　月　日開催
判　定	判　定	判　定
備　考 1. 回収率※ （水＋被験物質）系　100% （汚泥＋被験物質）系　100% ※試験液を直接分析機器に導入。 2. 実施機関 ・財団法人 化学物質評価研究機構 3. 特記事項 ・試験サンプルは塩酸塩を用い、物性値は塩酸塩の値である。 ・分解度の平均値が負の値に算出されたため、0 と表記した。	備　考	備　考

*1　東京化成工業添付資料による。　*2　化学物質の製造・輸入量に関する実態調査による。　*3 Kowwin v1.67 SRC-LOGKOW for Microsoft Windows による計算値。

Study No. 205154 (Test item K-1829)
Cultivating conditions:
Concentration
Test item ..... 100 (mg/L)
Reference item (aniline) ..... 100 (mg/L)
Activated sludge ..... 30 (mg/L)
Temperature ..... 25 ± 1 ℃
Duration ..... 28 days (Oct.30,2007 - Nov.27,2007)
Note: —

Vessel No.	Sample Description	BOD (mg)			
		7th day	14th day	21st day	28th day
[1]	Water + test item	0.0	0.0	0.0	1.1
[2]	Sludge + test item	1.3	2.1	2.8	5.0
[3]	Sludge + test item	1.0	1.9	2.7	4.8
[4]	Sludge + test item	1.3	2.2	2.9	4.2
[5]	Control blank [B]	2.2	4.2	7.1	7.7
[6]	Sludge + aniline	61.4	70.9	72.5	74.7

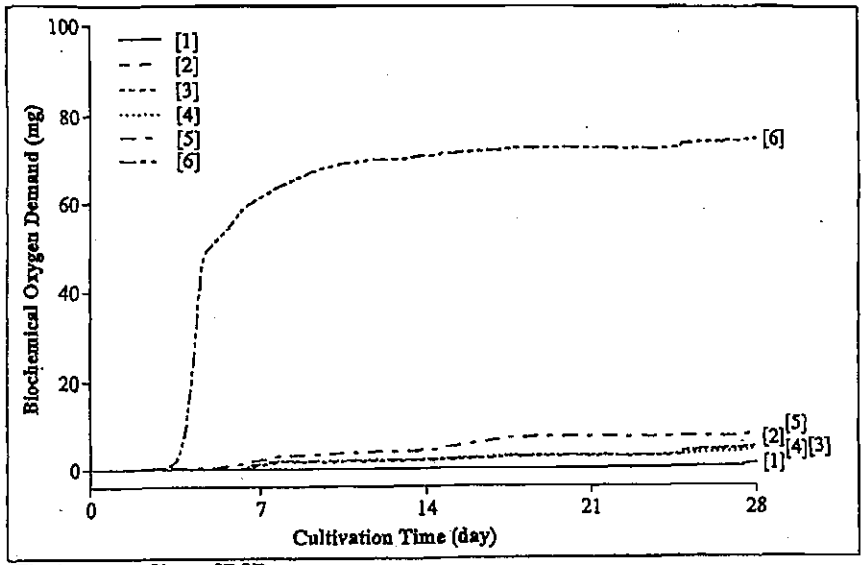


Fig. 1 Chart of BOD.

Nov.27,2007 Name _____

試験液の分析結果

28 日後の分析結果は下記のとおりであった。

なお、(水＋被験物質) 系、(汚泥＋被験物質) 系共に被験物質はほぼ理論量残留し、HPLC クロマトグラム上に被験物質以外のピークは認められなかった。

		(水+被験物質)系	(汚泥＋被験物質)系			理論量
		[1]	[2]	[3]	[4]	
BOD*1	mg	1.1	-2.7	-2.9	-3.5	77.7
DOC 残留量及び残留率 *1	mgC	15.7	15.1	15.0	15.2	15.0
	%	105	101	100	101	-
被験物質残留量及び残留率 (HPLC)	mg	30.0	29.9	29.9	29.7	30.0
	%	100	100	100	99	-

*1 (汚泥＋被験物質) 系は、汚泥ブランク系の値を差し引いて表示した。

分 解 度

28 日後の分解度は下記のとおりであった。

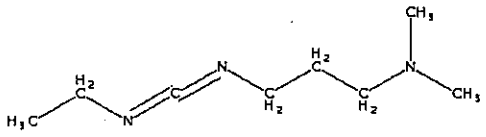
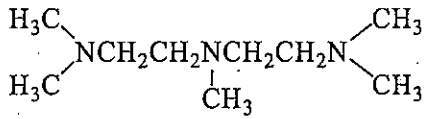
		(汚泥＋被験物質) 系			
		[2]	[3]	[4]	平 均
BOD 分解度	%	-3	-4	-5	0 (-4) *2
DOC 分解度	%	4	5	3	4
被験物質分解度 (HPLC)	%	0	0	1	0

*2 分解度の平均値が負の値に算出されたため、平均値を 0 としカッコ内にその計算値を示した。

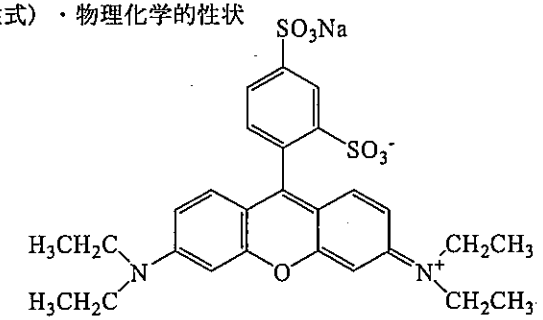
結 論

本試験条件下において、被験物質は微生物により分解されなかった。

Ｋ－１８２９の類似物質表

化合物名 (CAS 番号)	構造式	官報公示整理番号 (K- 番号)	分解度 (%)	分解判定 (年)	分配係数 (log Pow)	LC_{50} mg/L (ヒメダカ)	濃縮倍率	濃縮判定 (年)
N－[(エチルイミノ)メチリデン]－*N*, *N*′－ジメチルプロパン－1, 3－ジイルジアミン (1892-57-5)		2-1696 (K-1829)	標準(4 W) 2008年実施 BOD −3, −4, −5 (0) *1 TOC 4, 5, 3 (4) HPLC 0, 0, 1 (0) (塩酸塩にて試験実施)		−			
N－メチル－*N*, *N*－ビス(2－ジメチルアミノエチル)アミン (3030-47-5)		2-0147 (K-1379)	標準(4 W) 2000年実施 BOD 0, 0, 0 (0) TOC 0, 0, 1 (0) G C 0, 1, 1 (1)	難分解性 (2000)	2005 年実施 0.04 (フラスコ振とう法)		分配係数から類推	高濃縮性ではない (2005)

*1　分解度の平均値が負の値に算出されたため、0 と表記した。

整理番号　K－1830　（5－1504）	分解度試験	分解度試験	分解度試験
ナトリウム＝4－［6－（*N*, *N*－ジエチルアミノ）－3－（*N*, *N*－ジエチルアザニウミリデン）－3*H*－キサンテン－9－イル］ベンゼン－1，3－ジスルホナート　(3520-42-1)	事業対象年度　平成19年度	契約　年　月　日	契約　年　月　日
	試験期間　19. 9.12～19.12.14	試験期間　. . ～ . .	試験期間　. . ～ . .
構造式（示性式）・物理化学的性状	試験装置　(標)・揮	試験装置　標・揮	試験装置　標・揮
	試験濃度	試験濃度	試験濃度
	被験物質　100 mg/L	被験物質　mg/L	被験物質　mg/L
	汚泥　30 mg/L	汚泥　mg/L	汚泥　mg/L
	本試験期間　4 週間	本試験期間　週間	本試験期間　週間
	試験結果 間接 BOD　8, 5, 5 (6) %	試験結果 間接	試験結果 間接
	試験結果 直接 TOC　0, 1, 0 (0) %	試験結果 直接	試験結果 直接
	試験結果 直接 HPLC　-3, -2, -2 (0) %		
	審査部会　第81回 20年12月19日開催	審査部会　第　回 年　月　日開催	審査部会　第　回 年　月　日開催
	判定	判定	判定
	備考 1. 回収率※ （水＋被験物質）系　100% （汚泥＋被験物質）系　100% ※試験液を直接分析機器に導入。 2. 実施機関 ・財団法人 化学物質評価研究機構 3. 特記事項 ・分解度の平均値が負の値に算出されたため、0と表記した。	備考	備考

分子式　$C_{27}H_{29}N_2NaO_7S_2$　　分子量　580.65

純度*1　84.7%	外観　黒褐色粉末
不純物*1（物質名，含有率） 水分［乾燥減量（110℃）］　2.0% 無機塩［強熱残分（硫酸塩）］　13.3%	溶解度（対水，その他） 対水　100 g/L以上（20℃） 対アセトニトリル　1 g/L未満
融点　350℃以上（室温～350℃）において固体	1－オクタノール／水分配係数 -6.15*2
沸点　350℃以上（室温～350℃）において固体	
蒸気圧　1.39×10⁻⁵ Pa以下（80℃）	加水分解性 pH4, 7, 9　加水分解性なし
密度	
LD50	解離定数 －
IRチャートの有無　(有)・無	
用途　色素（染料、顔料、インク）	
生産量（　）　製造及び輸入　－	
試料　購入先　和光純薬工業	
経済産業公報発表年月日　年　月　日	

*1　和光純薬工業添付資料による。　　*2 Kowwin v1.67 SRC-LOGKOW for Microsoft Windowsによる計算値。

Study No. 205155 (Test item K-1830)

Cultivating conditions:

Concentration

Test item	100 (mg/L)
Reference item (aniline)	100 (mg/L)
Activated sludge	30 (mg/L)
Temperature	25 ± 1 ℃
Duration	28 days (Sep.13,2007 - Oct.11,2007)

Note: —

Vessel No.	Sample Description	BOD (mg)			
		7th day	14th day	21st day	28th day
[1]	Water + test item	0.9	0.9	1.3	1.7
[2]	Sludge + test item	4.9	7.6	9.3	10.7
[3]	Sludge + test item	3.8	6.1	7.5	8.9
[4]	Sludge + test item	4.1	6.3	7.2	8.9
[5]	Sludge + aniline	41.0	66.5	71.3	73.9
[6]	Control blank [B]	2.7	4.2	5.7	6.2

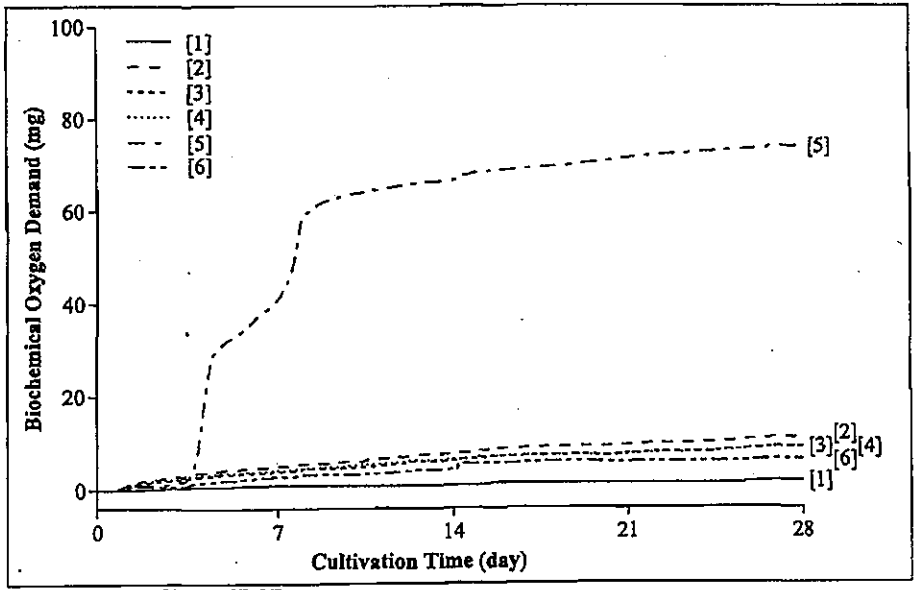


Fig. 1 Chart of BOD.

Oct.11,2007 Name

試験液の分析結果

28 日後の分析結果は下記のとおりであった。

なお、(水＋被験物質) 系、(汚泥＋被験物質) 系共に被験物質はほぼ理論量残留し、HPLC クロマトグラム上に被験物質以外のピークは認められなかった

		(水+被験物質)系	(汚泥＋被験物質)系			理論量
		[1]	[2]	[3]	[4]	
BOD*1	mg	1.7	4.5	2.7	2.7	58.9
DOC 残留量*1 及び残留率	mgC	18.2	18.3	18.0	18.1	18.7*2
	%	97	98	97	97	-
被験物質残留量及び残留率 (HPLC)	mg	29.9	30.7	30.6	30.5	30.5
	%	98	101	100	100	-

*1 (汚泥＋被験物質) 系は、汚泥ブランク系の値を差し引いて表示した。

*2 102 mg/L の被験物質標準溶液を 3 点調製し、それらの DOC 実測濃度の平均値から試験液中の理論量を算出した。

分 解 度

28 日後の分解度は下記のとおりであった。

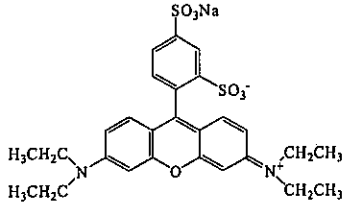
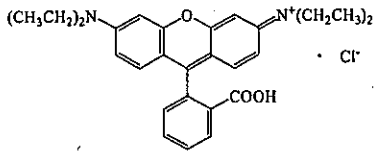
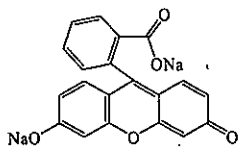
		(汚泥＋被験物質) 系			
		[2]	[3]	[4]	平 均
BOD 分解度	%	8	5	5	6
DOC 分解度	%	0	1	0	0
被験物質分解度 (HPLC)	%	-3	-2	-2	0 (-2)*3

*3 分解度の平均値が負の値に算出されたため、平均値を 0 としカッコ内にその計算値を示した。

結 論

本試験条件下において、被験物質は微生物により分解されなかった。

K－１８３０の類似物質表

化合物名 (CAS 番号)	構造式	官報公示整理番号 (K- 番号)	分解度 (%)	分解判定 (年)	分配係数 (log Pow)	LC_{50} mg/L (ヒメダカ)	濃縮倍率	濃縮判定 (年)
ナトリウム＝４－［６－（*N*, *N*－ジエチルアミノ）－３－（*N*, *N*－ジエチルアザニウミリデン）－３*H*－キサンテン－９－イル］ベンゼン－１，３－ジスルホナート (3520-42-1)		5-1504 (K-1830)	標準 (4 W) 2007年実施 BOD 8, 5, 5 (6) TOC 0, 1, 0 (0) HPLC -3, -2, -2 (0) *1		－			
２－（３－ジエチルイミニオ－６－ジエチルアミノ－３*H*－キサンテン－９－イル）安息香酸＝クロリド (3375-25-5)		5-1973 5-4056 (K-847)	標準 (4 W) 1987年実施 BOD 0, 0, 0 (0) TOC 3, 2, 0 (2) VIS (555 nm) 8, 8, 5 (7)	難分解性 (1987)	1987 年実施 1.9～2.0	33.9 (48 hr)	1987 年実施 １区 (100 μg/L) ：<0.2 ２区 (10 μg/L) ：<1.7 脂質含有率 3.9%	高濃縮性ではない (1987)
ジナトリウム＝２－（６－オキシド－３－オキソ－３*H*－キサンテン－９－イル）－ベンゾアート (518-47-8)		5-1416 (K-1825)	標準 (4 W) 2008年実施 BOD -2, 0, 1 (0) *1 TOC 0, 1, 1 (1) HPLC -1, 1, 1 (1)	難分解性 (2008)	－	>200 (96 hr)	2008 年実施 定常状態における濃縮倍率 １区 (0.46 mg/L) ：≦0.27 ２区 (0.046 mg/L) ：≦2.7 脂質含有率 開始前 2.94% 終了後 4.14%	高濃縮性ではない (2008)

*1　分解度の平均値が負の値に算出されたため、0 と表記した。

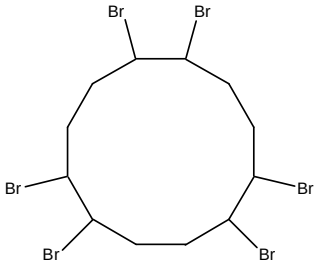
資料1－2

第一種特定化学物質へ該当するか否かの審議審査シート

（平成20年12月19日開催）

官報公示整理番号	CAS No.	物質名称	判定結果	頁
3-2254	25637-99-4 3194-55-6	1,2,5,6,9,10-ヘキサブロモシクロドデカン	一特相当とは判断されない	1

第一種特定化学物質へ該当するか否かの審議

官報公示整理番号	3-2254	CAS No.	25637-99-4 3194-55-6
判定結果	現時点で収集された情報からは、第一種特定化学物質に該当するとは判断されない。		
名称 構造式等	1,2,5,6,9,10-ヘキサブロモシクロドデカン  		
用途	発泡ポリスチレン用の難燃剤、繊維用の難燃剤 ※平成 20 年 3 月 26 日開催　化学物質審議会安全対策部会安全対策小委員会資料		
外観	灰褐色粉体		
分解性	難分解性		
蓄積性	高濃縮性		

WIL Research Laboratories WIL-186012 “A 90-day oral (gavage) toxicity study of HBCD in rats” (2001)

90 日間反復投与	投与方法	強制経口投与　溶媒：コーン油　Crl:CD(SD)IGS BR ラット
	純度	記載無し(3 ﾛｯﾄ使用)
	用量	３用量(100, 300, 1000 mg/kg/day)
	死亡	1000♂：1/15
	NOEL	NOEL：<100 mg/kg/day　【報告書では NOAEL：1000 mg/kg/day】
	推定根拠	血液生化学的検査(Alb↑：100 以上♂[13w]､TP↑：1000♂･100 以上♀[13w]､ T4↓：100 以上♂[13w]･100 以上♀[13w]) 絶対重量(肝↑：100 以上♂♀､前立腺↑：1000♂) 相対重量(肝↑：100 以上♂♀､前立腺↑：1000♂) 組織学的所見(肝－肝細胞空胞化：100 以上♂･300 以上♀)
	他の毒性	血液生化学的検査(Glb↑：300 以上♀[13w]､ γ-GTP↑：1000♀[3w･13w]･1000♂[13w]) 組織学的所見(肝－小葉中心性肝細胞肥大：1000♀､ 甲状腺－濾胞細胞肥大：300 以上♂♀)
	回復性	問題なし

厚生労働省既存化学物質安全性点検結果

Ema M, Fujii S, Hirata-Koizumi M, Matsumoto M. Two-generation reproductive toxicity study of the flame retardant hexabromocyclododecane in rats., Reprod Toxicol. 2008 Apr;25(3):335-51. Epub 2007 Dec 28

2 世代繁殖試験**【今回新たに収集された試験】**	投与方法	混餌投与　Crl:CD(SD)ラット
	純度	99.69%
	用量	3 投与群(150, 1500, 15000 ppm) 【[F0]♂:10.2, 101, 1008 mg/kg､[F0]♀:14.0, 141, 1363 mg/kg､[F1]♂:11.4, 115, 1142 mg/kg､[F1]♀:14.3, 138, 1363 mg/kg】
	死亡	【ケージ内事故死】1500［F1］♂：1/24、15000［F0］♂：1/24（切迫屠殺） 【試験途中死亡】1500［F1］♂：1/24、15000［F0］♂：1/24、15000［F0］♀：2/24（内 1 例：切迫屠殺）
	NOAEL	150 ppm（10.2 mg/kg 相当）

	推定根拠	親動物に対する毒性： 血液生化学的検査（TP↑・glb↑：1500 以上［F0］♂・15000［F1］♂・15000［F0］♀） 血中ホルモン量（TSH↑：1500 以上［F0*・F1］♀） 絶対重量（肝↑：1500 以上［F0］♂・15000［F1］♂・15000［F0・F1］♀） 相対重量（肝↑：1500 以上［F0］♂・15000［F1］♂・15000［F0・F1］♀） 組織学的所見（甲状腺—濾胞小型化：1500 以上［F0］♂・1500 以上［F0・F1］♀） F1 原始卵胞数↓：1500 以上 児動物に対する 毒性： 絶対重量（肝↑：1500 以上［F1］♂♀） 相対重量（肝↑：1500 以上［F1・F2］♂・1500 以上［F1］♀・15000［F2］♀） * 予備審査会では、150ppm の F0 雌の TSH 上昇は明確な組織学的変化を伴っていないことから、毒性影響とは判断しなかった。
	他の毒性	親動物に対する毒性： 体重↓：15000［F1］♂♀ 摂餌量↓：15000［F1］♂♀ 血中ホルモン量（T4↓：15000 ［F0］♂♀、FSH↑：15000［F0］♀） 絶対重量（甲状腺↑：15000［F0・F1］♂♀） 相対重量（甲状腺↑：15000［F0・F1］♂・15000［F1］♀） 児動物に対する 毒性： 生後 5-21 日の死亡発生率↑：15000［F2］ 生後 4 日・21 日生存率↓：15000［F2］ 体重↓：15000［F1・F2］♂・15000［F2］♀

他の毒性情報	[村井敏美、川崎浩之進、加納晴三郎、“殺虫剤および食品添加物などのラットにおける胎仔毒性に関する研究 (第 7 報) Hexabromocyclododecane の胎仔毒性”, 応用薬理 29, 981-986 (1985)] 発生毒性試験 Wistar ﾗｯﾄ(0.01, 0.1, 1%(混餌投与)) 妊娠 0～20 日 純度記載なし（HBCD 異性体混合物） (総摂取量として 0.13, 1.28, 12.0 g/kg 相当) 1%で母体への影響あり（肝重量増加、摂餌量減少） 生殖機能への影響なし、胎児への影響なし

[IUCLID（CAS No. 25637-99-4）（2005）より引用]
急性毒性
経口 LD_{50} ラット > 10 g/kg
吸入 LC_{50} ラット > 200 mg/L/1h
経皮 LD_{50} ウサギ > 8 g/kg
刺激性
ウサギ　眼及び皮膚　刺激性なし
感作性
Mouse lymphnode assay 感作性なし
Guinea pig maximization test　感作性なし(1 報)・感作性あり(2 報)
ヒト（パッチテスト）　感作性なし
反復投与毒性試験
SD ﾗｯﾄ　(125, 350, 1000 mg/kg/day(経口投与)) 28 日間 純度≧96～99.9%
NOAEL = 1000 mg/kg/day（1000 mg/kg/day でも毒性なし）
絶対重量（肝↑：350 以上♀・1000♂）
相対重量（肝↑：350 以上♂♀）
SD ﾗｯﾄ　(100, 300, 1000 mg/kg/day(経口投与))　90 日間 純度≧96～99.9%
NOAEL = 1000 mg/kg/day（1000 mg/kg/day でも毒性なし）
血液生化学的検査(Alb↑：100 以上♂[13w]、TP↑：1000♂･100 以上♀[13w]、Glb↑：300 以上♀[13w]、Cl↓：100 以上♂♀、T4↓：100 以上♂[13w]･100 以上♀[13w]、γ-GTP↑：1000♀[3w･13w]･1000♂[13w])
絶対重量(肝↑：100 以上♂♀､前立腺↑：1000♂)
相対重量(肝↑：100 以上♂♀､前立腺↑：1000♂)
組織学的所見(肝－肝細胞空胞化：100 以上♂･300 以上♀、肝－小葉中心性肝細胞肥大：1000♀、甲状腺－濾胞細胞肥大：300 以上♂♀))
SD ﾗｯﾄ　(1, 2.5, 5%(混餌投与)) 28 日間 純度記載なし
（940、2410、4820 mg/kg/day 相当）
NOAEL＝１％
絶対・相対重量（肝↑：1%以上♂♀）
組織学的所見（甲状腺肥大：1%以上♂♀）
SD ﾗｯﾄ　(0.16, 0.32, 0.64, 1.28%(混餌投与))　90 日間 純度記載なし
(120, 240, 470, 950 mg/kg/day 相当)
NOAEL = 1.28%
（肝臓での臓器重量の増加等及び脂肪沈着は可逆的変化）
変異原性試験
Ames 試験：　陰性（全 5 報とも）
In vitro 染色体異常試験：陰性
純度≧96～99.9%、溶媒：DMSO
ヒト末梢リンパ球
-/+S9mix 群：10, 19, 38, 75, 150, 300, 600 μg/ml
マウス小核試験：陰性
純度≧96～99.9%　マウス
3 投与群（500, 1000, 2000mg/kg）
In vitro Iatrogenic Recombination 試験：陽性

発がん性試験
$B6C3F_1$ ﾏｳｽ　(100, 1000, 10000ppm(混餌投与)) 18 ヶ月　純度記載なし
(13, 130, 1300 mg/kg/day 相当)
がん原性なし

	発生毒性試験 SD ﾗｯﾄ (250, 500, 1000mg/kg/day(経口投与)) 妊娠 6～19 日 純度≧96～99.9% 妊娠維持への影響なし（NOEL = 1000 mg/kg/day）、 母体への影響なし（NOEL = 1000 mg/kg/day）、胎児への影響なし 系統未記載ﾗｯﾄ (0.01, 0.1, 1% (混餌投与)) 妊娠 0～20 日 (5, 50, 500 mg/kg/day 相当) 純度記載なし 毒性影響なし 生体内運命 Wistar ﾗｯﾄ（500mg/kg/ﾗｯﾄ（経口投与））5 日間連続投与 糞便からの HBCD の排泄は投与量の 29～37%、尿からの排泄はみとめられない。 Isolated intestine loop の実験によれば HBCD は腸から吸収される。 HBCD は脂肪組織に蓄積したとみられる。（５日後に 0.3-0.7mg/g fat） 代謝物の有無は不明。 系統未記載ﾗｯﾄ (7-9mg/kg 14C-HBCD(経口投与)) 単回 体内からの半減期 約 27 時間（72 時間後に糞便中に 72%、尿中に 15%排泄） 吸収半減期 2 時間 脂肪組織からの半減期はもっと長いと考えられる。

[化学物質安全性（ハザード）評価シート（2002）より引用]

急性毒性

経口 LD_{50}　ラット > 10000 mg/kg
マウス > 6400 mg/kg

経皮 LD_{50}　ウサギ > 8000 mg/kg

吸入 LC_{50}　ラット > 200 mg/L、
> 202140 mg/m^3/4hr

腹腔内 LD_{50}　マウス = 3500 mg/kg

刺激性

ウサギ　眼及び皮膚　刺激性なし

モルモット　皮膚　刺激性なし

皮膚感作性

ヒト　感作性なし

モルモット　感作性なし（1 報）
軽度の感作性あり（2 報）

反復投与試験

SD ﾗｯﾄ (25000, 50000 ppm(混餌投与)) 28 日間 純度記載なし
全用量で肝重量の増加

SD ﾗｯﾄ（10000, 25000, 50000 ppm(混餌投与)）28 日間
純度記載なし（HBCD 異性体混合物）
全用量で肝重量の増加

SD ﾗｯﾄ (1600, 3200, 6400, 12800 ppm(混餌投与)) 13 週間 純度記載なし
6400 ppm 以上で肝臓の相対重量の増加、脂肪沈着
6 週間の回復期間後でも、12800 ppm での肝臓の相対重量の増加は残存

SD ﾗｯﾄ (125, 350, 1000 mg/kg/day(経口投与)) 28 日間
純度記載なし（HBCD 異性体混合物）
雄の 350 mg/kg/day 以上及び雌の全用量群で肝臓の相対重量の増加

変異原性試験

Ames 試験：

陰性　純度記載なし　溶媒記載なし

-/+S9mix	TA98、TA100、TA1537	3.15～3000 μg/plate

陰性　純度記載なし(HBCD 異性体混合物)　溶媒記載なし

-/+S9mix	TA98、TA100、TA1535、TA1537	～1000 μg/plate
-/+S9mix	TA98、TA100、TA1535	10～10000 μg/plate
-/+S9mix	TA98、TA100、TA1535、TA1537、TA1538	10～5000 μg/plate
-/+S9mix	TA98、TA100、TA1535、TA1537、TA1538	10～10000 μg/plate
-/+S9mix	TA98、TA100、TA1535、TA1537、TA1538	0.5～50 μg/plate
-/+S9mix	TA98、TA100、TA1535、TA1537、TA1538	2.5～260 μg/plate
-/+S9mix	*S. cerevisiae*	0.5～50 μg/plate

染色体異常試験

陰性　純度記載なし(HBCD 異性体混合物)　溶媒記載なし
ヒトリンﾊﾟ球
-/+S9mix 10～600 μg/mL

発生毒性試験

Wistar ﾗｯﾄ((0.01, 0.1, 1%(混餌投与))) 妊娠 0～20 日
純度記載なし(HBCD 異性体混合物)
１%で母体への影響あり（肝重量増加、摂餌量減少）
妊娠維持への影響なし、胎児への影響なし

	[Abstracts BFR 2001 Part 1 Overview Presentations, Risk Assessment and Risk management　p.14 EU Risk Assessment of HBCDD より引用] 急性毒性 　経口 LD_{50} ラット > 20 g/kg 感作性 　皮膚感作性あり 反復投与試験 　標的臓器は肝臓であり、LOAEL は 80 mg/kg/day 生殖発生毒性 　発生毒性は認められていない。 遺伝毒性試験 *In vitro* 試験結果から遺伝毒性なし

[デンマーク Environmental Project No. 568（2000）より引用]
急性毒性
経口 LD_{50} ラット > 10 000 mg/kg
経皮 LD_{50} ウサギ > 20000 mg/kg
吸入 LC_{50} ラット > 202 mg/L/4hr
刺激性
眼　刺激性なし（他の試験も同様の結果）
皮膚　30～60 分後に紅斑　24、48、72 時間後は症状なし（他の試験も同様の結果）
皮膚感作性
モルモット　誘導濃度 0.5%以上、惹起濃度 0.05%以上で陽性反応
誘導濃度 250000 ppm、惹起濃度 50000 ppm で陽性反応
反復投与試験
SD ﾗｯﾄ (1, 2.5, 5%(混餌投与)) 28 日間 純度記載なし
（約 0、833、2083、4167 mg/kg/day 相当）
NOAEL 算出不可
体重↓（2083 以上）
摂餌量↓（2083 以上）
絶対重量（肝↑：830 以上）
相対重量（肝↑：830 以上）
病理組織学的所見（肝－異常所見なし、
胸腺－小濾胞過形成・腺腫性過形成・上皮活性過多：用量依存性、
卵巣－卵形成↓：4167）
系統未記載ﾗｯﾄ（0.16, 0.32, 0.64, 1.28 %（混餌投与））13 週間 純度記載なし
（約 133～1067 mg/kg/day 相当）
NOAEL 算出不可
体重↓（1067♂）
摂餌量↓（1067♂）
絶対重量（肝↑：0.32 %以上）
病理組織学的所見（肝－脂肪沈着：用量依存性、
肝以外－異常所見なし）
で肝臓の相対重量の増加、脂肪沈着（）
回復期間（42 日間）後でも、肝臓の絶対重量の増加と脂肪沈着は完全には回復せず）
発がん性試験
$B6C3F_1$ ﾏｳｽ (100, 1000, 10000ppm(混餌投与)) 18 ヶ月　純度記載なし
(13, 130, 1300 mg/kg/day 相当)
この試験からがん原性を判断することは不可と判断された。

遺伝毒性試験
Ames 試験
大部分が陰性だが、1 報のみ TA100 及び TA1535 でﾌﾚｰﾑｼﾌﾄ変異が起こるとあり
In vivo UDS 試験：　陽性
In vitro Iatrogenic Recombination 試験：陽性（2 報）
発生毒性試験
Wistar ﾗｯﾄ (0.01, 0.1, 1% (混餌投与)) 妊娠 0～20 日
(6.7, 69, 658mg/kg/day 相当)　純度記載なし
母体毒性の NOAEL = 69 mg/kg/day
発生毒性の NOAEL = 658 mg/kg/day
摂餌量↓（658 母獣）
臓器重量（肝↑：658 母獣）
生体内運命
^{14}C-HBCD　72 時間後に糞便中に 70%、尿中に 16%排泄
脂肪組織からの半減期はもっと長いと考えられる。

	[Abstracts BFR 2001 Part 1 Overview Presentations, Risk Assessment and Risk management p.14 EU Risk Assessment of HBCDD より引用] 急性毒性 経口 LD_{50} ラット > 20 g/kg 感作性 皮膚感作性あり 反復投与試験 標的臓器は肝臓であり、LOAEL は 80 mg/kg/day 発生毒性 発生毒性は認められていない。 遺伝毒性試験 *In vitro* 試験結果から遺伝毒性なし
	[National Industrial Chemical Notification Assessment Scheme: Priority Existing Chemical Report No. 20（2001）より引用] 刺激性 ヒトでは刺激性なし 皮膚感作性 モルモットでは感作性は相反する結果が得られている 反復投与試験 28 日間ラット混餌投与試験及び 90 日間ラット混餌投与試験では、肝臓での臓器重量の増加等及び甲状腺の肥大がみとめられ、LOAEL はそれぞれ 900 mg/kg/day 及び 925 mg/kg/day（NOAEL は 450mg/kg/day）相当とされた。90 日間 ラット経口投与試験では、LOAEL = 80 mg/kg/day とされた。最近の 28 日間 ラット経口投与試験では、肝臓での臓器重量の可逆的増加がみとめられ、NOAEL = 1000 mg/kg/day とされた。 変異原性試験 *In vitro* 試験: 陰性 Recombination 試験： 陽性 発がん性試験 18 ヶ月間のマウス混餌投与試験においてがん原性なし 生殖発生毒性試験 生殖毒性の NOAEL = 50 mg/kg/day であるが、この試験は評価には不十分 生体内運命 HBCD は消化管から吸収されやすく、代謝及び排泄をうけ大部分は 72 時間以内に糞便中に排泄される。HBCD は主に脂肪組織に分布する

他の毒性情報**【今回新たに収集された情報】**	［Eriksson P, Fischer C, Wallin M, Jakobsson E, Fredriksson A, “Impaired behavior, learning and memory, in adult mice neonatally exposed to hexabromocyclododecane (HBCDD)”, Environmental Toxicology and Pharmacology 21, 317-322 (2006)］ 神経発生毒性試験（♂3ヶ月 齢） 生後 10 日に雌雄の児に単回強制経口投与、溶媒：20%脂肪乳化剤 (卵レシチンとラッカセイ油の混合物 (1:10)と水)、NMRI マウス 3-4 腹から選抜した３カ月齢のオス児の自発運動量測定（10 匹/群)、Morris 水迷路試験（１２-１７匹/群）を実施。 純度：98%以上 用量：0.9, 13.5 mg/kg 死亡：なし NOEL：< 0.9 mg/kg 推定根拠：自発運動試験 (運動↓：0.9・13.5[試験開始 0-20 分]、立ち上がり↓：0.9・13.5 [試験開始 0-20 分]) 他の毒性：自発運動 (運動↑：13.5 [試験開始 40-60 分]、立ち上がり↑：13.5 [試験開始 40-60 分]、総運動量↓：13.5 [試験開始 0-20 分]、総運動量↑13.5[試験開始 40-60 分])、Morris 水迷路試験 (潜伏時間↑：13.5 [習得期間第 4 日]、到達所要時間↑[試行期間第 1 日）]) OECD においては、「本試験は、ガイドライン及び GLP に沿って行われていないため、他の試験機関で確認試験を行うことが有益である」と評価している。 【SIAP (CAS No.25637-99-4, 3194-55-6)(SIAM24)より引用】 European Commission, Scientific Committee on Health and Environmental Risk (2008) でも同様の評価を行っている。 ［van der Ven LT, Verhoef A, van de Kuil T, Slob W, Leonards PE, Visser TJ, Hamers T, Herlin M, Hakansson H, Olausson H, Piersma AH, Vos JG, “A 28-Day Oral Dose Toxicity Study Enhanced to Detect Endocrine Effects of Hexabromocyclododecane in Wistar Rats”, Toxicological Sciences 94, 281-292 (2006)］ 28 日間反復投与試験 投与方法：28-33 日間強制経口投与　溶媒：コーン油　Wistar ラット (RIVM Cpb:WU) 純度：記載無し［α:β:γ 比は 10.28%:8.72%:81.01%］（微量のテトラブロモシクロドデカンおよびペンタブロモシクロドデカンを含む technical mixture） 用量：7 投与量（0.3, 1, 3, 10, 30, 100, 200 mg/kg/day） 死亡：0.3♀：1/5、3♂：2/5【投与過誤】 【数値は BMDL (ベンチマークドーズの 95%信頼下限値)、ただし病理組織学的検査の結果のみ CED (重要影響サイズ＝ベンチマークドーズ)】 overall BMDL：1.6 mg/kg/day 血液生化学的検査 (TT4↓：55.5♀、Cho↓：65.9♂、ALP↓：18.9♀、Glu↓：57.0♂・70.8♀、TP↑：200 以上♂・142.7♀、Alb↑：200 以上♂・197.5♀) 絶対重量 (下垂体↑：29.9♀、胸腺↓：104.2♂、甲状腺↑：1.6♀、肝臓↑：22.9♀) 病理組織学的検査 (甲状腺-濾胞細胞の高さ↑：47♀、核サイズ↑：39♂・25♀、空胞化↑：90♂・177♀、濾胞サイズ↓：199♂) 下垂体の免疫組織学的検査[最高投与群のみ検討] (TSH 産生細胞染色強度の比(高/低)↑:200♀) 肝—T4-UGT 活性↑： 4.1♀ 骨分析 (骨梁骨の鉱質密度：69.9♀、脛骨の骨端線部位-骨梁骨の鉱質密度：49.3♀) 免疫学的検査 [雄のみ実施] (脾臓-総細胞数↓：1.7♂、 ヘルパーT 細胞数↓：0.3♂、NK 細胞数↓：6.3♂) 回復性：実施せず ※SIAP（SIAM24）では、22.9mg/kg/day の雌の肝の絶対重量増加を overall BMDL として評価している。

［WIL Research Laboratories, Inc., WIL-186004, “A 28-day repeated dose oral toxicity study of HBCD in rats”, sponsored by Chemical Manufacturers Association, Brominated Flame Retardant Industry Panel (1997), WIL Research Laboratories, Inc., WIL-186004, “Addendum to the final report of a 28-day repeated dose oral toxicity study of HBCD in rats”, sponsored by Chemical Manufacturers Association, Brominated Flame Retardant Industry Panel (1998)］
反復投与試験
28 日間　強制経口投与　溶媒：コーン油　SD Crl:CD BR ラット
純度：記載無し (市販 HBCD の混合物：3 ロット使用)
用量：125, 350, 1000 mg/kg/day
死亡：なし
NOEL：< 125 mg/kg/day [報告書では NOAEL：1000 mg/kg/day]
推定根拠：相対重量 (肝↑：125 以上♀350 以上♂)
他の毒性：血液学的検査 (APTT↑：1000♂)
血液生化学的検査 (TP↑：350 以上♂･1000♀、Glb↑：1000♀、
Glu↑：1000♀、Cho↑：350 以上♀、Ca↑：1000♀)
絶対重量 (肝↑：1000♂･350 以上♀)
病理組織学的検査 (甲状腺-コロイド消失の重篤化：1000♂)
回復性：相対・絶対重量 (肝↑：1000♀)

［BASF Institute for Industrial Hygiene and Pharmacology, “Hexabromocyclododecane: 28-day feeding trials with rats” (1969)］
反復投与試験
28 日間　混餌投与　SD 系自家繁殖ラット
純度：記載無し (Hexabromide S)
用量：1.0, 2.5, 5.0 %
死亡：なし
NOEL：< 1.0%
推定根拠：絶対重量 (肝↑：1.0 以上♂♀) [肝・腎・心のみ測定]
相対重量 (肝↑：1.0 以上♂♀)
組織学的所見 (甲状腺－上皮の活性化：1.0 以上♂♀、小濾胞性過形成 (microfollicular hyperplasia)：1.0 以上♂♀)
他の毒性：一般状態 (状態不良 (poor condition)・脱毛･歩行蹌踉：2.5 以上♂♀)
体重↓ (2.5 以上♀5.0♂)
摂餌量↓ (2.5 以上♀5.0♂)
組織学的所見 (甲状腺－腺腫様増殖を伴う組織過形成：5.0♂♀、
卵巣－卵胞および成熟卵胞減少：5.0♀）
回復性：実施せず

［BASF Corporation, “Hexabromocyclododecane: 90-day feeding trials with rats” (1970)］
反復投与試験
90 日間　混餌投与　SD 系自家繁殖ラット
純度：記載無し (Hexabromid S)
用量：0.16, 0.32, 0.64, 1.28 %
死亡：1.28（♂1/30）
NOEL：<0.16%
推定根拠：絶対重量 (肝↑：0.16 以上♂♀) [肝・腎・心のみ測定]
相対重量 (肝↑：0.16 以上♂♀、心↓：1.28♂・0.16 以上♀)[肝・腎・心のみ測定]
他の毒性：体重↓ (1.28♂)
組織学的所見 (肝臓-脂肪顕出↑：0.16 以上♂・0.64 以上♀)
回復性：[1.28%のみ投与終了後 42 日間]
絶対重量 (肝↑：1.28♂♀) [肝・腎・心のみ測定]
相対重量 (肝↑：1.28♂♀、心↑：1.28♂)

［黒川雄二、井上達、川島邦夫、内田雄幸、門馬純子、“防炎加工剤 Hexabromocyclododecane のマウスにおける癌原性試験”、国立衛生試験所、安全性生物試験センター、毒性部 (1996)］
発がん性試験
18 ヶ月間混餌投与　SLc;$B_6C_3F_1$ マウス
純度：記載なし
用量：100, 1000, 10000 ppm
がん原性：なし
肝細胞癌、担癌、肺腺腫、白血病などの腫瘍性変化が認められたが、用量相関性が認められなかった。
他の毒性：肝臓において、細胞の過形成、増殖巣の出現、肝細胞の膨化を伴う変性、壊死、空胞化および脂肪化の混合した所見が HBCD 投与群で多く認められたが用量相関性は認められなかった。

［WIL Research Laboratories, Inc., WIL-186009, “A prenatal developmental toxicity study of hexabromocyclododecane (HBCD) in rats”, sponsored by Chemical Manufacturers Association, Brominated Flame Retardant Industry Panel (1999) ］
発生毒性試験
妊娠 6～19 日、強制経口投与　溶媒：コーン油　Crl:CD(SD)IGS BR ラット
純度：90.0 % (市販 HBCD の混合物：3 ロット使用)
用量：250, 500, 1000 mg/kg/day
NOAEL：1000 mg/kg/day
推定根拠：母体毒性および発生毒性なし

［Industrial Bio-Test Laboratories, Inc., P.O. No. 01515, “Mutagenicity of two lots of FM-100, lot 53 and residue of lot 3322 in the absence and presence of metabolic activation”, report to Velsicol Chemical Corporation (1977)］
復帰突然変異試験: 陰性
試験系：-S9mix 群: Salmonella typhimurium TA98, TA100, TA1535, TA1537
+S9mix 群: Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538
純度：記載なし (FM-100, Lot No.53)
溶媒：DMSO
濃度：-/+ S9mix 群: 25, 50, 100, 250 μg/10 μL
陽性対照：- S9mix 群: N-メチル-N-ニトロ-N-ニトロソグアニジン
+S9mix 群: 2-アミノフルオレン

［Pharmakologisches Inst., “Ames test for Hexabromid S” (1978)］
復帰突然変異試験: 陰性
試験系：Salmonella typhimurium TA100, TA1537, TA98
純度：1,2,5,6,9,10-ヘキサブロモシクロドデカン：～95 % (Hexabromid S)
溶媒：DMSO
濃度：-/+ S9mix 群: 31.5, 100, 315, 1000, 3000 μg/plate
陽性対照：- S9mix 群: N-メチル-N'-ニトロ-N-ニトロソグアニジン、
ベンゾ(a)ピレン 4,5-オキシド
+S9mix 群: 3-メチルコラントレン、ベンゾ(a)ピレン、2-アミノアントラセン

	［Life Science Research Israel Ltd., LSRI Project No. DSB/109/HBCD, “HBCD Blend; Assessment of mutagenic potential in histidine auxotrophs of Salmonella Typhimurium (the Ames test)” (1989)］ 復帰突然変異試験: 陰性 試験系：Salmonella typhimurium TA1535, TA100, TA1538, TA98, TA1537 純度：記載なし (HBCD Blend) 溶媒：DMSO 濃度：-/+ S9mix 群: 260, 130, 65, 6.5, 2.5 μg/plate 陽性対照：- S9mix 群: アジ化ナトリウム (TA1535, TA100)、2-アミノアントラセン (TA1535, TA100, TA1538, TA98, TA1537)、NPD (TA1538, TA98)、ICR191 (TA1537) +S9mix 群: 2-アミノアントラセン(TA1535, TA100, TA1538, TA98, TA1537)
	［Litton Bionetics, Inc., LBI Project No. 2547, “Mutagenicity Evaluation of 421-32B”, submitted to Ciba-Geigy Corporation (1976)］ 復帰突然変異試験: 陰性 試験系：Salmonella typhimurium TA1535, TA100, TA1538, TA98, TA1537 Saccharomyces cerevisiae D4 純度：記載なし (421-32B = Hexabromocyclododecane Dispersion) 溶媒：記載なし 濃度：-/+ S9mix 群: 0.5, 2.5, 5, 50 μg/plate 陽性対照：- S9mix 群: メチルニトロソグアニジン (TA1535, TA100, D4)、2-ニトロフルオレン (TA1538, TA98)、キナクリンマスタード (TA1537) +S9mix 群: 2-アントラセン (TA1535, TA100)、2-アセチルアミノフルオレン (TA1538, TA98)、8-アミノキノリン (TA1537)、ジメチルニトロソアミン (D4)
	［Gulf South Research Institute, “Mutagenicity test of GLS-S6-41A” (1978)］ 復帰突然変異試験: 陰性 試験系：Salmonella typhimurium TA98, TA100, TA1535, TA1537 純度：記載なし (GLS-S6-41A) 溶媒：DMSO 濃度：-/+ S9mix 群: 2, 40, 200, 1000 μg/plate 陽性対照：- S9mix 群: N-メチル-N-ニトロソ-N-ニトログアニジン (TA1535) +S9mix 群: ベンゾ(a)ピレン (TA98, TA100)、9-アミノアクリジン (TA1537) (TA98 の+S9mix 群において 40 μg/plate 以上で復帰変異株が増加したが、わずかな変化で、用量依存性は認められなかった)
	［SRI Research Institute, SRI Project LSC-5702, “In vitro microbiological mutagenicity studies of four Ciba-Geigy Corporation compounds”, prepared for Ciba-Geigy Corporation (1976)］ 復帰突然変異試験: 陰性 試験系：Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538 純度：記載なし (421-32-B = Hexabromocyclododecane Dispersion) 溶媒：DMSO 濃度：-/+ S9mix 群: 1, 10, 50, 100, 500, 1000, 5000 μg/plate 陽性対照：- S9mix 群: β-プロピオラクトン (TA100, TA1535)、2-(2-フリル)-3-(5-ニトロ-2-フリル)アクリルアミド (AF-2) (TA100)、9-アミノアクリジン (TA1537)、2-アントラミン (TA1538, TA98) +S9mix 群: 2-アントラミン (TA1538, TA98)

［Huntingdon Research Centre, “Ames metabolic activation test to assess the potential mutagenic effect of compound No.49” (1978)］
復帰突然変異試験: 陰性
試験系：Salmonella typhimurium TA98, TA100, TA1535, TA1537, TA1538
純度：記載なし (Organic bromide, Code number 49)
溶媒：DMSO
濃度：-/+ S9mix 群: 10, 100, 1000, 10000 μg/plate
陽性対照：+S9mix 群: 2-アミノアントラセン (TA98, TA100)、β-ナフチルアミン (TA1535)、ニュートラルレッド (TA1537)、2-アセチルアミノフルオレン (TA1538)

［Microbiological Associates, Inc., G96AO61.342, “Chromosome Aberrations in Human Peripheral Blood Lymphocytes (hexabromocyclododecane)”, sponsored by Chemical Manufactures Association (1996)］
染色体異常試験: 陰性
試験系：ヒト末梢血リンパ球
純度：記載無し
溶媒：DMSO
濃度：Initial assay
-/+ S9mix 群:0.25, 0.75, 2.5, 7.5, 25, 75, 250, 750, 2500 μg/mL
(20 hour harvest)
Independent assay
- S9mix 群: 10, 19, 38, 75, 150, 300, 600 μg/mL (20 hour harvest)
10, 19, 38, 75, 150, 300, 600 μg/mL (44 hour harvest)
+S9mix 群: 10, 19, 38, 75, 150, 300, 600 μg/mL (20 hour harvest)
10, 75, 150, 300, 600 μg/mL (44 hour harvest)
陽性対照：- S9mix 群: マイトマイシン C
+S9mix 群: シクロフォスファミド

［Helleday T, Tuominen KL, Bergman A, Jenssen D, “Brominated flame retardants induce intragenic recombination in mammalian cells”, Mutation Research 439, 137-147 (1999)］
組換え試験
試験系：Sp5 および SPD8 細胞株
純度：記載なし (1,2,5,6,9,10-hexabromocyclododecane)
溶媒：DMSO
濃度：Sp5: 2, 5, 10, 15, 20 μg/mL
SPD8: 3, 6, 10, 15, 20 μg/mL
陽性対照：カンプトテシン
結果：Sp5: 2.2 fold increase in reversion frequency with 43% growth inhibition at 20 μg/mL
SPD8: 1.9 fold increase in reversion frequency with 81% growth inhibition at 20 μg/mL

［BASF Aktiengesellschaft, Laboratory project No.: 26M0100/004018, "Cytogenetic study in vivo with hexabromcyclododecane in the mouse micronucleus test after two intraperitoneal administrations” (2000)］
小核試験：陰性
試験系：NMRI マウス(♂)（観察細胞：骨髄赤血球）
投与方法：腹腔内投与 (24 時間間隔で 2 回)
純度：ヘキサブロモシクロドデカン：90.0 %
溶媒：DMSO
用量：3 用量 (500, 1000, 2000 mg/kg):
毒性影響：立毛：500 以上、しゃがみこみ姿勢 (Squatting posture)：500 以上、一般状態の不良(Poor general state)：1000 以上
赤血球生成阻害：2000

環境調査	媒体	実施年度	検体	検出範囲	検出下限値
※1	水質	H15	0/60	―	0.087(μg/L)
	底質	H15	3/45	0.085～0.14	0.023(μg/g-dry)
	魚類	H16	3/18	0.043～0.077	0.0071（μg/g-wet）
備考	※1　H16、H17 版「化学物質と環境」（環境省環境保健部環境安全課）				

資料1－3

既存化学物質審査シート(人健康影響･生態影響)

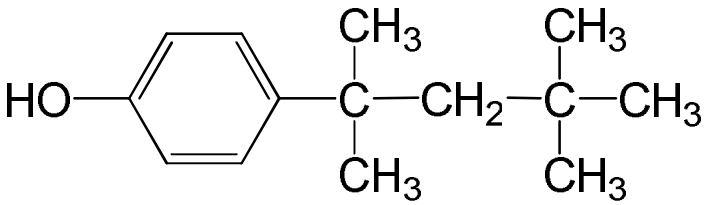
(平成20年12月19日開催)

官報公示整理番号	CAS No.	物質名称	判定結果		頁
			人健康影響	生態影響	
3-503	140-66-9	*p*－*tert*－オクチルフェノール	二監相当	三監相当 【告示済み】	1
4-44	843-55-0	1，1－ビス(4－ヒドロオキシフェニル)－シクロヘキサン		三監相当	3
3-2254	3194-55-6 25637-99-4	1，2，5，6，9，10－ヘキサブロモシクロドデカン		三監相当	4

既存化学物質審査シート

官報公示整理番号	3-503	CAS No.	140-66-9

判定結果	人健康影響　第二種監視化学物質相当 生 態 影 響　第三種監視化学物質相当【平成 18 年 7 月 18 日告示済み】

名称 構造式等	名　称：*p-tert*-オクチルフェノール 
用途	３－５０３として中間物、合成樹脂、接着剤、添加剤（ゴム用、油用、紙用）、洗剤等 ※化学物質の製造・輸入量に関する実態調査（平成１６年実績）
外観	白色結晶状固体
分解性	難分解性
蓄積性	高濃縮性でない

Ames	陰性 純度≧97%．溶媒（DMSO－溶解）．プレート法. TA98, TA100, TA1535, TA1537, WP2uvrA. 5000μg/plate まで実施した用量設定試験の結果を参考に、以下の濃度まで実施. （本試験Ⅰ） －S9mix 群：50μg/plate（TA1535, TA1537：25μg/plate 以上で菌の生育阻害） （TA98, TA100：最高用量で菌の生育阻害） 2000μg/plate（WP2uvrA：最高用量で菌の生育阻害） ＋S9mix 群：200μg/plate（TA98, TA100, TA1535, TA1537： 最高用量で菌の生育阻害） 2000μg/plate（WP2uvrA） （本試験Ⅱ） －S9mix 群：50μg/plate（TA1537：25μg/plate 以上で菌の生育阻害） （TA98, TA100, TA1535：最高用量で菌の生育阻害） 2000μg/plate（WP2uvrA：最高用量で菌の生育阻害） ＋S9mix 群：200μg/plate（TA1537：100μg/plate 以上で菌の生育阻害） （TA98, TA100, TA1535：最高用量で菌の生育阻害） 2000μg/plate（WP2uvrA：最高用量で菌の生育阻害）
染色体異常	陰性 純度≧97%．溶媒（DMSO－溶解）．CHL/IU. 0.1mg/mL まで実施した細胞増殖抑制試験の結果を参考に、以下の濃度まで実施. －S9mix 群：0.005mg/mL（細胞毒性のため、0.0025mg/mL まで観察） ＋S9mix 群：0.04mg/mL 24 時間処理群；0.016mg/mL（細胞毒性のため、0.008mg/mL まで観察） 48 時間処理群：0.016mg/mL（細胞毒性のため、0.008mg/mL まで観察）

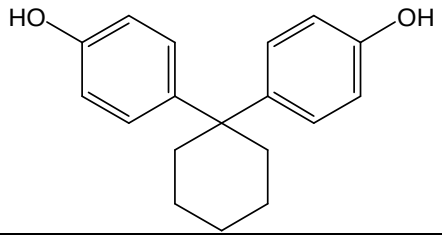
28 日間反復投与	投与方法	強制経口投与　溶媒：オリブ油
	純度	98.24%
	用量	3 用量(15, 70, 300 mg/kg/day)
	死亡	予備試験（500♀：1/2、1000♂：1/2、1000♀：2/2）
	NOEL	15 mg/kg/day
	推定根拠	一般状態（流涎：70 以上♂♀） 血液生化学的検査(A/G↓：70 以上♀）

	他の毒性	体重↓（300♂） 摂水量↑（300♂♀） 一般状態（自発運動量↓：300♂） 血液生化学的検査（Na↑：300♂♀、Alb↓・K↓：300♂、BUN↑･Cho↓・TG↑：300♀） 尿検査（尿比重↓･尿量↑・Na↓・Cl↓：300♂♀） 相対重量（腎↑:300♂♀、肝↑：300♀） 組織学的所見（腎－尿細管再生像：300♂♀）
	回復性	問題なし
人健康影響判定根拠	Ames 試験及び染色体異常試験は陰性であるが、NOEL 15mg/kg/day であることから第二種監視化学物質相当。	
備考		

既存化学物質審査シート

官報公示整理番号	4-44	CAS No.	843-55-0

判定結果	生 態 影 響　第三種監視化学物質相当

名称 構造式等	名　称：1，1－ビス（4－ヒドロオキシフェニル）－シクロヘキサン 
用途	－
外観	白色粉末
分解性	難分解性
蓄積性	高濃縮性でない

藻類生長阻害試験	生物種：　*Pseudokirchneriella subcapitata* 試験法：化審法 TG 培養方式：振とう培養 純度：100% 試験濃度：設定濃度　0.24、0.51、1.1、2.3、4.8＊ mg/L　＊調製可能最高濃度 実測濃度　0.21、0.45、0.92、2.0、3.6 mg/L（時間加重平均値） 助剤：DMF 95μL/L 72hEC50（実測値に基づく）> 3.6 mg/L 72hNOEC（実測値に基づく）= 0.92 mg/L
ミジンコ急性遊泳阻害試験	生物種：オオミジンコ *Daphnia magna* 試験法：化審法 TG 試験方式：半止水式、24 時間後に換水 純度：100% 試験濃度：設定濃度　0.47、0.84、1.5、2.6、4.7 mg/L 実測濃度　0.45、0.82、1.5、2.5、4.6 mg/L（時間加重平均値） 助剤：DMF 95μL/L 48hEC50（実測値に基づく）= 1.8 mg/L
魚類急性毒性試験	生物種：ヒメダカ *Oryzias latipes* 試験法：化審法 TG 試験方式：半止水式、24 時間毎に換水 純度：100% 試験濃度：設定濃度　0.48、0.85、1.5、2.7、4.8 mg/L 実測濃度　0.42、0.75、1.3、2.5、4.3 mg/L（時間加重平均値） 助剤：DMF 95μL/L 96hLC50（実測値に基づく）= 1.8 mg/L

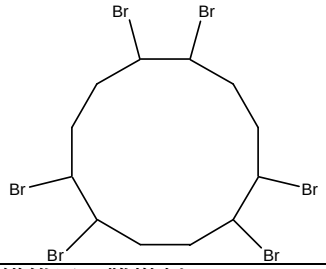
生態影響判定根拠	藻類生長阻害試験において 72hEC50>3.6mg/L、72hNOEC=0.92mg/L、ミジンコ急性遊泳阻害試験において 48hEC50=1.8mg/L であるが、魚類急性毒性試験において 96hLC50=1.8mg/L であることから第三種監視化学物質相当。

備考	試験用水溶解度： 藻類培地：　4.8 mg/L、Elendt M4 medium：　4.7 mg/L、脱塩素水道水：　4.8 mg/L

既存化学物質審査シート

官報公示整理番号	3-2254	CAS No.	3194-55-6 25637-99-4

判定結果	生 態 影 響　第三種監視化学物質相当

名称 構造式等	名　称：１，２，５，６，９，１０－ヘキサブロモシクロドデカン 
用途	発泡ポリスチレン用の難燃剤、繊維用の難燃剤 ※平成 20 年 3 月 26 日開催　化学物質審議会安全対策部会安全対策小委員会資料
外観	無臭白色個体
分解性	難分解性
蓄積性	高濃縮性

生態毒性情報	［SIAP（OECD/HPV プログラム）より引用］ 藻類に対する毒性値として ・*Skeletonema costatum*　72hEC50= 0.052 mg/L※ ミジンコに対する毒性として ・*Daphnia magna*　48hEC50> 0.0032 mg/L ・*Daphnia magna*　21dNOEC（成長、死亡）= 0.0031 mg/L 21dNOEC（繁殖）= 0.0056 mg/L 魚類に対する毒性として ・*Oncorhynchus mykiss*　96hLC50> 0.0025 mg/L ・*Oncorhynchus mykiss*　NOEC（ふ化成功率、ふ化時間、浮上時間、成長、死亡）≧0.0037 mg/L ※化審法テストガイドラインの推奨種を用いた試験結果でないことから、参考値として記載した。
生態影響判定根拠	ミジンコ急性遊泳阻害試験、魚類急性毒性試験及び魚類初期生活段階毒性試験において溶解限度で影響が認められないが、ミジンコ繁殖阻害試験において 21dNOEC（繁殖）=0.0056 mg/L であることから、第三種監視化学物質相当。

環境調査※1	媒体	実施年度	検体	検出範囲	検出下限値
	水質	H15	0/60	―	0.087(μg/L)
	底質	H15	3/45	0.085～0.14	0.023(μg/g-dry)
	魚類	H16	3/18	0.043～0.077	0.0071（μg/g-wet）

備考	※１　H16、H17 版「化学物質と環境」（環境省環境保健部環境安全課） 対水溶解度（20℃）：0.066 mg/L（sum of α-, β- and γ-HBCDD） 0.049 mg/L（α-HBCDD）、0.015 mg/L（β-HBCDD）、0.002 mg/L（γ-HBCDD） 出典： MacGregor and Nixon, 2004

資料１－４

平成 20 年度第 8 回薬事・食品衛生審議会薬事分科会化学物質安全対策部会化学物質調査会
化学物質審議会第 81 回審査部会
第 84 回中央環境審議会環境保健部会化学物質審査小委員会
合同審議会議事録
【第一部】

１．日　時：平成 20 年 12 月 19 日（金） 13:30～14:25
２．場　所：三田共用会議所　４階　第４特別会議室
３．出　席（五十音順、敬称略）

薬事・食品衛生審議会薬事分科会化学物質安全対策部会化学物質調査会委員

有馬　郷司	江馬　眞（座長）	菅野　純
清水　英佑	高木　篤也	西原　力
林　　真	前川　昭彦	安田　峯生
吉岡　義正		

化学物質審議会審査部会委員

内田　直行	北野　大（部会長）	清水　英佑
竹内　和彦	竹下　達也	田中　明人
西原　力	藤木　素士	前川　昭彦
米澤　義堯		

中央環境審議会環境保健部会化学物質審査小委員会委員

菅野　純	白石　寛明	米元　純三
田辺　信介	中杉　修身（委員長）	吉岡　義正
田中　嘉成		

事務局

厚生労働省	山本化学物質安全対策室長
経済産業省	森田化学物質安全室長
環境省	戸田化学物質審査室長　　他

４．議　　題
　１．前回審議結果の確認
　２．既存化学物質の審議等について
　　（１）分解性について

（２）難分解性・高濃縮性判定済みの既存化学物質について

（３）人健康影響・生態影響について

（４）化学物質排出把握管理促進法の第一種及び第二種指定化学物質の一部を化審法第二種及び第三種監視化学物質に指定することについて

３．その他

○事務局（環境省）　お時間が参りましたので、ただいまから平成 20 年度第８回薬事・食品衛生審議会薬事分科会化学物質安全対策部会化学物質調査会、化学物質審議会第 81 回審査部会及び第 84 回中央環境審議会環境保健部会化学物質審査小委員会の合同審議会を開催したいと思います。

本日は、いずれの審議会も開催に必要な定足数を満たしており、それぞれの審議会は成立していることをまずご報告させていただきます。

また、各審議会から本日の会合への具体的伝達手続はそれぞれの省により異なりますが、化審法第 41 条に基づく新規化学物質の判定に関する諮問が大臣よりなされている審議会もございますので、よろしくお願いいたします。

なお、本審議会は既存化学物質の審議と新規化学物質の審議を第１部と第２部に分けて実施し、本日は 13 時半から 15 時半までを第１部として既存化学物質の審議を公開で行います。終了後、休憩を挟みまして、第２部として通常の新規化学物質等の審議を行いますので、どうぞよろしくお願いいたします。

それでは、審議に入ります前に、お手元にお配りした資料の確認を行いたいと思います。

まず、議事次第がございます。あと、それぞれホチキス止めで資料１－１、１－２、１－３、１－４がございます。同じく、すべてホチキス止めで資料２－１、２－２、２－３、２－４、２－５、２－６、２－７までございます。あと参考資料といたしまして、これもホチキスで止めてありますが、参考１、参考２－１と２－２を同時に綴じた資料がございます。その下に、Ａ３判を折り畳みました参考３、１枚紙で参考４、さらに参考５がございます。

あと、資料番号は振っておりませんが、右上に（参考資料）と書いてあります「ＰＲＴＲ及びＭＳＤＳ対象化学物質の選定基準の詳細」という資料も一番下につけております。

過不足等ございましたら事務局にお申しつけください。

本日の全体の議事進行につきましては、中央環境審議会環境保健部会化学物質審査小委員会の中杉委員長にお願いしたいと思います。

どうぞよろしくお願いいたします。

○中杉委員長　初めに、第１部の会議の公開の是非についてお諮りします。

各審議会におきましての公開につきましては、それぞれ規定のあるところでございますけれども、本日の会議のうち第１部については、公開することにより公正かつ中立な審議に著しい支障を及ぼすおそれがある場合、または特定な者に不当な利益もしくは不利益をもたらすおそれがある場合等、非

公開とするべき場合に該当しないと考えますので、公開したいと思いますが、よろしいでしょうか。

それでは、本日の第１部は公開といたします。

なお、公開の会議の議事録は、後日ホームページ等で公開されますので、あらかじめご承知おきお願いいたします。

それでは、議事次第に従いまして、まず議題１、前回審議結果の確認について、事務局から資料のご説明をお願いいたします。

○事務局（厚生労働省）　それでは、ご説明させていただきます。

資料１－３をごらんください。

審査シートの３ページになりますけれども、１，５－ジアミノナフタレンにつきまして、審査シートの記載方法について先生方からご意見をいただきましたので、修正したものを配付させていただいております。

発がん性について、ＮＴＰのデータでがん原性ありと評価されておりまして、４ページになりますけれども、ＩＡＲＣの総合評価のところ、一番下に Group３：『ヒトに発がん性を示すとしては分類できない』という一文を記載させていただいていたんですけれども、その評価の過程についても記載すべきであるというご指摘に従いまして、「発がん性に対する証拠の程度」を追記させていただいております。

以上、ご報告申し上げます。

○中杉委員長　よろしいでしょうか。

ほかにご質問、修正点ございませんようでしたら、今後の扱いについてご説明ください。

○事務局（環境省）　ただいまの資料１－１から１－４でございますけれども、もし他にご意見等ございましたら、本日の会議終了までにお申し出いただければと思います。特にご意見等ございませんでしたら、内部の手続が終了次第、各省のホームページ上で公開させていただきます。

よろしくお願いいたします。

○中杉委員長　よろしいでしょうか。

それでは、次に移ります。

○北野部会長　それでは議題２、既存化学物質の審議等に入りたいと思います。

まず分解性について、事務局からご説明をお願いします。

○事務局（経済産業省）　資料２－１に基づきまして、まとめてご説明させていただきます。

１ページをごらんください。

整理番号 1831、本物質の分解度試験の結果でございますが、ＢＯＤが平均 92%、ＨＰＬＣが 100%でした。以上の結果より、判定案としては、良分解性とさせていただいております。

続きまして、４ページをごらんください。

整理番号 1822、本物質については、ナトリウム塩を用いて分解度試験を行いました。

結果でございますが、ＢＯＤが平均２％、ＴＯＣが０％、ＨＰＬＣが０％という結果が得られました。この結果より、判定案といたしましては難分解性とし、後続の試験案として濃縮度試験を提案させていただきます。

続きまして、８ページをごらんください。

整理番号 1829、本物質につきましては、塩酸塩を用いまして分解度試験を行いました。

分解度試験の結果でございますが、ＢＯＤが平均０％、ＴＯＣ４％、ＨＰＬＣが０％という結果が得られました。この結果より、判定案といたしまして難分解性、後続の試験案として濃縮度試験を提案させていただきます。

最後に、11 ページをごらんください。

整理番号 1830、本物質の分解度試験の結果でございますが、ＢＯＤが平均６％、ＴＯＣが０％、ＨＰＬＣが０％という結果が得られました。この結果より、判定案といたしまして難分解性、後続の試験案として濃縮度試験を提案させていただいております。

以上４物質について、ご審議よろしくお願いいたします。

○北野部会長　ありがとうございました。

資料２－１の４物質ですが、１つずついきましょうか。

まずＫ番号 1831、良分解性という判定をしたいということですが、いかがでしょう。よろしいですか。

では、この物質については事務局案どおり、良分解性とします。

次の物質、Ｋ1822 です。これは難分解性と判定したいんですが、いかがでしょうか。難分解性でよろしいですか。

そうしますと難分解性で、次は濃縮度試験という、これは分配係数を適用するかどうか、そこはどういきますか。

○事務局（経済産業省）　まずは分配係数で、今の予測では 0.32 と極めて低い分配係数ですので、

これでまず実測してみて、3.5 を超えるようであれば濃縮度試験に移りたいと思います。

○北野部会長　ありがとうございました。

　では、これは難分解性で、分配係数を確認する。その結果によって、必要であれば濃縮度試験を行うということですね。

　ありがとうございました。

　３番目、1829 です。これも難分解性と判定したいという事務局案ですが、いかがでしょう。よろしいでしょうか。

　その後の濃縮度試験についても、1822 と同じ取り扱いでよろしいですね。はい、ありがとうございました。

　それでは最後の物質、1830 です。これも難分解性と判定したいということですが、いかがでしょうか。よろしいでしょうか。

　後の濃縮度試験も、前の２物質と同じ取り扱いでお願いします。

　以上、分解性の判定を終わります。

○江馬座長　次に、議題２の（２）難分解性・高濃縮性判定済みの既存化学物質について、事務局から説明をお願いします。

○事務局（厚生労働省）　それでは、ご説明させていただきます。

　資料２－２及び２－３をご参照ください。

　資料２－２「第一種特定化学物質へ該当するか否かの審議審査シート」について、ご説明させていただきます。

　まず１ページに記載させていただいておりますが、官報公示整理番号 3-2254、名称が１，２，５，６，９，10－ヘキサブロモシクロドデカンとなっております。構造式は、記載のとおりです。用途は、発泡ポリスチレン用の難燃剤、繊維用の難燃剤となっております。

　分解性につきましては難分解性、蓄積性につきましては高濃縮性と判定いただいておりまして、平成 16 年９月 22 日に第一種監視化学物質として指定されております。

　当該物質につきまして、今回、新たに収集された試験につきまして、国立医薬品食品衛生研究所の山本主任研究官よりご説明いただきます。

○事務局（厚生労働省）　それでは、説明させていただきます。

　まず最初に、今回新たに収集された情報として、１ページの下のほうにございますが、厚生労働省

既存化学物質安全性点検の２世代繁殖試験の結果をご説明いたします。

投与方法ですが、混餌投与で、ＣＤラットを用いております。

用量は、３投与群で 150、1,500、15,000ppm で、平均摂餌量から計算いたしますと、摂餌量はＦ０の雄で 10.2、101、1,008 mg/kg、以下Ｆ０の雌、Ｆ１の雄、Ｆ１の雌については、表のようになっております。

次に死亡ですけれども、ケージ内事故に起因すると思われる死亡が中低用量群、雄、１例、また、切迫屠殺したものが高用量群Ｆ０雄、１例でございました。

試験途中の雄動物の死亡は交配前投与期間の投与７週に中用量群で１例、及び第５週に高用量群で１例観察されました。しかし、いずれも死亡前に一般状態の変化はございませんでした。

次に、雌動物の試験途中の死亡ですけれども、高用量群でＦ０で２例見られました。そのうち１例は、交配前投与期間に一般状態の悪化のため切迫屠殺いたしました。もう一例は、難産のために妊娠 21 日に死亡いたしました。

このように死亡はございますが、いずれも例数は少なく、発生時期や世代間や性別を通して一貫性が見られるものはございませんので、これは被験物質による影響ではないと考えます。

２ページ、推定根拠です。

まず、親動物に対する毒性としては、標的臓器として肝臓、腎臓、卵巣の３つが見られます。肝臓に対しては組織学的所見を伴わない肝重量の増加、及びこれに関係すると思われる血液生化学的検査の項目に変化が見られます。

甲状腺ですが、組織学的所見の濾胞小型化と、血中ホルモン量の甲状腺に関連した項目の変化が見られました。

卵巣に対しては、Ｆ１原始卵胞数の減少が認められましたが、Ｆ１雌親の各種生殖パラメータやＦ２胎児の着床数などには異常は見られませんでした。

次に、次代に対する毒性といたしましては、組織学的所見を伴わない離乳時の肝重量の増加が見られました。

以上を推定根拠に、ＮＯＡＥＬは 150ppm、10.2 mg/kg 相当と推定されております。

これ以外の毒性といたしましては、親動物に対しては、体重、摂餌量の減少、甲状腺に関連する血中ホルモン量の変化及び甲状腺の臓器重量の増加が見られます。次代に対する毒性といたしましては、Ｆ２児の生後死亡率の上昇、哺乳時生存率の低下及び離乳時の哺乳期間の体重減少が見られました。

２ページ以降に他の毒性情報を参考として挙げておりますが、９ページをごらんください。

これ以降には、今回、新たに収集された他の毒性情報を参考データとして載せてございます。

この中で、特に最初のエリクソンらの報告について、ＮＯＥＬが非常に低いので、説明させていただきます。

このエリクソンの神経発生毒性試験ですけれども、ＮＭＲＩマウスを用いて、用量は 0.9 と 13.5 ㎎/kg で、生後 10 日の雄・雌児に単回強制経口投与いたしました。その結果、推定根拠と見られるような自発運動試験をもとに、ＮＯＥＬを 0.9 ㎎/kg 未満と推定しております。他の毒性では、そのように自発運動や水迷路試験のデータがあります。

この試験ですけれども、下に書いてありますように、ＯＥＣＤにおいては、本試験はガイドライン及びＧＬＰに沿って行われていないため、他の試験機関で確認試験を行うことが有益であると評価しております。

この結果については、予備審査会でもご議論いただきましたが、特殊な条件下で行われた単独の実験であること、再現性を含め検証が必要なこと、現在のところ、この一報以外に動物試験で神経発生毒性の報告はないことなどを考えると、新たな神経毒性の可能性について懸念が啓示されたものとは考えますが、現時点で規制を作用するデータとして用いることについては慎重に対処すべきであり、国際機関でも同様に、エリクソンらの試験結果の評価については慎重な態度を示していますので、引き続き国際動向に配慮しつつ、さらなる情報収集に努めるべきであるとの結果に予備審査会では至りました。

１ページにお戻りいただきまして、このような現状を踏まえて、現時点では先ほどご説明した２世代繁殖試験のＮＯＡＥＬ150ppm、10.2 ㎎/kg 相当から毒性を評価した結果、事務局案として「現時点で収集された情報からは、第一種特定化学物質に該当するとは判断されない」となりました。

ご審議お願いいたします。

○江馬座長　新たな情報として、２世代繁殖試験、それから９ページで説明していただきました神経発生毒性試験、その下の 28 日間の試験等があります。

ただいまの説明につきまして、コメントございましたらお願いします。

○西原委員　毒性の専門ではないので、ちょっと教えてほしいんですけれども、２世代繁殖試験というのは非常に難しいものなんですか。いや、死亡例が何例か出ていますね。通常このくらいは出るものですか。

○江馬座長　この死亡例の中には事故によるものも入っていまして、1群 20 から 24 匹で 4 群構成と動物が結構多いということで、このぐらい出ることもあるかなとは思います。

○田辺委員　このＨＢＣＤはα、β、γと異性体があると思うんですが、この試験はどの異性体のデータでしょうか。

○江馬座長　α、β、γでそれぞれ 8.5、7.9、83.7%です。

○菅野委員　起きている変化自体は肝臓に対する影響が主体であって、それに引き続く、いわゆる甲状腺ホルモン、サイロキシンの収支ですね、肝臓による排泄増加が加わって、それによって甲状腺刺激、ＴＳＨが上がって甲状腺が腫れる、それがメインの変化であろう。ＦＳＨが上がるのに関しては、卵巣に変化があったが軽いと考えるということで、全体の判定はこの予備審査の判定でよろしいのではないかと思います。

○江馬座長　そのほか、よろしいでしょうか。特に毒性の先生方、コメントありましたら。

○前川委員　今もおっしゃいましたように、毒性としてはメインは肝臓ですね。それと卵巣に対する影響ということです。甲状腺は、肝臓での甲状腺ホルモンの代謝を促進した結果としてＴＳＨが上がった、そのために甲状腺に変化が起こったということですので、標的臓器と言えば標的臓器ですけれども、基本的には二次的な変化である、メインは肝臓であるということです。

それから、今回、新たに卵巣の原始卵胞の数が減っているというデータが出ておりますけれども、卵巣自身への影響は、これまでのデータでも幾つか指摘されております。

それから、甲状腺に対する影響あるいは肝臓に対する影響も、ある意味では、これまでのデータで指摘されたものが今回、よりクリアな形で出てきたということかと思います。

ですから、毒性の内容としては、そんなに強いものではないということですね。

それから、胎児に対する影響もないわけではないんですけれども、ただ、気にかかりますのは、今回のデータでもそうですけれども、Ｆ１、Ｆ２の両方を見ているんですけれども、影響としてはＦ２のほうがより強くなっているといったことですね。その辺のところは気にかかるデータではあります。ですけれども、ＮＯＥＬの 10.2 ㎎/kg 云々というのは、これまで一特とされております物質に比べましても、そんなに低いものではない。毒性の内容としても、そんなに重篤なものではないといったことからも、一特にするようなデータではないかと思います。

○江馬座長　そのほか、よろしいでしょうか。

○安田委員　難分解、高蓄積性の物質ということで、気になるのは体内動態がどうなるか、体内負荷

量がどうなるかといったところですが、その辺についてのデータはいかがでしょうか。

○江馬座長　それほどデータは出ていないと思うんですが、１つ、肝臓にたまるというデータは出ていたと思います。それ以外はちょっとわかりません。

そのほか、よろしいでしょうか。

よろしいようでしたら、本物質は事務局案どおり「現時点で収集された情報からは、第一種特定化学物質に該当するとは判断されない」としたいと思います。

どうもありがとうございました。

○中杉委員長　続きまして、議題２の（３）人健康影響・生態影響についてでございます。

資料２－４でございますが、３物質ございますので、１つずつ。

最初に、3-503 について、事務局から資料のご説明をお願いいたします。

○事務局（厚生労働省）　それでは、ご説明いたします。

資料２－４、審査シート１ページをごらんください。

官報公示整理番号 3-503 の物質でして、名称は p-tert-オクチルフェノール、構造式等は記載のとおりです。

本物質は、人健康影響に関する試験が実施されております。順にご説明いたします。

まずＡｍｅｓ試験、陰性。染色体異常試験、陰性。28 日間反復投与毒性試験につきましては、ＮＯＥＬを 15 とさせていただいております。

判定根拠、２ページでございますが、Ａｍｅｓ試験及び染色体異常試験は陰性であるが、ＮＯＥＬ 15 であることから、第二種監視化学物質相当とさせていただいております。

ご審議のほどよろしくお願いいたします。

○中杉委員長　それでは、まず構造から、コメントございましたらお願いいたします。

○西原委員　これは内分泌攪乱物質として有名になった物質、オクチルフェノールの代表的物質で、女性ホルモンレセプターと結合してメス化を引き起こすと考えられています。

○中杉委員長　そのほかコメントございますか。よろしいでしょうか。

それではスクリーニング毒性試験のほうですけれども、Ａｍｅｓ染色体異常についてコメントございますでしょうか。

○林委員　Ａｍｅｓ、染色体ともに陰性で、特に問題ございません。

○中杉委員長　よろしいでしょうか。

それでは、28 日間反復投与毒性試験の結果について、コメントをお願いいたします。

○高木委員　本物質の標的臓器としては、腎臓がメインなものです。実際に血液検査でＢＵＮ等の増加が見られております。

評価についてはこのとおりだと思うんですけれども、見ている臓器が心臓、肝臓、腎臓、副腎、脾臓だけが組織学的検索をしていて、それ以外は見ていないというのが、ちょっと引っかかる点ではあります。ただ、その中でも影響がとらえられているということで、それ以上は追究できないかと思います。

あと、記載のことですけれども、雄の尿のカリウムが最高用量の 300 ㎎/kg で減少しているので、それをつけ加えていただければいいと思います。

○中杉委員長　ほかに追加でコメントございますでしょうか。

○前川委員　今、ご説明がありましたように、この試験は 300 を最高にして３用量でなされているんですけれども、1,000 でなくて 300 にした理由は、そこにも書いてありますように、予備試験で 500 以上で死亡が見られているということです。そういう意味で最高用量を 300 にして、その結果、さっきご説明がありましたように、特に腎臓への影響を示唆するような所見が出ている。それとともに、相対重量で肝臓の重量も増えております。

ただ、腎臓に関しましては腎臓の尿細管に病理組織学的な変化が出ておりますけれども、肝臓に関しましては単に重量の増加だけで、病理の所見は全く出ておりません。ですから、メインの標的臓器は腎臓ということでよろしいかと思います。

それから、一般状態その他から見まして、先ほどもご説明がありましたように他の臓器は検索されていないというお話ですけれども、一応他の所見などとも照らし合わせてみれば、それなりに評価はできるであろうと思います。

○菅野委員　腎臓に関しては尿量が増えたり、Na、Cl 両方下がって、いわゆる尿細管性の尿崩症的になっているんだと思います。

あと、ホルモン活性の云々なんですが、これは臓器を見ていないんですね。ですが、大人の動物でホルモン活性を見ても、普通フィードバックがかかって変化が見られないことが多いので、むしろこちらの腎臓の毒性のほうがホルモン活性によるＮＯＥＬより低いのだろうなと思いますので、ここではあえて取り上げなくてよろしいかと。この試験法では弱いホルモン活性は見られないということでよろしいんだと思います。

○西原委員　すみません、「構造からコメント」と言われたので言ったまでで。

○中杉委員長　結論としては、これでよろしいということですね。

ほかにご意見ございますでしょうか。

ほかにないようでしたら、この物質はＮＯＥＬが 15 ということで、事務局案どおり、第二種監視化学物質相当という判定をさせていただきます。ただ、尿検査のところの追加をしておいてください。

○事務局（厚生労働省）　承知いたしました。

○北野部会長　それでは次に、公示番号 4-44 ですか、１，１－４ヒドロオキシフェニル－シクロヘキサンについて、ご説明をお願いします。

○事務局（環境省）　審査シート３ページをごらんください。

記載の物質につきまして、化審法テストガイドラインに基づく３種の生態影響試験が実施されております。

魚類急性毒性試験におきまして、96 時間ＬＣ50 が 1.8㎎/L との結果が得られております。

生態影響判定根拠でございますが、藻類生長阻害試験において 72 時間ＥＣ50 が 3.6㎎/L を上回り、72 時間ＮＯＥＣが 0.92㎎/L、ミジンコ急性遊泳阻害試験において 48 時間ＥＣ50 が 1.8㎎/L であるが、魚類急性毒性試験において 96 時間ＬＣ50 が 1.8㎎/L であることから、第三種監視化学物質相当とさせていただいております。

ご審議よろしくお願いいたします。

○北野部会長　この物質について構造上の知見があったら承りたいと思いますが、いかがでしょうか。

○西原委員　この物質もビスフェノールＡの類似体ということで、女性ホルモン活性がある可能性はあります。この濃度でメダカで影響が見られるかどうかは、私ちょっとわかりませんけれども。短い時間ですから、それは出てこないと思います。

○北野部会長　それでは、生態毒性試験の中身について議論していきたいと思いますが、いかがでしょうか。

○吉岡委員　この３つの試験方法及び試験結果とも、合理的なものだと思って見ております。

毒性を見ますと、藻類生長阻害試験が 3.6㎎/L 以上となっておりまして、これだけ非常に緩いように見えますが、データから見ると、このＥＣ50 はおおよそ４㎎/L ぐらいになるのではないかと予想されます。

○北野部会長　３つの試験について、ほぼ妥当であるというご意見ですが、ほかの先生方、いかがで

しょうか。よろしいですか。

判定根拠も、これでよろしいですね。

それでは、この物質につきましても事務局案どおり、第三種監視化学物質相当とさせていただきます。

○江馬座長　次に、3-2254、事務局から説明をお願いします。

○事務局（環境省）　審査シート４ページでございます。

当該物質は、先ほど「第一種特定化学物質には該当しない」とご判定いただいた物質でございます。

本物質につきまして、ＯＥＣＤ／ＨＰＶプログラムのＳＩＡＰに生態影響に関する情報がございましたので、今回、ご審議いただきたいと考えております。

結果は記載のとおりでございまして、藻類生長阻害試験でございますが、こちらは化審法テストガイドラインの推奨種を用いた試験結果ではございませんが、ＳＩＡＰにおいて、藻類に対する試験として最も信頼性のあるデータと評価されていることから、今回、こちらに記載させていただきました。

生態影響判定根拠でございますが、ミジンコ急性遊泳阻害試験、魚類急性毒性試験及び魚類初期生活段階毒性試験において溶解限度で影響が認められないが、藻類生長阻害試験において 72 時間ＥＣ50 が 0.052mg/L、ミジンコ繁殖阻害試験において 21 日間ＮＯＥＣが 0.0056mg/L であることから、第三種監視化学物質相当とさせていただいております。

なお、エコ調査の結果もございますので、こちらに記載させていただいております。

ご審議よろしくお願いいたします。

○江馬座長　ただいまの説明につきまして、まず構造の面からコメントをお願いします。

○西原委員　構造面は特にありません。先ほどのときに私、質問すべきだったかもしれません。もしデータがあれば教えてほしいんですが、この物質の製造量とか輸入量はどのぐらいのものですか。

○事務局（経済産業省）　平成 19 年度で、供給量としては 3,200 トン。供給量というのは製造量、輸入量合わせて 3,200 トン、出荷量としては 3,400 トンございます。

○江馬座長　そのほか、コメントございませんでしょうか。

○吉岡委員　生態毒性の関係ですけれども、論文ということで、ミジンコと魚類については恐らく問題はないだろうと思っております。試験方法及び結果ともですね。

一番問題が残りますのは、藻類に対する毒性値として、この値を生態影響の判定根拠の中に加えるべきであるかという点だと思います。実は、このプログラムの中で上がっておりますデータといたし

ましては５点ございまして、そのうち２点はセネデスムスを用いました、いわゆるＯＥＣＤの試験法の生物を用いました試験結果でございます。その試験結果のＥＣ50 といった値は、溶解度以上の値になっておりまして、通常の試験ならば「まあ問題はなかろう」ということで通過していくべきものでございます。しかしながら、そこに書かれております藻類の種類、これは海産の藻類、珪藻類の１種ですけれども、このものに対して文献を集めてみると３つあって、その３つのうちで、実は毒性値がピタッと決まっている文献というのはないのです。大体この付近であろうという点と、それから、１濃度区だけやってみたら 50%に近い値が出てきたというところ、それを総合的に判断して「まあこの辺じゃないか」ということで、0.052mg/L という数字が上がってきているところでございます。

１つの点は、きちんとした濃度設定が行われて決められたＥＣ50 ではないということ、２つ目の点といたしましては、ＯＥＣＤ試験法に載っていない種類を用いた試験を化審法の基準として採用するかどうかという点が問題になろうかと思います。

これは１人では決められませんので、他の先生方のご意見も伺いたいと思います。

○江馬座長　というご意見なんですが、他の先生方、コメント、ご意見ございましたらお願いします。

それから、事務局から何かありましたら。

○事務局（環境省）　海産系の藻類の結果を判定根拠に記載すべきでないというご意見ですが、結果として、ミジンコの毒性値から三監相当には変わらないということかと思います。淡水系の藻類の結果をこちらに記載するということもございますが、そういった対応でよろしいでしょうか。

○吉岡委員　私が言ってもいいのかどうかわかりませんけれども、とりあえず、藻類のどれを載せるかはペンディングにして、詳細な議論を重ねてからでないとはっきりした結論を今すぐには出せないのではないかと思います。

とりあえずこの物質につきましては、仮に藻類の試験がなくても三監相当の判定は可能でございますから、処理としてはそのようにしておいて、今後も例えば文献のデータの中で今まで見たこともないような種類の魚が出てきた、その試験があったときにそれをどうするかという問題になってくる。そういう大きなことにつながってまいりますので、とりあえずペンディングにしておいて、判定のところはミジンコの繁殖毒性で行うという案、折衷案みたいなものですけれども、それでいかがでしょうか。

○中杉委員長　幸いにして、今回はこれを外しても三監相当ということなので、吉岡先生が言われたとおりでよろしいのではないかと私も判断をいたします。もう少し議論が必要だと思うんですね。

記載をどうするかというのは難しい話なので、それは事務局と少し相談したいと思いますけれども、判定としては三監相当で、藻類は根拠にしないということで、とりあえず。

いずれそれを根拠にしなければいけないものが出てくるだろうと思いますので、その前に議論しておかなければいけないとは思いますけれども。

○江馬座長　ミジンコの試験を根拠にして三監相当ということで、よろしいでしょうか。藻類のことにつきましては議論をいただくということで、よろしくお願いします。

判定案は、事務局案どおりとさせていただきます。

○中杉委員長　これは先ほど一特でないという判断をしたもので、一監ではあるんですよね。一監であって三監であるという扱いなんですね。三監であるということは、管理の仕方として事業者の方が何をしなければいけないというのは、一監にしておけば、もうそれで十分なはずなんだけれども、三監にするというのは「これは生態影響が懸念されるよ」ということをアナウンスするという意味があると思うんですね。そういうことで言いますと先ほどの健康影響も、一特ではないけれども、この結果、仮に 10.幾つというのを採用するとしたら二監相当の判定になるわけですよね。これは今の 25 以下ですか、そういう判定に単純に持っていくと、そういうふうになります。そういうふうなことで、二監相当としておくのがいいのかもしれない。それができるかどうかというのも１つあります。

もう一つは、今、化審法の改正を議論していますから、当然この二監、三監のそういうややこしい話は先送りになるので、今の段階ではこれは必ずしも二監にしなくてもいいかと思いますけれども、「これは人健康影響は二監相当ですよ」ということは何かの形で事業者の方にアナウンスをしておく必要があるだろう。ただ蓄積性があるだけではないよということは注意したほうがいいのではないかと思います。

○事務局（経済産業省）　ただいまの二監相当かどうかというのは、28 日間のデータで 25 というところなので、これは２世代繁殖試験の結果と同一には扱えないのかなと思います。

ただ一方、おっしゃるように、生態毒性は相当強くなっております。事業者のほうはこういう状況を、今日の結果を受けたというよりは、生態毒性のところとか高濃縮である、あと量も多いということで、排出量を削減していく取り組みを始めております。将来的には相当量減っていくかなというふうに想定されております。

今後も、今日のご意見を踏まえて、製造事業者及び取り扱い事業者には排出削減に向けた、またはその管理に向けた取り組みをしてほしい旨、伝えたいと考えております。

○中杉委員長　これは今度、優先取り組み物質のほうの体系にしても、一監の流れというのは別になってしまっているので、その具体的な中身をどうするかという議論をするときに、そこら辺も踏まえて、今、言われるように、これが 20 だからというふうにすぐにならないのは理解しましたけれども、何か考えていく必要があるかなと思いますので、一言だけ申し上げました。

○田辺委員　この物質は、いわゆる環境モニタリングあるいは生物モニタリングの調査データが最近、学術レベルでも随分増えているんですが、それでも、やはり広く検出されておりますので、そういう意味でも、もう少しこれは慎重に議論を進めたほうがいいのではないかと思いますので、ちょっとつけ加えておきます。

○中杉委員長　それでは、議題２の（３）につきましては以上ということで、次に議題２の（４）化管法の第一種及び第二種指定化学物質の一部を化審法の第二種及び第三種監視化学物質に指定することについて、事務局から資料のご説明をお願いいたします。

○事務局（環境省）　お手元の資料２－７をごらんください。

こちらの資料ですけれども、一言で言いますと、化管法の指定化学物質の選定のプロセスにおきまして確認された毒性を根拠に、化審法の二監あるいは三監の判定を行うといったことについて説明した資料でございます。

１.、２．でそれぞれ背景と今回の手続についてご説明しております。

まず１．でございますが、化学物質排出把握管理促進法、通常化管法と呼んでおりますけれども、化管法のＰＲＴＲの対象になる第一種指定化学物質及びＭＳＤＳの対象になる第二種指定化学物質のうち、当該化学物質について収集された科学的知見並びに分解性、蓄積性に関する既存点検結果から判断いたしまして、化審法における第二種及び第三種監視化学物質の要件に該当するものについては、これまでも順次、第二種、第三種監視化学物質として指定してきたというところでございます。

ご参考として、次のページに、化管法でどういった科学的知見を根拠に指定されているかをつけております。こちらにありますように、人健康影響の観点、生態毒性の観点から、化審法と類似のエンドポイントに着目した指定が行われている状況でございます。

また１ページにお戻りいただきまして、２．でございます。

最近の動きといたしまして、今年 11 月 21 日付けで、化管法の施行令の一部を改正する政令が公布されております。その政令におきまして新たに化管法の第一種及び第二種指定化学物質に指定された物質につきまして、次に示しております考え方に従って、化審法上の第二種、第三種監視化学物質と

して指定することとしたいということでございます。

考え方について申し上げます。

まず（１）第二種監視化学物質への指定でございます。

以下の化学物質を除外した上で、既存点検結果等から難分解性であり高蓄積性でないと判断されている化学物質について、第二種監視化学物質と指定したいと思います。除外する物質ですが、①として、化審法の審査対象外の化学物質。これは専ら医薬品あるいは農薬として使用されているものなどがあります。②といたしまして、既に化審法の第一種・第二種特定化学物質に指定されている化学物質。③といたしまして、人健康影響以外の観点から対象となった化学物質。これらを除いた上で、化審法の第二種監視化学物質として指定することとしたいと思います。

続きまして（２）第三種監視化学物質の指定の考え方でございますが、以下の化学物質を除外した上で、既存点検結果等から難分解性であると判断されている化学物質をまず選定いたします。除外する項目ですが、①は二監指定と同様です。化審法の審査対象外のものは除外します。②も同様で、化審法第一種・第二種特定化学物質に指定されている化学物質を除外いたします。③といたしまして、生態毒性以外の観点で対象となった化学物質、これについても除外します。それらを除外して選定された化学物質につきまして、２）でございますが、監視化学物質への該当性の判定等に係る試験方法及び判定基準、通常の審査で見ていただいている判断基準ですが、この判定基準に基づきまして、第三種監視化学物質に該当することが明らかなものについて、第三種監視化学物質に指定するものでございます。

具体的な指定予定物質等につきましては、後ろに別添でつけております。

おめくりいただきまして、右上に（別添１－１）と書いてあります表が、化審法の第二種監視化学物質へ新たに指定を予定している物質でございます。22 種類ございます。それに関する根拠データにつきましては、おめくりいただきまして（別添１－２）と書いてあるもので、それぞれの物質についての根拠データを整理したものでございます。

２枚めくっていただきますと、右上に（別添２－１）とついた資料がございます。この資料が化審法の第三種監視化学物質へ新たに指定を予定している物質でございます。これが計 43 物質ございます。その後ろに（別添２－２）といたしまして、これら 43 物質についての指定の根拠データをつけております。

詳しいご説明は省略させていただきますが、このような考え方に沿いまして、これらの物質につい

て化審法上の判定をすることとさせていただきたいというご提案でございます。

○中杉委員長　これは化管法が最初にできたときに、第一次といいますか、対象物質とされたものについて、同様の考え方で、当時の指定化学物質にさせていただいたということがございますので、それと同じようなことを化管法の見直しが行われたので行いたいということでございます。

ご意見等ございますでしょうか。いかがでしょう、よろしいでしょうか。

一応ここでご判断いただく必要があって、持ち越しというわけにはいかないですよね。

○事務局（環境省）　もし何かありましたら、今回いただきたいと思います。

○中杉委員長　この物質はおかしいとか、この根拠はおかしいということがございましたら、一応はこれまでと判断の手続は同じ形にして、事務局のほうで選んだということでございますが、よろしいでしょうか。

特段のご意見がないようですので、ご了承いただいたものと考えてよろしいでしょうか。

それでは、そのようにさせていただきます。

最後に議題３、その他ですけれども、事務局のほうから何かありますでしょうか。

○事務局（環境省）　特段ございません。

○中杉委員長　それでは、本日の審議会の第１部は、これで終了したいと思います。

予定より大分スムーズに進んでおりますので、ここで休憩をとって、２時 45 分から第２部、新規化学物質等の審議を開始いたします。

なお、第２部につきましては新規化学物質の審査でございますので、非公開とさせていただきます。傍聴者の方におかれましては、ご退室いただきますようにお願い申し上げます。

どうもありがとうございました。

資料２－１

残留性有機汚染物質に関するストックホルム条約の新規対象物質を化審法第一種特定化学物質に指定することについて(案)

平成２１年6月２６日

厚生労働省医薬食品局審査管理課化学物質安全対策室
経済産業省製造産業局化学物質管理課化学物質安全室
環境省総合環境政策局環境保健部企画課化学物質審査室

【背景】

１．　残留性有機汚染物質に関するストックホルム条約（平成１６年５月発効。以下「ＰＯＰｓ条約」という。）においては、難分解性、生物蓄積性、毒性及び長距離移動性を有する POPs（Persistent Organic Pollutants、残留性有機汚染物質）による人の健康の保護及び環境の保全を図るため、各国が国際的に協調して、条約の対象物質について、製造及び使用を原則禁止する等の措置を講じることとしている（参考１）。我が国においては、平成１７年に国内実施計画を定め、対象物質に関する製造、使用、輸入及び輸出の規制については、化審法、農薬取締法、薬事法、及び外為法に基づき、所要の措置が講じられているところである。化審法においては、現在のＰＯＰｓ条約対象物質のうち、意図的に製造されることのない PCDD 及び PCDF を除いた１０物質について、第一種特定化学物質（以下「一特」という。）に指定し、製造、輸入の許可制（事実上禁止）、使用の制限及び届出制（事実上禁止）等の措置を講じている。

２．　ＰＯＰｓ条約における対象物質の追加のための手続きとしては、締約国から提案のあった候補物質について、残留性有機汚染物質検討委員会（以下「ＰＯＰＲＣ」という。）において、締約国等から提供された科学的知見に基づき、条約で定められた手順に基づく検討を行うこととされている（我が国からは、委員として北野大　明治大学教授が第１回より継続的に出席。検討の手順については参考２を参照。）。昨年秋までに、４回のＰＯＰＲＣが開催されており、その結果、締約国会議に対して、９種類の物質について、附属書 A（廃絶）、附属書 B（制限）又は附属書 C（非意図的放出の削減）へ追加する旨の勧告を行うことが決定された。

３．　本年５月に開催された第４回締約国会議においては、上記勧告を踏まえ、当該９種類の物質を附属書に追加することが検討された。その結果、各物質について、参考３のとおり附属書に新たに追加することが決定された。これら物質については、今後、条約の下で、製造、使用等を廃絶・制限する措置等が講じられることとなる（改正される附属書の発効は、国連事務局による各国への通報から１年後）。

【化審法による対応】

４．　今回附属書に追加されることとなった化学物質については、①ＰＯＰｓとしての要件（参考４）を満たすことがＰＯＰＲＣにより既に科学的に評価されており（別添１～９を参照）、これらの要件は化審法の一特と同様に、分解性、蓄積性並びに人等への毒性を考慮したものであること、②工業化学品として意図的に製造される可能性がある物質であることから、下表のとおり、速やかに化審法の一特に指定し、現在のＰＯＰｓ条約

対象物質と同様に、関係法令とも連携しつつ、原則、これら物質の製造・使用等を禁止するための所要の措置を講ずることとしたい。

５． なお、これら物質のうち「PFOS とその塩及び PFOSF」については、日本としても、条約で認められた範囲で我が国に必須の特定の用途について適用除外の登録等を行う予定であり、今後、化審法等の国内担保法体系において、その用途の内容及び管理のために必要な措置等を引き続き検討する予定である。

ＰＯＰｓ条約への新規追加に伴い化審法第一種特定化学物質へ指定を行う物質(案)

No.	化学物質名	CAS番号	化審法官報公示整理番号
1	ペルフルオロ（オクタン－１－スルホン酸）（別名ＰＦＯＳ）又はその塩	1763-23-1 2795-39-3* 4021-47-0* 29457-72-5* 29081-56-9* 70225-14-8* 56773-42-3* 251099-16-8*	2-1595 2-2810
2	ペルフルオロ（オクタン－１－スルホニル）＝フルオリド（別名ＰＦＯＳＦ）	307-35-7	2-2803
3	ペンタクロロベンゼン	608-93-5	3-76
4	*r*－1, *c*－2, *t*－3, *c*－4, *t*－5, *t*－6－ヘキサクロロシクロヘキサン（別名α－ヘキサクロロシクロヘキサン）	319-84-6	3-2250 9-1652
5	*r*－1, *t*－2, *c*－3, *t*－4, *c*－5, *t*－6－ヘキサクロロシクロヘキサン（別名β－ヘキサクロロシクロヘキサン）	319-85-7	3-2250 9-1652
6	*r*－1, *c*－2, *t*－3, *c*－4, *c*－5, *t*－6－ヘキサクロロシクロヘキサン（別名γ－ヘキサクロロシクロヘキサン又はリンデン）	58-89-9	3-2250 9-1652
7	デカクロロペンタシクロ［5．3．0．$0^{2,6}$．$0^{3,9}$．$0^{4,8}$］デカン－５－オン（別名クロルデコン）	143-50-0	
8	ヘキサブロモビフェニル	36355-01-8	
9	テトラブロモ（フェノキシベンゼン）（別名テトラブロモジフェニルエーテル）	40088-47-9**	3-61
10	ペンタブロモ（フェノキシベンゼン）（別名ペンタブロモジフェニルエーテル）	32534-81-9**	
11	ヘキサブロモ（フェノキシベンゼン）（別名ヘキサブロモジフェニルエーテル）	68631-49-2*** 207122-15-4***	3-2845
12	ヘプタブロモ（フェノキシベンゼン）（別名ヘプタブロモジフェニルエーテル）	446255-22-7*** 207122-16-5***	3-3716****

*ペルフルオロオクタンスルホン酸塩の例

**商業用ペンタブロモジフェニルエーテルに含まれる代表的な異性体

***商業用オクタブロモジフェニルエーテルに含まれる代表的な異性体

****ジフェニル＝エーテルの臭素化物（Br_{1}＝7～9）として

参考１　ＰＯＰｓ条約の概要

参考２　新規ＰＯＰｓの追加フロー

参考３　第４回締約国会議において決定された事項

参考４　ＰＯＰｓ条約附属書Ｄに規定されている情報の要件及び選別のための基準

別添１～９　ＰＯＰＲＣにおいて作成された危険性の概要（Risk Profile）

（参考１）**残留性有機汚染物質に関するストックホルム条約（POPs 条約）の概要**

１．目　的

リオ宣言第15原則に掲げられた予防的アプローチに留意し、毒性、難分解性、生物蓄積性及び長距離移動性を有するPOPs（Persistent Organic Pollutants、残留性有機汚染物質）から、人の健康の保護及び環境の保全を図る。

２．各国が講ずべき対策

①PCB等9物質の製造、使用の原則禁止及び原則制限（DDTのみ）
②ダイオキシン、PCB等4物質の非意図的生成物質の排出の削減
③POPsを含む在庫・廃棄物の適正管理及び処理
④これらの対策に関する国内実施計画の策定
⑤その他の措置
・条約対象12物質※1と同様の性質を持つ有機汚染物質の製造・使用を防止するための措置
・POPsに関する調査研究、モニタリング、情報提供、教育等
・途上国に対する技術・資金援助の実施

３．条約の発効

平成16年5月17日発効（日本は平成14年8月30日に締結済）。平成21年5月1日現在162ヶ国(+EC)が締結。

４．条約発効後の動き

対象物質追加の検討を行うPOPs検討委員会会合を、平成17～20年の各年11月に開催。平成21年5月に開催されたCOP4において新たに9物質※2の追加が決定された。

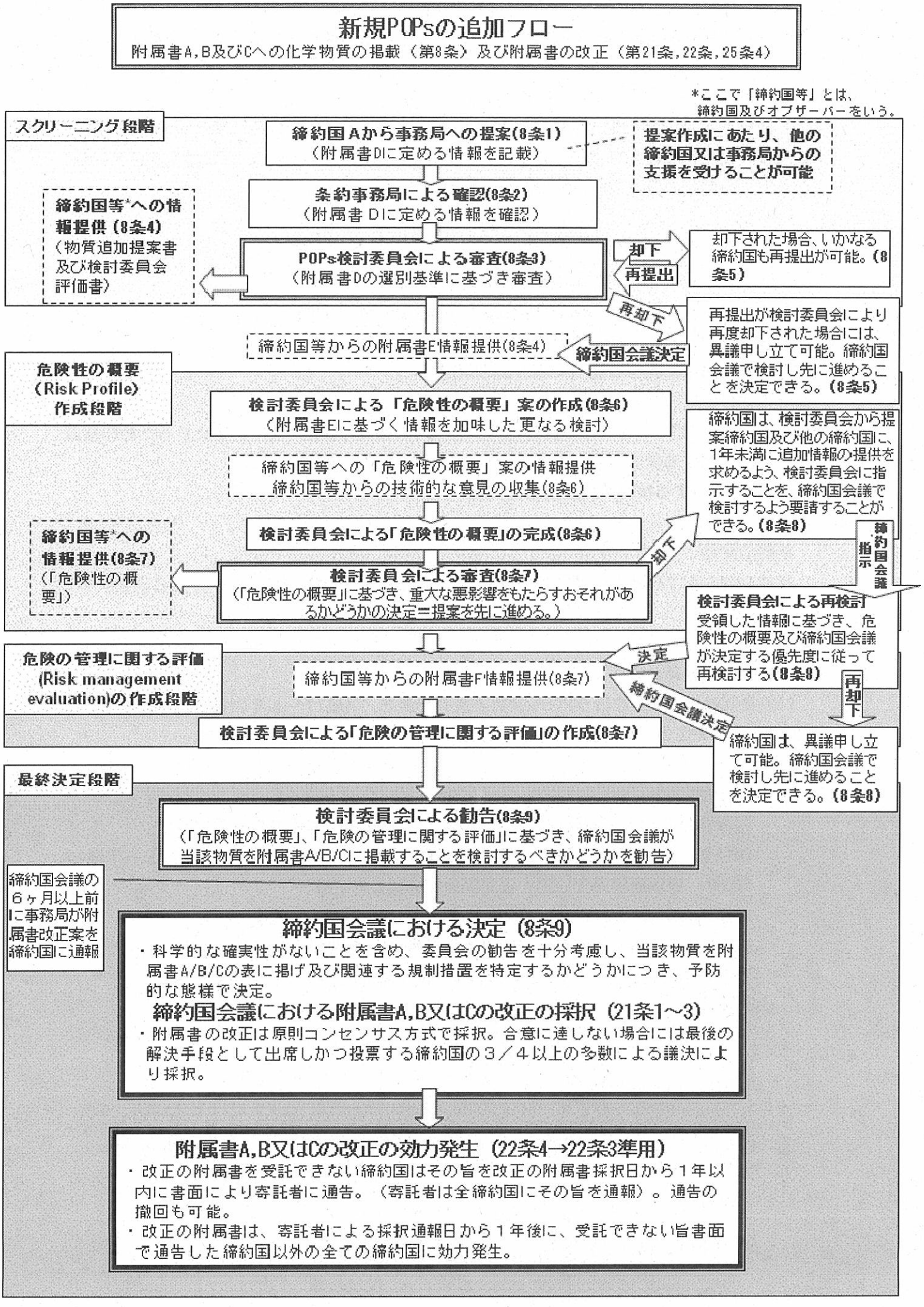
５．我が国の対応

○　対象物質の製造・使用禁止等については、化審法、農薬取締法等で措置。
○　関係省庁連絡会議（議長は環境保健部長）において国内実施計画を作成し、平成17年6月、地球環境保全に関する関係閣僚会議にて了承。
○　我が国の主導により東アジアPOPsモニタリング事業を実施。
○　POPs検討委員会に北野大　明治大学教授を、条約有効性評価のための調整グループ及び地域組織グループに柴田康行　国立環境研究所化学領域長を派遣。

※1　対象物質：
アルドリン、ディルドリン、エンドリン、クロルデン、ヘプタクロル、トキサフェン、マイレックス、ヘキサクロロベンゼン、PCB、DDT、ダイオキシン・ジベンゾフラン

※2　COP4 において追加された物質：
クロルデコン、リンデン、テトラ・ペンタブロモジフェニルエーテル、ヘキサブロモビフェニル、ペルフルオロオクタンスルホン酸及びその塩、パーフルオロオクタンスルホン酸フルオリド（PFOS 及びその塩、PFOSF）、ペンタクロロベンゼン、ヘキサ・ヘプタブロモジフェニルエーテル、α-ヘキサクロロシクロヘキサン（α-HCH）、β-ヘキサクロロシクロヘキサン（β-HCH）

（参考２）新規ＰＯＰｓの追加フロー



（参考３）第４回締約国会議において決定された事項

○附属書Aへの追加

物質名	主な用途	決定された主な規制内容	※
テトラブロモジフェニルエーテル、ペンタブロモジフェニルエーテル	プラスチック難燃剤	・製造・使用等の禁止 （以下の用途を除外する規定あり） -当該物質を含有する製品のリサイクル	9,10
クロルデコン CAS No:143-50-0	農薬	・製造・使用等の禁止	7
ヘキサブロモビフェニル CAS No:36355-01-8	プラスチック難燃剤	・製造・使用等の禁止	8
リンデン（γ－ＨＣＨ） CAS No:58-89-9	農薬	・製造・使用等の禁止 （以下の用途を除外する規定あり） -アタマジラミ、疥癬の医薬品用の製造と使用	6
α－ヘキサクロロシクロヘキサン CAS No:319-84-6	リンデンの副生物	・製造・使用等の禁止	4
β－ヘキサクロロシクロヘキサン CAS No:319-85-7	リンデンの副生物	・製造・使用等の禁止	5
ヘキサブロモジフェニルエーテル、ヘプタブロモジフェニルエーテル	プラスチック難燃剤	・製造・使用等の禁止 （以下の用途を除外する規定あり） -当該物質を含有する製品のリサイクル	11,12

○附属書Bへの追加

物質名	主な用途	決定された主な規制内容	※
ペルフルオロオクタンスルホン酸（PFOS）とその塩、ペルフルオロオクタンスルホン酸フルオリド（PFOSF） CAS No: 1763-23-1 CAS No: 307-35-7	撥水撥油剤、界面活性剤	・製造・使用等の禁止 （以下の目的・用途を除外する規定あり） -写真感光材料 -半導体用途 -フォトマスク -医療機器 -金属メッキ -泡消火剤 -カラープリンター用電気電子部品 -医療用 CCD カラーフィルター　など	1,2

○附属書A及びCへの追加

物質名	主な用途	決定された主な規制内容	※
ペンタクロロベンゼン CAS No: 608-93-5	農薬	・製造・使用等の禁止 ・非意図的生成による排出の削減	3

（注意）上記の表中の情報は省略・簡略化しているため、規制内容の詳細については、条約事務局のホームページ（http://www.pops.int/）から会議文書を御確認いただきたい。

※２ページに記載の物質リストとの対応。

（参考４） ＰＯＰｓ条約附属書Ｄに規定されている情報の要件及び選別のための基準

ＰＯＰＲＣでは、締約国から提案のあった化学物質ごとに、附属書Ｄに定められた選別のための基準（下記を参照）に基づき審査を実施後、附属書Ｅに沿って、これら情報を更に考慮、評価した上で、当該化学物質が、長距離にわたる自然の作用による移動の結果として、世界的規模の行動を正当化するようなヒトの健康又は環境に対する重大な悪影響をもたらすかどうかの評価を行うため、危険性の概要（Risk Profile）の作成が行われる。

化学物質の特定	商品名、商業上の名称、別名、ケミカル・アブストラクツ・サービス（ＣＡＳ）登録番号、国際純正・応用化学連合（ＩＵＰＡＣ）の名称その他の名称
	構造（可能な場合には異性体の特定を含む。）及び化学物質の分類上の構造
残留性 （次のいずれか）	化学物質の水中における半減期が２ヶ月を超えること、土中における半減期が６ヶ月を超えること又は堆積物中における半減期が６ヶ月を越えることの証拠
	この条約の対象とすることについての検討を正当とする十分な残留性を化学物質が有することの証拠
生物蓄積性 （次のいずれか）	化学物質の水生種の生物濃縮係数若しくは生物蓄積係数が五千を超えること又はこれらの資料がない場合にはオクタノール／水分配係数の常用対数値が五を越えることの証拠
	化学物質に他に懸念される理由（例えば、他の種における高い生物蓄積性、高い毒性、生態毒性）があることの証拠
	化学物質の生物蓄積の可能性がこの条約の対象とすることについての検討を正当とするのに十分であることを示す生物相における監視に基づく資料
長距離にわたる自然の作用による移動の可能性 （次のいずれか）	化学物質の放出源から離れた地点における当該化学物質の潜在的に懸念すべき測定の水準
	化学物質が別の環境に移動した可能性とともに、大気、水又は移動性の種を介して長距離にわたり自然の作用により移動した可能性を示す監視に基づく資料
	化学物質がその放出源から離れた地点における別の環境に移動する可能性とともに、大気、水又は移動性の種を介して長距離にわたり自然の作用により移動する可能性を示す環境運命の性質又はモデルによる予測結果。主に大気中を移動する化学物質については、大気中における半減期が二日を超えるべきである。
悪影響 （次のいずれか）	この条約の対象となる化学物質とすることについての検討を正当とする人の健康又は環境に対する悪影響を示す証拠
	人の健康又は環境に対する損害の可能性を示す毒性又は生態毒性の資料

別添1

ペルフルオロオクタンスルホン酸の危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 活性汚泥、底質培養物、土壌培養物中での好気的生分解試験及び下水汚泥での嫌気的生分解試験では、分解の兆候はまったく示されなかった。 【光分解性】 ・直接または間接光分解の証拠は見られなかった（EPA OPPTS ﾌﾟﾛﾄｺﾙ 835.5270）。 ・25℃における間接光分解の半減期は3.7年以上と算出された。 【加水分解性】 ・分解はまったく示されなかった（EPA OPPTS ﾌﾟﾛﾄｺﾙ 835.2210） ・半減期は41年以上とされた。 ※ＰＦＯＳＦは水中で速やかに加水分解されＰＦＯＳを生成する知見が別途得られている。	【BCF（経鰓的生物濃縮係数）】 ・ﾆｼﾞﾏｽ： BCF =2900（肝臓），3100（血漿） ・丸ﾊｾﾞ：BCF =約2400（全魚体） ・ﾌﾞﾙｰｷﾞﾙｻﾝﾌｨｯｼｭ：BCFk =2796 ※上記の値は、POPs条約付属書Dの基準値（BCF＜5000）以下であるが、PFOSの物性の一つである非脂肪組織中の蛋白質親和性を考慮すると、脂溶性物質を対象に設定されているBCF基準値のPFOSへの適用は不適切な可能性がある。 【BMF（経口的生物濃縮係数）】 ・ﾐﾝｸ：BMF=22（魚中の濃度から推計） ・ﾎｯｷｮｸｸﾞﾏ：BMF＞160（ﾎｯｷｮｸｱｻﾞﾗｼ中の濃度から推計） ※人為的発生源から最も遠く離れた北極圏の動物において高濃度のPFOSが検出されていることに留意。魚類･魚食性鳥類など食物連鎖上の低位種においてもPFOSが検出。また、ﾜｼなど捕食生物種は、低位にある鳥類よりも高濃度のPFOSを蓄積することが認められている。このことは、PFOSの残留性と長期蓄積性によるものである。	【反復投与毒性】 アカゲザル（強制経口90日）： 4.5mg/kg/dayで全数死亡、 0.5mg/kg/dayで消化管毒性 （カリウム塩） ラット（経口90日）：18mg/kg/dayで全数死亡、6mg/kg/dayで半数死亡、 2mg/kg/dayで体重及び臓器重量変化 （カリウム塩） カニクイサル（26週）：LOEL 0.03mg/kg/day 主な毒性は、胸腺萎縮（♀）、HDL、コレステロール、T3低下 ラット（混餌2年）：0.06（♂）、 0.07mg/kg/day（♀）で肝細胞の病理組織的変化 【発生毒性】 ラット（二世代経口）： NOAEL:0.1mg/kg/day 0.4mg/kg/dayでF1児体重増加量低下、 1.6mg/kg/dayでF1世代生存率低下、母体体重低下等（カリウム塩） ラット（♀）：妊娠17-20日目の 25mg/kgで全児死亡	【慢性毒性】 ユスリカ *Chironomus tentans* ： 10dNOEC=0.0491 mg/L（成長･生存）

	・PFOS は疎水性・疎油性であるため POPs に特有な脂肪組織に蓄積するという典型的パターンに該当しない。また、PFOS は物理化学的特性が特異なため、生物蓄積のﾒｶﾆｽﾞﾑは他の POPs と異なる。		

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Persistent Organic Pollutants Review Committee
Second meeting
Geneva, 6–10 November 2006

Report of the Persistent Organic Pollutants Review Committee on the work of its second meeting

Addendum

Risk profile on perfluorooctane sulfonate

At its second meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on perfluorooctane sulfonate, on the basis of the draft contained in document UNEP/POPS/POPRC.2/11. The text of the risk profile, as amended, is provided below. It has not been formally edited.

K0653903 151206

PERFLUOROOCTANE SULFONATE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its second meeting

November 2006

CONTENTS

EXECUTIVE SUMMARY

1 INTRODUCTION

1.1 Chemical Identity of the proposed substance

On July 14, 2005, the government of Sweden made a proposal for listing perfluorooctane sulfonate (PFOS) and 96 PFOS-related substances in Annex A of the Stockholm Convention on Persistent Organic Pollutants (POPs).

Chemical name: Perfluorooctane Sulfonate (PFOS)

Molecular formula: $C_8F_{17}SO_3^-$

PFOS, as an anion, does not have a specific CAS number. The parent sulfonic acid has a recognised CAS number (CAS No. 1763-23-1). Some examples of its commercially important salts are listed below:

Potassium salt (CAS No. 2795-39-3)

Diethanolamine salt (CAS No. 70225-14-8)

Ammonium salt (CAS No. 29081-56-9)

Lithium salt (CAS No. 29457-72-5)

Structural formula:

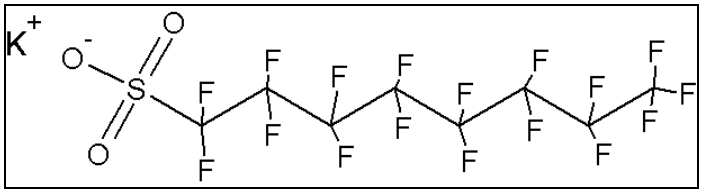

Figure 1. Structural formula of PFOS shown as its potassium salt

PFOS is a fully fluorinated anion, which is commonly used as a salt or incorporated into larger polymers. PFOS and its closely related compounds, which contain PFOS impurities or substances which can give rise to PFOS, are members of the large family of perfluoroalkyl sulfonate substances. In its regulatory measures on PFOS, the EU has addressed all molecules having the following molecular formula: $C_8F_{17}SO_2Y$, where Y = OH, metal or other salt, halide, amide and other derivatives including polymers (European Union 2006).

The physical and chemical properties of the potassium salt of PFOS are listed in Table 2.

Table 2. Physical and chemical properties of PFOS potassium salt.

(Data from OECD, 2002, unless otherwise noted).

Property	Value
Appearance at normal temperature and pressure	White powder
Molecular weight	538 g/mol
Vapour Pressure	3,31 x 10^{-4} Pa
Water solubility in pure water	519 mg/L (20 ± 0,5ºC) 680 mg/L (24 - 25ºC)
Melting point	> 400 ºC
Boiling point	Not measurable
Log K_{OW}	Not measurable
Air-water partition coefficient	< 2 x 10^{-6} (3M, 2003a)
Henry's Law Constant	3,09 x 10^{-9} atm m^3/mol pure water

PFOS can be formed (by environmental microbial degradation or by metabolism in larger organisms) from PFOS-related substances, i.e., molecules containing the PFOS-moiety depicted in Figure 1. Although the ultimate net contribution of individual PFOS-related substances to the environmental loadings of PFOS cannot be predicted readily, there is a potential that any molecule containing the PFOS moiety could be a precursor to PFOS.

The majority of PFOS-related substances are polymers of high molecular weights in which PFOS is only a fraction of the polymer and final product (OECD, 2002). PFOS-related substances have been defined somewhat differently in different contexts and there are currently a number of lists of PFOS-related substances (Table 3). The lists contain varying numbers of PFOS-related substances that are thought to have the potential to break down to PFOS. The lists overlap to varying extents depending on the substances under consideration and the overlap between national lists of existing chemicals.

Table 3. Number of PFOS-related substances as proposed by UK – DEFRA, US – EPA, OECD, OSPAR, and Canada

Source	Number of PFOS-related substances
RPA and BRE (2004)	96
US - EPA (2002, 2006)	88[1] + 183[1]
OECD (2002)	172[1] (22 classes of perfluoroalkyl sulfonate substances)
OSPAR (2002)	48
Environment Canada (2006)	57

[1] Perfluorinated substances with different carbon chain lengths are included in the list.

A large number of substances may give rise to PFOS and thus contribute to the contamination problem. DEFRA in the United Kingdom (RPA and BRE, 2004) has recently proposed a list of 96 PFOS-related substances. However, the properties of the 96 substances have not generally been determined. According to 3M (submission to the secretariat of Stockholm Convention (SC), 2006), they may have very different environmental characteristics such as solubility, stability and ability to be absorbed or metabolised. Nevertheless, the document by the United Kingdom infers that all of these substances would give rise to the final degradation product of PFOS (RPA and BRE, 2004).

Environment Canada's ecological risk assessment defines PFOS precursors as substances containing the perfluorooctylsulfonyl ($C_8F_{17}SO_2$, $C_8F_{17}SO_3$,, or $C_8F_{17}SO_2N$) moiety that have the potential to transform or degrade to PFOS (Environment Canada, 2006). The term "precursor" applies to, but is not limited to, some 51 substances identified in the ecological assessment. However, this list is not considered exhaustive, as there may be other perfluorinated alkyl compounds that are also PFOS precursors. This information was compiled based on a survey to industry, expert judgement and CATABOL modelling, in which 256 perfluorinated alkyl compounds were examined to determine whether non-fluorinated components of each substance were expected to degrade chemically and/or biochemically and whether the final perfluorinated degradation product was predicted to be PFOS. While the assessment did not consider the additive effects of PFOS and its precursors, it is recognized that the precursors to PFOS contribute to the ultimate environmental loading of PFOS. Precursors may also play a key role in the long-range transport and subsequent degradation to PFOS in remote areas, such as the Canadian Arctic.

1.2 Conclusion of the POP Review Committee on Annex D information

The Persistent Organic Pollutants Review Committee (POPRC) evaluated Annex D information at the First meeting of the POPRC, Geneva, 7-11 November 2005, and concluded that PFOS information meets the screening criteria specified in Annex D (decision POPRC-1/7: Perfluorooctane sulfonate).

1.3 Data sources

This document on PFOS mainly builds on information that has been gathered in the hazard assessment report prepared by the UK and the USA for the OECD, and in the UK risk reduction strategy:

OECD (2002) Co-operation on Existing Chemicals - Hazard Assessment of Perfluorooctane Sulfonate and its Salts, Environment Directorate Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, Organisation for Economic Co-operation and Development, Paris, 21 November 2002.

RPA AND BRE (2004) Perfluorooctane Sulfonate – Risk reduction strategy and analysis of advantages and drawbacks, Final Report prepared for Department for Environment, Food and Rural Affairs and the Environment Agency for England and Wales.

Recent relevant information from the open scientific literature (up to May 2006) is also included. Data submitted by Parties and observers, which have been considered, are also included in this report when they add new information.

1.4 Summary of assessment and management under other programs

The hazard assessment of PFOS, prepared by the OECD in 2002, concluded that the presence and the persistence of PFOS in the environment, as well as its toxicity and bioaccumulation potential, indicate a cause of concern for the environment and human health.

An environmental risk assessment, prepared by the UK-Environment Agency, and discussed by the EU member states under the umbrella of the existing substances regulation (ESR DIR 793/93) shows that PFOS is of concern.

The final Environment Canada/Health Canada assessments of PFOS, its salts and its precursors were released in July 2006. The ecological risk assessment has concluded that PFOS and its salts are persistent and bioaccumulative, and that PFOS, its salts and its precursors have immediate or long-term harmful effects on the environment (Environment Canada, 2006).

The EU has recently decided on restrictions on the marketing and use of PFOS (European Union, 2006). The measures cover PFOS acid, its salts and PFOS derivatives, including PFOS polymers. The decision prohibits the placing on the market and use of these compounds as a substance or constituent of preparations in a concentration equal to or higher than 0,005% by mass. Furthermore, semi-finished products and articles, containing PFOS more than 0,1% by mass are prohibited. Some derogations are, however, granted in the decision. These include certain uses in photolithography processes, in photographic coatings and in metal plating, hydraulic fluids for aviation and fire fighting foams that have already been placed on the market.

The UK and Sweden have proposed the following classification for PFOS in EU (2005):

T Toxic

R40 Carcinogen category 3; limited evidence of carcinogenic effect

R48/25 Toxic; danger of serious damage to health by prolonged exposure if swallowed

R61 May cause harm to the unborn child

R51/53 Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment has.

Norway is now considering a proposal to prohibit the use of fire fighting foams containing PFOS and PFOS-related compounds, which is the major use of these compounds today in Norway.

The Environmental Protection Agency (EPA) in the USA finalized two Significant New Use Rules (SNURs) in 2002, requiring companies to inform the EPA before manufacturing or importing 88 listed PFOS-related substances. The EPA proposed an additional SNUR under section 5(a)(2) of the Toxic Substances Control Act (TSCA) in March 2006 to include within the scope of this regulation another 183 perfluoroalkyl sulfonates with carbon chain lengths of five carbons and higher. The EPA further proposed an amendment to the Polymer Exemption rule in March 2006 which would remove from exemption polymers containing certain perfluoroalkyl moieties consisting of CF3- or longer chains, and would require that new chemical notifications be submitted on such polymers.

1.5 Status of the chemical under international conventions

OSPAR: PFOS was added to the list of Chemicals for Priority Action in June 2003.

Persistent Organic Pollutants Protocol to the Long-Range Transboundary Air Pollution Convention ("LRTAP"): The Executive Body of the UNECE LRTAP Convention agreed that PFOS be considered a POP as defined under the Protocol on POPs and requested that the UNECE Task Force on POPs continue with the review of the substance and exploring management strategies.

2 SUMMARY INFORMATION RELEVANT FOR THE RISK PROFILE

2.1 Sources

2.1.1 Production and trade

The main production process of PFOS and PFOS-related substances is electro-chemical fluorination (ECF), utilized by 3M, the major global producer of PFOS and PFOS-related substances prior to 2000.

Direct fluorination, electro-chemical fluorination (ECF):

$$C_8H_{17}SO_2Cl + 18\ HF \rightarrow C_8F_{17}SO_2F + HCl + \text{by products}$$

The reaction product, perfluorooctanesulfonyl fluoride (PFOSF)[1] is the primary intermediate for synthesis of PFOS and PFOS-related substances. The ECF method results in a mixture of isomers and homologues with about 35-40% 8-carbon straight chain PFOSF. However, the commercial PFOSF products were a mixture of approximately 70% linear and 30% branched PFOSF derivate impurities. The global production of PFOSF by 3M until the production ceased is estimated to have been 13,670 metric tonnes (1985 to 2002), with the largest yearly production volume, 3700 metric tonnes of PFOS and PFOS related substances, in 2000 (3M, Submission to SC, 2006). PFOSF may be further reacted with methyl- or ethylamine to form *N*-ethyl- and *N*-methyl perfluorooctane sulfamide and subsequently with ethylene carbonate resulting in *N*-ethyl- and -methyl-perfluorooctane sulfamidoethanol (*N*-EtFOSE and *N*-MeFOSE). *N*-EtFOSE and *N*-MeFOSE were the principal building blocks of 3M's product lines. PFOS is formed after the chemical or enzymatic hydrolysis of PFOSF (3M, 1999).

Other production methods for perfluoroalkylated substances are telomerisation and oligomerisation. However, to which extent these methods are applied for production of PFOS and PFOS-related substances is not evident.

[1] In the OECD report, 2002, perfluorooctanesulfonyl fluoride is abbreviated POSF.

On 16 May 2000, 3M announced that the company would phase-out the manufacture of PFOS and PFOS-related substances voluntarily from 2001 onwards. By the end of 2000, about 90 % of 3M's production of these substances had stopped and in the beginning of 2003 the production ceased completely.

3M´s voluntary phase-out of PFOS production has led to a reduction in the use of PFOS-related substances. This is due not only to the limited availability of these substances (3M had at the time the greatest production capacity of PFOS-related substances in the world), but also to action within the relevant industry sectors to decrease companies´ dependence on these substances.

The US Environmental Protection Agency (US EPA) compiled a list of non-US companies which are believed to supply PFOS-related substances to the global market. Of these (and excluding the plant of 3M in Belgium), six plants are located in Europe, six are located in Asia (of which four are in Japan) and one in Latin America (OECD, 2002). However, this list may not be exhaustive or current.

According to the recent submission from Japan to the secretariat of the Stockholm Convention, 2006, there is one manufacturer in Japan still producing PFOS and with a production amount of 1-10 tonnes (2005). The submission from Brazil states that lithium salt of PFOS is produced but that no quantitative data is available.

2.1.2 Uses

Perfluorinated substances with long carbon chains, including PFOS, are both lipid-repellent and water-repellent. Therefore, the PFOS-related substances are used as surface-active agents in different applications. The extreme persistence of these substances makes them suitable for high temperature applications and for applications in contact with strong acids or bases. It is the very strong carbon-fluorine binding property that causes the persistence of perfluorinated substances.

The historical use of PFOS-related substances in the following applications has been confirmed in the US and the EU.

- Fire fighting foams
- Carpets
- Leather/apparel
- Textiles/upholstery
- Paper and packaging
- Coatings and coating additives
- Industrial and household cleaning products
- Pesticides and insecticides

In the UK study (RPA and BRE, 2004), detailed information has been received from the following sectors that currently use PFOS-related substances:

- Use of existing fire fighting foam stock
- Photographic industry
- Photolithography and semiconductor
- Hydraulic fluids
- Metal plating

The sectors presented above account for the UK but are considered to be representative for EU. However, deviation in the current use pattern between EU countries cannot be excluded.

PFOS and its precursors are not manufactured in Canada but rather are imported as chemicals or products for Canadian uses. They may also be components in imported manufactured articles. It is estimated that the majority of PFOS has been used as water, oil, soil and grease repellents (e.g. on fabric, leather, paper, packaging, rugs and carpets) and as surfactants (e.g. in fire fighting foams and coating additives) (Environment Canada, 2006).

PFOS and its precursors are not manufactured in the US, but can be imported either as chemicals or in products for the specific limited uses that were excluded from regulation. These comprise use as an anti-erosion additive in aviation hydraulic fluids; use as a component of a photoresist substance, including a photo acid generator or surfactant, or as a component of an anti-reflective coating, used in a photomicrolithography process to produce semiconductors or similar components of electronic or other miniaturized devices; use in coatings for surface tension, static discharge, and adhesion control for analog and digital imaging films, papers, and printing plates, or as a surfactant in mixtures used to process imaging films; and use as an intermediate only to produce other chemical substances to be used solely for these uses. Historically, PFOS and its precursors were also used as surfactants in fire fighting foams and in industrial and household cleaning products; in carpet, textile, leather, and paper coatings; and in termite and ant bait insecticide products. Stocks of PFOS and PFOS-containing products that were in existence at the time the US regulations were promulgated in 2002 could continue to be used in any application until they were consumed without violating the regulation, except that the PFOS-related insecticide products are subject to a phase-out agreement prohibiting their use after 2015.

The table below outlines the estimated current demand for PFOS-related substances in these applications in the EU (RPA and BRE, 2004).

Estimated Current (2004) Demand for PFOS Related Substances in the EU	
Industry Sector	Quantity (kg/year)
Photographic industry	1,000
Photolithographic and semi-conductors	470
Hydraulic fluids	730
Metal plating	10,000

In the survey on production and use of PFOS and related substances performed by OECD in 2004 (published 2005), data concerning PFOS were difficult to separate from data on other perfluoroalkyl sulfonates.

Fire Fighting Foams

The fire fighting foams can be grouped in two main categories:

- Fluorine-containing foam types (some of them consist of PFOS-related substances)
- Fluorine-free foam types

Since the announcement of the voluntary cessation of production of PFOS-related substances by 3M, the presence of PFOS in fire fighting foams has gradually decreased (RPA and BRE, 2004).

Historically, in Canada, the most significant imports of PFOS, itself, were in the form of the potassium salt, used for fire-fighting foams (Environment Canada, 2006). Canada has also identified that existing stocks of PFOS-containing fire fighting foams could be a continued significant source of releases.

An industry survey conducted in the US by the Fire Fighting Foam Coalition in 2004 reported that the total inventory of aqueous film-forming foam in the US was approximately 9.9 million gallons, of which about 45% was PFOS-based stocks produced before 2003, with the other 55% comprised of telomer-based foams.

Textile, Carpet and Leather Protection

PFOS-related substances have been used to provide soil, oil and water resistance to textiles, apparels, home furnishings and upholstery, carpets, and leather products. Since 3M´s withdrawal from the market, PFOS-related substances are used to a much smaller extent for these applications (RPA AND BRE, 2004).

Paper and Packaging Protection

PFOS-related substances have been used in the packaging and paper industries in both food packaging and commercial applications to impart grease, oil and water resistance to paper, paperboard and packaging substrates. According to 3M, fluorochemicals were used for both food contact applications (plates, food containers, bags and wraps) and non-food applications (folding cartons, containers and carbonless forms and masking papers). Since 3M´s withdrawal from the market, PFOS related substances are used to a much smaller extent for these applications (RPA and BRE, 2004).

Coatings and Coating Additives

3M indicates that prior to its voluntary phase-out of PFOS production, the company would sell fluorochemical polymer coatings and coating additives which were used undiluted or diluted with water or butyl acetate to impart soil or water repellence to surfaces (including printing circuit boards and photographic film) (RPA and BRE, 2004).These polymers contained fluorocarbon residuals at a concentration of 4% or less. Other applications for aqueous coatings are to protect tile, marble and concrete. It is unclear which of these products were actually based on PFOS-related substances.

A survey in the UK among members of the British Coatings Federation (BCF) showed that the use of PFOS-related substances for these purposes is very limited (RPA and BRE, 2004).

Industrial and Household Cleaning Products (Surfactants)

3M PFOS-based products were sold in the past to a variety of formulators to improve the wetting of water-based products marketed as alkaline cleaners, floor polishes (to improve wetting and levelling), denture cleansers and shampoos. Several of these products (alkaline cleaners, floor polishes, shampoos) were marketed to consumers; some products were also sold to janitorial and commercial services. A number of the alkaline cleaners were spray-applied.

With regard to the UK cleaning products industry, the responses received do not indicate the use of PFOS-related substances in industrial and household cleaning products. Based on information provided in product registers, the Swedish National Chemicals Inspectorate (KemI) has indicated that PFOS-related substances are still being used in Sweden for both industrial and household use (RPA and BRE, 2004).

Photographic Industry

PFOS-based chemicals are used for the following purposes in mixtures, in coatings applied to photographic films, papers, and printing plates (RPA and BRE, 2004):

- Surfactants
- Electrostatic charge control agents;

- Friction control agents;
- Dirt repellent agents; and
- Adhesion control agents

Photolithography and Semiconductors

Photoresist

Semiconductor manufacturing comprises up to 500 steps, of which there are four fundamental physical processes:

- Implant
- Deposition
- Etch
- Photolithography

Photolithography is the most important step towards the successful implementation of each of the other steps and, indeed, the overall process. It shapes and isolates the junctions and transistors; it defines the metallic interconnects; it delineates the electrical paths that form the transistors; and joins them together. Photolithography reportedly represents 150 of the total of 500 steps mentioned above. Photolithography is also integral to the miniaturization of semiconductors (RPA and BRE, 2004).

PFOS is used as a photoacid generator (PAG) in a mechanism called chemical amplification that increases the sensitivity of photoresist to allow etching images smaller than wavelength of light.

Antireflective Coatings

A number of resist suppliers sell antireflective coatings (ARC), subdivided into Top (TARC) and Bottom (BARC) coatings and used in combination with deep ultra violet (DUV) photoresist. The process involves placing a thin, top coating on the resist to reduce reflective light, in much the same way and for the same purposes that eyeglasses and camera lenses are coated.

Hydraulic Fluids for the Aviation Industry

Hydraulic fluids were initially used in aircraft to apply brake pressure. As larger and faster aircraft were designed, greater use of hydraulic fluids became necessary. An increase in the number of hydraulic fluid fires in the 1940s necessitated work towards developing fire resistant fluids. The first of these fluids was developed around 1948, when fire resistant hydraulic fluids based on phosphate ester chemistry were developed.

Perfluorinated anions act by altering the electrical potential at the metal surface, thereby preventing the electrochemical oxidation of the metal surface under high fluid flow conditions (RPA and BRE, 2004). As a result, hydraulic fluids based on phosphate ester technology and incorporating additives based on perfluorinated anions are used in all commercial aircraft, and in many military and general aviation aircraft throughout the world, as well as by every airframe manufacturer (RPA and BRE, 2004).

Metal Plating

The main uses of PFOS-related substances in metal plating are for chromium plating, and anodising and acid pickling. PFOS related substances lower the surface tension of the plating solution so that mist containing chromic acid from the plating activity is trapped in solution and is not released to air (RPA and BRE, 2004).

Other

There is information on other historical or current PFOS applications such as in pesticides, medical applications, mining and oil surfactants, flame retardants and in adhesives. Based on current understanding, these applications represent a minor part of known PFOS applications and are therefore not further elaborated in this profile.

2.1.3 Releases to the environment

There is to date very limited information regarding the emissions and pathways of PFOS to the environment. The occurrence of PFOS in the environment is a result of anthropogenic manufacturing and use, since PFOS is not a naturally occurring substance.

Releases of PFOS and its related substances are likely to occur during their whole life cycle. They can be released at their production, at their assembly into a commercial product, during the distribution and industrial or consumer use as well as from landfills and sewage treatment plants after the use of the products (3M, 2000).

Manufacturing processes constitute a major source of PFOS to the local environment. During these processes, volatile PFOS-related substances may be released to the atmosphere. PFOS and PFOS-related substances could also be released via sewage effluents (3M, 2000). High local emissions are indicated by one study that showed extremely high concentrations of PFOS in wood mice collected in the immediate vicinity to 3M's fluorochemical plant in Antwerpen, Belgium (Hoff et al., 2004). High concentrations of PFOS were also found in liver and blood from fish collected in the Mississippi River at the immediate vicinity of another 3M fluorochemical plant at Cottage Grove in Minnesota (MPCA, 2006).

Fire training areas have also been revealed to constitute a source of PFOS emissions due to the presence of PFOS in fire-fighting foams. High levels of PFOS have been detected in neighbouring wetlands of such an area in Sweden (Swedish EPA, 2004) as well as in groundwater in the US close to a fire-training area (Moody et al., 2003).

An investigation on the uses of PFOS and PFOS-related compounds in Norway in 2005 shows that approximately 90% of the total use is in fire extinguishers (Submission to SC, 2006). Estimated releases of PFOS related to fire extinguishers are at least 57 tonnes since 1980 to 2003 (2002; 13-15 tonnes). Remaining quantities of fire extinguisher foam in Norway are estimated to be a minimum of 1.4 million litres, which corresponds to an amount of approximately 22 tonnes PFOS. Releases from the municipal sector in Norway, 2002, were estimated to be 5-7 tonnes (Submission to SC, 2006).

The use of PFOS in semiconductors is estimated to result in a release of 43 kg per year in the EU, according to the Semiconductur Industry Association (SIA) (SIA, Submission to SC, 2006). This corresponds to 12 % of the total PFOS use in this application. PFOS released in the USA from semiconductors is estimated to be in the same range (SIA, 2006).

The releases of sulfonated perfluorochemicals, including PFOS or PFOS-related substances, from different product usages have been estimated (3M Speciality Materials, 2002). For example, garments treated with home-applied products, are expected to lose 73 % of the treatment during cleaning over a 2-year life span. A loss of 34 % to air is expected from spray can products during use, while up to 12.5 % of the original content may be remaining in the cans at the time of disposal.

One route for PFOS and PFOS-related substances to the environment may be through sewage treatment plants (STPs) and landfills, where elevated concentrations have been observed compared to background concentrations. Once released from STPs, PFOS will partially adsorb to sediment and organic matter. A substantial amount of PFOS may also end up in agricultural soil, due to the

application of sewage sludge. The primary compartments for PFOS are therefore believed to be water, sediment and soil (RIKZ, 2002).

Dispersion of PFOS in the environment is thought to occur through transport in surface water, or oceanic currents (Yamashita *et al*., 2005, Caliebe *et al*., 2004), transport in air (volatile PFOS-related substances), adsorption to particles (in water, sediment or air) and through living organisms (3M, 2003a).

One major obstacle when trying to estimate the releases of PFOS to the environment is that PFOS can be formed through degradation of PFOS-related substances. The rate and the extent of that formation are presently unknown. In a study on Swedish STPs, higher concentrations of PFOS were found in the effluents compared to incoming sewage water, which could indicate that PFOS was formed from PFOS-related substances (Posner and Järnberg, 2004).

2.2 Environmental fate

2.2.1 Persistence

PFOS is extremely persistent. It does not hydrolyse, photolyse or biodegrade in any environmental condition tested (OECD, 2002).

A study on the hydrolysis of PFOS in water has been performed following US-EPA OPPTS protocol 835.2210. The study was conducted at pH varying from 1.5 – 11.0 and at a temperature of 50°C, to facilitate hydrolysis, but did not indicate any degradation of PFOS. The half-life of PFOS was set to be greater than 41 years.

A study on the photolysis of PFOS in water following US-EPA OPPTS protocol 835.5270 has been conducted. No evidence of direct or indirect photolysis was observed under any of the conditions tested. The indirect photolytic half-life of PFOS at 25°C was calculated to be more than 3.7 years.

Biodegradation of PFOS has been evaluated in a variety of tests. Aerobic biodegradation of PFOS has been tested in activated sewage sludge, sediment cultures and soil cultures in several studies. Anaerobic biodegradation has been tested in sewage sludge. None of the studies demonstrated any signs of biodegradation.

Modelling with a simulator program of microbial degradation, the CATABOL system, and expert judgment predicted that of 171 studied perfluorinated substances over 99% would biodegrade to extremely persistent perfluorinated acids. Of them, 109 substances were predicted to end up as perfluorinated sulfonic acids, including PFOS, and 61 as perfluorinated carboxylic acids (Dimitrov et al., 2004).

The only known condition whereby PFOS is degraded is through high temperature incineration under correct operating conditions (3M, 2003a). Potential degradation at low temperature incineration is unknown.

2.2.2 Bioaccumulation

It should be noted that PFOS does not follow the “classical” pattern of partitioning into fatty tissues followed by accumulation, which is typical of many persistent organic pollutants. This is because PFOS is both hydrophobic and lipophobic. Instead, PFOS binds preferentially to proteins in the plasma, such as albumin and β-lipoproteins (Kerstner-Wood et al., 2003), and in the liver, such as liver fatty acid binding protein (L-FABP; Luebker et al., 2002). Because of the unusual physical-chemical characteristics of PFOS, the mechanism of bioaccumulation probably differs from other POPs.

In a study following OECD protocol 305, the bioaccumulation of PFOS in bluegill sunfish (*Lepomis macrochirus*) has been tested. The whole-fish kinetic bioconcentration factor (BCFK) was determined to be 2796 (3M, 2002).

In another study on rainbow trout (*Oncorhynchus mykiss*), a bioconcentration factor (BCF) in liver and plasma was estimated to be 2900 and 3100, respectively (Martin, *et al*., 2003).

When strictly looking at the BCF values, it is clear that these values are below the numeric BCF criteria in Stockholm Convention Annex D (the reported BCF values are below 5000) but, in this particular case, as noted above, the BCF numeric criteria may not adequately represent the bioaccumulation potential of the substance. Monitoring data from top predators at various locations show highly elevated levels of PFOS and demonstrate substantial bioaccumulation and biomagnification (BMF) properties of PFOS. It is notable that the concentrations of PFOS found in livers of Arctic polar bears exceed the concentrations of all other known individual organohalogens (Martin et al., 2004a). Based on the concentration of PFOS in predators (e.g., the polar bear) in relation to the concentration in their principal food (e.g., seals), hypothetical BMF values can be calculated. Such data are reported in Table 4. It should be noted that there are uncertainties in these comparisons. Even if either liver or blood concentrations are compared in two species, species differences in specific protein binding in that particular compartment may affect the concentration in the organ without having affected the whole-body concentration of the substance.

Table 4. Measured concentrations of PFOS in biota from various locations. Calculated BMF is shown where applicable.

Species and Location	Concentrations of PFOS	Reference
• Polar Bear, Canadian Arctic	- Concentrations of PFOS in liver (1700 – > 4000 ng/g) exceeding all other individual organohalogens. - BMF > 160 based on concentrations in Arctic seals.	Martin et al., 2004a.
• Arctic fox, Canadian Arctic	- Very high concentrations of PFOS in liver (6.1 - 1400 ng/g)	Martin et al., 2004a.
• Mink, US	- Very high concentrations of PFOS in liver (40 - 4870 ng/g). - BMF = 22 based on data from fish in the same area. - nother mink study also show very high concentrations of PFOS in liver (1280 - 59 500 ng/g, mean 18 000 ng/g,) - BMF ~145 to ~4000 based on data from their prey such as crayfish (whole body), carp (muscle) and turtles (liver	Giesy and Kannan, 2001 Kannan et al., 2005

• Bald Eagle, US	- Very high concentrations of PFOS in plasma (1 – 2570 ng/g).	Giesy and Kannan 2001.
• Dolphin, US	- Very high concentrations of PFOS in liver (10 – 1520 ng/g).	3M, 2003a.
• Seal in the Bothnian Sea, Finland	- Very high concentrations of PFOS in liver (130 – 1100 ng/g). - BMF > 60 based on data from salmon in the same area.	Kannan et al., 2002

In a study by Kannan et al. (2005), the whole body BCF for round gobies (*Neogobius melanostomus)* was calculated to be approximately 2400, which is comparable with laboratory data. PFOS concentrations in fish (whole body of round gobies) compared to concentrations in liver of salmon results in BMFs of approximately 10-20. In bald eagles, the mean PFOS concentration in the livers, 400 ng/g ww, gives a BMF of four to five when compared to fish at higher trophic levels in the study. For mink, BMFs from 145 to 4000 can be calculated when based on the mean liver concentration, 18 000 ng/g ww, compared to their prey items such as crayfish (whole body), carp (muscles) and turtles (liver).

In general, data show that animals at higher trophic levels have higher concentrations of PFOS than animals at lower trophic levels, indicating that biomagnification is taking place. For instance, a trophic magnification factor (TMF) of 5,9 was calculated for PFOS based on a pelagic food web including: one invertebrate species, Mysis; two forage fish species, rainbow smelt and alewife; and a top predator fish species, lake trout. A diet-weighted bioaccumulation factor of approximately 3 was determined for the trout (Martin et al., (2004b).

Morikawa *et al.* (2005) showed a high bioaccumulation in turtles. Results from a study performed by Tomy *et al*. (2004a) indicated that PFOS biomagnified in an eastern Arctic marine food web (liver concentrations of PFOS were used for seabirds and marine mammals). Houde *et al.* (2006) showed PFOS biomagnification in the Atlantic Ocean bottlenose dolphin food web.

A study by Bossi *et al*. (2005a) further supports that biomagnification is taking place. In this study, a preliminary screening of PFOS and related compounds has been performed in liver samples of fish, birds and marine mammals from Greenland and the Faroe Islands. PFOS was the predominant fluorochemical in the biota analyzed, followed by perfluorooctane sulfonamide (PFOSA). The results from Greenland showed a biomagnification of PFOS along the marine food chain (shorthorn sculpin < ringed seal < polar bear).

It is assumed that the main and most relevant route of exposure to PFOS for birds is through the diet as biomagnification in bird tissues can occur this way. BMFs above one are reported for several bird species collected in the Gulf of Gdansk (Gulkowska *et. al.* 2005). Kannan *et al*. (2005) reported a BMF of 10 to 20 in bald eagles (relative to prey items). Tomy *et al*. (2004a) calculated a trophic level BMF for black-legged kittiwake:cod of 5.1 and a BMF for glaucous gull:cod of 9.0. Newsted *et al.* (2005) indicated that PFOS has relatively shorter half-lives in blood and liver tissue in birds compared to mammals. For example, the estimated elimination half-life for PFOS from serum is 13.6 days in male mallards whereas in male rats, it is greater than 90 days. A recent study has suggested that PFOS is excreted relatively rapidly from birds (Kannan *et al*., 2005). However, if birds are chronically exposed to PFOS in their diet, biomagnification can still occur. Environmental monitoring of birds in northern parts of their range in fact indicates accumulation of PFOS.

The fact that PFOS binds to proteins leads to the relevant question -- *at what concentrations of PFOS will the binding sites on these proteins be saturated?* Serum albumin is most likely the binding pool of PFOS (Jones *et al*., 2003) and several studies have been carried out with regard to bioconcentration in plasma. In Ankley *et al*. (2005), the bioconcentration in fish was studied at concentrations of PFOS in water up to 1 mg /L; the concentration of PFOS in water and plasma followed an almost linear relationship in the doses tested up to 0.3 mg/l without any signs of saturation (1 mg/l was not tested due to mortality at that dose). This is far above environmentally relevant concentrations.

In a study by 3M (2003a), the bioconcentration factor (BCF) in whole fish was determined to be approximately 2800 at a PFOS concentration of 86 µg/l, based on calculations of uptake and depuration of PFOS. Steady-state levels were attained after 49 days of exposure. Depuration occurred slowly and 50% clearance for whole fish tissues was estimated to be 152 days. Due to mortality, a BCF could not be calculated for the other concentration used, 870 µg/l. Thus, it is not likely that saturation of serum protein binding sites will limit the bioconcentration of PFOS in fish. In Cynomolgus monkeys, cumulative doses of PFOS (0,03, 0,15, or 0,75 mg/kg/day, orally, for 182 days) showed a linear increase in plasma at the low- and mid-dose groups while a nonlinear response was showed in the high-dose group (Covance Laboratories, Inc. 2002a). We are not aware of similar data in other mammals, but considering the high level of bioaccumulation observed in mammals, and that mammalian serum contains high concentrations of protein, binding sites are not likely to limit the bioaccumulation of PFOS in environmentally exposed mammals.

2.2.3 Long-range environmental transport

The potassium salt of PFOS has a measured vapour pressure of 3.31×10^{-4} Pa (OECD, 2002). Due to this vapour pressure and a low air-water partition coefficient ($< 2 \times 10^{-6}$), PFOS itself is not expected to volatilise significantly. It is therefore assumed to be transported in the atmosphere predominantly bound to particles, because of its surface-active properties, rather than in a gaseous state.

Some of the PFOS-related substances have a considerably higher vapour pressure than PFOS itself, and are as a result more likely to be volatile. The vapour pressures of precursors, such as N-EtFOSEA and N-MeFOSEA, may exceed 0.5 Pa (1000 times greater than that of PFOS) (Giesy and Kannan 2002). Other PFOS precursors considered volatile include N-EtFOSE alcohol, N-MeFOSE alcohol, N-MeFOSA and N-EtFOSA (3M, 2000). These precursors to PFOS could evaporate into the atmosphere and be more widely transported through air than is possible for PFOS itself. Once in the atmosphere, they can remain in gas phase, condense on particles present in the atmosphere and be carried or settle out with them, or be washed out with rain (3M, 2000). Martin *et al*. (2002) measured the air in Toronto and Long Point, Ontario, for some precursors of PFOS. They found an average N-MeFOSE alcohol concentration of 101 pg/m^3 in Toronto and 35 pg/m^3 at Long Point. The average concentrations of N-EtFOSE alcohol were 205 pg/m^3 in Toronto and 76 pg/m^3 in Long Point.

For precursors released to water, the vapour pressure may be significant enough to allow the substance to enter into the atmosphere. For N-EtFOSE alcohol, the tendency to leave the water phase is indicated by its relatively high Henry's law constant (1.9×10^3 Pa·m^3·mol^{-1}) (Hekster *et al*. 2002). It has been reported that when these PFOS precursors are present as residuals in products, they could evaporate into the atmosphere when the products containing them are sprayed and dried (3M, 2000).

PFOS has been detected in rainwater from an urban center in Canada with a concentration of 0.59 ng/L. Whether or not PFOS originates from precursors either being transported and subsequently wet deposited and degraded to PFOS, or atmospherically degraded and then wet deposited, is unclear. Measurements of potential precursors for PFOS were not performed in this study (Loewen *et al*, 2005)

The atmospheric half-life of PFOS is expected to be greater than two days. This statement, while not specifically tested, is based on the fact that PFOS has exhibited extreme resistance to degradation in all tests performed. However, an atmospheric half-life of 114 days has been calculated for PFOS using an AOP computer modeling program v1.91 (Environment Agency,, 2004). The indirect photolytic half-life of PFOS at 25°C has been estimated to be more than 3.7 years (OECD, 2002).

How perfluoralkyl acid substances have come to be globally disseminated in the environment has been the key question, since, for example, the vapour pressure and Henry's law constant of PFOS indicates it is too involatile and therefore unlikely to enter directly into the atmosphere (Stock *et al.* 2004). Therefore it has been hypothesized that PFOS must be globally distributed via more volatile, neutral airborne contaminants that undergo long-range transport and then degrade to yield the free acids.

In support, Stock *et al.* (2004) have recently reported that polyfluorinated sulfonamides are widely distributed throughout the North American troposphere. Mean concentrations ranged from 22-403 pg/m^3 with the dominant polyfluorinated contaminant dependent on the sampling location.

High mean concentrations of N-methyl perfluorooctane sulfonamidoethanol (NMeFOSE) of 359 pg/m^3, were identified in the air of Griffin, Georgia. The authors speculate that, as Griffin is located in the midst of the main carpet manufacturing and treatment zone of the US, it probably is entering the environment from carpet treatment products, many of which consist of fluorinated molecules linked to polymeric materials. For example, it is possible that free chemical may be left in the carpet fibres, with publicly available information on 3M produced products indicating the concentration of free polyfluorinated sulfonamides is typically 1-2% or less. Alternatively, it is postulated that chemically bound NMeFOSE may also be released from carpets due to chemical, physical, and/or biological degradation processes.

Support for this hypothesis comes from Shoeib *et al.* (2004), who measured both NMeFOSE and the related N-ethyl perfluorooctane sulfonamidoethanol (NEtFOSE) in both indoor and outdoor air. Mean indoor air concentrations for these were 2590 and 770 pg/m^3, respectively, and the ratios between indoor and outdoor air were 110 and 85, respectively. Again carpets were identified as a possible source of NMeFOSE, and high usage of paper in the building as a possible source of NEtFOSE. Paper products were also suggested by Stock *et al.* (2004) as a possible source for the high levels of NEtFOSE in the air of Reno, Nevada.

Recently Dinglasan-Panlilio and Maybury (2006) have demonstrated that residual fluorinated substances detected in materials, including 0.39% of a perfluoroalkyl sulfonamido alcohol present in a commercially available carpet protector product, are the likely sources for these volatile precursors. Further N-methyl perfluorobutane sulfonamidoethanol (NMeFBSE) has been demonstrated in the laboratory to degrade to perfluorobutane sulfonate (PFBS), albeit in low yield (D'eon et al, 2006).

PFOS has been measured in a wide range of biota in the Northern Hemisphere such as the Canadian Arctic, Sweden, the US and the Netherlands. In a study by Martin *et al.* (2004a), the levels of PFOS were measured in liver samples from biota in the Canadian Arctic and were found in the vast majority of the species examined. The presence of PFOS in Arctic biota, far from anthropogenic sources, demonstrates the potential of PFOS for long-range transport. The mechanisms of this transport are not known, but it could be due to the transport of volatile PFOS-related substances that eventually degrade to PFOS.

While precursors will undergo degradation once released to the environment, transformation rates may vary widely. Precursors that reach a remote region through the atmosphere or other media may be subject to both abiotic and biotic degradation routes to PFOS (Giesy and Kannan 2002a; Hekster *et al*. 2002). The mechanisms of this degradation are not well understood. When rats metabolize N-MeFOSE-based compounds, several metabolites have been confirmed in tissue samples, including PFOS and N-MeFOSE alcohol (3M Environmental Laboratory 2001a, 2001b). PFOS appears to be the final product of rat and probably other vertebrate metabolism of POSF-based substances.

A recent study performed with rainbow trout (*Onchorhynchus mykiss)* liver microsomes has demonstrated that *N*-ethyl perfluorooctanesulfonamide (N-EtPFOSA) is a precursor of PFOS in fish (Tomy et al., 2004b). These findings combined with the recent measurements of concentrations up to 92.8 ± 41.9 ng/g wet weight of *N*-EtPFOSA in aquatic organisms from Arctic regions (Tomy et al., 2004a) strengthen the hypothesis that perfluorinated sulfonamides are one of the volatile precursors of PFOS transported over long distances to the Arctic. However, the hypothesis that these volatile precursors reach the Arctic latitudes by atmospheric transport has not yet been confirmed by atmospheric measurements (Bossi et al., 2005b)

2.3 Exposure

2.3.1 Measured environmental levels

A screening study was assigned by the Swedish Environmental Protection Agency (Swedish EPA) and performed by ITM, Institute of Applied Environmental Research, on the levels of PFOS in the Swedish environment (Swedish EPA, 2004). The results showed highly elevated levels of PFOS in a wetland in the vicinity of a fire drill area with a declining gradient out in the adjacent bay (2.2 – 0.2µg/L). Elevated levels were also detected outside sewage treatment plants (STPs) and landfills. Effluents from STPs contained levels of PFOS up to 0.020 µg/L and leachate levels from landfills were between 0.038 – 0.152 µg/L.

The occurrence of PFOS and other perfluoroalkyl sulfonate substances in open ocean waters such as the Atlantic and the Pacific Ocean have been investigated. The detection of PFOS in oceanic waters suggests another potential long-range transport mechanism to remote locations such as the Arctic. The results showed that PFOS is present in central to western Pacific Ocean regions in concentrations ranging from 15 – 56 pg/L, comparable to the concentrations in the mid-Atlantic ocean. These values appear to be the background values for remote marine waters far from local sources (Taniyasu *et al*., 2004). PFOS was also detected in oceanic waters in several coastal seawaters from Asian countries (Japan, China, and Korea) at concentrations ranging from 1.1 - 57 700 $pg.L^{-1}$ (Jin *et al.*, 2004; Yamashita *et al*., 2005). PFOS was also observed in the North Sea (estuary of the river Elbe, German Bight, southern and eastern North Sea) (Caliebe *et al*., 2004).

In a study in cities across China, PFOS was detected in all water samples (surface and sea water, groundwater, municipal and industrial effluents and tap water), showing that PFOS pollution existed generally in water compartments in China. Concentrations were generally at levels of approximately 1 ngéL (Jin *et al.*, 2004).

Studies in the US have identified the presence of PFOS in surface water and sediment downstream of a production facility, as well as in wastewater treatment plant effluent, sewage sludge and landfill leachate at a number of urban centres in the US (3M Multi City study, reviewed in OECD (2002) and 3M (2003a). Four of the cities (Decatur (AL), Mobile, Columbus (GA), Pensacola) were cities that have manufacturing or industrial use of fluorochemicals; two of the cities (Cleveland (TN), Port St. Lucie) were control cities that do not have significant fluorochemical activities. The ranges of PFOS levels in these cities are provided in Table 5.

Table 5. Environmental Levels of PFOS in Six US Urban Centres in the US (from OECD, 2002)

Medium	Range of PFOS levels (µg/L or µg/kg)
Municipal wastewater treatment plant effluent	0.041 - 5.29
Municipal wastewater treatment plant sludge	0.2 - 3.120 (dry weight)
Drinking water	ND - 0.063
Sediment	ND - 53.1 (dry weight)
Surface water	ND - 0.138
'Quiet' water	ND - 2.93

Note: ND: not detected

The control cities' samples generally inhabited the lower end of the above ranges, except for the municipal wastewater treatment plant effluent and sludge findings for one of the control cities (Cleveland), which were intermediate in their ranges, and the 'quiet' water samples at control city (Port St. Lucie), which were the highest. In Canada, suspended sediment samples were collected annually at Niagara-on-the-Lake in the Niagara River over a 22 year period (1980-2002). PFOS concentrations ranged from 5 to 1100 $pg.g^{-1}$ (Furdui *et al.,* 2005). Preliminary findings suggest that PFOS concentrations increased during the study period from < 400 $pg.g^{-1}$ in the early 1980s to > 1000 $pg.g^{-1}$ in 2002.

Samples of effluent from fifteen representative industry sectors have been analysed for PFOS (Hohenblum *et al*, 2003). The industry sectors were printing (1 site), electronics (3), leather, metals, paper (6), photographic and textiles (2). The PFOS levels ranged from 0-2.5 µg/L (2.5 µg/L for leather, 0.120 µg/l for metal, 0.140-1.2 µg/l at four paper sites, 1.2 µg/l for photographic, not found in textiles or electronics).

Groundwater from below an air force base in Michigan, US, has been sampled (Moody et al, 2003). Fire fighting foams containing PFOS had been used there in training exercises from the 1950s to 1993 when the base was decommissioned. The groundwater was found to contain PFOS, at levels from 4 - 110 µg/l.

Sixteen Great Lakes water samples (eight locations) were analysed for perfluorooctane surfactants. PFOS was present in all samples with a concentration range of 21-70 ng/L. Three PFOS precursors were also found in the water samples. N-EtFOSAA (4.2-11 ng/L) and PFOSA (0.6 -1.3 ng/L) were present in nearly all samples while PFOSulfinate was identified at six out of eight locations (2.2-17 ng/L) (Boulanger et al, 2004). PFOS was detected in surface water as a result of a spill of fire-fighting foam from the Toronto International Airport into nearby Etobicoke Creek. Concentrations

of PFOS ranging from <0.017 to 2210 $\mu g.L^{-1}$ were detected in creek water samples over a 153-day sampling period. PFOS was not detected at the upstream sample site (Moody *et al*. 2003).

PFOS and related fluorochemicals have been detected in animals in a number of studies in a variety of locations around the globe. Generally, the highest concentrations are found in top predators in food chains containing fish. The highest North American or circumpolar concentration of PFOS in mammal tissue reported in the published literature is 59 500 $\mu g.kg^{-1}$ ww in mink liver from USA (Kannan *et al*., 2005a).

Martin *et al.* (2004a) measured the levels of PFOS in liver samples from biota in the Canadian Arctic. PFOS was found in the vast majority of the samples and higher levels were found in animals at the top of the food chain. The highest levels were found in polar bear, with a mean level of 3100 ng/g from seven animals (maximum value > 4000 ng/g). The concentrations of PFOS in polar bear are 5-10 times higher than the concentration of all other perfluoroalkyl substances and were higher than any other previously reported concentrations of persistent organochlorine chemicals (e.g., PCBs, chlordane or hexachlorocyclohexane) in polar bear fat (Martin *et al.,* 2004a). PFOSA, a precursor to PFOS, was also found in most of the samples. The concentration of PFOSA was higher than that of PFOS in fish, but not in mammals. This could indicate that PFOSA has been metabolised to PFOS in mammals and the high concentrations may be the result of both direct exposure to PFOS and metabolism from PFOSA.

PFOS is found in birds worldwide. In North America, PFOS has been found in eagles in the Great Lakes, mallards in the Niagara River, loons in northern Quebec, gulls in the Arctic and in Canadian migratory species in the United States (e.g., common loon in North Carolina). In Canadian or Canada-US migratory species, concentrations have been measured in liver ranging from not detectable to 1780 ng/g for loon in northern Quebec and bald eagle in Michigan, in blood plasma ranging from <1- 2220 ng/g blood plasma in bald eagles, and in eggs and egg yolk ranging from 21-220 ng/g in double-crested cormorant in Manitoba. In several monitoring studies, piscivorous water birds were found to have some of the highest liver and serum PFOS concentrations compared to other species (Newsted *et al.,* 2005). In a study of birds in the Niagara River Region, piscivorous birds (common merganser, bufflehead) contained significantly greater PFOS concentrations than non-piscivorous birds (Sinclair *et al*., 2006). Preliminary data on temporal trends show an increase in bird PFOS concentrations, in two Canadian Arctic species (thick-billed murres and northern fulmars) from 1993 to 2004 (Butt *et al*., 2005). It is noted that concentrations of PFOS in plasma have been reported in eagle, gulls and cormorants around the Great Lakes and in the Norwegian Arctic ranging from <1 ng/g to 2220 ng/g .

Kannan and Giesy (2002b) have summarised results of analyses on archived tissue samples. The tissues analysed came from marine mammals, birds, fish, reptiles and amphibians from around the world, including the Arctic and Antarctic Oceans. Samples collected in the 1990s were used. Around 1700 samples were analysed, with concentrations in liver, egg yolk, muscle or blood plasma determined. The detection limit varied from 1 ng/g to 35 ng/g wet weight. A summary of the results is shown in Table 6.

Table 6. Maximum concentrations of PFOS in various species as well as frequency of detection. Based on Kannan and Giesy (2002a)

Species	Maximum concentration ng/g wwt	Frequency of detection
Marine mammals	1520	77%
Mink and otter	4900	100%
Birds	2570	60%
Fish	1000	38%

PFOS was detectable in most of the samples, including those from remote marine locations, at concentrations >1 ng/g. The authors compared the results from remote areas with those from more industrial locations and noted that PFOS is widely distributed in remote regions, including the Polar Regions, but that the levels found in more urban and industrial areas (e.g. the Baltic, Great Lakes) are several times higher. The tissues of fish-eating birds in Canada, Italy, Japan and Korea all contained detectable levels of PFOS, suggesting that they are exposed through the fish they consume. A summary of several studies is given in Table 7.

Table 7. Monitored levels of PFOS in animals (data from selected studies, based on OECD, 2002)

Description	Reference	Reported Highest Concentrations (Max, Mean)	Location
Global monitoring survey of marine mammals (Florida, California, Alaska, northern Baltic Sea, Mediterranean Sea, Arctic, Sable Island (Canada)	A	Bottlenose dolphin (liver, n = 26): Max: 1520 ng/g wet wt. Mean: 420 ng/g wet wt.	Florida
		Ringed seal (liver, n = 81): Max: 1100 ng/g wet wt. Mean: 240 ng/g wet wt.	Northern Baltic Sea
Survey of mammals, birds and fish in the Canadian Arctic	B	Polar bear (liver, n = 7): Max: > 4000 ng/g wet wt. Mean: 3100 ng/g wet wt.	Canadian Arctic

Description	Reference	Reported Highest Concentrations (Max, Mean)	Location
		Arctic fox (liver, n = 10): Max: 1400 ng/g wet wt. Mean: 250 ng/g wet wt.	
Survey of fish (US, Europe, North Pacific Ocean, Antarctic)	C	Fish (muscle, n = 172): Max: 923 ng/g wet wt. Mean. 40 ng/g wet wt.	Belgian estuary
		Carp (muscle, n = 10): Max: 296 ng/g wet wt. Mean: 120 ng/g wet wt.	US Great Lakes
Survey of fish-eating birds (US, Baltic Sea, Mediterranean Sea, Japanese coast, Korean coast)	D	Bald eagle (plasma, n = 42): Max: 2570 ng/mL Mean: 520 ng/mL	Midwest US
Survey of mink and river otter in the US	E	Mink (liver, n = 77): Max: 4870 ng/g wet wt. Mean: 1220 ng/g wet wt.	US
		River otter (liver, n = 5): Max: 994 ng/g wet wt. Mean: 330 ng/g wet wt.	US
Survey of oysters in the US (Chesapeake Bay & Gulf of Mexico)	F	Oyster (Whole body, n =77) Max: 100 ng/g wet wt. Mean: 60 ng/g wet wt.	US
Fish samples upstream and downstream of 3M facility in Decatur, Alabama, US	G	Fish (whole body): Mean (upstream): 59.1 µg/kg wet wt. Mean (downstream): 1,332 µg/kg wet wt.	Decatur, US
Swedish urban and background	H	Perch: 3 - 8 ng/g (urban sites in the vicinity of	Sweden (Lake Mälaren)

Description	Reference	Reported Highest Concentrations (Max, Mean)	Location
fish samples		municipal STPs); 20-44 ng/g in Lake Mälaren and near Stockholm	

Sources: A: 3M (2003a), B: Martin *et al.* (2004a); C: Giesy and Kannan (2001c) in 3M (2003a); D: Giesy and Kannan (2001b) in 3M (2003); E: Giesy and Kannan (2001d) in 3M (2003a); F: Giesy and Kannan (2001e) in 3M (2003); G: Giesy and Newsted (2001) in OECD (2002); H: Holmström *et al.* (2003).

Concentrations of PFOS in guillemot (*Uria aalge*) eggs from Stora Karlsö in the Baltic Sea have been measured retrospectively from 1968 to 2003 (Holmström et al, 2005). The results shown in Figure 2 display a trend of increasing concentrations since 1968 (17 – 623 ng/g).

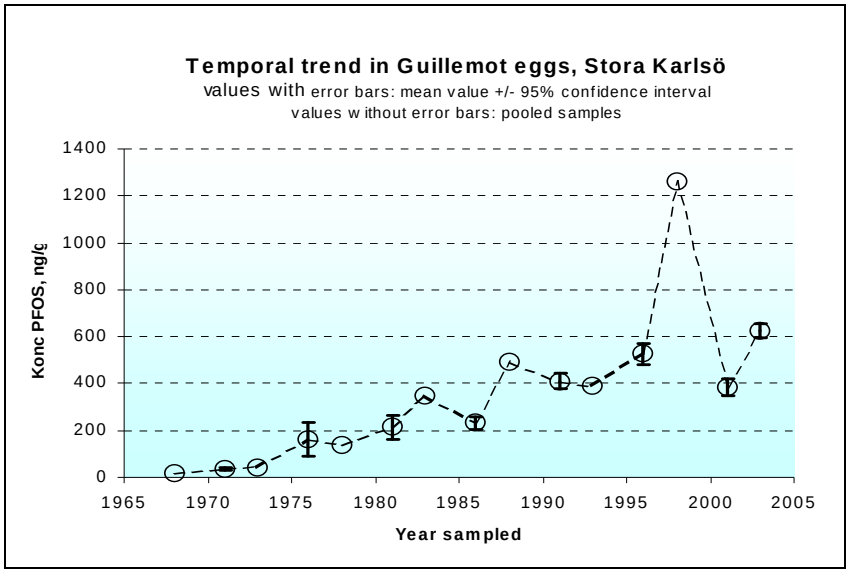

Figure 2. Measured concentrations of PFOS in Guillemot (*Uria aalge*) eggs sampled at Stora Karlsö in the Baltic Sea between the years 1968 – 2003. The graph is taken from the report "Screening av perfluorerade ämnen" by the Swedish EPA, Environmental Assessment Department (2004).

2.3.2 Bioavailability

Studies on fish have shown that PFOS has bioconcentration properties. In studies on bluegill sunfish (*Lepomis macrochirus*) and rainbow trout (*Oncorhynchus mykiss*), bioconcentration factors (BCFs) have been estimated to be 2796 (whole fish) as well as 2900 (liver) and 3100 (plasma), respectively. The major route of uptake is believed to be through the gills (Martin *et al.*, 2003).

Since PFOS is released from sewage treatment plants to the environment i.e. through water, one major route for PFOS into local food chains could be through fish. PFOS has shown a high oral uptake (95%) within 24 hours in the gastro-intestinal (GI) tract in studies on rats (OECD, 2002). Taken together, this could constitute the basis of the highly elevated levels that have been observed in top predators in food chains containing fish.

This could also be corroborated by two separate human monitoring studies on the Swedish population where the levels of PFOS in whole blood was higher (27.2 ng/g, 3.0 – 67, n = 10) in females with a high consumption of fish (Berglund, 2004) compared to samples from females in the general population (17.8 (ng/g, 4.6 – 33, n = 26) (Kärrman *et al.,* 2004).

In humans, the highest concentrations of PFOS have been detected in workers at 3M's manufacturing plant for perfluorochemicals in Decatur, US, where the levels in serum in the last year of measurement (2000) ranged between 0.06 – 10.06 ug/g (n = 263, OECD, 2002).

In a study of the general population, blood samples from families including three generations living in 12 European countries were tested for a large number of chemicals including PFOS and PFOSA. PFOS was present in 37 of 38 samples with concentrations from 0.36 to 35.3 ng/g blood, while PFOSA was present in 36 of 38 samples with concentrations from 0.15 to 2.04 ng/g blood (WWF, 2005).

Pooled serum samples from 3802 Australian residents, collected 2002-2003 and divided in relation to age, gender and region, were analysed for perfluoroalkylsulfonates, perfluoroalkylcarboxylates and PFOSA (Kärrman et al., 2006). PFOS and PFOSA were quantified in all pooled serum samples with a total range of 12.7-29.5 ng/ml (mean 17.2 ng/ml) and 0.36-2.4 ng/ml (mean 0.81 ng/ml), respectively. For PFOS, a significant correlation between age and concentration was shown. No substantial difference was found in levels of perfluorinated compounds between the urban and rural regions. According to gender some differences were shown for some of the age groups.

2.4 Hazard assessment for endpoints of concern

2.4.1 Mammalian Toxicity

Evidence of the mammalian toxicity of PFOS is available from acute, sub-chronic and chronic exposures to rats, sub-chronic exposures to monkeys, and a two-generation study on rats. Results are available from reproductive and teratogenicity studies on rats and rabbits. Details of these studies are not included here, they can be found in the assessment made by OECD (2002). The most relevant data for this risk profile are:

- A 90-day study on rhesus monkeys exposed to PFOS potassium salt via gavage at the doses 0, 0.5, 1.5 and 4.5 mg/kg bw/day. At 4.5 mg/kg bw/day all monkeys (4) died or were sacrificed in moribound condition. No deaths were observed at 0.5 or 1.5 mg/kg bw/day, but there were signs of gastrointestinal toxicity. A NOAEL could not be established since the lowest dose was a LOAEL (Goldenthal et al., 1978a).
- A 90-day oral repeated dose toxicity study in rats that were fed diets containing 0, 30, 100, 300, 1000 and 3000 mg PFOS potassium salt per kg diet. All rats died when fed diets containing 300 mg/kg PFOS and above (equivalent to 18 mg/kg bw/day and above). At 100 mg/kg (6 mg/kg bw/day), 50% (5/10) of the animals died. All rats receiving diets containing 30 mg/kg PFOS (2.0 mg/kg/day) survived until the end of the study, but small changes in body and organ weights were reported. Since the lowest dose tested was a LOAEL, a NOAEL could not be established (Goldenthal et al., 1978b).
- A two-generation reproductive toxicity study on rats that were fed PFOS potassium salt via gavage at the doses 0.1, 0.4, 1.6, and 3.2 mg/kg bw/day. At the doses 1.6 and 3.2 mg/kg bw/day a significant reduction in the viability of the F1 generation was observed. In the 1.6 mg/kg bw/day group, 34% (86/254) of the F1 pups died within four days after birth. In the 3.2 mg/kg bw/day group, 45% (71/156), of the F1 pups died within one day after delivery. None of these pups survived beyond day 4. Maternal toxicity at 1.6 and 3.2 mg/kg bw/day was manifested as reduced

food consumption, body weight gain, and terminal bodyweight. Localised alopecia was also observed at 3.2 mg/kg bw/day. The LOAEL in this study was 0.4 mg/kg bw/day based on significant reductions in pup weight gain in the F1 generation animals. The NOAEL was 0.1 mg/kg bw/day (Christian et al., 1999). A new study by Luebker *et al.* (2005) supports these results.

- Cynomolgus monkeys administered PFOS for 26 weeks were observed to have thymic atrophy (females), and reduced high density lipoprotein, cholesterol, triiodothyronine, total bilirubin levels (males) (Covance Laboratories, Inc. 2002a). The LOEL dose was 0.03 $mg.kg^{-1}$ bw/day at which average mean female and male concentrations in sera and liver were 19.8 $\mu g.mL^{-1}$ and 14.5 $\mu g.g^{-1}$, respectively.
- A 2-year dietary rat study in which histopathological effects in the liver were seen in males and females at intakes as low as 0.06–0.23 mg PFOS/kg bw per day and 0.07–0.21 mg PFOS/kg bw per day, respectively (Covance Laboratories, Inc. 2002b). Average values were determined for males and females to establish LOELs of 40.8 ug/g in liver and 13.9 mg/L in serum.

A study by Grasty *et al.* (2003) concluded that exposure of pregnant rats to PFOS late in gestation, at 25 mg/kg b.w. PFOS by oral gavage on gestation day (GD) 17-20 or 50 mg/kg PFOS on GD 19-20, is sufficient to induce 100% pup mortality and that the causative factor may be inhibition of lung maturation. However, in a subsequent study by Grasty *et al.* (2005), the mechanism behind pup mortality could not be established.

2.4.2 Ecotoxicity

Environmental toxicity data for PFOS is predominantly found for aquatic organisms such as fish, invertebrates and algae, and for birds.

PFOS has shown moderate acute toxicity to fish. The lowest observed LC_{50} (96h) was estimated to be 4.7 mg/l in a study where fathead minnow (*Pimephales promelas*) were exposed to the lithium salt of PFOS. The lowest NOEC, 0.3 mg/l, has been observed in *Pimephales promelas* at prolonged exposure (42d) and was based on mortality (OECD, 2002). The lowest LC_{50} (96h) for aquatic invertebrates has been observed in the mysid shrimp (*Mysidopsis bahia)* and was estimated to be 3.6 mg/l. The lowest NOEC value has been observed in *Mysidopsis bahia* at 0.25 mg/l (OECD, 2002).

A study by Macdonald *et al*. (2004) reported a 10-day NOEC of 0.0491 mg/L for the growth and survival of the aquatic midge (Chironomous *tentans*). The authors concluded that PFOS is 2-3 orders of magnitude more toxic to chironomids than to other aquatic organisms possibly through some kind of interaction with haemoglobin, which is present at all levels of dissolved oxygen (DO) in chironomids as opposed to daphnids, where haemoglobin is produced only in response to declining DO levels.

The most sensitive algae appear to be the green algae *Pseudokirchnerilla subcapitata* with a IC_{50} (96h, cell density) of 48.2 mg/L. The lowest NOEC value for algae was determined in the same study for *Pseudokirchnerilla subcapitata*, 5.3 mg/L (Boudreau *et al.,* 2003).

Mallard and bobwhite quail were exposed to PFOS in feed for up to 21 weeks and a variety of endpoints examined including changes in adult body and organ weights, feed consumption rate, fertility, hatchability, and offspring survival. At a dose of 10 mg/kg diet PFOS, effects in male mallards (*Anas platyrhyncos)* included reduced testes size and decreased spermatogenesis (3M, 2003b). At this dose, the concentrations of PFOS in serum and liver were 87.3 ug/mL and 60.9 ug/g, respectively (3M, 2004). For quail (*Colinus virginianus*), at 10 mg/kg in diet, minor effects were observed in adults, including an increase in liver weight (females), an increase in the incidence of small testes size (males), and reduction in survivability in quail chicks as a percentage

of eggs set. Concentrations in serum and liver of adult quail females was 84 $\mu g.mL^{-1}$ serum (week 5, pre-reproductive phase), and 8.7 $\mu g.mL^{-1}$ serum (week 21) and 4.9 $\mu g.kg^{-1}$ wet weight liver; in adult quail males, concentrations were 141 $\mu g.mL^{-1}$ serum and 88.5 $\mu g.g^{-1}$ wet weight liver (3M, 2003c).

3 SYNTHESIS OF THE INFORMATION

Perfluorooctane sulfonate (PFOS) is a fully fluorinated anion, which is commonly used as a salt in some applications or incorporated into larger polymers. Due to its surface-active properties, it has historically been used in a wide variety of applications, typically including fire fighting foams and surface resistance/repellency to oil, water, grease or soil. PFOS can be formed by degradation from a large group of related substances, referred to as PFOS-related substances (see definition on page 4).

Due to their intrinsic properties, PFOS and its related substances have been used in a wide variety of applications. While historically, PFOS and PFOS-related substances have been used in eight different sectors as shown in Section 2.1.2. above, the present use in industrialized countries seems to be limited to five sectors, see 2.1.2. It is not known whether this also reflects the global use.

PFOS and PFOS-related substances can be released to the environment at their manufacture, during their use in industrial and consumer applications and from disposal of the chemicals or of products or articles containing them after their use.

The rate and the extent of the formation of PFOS from its related chemicals are largely unknown. Lack of data makes it very difficult to estimate the net contribution of the transformation of each of the PFOS-related substances to the environmental loadings of PFOS. However, based on its extreme stability, it is expected that PFOS is likely to be the final degradation product of all PFOS-related substances.

PFOS is extremely persistent. It has not shown any degradation in tests of hydrolysis, photolysis or biodegradation in any environmental condition tested. The only known condition whereby PFOS is degraded is through high temperature incineration.

With regard to bioaccumulation potential, PFOS meets the Annex D criteria given the highly elevated concentrations that have been found in top predators such as the polar bear, seal, bald eagle and mink. Based on the concentrations found in their prey, high BMFs have been estimated for these predators. BCF values in fish, although (rather) high do not in themselves meet the specific numeric criteria. However, due to the properties of PFOS, which binds preferentially to proteins in non-lipid tissues, application of numeric criteria for BCF or BAF, which are derived based on consideration of lipid-partitioning substances, may be inappropriate for PFOS. Most notable and alarming are the high concentrations of PFOS that have been found in Arctic animals, far from anthropogenic sources. PFOS has been detected in higher trophic level biota and predators such as fish, piscivorous birds, mink, and Arctic biota. Also, predator species, such as eagles, have been shown to accumulate higher PFOS concentrations than birds from lower trophic levels. Even with reductions in manufacturing of PFOS by some manufacturers, wildlife, such as birds, can continue to be exposed to persistent and bioaccumulative substances such as PFOS simply by virtue of its persistence and long-term accumulation.

According to available data, PFOS meets the criteria for the potential for long-range transport. This is evident through monitoring data showing highly elevated levels of PFOS in various parts of the northern hemisphere. It is especially evident in the Arctic biota, far from anthropogenic sources. PFOS also fulfils the specific criteria for atmospheric half-life.

PFOS fulfils the criteria for adverse effects. It has demonstrated toxicity towards mammals in sub-chronic repeated dose studies at low concentrations, as well as rat reproductive toxicity with mortality of pups occurring shortly after birth. PFOS is toxic to aquatic organisms with mysid shrimp and *Chironomus tentans* being the most sensitive organisms.

Table 8. POP characteristics of PFOS (studies performed with the potassium salt of PFOS, unless otherwise noted).

Criterion	Meets the criterion (Yes/No)	Remark
Persistence	Yes	Extremely persistent. No degradation recorded in chemical or biological tests
Bioaccumulation	Yes	Found in highly elevated concentrations in top predators. Calculated hypothetical BMFs = 22 - 160. BCF in fish = 2796 - 3100.
Potential for Long-Range Environmental Transport	Yes	Atmospheric half life > 2 days (estimated value based on photolytic half life > 3.7 years)
Toxicity	Yes	Sub-chronic exposure: Mortality in monkeys at 4.5 mg/kg bw/day. Reproductive toxicity: mortality in rat pups at 1.6 mg/kg bw/day. Acute toxicity to Mysid shrimp (*Mysidopsis bahia)*: LC_{50} (96h) = 3.6 mg/L Acute toxicity to fish, Fathead minnow (*Pimephales promelas*): LC_{50} = 4.7 mg/L[1]

[1]The study compound was the lithium salt of PFOS

A risk quotient analysis, where known or potential exposures are integrated with known or potential adverse environmental effects, have been performed on PFOS for the wildlife in Canada (Environment Canada, 2006). The results indicate that the higher trophic level mammals may be at risk at current environmental concentrations of PFOS.

In the risk quotient analyses for polar bear, the highest concentration was found in South Hudson Bay with a maximum concentration of 3.77 $\mu g.g^{-1}$ ww liver (range 2.00-3.77 $\mu g.g^{-1}$, mean 2.73 $\mu g.g^{-1}$ ww liver, Smithwick *et al*. 2005). In comparing this value of 3.77 $\mu g.g^{-1}$ ww liver of PFOS in polar bear with a critical toxicity value of 40.8 $\mu g.g^{-1}$ ww liver for histopathological effects in liver

of rats (a 2-year study, Covance Laboratories, Inc. 2002), the difference is only about a factor 10. Using an application factor of 100[2], as was used in the Canadian Ecological Screening Assessment Report, a risk quotient of 9.2 was calculated, where values above one indicate risk. Risk quotients were also calculated on toxicological endpoints from other studies in rats and monkeys but with the same maximum exposure concentration from the south Hudson Bay polar bear, showing risk quotients from 2.1 to 19.

Concentrations in Canadian Arctic polar bear are among the highest in polar bears worldwide but the exposure concentrations are not considered an anomaly given similar concentrations in polar bears in other North America and European Arctic locations and high concentrations in other wildlife globally as shown above.

Risk quotients were also calculated for a number of bird species that are native to Canada, including many piscivorous birds and migratory species. The range of risk quotients is either above or approaching one that indicates potential for harm at concentrations observed in native species, including migratory species (Environment Canada, 2006).

4 CONCLUDING STATEMENT

PFOS is a synthetic substance of anthropogenic origin with no known natural occurrence. It can be concluded therefore that the presence of PFOS and its precursors in the environment are the result of anthropogenic activities and that PFOS found in remote areas far from possible sources has been brought there through long-range environmental transport. While PFOS related substances may be degraded to PFOS, PFOS itself is extremely persistent in all media and can bioaccumulate and biomagnify in mammals and piscivorous birds.

The voluntary phase out of PFOS production by the major producer in the USA has led to a reduction in the current use of PFOS-related substances. However, it can be assumed that it is still produced in some countries and it continues to be used in many countries. Given the inherent properties of PFOS,[3] together with demonstrated or potential environmental concentrations that may exceed the effect levels for certain higher trophic level biota such as piscivorous birds and mammals; and given the widespread occurrence of PFOS in biota, including in remote areas; and given that PFOS precursors may contribute to the overall presence of PFOS in the environment, it is concluded that PFOS is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

[2] An application factor of 100 applied for extrapolation from laboratory to field conditions and for intraspecies and interspecies variations in sensitivity, and extrapolation from the observed effects level to a no-effect level.

[3] A decision on the inclusion of PFOS precursors has been postponed until the Committee has evaluated the information requested under Annex F.

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別添2

ペンタクロロベンゼンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 分解しない（OECD TG 301C）	【ｵｸﾀﾉｰﾙ/水分配係数】 logKOW=4.88-6.12（推奨値 5.17-5.18）	【反復投与毒性】 ［ラット　混餌：100 日］ NOEL：18.2mg/kg/day（♀） LOEL：8.3mg/kg/day（♂） 8.3mg/kg/day 以上（♂）で腎重量増加、腎硝子滴 37.5mg/kg/day 以上（♀）で肝重量増加及び肝細胞肥大 81.1mg/kg/day（♂）及び 78.7mg/kg/day（♀）でヘモグロビン減少、白血球増加等	【慢性毒性】 カダヤシ *Gambusia affinis* ： 42dEC10=0.002 mg/L（成長） タイワンガザミ *Portunus pelagicus* ： 40dEC10=0.014 mg/L（成長）
【光分解性】 大気中で、主として OH ﾗｼﾞｶﾙとの反応により光酸化される。日光照射下の表層水での分解は早く、4 時間で 41%が消失。	【BCF（経鰓的生物濃縮係数）】 ・魚：BCF=1085-23000 ・軟体動物：BCF=833-4300 ・甲殻類：BCF=577-2258	［ラット　混餌：13 週］**(NTP)** NOEL：2.4mg/kg/day（♂）、 24mg/kg/day（♀） 2.4mg/kg/day 以上（♂）で絶対・相対肝重量増加、2.4mg/kg/day 以上（♀）で体重減少、7.2mg/kg/day 以上（♂）で組織学的所見を伴う腎重量増加、 24mg/kg/day（♂）以上で精子異常、小葉中心性肝細胞肥大、72mg/kg/day（♀）で腎毒性 【催奇形性】 ラット：50mg/kg/day の母体暴露で肋骨数過剰、胸骨異常の報告	
【半減期】 ・大気中：推定値は 45-467 日。OH ﾗｼﾞｶﾙとの反応による半減期の計算値は 277 日。ﾓﾃﾞﾙﾃﾞｰﾀに基づく半減期は 65 日。分解ﾌﾟﾛｾｽのみを考慮した場合の推定半減期は 155 日 ・水中：表層水中の推定半減期は 194-1250 日。更に深いところでの嫌気性生分解による推定半減期は 776-1380 日。 ・土壌中：ｽﾊﾟｲｸした下水汚泥改良土壌中で半量は揮発により素早く消失し、残り半量の半減期は 187-1550 日。好気性のﾛｰﾑ砂質土壌中の半減期は 194-345 日。湖水の砂状底質中で 150 日後に 75%が分解し、これに続く一次代謝物の半減期は 50 日。温帯地域の有機土壌と底質中の推定半減期は 6 年。			

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Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Third meeting
Geneva, 19–23 November 2007

Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Risk profile on pentachlorobenzene

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on pentachlorobenzene, on the basis of the draft contained in document UNEP/POPS/POPRC.3/15. The text of the risk profile, as amended, is set out below. It has not been formally edited.

K0763738 171207

PENTACHLOROBENZENE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

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EXECUTIVE SUMMARY

The European Community and its Member States being Parties to the Stockholm Convention have proposed pentachlorobenzene (PeCB) to be listed to the Convention. The Persistent Organic Pollutants Review Committee concluded that PeCB fulfilled the screening criteria set and decided to establish an ad hoc working group to review the proposal further.

Most of the countries who submitted information to the UNEP secretariat reported no production or use of PeCB (Czech Republic, Germany, Lithuania, Mauritius, Turkey, Canada), which is in agreement with the information in the dossier submitted. Past uses of PeCB are PeCB as a component in PCB products, in dyestuff carriers, as a fungicide and a flame retardant and as a chemical intermediate e.g. for the production of quintozene. Major U.S. and European manufacturers of quintozene have changed their manufacturing process to eliminate this use of PeCB. PeCB is also present at low levels as an impurity in several herbicides, pesticides and fungicides. In the United States, some pesticide manufacturers have changed their manufacturing processes to reduce the concentration of HCB impurities in their products, and these changes may have reduced concentrations of PeCB contaminants also. PeCB is also a low level degradation product of some pesticides. Literature sources show that PeCB is of no commercial significance. No trade or stockpiles have been reported.

Nowadays PeCB enters the environment through various sources of which PeCB as a byproduct of incomplete combustion is the largest current source. However, there is considerable uncertainty on the release of PeCB by various sources and available data are limited to the United States and Canada. The limited data available makes it difficult to provide a proper global estimate on amounts and trends. Total estimated annual global emissions of PeCBs based on the US-TRI database were 85.000 kg/yr.

PeCB should be considered as persistent given the estimated and experimental half lives in atmosphere, soils, sediments, and water. According to the available data PeCB has a high bioaccumulation potential. Log Kow values vary between 4.88 and 6.12, with recommended values of 5.17-5.18. BCF values range from 1085 - 23000 L/kg for fish, 833 – 4300 L/kg for mollusca, and 577 – 2258 L/kg for crustacea. Due to the fact that biotransformation of PeCB will be insignificant and the substance is very hydrophobic, the compound may also have a high biomagnification potential.
PeCB is moderately toxic to humans and is not classified as a carcinogen. Within the European Union PeCB is classified as a substance which is very toxic to aquatic organisms (LC50 for fish, daphnia or algae ≤ 1 mg/L). Limited data are available on terrestrial ecotoxicity and data for toxicity to birds are lacking.

Physical and chemical characteristics, such as water solubility, vapour pressure and Henry's Law Constant, are within the range of the other POPs. PeCB can be photo-oxidized in the atmosphere, largely through reactions with hydroxyl (OH) radicals. However, estimated half-lives of PeCB in air of 45 to 467 days were reported. Considering its physical and chemical characteristics and persistence in air, PeCB has a potential for long range transport through the atmosphere. This is supported by the presence of PeCB in environmental compartments, including biota, from remote regions.
PeCB is spread widely in the environment on a global scale. Measured levels of PeCB in abiotic and biotic media in remote regions such as the (ant) arctic environment are available, as well as monitoring data on PeCB in abiotic and biotic media of temperate zones. In general, data from developed countries indicates that concentrations of PeCB in the temperate zones of the world seem to decrease. For the (ant)arctic area, only recent data are available which do not allow to derive a trend.

Based on the available evidence, PeCB is likely, as result of its long range environmental transport, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

1 Introduction

The European Community and its Member States being Parties to the Stockholm Convention have proposed PeCB to be listed in Annex A, B and/or C to the Convention pursuant to paragraph 1 of Article 8 of the Convention. The complete original proposal is contained in document UNEP/POPS/POPRC.2/INF/5. A summary of the proposal prepared by the Secretariat was provided in document UNEP/POPS/POPRC.2/13.

The acceptance of the original proposal for further consideration by the Persistent Organic Pollutants Review Committee implies that the properties of the substance fulfilled the screening criteria set out in Annex D of the Convention. The next step is to prepare a risk profile for the substance as described in Annex E. This draft risk profile has been prepared following the decision of the Committee, at its second meeting in November 2006, to establish an ad hoc working group to review the proposal further in accordance with the provisions of the Convention (Decision POPRC-2/7).

All data in this document are presented according to the International System of Units (SI) and, therefore, many have been recalculated from other units in the data sources. Furthermore, all concentrations are presented based on kg or L (e.g. µg/kg or mL/L).

1.1 Chemical Identity of the proposed substance

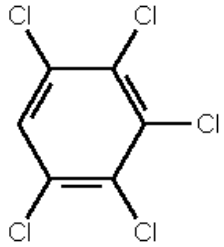
1.1.1 Names and registry numbers

PeCB belongs to the group of chlorobenzenes, which are characterised by a benzene ring in which the hydrogen atoms are substituted by one or more chlorines. The chlorobenzenes are neutral, thermally stable compounds with increasing stability and higher melting and boiling points with increasing chlorine substitution. PeCB has a very low solubility in water (Rossberg et al., 2006).

IUPAC Name: benzene, pentachloro-
CAS Chemical Name:
Synonyms: 1,2,3,4,5-pentachlorobenzene; Pentachlorobenzene; PCB; PeCB; QCB; quintochlorobenzene
CAS Registry Number: 608-93-5
EINECS Number: 210-172-0
Trade names: -

1.1.2 Structure

1,2,3,4,5-Pentachlorobenzene



1.1.3 Physico-chemical properties

Mackay et al (2006) provided a recommended value of 0.11 Pa at 20 ^{o}C. Water solubility at 25 ^{o}C varied between 0.135 and 3.46 mg/L, whereas the recommended value in various sources was around 0.55 mg/L. The log Kow values in Mackay et al (2006) varied between 4.88 and 6.12. This source and the PHYSPROP and CHEMFATE databases recommend values of 5.17-5.18 as most reliable. A full listing of the physical and chemical properties of PeCB is listed in Annex II, Table 1.1 in UNEP/POPS/POPRC.3/INF/21.

1.2 Conclusion of the Persistent Organic Pollutants Review Committee on the Annex D information on Pentachlorobenzene

At its second meeting on 6-10 November 2006, the POP Review Committee applied the screening criteria specified in Annex D to the Stockholm Convention, and concluded, in accordance with paragraph 4 (a) of Article 8 of the Convention, that it was satisfied that the screening criteria were fulfilled for PeCB. The Committee decided furthermore, in accordance with paragraph 6 of Article 8 of the Convention and paragraph 29 of decision SC-1/7 of the Conference of the Parties to the Stockholm Convention, to establish an ad hoc working group to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention. It invited, in accordance with paragraph 4 (a) of Article 8 of the Convention, Parties and observers to submit to the Secretariat the information specified in Annex E of the Convention before 2 February 2007.

1.3 Data sources

Information on the data sources (references and other literature) has been provided in UNEP/POPS/POPRC.3/INF/21 Annex I and III. Where the reviews mentioned above have been cited, the text quoted (or quoted with modifications) includes the references cited in the original review. These references are not shown individually in the reference list. The following parties and observers have answered the request for information specified in Annex E of the Convention: Canada, Czech Republic, Germany, Japan, Lithuania, Mauritius, Switzerland, Turkey, United States of America, International POPs Elimination Network (IPEN), and the International Council of Chemical Associations/World Chlorine Council (ICCA-WCC).

1.4 Status of the chemical under international conventions

PeCB is not included in any international convention. The European Commission has submitted a proposal to include PeCB to the Protocol to the 1979 Convention on Long Range Transboundary Air Pollution (LRTAP) on Persistent Organic Pollutants to the Executive Secretariat of the United Nations Economic Commission for Europe in 2006 (European Commission, 2007). The objective of the LRTAP POPs protocol is to control, reduce or eliminate discharges, emissions and losses of persistent organic pollutants. The UNECE Task Force on POPs identified the following options for possible inclusion of PeCB into the Protocol:
(a) Listing of PeCB in annex I to the Protocol in order to prevent production and use;
(b) Listing of PeCB in annex I and annex III to the Protocol. [ECE/EB.AIR/WG.5/2007/14]

PeCB is identified as a priority substance within the European Water Framework Directive (2000/60/EC). Within the list of these priority substances so-called priority hazardous substances are identified which are of particular concern for the freshwater, coastal and marine environment. These substances will be subject to cessation or phasing out of discharges, emissions and losses within 20 years after adoption of the Directive. The European Commission has proposed to include PeCB as a priority hazardous substance. [COM(2006) 397 final]. PeCB is listed on the OSPAR 1998 List of Candidate Substances (OSPAR, 1998).

2 Summary information relevant for the risk profile

2.1 Sources

Production, use and sources of release have been described extensively in the two documents submitted by Canada (Government of Canada, 1993, 2003), the proposed risk management strategy for PeCB by Canada (Environment Canada, 2005) and the document submitted by the ICCA/WCC (2007). Additional information was retrieved from the documents submitted by other Parties and Observers and from the open literature.

2.1.1. Production, trade, stockpiles

The submission document for PeCB reported that PeCB was not produced anymore within Europe and North America (Van de Plassche et al., 2002). PeCB has not been reported by EU Industry as an HPVC or LPVC (http://ecb.jrc.it/esis/). Most of the countries who submitted information to the UNEP secretariat reported no production (Canada , Czech Republic, Germany, Lithuania, Mauritius, Turkey, and USA). No intentional production was mentioned in the document submitted by the ICCA/WCC and according to Ullmann's Encyclopedia of Industrial Chemistry PeCB is of no economic significance (Rossberg et al., 2006). No trade or stockpiles have been reported.

2.1.2. Uses

Canada and the USA reported that there is no current domestic commercial demand for PeCB and that PeCB is not used as an end product. Ullmann's Encyclopedia of Industrial Chemistry does not mention any present use of PeCB (Rossberg et al., 2006). However, various past uses or unintentional uses of PeCB are mentioned in the literature:

1. PeCB was a component of a chlorobenzenes mixture used to reduce the viscosity of PCB products employed for heat transfer (Environment Canada, 2005), but new regulations prohibiting new uses of PCB-containing dielectric fluids resulted in a decline of the use of PeCB after 1980. PCBs are still in use in some old electrical equipment in North America and Europe so that there is a small potential for release of PeCB from this source (Environment Canada, 2005). It can be presumed that some PCBs are also still in use elsewhere in the world and some fraction of them contain PeCB. PCBs are being taken out of service in many countries of the world so that any related PeCB emissions are expected to decrease with time.

2. Formerly, PeCB and TeCB could be found in dyestuff carriers. The applications in dye carriers have been discontinued (Environment Canada, 2005). It is not clear from the Canadian document if PeCB, TeCB or both have been used in dyestuff carriers.

3. PeCB can be found as an impurity in several herbicides, pesticides and fungicides currently in use in Canada (Environment Canada, 2005). The US EPA carried out a study to assess the dietary cancer risk of hexachlorobenzene and PeCB as impurities in chlorothalonil, PCNB, picloram, and several other pesticides. PeCB was identified in pentachloronitrobenzene (quintozene), endosulfan, chlorpyrifos-methyl, atrazine, and clopyrilid, but not in simazine, chlorothalonil, picloram and dacthal (US EPA, 1998). Technical grade hexachlorobenzene (HCB) contains about 98 % HCB, 1.8 % pentachlorobenzene and 0.2 % 1,2,4,5-tetrachlorobenzene (WHO-IPCS, 1997). HCB is already listed in annex A and C of the Stockholm convention and it may thus be expected that HCB is of minor importance as a source for PeCB. The present situation for the other pesticides is unknown.

4. The use of PeCB as chemical intermediate is mentioned in WHO-IPCS (1991). So far, only the use as an intermediate in the manufacture of pentachloronitrobenzene (quintozene) has been found in the literature. PeCB is present as an impurity in this fungicide. Van de Plassche et al. (2002) report on the production and use of quintozene in various countries and indicated that the use outside the UNECE region is unknown. Van de Plassche et al. (2002) stated: 'Nowadays, quintozene is manufactured using another production process without PeCB. Amvac does not know of any current quintozene producer using PeCB as feedstock. They conclude that it is unlikely that there are any stockpiles of quintozene containing appreciable quantities of PeCB.' Feiler (2001) in ICCA/WCC (2007) reported that quintozene is now being made by chlorination of nitrobenzene instead of using PeCB as an intermediate. The available data suggest a decrease in PeCB use for the preparation of quintozene. However, this conclusion is based on data for Europe and North America only.

5. PeCB may have been used in the past as a fungicide and as a flame retardant (Van de Plassche et al., 2002). WHO-IPCS (1991) mentions that PeCB was formerly used in a pesticide to combat oyster drills. No further sources of these applications have been found.

6. Less than 0.1 kg per year of pure PeCB was imported into Canada from the United States for use as a laboratory reagent (Government of Canada, 1993). The use as laboratory reagent, based on data applicable to 1995, is also mentioned in Government of Canada (2003). The present situation is unknown.

From the data submitted and data in the literature it is obvious that production and use of PeCB in Europe and North America are negligible. The situation in other parts of the world is less clear.

2.1.3. Releases to the environment

The proposed risk management strategy for PeCB prepared by Environment Canada in 2005 mentions various routes through which PeCB can be released into the Canadian environment (Environment Canada, 2005). The main sources of release in Canada are barrel burning of house-hold waste , wood treatment plants and in service utility poles, pesticide use, dielectric fluid spill and cleanup, municipal solid waste incineration, hazardous waste incineration, magnesium production, solvent use and long range transport. As potential sources of release are mentioned: magnesium production (less than 2% of total annual releases), chlorinated solvents (negligible), secondary copper and aluminium processing (no data), chemical manufacturing (unlikely), iron and steel mills (scarcity of data), petroleum refineries (unlikely), wastewater treatment plants

(unlikely), textile mills (unlikely), long range transport (amount not known, expected to decrease) (Table 2.1, Annex II, UNEP/POPS/POPRC.3/INF/21).

The sources of release and potential sources are described more extensively in Environment Canada (2005). The total release provided by Environment Canada in the risk management strategy of PeCB (Environment Canada, 2005), 41.9 kg/yr, is a factor of 10 lower than the release of >580 kg/yr provided in the Priority substances list assessment report for PeCB (Government of Canada, 1993), submitted by Canada for the drafting of this Risk profile. The most significant sources in the Canadian risk management report (Environment Canada, 2005), barrel burning of household waste (21,93 kg/yr), municipal solid waste incineration (2.36 kg/yr), hazardous waste incineration (1.84 kg/yr) and magnesium production (1.53 kg/yr), were not identified as sources in 1993.

Data on releases of PeCB in the USA can be found in the U. S. EPA Toxics Release Inventory (TRI) (US EPA 2007a, http://www.epa.gov/tri/tridata/index.htm#pdr). The TRI contain release data for 2000 – 2004. Total releases vary between 1512 and 763 kg PeCB/yr and include air emissions, surface water discharges, underground injection, on site releases to land and transfers off-site to disposal. Air emissions between 2000 and 2004 were 74, 34, 37, 40 and 100 kg/yr respectively. Water emissions are in the same order of magnitude (See Table 2.2, Annex II, UNEP/POPS/POPRC.3/INF/21). The US also indicated in their comments that the data provided by TRI on "on-and-off-site releases" include amounts that would not be released to the environment because they were subject to treatment or other management activities. The TRI data does not cover all the industry sectors, which implies that total releases in the US can be much higher than those provided. Release data from other countries are not yet available.

The ICCA/WCC provided a document with an estimation of the annual global emissions of PeCB based on the U. S. Toxics Release Inventory (TRI) (ICCA/WCC, 2007). PeCB formation has been observed during combustion of municipal solid waste. The reported emission factors varied primarily due to differences in combustion conditions rather than fuel composition or waste content. The combustion of PVC may be a source of PeCB formation (Kim et al., 2004; Aracil et al., 2005; Muller et al., 1997), but the relative importance of this source is debated. There are other processes which produce a variety of chlorinated aromatics that may contribute to PeCB even if PeCB has not been explicitly detected and reported yet. Total estimated annual global emissions of PeCBs by ICCA/WCC (2007) were 85.000 kg/yr, about 2000 times the amount estimated for Canada and 850 times the total release of the United States. Most of the emission sources are similar with those provided in the Canadian risk management document (Environment Canada, 2005), but some are different. Hazardous waste incineration and wood treatment plants are lacking in the ICCA/WCC study, whereas combustion of coal and combustion of biomass, which amounts half of the total global emissions, are lacking in the Canadian study. Other PeCB sources could include quintozene degradation, titanium dioxide production, and ore treatment for the production of metals including magnesium, copper, niobium, and tantalum (ICCA/WCC 2007 citing Beck and Hansen, 1974; Knutzen and Oehme, 1989; Doering et al., 1992, and Vogelgesang 1986). No quantitative estimates are provided, because there is no quantitative information on which to base them. Although chemical manufacturing was thought to be unlikely as a source, the highest reported chlorobenzene concentrations in Canadian sediment have been observed near industrial sites (Government of Canada, 2003).

In conclusion, PeCB can enter the environment through various sources of which PeCB as a byproduct of incomplete combustion is the most significant current source. Nearly all fuels contain some chloride, especially biomass and waste. In industrial chlorination reactions it is possible that PeCB is produced as a byproduct and it probably accounts for some of the emissions reported. For a number of potential sources, such as copper and aluminum processing plants and steel mills no or limited data are available. From the data provided in the various documents one may expect a decrease of releases through past intentional use, due to phasing out of PeCB. In the case of unintentional releases as a byproduct of combustion a decrease can be expected in those cases where measures were taken to reduce the releases of other byproducts/emissions. The global estimate should be considered taking into account these uncertainties and the variation in industrial and waste handling processes among the various countries.

2.2 Environmental fate

2.2.1 Persistence

Pentachlorobenzene (PeCB) can be photo-oxidized in the atmosphere, largely through reactions with hydroxyl (OH) radicals (CEPA, 1993). There are no experimental data on atmospheric degradation, but the estimated half-life of PeCB is 45 to 467 days. For PeCB, the calculated half-life in air based on reaction with OH-radicals is 277 days (EPISUITE, US EPA, 2007b). Vulykh et al. (2005) estimate a half-life in air of 65 days based on modelling data. This estimate is the

result of degradation as well as dry and wet deposition and gaseous exchange with various surfaces. The atmospheric half-life of PeCB due to the degradation process only is estimated to be 155 days.

In the OECD TG 301C test PeCB was non-biodegradable (NITE, 2007). Photodegradation of PeCB is fast in surface water under sunlight irradiation: 41% loss after 24 hours (HSDB, February 2000). The half-life of PeCB in surface water was estimated to range from 194 to 1250 days, the estimated half-life for the anaerobic biodegradation in deeper water ranged from 776 to 1380 days (CEPA, 1993).

Wang et al. (1994) studied PeCB in spiked (4.5 µg/kg) and sewage sludge-amended soil (3 µg/kg) at 20-30 °C. Half of the dosage of PeCB is lost rapidly by volatilization, followed by degradation with half-lives of 187 days (spiked soil; 1.4 o.m.) to 1550 days (amended soil, 4.5% o.m.). Formation of bound residues is a relatively minor route of dissipation on soil. Scheunert et al. (1985) recovered 1% of a 2 mg/kg dosage as bound residue after 126 days. Under aerobic conditions PeCB is persistent in soil.

Beck and Hansen (1974) found disappearance half-lives based on duplicate samples, of 194 – 345 days in an aerobic loamy sand soil (1.9% o.m.); 18-20°C) treated at 7 mg/kg. Standard deviations were 20 to 25%. The 95% confidence limits are thus 112-726 and 289-3176 days. Since the values were based on duplicates, the total range of 112-3176 days represents the experimental results. Soils were kept in 10L buckets covered with two plastic sheets. During the experiment that lasted 600 days, water losses were compensated; apparently the total water content of the soil evaporated from the soils every 100 days (Bro-Rasmussen et al., 1970). The reported disappearance values are based on log(2)/k; instead of ln(2)/k. Correct half lives thus span the range of 260 – 7300 days. The contribution of volatilization of PeCB to these half lives is unknown.

Susarla et al. (1997) investigated the degradation of HCB in a methanogenic slurry of sandy sediment (<1% o.m.) with lake water (1:3 v/v), spiked at 1.14 mg/L. After 75% of the HCB had degraded after 150 days, the degradation of the primary metabolite PeCB followed first order kinetics with a half life of approximately 50 days at 25 °C. Masunaga et al. (1996) investigated the degradation of PeCB in sulfidogenic estuarine sediments that had been pre-exposed to various chemicals from local industries. Sediment slurries contained 272 g/kg solids; of which 12% can be lost by ignition, and were kept at 25°C. PeCB half-life was 18 days. In autoclaved samples the half-life was 990 days.

In sediment cores of Ketelmeer in The Netherlands, that had been selectively enriched with HCB to get a dechlorinating anaerobic community, PeCB is not persistent: the adapted anaerobic microflora gives half-lives of about 6 days at 25 °C when spiked at 50 µg/L (Beurskens et al., 1994). A mixture of clay loam soil (5.38% o.m.) and a sterile medium (50 g soil and 70 ml medium) was incubated anaerobically at room temperature after inoculation with a 10% slurry of an adapted microbial culture. The soil was spiked with 14.2 mg/L HCB, 25 mg/L PeCB, and 254.1 mg/L 1,2,4-TCB. Concentrations of PeCB decreased with a half-life of approximately 23 days. Chlorobenzene accumulated as the major metabolite after 80 and 142 days to 1 mmol/L (Ramanand et al., 1993). So far, only one bacterial strain which reductively dechlorinates chlorobenzenes has been isolated (Adrian and Görisch, 2002).

Comparison of PeCB concentrations in Ketelmeer sediment (The Netherlands) sampled and measured in 1972 to concentrations in samples taken in 1988 from sediment layers deposited around 1970, showed a small but statistically significant decline of 35%. HCB had decreased by 80%. Lower chlorinated benzenes like di- and tetrachlorinated benzenes had increased up to 80% (Beurskens et al., 1993). Lake Ketelmeer sediment contains 9-13% o.m. (Aarnoutse et al., 1996; Cornelissen and Gustafsson, 2004). In a UK soil (Woburn) that had received 25 separate sewage sludge applications in 20 years time (until 1961), approximately 21% of the added PeCB was still in the soil 30 years after application had stopped (Wang et al., 1995). This soil received about 25% of its dry weight in sludge. Assuming that sludge contained 80% organic matter and a 2% organic matter breakdown per year, the mean o.m. content was 15%. Input of HCB during these years was about 4 times higher than the PeCB input; and HCB residues also declined to 22% in these 30 years.

Experimental data on degradation of PeCB in water are lacking. PeCB is expected to dissipate from the water phase to the sediment or into the air. PeCB is persistent in soils and sediments under aerobic conditions. In anaerobic sediment-water slurries PeCB is considered persistent, except at temperatures above 10°C in combination with low organic matter contents. Higher organic matter contents seem to drastically increase the persistency. Actual field measurements of PeCB may overestimate persistency as a result of formation of PeCB from HCB. The true field half life of PeCB is estimated around 6 years in organic soil and sediment in the temperate zone.

PeCB should be considered as persistent given the magnitude of estimated and experimental half-lives in atmosphere, soils, sediments, and water. Persistence in the environment depends on the rate of photo-oxidation, the presence of oxygen and organic matter.

2.2.2 Bioaccumulation

PeCB is highly hydrophobic. Mackay et al. (2006) report log K_{ow} values between 4.88 and 6.12, with recommended values of 5.17-5.18. Therefore, it can be assumed that the compound has a high bioaccumulation potential. This is confirmed by the data shown in Table 2.3, Annex II, UNEP/POPS/POPRC.3/INF/21 which summarizes values considered reliable according to the Klimisch criteria (Klimisch, 1997).

BCFs range from 1085 - 23000 L/kg for fish; 833 – 4300 L/kg for mollusca, and 577 – 2258 L/kg for crustacea. It should be noted that for the lowest BCF data for fish it is not explicitly clear if exposure concentrations have been measured (Schuler et al., 2007). If these BCFs are based on nominal instead of measured exposure concentrations, then they are probably lower than the 'real' BCFs based on measured concentrations.

In conclusion, these values show that PeCB can be considered to have a high bioaccumulation potential. Due to the high logK_{ow} and the fact that biotransformation may be insignificant (Schuler et al., 2006, 2007), the compound may also have a biomagnification potential. However, data on the biomagnification of PeCB are lacking.

2.2.3 Potential for Long range environmental transport

Overall persistence and long-range transport potential were estimated for five new POP candidates (including PeCB) with the OECD Pov & LRTP Screening Tool using the input properties in the POPRC proposal documents (Wegmann et al, 2007). The tool does not provide absolute levels in the environment, but facilitates comparison with earlier identified POP substances. The authors conclude that, although there are considerable uncertainties in the chemical characteristics of the five chemicals investigated, the POP candidates (including PeCB) have Pov and LRTP properties similar to those of several earlier identified POPs.

There is also evidence for long range transport of PeCB based on calculations of the transport distance of PeCB through the atmosphere. Mantseva et al. (2004) developed a multi-compartment transport model for the evaluation of long-range atmospheric transport and deposition of POPs. Based on this model assessment a transport distance in Europe of over 8 000 km is calculated for PeCB. The model is described in detail by Vulykh et al. (2005) who assessed a transport distance of 8 256 km. Based on measured concentrations in air samples of North America an empirical estimation of 13 338 km was made for the long rang transport of PeCB through air (Shen et al., 2005). This distance is larger than that of the other organochlorine pesticides that were part of this study including the currently listed POPs dieldrin, DDT and heptachlor.

Monitoring data also indicate that PeCB is subject to long range transport. PeCB was detected in air and precipitation at various locations in the world, many of those far from its sources. In all air samples collected in 2000-2001 at the 40 sampling stations in North America (including 5 arctic stations), PeCB was detected. The measured concentrations were relatively constant across the continent, averaging 0.045 ng/m^3 with a range of 0.017 to 0.136 ng/m^3 (Shen et al., 2005). According to the authors, the small spatial variability across the Northern Hemisphere indicates that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global atmosphere. The presence of PeCB has been reported in several abiotic (air, rainwater, water, sediment and soil) and biotic (fishes, birds, mammals) matrices at remote regions including the arctic region and Antarctica. These are described in detail in the section Exposure.

In conclusion, modeling, monitoring data of PeCB in air, as well as PeCB's chemical properties indicate that this substance has a considerable potential for long range environmental transport. The presence of PeCB in matrices from remote regions, some that can only have received PeCB after transport via air, supports the conclusion that PeCB is subject to long range transport.

2.3 Exposure

PeCB is spread widely in the global environment. The first two sections will focus on the levels of PeCB in abiotic and biotic media in remote regions such as the (ant)arctic environment. The third section will focus on monitoring data on PeCB in abiotic and biotic media of temperate zones, as well as observed trends. The last section discusses human exposure.

2.3.1 Levels in abiotic environmental matrices of remote regions

Atmospheric concentrations of PeCB have been measured at various locations around the world. Concentrations in air collected at Alert (Northwest Territories, Canada) ranged from 0.0031 to 0.135 ng/m^3 (Government of Canada, 1993). Measured concentrations across North America averaged 0.045 ng/m^3 with a range of 0.017 to 0.136 ng/m^3 (Shen et al., 2005). They also observed that atmospheric levels of organochlorine compounds including PeCB increased with increasing elevation in the Canadian Rocky Mountains.

PeCB was found in all water samples collected during a study of the distribution of chlorinated organics in the North Pacific Ocean, the Bering and Chukchi streets (ICCA/WCC 2007 citing Strachan et al., 2001). Concentrations of PeCB in the dissolved phase averaged 0.016 ng/L, while suspended solids represented only a small fraction of the total amount of PeCB. Bottom sediment samples taken from harbours in northern Norway and the Kola Peninsula in the arctic contained PeCB in concentrations ranging from 2 to 5 µg/kg dry weight. PeCB concentrations in four Alaskan arctic lakes sampled from 1991 to 1993 averaged 0.10 ±0.10 µg/kg dry weight (ICCA/WCC, 2007 citing Allen-Gil et al., 1997). Concentrations in soil samples from the coastal areas of Victoria Land (Antarctica) varied between 0.4 and 1.3 µg/kg dry weight (Borghini et al., 2005). In these soil samples PeCB was the dominant organic compound. Muir et al. (1995 as cited by ICCA/WCC, 2007) reported PeCB in sediment of a series of remote lakes in northern Canada. Sediment surface layer concentrations (representing a period of time estimated between 1979-1988) of PeCB in these northern lake ranged from less than 0.01 to 0.73 µg/kg sediment.

2.3.2. Levels in biota of remote regions

Contamination of the environment and biota in remote regions can be a threat to vulnerable species and ecosystems. PeCB is detected in mosses, fish, penguin eggs, seals and predatory mammals in the arctic and antarctic regions.

PeCB concentrations in mosses from coastal areas of Victoria Land (Antarctica) varied between 1 and 2.4 µg/kg dry weight (Borghini et al., 2005). The mosses do not have a root system and their supply is largely dependent on atmospheric deposition. The measured PeCB concentrations in both mosses were higher than those of the currently listed POPs HCB and DDT that were also included in this study. PeCB concentrations in mosses growing in the Andean Mountains at elevations between 700-4500 m ranged from 0.2 – 2.4 µg/kg dw (Grimalt et al., 2004). This study shows that PeCB is likely subject to cold-trapping. An inverse relationship was established with higher PeCB concentrations at lower temperatures. A similar relationship was established for mountain soils in Tenerife (Ribes et al., 2002).

Concentrations (µg/kg wet weight) of PeCB in organs from fish from Alaska and Northwestern Russia and other arctic locations varied between 0.06 ±0.08 and 5.06 µg/kg wet weight PeCB (ICCA/WCC, 2007 citing Allen-Gil et al., 1997, citing Muir et al., 2003, citing Arend et al., 2001, Vorkamp et al., 2004; Corsolini et al., 2006).

In Greenland PeCB was observed at levels of 23 µg/kg lipid weight in ptarmigan liver (1.5 µg/kg wet weight) and 8 µg/kg lipid weight in kittiwake muscle (1.1 µg/kg wet weight) (Vorkamp et al., 2004). Adelie penguin eggs (Antarctic) contained 0.68 µg/kg ww PeCB (Corsolini et al., 2006).

Inuit hunter collected tissue samples of ringed seals from the east and west sides of the Northwater Polnya between Canada and Greenland during the spring of 1998 (ICCA/WCC, 2007 citing Fisk et al., 2002). The concentration (wet weight) of PeCB in these sampled ranged from 7.3 ±1.9 µg/kg in male ringed seals to 8.4 ±1.1 µg/kg in females from the west side. Seals from the east side (Quebec) contained 5.0 ±0.5 µg/kg (males) and 7.0 ±1.5 µg/kg (females). Seals from the White Sea in Northwestern Russia collected in the period 1992-1998 contained PeCB at concentrations ranging from 0.9 (bearded seal) to 12.0 µg/kg lipid weight (harp seal) in their blubber (ICCA/WCC, 2007 citing Muir et al., 2003). The mean concentration (± standard deviation of the 10 samples) of PeCB in 1992 was 11±2.0 ng/g lipid weight whereas the concentration of PeCB in 1998 was 5.0±1.8 ng/g lipid weight. PeCB concentrations in bowhead whales collected between 1994 and 1998 averaged at 0.3 ± 0.1 and 0.8 ± 0.1 µg/kg wet weight in liver and blubber, respectively (ICCA/WCC, 2007 citing Hoekstra et al., 2002). St. Lawrence Bay (Canada) Beluga Whale blubber was found to contain 24.5 (1.56 – 1510) µg/kg (lipid weight) PeCB for females and 144.5 (1.5 - 1500) µg/kg for males (ICCA/WCC, 2007 citing Hobbs et al., 2003). In Greenland, blubber of musk ox (captured between 1998 and 2001) was reported to contain 0.32 µg/kg lipid weight PeCB (equivalent to 0.29 µg/kg ww) (Vorkamp et al., 2004).

PeCB has also been detected in polar bears. The compound was present in all 15 fat and plasma samples taken from polar bears from the arctic Svalbard islands (Gabrielsen et al., 2004) at an average concentration of 7.9 and a maximum of

13.9 µg/kg (wet weight). Similar concentrations are observed in polar bears from Alaska, Canada and East-Greenland, according to the authors. Concentrations and body burdens of chlorobenzenes (including PeCB) in polar bears of different ages have been studied before and after their seasonal fasts (ICCA/WCC, 2007 citing Polischuk et al., 2002). The authors conclude that no PeCB is metabolized or excreted during the fast, leading to increasing concentrations of the compound in fat tissue. Amounts of PeCB in cubs is reported to be greater than in adults due to the fact that nursing bear cubs receive an increased amount of PeCB.

The accumulation of PeCB has also been measured in the arctic fox during 1999-2001 (ICCA/WCC 2007, citing Hoekstra et al., 2003). The animals were collected some distance from human habitation to minimize effects of garbage scavenging. About 20 animals were collected at each site. PeCB concentrations (µg/kg) found in arctic foxes were0.61 ± 0.12 in muscle (Arivat), 0.29 ± 0.06 in muscle (Holman), 0.57 ± 0.11 in liver (Holman), 0.55 ± 0.20 in muscle (Barrow) and 0.73 ± 0.17 in liver (Barrow). Hoydal and Dam (2003) measured concentrations of <0.1 – 37 ng/g wet weight in biota captured in the environment of the Faroe Islands.

King et al (2003) studied the chlorobenzenes spilled after an accident in the Gulf of St Lawrence. There was a rapid decline in tri- to peCB concentrations in snow crabs from sampling location 1 [near the spill] between 1996 and 1998. From 1998 to 2000 the chlorobenzenes concentrations in snow crabs persisted at low levels. In 1996, chlorobenzenes concentrations at locations 2 to 11 were much lower than at location 1, but showed no consistent decrease with time.

2.3.3. Levels at temperate regions including trends

A large quantity of monitoring data exists on PeCB detected in abiotic matrices as well as in biota in temperate zones, mainly originating from developed countries. In general, concentrations of PeCB in the temperate zones of the world seem to decrease. This pattern is representative for that of most POPs. For the (ant)arctic area, only recent data are available which do not allow to derive a trend.

A study of the influence of emission sources on atmospheric PeCB concentrations in Germany showed that concentrations were higher at industrial or urban locations (ranging from 0.057 to 0.286 ng/m^3) than at a rural reference site (0.031 ng/m^3) (ICCA/WCC 2007 citing Wenzel et al., 2006). Concentrations at the rural site are comparable to the average atmospheric concentration measured by the Integrated Atmospheric Deposition Network (IADN) above the North American Great Lakes in 2000, i.e., about 0.072 ng/m^3 (ICCA/WCC 2007 citing Buehler et al., 2004)

A clear trend of the presence of PeCB in the environment can be derived from its presence in sediment cores. Sediment cores from the industrially impacted area from Lake Ontario near the mouth of the Niagara River (Canada) show an increase in PeCB concentration from early 1900 until the period 1960-1970 (peak concentration of over 100 µg/kg) after which concentrations declined to about 10% of the peak concentration by 1980 (ICCA/WCC, 2007 citing Durham and Oliver, 1983 and NYDEC, 1998). Also PeCB concentrations in the Niagara river water dropped from 0.351 to 0.093 ng/L during the period 1987-1997 (ICCA/WCC 2007, citing Williams et al., 2000). However, data in the mussel watch programme for the Niagara river do not show a decrease in PeCB concentrations between 1997 and 2000 on several locations (Ministry of the Environment Ontario, 1999, 2003). Concentrations of PeCB in sediment of the Ketelmeer in The Netherlands dropped by 37% in the period 1972-1988 (Beurskens et al., 1993).

PeCB concentrations in Herring Gull eggs from Muggs Island / Leslie spit (Canada) have dropped from 50 µg/kg in 1970 to non-detected at 1 µg/kg in the mid 1990s (ICCA/WCC 2007, citing Bishop et al., 1992; Petit et al., 1994; Pekarik et al., 1998; Jermyn-Gee et al., 2005; Havelka, 2006). Calambokidis et al (1999) studied persistent pollutants in Harbor Seals (Phoca vitulina) in Puget Harbor (US) during the period 1984-1997. They concluded that total TEQ showed a near significant decline by year (p=0.07) and that other pesticides also showed general declining trends. Only for HCB, total chlorobenzenes, and chlordanes was the decline statistically significant. Only recent data (last 15 years) are summarized in Table 2.4 for abiotic and Table 2.5 for biota matrices in Annex II, UNEP/POPS/POPRC.3/INF/21.

During a survey within the Danube Regional Project for the European Water Framework Directive, PeCB was detected in almost all sediment samples at concentration levels of 0.0001 – 3.5 mg/kg and in most of the suspended solid samples at concentration levels of 0.001 – 0.028 mg/kg (Slobodník and Dogterom, 2003). The ATSDR database from the US Government contains 41 records of polluted sites with PeCB. Maximum concentrations of PeCBs at these sites vary between 147 and 5100 mg/kg in sediments and between 0.43 and 2040 mg/kg in soil. Concentrations in fish vary between 0.00019 and 2.4 µg/g (ATSDR, 2007). Neither references mention if these concentrations are based on wet or dry weight basis.

2.3.4. Human exposure

Occupational exposure to PeCB may be through inhalation and dermal contact with this compound at workplaces where PeCB is produced or used. Examples are wood treatment plants, dielectric fluid spill and cleanup, municipal solid waste incinerators, hazardous waste incinerators, and magnesium production plants. Exposure may also arise in occupational settings where the pesticide quintozene is produced and used. The general population may be exposed to PeCB via inhalation of ambient air, ingestion of food and drinking water. Case reports of adverse effects in individuals, or epidemiological studies of populations exposed to PeCB have not been identified (Government of Canada, 1993).

PeCB has been detected in breast milk and found to accumulate in human placenta (Shen et al., 2007). The mean concentration of PeCB in the breast milk of Canadian women taken 3 to 4 weeks after parturition was < 1 µg/kg (trace) with a maximum value of 1 µg/kg. In this survey, the compound was detected in 97% of the 210 samples analyzed (detection limit and sampling period unspecified) (Government of Canada, 1993 citing Mes *et al.,* 1986). In the breast milk of women of Canadian indigenous population, "trace" (< 1 µg/kg) amounts of PeCB were observed in 17% of the 18 samples (detection limit not specified) (Government of Canada, 1993 citing Davies and Mes, 1987). Two other studies investigating PeCB in human milk reported concentrations in the range of 1 to 5 µg/kg (WHO-IPCS, 1991). PeCB has also been measured in abdominal, mammary, and perirenal fat tissue from 27 adult Finnish males and females (Smeds and Saukko, 2001). Workers with occupational exposure to PeCB were found to have higher levels of the substance in blood than control groups (Lunde and Bjorseth, 1977).

2.3.5. Bioavailability

The Environmental Health Criteria on chlorobenzenes (WHO/IPCS, 1991) concluded that limited evidence was available showing that sediment-bound residues of chlorobenzenes are bioavailable to organisms; i.e., aquatic invertebrates can take up residues from sediment, and plants, from soil. Since then, more information on the bioavailability of hydrophobic substances became available.

Bioavailability of chlorobenzenes is inversely proportional to the organic carbon content of the soil or sediment (Government of Canada (2003) citing e.g. van Gestel and Ma, 1988; Hulzebos et al., 1993). It was furthermore stated in the Canadian Follow-up Report that persistent substances can remain bioavailable for long periods of time, thereby increasing the probability and duration of potential exposure relative to compounds that do not persist in the environment.

It is generally accepted that not all fractions of organic pollutants bound on sediments or soils are equally toxic due to their various resistances to desorption. The resistant and sequestered fractions of PeCB are environmentally less harmful than the more readily desorbing, labile, or available fractions. The large fraction of water soluble organic matter in the sediments is potentially highly mobile and could be easily resuspended or leached to the overlying water column. If the soluble organic matter carries the major amount of PeCBs as expected, continuous contamination of the water body from the sediments is very likely. Qiao & Farrell (1996) carried out experiments with PeCB in rainbow trout and concluded that mass balance analysis suggests that the appearance of HCBP and PeCB in the fish after 6 days could not be accounted for solely by the amount of chemical dissolved in the water at the time when the fish were introduced. The chemical uptake in fish with the pharynx plugged, to eliminate the gut uptake route, was similar to that in control fish. Because direct access to bottom sediments did not alter chemical uptake, they concluded that hydrophobic chemicals such as PeCB and HCBP associated with suspended sediments from the Fraser River can readily desorb and be taken up across the gill. Åkerblom (2007) concluded that pesticide sorption to organic particles in standardized toxicity tests is fast and efficient and that substances bound to the sediment may act as a reservoir, continuously supplying the pore water with low pesticide concentrations.

As organic pollutants bound to sediment or organic matter may still become available, an evaluation should focus on sorption and desorption kinetics of PeCB and modifying circumstances rather than on statements on bioavailability. Such data are however scarce.

2.4 Hazard assessment for endpoints of concern

2.4.1. Toxicity

Toxicokinetics
Toxicokinetic studies with rats show that after an oral dose, the substance is distributed to the blood and tissues (Umegaki et al., 1993; ICCA/WCC, 2007 citing Thomas and coauthors). Linder et al., (1980) observed that rats fed with PeCB accumulated approximately 1.5 – 2.2 times the dietary concentration in their adipose tissues. Umegaki et al., (1993) studied the kinetics of PeCB in blood and tissues of rats given a single oral dose by gavage of either 15 mg or 20 mg. PeCB was observed in the blood, liver, kidney, brain, and fat tissue as well as in the feces (4.8% of the dose). In the blood, also the major metabolite pentachlorophenol was observed.

Den Besten et al (1994) studied the urinary metabolite profile of PeCB in the rat after dietary exposure for 13 weeks. PeCB was metabolized to the major metabolites pentachlorophenol (PCP), 2,3,4,5-tetrachlorophenol (TCP), mercaptotetrachloro-phenol (MTCP), the glucuronide derivative of pentachlorothiophenol (PCTP), and the minor metabolites tetrachlorohydroquinone (TCHQ), methylthiotetrachlorophenol (MeTTCP), hydroxytetrachlorophenyl sulphoxide (HTCPS), and bis(methylthio)-trichlorophenol (bis-MeTTriCP). The study also revealed that oxidation of PeCB to 2,3,4,5-TCP was not mediated by cytochrome P450IIIA. In the urine of rabbits exposed to a single oral dose of PeCB, also pentachlorophenol and 2,3,4,5-tetrachlorophenol was observed (Slooff et al., 1991, citing Kohli et al., 1976).

A study with coyotes showed that PeCB is excreted in the faeces (Johnston et al., 1997). Coyotes were dosed with PeCB (single dose of 130, 260 or 520 mg). In both studied matrices, faeces and adipose tissue, residues of PeCB were determined. PeCB was detectable in faeces for six months post-dosing. In the faeces, also the metabolites pentachlorophenol and 2,3,4,5-tetrachlorophenol were detected.

Data on other than the oral exposure route are limited available. WHO-ICPS (1991) indicates that the chlorobenzenes are less readily absorbed through the skin, but that levels of the same isomer of the chlorobenzenes in various tissues appear to be similar, regardless of the route of administration. The ingestion of a lethal dose leads to respiratory paralysis, while the inhalation of high doses causes local irritation and depression of the central nervous system WHO-ICPS (1991).

Acute toxicity
PeCB has been tested on rats and mice. Results of acute toxicity tests are available for oral and dermal exposure (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). LD_{50}s for PeCB (by gavage in peanut oil) are 940 to 1125 mg/kg bw in adult and weanling rats and 1175 and 1370 mg/kg bw in Swiss Webster mice (Linder et al., 1980 cited in Government of Canada, 1993). Decreased activity and tremors were observed in both species at sublethal doses; the kidneys, liver and adrenal glands of rats were also enlarged. In some rats, the gastric mucosa was hyperaemic, and a slight reddish fluorescence of the gastrointestinal tract was observed in both rats and mice under ultraviolet light, suggesting porphyria (Government of Canada, 1993). In the study of Allen et al., (1979, cited in Slooff, 1991), a LD50 of 250 mg/kg bw was observed in rats. Ariyoshi et al., (1975, cited in Slooff, 1991) observed an increase of cytochrome P450 content in rats as well as an increase in the activity of two hepatic enzymes after oral administration of 250 mg/kg bw once daily during 3 days.

To determine a dermal LD50 one concentration (i.e., 2500 mg/kg bw) was tested on rats, but no toxic effects were seen at this dose (Linder et al., 1980 cited in Slooff, 1991). Based on this study, a NOEC of > 2500 mg/kg bw can be established for dermal exposure.

PeCB is classified in the European ESIS database as R22, harmful if swallowed (European Chemicals Bureau, 2007). WHO-IPCS (1991) reported that data on skin and eye irritation potential and on sensitization potential were mainly restricted to 1,2,4-trichlorobenzene. No data were available for PeCB.

Subchronic toxicity

PeCB has been tested on rats and mice. Results of (sub)chronic toxicity tests are available for dietary exposure, see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21. In female Sherman rats ingesting diets containing 500 mg/kg and greater (> 37.5 mg/kg bw/day) PeCB for 100 days, there was an increase in liver weight and hypertrophy of hepatic cells (Linder et al., 1980). There was also an increase in kidney weights and renal hyaline droplet formation in males at exposure levels ≥125 mg/kg (equivalent to ≥8.3 mg/kg bw/day). In addition, at 1 000 mg/kg (equivalent to 81.1 mg/kg bw/day for males and 78.7 mg/kg bw/day for females), the effects observed were: an increase in adrenal weight and focal areas of renal tubular atrophy and interstitial lymphocytic infiltration in males; an increase in kidney weight in females; a decrease in haemoglobin and an increase in white blood cells in both sexes; and decreases in red blood cells and haematocrit in males. The no-observed-effect-level (NOEL) in female rats, derived on the basis of the results of this study, was 250 mg/kg (equivalent to 18.2 mg/kg bw/day); the lowest-observed-effect-level (LOEL) in males was 125 mg/kg (equivalent to 8.3 mg/kg bw/day) (calculations by Government of Canada, 1993).

In a study of NTP (1991) rats and mice were exposed to PeCB through their diet. Observed effects were among others: decreases in the mean body weights of male rats at exposure levels ≥ 1 000 mg/kg diet and in females at all concentrations (≥ 33 mg/kg), increase in absolute and relative liver weights (33 mg/kg in males), centrilobular hepatocellular hypertrophy (as low as 330 mg/kg for males), increases in kidney weights and renal histopathological effects at concentrations as low as 100 mg/kg, nephrotoxic effects in females (≥ 1 000 mg/kg), increase of the concentration of protein in the urine in male and female rats at ≥ 1 000 mg/kg, decrease of free thyroxin and total thyroxin concentrations in male and female rats indicating moderate hypothyroxinemia and abnormalities were observed at concentrations of ≥330 mg/kg in females and ≥ 1 000 mg/kg in males. The incidence of abnormal sperm in males was also increased at both dietary concentrations at which it was examined (330 and 2 000 mg/kg). On the basis of histopathological lesions, the authors considered the NOELs to be 33 mg/kg in male rats and 330 mg/kg in females (approximately 2.4 and 24 mg/kg bw/day, respectively) (calculations by Government of Canada, 1993).

In PeCB exposed mice in the same study NTP (1991), observed effects were among others: ventral swelling and ruffled fur (2 000 mg/kg), increase of kidney weights (≥330 mg/kg in males), functional effects on the thyroid at all concentrations in both sexes (≥33 mg/kg), increase in liver weights (at 100 mg/kg in males). The only exposure-related histological lesion in mice of either sex was centrilobular hepatocellular hypertrophy and minimal necrosis, observed at all concentrations in males and at ≥ 330 mg/kg (equivalent to 68 mg/kg bw/day) in females. On the basis of the histopathological lesions, the authors considered the NOEL in female mice to be 100 mg/kg (approximately 22 mg/kg bw/day). No NOEL for males could be established (LOEL = 33 mg/kg or approximately 5.2 mg/kg bw/day) (calculations by Government of Canada, 1993).

In contrast to ingestion, WHO-ICPS (1991) does not provide data on dermal exposure and inhalation of PeCB, which indicates that such data are limited. The lowest NOELs reported for the ingestion of PeCB were between 2.4 and 24 mg/kg per day. Ingestion of high doses by rats and mice resulted in hepatic and renal toxicity.

Mutagenicity and carcinogenicity

Epidemiological studies of exposed populations are not available and information on carcinogenicity in experimental animals has not been identified. PeCB showed no genotoxicity in a small number of *in vitro* and *in vivo* studies of a limited range of investigated genetic endpoints.

PeCB has been tested negative in the Ames test (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). Based on limited available data, mutagenicity in *S. typhimurium* with and without metabolic activation, effects on chromosomes in Chinese Hamster ovary cells *in vitro,* and micronuclei in peripheral blood smears in animals from the NTP sub-chronic study, PeCB has been assessed as not genotoxic (Haworth et al., 1983 and NTP, 1991 cited in Government of Canada, 1993). Several studies (Thomas et al., 1998 and Gustafson et al., 2000; Ying et al., 2001) investigated the tumor-promoting activity in medium term carcinogenicity assays of various chlorobenzene isomers including PeCB. The results suggest that PeCB promotes glutathione *S*-transferase (GSTP1-1) positive preneoplastic foci formation in rat liver, following diethylnitrosamine (DEN) initiation.

Both Health Canada and U.S. EPA have reviewed the cancer toxicity data of PeCB. The cancer weight-of-evidence classification is based on all routes of exposure. Neither group derived a risk value. Both groups concluded that the substance is unclassifiable with respect to its carcinogenicity in humans due to the lack of data. PeCB is not classified as a carcinogen by IARC or by the EU (European ESIS database).

Reproductive and developmental toxicity
Available studies concerning the embryotoxicity, foetotoxicity and teratogenicity of PeCB include one study in rats (and one in mice (Villeneuve and Khera, 1975 and Courtney et al., 1977, cited in Government of Canada, 1993) (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). Results of the study of Villeneuve and Khera (1975) indicated that PeCB is foetotoxic (an increased incidence of extra ribs and sternal defects was observed in the offspring) at maternal exposure doses of 50 mg/kg bw/day. The exposure concentration was below the concentration that induced toxic effects in the mothers. In mice, no embryotoxic, foetotoxic or teratogenic effects were observed in the offspring at doses which were maternally toxic (50 mg/kg bw/day and above)(Courtney et al., 1977). In the only identified study on reproductive toxicity of PeCB, Linder et al. (1980) reported that suckling pups of PeCB treated mothers fed ≥ 250 mg/kg developed tremors (LOAEL = 18.2 mg/kg/day). At 1000 mg/kg, most sucklings died before weaning.

The studies above are also cited in WHO-ICPS (1991) who conclude that there is some evidence that the higher chlorinated benzenes (TCBs, TeCBs, PeCB) are embryotoxic or fetotoxic at dose levels that are not maternally toxic. WHO-ICPS (1991) also remark that the available data are not consistent and that the toxicities of the various isomers of the TCBs and TeCBs for the mother and fetus vary considerably. Most reported effect (NOAEL, NOEL) and no effect levels (LOAEL, LOEL) vary between 17 and 200 mg/kg PeCB per day.

PeCB showed high oral toxicity with LD50 doses as low as 250 mg/kg bw in rats. From the limited data available, dermal LD50s are higher. Data on skin and eye irritation potential and on sensitization potential are limited. In contrast to ingestion, WHO-ICPS (1991) does not provide data on dermal exposure and inhalation of PeCB, which indicates that such data are limited. The lowest NOELs reported for the ingestion of PeCB were between 2.4 and 24 mg/kg bw per day. Ingestion of high doses by rats and mice resulted in hepatic and renal toxicity.

PeCB showed no genotoxicity in a small number of *in vitro* and *in vivo* studies of a limited range of investigated genetic endpoints. Data on mutagenity and carcinogenity are limited. Both Health Canada and US-EPA concluded that the PeCB is unclassifiable with respect to its carcinogenicity in humans due to the lack of data. PeCB is not classified as a carcinogen by IARC, nor by the EU (European ESIS database). There is some evidence that PeCB is embryotoxic or fetotoxic at dose levels that are not maternally toxic.

2.4.2. Ecotoxicity

Aquatic toxicity
Acute and chronic toxicity data are available for both freshwater (see Table 2.7, Annex II, UNEP/POPS/POPRC.3/INF/21) and marine organisms (see Table 2.8, Annex II, UNEP/POPS/POPRC.3/INF/21). The lowest acute toxicity values are 100 µg/L for freshwater fish species (EC50) and 87 µg/L for a marine crustacean (LC50). The lowest chronic values (NOECs) are 2 µg/L for a freshwater fish and 14 µg/L for a marine crustacean. According to these findings, species sensitive to PeCB can be found in both the freshwater and the marine environment.

Within the European Union PeCB is classified as a substance which is very toxic to aquatic organisms and which may cause long-term adverse effects in the aquatic environment (Risk phrases N; R50 and R53) (European Chemicals Bureau, 2007). This classification is based on the fact that the substance is very toxic to fish, daphnia or algae (LC50 ≤1 mg/L) and the substance is not readily degradable or bioaccumulative.

Soil and sediment toxicity
Limited data are available for soil and sediment. Tests with various chlorobenzenes were carried out by Van Gestel et al (1991). Two earthworm species were raised on a natural sandy soil (KOBG) and an artificial OECD standard soil. Average LC50 values varied between 115 and 238 mg/kg dry weight, whereas LC50 values in pore water varied between 55.1-117.7 µg/L. Van Gestel et al (1991) concluded that based on pore water concentrations earthworms are more sensitive to PeCB than fish, but that this may be due to differences in test design.

Only one study on the toxicity of PeCB in plants was identified. Duplicate tests were carried out in which *Lactuca sativa* seedlings were grown on OECD soil contaminated with PeCB. The seedlings were harvested after 7 and 14 days. EC50 values varied between 56 and 862 mg/kg dw (Hulzebos et al. 1993). Experiments in solution resulted in an EC50 value of ±1.0 mg/L. Details of the tests are provided in Table 2.9, Annex II, UNEP/POPS/POPRC.3/INF/21.

Toxicity to birds
No toxicity data on birds are available for PeCB.

Multiple chemicals and toxicological interactions
Annex E request information on toxicological interactions involving multiple chemicals (Annex E, b). Limited information is available on this subject. Yoo et al (2003) report on their studies on the kinetics of PeCB: "The kinetics and toxicity of pentachlorobenzene were assessed using a freshwater (*Hyalella azteca*) and marine amphipod (*Leptocheirus plumulosus*). The results of these studies demonstrated the additive toxicity of PeCB with other organic chemicals (pyrene)."

Comparison of exposure and effect data
Several methods, exposure routes and species with very different feeding strategies were used by ICCA/WCC to determine the lethal and critical body burden of PeCB. Based on the general knowledge on substances with a narcotic mode of action and the available data on PeCB, such as the *Hyalella* growth/mortality study and other information discussed, an estimation of 25 mg/kg PeCB/kg (0.1 mmol) was tentatively proposed by ICCA/WCC (2007) as a Critical Body Burden for chronic effects.

A very recent publication of Schuler et al (2007b) has reported critical whole body residues of pentachlorobenzene of 58 mg/kg and 5 mg/kg for *Hyalella azteca* and *Chironomus tentans* respectively. These residue levels are lower than the highest concentrations reported for temperate regions in Table 2.5 in the Annex POPRC3/INF21 and 150-1500 times higher than the highest values of <0.1 – 37 µg/kg wet weight in biota reported for the Faroe Islands by Hoydal and Dam (2003). Other concentrations reported from remote areas are of the same order of maginitude, e.g. Adelie penguin eggs (Antartic) contained 0.68 µg/kg ww (Corsolini et al., 2006) and whole body concentrations from fish in the White Sea were up to 5 µg/kg ww (ICCA/WCC, 2007 citing Muir et al., 2003).

The World Chlorine Council (ICCA/WCC, 2007) has provided information related to two other approaches. The first approach focused on PeCB organic carbon concentrations in sediments from Canadian lakes and showed that in both rural and remote sites, PeCB organic carbon concentrations were 410-75000 times lower than Environment Canada's "estimated no effect value" for freshwater benthic organisms. In the second approach, comparisons were made between exposure estimations for a pisciverous predator and for polar bear using assumptions considered by the WCC as "worst case assumptions", and effect levels derived from human Reference Dose and Tolerable Daily Intakes from USA and Canada. These estimations of exposure were 13 and 20 times lower than the derived effect levels, respectively.

The available information has not been sufficient for confirming if the values given above represent real critical body burdens or just expressions of internal dose or whole body residues levels. Both concepts have fundamental differences related to the understanding of the mechanism of action of the chemical. Nevertheless, it should be noted that expressing the toxicological effects as internal dose or, whenever possible, critical body burdens, improves the effect assessment but only reduces partially its uncertainty. In addition, all the uncertainty related to the exposure assessment remains. While monitoring levels above critical body burdens or internal toxic doses clearly indicate a risk, the fact that current measured concentrations are below these triggers should in no case be interpreted as a confirmation of the absence of risk, particularly in the assessment of POPs and POPs candidates.

3 Synthesis of the information

Pentachlorobenzene is a chlorinated organic compound. According to available data, pentachlorobenzene should be considered as persistent given the considerable number of estimated and experimental half-lives in atmosphere, soils, sediments, and water. Persistence in the environment depends on the rate of photo-oxidation, the presence of oxygen and organic matter. Pentachlorobenzene meets the criterion on bioaccumulation. BCF values for pentachlorobenzene range from 1085 – 23 000 L/kg for fish, 833 – 4 300 L/kg for mollusca, and 577 – 2258 L/kg for crustacean. Biomagnification may be expected due to the high $\log K_{ow}$ and the fact that biotransformation is insignificant. However, data on the biomagnification of pentachlorobenzene are lacking.

The available data support the potential for long range transport of pentachlorobenzene. The physical and chemical characteristics are within the range of the other POPs. Model estimations on the transport distance resulted in distances of 8 000 km, while estimates based on air measurements suggested 13 338 km. Monitoring data also indicate that PeCB is subject to long range transport. PeCB was detected in air and precipitation at various locations in the world, many of those

far from its sources. The small spatial variability across the Northern Hemisphere observed in some studies also indicate that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global hemisphere.

A large quantity of monitoring data exists on PeCB detected in abiotic matrices as well as in biota in temperate zones, mainly originating from developed countries. In general, concentrations of PeCB in the temperate zones of the world seem to be decreasing. This pattern is representative for most POPs. For the Arctic and Antarctic area, only recent data are available which do not enable a trend to be derived.

Case reports of adverse effects in individuals, or epidemiological studies of populations exposed to PeCB have not been identified. The only risk phrase for pentachlorobenzene in the European ESIS database is R22, harmful if swallowed. Lowest LD50 observed for acute exposure was 250 mg/kg bw. Repeat-dose mammalian toxicity tests result in evidence of hepatic, nephric, hematological, and developmental toxicity for this chemical. According to the American Hazardous Substances Data Bank pentachlorobenzene is not classifiable as to human carcinogenicity because there are no human data and no animal data available. PeCB is moderately toxic to humans. Pentachlorobenzene is very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. Data on soil and sediment organisms are limited or lacking.

Bioavailability of pentachlorobenzene is inversely proportional to the organic carbon content of the soil or sediment. However, experiments suggest that hydrophobic chemicals bound to the sediment or suspended sediment may act as a reservoir and result in continuous uptake. There are limited quantitative data on this process for pentachlorobenzene.

The data from Europe and North America show that production and use of pentachlorobenzene has ceased over the last decades, but it cannot be excluded that PeCB is produced or used elsewhere. Unintentional release of pentachlorobenzene as a byproduct of incomplete combustion appears to be the largest current source. However, this conclusion is based on data for Europe and North America only.

An important element in the assessment of the potential risk of PeCB is the assessment of the risk associated with intended and non-intended uses. This distinction is not possible with the current information but it should be very useful for the decision making process. Such an analysis would request precise information on the amounts released by intentional production and use in the past and the unintentional releases plus a correction for the degradation rate of the substance after release. Data on past production and use are currently lacking.

PeCB meets all screening criteria on long range transport, persistence, bioaccumulation and toxicity. Generally, environmental concentrations seem to be decreasing. Production and use have ceased in Europe and North America, but data from other parts of the world are limited. Unintentional release as a byproduct of incomplete combustion appears to be the most important source of PeCB in the environment.

The available information does not allow the Committee to distinguish between the environmental burden caused by intentional use and the burden caused by the unintentional production and releases of PentaCB. Clarifying this distinction would help the Committee to prepare the risk management evaluation and to formulate its final conclusions. Hence, additional data on this issue should be sought.

4 Concluding statement

PeCB is persistent in the environment and is bioaccumulative. The small spatial variability in the ranges of air concentrations across the Northern Hemisphere indicates that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global hemisphere. There are monitoring data from remote areas, backed up by modelling results that suggest that pentachlorobenzene can be transported over great distances. Pentachlorobenzene is moderately toxic to humans, but is very toxic to aquatic organisms.

As a result of the long range transport of PeCB, neither a single country nor a group of countries alone can abate the pollution caused by this substance. Unintentional release of PeCB, as a byproduct of incomplete combustion, appears to be the largest current source. Measures to reduce these releases can only be taken at a global scale. Although the production and use of pentachlorobenzene seems to have ceased in most countries, its reintroduction remains possible. This could lead to increased releases and levels in the environment. Based on the available evidence, PeCB is likely, as a result of its long

range environmental transport, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

As the distinction between the environmental burden caused by intentional use and the burden caused by unintentional production and releases would support the preparation of the risk management evaluation and making the final recommendation, the Committee considers that an additional effort should be made to fill this gap.

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別添3

α－ヘキサクロロシクロヘキサンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 生分解は嫌気的条件で起こる。 【光分解性】 日光照射下での水溶液中の半減期は 4-6 日。固い表面上では半減期は 91 時間。 【加水分解性】 ・半減期は温度依存性を示し、pH 8 (20℃) で 0.8 年。pH 7.8 (5℃) で 26 年。北極海で 63 年 【半減期】 ・水中：高緯度北極圏湖沼で 0.6 年-1.4 年と推定。東部北極海ではｴﾅﾝﾁｵ選択性の分解により、(＋)異性体は 5.9 年、(-)異性体が 23.1 年。加水分解が考慮される場合は、(＋)異性体は 5.4 年、(-)異性体が 16.9 年。 ・土壌中：亜熱帯地域のｲﾝﾄﾞの砂質ﾛｰﾑで 55 日。温帯地域では 161 日。ｶﾅﾀﾞの砂質ﾛｰﾑでの長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 15 年後に 4%が残留。高緯度北極圏湖沼堆積物で 2 年と推定。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKOW=3.8 【BCF (経鰓的生物濃縮係数)】 ・単細胞緑藻類：BCF=200-2700 (乾重量ﾍﾞｰｽ) ・鞭毛藻：BCF=13000(脂質ﾍﾞｰｽ) ・無脊椎動物：BCF=60(脂質ﾍﾞｰｽ 8000)-2750 ・ｾﾞﾌﾞﾗﾌｨｼｭ：BCF=1100(OECD TG 305E) ・ﾆｼﾞﾏｽ：BCF=1100-2800 【BMF (経口的生物濃縮係数)】 ・動物ﾌﾟﾗﾝｸﾄﾝ、ﾎｯｷｮｸｸﾀﾞﾗ：BMFs＞1 ・海鳥 (ﾋﾒｳﾐｽｽﾞﾒとﾊｼﾞﾛｳﾐﾊﾞﾄを除く) BMFs＜1 (alphaHCH は新陳代謝されるため) ・ﾜﾓﾝｱｻﾞﾗｼ：BMF= 2.5 (脂肪組織) ・ﾎｯｷｮｸｸｼﾞﾗ：BMF=9.85 ・結論として、北極の生態系において、効果的な蓄積性が見られる。 【FWMF (食物連鎖による経口的生物濃縮係数)】 ・FWMFs＞1 (北極海の食物連鎖の研究)	【反復投与毒性】 ラット (混餌 107 週)：NOAEL 50mg/kg 主な毒性は、100mg/kg で肝肥大及び肝細胞の病理組織学的変化、800mg/kg で成長遅延、死亡率増加及び腎障害 ラット (混餌 90 日)：NOAEL 0.1mg/kg/day 主な毒性は、0.5mg/kg/day で肝重量増加及び白血球数減少、2.5mg/kg/day で肝実質細胞肥大等、 12.5mg/kg/day で肝、心、腎及び副腎相対重量増加、成長遅延 【発がん性】 肝腫瘍 IARC グループ 2B (possibly carcinogenic to human) 【その他】 農薬、肥料の HCH 暴露により、感覚異常、頭痛、倦怠、嘔吐、振戦等 急性毒性試験において、背弯姿勢、呼吸困難、振戦、痙攣等神経症状 マウス：0.5mg/kg/day で血清中 IgG、IgM 減少	

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Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Risk profile on alpha hexachlorocyclohexane

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on alpha hexachlorocyclohexane, on the basis of the draft contained in document UNEP/POPS/POPRC.3/17. The text of the risk profile, as amended, is provided below. It has not been formally edited.

K0820043 300108

ALPHA HEXACHLOROCYCLOHEXANE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

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Executive summary

Mexico, being a Party to the Stockholm Convention, proposed lindane as well as alpha- and beta-hexachlorocyclohexane to be included in Annex A, B or C of the Stockholm Convention. After the risk profile on lindane had already been agreed at the last meeting of the Review Committee in November 2006, the Committee concluded that alpha-HCH also complied with the screening criteria laid down in Annex D of the Convention and that further elaboration of the proposal and preparation of a draft risk profile should be done.

After almost forty years of extensive use worldwide, there has been a gradual replacement of technical hexachlorocyclohexane (HCH) by lindane (gamma-HCH). No significant uses of technical HCH have been reported after 2000. However, releases into the environment may also occur from lindane production as well as from hazardous waste sites, landfills and contaminated sites. Because of its hazard profile and widespread abundance, technical HCH (including alpha-HCH as the main isomer) is subject to national and international regulations and prohibitions.

Alpha-HCH is susceptible to abiotic and biotic degradation at variable rates and degrees, depending on e.g. environmental media, site and climate. Alpha-HCH is expected to rapidly degrade in tropical conditions, whereas it accumulated in colder climates. Alpha-HCH is moderately persistent in soil. Based on values from aquatic compartments i.e. Arctic freshwater and sea water, it can be concluded that alpha-HCH shows high persistence in water in colder regions.

The physico-chemical properties of alpha-HCH allow the dispersal of the substance from its sources to the Arctic by a combination of long-range atmospheric transport and ocean currents. High levels of alpha-HCH have been detected in the Arctic Ocean, where it has built a large reservoir and is present in marine as well as in terrestrial species.

Alpha-HCH exposure levels in local areas have declined after worldwide prohibitions and restrictions. However regions with recent exposure and/or high pollution can still show elevated levels. A special concern also arises from exposure of hazardous waste sites and dumping grounds from disposed alpha-HCH residues from lindane production. Due to its persistence, alpha-HCH can still be detected regularly at low background levels in the environment. Elevated levels have also been reported from the Arctic (levels in the Arctic Ocean are higher than in temperate oceans and lakes). Though alpha-HCH levels in air decreased more than twenty-fold from the 1980s onwards, there has been only a modest change in higher marine and terrestrial predators e.g. fur seals or polar bears.

Because alpha-HCH is present in the terrestrial and aquatic food chains, alpha-HCH may bioaccumulate and biomagnify in biota and Arctic food webs. The biomagnification factors (predator-prey comparison) for many of the examined species are greater than 1 (one). Some animals, especially birds, but also mammals, have the potential to metabolize alpha-HCH. As this is an enantioselective biotransformation, a distinctive accumulation of (+) or (-) alpha-HCH can occur in mammals (depending on the species).

Alpha-HCH is the isomer with the highest neurotoxic potential beside gamma-HCH. Alpha-HCH has been classified as possibly carcinogenic to humans (group 2B) by the International Agency for Research on Cancer (IARC), based on inadequate evidence of carcinogenicity in humans and sufficient evidence for carcinogenicity to animals. Alpha-HCH causes liver hyperplasia and liver tumours in (laboratory) rodents. From animal experiments it is known that alpha-HCH affects the immune system; immunosuppressive effects were observed in humans exposed to technical HCH as well. Epidemiological studies indicate an elevated incidence of breast cancer after exposure to alpha-HCH as well as hormonal disorders leading to infertility and abortions. A possible association with intrauterine growth retardation and aplastic anaemia has been postulated.

Based on the hazard profile and the exposure scenarios it can be concluded that alpha-HCH may adversely affect wildlife and human health in contaminated regions. The United States Environmental Protection Agency (USEPA) estimated, based on daily intake rates for the Arctic population, elevated cancer rates, though estimates are very conservative. It has to be considered that the liver is the target organ for all HCH-isomers, thereby leaving the risk of additive effects. Moreover the indigenous Arctic population as well as wildlife are exposed to a broad range of POPs including all HCH isomers and other pollutants leading to probably additive effects. Nevertheless Arctic public health authorities believe the significant social, cultural and economic benefits of traditional foods outweigh the risks of contaminants such as HCH at present but give another reason for the quick control and elimination of all HCH isomers from traditional foods.

For these reasons global action on alpha-HCH is warranted.

1 Introduction

In the proposal by Mexico to include lindane in Annex A, B or C of the Stockholm Convention and in the ensuing discussions, it was concluded that "other isomers of hexachlorocyclohexane should also be considered" (UNEP/POPS/POPRC.2/10). Thus Mexico submitted a proposal for listing alpha-hexachlorocyclohexane in Annexes A, B or C of the Stockholm Convention on 26th July 2006 (UNEP/POPS/POPRC2./INF/7). Austria (on behalf of Germany) prepared the first working draft on alpha-HCH.

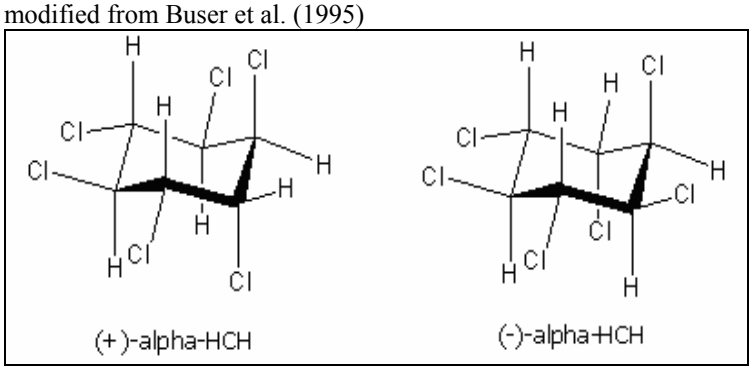
Alpha-HCH is one of the five stable isomers of technical HCH, an organochlorine pesticide formerly used in agriculture. The modes of action of the HCH isomers differ quantitatively and qualitatively with regard to their biological activity in the central nervous system as the main target organ. Alpha-HCH is mainly stimulating to the central nervous system, but the final effect of the mixed isomers depends on the composition (IPCS, 2001). In general, HCHs are among the most studied pesticides with respect to their environmental fate and effects (Breivik et al., 1999).

1.1 Chemical Identity

Chemical name: Alpha-hexachlorocyclohexane (alpha-HCH)
IUPAC name: (1a,2a,3b,4a,5b,6b)-Hexachlorocyclohexane
Common synonyms: 1,2,3,4,5,6-hexachlorocyclohexane, alpha isomer, (1alpha,2alpha,3beta,4alpha,5beta,6beta)-1,2,3,4,5,6-hexachlorocyclohexane, alpha-1,2,3,4,5,6-Hexachlorocyclohexane; alpha-benzene hexachloride, alpha-BHC, alpha-HCH, alpha-lindane; benzene-trans-hexachloride, Hexachlorocyclohexane-Alpha (Chemfinder, 2007)

Alpha-HCH is a chiral molecule; the enantiomers are shown in Figure 1.
CAS number:
Racemic: 319-84-6, (+) alpha-HCH: 11991169-2, (-) alpha-HCH: 119911-70-5
Chemical formula: $C_6H_6Cl_6$
Molecular weight: 290.83

Figure1: Structure of alpha-HCH,
modified from Buser et al. (1995)



Stability and persistence of HCH isomers are attributed to the orientation of the chlorine atoms on the molecule. Axial chlorine atoms may probably provide available sites for enzymatic degradation. Alpha-HCH exhibits 4 axially and 2 equatorially orientated chlorine atoms. Thus it is thought that the molecule is more susceptible to degradation than the beta-isomer (Philips et al., 2005).

1.1.1 Physico-chemical properties

The physico-chemical properties (see Table 1 for selected properties) of alpha-HCH allow for long-range transport and "cold condensation", an enrichment of the substance in cold climates compared to concentrations near sources, on altitudinal and latitudinal scales described by Wania and Mackay (1996). Alpha-HCH can volatilize due to its vapour pressure and low octanol-air partition coefficient from soil surfaces. The Henry's law constant is relatively low and decreases with temperature.

Table 1. Selected physico-chemical properties

Melting Point (K)	432 [1]
Boiling Point (K)	561 [1]
Water solubility (mol*m^{-3} at 25 °C)	0.33 [2]
Vapour pressure (Pa at 25 °C)	0.25 [2]
Henry´s Law Constant (Pa m^3 mol^{-1})	0.74 [2]
Log Kow (25°C)	3.9 [2]
Log Koa (25°C)	7.5 [2]
Physical state	crystalline solid [1]

[1] ATSDR (2005)
[2] Xiao et al. (2004)

1.2 Conclusion of the POP Review Committee of Annex D information

The POP Review Committee evaluated the proposal regarding alpha-HCH submitted by Mexico (UNEP/POPS/POPRC.2/INF/7 as summarized by the Secretariat in document UNEP/POPS/POPRC.2/15) according to the requirements in Annex D of the Stockholm Convention at its second meeting in Geneva. In Decision POPRC-2/9 the Committee reached the conclusion that alpha-HCH meets the screening criteria specified in Annex D. The Committee also decided to establish an ad-hoc working group to review the proposal further and prepare a draft risk profile in accordance with Annex E of the Convention.

1.3 Data sources

The draft risk profile is based on the following data sources:

- Proposal submitted by Mexico for listing alpha-hexachlorocyclohexane in Annexes A, B and/or C of the Convention (UNEP/POPS/POPRC2./INF/7), 2006.
- Decision POPRC-2/9 of the Review Committee, 2006.
- Information submitted by Parties and observers according to Annex E of the Convention: specific and/or scientific information: Czech Republic, Germany, International POPs Elimination Network (IPEN), Japan, Switzerland, United States of America; general information: Algeria, Crop Life International, Kingdom of Bahrain, Mauritius, Mexico, Qatar, Republic of Lithuania and Turkey. This information is available on the Convention's website. (http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/submissions.htm).
- Assessment of lindane and other hexachlorocyclohexane isomers, USEPA, 2006. http://www.epa.gov/oppsrrd1/REDs/factsheets/lindane_isomers_fs.htm
- International Programme on Chemical Safety, ALPHA- and BETA-HEXACHLOROCYCLOHEXANES, Environmental Health Criteria 123, World Health Organization. Geneva, 1992. http://www.inchem.org/documents/ehc/ehc/ehc123.htm
- Toxicological profile for hexachlorocyclohexanes, United States of America Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 2005. http://www.atsdr.cdc.gov/toxprofiles/tp43.html
- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. 2006. North American Commission for Environmental Cooperation http://www.cec.org/pubs_docs/documents/index.cfm?varlan=english&ID=2053

In addition to these information sources, a literature search of public data bases was conducted. The following databases were used: ECOTOXicology database (Ecotox, http://www.epa.gov/ecotox/) Hazardous Substances Data Bank (HSDB, http://toxnet.nlm. nih.gov/cgi-bin/sis/htmlgen?HSDB), Pubmed (http://www.ncbi.nlm.nih.gov /entrez/query.fcgi?DB=pubmed), Environmental Fate Data Base (EFDB http://www.syrres. com/esc/efdb_info.htm. In general search terms include the chemical name or CAS number and/or a combination of technical terms because of the multiplicity of entries. For the same reason, specific topical and updated articles were also considered. The reports listed above contained individual references which have not been listed specifically in this draft risk profile. Additional references are provided in UNEP/POPS/POPRC.3/INF/27.

1.4 Status of the chemical under international conventions

Alpha-HCH is a constituent of technical HCH, which is regulated by at least two international agreements. The first one is the 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs) under the Convention on Long-Range Transboundary Air Pollution. Technical HCH is listed in Annex II of the protocol which restricted its use to an intermediate in chemical manufacturing only.

The second agreement is the Rotterdam Convention on the Prior Informed Consent (PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. HCH (mixed isomers) is subject to the PIC Procedure and is listed in Annex III of the Convention.

Canada, Mexico and the United States signed the North American Regional Action Plan (NARAP) on Lindane and other Hexachlorocyclohexane isomers in 2006. The goal of the NARAP is to reduce the risks associated with the exposure of humans and the environment.

In the European Union, the production and use of technical HCH as an intermediate in chemical manufacturing will be phased out by the end of 2007 at the latest (Regulation (EC) No 850/2004). HCHs are also among the priority substances (Decision No 2455/2001/EC) of the adopted EU Water Framework Directive 2000/60/EC.

Hexachlorocyclohexane isomers, including the alpha-isomer, are on the List of Chemicals for Priority Action under the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic. The objective is the prevention of pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances.

2 Summary information relevant for the risk profile

2.1 Sources

2.1.1 Production

Alpha-HCH by itself is neither intentionally produced nor placed on the market. It is produced as the main constituent of technical HCH which is used as organochlorine insecticide or chemical intermediate to manufacture enriched gamma-HCH (lindane). Currently no production data on technical HCH have been reported, whereas manufacture of lindane still takes place (IHPA, 2006).

HCH is manufactured by photochemical chlorination of benzene which leads to the formation of mainly five stable HCH isomers. The yields of different isomers vary due to technical differences in the production process. The reported ranges are: alpha-HCH (55 - 80%), beta-HCH (5 - 14%), gamma-HCH (8 - 15%), delta-HCH (6 - 10%) and epsilon-HCH (1 - 5%) (Breivik et al., 1999). Further details on the production and reuse of HCH residuals can be found in UNEP/POPS/POPRC.2/17/Add.4 (Risk Profile on Lindane) and IHPA (2006). The following countries which submitted information according to Annex E stated that there was currently no production or use of alpha-HCH: Czech Republic, Germany, Mauritius, Mexico, Norway, Qatar, Republic of Lithuania, Turkey, Switzerland, and the United States of America.

2.1.2 Trade and stockpiles

Technical HCH was rapidly introduced in the 1940s on a large scale on the market, due to its universal insecticidal properties. The promising market opportunities worldwide arose in the search for an inexpensive alternative to DDT (IHPA, 2006). However, due to the decreasing effectiveness of the gamma> alpha> beta-isomer in controlling insects (Baumann et al., 1980) technical HCH was gradually replaced by lindane (> 99% gamma-HCH). However, the manufacture of lindane has resulted in a huge amount of HCH residuals, which must be disposed of or otherwise managed. IHPA (2006) calculated 1.9 to 4.8 million tons of HCH residuals based on global lindane production, in the absence of exact data. These estimates are far beyond the values reported by Walker et al. (1999) who reported stockpiles of approximately 2 785 tons of technical HCH and 45 tons of unspecified HCH material in Africa and the Near East.

2.1.3 Uses

Around 10 million tons of technical HCH were released into the environment between 1948 and 1997 (Li et al., 1999). Breivik et al. (1999) estimated technical HCH usage at approximately 400 000 tons in Europe alone between 1970 and 1996. The data illustrate the large uncertainties of these estimates. According to Li and Macdonald (2005) global usage of technical HCH was dominated by 10 countries headed by China, which consumed almost half of the total global quantity. The other countries were (in order of decreasing usage): Former Soviet Union, India, France, Egypt, Japan, United States, East Germany, Spain and Mexico. Usage of technical HCH was banned in most western countries and Japan in the 1970s but continued in China and Russia until 1983 and 1990. In 1990, India also banned technical HCH for agricultural use but

kept it for public health uses (AMAP, 2004a). Technical HCH usage steadily declined and now technical HCH is virtually no longer used worldwide. However, there are indications that the use of stockpiles, limited use for public health purposes and/or illegal use cannot be excluded (Zhulidov et al., 2000; Bakore et al., 2004; Qian et al., 2006).

2.1.4 Releases to the environment

There are several pathways of alpha-HCH for entering the environment. Historically, alpha-HCH was released during the manufacture of technical HCH and its use as a pesticide. Alpha- and beta-HCH have the same global emission patterns which, however, differ in scale. Li and Macdonald (2005) estimated the global usage of alpha-HCH (based on data on technical HCH) at 6 millions tonnes, with 4.3millions tonnes emitted into the atmosphere. After the 1940s emissions of alpha-HCH increased and peaked in the early 1970s. Due to the ban on the use of alpha-HCH in North America, in European countries and Japan, emissions decreased but reached again a peak in the 1980s because of frequent usage in Asian countries. After the 1980s, figures dropped due to further prohibitions and restrictions e.g. in China. Releases of alpha-HCH into the environment are also possible from hazardous waste sites (USEPA, 2006), stockpiles and residues of lindane production, which are not always controlled or maintained safely (IHPA, 2006). Also, contaminated sites (e.g. from former production plants) may contribute to the environmental burden of alpha-HCH (Concha-Grana et al., 2006). Germany (submitted Annex E information, 2007) reported that there are still a few isolated local sources i.e. landfills and dumps in the former GDR (East Germany) from applications of technical HCH. As a result, higher concentrations of alpha-HCH in fish of the river Elbe near the former production site were detected after heavy rainfalls and floods in 2003. However, quantitative estimates of releases from hazardous waste sites and landfills are not available.

2.2 Environmental fate

2.2.1 Persistence

Alpha-HCH is, in principle, degradable in environmental compartments by abiotic processes such as photodegradation or hydrolysis. Based on laboratory experiments from Ngabe et al. (1993), hydrolytic half-lives of alpha-HCH show strong temperature dependence. At 20°C, pH 8 the DT50 was 0.8 years whereas it increased at lower temperature (5°C, pH 7.8) to 26 years. Based on these degradation rates Harner et al. (1999) calculated a DT50 of alpha-HCH in the Arctic Ocean of 63 years.

In general, HCH-isomers do not absorb light > 290 nm. Thus it is expected that photolysis plays a minor role in the removal of alpha-HCH. Deo et al. (1994) reported half-lives of alpha-HCH in aqueous solution exposed to sunlight of 4 to 6 days. While the mechanism of this degradation is uncertain, it was shown that alpha- as well as gamma-HCH break-down by indirect photolysis with photosensitizing agents that may transfer the excitation energy to HCH (ATSDR, 2005; USEPA, 2006). Regarding photodegradation on hard surfaces, a half-life equal to 91 hours on a thin film has been reported (ATSDR, 2005). However, the relevance of this result is questionable when taking into consideration the arguments mentioned above.
The measured atmospheric OH rate constant of 1.4×10^{-13} cm^3/molecule-sec resulted in a corresponding half-life of 115 days (ATSDR, 2005) (using an average hydroxyl radical concentration of 5×10^5 molecule/cm^3 according to the TGD (2003)).

In conclusion, abiotic degradation is very slow especially at lower temperatures. Photolysis in aqueous media and air is considered to play an insignificant role in the degradation of alpha-HCH.

Biotic degradation of alpha-HCH has been found to take place in pure cultures, soil slurries, soil (semi-)field studies, sediment and water. Initially it was thought that HCH biodegradation in soil occurs under anaerobic conditions. However, several investigations show that alpha-HCH is aerobically degraded, in some cases even faster than anaerobically. Breakdown was also reported for methanogenic and sulfate reducing conditions (Phillips et al., 2005).

The anaerobic metabolic pathway of alpha-HCH leads via dechlorination to tetrachlorocyclohexene. Dichlorophenol and trichlorophenol as well as chlorobenzene and benzene were formed under methanogenic conditions, the last two as stable end products. These metabolites can be further mineralised aerobically or anaerobically (Bachmann et al., 1988; Phillips et al., 2005). In pure cultures as well as in flooded soil gamma-HCH is the most easily dechlorinated isomer followed by alpha-HCH under anaerobic conditions (Jagnow et al., 1977; MacRae et al., 1967).

Under aerobic conditions alpha-HCH was dehydrochlorinated to pentachlorocyclohexane in soil slurries. Further conversion to tetrachlorobenzene or trichlorobenzene may occur to yield dichlorobenzene (Deo et al., 1994). The aerobic degradation pathway of gamma-HCH was extensively studied with *Shingobium sp.* and results in several metabolites. It was suggested that alpha-HCH follows the same pathway than gamma-HCH. Complete mineralization of alpha-HCH was shown in laboratory studies under aerobic conditions (Phillips et al., 2005).

In general, climatic conditions as well as soil texture and organic matter altering substance sorption, water content, pH and bacterial growth influence degradation rates (IPCS, 1992). The moisture content of the soil enhances losses of alpha-HCH, which is attributed to higher volatility and/or microbial degradation (Chessells et al., 1988; Phillips et al., 2005). Bacteria capable of degrading HCHs at extreme temperatures (< 5 °C or > 40°C) have not yet been reported (Phillips et al., 2005).

Data on laboratory soil studies or field investigations are limited. Under various field conditions it is assumed that degradation rates are in the order of alpha > gamma > > beta (Suzuki et al., 1975, Stewart and Chisholm, 1971; cf. also section 1.1). Singh et al. (1991) reported field half-lives (i.e. dissipation, including losses by leaching and volatilisation) of around 55 days on cropped and uncropped plots in a sandy loam in India under subtropical conditions. This result is consistent with findings from Kaushik (1989) who reported an even shorter half-life for technical HCH under similar study conditions. Also, in temperate climate Doelman et al. (1990) observed in a semi-field study with contaminated soil > 50 % removal after 161 days, mainly attributed to a quick decline in the first few weeks, whereas degradation slowed down afterwards. Suzuki et al. (1975) also suggested that low residue levels (below 0.1 ppm) may resist microbial and physico-chemical action. Low concentrations of alpha-HCH may persist in the environment indefinitely because of low affinity of enzymes or transport system responsible of HCH degradation (Phillips et al., 2005). Stewart and Chisholm (1971) observed in a long-term field study after an application of technical HCH, 4 % of the alpha-isomer after 15 years in a sandy loam in Canada. In addition, Chessells et al. (1988) showed that after a 20 year application history of technical HCH on sugar cane in Queensland, Australia, alpha-HCH with the highest initial concentration is substantially less prevalent in the field and the detected levels were twice as much as the levels of the gamma-isomer.

Abiotic processes are not enantioselective, but biodegradation may be. If nonracemic alpha-HCH residues in the environment or biota are measured, enzymes are involved. However, racemic residues do not exclude the possibility of biotic degradation (cp. Suar et al., 2005). Also for monitoring purposes enantiomeric fractions (EFs, calculated by the formula EF = ER/(ER+1), ER = enantiomeric ratio: (+) /(-) alpha-HCH, Kallenborn et al., 2001) have been quantified for the characterisation of residues. Hegeman and Laane (2002) investigated the enantiomeric distribution of alpha-HCH in different environmental compartments obtained from 618 measurements. In general, the abiotic compartments showed average EFs close to 0.5. In soil, the preference tended to be the degradation of the (-) alpha-HCH (EF > 0.5), whereas in water an opposite tendency was found. Kurt-Karakus et al. (2005) reported a range of EFs for alpha-HCH of 0.4 - 0.89 (mean 0.5) in global background soils which covered a greater range than the EFs in ambient air of North America (0.47 - 0.52), suggesting that post-deposition degradation had taken place. However, since EFs vary considerably with site, caution is needed when using enantiomeric signatures in the air as a marker of reemissions from (soil) surfaces.

Based on the K_{oc} value and confirmed by field data, alpha-HCH is expected to have a low leaching potential (HSDB, 2006; Singh et al., 1991). However, groundwater pollution may occur in highly contaminated areas (Law et al., 2004). Detailed information regarding the relevance of isomerisation in the environment can be found in the risk profile on lindane (UNEP/POPS/POPRC.2/17/Add.4).

Alpha-HCH is able to biodegrade in sea water/sediment samples (HSDB, 2006) and freshwater (Padma and Dickhut, 2002). Helm et al. (2002) estimated the half-lives for alpha-HCH in a high Arctic lake at 0.6 to 1.4 years. For the Eastern Arctic Ocean enantioselective degradation for the (+) alpha- and (-) alpha-HCH with half-lives of 5.9 and 23.1 years was observed. If breakdown with hydrolysis was taken into consideration, the overall half-lives were 5.4 and 16.9 years for the (+) and (-) alpha-isomer respectively (Harner et al., 1999). Though sediment degradation rates are poorly known and thus the estimates are less certain, the half-life for alpha-HCH in sediments of a high Arctic lake was assumed to be approximately 2 years (Helm et al., 2002). Some data on α-HCH levels in sediment cores 30-40 years of age indicate long half-lives of α-HCH in sediments from different geographical areas (Barra et al., 2001; Rawn et al., 2001; Riching et al., 2005)

2.2.2 Bioaccumulation

The octanol-water partition coefficient (log Kow = 3.8) for alpha-HCH indicates a potential for bioaccumulation (ATSDR, 2005), though it is below the value of 5 stated in Annex D paragraph 1(c)(i) of the Stockholm Convention. A wide range of bioconcentration factors (BCFs) have been reported in several studies. For green algae, bioconcentration factors varied from about 200 in *Chlorella pyrenoidosacells* to 2700 (dry weight basis) and 13000 on a lipid basis, respectively in *Dunaliella*. Studies of invertebrates show BCFs in the range of 60 (8000 on a lipid basis) in *Artemia* to 2700 in polychaetes, depending on the lipid content of the animals (IPCS, 1992).

The BCF (whole body) for alpha-HCH according to the former OECD test guideline 305 E in zebra fish was equal to 1 100 under steady state conditions with uptake constants (k1) of 50 and clearance rate constants (k2) of 0.045. These values are similar to those of gamma-HCH (BCF 850, k1 = 50.8, k2 = 0.055) (Butte et al., 1991). Oliver et al. (1985) reported BCFs (whole body) ranging from 1 100 to 2 800 in rainbow trout.

In general, studies from Arctic marine food webs show food web magnification factors (FWMFs), which represent the mean rate of increase per trophic level in the food chain, greater than 1. The BMFs (biomagnification factor, predator-prey comparison) of alpha-HCH in zooplankton and Arctic cod are greater than 1, showing a potential for biomagnification. BMFs of alpha-HCH in seabirds were generally less than 1 with the exception of dovekie and black guillemot. Ringed seals showed a BMF of 2.5 (Moisey et al., 2001). It is suggested that alpha-HCH isomer has the potential to biomagnify in aquatic food webs and may increase at lower as well as in upper trophic levels, especially in marine mammals (USEPA, 2006; Hoekstra et. al., 2003a). The report of Hoekstra et al. (2003b) also confirms this presumption with a BMF of 9.85 in bowheads for alpha-HCH.

Fisk at al. (2001) reported on the influence of chemical and biological factors on the trophic transfer of POPs including alpha-HCH. In general, the highest BMF should be seen in homeothermes (birds and mammals) compared to poikilothermes (fish, invertebrates) attributed to their greater energy requirements. Within the homeothermes, seabirds usually have the highest BMFs, consistent with the greater energy demand in birds. But this is not applicable for alpha-HCH. Most seabirds appear to be able to induce the cytochrome P450 such as CYP2B, which are enzymes to metabolize alpha-HCH, so the ranking from highest to lowest biotransformation ability (usually for OCs: marine mammals > seabirds > fish > zooplankton) is not applicable for this compound. The BMF of alpha-HCH in poikilothermes is 1.3 and equal to that in homeothermes (Hop et al., 2002).

As alpha-HCH is a chiral compound, the determination of the ER or EF is important in order to understand species-specific metabolism and biotransformation. No enantioselective biotransformation in rainbow trout for alpha-HCH was observed by Konwick et al. (2006) in a dietary study showing consistent EFs in the fish. In an experiment of Wong et al. (2002) alpha-HCH was racemic throughout the course of the experiment with rainbow trout, fed with treated food. These results are in contrast with reports of enantioselective biotransformation in other species. The EF in benthic invertebrates, zooplankton and fish was 0.45 as a maximum. Ringed seals showed an EF of 0.51, while the EFs in seabirds range from 0.65 (dovekie) to 0.97 in glaucous gulls (Moisey et al., 2001). This suggests that seabirds preferentially metabolize the (-) enantiomer. Associated with a BMF of < 1 in seabirds, it has been found that both enantiomers of alpha-HCH are metabolized in birds (dovekie and black guillemot seem to have a lower capacity).

The EF of 0.51, considered together with the BMF of 2.5 in seals, indicates that mammals are not able to biotransform alpha-HCH in great amounts (Moisey et al., 2001). Nevertheless, Wiberg et al. (2000) found residues of alpha-HCH with nonracemic ERs in seals as well as in polar bears. According to Hoekstra et al. (2003b) accumulation of the (+) enantiomer occurs in bowhead whale and beluga, but (-) alpha-HCH enriches in bearded seal. Ringed seal show a slight accumulation of the (+) enantiomer (Hoekstra et al., 2003b) but sometimes the alpha-HCH residues are racemic (Fisk et al., 2002). This indicates an enantiospecific biotransformation and accumulation of alpha-HCH in the food chain. When investigating the EFs in krill, cod and penguin eggs, Corsolini et al. (2006) also found enantioselective biotransformation with an increase by 14 % of (+) alpha-HCH from the lower to the higher trophic level (from krill to penguin). There are interspecies differences in the enantiomeric profile of alpha-HCH in marine mammals, too. The BMF for calanus to bowhead for example is high (near 10 with a (+) alpha-HCH fraction of 16 and 4.5 of (-) alpha-HCH) (Hoekstra et al., 2003b).

Moisey et al. (2001) showed different BMFs in doveky, depending on the prey. Summed up, biomagnification is affected by many parameters such as contamination in biota, and consequently of food (prey), the trophic level and the ability to biotransform alpha-HCH.

Kelly at al. (2007) have recently shown that, for substances with a log Koa >6 and a log Kow >2, the fish BCF is not a good predictor of biomagnification in air-breathing animals. This is also well illustrated by beta-HCH, in the marine mammalian and terrestrial food webs. as such compounds biomagnify strongly up to 3000- and 400-fold respectively. Alpha-HCH also meets these criteria.

Not only in the arctic food web, but also in organs of fur seals from the Pacific coast of Japan and double crested cormorants from the great lakes, alpha-HCH was detected (with an alpha-HCH ER from 1 in the muscle to 1.58 in fat). High alpha-HCH ERs were found in the brain of the cormorants (> 3.6) (Iwata et al., 1998). Willet et al. (1998) inferred from high alpha-HCH concentrations in marine mammal brain that this compound can cross the blood/brain barrier. Ulrich et al. (2001) also found in studies with rats that the alpha-HCH ER in brain, ranging from 2.8 to 13.5, is not caused by an enantioselective metabolism but that selective retention might be responsible.
Braune et al. (1999) detected alpha-HCH residues in the fat of caribou. Residues of alpha-HCH could also be found in livers and the adipose tissue of arctic foxes. The alpha-HCH ER of 2.2 in the liver, and 1.1 in the adipose tissue, indicates a stereoselective bioaccumulation also in terrestrial mammals (Klobes et al., 1997).

In conclusion high levels are found in Arctic biota because of the bioaccumulation potential of alpha-HCH (as a product of bioconcentration and biomagnification) and the historically particularly efficient deposition processes of this substance in the Arctic waters. The efficient accumulation is an effect of the combination of the physico-chemical properties of

alpha-HCH and the low temperature in the Arctic. In other words, alpha-HCH effectively accumulates in the Arctic ecosystem as a whole.

2.2.3 Long range environmental transport

Monitoring data on the environment including biota from remote regions such as the Arctic or Antarctica, where technical HCH has not been used, provide evidence of the long-range transport potential of alpha-HCH. Also the physico-chemical properties in combination with its stability allow alpha-HCH to undergo long range transport in the atmosphere. Primary emissions from the source regions (mainly in Asia) and Arctic air concentrations have synchronously decreased, suggesting a rapid dispersion of alpha-HCH from its sources to remote regions (Li and Bidleman, 2003). Especially high concentrations compared to the source regions were reported for the Arctic Ocean (see Table 2). It is assumed that after long range transport alpha-HCH accumulated in the cold water due to its low Henry's law constant and built a large reservoir (Li and Macdonald, 2005). HCHs including alpha-HCH are the most abundant pesticides in the Arctic air and water (Walker et al., 1999).

To understand pathways and the fate of alpha-HCH in the upper Arctic Ocean, Li et al. (2004) developed an Arctic Mass Balance Box Model. They concluded that the highest load of 6 670 tonnes was reached in 1982 mainly by gas exchange and ocean currents and decreased thenceforward by an average annual rate of approximately 270 tons/year. After 1990, ocean currents become the dominant input of alpha-HCH in the Arctic Ocean. However, the portion of alpha-HCH entering the Arctic atmosphere via long range transport from source regions played a prominent role (especially in the beginning). After the early 1990s alpha-HCH in the Arctic air came from both atmospheric transport and volatilization from the Arctic Ocean. It was suggested that a complete elimination of alpha-HCH mainly by degradation and ocean currents would require another two decades. In total 27 700 tons alpha-HCH were transported between 1945 and 2000 via long range transport to the Arctic Ocean.

According to model calculations with the OECD Pov and LRTP Screening Tool, alpha-HCH has similar persistence and long-range transport properties compared to already identified POPs such as PCBs and organochlorine pesticides (Wegmann et al., 2007). Model input properties of the chemicals include partition coefficients in air-water and octanol-water as well as half-lives in air, water and soil and the Henry's Law constant (based on figures contained in UNEP/POPS/POPRC2./INF/7). The model considers all environmental compartments quantitatively. The results of the model do not indicate absolute levels in the environment but help to compare possible POPs with identified POPs (reference chemicals: PCB congeners 28, 101, 180, HCB, carbon tetrachloride and alpha-HCH) according to their environmental persistence and potential for long range transport. Uncertainties in the chemical properties were investigated by Monte Carlo uncertainty analysis.

2.3 Exposure

Exposure to alpha-HCH resulted from the use of technical HCH, and from the production and manufacture of technical HCH and lindane. Because of the persistence high exposure is also expected in contaminated areas due to extensive use, former production, disposal sites and stockpiles. Though usage of technical HCH has practically ceased worldwide monitoring data based on the ratio of the alpha-/gamma-isomer still suggest possible releases of technical HCH in certain areas (Zhang et al. 2003; Qian et al., 2006; Zhulidov et al., 2000).

Human exposure to alpha-HCH results mostly from ingestion of contaminated plants, animals and animal products. Inhalation of ambient air and consumption of drinking water are further sources of exposure, although to a minor extent. As shown by a French pilot study alpha-HCH was detected in indoor air and on the hands of the general population in the Paris area in 42 and 35 % of the samples. Levels were low and ranged up to 1.8 ng/m^3 in air and up to 8.5 ng/hand (Bouvier et al., 2006).

Monitoring data from a wide range of biota including humans suggest that significant uptake from the environment occurs, which demonstrates the bioavailability of alpha-HCH. Infants may be exposed during fetal development and breastfeeding.

2.3.1 Environmental monitoring data from local areas

Generally, environmental levels in local areas have dropped after restrictions and prohibitions of the usage of technical HCH (IPCS, 1992; see also Table 2). However, monitoring data show its ubiquitous distribution in all environmental media e.g. in monitoring activities in the Czech Republic (submitted Annex E information by the Czech Republic, 2007), in lichens of various locations in Switzerland (values given in table 2) or in a recently performed monitoring programme in Japan. Alpha-HCH had been detected in Japan in all but 7 fish specimens. The reported values are as follows: water 0.013 - 5.7 ng/l, sediment trace - 5.7 ng/g dw (dry weight), shellfish up to 1.8 ng/g ww (wet weight), fish up to 2.9 ng/g ww, bird 0.1 - 1.6 ng/g ww, air (warm and cold season) 0.02 - 3.2 ng/m^3 and 0.01 - 0.68 ng/m^3 (submitted Annex E information by Japan, 2007).

Table 2. Selected monitoring data of abiotic compartments and vegetation (values refer to alpha-HCH except otherwise stated)

Compartment	Country/region	Levels	Comments	References	Year
Air	Great Lakes, rural	< 1 - 84 pg/m^3	alpha-HCH, mean values, gas phase	Sun et al., 2006b	1992-2003
	Great Lakes, Chicago	52 pg/m^3	alpha-HCH, mean value, gas phase	Sun et al., 2006b	1996-2003
	Niigata, Japan	92 pg/m^3	Annual average, according to the authors a result of long-range trasport	Murayama et al., 2003	2000-2001
	Czech Republic (Kosetice)	**38**/21/17/22/**13** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1999-2003
	Finland (Pallas)	**24**/28/18/15/17/18/**9** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1996-2003
	Iceland (Storhofdi)	**17**/16/15/15/10/8/10/5/**7** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1995-2003
	Norway (Lista)	**94**/94/76/69/52/61/50/37 /25/19/17/17/**12** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1991-2003
	Sweden (Aspvreten)	**43**/57/61/50/-/67/**16** pg/m^3	Air and aerosol, annual mean concentrations	EMEP measurement, data online	1995-2002
	Ny-Aslund (Svalbard, Norway)	73 pg/m^3	∑HCHs, mostly alpha-HCH, highest annual average value reported in 1996	AMAP, 2004a	1996-1988
	Barents Sea and eastern Arctic Ocean	11 - 68 pg/m^3		Harner et al. (1999)	1999
	Arctic	23 +/- 10 pg/m^3	Uniform distribution, arithmetic mean, measurements from 4 Arctic sites	Su et al., 2006	2000-2003
Precipitation	Belgium (Knokke)	4.1 - 0.5 ng/l	annual mean concentrations	EMEP measurement data online	1996-2003
	Germany (Zingst)	1 - 0.3 ng/l	annual mean concentrations	EMEP measurement data online	1999-2003
	Finland (Pallas)	< 1 ng/l	precipitation + dry deposition annual mean concentrations	EMEP measurement data online	1996-2003
	Norway (Lista)	2.7 - 0.4 ng/l	annual mean concentrations	EMEP measurement data online	1991-2003
	Sweden (Aspvreten)	2.7 - 0.4 ng/l	annual mean concentrations	EMEP measurement data online	1995-2002
	Canada/Great Lakes	1 - 40 ng/L	81 samples	IPCS, 1992	1976-77
Soil	Russian Arctic	0.2 - 0.5 ng/g dw	∑HCHs, predominantly alpha-HCH, soil including peat and litter	AMAP, 2004a	200-2001
	Antarctica	< 0.01 – 0.026 ng/g dw		Borghini et al., 2005	1999
Seawater	Northern Barents Sea, Eastern Arctic Ocean	910 (350 - 1630) pg/l	Sample period: July-September	Harner et al., 1999	1996
	North American Arctic Ocean	~ 7.5 µg/m^3		Li and Macdonald, 2005	1983
	Canadian Archipelago and southern Beaufort Sea	3.5 (1.1 – 5.4) ng/L	Surface water, measurements in summer	Bidleman et al., 2007	1999
Freshwater, rivers	Russian north rivers	< 1 - 69 ng/l	Seven-year weighted mean concentrations	AMAP, 2004a	1190-1996
River and estuarine waters	Eastern and southern Asia and Oceania	up to max. 470 ng/l		Iwata et al., 1994	1989-1991
Sediment (Lake)	Southern Sweden	9.2 ± 6.3 ng/g dw	∑HCHs, data from the Swedish Monitoring Program, 2002	AMAP, 2004a	2002
Vegetation (lichen)	Taymir (Russia)	7 ng/g dw	Highest concentration in lichen compared to samples from Alaska, Urals and Kola	AMAP, 2004a	1991-1993

Compartment	Country/region	Levels	Comments	References	Year
	Switzerland	0.5 - 4 µg/kg dw	From various locations (e.g. cities, industry, rural)	Submitted Annex E information by Switzerland, 2007	2002
Moss	Antarctica	0.43 – 4 ng/g dw		Borghini et al., 2005	1999

Environmental levels can still be high in the proximity of sources. HCH concentrations in contaminated soil of 40 - 225mg/kg were found in the topsoil around a chemical plant in Albania (UNEP, 2003). Mean levels of 0.02 mg/kg were reported for soils from the Pearl River Delta in China, Russian soils near the Lena River contained 0.001 - 0.017 mg/kg HCH (UNEP, 2003). Levels of up to 12 000 mg/kg were detected in soil of a highly polluted area in Spain (Concha-Grana et al., 2006)

Levels in biota vary, depending on the location (recent usage and/or high pollution) and species. Alpha-HCH is in most cases the dominant isomer in fish (Willett et al., 1998). E. g. concentrations of HCHs (mainly the alpha-isomer) in several fish species from India ranged between 6 to 68 ng/g ww. Fish samples collected from the Nile River near Cairo in 1993 showed a concentration of alpha-HCH of 0.5 ng/g ww (UNEP, 2003).

Alpha-HCH was also determined in eggs of Dalmatian Pelican (*Pelecanus crispus*) as well as in eels (*Anguila anguila*), the main pelican prey species collected in the wetlands of Amvrakikos Gulf in Greece for a two year period, 1992 and 1993. The concentration in pelican eggs was 7.9 ± 3.2 ng/g and 6.5 ± 2.5 ng/g ww in eels (UNEP, 2003). Concentrations of alpha-HCH in perch from the Latvian coast were up to 21 ng/g lw (lipid weight) (range 50 - 60), which were considered as background load. Elevated levels of up to 126 ng/g lw were attributed to a recent discharge of technical HCH (Olsson et al., 1999).

A local source of alpha-HCH was the usage of technical HCH by indigenous human populations in the Russian north against nuisance insects parasitizing domesticated reindeer (Li et al., 2004). However, no quantitative estimates of these exposure levels exist.

2.3.2 Exposure as a result of long range environmental transport

Highest measured levels of alpha-HCH have been reported for higher latitudes in air (e.g. Svalbard, Alert) as well as in seawater (Harner et al., 1999). As shown in table 2, alpha-HCH in air (e.g. from 94 pg/m^3 in 1992 to 12 pg/m^3 in 2003 in Norway) has decreased. AMAP (2004a) also summarized that concentrations of HCHs in Arctic air have been low since the mid 1990s due to worldwide prohibitions and restrictions. Before, in the 1980s, levels as high as approximately 900 pg/m^3 were measured in Arctic air (Li et al., 2002). Seawater levels in the eastern Arctic Ocean were generally lower than in the western part (Harner et al., 1999). Surface concentrations are highest in the Central Canadian Arctic Archipelago, intermediate in the Beaufort/Chukchi Seas and at the North Pole. In the 1990s levels in the Canadian Arctic Ocean were higher than anywhere else in the global marine environment (AMAP, 2004a).

This spatial distribution is also reflected in the levels in biota. Hoekstra et al. (2002) found that bowhead whales exhibit a reversal in their blubber alpha-/beta-HCH ratios on their migration route between the Bering to the Beaufort Sea. Levels in beluga blubber decreased from approximately 190 to 140 ng/g lw between 1982 and 1997 in the southeast Baffin Bay (AMAP, 2004a). Levels of up to 196 ng /g ww were reported from Alaska (submitted Annex E information by IPEN, 2007) and of up to 344 ng/g ww from Arviat (Stern et al., 2005). Minke whales from Greenland had higher concentrations of the prevalent alpha-isomer in blubber (mean levels 40 - 55 ng/g ww), than individuals from the North Sea (below 30 ng/g) (AMAP, 2004a). No decline of ∑HCHs in blubber of narwhal from the Canadian Arctic was observed between 1982 and 1999.

Concentrations in ringed seal of the Canadian Arctic showed no significant change of ∑HCH concentration from the 1970s. The elevated residues of HCH isomers in marine mammals of the Canadian Archipelago are likely due to the high concentrations of HCH isomers in the water because HCH isomers are the most abundant organochlorines in the Arctic Ocean (NARAP, 2006).

No temporal trend for Arctic cod and dab from the costal waters of Iceland was found for the period from 1991 to 2000, whereas results from Norway revealed a significant decrease (from 23 to 4 ng/g lw) of alpha-HCH residues in Arctic cod liver between 1987 to 1998 (Sinkkonen and Paasivirta, 2000).

Alpha-HCH has been detected in the muscle and liver of Arctic foxes (1.5 and 3 ng/g ww) in Canada (AMAP, 2004a). Levels in polar bear also reflect the spatial distribution of alpha-HCH being highest in Alaskan populations (in male polar bear up to 593 ng/g lw). No decline of alpha-HCH levels were reported for female polar bears in western Hudson Bay (concentrations up to 260 ng/g lw) from 1991 – 2002 (Verreault et al., 2005). Residues of alpha-HCH in East Greenland polar bears increased from 18 - 25 % during the 1990s (AMAP, 2004a).

2.3.3 Food

Daily intake values of alpha-HCH for the general population in adult human diets between 1986 and 1991 in the United States were reported to be 0.008 µg/kg. In the USA, the age dependent average daily intake of alpha-HCH declined from 3.3 – 16.1 ng/kg bodyweight (bw; 1982 – 84) to 0.5 – 2.7 ng/kg bw (1986 – 91) (ATSDR, 2005). In the Total Diet Study conducted by FDA in 2003 on 100 food items, alpha-HCH was detected in 35 items (submitted Annex E information by IPEN, 2007). In a Total Diet Study from Canada (1993 - 96), an average daily dietary intake of 0.37 ng/kg bw alpha-HCH was reported (Health Canada, 2003, in EFSA, 2006). Within the European countries, representative dietary intake studies are scarce. One was performed in the Czech Republic. The median daily intake values for alpha-HCH declined from 4.3 ng/kg bw in 1994 to 1.6 ng/kg bw in 2002 (EFSA, 2005). A local diet study carried out in Spain in the years 1990/91 estimated daily intakes below 0.1 µg alpha-HCH (Urieta et al., 1996).

Alpha-HCH has been found in cow's milk in countries where HCH had been used recently. Mean levels of alpha HCH in cow's milk of two different regions in India were 0.012 mg/kg lipid and 0.0045 mg/kg lipid, respectively (ATSDR, 2005). 140 bovine milk samples from 14 districts of Haryana, India (sampled within 1998 - 1999) were analysed for organochlorine pesticide residues. Four percent of the samples exceeded the maximum residue limit (MRL) of 0.05 mg/kg as recommended by WHO for alpha-HCH (Sharma et al., 2006). A monitoring study (192 samples) of cow's milk from Mexico revealed 0.001 - 0.201 mg/kg alpha-HCH (ATSDR, 2005).

Fish and clam samples from India contained 0.01 – 0.02 mg/kg ww and 0.26 mg/kg ww alpha-HCH respectively (Nair and Pillai, 1992). High levels of alpha-HCH in the food chain are documented for the arctic region (AMAP, 2004b; levels are reported under section 2.3.2.). Indigenous populations in the Arctic are particularly vulnerable from dietary exposure to alpha-HCH through subsidence food such as caribou, fish, seal and whale.

2.3.4 Body burden

Median levels of alpha-HCH in 25 American patients were 0.04 ng/g in the whole blood and 1.1 ng/g (maximum 9.6 ng/g) in biopsy fat (ATSDR, 2005). A Spanish study reported mean alpha-HCH levels of 1.43 µg/g (maximum 6.75 µg/g) in fat samples of children living in farm areas (Olea et al., 1999). Alpha-HCH has been detected in 1.7 % of the 4822 blood samples of German adults from 120 locations (detection limit: 0.1 µg/l) (Becker et al., 1998). Alpha-HCH was detected in blood serum from three of 186 (=1.6 %) Brazilian children (mean: 1.8 ppb) (ATSDR, 2005). Alpha-HCH has been detected in all samples (n = 142) of an eastern Romanian study in 2005 with a median concentration of 31 ng/g lipid (range 3 - 146 ng/g) (Dirtu et al., 2006). High concentrations were reported for India, due to agricultural use and malaria control. Blood serum contained up to 0.45 mg/l alpha-HCH, whereas adipose tissue contained up to 0.30 mg/kg. Breast milk contained 0.16 mg/l (mean) (Nair and Pillai, 1992). Scheele et al. (1998) investigated levels of several organochlorine compounds including alpha-HCH in bone marrow of 29 adults from Germany (collected between 1980 and 1991). Compared to adipose tissue, with generally highest levels of organochlorine compounds, alpha-HCH concentrations were 10-fold higher in bone marrow (mean: 0.050 mg/kg on dry lipid weight; max: 0.476 mg/kg). Alpha-HCH has also been detected in semen (ATSDR, 2005).

2.3.5 Exposure of children

Children are at specific developmental stages more vulnerable to risks from chemical substances than adults. It is unclear if children are more susceptible than adults to health effects from exposure to alpha-HCH although it is known that the developing brain is sensitive to the effects of different POPs. The specific enrichment of alpha-HCH in the mammalian brain might be a reason of concern. Placental transfer of alpha-HCH in humans is well documented (ATSDR, 2005; Falcon et al., 2004; Shen et al., 2006). Alpha-HCH accumulates to a higher extent in human placenta than in breast milk.

Mean alpha-HCH levels in breast milk of a Finnish cohort (43 mothers, 1997 – 2001) were 0.19 ng/g lipid, whereas placenta mean concentrations of alpha-HCH were 3.47 ng/g lipid. In a Danish cohort (43 mothers, 1997 – 2001), mean concentrations of 0.51 ng/g lipid in breast milk and 1.53 ng/g lipid in placenta were detected. A specific metabolic activity of the placental tissue is suspected (Shen et al., 2006). It could be shown that in case of restrictions of use, alpha-HCH concentrations in breast milk decline continuously. In Germany alpha-HCH was still found in 28 % of the breast milk samples analysed in 1984/85 whereas it could not be detected in 1990/91 and 1995 samples (Ott et al., 1999). More than 2 000 individual human milk samples from women living in Western Germany collected and analysed between 1984 and 2001 indicated that alpha HCH concentration declined from > 0.01 mg/kg fat to levels below detectability (detection limit of 0.001 mg/kg fat) (Fürst, 2004). In the framework of the 3rd WHO human milk field study, HCHs were analysed in 16 human milk pools from ten European countries. In Bulgaria, Russia and Ukraine, alpha-HCH was detected in

concentrations between 0.002 – 0.006 mg/kg lipid, whereas in the samples of Czech Republic, Germany, Ireland, Italy, Luxembourg, Norway and Spain alpha-HCH was not detectable (detection limit: 0.001 mg/kg lipid). In Nairobi, Kenya, 8.8% of 216 breast milk samples contained detectable alpha-HCH with a mean concentration of 0.013 mg/kg milk fat and a range of 0.002 – 0.038 mg/kg (Kinyamu et al., 1998). Breast milk samples from India contained 0.16 mg/l (mean) (Nair and Pillai, 1992). Another Indian study reports 0.045 mg/l alpha-HCH in breast milk (Nair et al., 1996). It can be concluded that alpha-HCH concentrations in breast milk strongly depend on exposure and that in several East European and developing countries concentrations are still very high.

2.4 Hazard assessment for endpoints of concern

Compared to technical HCH and lindane, limited data are available for alpha-HCH. A limited number of subchronic and chronic oral toxicity studies exist. No animal studies of the toxicity of alpha-HCH via inhalation and dermal application have been conducted. Studies on developmental, teratogenic and reproductive effects of alpha-HCH are missing. There is a lack of dose-response data after oral exposure for all relevant species. For the present risk profile, the most important findings concerning the hazard assessment have been reviewed. For more details please consider the reports listed under heading 1.2.

Acute Toxicity/ Neurotoxicity: Oral LD50 values range between 1000 and 4000 mg/kg bw for mice and between 500 and 4 674 mg/kg bw for rats. The signs of poisoning were central nervous stimulation: excitation, hunched posture, rough fur, dyspnoea, anorexia, tremors, convulsions, and cramps (IPCS, 1992).

Subchronic toxicity: In a 90-day study on rats carried out with dose levels of 0, 2, 10, 50, or 250 mg alpha-HCH/kg diet, growth was retarded and relative weight of organs (liver, heart, kidneys, and adrenals) increased at 250 mg/kg diet (equivalent to 12.5 mg/kg bw/day). At levels of 50 and 250 mg/kg, liver enzyme activities were modified and liver parenchyma cells enlarged. Liver weight increased at dose levels of 10 mg/kg diet (equivalent to 0.5 mg/kg bw/day) and reductions in white blood cell count were noted. Signs of immunosuppression (reduced serum levels of immunoglobulins G and M) were observed at 50 and 250 mg/kg diet. The NOAEL was 2 mg/kg alpha-HCH/kg diet (equivalent to 0.1 mg/kg bw/day; the LOAEL was 10 mg/kg diet) (IPCS, 1992).

Chronic Toxicity: When groups of 10 female and 10 male weanling Wistar rats were administered daily diets containing 0, 10, 50, 100, or 800 mg alpha-HCH /kg food (in corn oil) for 107 weeks, the highest dose level resulted in growth retardation, increased mortality, and slight kidney damage. With daily doses of 100 or 800 mg/kg, liver enlargement and histopathological changes in the liver were found. However, there were no liver changes at 50 mg/kg diet (NOAEL 50 mg/kg, LOAEL 100 mg/kg diet) (Fitzhugh et al., 1950).

Genotoxicity: Alpha-HCH was not mutagenic to bacteria (*Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537) with and without metabolic activation and did not induce DNA damage in bacteria. However, alpha-HCH induced DNA-fragmentation in human and rat hepatocytes. Oral exposure to alpha-HCH resulted in mitotic disturbances including an increased mitotic rate and increased frequency of polyploid hepatic cells in mice (ATSDR, 2005).

Carcinogenicity: Studies of the carcinogenicity of alpha-HCH are limited. Several studies in mice were performed, but their value is limited. Nevertheless, it is clear from the results that alpha-HCH, at high dose levels, produces nodular hyperplasia and hepatocellular carcinomas in mice (the incidence varying according on the strain) and also in rats (low incidence). Studies on initiation promotion and mode of action indicate that the neoplastic response observed with alpha-HCH is most likely due to a non-genotoxic mechanism. Alpha-HCH has been shown to promote tumors in the liver of mice and rats (IPCS, 1992). The International Agency for Research on Cancer (IARC) classified alpha- HCH in group 2B: possibly carcinogenic to humans. USEPA categorized alpha-HCH as probable human carcinogen. The department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans (ATSDR, 2005).

Immunotoxicity: Mice, treated with alpha-HCH (50 and 250 mg/kg/day- i.e. 0.5 and 2.5 mg/kg/bw/day) showed signs of immunosuppression (reduced serum levels of immunoglobulins G and M).

Effects in Humans: Adverse effects such as neurophysiological and neuropsychological disorders and gastrointestinal disturbances have been reported for workers exposed to technical HCH during pesticide or fertilizer formulation. Workers suffered from paraesthesia of the face and extremities, headache and giddiness, malaise, vomiting, tremors, apprehension, confusion, loss of sleep, impaired memory and loss of libido. Serum enzyme and IgM levels were enhanced (ATSDR, 2005). Inhalation of HCH (mixed isomers) may lead to irritation of the nose and throat (IPCS, 2006). The observation of serious hepatic effects in animals (e.g., fatty degeneration and necrosis) suggests that the same results could potentially occur in workers following prolonged occupational exposure to HCH isomers.

A German study on organochlorine compounds in the peripheral blood of 486 women with hormonal disorders and/or infertility revealed that alpha-HCH concentrations were significantly higher in women with uterine fibroids, antithyroidal antibodies, luteal insuffiency and women highly susceptible to allergies. Obese women and women with a history of abortion had the highest HCH levels in blood (Gerhard, 1993).

In a pilot study with limited statistical power a possible association between exposure to organochlorines and the risk of childhood aplastic anaemia was shown. Alpha-HCH was significantly higher in children with aplastic anaemia than in those of controls ($p < 0.05$) (Ahamed et al., 2006).

The association between alpha-HCH exposure and intrauterine growth retardation (IUGR, < 10th percentile of birth weight for gestational age) was examined in India. Statistically significant associations ($p < 0.05$) between maternal blood levels of alpha-HCH and interauterine growth retardation were found (Siddiqui et al., 2003)

Effects in non-target organisms: Data on effects in non-target species are extremely limited. Alpha-HCH is acutely toxic to aquatic organisms. Effect concentrations in algae, zooplankton (brine shrimp and water flea) and fish of < 1 mg/l were reported (detailed values in IPCS, 1992; ECOTOX database, 2007). A LC50 of approximately 1.4 mg/l was determined in an acute test (duration 24 hours) in zebra fish (Oliveira-Filho and Paumgarten, 1997). In a long term study (70 days) with snails (*Lymnaea stagnalis*) a 50 % reduction of reproduction was found at a concentration of 65 µg/l. In fish no histopathological changes or influence on growth and behaviour could be detected in long-term experiments (test concentration 800 µg/L, duration 50 days, species guppies or pellets containing 10 - 1250 mg alpha-HCH/kg, duration 3 months, species rainbow trout) (IPCS, 1992). Monitoring data on Arctic polar bears revealed a negative correlation with retinol concentrations and HCHs, which may impact a wide range of biological functions (AMAP, 2004a).

Risk characterisation
USEPA performed a dietary risk assessment for Alaskan communities for alpha and beta-HCH in 2006. USEPA estimated alpha-HCH exposures for Alaskan communities in the range of 0.00057 - 0.0039 mg/kg bw/day for adults, 0.0021 - 0.051 mg/kg bw/day for children (age 1 - 6) and 0.00073 - 0.0050 mg/kg bw/day for children (age 7 - 12). The risk is expressed as a percentage of a maximum acceptable dose or reference dose (RfD). A level of concern is reached if the dietary risk exceeds 100% RfD (USEPA, 2006). The RfD value of 0.001 mg/kg/day for chronic exposure is based on a NOAEL of 0.1 mg/kg/day (the LOAEL is 0.5 mg/kg/day) established in a subchronic toxicity study in rats and applying an uncertainty factor of 100 (USEPA, 2006). For inhalation the reference concentration (RfC) of alpha-HCH is 0.00025 mg/m^3 based on a NOAEL of 0.025 mg/m^3 for observations of liver and kidney toxicity determined in an subchronic inhalation study in rats and applying an uncertainty factor of 100 (RIVM, 2001 in USEPA, 2006).

The acute dietary exposure estimates are not of concern according to USEPA (2006). USEPA's dietary risk assessment indicates that the chronic dietary exposure estimates for alpha-HCH are above the levels of concern for high-end dietary intake estimates. The cancer dietary risk estimates for alpha-HCH are also above the level of concern for both low and high-end dietary intake estimates. According to EPA, the risk values (% cRfD) are 57 - 390 for adult males, 67 – 460 for adult females, 210 – 5 100 for children (1 - 6 years) and 73 - 500 (7 - 12 years). The estimated cancer risk for adult males is 3.2×10^{-3} to 2.5×10^{-2} and 4.2×10^{-3} to 2.9×10^{-2} for adult females. It should be noted that these estimated incidences are at least four orders of magnitude higher than a general accepted cancer risk of 1×10^{-6}. Even though this risk estimation is very conservative due to the basic maximum detected levels it can be concluded that the dietary risks are of concern. Additionally, it has to be mentioned that the target organ of chronic toxicity is the liver and it can be expected that HCHs effects might be additive.

3 Synthesis of the information

Technical HCH, a mixture of five stable HCH-isomers, contains 55 – 80 % alpha-HCH and was used extensively worldwide as an organochlorine pesticide. Though usage of technical HCH is negligible nowadays, releases into the environment may still occur. Local sources include hazardous waste sites, contaminated sites, stockpiles and landfills or dumping grounds. Though no quantitative estimates of these releases exist, the amounts of HCH residuals in the form of by-products from lindane production are assumed to range between 1.6 - 1.9 to 4.8 million tonnes. In addition, many sites are expected to cause environmental pollution and are not maintained or controlled appropriately.

The physico-chemical properties of alpha-HCH facilitate long-range atmospheric transport and allow for "cold condensation" on a global scale. In addition, the low Henry's Law Constant contributes to achieve high levels in the Arctic Ocean. Moreover, it was shown that Arctic air concentrations mimicked global usage data directly until the early 1990s. Also, monitoring data from remote regions e.g. the Arctic and Antarctica suggested that detected levels, which were sometimes higher than in source regions, originate from long range transport.

Hydrolysis contributes to the overall removal of alpha-HCH in aqueous solution under alkaline pH, but under environmental conditions has minor importance. Alpha-HCH may undergo enantioselective degradation which depends on the site and medium. Reported half-life and residue analyses in soil suggest moderate persistence. However, certain environmental conditions e.g. low concentrations or low temperatures resulted in longer half-lives. Half-lives for alpha-HCH in Arctic lakes were up to 1.4 years, whereas in the Eastern Arctic Ocean enantioselective degradation resulted in a range of approximately 5 to 17 years.

Alpha-HCH may bioaccumulate and biomagnify in biota and Arctic food webs. The BMFs as well as FWMFs in invertebrates, fish and terrestrial and marine mammals were greater than 1. Because of the individual potential to metabolize alpha-HCH, birds do not fit into this scheme. Most birds show BMFs < 1, independent of the trophic level. Especially in mammals, an enantiospecific accumulation of (+) or (-) alpha-HCH occurs (depending on the species). Combined with the lower potential for biotransformation alpha-HCH, - reaches high BMFs in mammals, with the highest concentrations in brain tissue (especially the (+) enantiomer). As all HCHs act on the central nervous system, this has to be seen with caution. To date, however, no enantiomer-specific toxicity studies for alpha-HCH are available and the reasons for the enrichment and differences are largely unclear.

Alpha-HCH has been shown to be neurotoxic, hepatotoxic, and to cause immunosuppressive effects and cancer in laboratory animals. The International Agency for Research on Cancer (IARC) has classified alpha-HCH in group 2B, possibly carcinogenic to humans. Several epidemiological studies indicate that alpha-HCH might play a role in human breast cancer. Alpha-HCH is a known tumour promoting agent.

Alpha-HCH may adversely affect human health in contaminated areas as well as in Arctic regions. Based on the available toxicity data of alpha-HCH, it can be concluded that current concentrations of alpha-HCH in food and human breast milk are a matter of concern. The estimated daily intake of alpha-HCH of Arctic indigenous people exceeds safe intake reference values, even though estimation is very conservative. The dietary risks of these populations are of concern. Nevertheless it should be emphasized that traditional foods have unique social, cultural, spiritual and economic value and therefore it is strongly recommended to avoid foods in which alpha-HCH levels are of concern.

4 Concluding statement

Though most countries have banned or restricted the use of technical HCH as a pesticide, replacing it in most cases by the use of lindane, the lindane production process has produced huge amounts of HCHs residuals. The continued production and existing stockpiles of these waste isomers have been a worldwide problem and contribute to the releases into the environment.

Releases into the environment have dramatically decreased over the past 30 years, but levels in the environment suggest that alpha-HCH may persist in the environment (at lower concentrations). The cold Arctic Ocean, which is now eliminating alpha-HCH, was a sink which preserved the chemical from rapid degradation. Levels in Arctic biota do not thoroughly reflect the decreasing trend of the abiotic compartments.

Alpha-HCH is present in the terrestrial and the aquatic food chains and concentrations are a human health concern. High exposure is expected in polluted areas, which are still present around the globe. High exposure ois also possibly expected as a result of long-range transport in the Arctic region. In addition, humans and wildlife are exposed to various contaminants that can influence the toxicological effects of alpha-HCH in an additive way. Based on the inherent properties, together with estimated daily intakes of alpha-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of alpha-HCH in biota, including in remote areas far from likely sources, it is concluded that the substance is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

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別添4

β－ヘキサクロロシクロヘキサンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【光分解性･加水分解性】 非生物的な分解ﾌﾟﾛｾｽ（光分解や加水分解）では分解しない。 【半減期】 ･大気中：56 日(計算値) ･水中：水及び底質中の半減期のﾃﾞｰﾀはないものの、ﾓﾆﾀﾘﾝｸﾞに基づき残留性があり、容易に分解しないと推定される。 ･土壌中：亜熱帯地域のｲﾝﾄﾞの砂質ﾛｰﾑで 100 及び 184 日。温帯地域では嫌気性条件下で分解せず。ｶﾅﾀﾞの砂質ﾛｰﾑでの長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 15 年後に 44%が残留。日本の農地での長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 570 日後に 30%が残留。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKow=3.78 【BCF（経鰓的生物濃縮係数）】 ｾﾞﾌﾞﾗﾌｨｼｭ：BCF=1460 【FWMF（食物連鎖による経口的生物濃縮係数）】 ･FWMFs＞1（北極海の食物連鎖の研究） ･FWMF=7.2（高塩素処理された PCB に相当） ･FWMF=2.9（ﾎﾞｰﾌｫｰﾄ･ﾁｭﾄｺ海の食物連鎖の研究による計算値） 【BMF（経口的生物濃縮係数）】 ･ｶﾀﾂﾑﾘに高い蓄積性が見られ、その捕食者（小さいｼﾗｻｷﾞなど）の BMF は 1 を超える。 ･ﾛｼｱのﾁｭｺﾄ半島の先住民の母乳含まれる betaHCH のﾚﾍﾞﾙが高い。	【反復投与毒性】 ラット（混餌　52 週）：LOAEL 0.5mg/kg/day 肝肥大、肝細胞の組織学的変化、ほぼ全動物死亡 ラット（混餌　13 週）：NOAEL 0.1mg/kg/day 主な毒性は、0.1mg/kg/day 以上で肝臓影響、2.5mg/kg/day 以上で胸腺重量減少、精巣萎縮、卵巣萎縮等、12.5mg/kg/day で死亡（運動失調、昏睡）、成長遅延、白血球･赤血球減少等 【発がん性】 マウス（26 週）：34mg/kg/day で肝腫瘍 IARC グループ2 B（possibly carcinogenic to human） 【生殖毒性】 ラット（2世代繁殖試験）：NOAEL 0.1mg/kg/day 死亡率増加、不妊 ラット：20mg/kg/day を母胎投与で児死亡率増加 ミンク等で性周期かく乱、生殖器萎縮等の報告 【その他】	【慢性毒性】 グッピー　*Poecilia reticulata*　：4-12週間試験　NOEC=0.032 mg/L（組織学的変化）。エストロゲン活性により、雄魚において、ビテロゲニン生成の変化、精巣の萎縮、雌雄同体現象、下垂体の変質が起こった。 ニワトリ：β -HCHを含む様々な有機塩素化合物に高濃度に曝露された雌が1回目及び2回目に産卵した雛鳥の身体状況が劣っていた。

		農薬、肥料の HCH 暴露により、感覚異常、頭痛、倦怠、嘔吐、振戦等 急性毒性試験において、背弯姿勢、呼吸困難、振戦、痙攣等神経症状 マウス（経口　30 日）：60mg/kg/day でリンパ球増殖、NK 活性減少	

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Geneva, 19–23 November 2007

Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Risk profile on beta hexachlorocyclohexane

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on beta hexachlorocyclohexane, on the basis of the draft contained in document UNEP/POPS/POPRC.3/18. The text of the risk profile, as amended, is set out below. It has not been formally edited.

K0763739 181207

BETA HEXACHLOROCYCLOHEXANE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

TABLE OF CONTENTS

Executive summary

Mexico, being Party to the Stockholm Convention, proposed lindane as well as alpha- and beta-hexachlorocyclohexane to be included in Annex A, B or C of the Stockholm Convention. After the risk profile on lindane had already agreed at the last meeting of the Review Committee in November 2006, the Committee concluded that beta-HCH also complied with the screening criteria laid down in Annex D of the Convention and further elaboration of the proposal and preparation of a draft risk profile should be done.

After almost forty years of extensive use worldwide, there has been a gradual replacement of technical hexachlorocyclohexane (HCH) by lindane (gamma-HCH). No significant uses of technical HCH have been reported after 2000. However releases into the environment may also occur from lindane production as well as from hazardous waste sites, landfills and contaminated sites. Because of its hazard profile and widespread abundance, technical HCH (including beta-HCH) is subject to national and international regulations and prohibitions.

Abiotic degradation processes do not play an important role in the fate of beta-HCH in the environment. Thus photolysis and hydrolysis are not significant. Under favourable conditions, beta-HCH is susceptible to biodegradation. However, compared to the gamma- and alpha-HCH, it is the most recalcitrant isomer. Laboratory and field data including a long-term soil study suggest that beta-HCH is persistent in soil, especially under low temperatures. It is mainly associated with particles and has a low leaching potential.

The physico-chemical properties of beta-HCH allow the dispersal of the substance from its sources to the Arctic mainly by long-range environmental transport via ocean currents. Beta-HCH has been detected in the Arctic Ocean and is present in marine, terrestrial species, and humans.

Beta-HCH exposure levels in local areas have declined after worldwide prohibitions and restrictions. However regions with recent exposure and/or high pollution can still show elevated levels. A special concern also arises from exposure of hazardous waste sites and dumping grounds from disposed beta-HCH residues from lindane production.

Due to its persistence, beta-HCH can still be detected at low background levels in all environmental media except in regions with recent usage and/or high pollution. Data from the abiotic environment in the Arctic are scarce, partly due to low levels compared with the other HCH isomers. In contrast to this fact, fairly high concentrations in Arctic biota including marine mammals and birds were detected with increasing levels.

Beta-HCH is present in terrestrial and aquatic food chains. Beta-HCH may bioaccumulate and biomagnify in biota and Arctic food webs, especially in upper trophic levels. In humans, accumulation in fat tissue and high concentrations in blood and breast milk may occur. Beta-HCH transfers from mothers to embryos and nursing infants.

Beta-HCH is acutely toxic to aquatic organisms and shows estrogenic effects in fish. Reduced fitness of offspring in birds as well as reduced retinol concentrations in polar bears is associated with beta-HCH and HCHs levels.

Toxicological studies with beta-HCH have demonstrated neurotoxicity and hepatotoxicity. Also, reproductive and immunosuppressive effects and effects on fertility were seen in laboratory animals. Beta-HCH has been classified in group 2B as possibly carcinogenic to humans by the International Agency on Research and Cancer (IARC). Several epidemiological studies indicate that beta-HCH might play a role in human breast cancer.

Human exposure to beta-HCH results mostly from ingestion of contaminated plants, animals and animal products. High exposure is expected in contaminated areas due to extensive use, former production, disposal sites and stockpiles.

Given the hazard profile and the exposure levels in the environment including the food chain, it can be concluded that beta-HCH may adversely affect wildlife and human health in contaminated and remote regions including the Arctic region. Arctic public health authorities believe the significant social, cultural and economic benefits of traditional foods outweigh the risks of contaminants such as HCH at present but give another reason for the quick control and elimination of all HCH isomers from traditional foods.

Based on the hazard profile, together with estimated daily intakes of beta-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of beta-HCH in biota, including in remote areas far from likely sources, it is concluded that the substance is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

1 Introduction

During the procedure for adding lindane to Annex A of the Stockholm Convention, the POPs Review Committee discussed the proposal of lindane and concluded that "other isomers of hexachlorocyclohexane should also be considered" (UNEP/POPS/POPRC.2/10). Thus Mexico submitted a proposal for listing beta hexachlorocyclohexane in Annexes A, B or C of the Stockholm Convention on 26th July 2006 (UNEP/POPS/POPRC2./INF/8). Austria on behalf of Germany prepared the first working draft on beta-HCH.

Beta-HCH is one of the five stable isomers of technical HCH, an organochlorine pesticide formerly used in agriculture. The modes of action of the HCH isomers differ quantitatively and qualitatively with regard to their biological activity in the central nervous system as the main target organ. Beta-HCH is mainly a depressant and the final effect of the mixed isomers depends on the composition (IPCS, 2001). In general HCHs are among the most studied pesticides with respect to environmental fate and effects (Breivik et al., 1999).

1.1 Chemical Identity

Chemical name: Beta-hexachlorocyclohexane (beta-HCH)

IUPAC name: (1-alpha, 2-beta, 3-alpha, 4-beta, 5-alpha, 6-beta)-Hexachlorocyclohexane

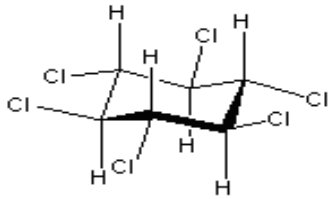
Common synonyms: beta-1,2,3,4,5,6-Hexachlorocyclohexane; beta-Benzenehexachloride; beta-BHC, benzene-cis-hexachloride; beta-HCH; beta-Hexachlorocyclohexane; beta-Hexachlorocyclohexane; beta-isomer; beta-lindane; Hexachlorocyclohexane-Beta; trans-alpha-benzenehexachloride; beta-benzenehexachloride (Chemfinder, 2007)

CAS number: 319-85-7

Chemical formula: $C_6H_6Cl_6$

Molecular weight: 290.83

Figure 1: Structure of beta-HCH (modified from Buser et al.,1995)



beta-HCH

1.1.1 Physico-chemical properties

Selected physico-chemical properties of beta-HCH are provided in Table 1. Beta-HCH is more soluble in water and octanol compared to other organochlorine pesticides. Its chemical structure seems to confer the greatest physical and metabolic stability (e.g. beta-HCH has a lower vapour pressure and a higher melting point than the alpha-isomer). The physico-chemical properties (a selection is given in Table 1) of beta-HCH allow for "cold condensation", an enrichment of the substance in cold climates compared to concentrations near sources, on altitudinal and latitudinal scales described by Wania and Mackay (1996).

The Henry's Law Constant is a factor of 20 lower than for alpha-HCH and decreases significantly with water temperature which favours partitioning from air to water. Also its relatively high log K_{oa} promotes partitioning from air to environmental organic phases. This is probably one reason why transportation pathways of alpha- and beta-HCH diverge in the environment (Li and Macdonald, 2005). Based on an extensive data analysis of the physico-chemical properties of alpha-, beta- and gamma-HCH Xiao et al. (2004) concluded that its different environmental behaviour is caused by a higher solubility in water and octanol rather than the lower volatility compared to the gamma- and alpha-isomer.

Table 1: Selected physico-chemical properties of beta-HCH

Melting Point (K)	314-315 [1]
Boiling Point (K)	333 at 67 Pa [1]
Water solubility (mol*m^{-3} at 25 °C)	1.44 [2]
Vapour pressure (Pa at 25 °C)	0.053 [2]
Henry´s Law Constant (Pa m^3 mol^{-1})	0.037 [2]
Log Kow (25°C)	3.9 [2]
Log Koa (25°C)	8.7 [2]
Physical state	crystalline solid [1]

[1] ATSDR (2005)
[2] Xiao et al. (2004)

1.2 Conclusion of the POP Review Committee of Annex D information

The POP Review Committee evaluated the proposal regarding beta-HCH submitted by Mexico (UNEP/POPS/POPRC.2/INF/8 as summarized by the Secretariat in document UNEP/POPS/POPRC.2/16) according to the requirements in Annex D of the Stockholm Convention at its second meeting in Geneva. In Decision POPRC-2/10 the Committee reached the conclusion that beta-HCH meets the screening criteria specified in Annex D. The Committee also decided to establish an ad hoc working group to review the proposal further and prepare a draft risk profile in accordance with Annex E of the Convention.

1.3 Data sources

The draft risk profile is based on the following data sources:

- Proposal submitted by Mexico for listing alpha- and beta-HCH in Annexes A, B and/or C to the Convention (UNEP/POPS/POPRC2./INF/8), 2006.
- Decision POPRC-2/10 of the Review Committee, 2006.
- Information submitted by parties and observers according to Annex E of the Convention: specific and/or scientific information: Czech Republic, France, Germany, International POPs Elimination Network (IPEN), Japan, Norway, Switzerland, United States of America, general information: Algeria, Crop Life International, Kingdom of Bahrain, Mauritius, Mexico, Qatar, Republic of Lithuania and Turkey. This information is available on the Convention's website (http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/submissions.htm)
- Assessment of lindane and other hexachlorocyclohexane isomers, USEPA, 2006. http://www.epa.gov/oppsrrd1/REDs/factsheets/lindane_isomers_fs.htm
- International Programme on Chemical Safety, ALPHA- and BETA-HEXACHLOROCYCLOHEXANES, Environmental Health Criteria 123, World Health Organization. Geneva, 1992. http://www.inchem.org/documents/ehc/ehc/ehc123.htm
- Toxicological profile for hexachlorocyclohexanes, United States of America Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, 2005. http://www.atsdr.cdc.gov/toxprofiles/tp43.html
- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. 2006. North American Commission for Environmental Cooperation http://www.cec.org/pubs_docs/documents/index.cfm?varlan=english&ID=2053

In addition to these information sources a literature search of public data bases was conducted. The following databases were used: ECOTOXicology database (Ecotox, http://www.epa.gov/ecotox/) Hazardous Substances Data Bank (HSDB, http://toxnet.nlm. nih.gov/cgi-bin/sis/htmlgen?HSDB), Pubmed (http://www.ncbi.nlm.nih.gov /entrez/query.fcgi?DB=pubmed), Environmental Fate Data Base (EFDB http://www.syrres. com/esc/efdb_info.htm. In general search terms include the chemical name or CAS number and/or a combination of a technical term because of the multiplicity of entries. For the same reason, specific topical and updated articles were also considered.

The reports listed above contained individual references which were not listed again in this draft risk profile. References referred to in this document are provided in UNEP/POPS/POPRC.3/INF/28.

1.4 Status of the chemical under international conventions

Beta-HCH is a constituent of technical HCH, which is regulated at least by two international agreements. The first one is the 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs) under the Convention on Long-Range Transboundary Air Pollution. Technical HCH is listed in Annex II of the protocol which restricted its use to an intermediate in chemical manufacturing only.

The second agreement is the Rotterdam Convention on the Prior Informed Consent (PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. HCH (mixed isomers) is subject to the PIC Procedure and is listed in Annex III of the Convention.

Canada, Mexico, and the United States signed the North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane Isomers in 2006. The goal of the NARAP is for the three member countries to cooperatively take actions to reduce the risks associated with the exposure of humans and the environment to lindane and other HCH isomers.

In the European Union the production and use of technical HCH as an intermediate in chemical manufacturing will be phased out by the end of 2007 at the latest (Regulation (EC) No 850/2004). HCHs are also one of the priority substances (Decision No 2455/2001/EC) of the adopted EU Water Framework Directive 2000/60/EC.

Hexachlorocyclohexane isomers, including the beta-isomer, are on the List of Chemicals for Priority Action under the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic. The objective is the prevention of pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances.

2 Summary information relevant for the risk profile

2.1 Sources

2.1.1 Production

Beta-HCH by itself is neither intentionally produced nor placed on the market. It is produced as constituent of technical HCH used as organochlorine insecticide or chemical intermediate to manufacture enriched HCH (lindane). Currently no production data on technical HCH have been reported, whereas manufacture of lindane still takes place (IHPA, 2006).

Further details on the production and reuse of HCH residuals can be found in UNEP/POPS/POPRC.2/17/Add.4 (Risk Profile on Lindane) and IHPA (2006).

The following countries which submitted information according to Annex E stated that there was currently no production or use of beta-HCH: Czech Republic, Germany, Mauritius, Mexico, Norway, Qatar, Republic of Lithuania, Turkey, Switzerland and the United States of America.

2.1.2 Trade and stockpiles

Please see section 2.1.2 of the risk profile on alpha-HCH.

2.1.3 Uses

Please see section 2.1.3 of the risk profile on alpha-HCH.

2.1.4 Releases to the environment

There are several pathways for beta-HCH for entering the environment. Historically beta-HCH was released during the manufacture of technical HCH and its use as a pesticide. Li et al. (2003) estimated global emissions of beta-HCH from the usage of technical HCH between 1945 and 2000 at 850 000 tonnes, of which 230 000 tonnes were emitted into the atmosphere over the same period. In 1980, the usage of beta-HCH was around 36 000 tonnes, and the calculated primary emissions were 9 800 tonnes (83 % attributed to the application and 17 % to soil residues due to prior applications). In 1990, figures dropped to 7 400 (usage) and 2 400 tons (emissions). In 2000, emissions of beta-HCH from soil residues were 66 tonnes in the absence of direct usage of technical HCH. Also, as a result of the ban on technical HCH in northern countries, global emissions of beta-HCH have undergone a “southward tilt” (Li et al., 2003).

Releases of beta-HCH into the environment are also possible from hazardous waste sites (USEPA, 2006), stockpiles and residues of lindane production, which are not always controlled or maintained safely (IHPA, 2006). Also, contaminated sites (e.g. from former production plants) may contribute to the environmental burden of beta-HCH (Concha-Grana et al., 2006). Germany (submitted Annex E information, 2007) reported that there are still a few isolated local sources i.e. landfills and dumps in the former GDR (East Germany) from applications of technical HCH. As a result, higher concentrations of beta-HCH in fish of the river Elbe near the former production site were detected after heavy rainfalls and floods in 2003. However, quantitative estimates of releases from hazardous waste sites and landfills are not available.

2.2 Environmental fate

2.2.1 Persistence

Investigations of the hydrolysis and photolysis of beta-HCH are extremely limited. Only one literature study regarding photodegradation has to date been available. A photodegradation half-life for a thin film of beta-HCH equal to 152 hours has been reported (ATSDR, 2005). The relevance of this result is questionable with respect to the chosen test design which does not comply with internationally accepted test guidelines on photolysis and, as pointed out by ATSDR (2005) no absorption bands were observed in the studied spectral region. In general, photolysis is not expected to be an important environmental fate process for beta-HCH since no absorption of light > 290 nm takes place.

Based on the calculated atmospheric OH rate constant of $5.73x10^{-13}$ cm^3/molecule-sec (HSDB, 2006) the estimated half-life is 56 days (using an average hydroxyl radical concentration of $5x10^5$ molecule/cm^3 according to the TGD (2003)).

USEPA (2006) concluded that HCH isomers are resistant to abiotic processes like photolysis and hydrolysis (except at basic pH).

Beta-HCH is in principle biodegradable under oxic and anoxic conditions. However several studies have suggested that significant degradation does mainly occur under anaerobic conditions (Middeldorp et al., 1996). Degradation was observed in pure cultures, soil slurry, soil microcosm, field studies and via bioremediation techniques in the soils of contaminated sites (Phillips et al., 2005). Effectiveness of removal varied depending on the test design and environmental factors.

In general the metabolic pathway of beta-HCH occurs anaerobically via dechlorination to tetrachlorocyclohexene and dichlorocyclohexadiene, an unstable metabolite. Chlorobenzene and benzene were formed as stable end products under methanogenic conditions. These metabolites can be further aerobically or anaerobically mineralised (Phillips et al., 2005). Compared to other HCH isomers laboratory data using radio-labelled beta-HCH have shown only minimal and incomplete mineralization (Sahu et al., 1995).

Beta-HCH is considered to be the most recalcitrant isomer due to its chemical structure (Decision POPRC-2/10, 2006). Under favourable laboratory conditions several strains of bacteria e.g. *Bacillus brevis*, *Bacillus circulans*, *Dehalobacter sp.* in conjuction with *Sedimentibacter sp.,* isolated from HCH polluted sites, have been identified as beta-HCH degraders (Gupta et al., 2000; van Doesburg et al., 2005). But only a few e.g. *Sphingobium sp.* were able to transform beta-HCH under aerobic conditions (Sharma et al., 2006).

Research on the intrinsic stimulation and additives for soil bioremediation of beta-HCH polluted sites is under way (e.g. Kumar et al., 2005; MacRae et al., 1984) but to remove the isomer remains a difficult challenge (Phillips et al., 2005). Regarding the effects on the intrinsic soil microbial population of an uncontaminated soil, Bhatt et al. (2006) showed that the application of technical HCH disturbed the microbial community irreversibly.

In general, climatic conditions as well as soil texture and organic matter altering substance sorption, water content, pH and bacterial growth influence degradation rates (IPCS, 1992). Phillips et al. (2005) stated that bacteria capable of degrading HCHs at extreme temperatures (< 5 °C or > 40°C) have not yet been reported.

Data on laboratory soil studies or field investigations are limited. Singh et al. (1991) reported half-lives of 100 and 184 days on cropped and uncropped plots respectively, in a sandy loam in India under subtropical conditions. The applied formulated HCH was immediately incorporated into the top layer of the soil. Soil samples were taken randomly from the plots in 0-15 cm depths. No quantitative information on losses of beta-HCH by volatilisation or leaching during the experiment is available in the citied study. In a temperate climate Doelman et al. (1990) observed in a semi-field study with contaminated soil no degradation of beta-HCH under anaerobic conditions. Stewart and Chisholm (1971) observed in a long-term field study after an application of technical HCH, 44 % of the beta-HCH isomer after 15 years in a sandy loam in Canada. Approximately 30 % of beta-HCH (from applied technical HCH) was observed after 570 days in a field test in Japan on agricultural field plots (Suzuki et al., 1975). Also, Chessells et al. (1988) showed that after a 20 year application history of technical HCH on sugar cane in Queensland, Australia, beta-HCH was found in concentrations which are more than one order of magnitude higher compared to the other isomers. Volatilisation from soil surfaces is considered not to be an important fate process (HSDB, 2006; Singh et al., 1991).

Beta-HCH was stable in a sediment/water study under laboratory conditions. In addition, isomerisation of alpha- to the beta-HCH isomer was observed (Wu et al., 1997). Detailed information regarding isomerisation can be found in the risk profile on lindane (UNEP/POPS/POPRC.2/17/Add.4). Levels of the beta-HCH isomer compared to alpha-, gamma- and delta-HCH were highest in porewater (1 423 ng/l) compared to concentrations in surface water (92.5 ng/l) and sediment (3.9 ng/g) of the Minjiang River Estuary, China (Zhang et al., 2003). No degradation half-lives in water or sediment are available, however, based on monitoring studies, it can be assumed that beta-HCH is persistent and does not undergo degradation easily.

2.2.2 Bioaccumulation

The octanol-water partition coefficient (log K_{ow} = 3.78) for beta-HCH indicates that it has a potential to bioaccumulate, especially in combination with its shown persistence in animal tissue (Walker et al., 1999),

The BCF according to the former OECD test guideline 305 E in zebra fish was equal to 1 460, which was the highest BCF (whole body) compared to determined values for alpha- (1 100) and gamma-HCH (850) (Butte et al., 1991). According to the ECOTOX database this was also the highest reported BCF. Nonetheless, the screening criteria were considered fulfilled by POPRC for beta-HCH as set out in the evaluation contained in the annex to its decision POPRC-2/10.

Several studies suggest that the relative proportions of HCH isomers vary dramatically across species in the Arctic marine food web (USEPA, 2006). Concentrations of beta-HCH increased with the trophic level especially in upper trophic levels (marine mammals) (USEPA, 2006; Hoekstra et al., 2003). Whereas it is assumed that organochlorine (OC) profiles in mammals are mainly influenced by their ability to biotransform and excrete OCs, high detected levels of beta-HCH in various mammalian species are another indication of its recalcitrant nature and slow elimination. Hop et al. (2002) showed that beta-HCH biomagnifies differently in poikilotherms and homeotherms. Beta-HCH increased more among homeotherms (birds and mammals) with the trophic level. Fisk et al. (2001) reported the highest BMF (biomagnification factor) in birds compared to the other trophic levels, but migration and prey items are also considered to influence the variability of the BMFs. These data are in line with findings from Moisy et al. (2001). In general, studies from Arctic marine food webs show that BMFs for nearly all examined species as well as obtained food web magnification factors (FWMFs), which represent the mean rate of increase per trophic level in the food chain, are greater than 1. For example Fisk et al. (2001) reported a FWMF of 7.2 which is comparable to higher chlorinated PCBs. A FWMF of 2.9 was calculated by Hoekstra et al. (2003) for the marine food web in the Beaufort-Chukchi Sea. However in sub-Arctic waters e.g. the White Sea, values for for beta-HCH were lower compared to the other food web studies. Differences in feeding habits and availability/levels of contaminants were suggested as being responsible by Muir et al. (2003).

Also, in the terrestrial food chain, beta-HCH may biomagnify. Data obtained from an investigation in south India showed that HCHs were the predominant OCs in biota. Elevated concentrations were measured in snails and subsequently their predators (e.g. little egret) showed BMFs above 1 (Senthilkumar et al., 2001). Also Wang et al. (2006) found beta-HCH as a major compound in mollusks (submitted Annex E information by IPEN, 2007).

Kelly at al. (2007) have recently shown that, for substances with a logKoa >6 and a logKow >2, the fish BCF is not a good predictor of biomagnification in air-breathing animals. This is well illustrated by beta-HCH, in the marine mammalian and terrestrial food webs, as such compounds biomagnify strongly up to 3000- and 400-fold respectively.

Fish, marine and terrestrial mammals as well as birds are the major nutrition sources of several human Arctic population groups and thus exposure through diet is much more likely than for most populations in the developed world. Levels of beta-HCH in breast milk among women from indigenous people on the Chukotka Peninsula, Russia (Chukotsky rayon, mean value 370 ng/g lipids) are highest compared to other northern towns of Russia and to levels in Canada (Nunavik, by 30 times; AMAP, 2004). Also, concentrations of maternal blood sampled between 1994 and 1997 were highest in Russian mothers (Arctic non-indigenous population, serum concentration 223 µg/kg lipid), but elevated levels were also found in Iceland (23 µg/kg) and in the Canadian Arctic (AMAP, 2003).

2.2.3 Long-range environmental transport

Many studies and monitoring data have detected beta-HCH regularly in the Arctic environment as well as in biota (e.g. AMAP, 2004; AMAP, 2003). Because technical HCH, including beta-HCH, was never extensively used in this remote area, this is evidence of its long range transport (UNEP/POPS/POPRC.2/17/Add.4).

Based on monitoring data from Arctic air, beta-HCH appears to be less subject to direct atmospheric loading into the high Arctic. This can possibly be explained by differences in the Henry's Law Constant and the air/octanol partition coefficient that show enhanced affinity to organic matter (Li et al., 2002). Thus rain scavenging is much more efficient for beta- than for alpha-HCH and besides, the frequency of precipitation is considerably higher in the North Pacific compared to the Arctic. This suggests that beta-HCH enters the Arctic probably by mechanisms involving wet deposition or partitioning into the North Pacific surface water and subsequently entering the Arctic in ocean currents passing through the Bering Strait (Li et al., 2003). The Bering and Chukchi Seas are the most vulnerable locations for beta-HCH loadings (Li et al., 2002). Concentrations of beta-HCH around the Bering Strait in the 1990s reached approximately 1.2 ng/l (Li and Macdonald, 2005). Thus "cold condensation" also occurred for beta-HCH, but mainly in the Pacific Ocean and Bering Sea upstream of the Arctic Ocean. Thus beta-HCH reached the Artic later compared to alpha-HCH and differed in its spatial distribution (Li et al., 2002). This spatial and temporal distribution is also reflected in residue levels in marine and terrestrial mammals as well as in local residents (Li and Macdonald, 2005).

Measurement of beta-HCH in high mountains in the Czech Republic is another proof for its long-range transport potential (submitted Annex E information by the Czech Republic, 2007).

According to model calculations with the OECD Pov and LRTP Screening Tool beta-HCH has similar persistence and long-range transport properties compared to already identified POPs such as PCBs and OCs (Wegmann et al., 2007). Model input properties of the chemicals include partition coefficients in air-water and octanol-water as well as half-lives in air, water and soil and the Henry's Law constant (based on figures contained in UNEP/POPS/POPRC2./INF/8). The model considers all environmental compartments quantitatively. The results of the model do not indicate absolute levels in the environment but help to compare possible POPs with identified POPs (reference chemicals: PCB congeners 28, 101, 180, HCB, carbon tetrachloride and alpha-HCH) according to their environmental persistence and potential for long range transport. Uncertainties in the chemical properties were investigated by Monte Carlo uncertainty analysis.

2.3 Exposure

Direct exposure to beta-HCH resulted from the production (including manufacture of lindane) and use of technical HCH. Because of the persistence, high exposure is also expected in contaminated areas due to extensive use, former production, disposal sites and stockpiles. Though usage of technical HCH has practically ceased worldwide monitoring data based on the ratio of the alpha/gamma-isomer still suggest possible releases of technical HCH in certain areas (Zhang et al. 2003; Qian et al., 2006; Zhulidov et al., 2000).

Exposure of the general public results mostly from the ingestion of contaminated plants, animals and animal products. Inhalation of ambient air and consumption of drinking water are further sources of exposure, although to a minor extent. Intake through indoor air may be considerable for people living in houses treated for pest-control purposes. Infants may be exposed during fetal development and breastfeeding.

2.3.1 Environmental monitoring data from local areas

Generally environmental levels in local areas have dropped after restrictions and prohibitions of the usage of technical HCH (IPCS, 1992). However, monitoring data show its ubiquitous distribution in all environmental media. For example, beta-HCH (up to 15 µg/kg dry substance) has been detected using passive monitoring in lichens in various locations (e.g. cities, industry, rural) in Switzerland (submitted Annex E information by Switzerland, 2007). Also, a recently (2004) performed monitoring programme in Japan revealed that beta-HCH had been detected in all specimens. The reported values (range) are as follows: water 0.031-3.4 ng/l, sediment 0.004-53 ng/g dry weight, shellfish 0.22-1.8 ng/g wet weight, fish trace-1.1 ng/g wet weight, bird 1.1-4.8 ng/g wet weight, air (warm and cold season) 0.53-110 pg/m^3 and 0.32-78 pg/m^3 (submitted Annex E information by Japan, 2007). The Czech Republic (Annex E information, 2007) reported that, with regard to HCHs, the most severe situation is in central and southern Moravia, where sediment particles are found in amounts of tens of ng/g and in some cases even in hundreds of ng/g (no information on which basis the concentrations are expressed was submitted).

However, heavily contaminated soils were found in the proximity of sources. HCH concentrations of 40 - 225 mg/kg were found in the topsoil around a chemical plant in Albania. Mean levels of 0.02 mg/kg were reported for soils from the Pearl River Delta in China, while Russian soils near the Lena River contained 0.001-0.017 mg/kg HCH (UNEP, 2003).

Compared to the other HCH isomers, concentrations of beta-HCH in the air are low. Elevated levels were detected in higher mountains (Mount Everest Region) of 11.2 pg/m^3 compared to up to 1 pg/m^3 in the Arctic (Li et al., 2006). Seasonal changes in beta-HCH concentrations in Japan (mean 23 pg/m^3) in 2000 were probably caused by re-emissions from a terrestrial source (Murayama et al., 2003). Unlike alpha- and gamma-HCH observed concentrations of beta-HCH in air at most locations near the Great Lakes in North America did not show significant trends between 1990 and 2003. The highest concentration was observed in Chicago with a maximum of 73 pg/m^3 (mean 12 pg/m^3, 1999-2003, gas phase, Sun et al., 2006a). Regarding the occurrence of beta-HCH in precipitation samples from the same region (mean concentrations 0.16 - 0.64 ng/l) a significant increase in concentrations at three Great Lakes stations over the last decade was observed (Sun et al., 2006b).

Levels in biota vary, depending on the location (recent usage and/or high pollution) and species. For example, concentrations of HCHs (mainly the beta-isomer) in one fish species (*Java tilapia*) from India amounted to up to 2 000 ng/g wet weight (Senthilkumar et al., 2001). Fish samples collected from the Nile River near Cairo in 1993 showed a concentration of beta-HCH of 1.5 ng/g wet weights (UNEP, 2003). Alpha-HCH is in most cases the dominant isomer in fish (Willett et al., 1998).

A global sampling study of free-range chicken eggs found that of 30 egg samples taken from 17 different geographic locations, beta-HCH was detected in all samples. Levels were particularly high in samples taken in Senegal and India. (Blake, 2005).

Birds and bats can accumulate higher concentrations of beta-HCH. According to submitted Annex E information by Norway (2007) Bustnes et al. (2006) concluded that beta-HCH levels in blood and eggs were higher in the endangered subspecies compared with the increasing subspecies of the black-backed gulls in Norway. One explanation might be the migration route through the Black Sea where HCH levels are considerable high.

In a study of resident and migratory birds collected from South India, the organochlorine contamination pattern varied depending on the migratory behaviour. Resident birds living in the same region for their entire life span contained relatively greater concentrations of HCHs (14-8800 ng/g wet weight). Long distance migratory birds which have their breeding grounds in Europe, Russia, the Middle East, Papua New Guinea and Australia contained HCHs at levels of 19-5500 ng/g. Among various HCH isomers, beta-HCH was the predominant contaminant in all the bird species (UNEP, 2003). Similar levels were reported in a later investigation (Senthilkumar et al., 2001) including residue levels of HCHs in egg yolks (range 350-49000 ng/g fat weight). Again beta-HCH was the predominant isomer in birds (no detailed values for beta-HCH were reported). In addition, HCHs concentrations (mainly the beta-isomer, up to 330 ng/g wet weight) in Indian bats were investigated, which were higher in 1998 than in 1995 and highest compared to other parts of the world.

A local source of beta-HCH was the usage of technical HCH in the Russian north against nuisance insects on domesticated reindeer by indigenous human populations (Li et al., 2004). However, no quantitative estimates of these exposure levels exist.

2.3.2 Exposure as a result of long-range environmental transport

The main transportation pathway of beta-HCH to the Arctic is assumed to be ocean currents (Li et al., 2002). Compared to levels of alpha-HCH in sea water, beta-HCH levels were lower - partly due to reduced emissions and different spatial and temporal distributions, e.g. beta-HCH reached its peak (approximately 0.3 ng/l) in the north American Arctic Ocean in 1994, around 10 years after the alpha-HCH levels had reached their peak. Enrichment of the upper waters of the North Pacific Ocean and Bering Sea (approximately 1.3 ng/l 1988-1999) caused higher concentrations in the Chukchi Sea and subsequent decreases towards the Arctic interior ocean (Li and Macdonald, 2005). Data on beta-HCH from surface water of the Canadian Archipelago in 1999 showed concentrations of 0.1 ng/l (Bidleman et al., 2007).

This spatial distribution is also reflected in the levels in biota. Hoekstra et al. (2002) found that bowhead whales exhibit a reversal in their blubber alpha-/beta-HCH ratios on their migration route between the Bering to the Beaufort Sea. Also elevated residues of HCH isomers in marine mammals of the Canadian Archipelago are likely due to the high concentrations of HCH isomers in the water because HCH isomers are the most abundant organochlorines in the Arctic Ocean (NARAP, 2006).

Beta-HCH is not so abundant in the Arctic abiotic environment and therefore it has not been studied as well as the other HCH isomers. Measured levels in the Arctic air (e.g. < 1 pg/m^3 from six Arctic circumpolar located sites between 2000-2003, Su et al. (2006)) and in terrestrial as well as freshwater ecosystems were low (AMAP, 2004). HCHs also show a high degree of spatial variability in the levels of contamination across the Russian north (AMAP, 2004).

Levels in the Arctic terrestrial environment (including carnivores) are much lower than in the marine compartment and its predators. However, beta-HCH has been detected in the fat of male Arctic foxes (up to 810 ng/g wet weight) in Alaska (AMAP, 2004). The highest levels of HCH in polar bears were detected in the Beaufort Sea population (approx. 770 ng/g wet weight in fat). Beta-HCH accounted for 93 % of HCH residues.

The metabolism of beta-HCH is very limited in Arctic seabirds, and therefore beta-HCH is detected more readily than alpha- and gamma-HCH. But concentrations vary notably between species, depending on the trophic position and migration. Higher levels of beta-HCH were observed in the North American Arctic in closer proximity to Asia where HCH was recently used. Levels were below 1 ng/g in bird tissue and 30 ng/g wet weight in eggs (AMAP, 2004).

Regarding temporal trends, it was shown that beta-HCH levels in seabirds, ringed seals and polar bears increased, whereas belugas showed no difference from 1982 to 1997 (AMAP, 2004).

2.3.3 Food

Daily intake values of beta HCH for the general population in adult human diets between 1986 and 1991 in the United States were reported to be below 0.001 µg/kg /day The average concentration of beta-HCH in 234 ready-to-eat foods was 0.0027 µg/kg (no information on which basis the concentrations are expressed, ATSDR, 2005). In the Total Diet Study conducted by USFDA in 2003 on 100 food items, beta-HCH was detected in 12 items (submitted Annex E information by IPEN, 2007). In the USA, the average daily intake of beta-HCH was <0.1-0.4 ng/kg body weight (bw) (depending on age) during the years 1982-1984 and was generally below 0.1 ng/kg bw during the years 1986-1991 (ATSDR, 2005). In a total diet study from Canada (1993-1996), an average daily dietary intake of 0.39 ng/kg bw beta-HCH was reported (EFSA, 2005). In fat-containing food products, levels ranged up to 0.03 mg/kg (fat) but in milk products levels up to 4 mg/kg (fat) were detected (WHO, 2003). In the United States and Canada levels in food are slowly decreasing. Within the European countries representative dietary intake studies are scarce. One was performed

in the Czech Republic. The median intake values for beta-HCH declined from 8.4 ng/kg bw in 1994 to 2.1 ng/kg bw in 2002 (EFSA, 2005). A local diet study from Spain showed elevated daily intakes of 0.1 µg beta-HCH (Urieta et al., 1996). Fish and clam samples from India contained 0.001 and 0.02 mg beta-HCH/kg wet weight respectively (Nair and Pillai, 1992). Because of the global trade of foodstuffs, feed ingredients and food products from regions with ongoing or recent use of HCHs, which are supposedly more contaminated, might be imported by countries where technical HCH has already been phased out.

High levels of beta-HCH levels in food are documented for the Arctic Region (AMAP, 2004). Subsistence foods in Alaskan communities from the years 1990 to 2001 were analysed for total HCH in order to estimate dietary intakes by indigenous people. Highest concentrations were found in marine mammals of whale (391 ng/g) and seal (215 ng/g). High concentrations were documented for walrus (20 ng/g), whitefish (20 ng/g) and salmon (26 ng/g). Berries contained 10 ng/g and ducks 7 ng/g (no specification if values referring to whole body or lipid basis reported) (USEPA, 2006).

2.3.4 Body burden

2.3.4.1 General population

Beta-HCH is the most prevalent HCH-isomer in human fatty tissue. The half-life of beta-HCH after inhalation exposure in the body is 7.2-7.6 years (ATSDR, 2005). Human biomonitoring studies in the United States showed that median levels of beta HCH in post-mortem human adipose tissue samples decreased over time (0.45 ppm in 1970 to 0.16 ppm since 1981*)* (ATSDR, 2005).

A comparison between body compartments showed median levels of 0.13 ng/g in whole blood and 18 ng/g in adipose tissue (ATSDR, 2005). According to the results of the National Reports on Human Exposure to Environmental Chemicals, beta-HCH serum concentrations in the US population have been declining since 1970. For all tested age groups (12 years and older), the 95th percentile of beta-HCH serum concentrations on a lipid-weight basis decreased from 68.9 in the years 1999-2000 to 43.3 ng/g in the years 2001-2002. Concentration levels (2001/2002) in females were higher (54.5 ng/g) than in males (29.2 ng/g). Highest concentration levels were found in the Mexican Americans (84.4 ng/g). Comparably low levels were found in the age group 12-19 years (8.44 ng/g) (CDC, 2005). Age-related increases in the levels of beta-HCH have been observed in several studies and documented by the German Commission on Biological Monitoring (Ewers et al., 1999).

Comparably high concentrations were detected in human blood serum samples from Romania. Beta-HCH was detected in all samples (n = 142) with a median concentration of 923 ng/g lipid (range 38-11690 ng/g) (Dirtu et al., 2006). High concentrations were reported for India due to agricultural use and Malaria control activities. Blood serum samples from India contained up to 0.02 mg beta-HCH/l, whereas adipose tissue contained up to 0.18 mg/kg (Nair and Pillai, 1992).

2.3.4.2 Indigenous population

Beta-HCH concentrations in blood plasma samples from different regions and ethnic groups of indigenous mothers of the Arctic were 0.04 - 0.11 µg/l (Canada), 0.07-0.56 µg/l (Greenland), 0.12 - 0.53 µg/l (Alaska), 0.31 - 3.1 µg/l Russian Arctic (maximum level: 11.6 µg/l), 0.16 - 0.21 µg/l (Iceland), 0.05 - 0.09 µg/l (Norway, Finland and Sweden) and 0.11 µg/l from the Faroe Islands (AMAP 2004, values given as geometric means, with the exception of Alaska which are given as arithmetic means). The highest concentrations in blood samples of the indigenous population were reported for the Russian Arctic.

Comparative investigations of the maternal blood and cord blood of indigenous mothers for beta-HCH in the Russian Arctic were highly dependent on the residential area. The mothers with the highest exposure (Chutkotsky District) had blood concentrations (µg/l plasma, geometric mean and range) of 2.0 (0.6 - 7.6) µg/l whereas the cord blood contained 0.8 (n.d.- 8.0) µg/l (AMAP, 2004:2). The variation in body burden for indigenous people may also be due to local sources in addition to variations in consumption of local marine foods (AMAP, 2004:2).

2.3.5 Exposure of children

Children are at specific developmental stages more vulnerable against chemical substances than adults. It is not known if children are more susceptible than adults to health effects from exposure to beta-HCH. Placental transfer of HCH in humans has been well documented (ATSDR, 2005; Falcon et al., 2004; Shen et al., 2006). Beta-HCH is lipophilic and accumulates in adipose tissue and breast milk. This is another relevant exposure source for children (USEPA, 2000). Several studies concerning beta-HCH in breast milk are listed in Table 2. It could be shown, that due to restrictions of use, concentrations are constantly declining.

It can be concluded that beta-HCH concentrations in breast milk are highly exposure-dependent. Whereas in some areas concentrations are very low, i.e. 13 ng/g in Poland, in other areas i.e. Russia, Ukraine, Romania they are very high (up to > 800 ng/g). In general it can be expected that in several East European and developing countries concentrations

are still very high. Especially high concentrations were reported for India and China (Wong et al., 2002). Extremely high levels were also reported for cotton pickers in Pakistan (UNEP, 2003).

Due to bioaccumulation in the Arctic marine food web, high concentrations were found in the breast milk of indigenous mothers of Arctic regions.

Table 2. Concentrations of beta HCH in breast milk

Country/region	Levels (lipid weight basis)	Comments	References	Year
Germany	0.12 mg/kg	Start of Monitoring program 1984	Fürst et al. in EFSA, 2005	1984
Germany	0.02 mg/kg	Continuous Monitoring since 1984	Fürst et al. in EFSA, 2005	2001
Spain	0.24 µg/g	51 samples	Hernandez et al. in Wong, 2002	1991
Canada	0.6-0.8ng/g	Lower concentration: population near Great lakes	Mes and Malcolm in ATDSR, 2005	1992
Canada	0,02 µg/g	497 samples	Newsome and Ryan in Wong, 2002	1992
Brazil	0.27 µg/g	40 samples	Paumgartten et al. in Wong, 2002	1992
Russia Murmansk	853 ng/g	15 samples	Polder et al. in Dirtu, 2006	1993
Russia Nonchegorsk	740 ng/g	15 samples	Polder et al. in Dirtu, 2006	1993
Ukraine	731 ng/g	200 samples	Gladen et a.l in Dirtu, 2006	1993-1994
Czech Republic	71 ng/g	17 samples	Schoula et al. in Dirtu, 2006	1993-1994
Kazakstan	2.21µg/g	33-76 samples	Hooper et al., in Won, 2002	1994
Siberian Russia	40 -142 µg/kg (geom.means)	Arctic Monitoring Assessment Programme	Klopov et al. 1998, 2000 in AMAP 2004	1994-1995
Northern Russia	120 -401 µg/kg (geom.means)	Arctic Monitoring Assessment Programme	Polder et al. in AMAP 2004	1994-1995
Australia	0.35µg/kg	60 samples	Quinsey et al in Wong, 2002	1995
Afrika, Uganda,	0.005-0.25 mg/kg	-	Ejobi et al. in ATDSR, 2005	1996
India	8.83 µg/kg	Delhi, Age group: 20-30 61 samples	Banerjee et al. in Wong, 2002	1997
India	0.022 – 0,078 mg/kg	Region under Malaria control	Dua et al. in ATDSR, 2005	1997
Pakistan	0 – 0.90 mg/kg	Cotton pickers	Masud and Parveen, 1998 in UNEP, 2003	1998
Nairobi, Kenya	0.0830-0.026 mg/kg	Urban population	Kinyamu et al.	1998
Japan, Osaka,	5.43 µg/g	Estimated use in Japan: 400 000 tons	Konishi et al. 2001	1972
Japan, Osaka,	0.21 µg/g	Ban of organochlorine compounds in 1970ies	Konishi et al. 2001	1998
Romania, Iassay	640 ng/g	19 samples	Covaci et al. in Dirtu, 2006	2000
Czech Republic	56 ng/g	43 samples	Cajka and Hajslova in Dirtu, 2006	2000
China, Hong Kong	15.96 µg/g	Uncontrolled agricultural use	Wong et al. 2002	1985
China, Hong Kong	0.95 µg/g	115 samples	Wong et al. 2002	1999
China, Guangzhou	1.11 µg/g	54 samples	Wong et al. 2002	2000
Turkey	149 ng/g	37 samples	Erdoorul et al. in Dirtu, 2006	2003
Poland	13 ng/g	22 samples	Jaraczewska et al. in Dirtu, 2006	2004
Sweden, Copenhagen	13.64/12.29 ng/g	Cases/Controls Cryptorchidism- study	Daamgard et al.	2006

2.3.6 Information on Bioavailability

Beta-HCH is moderately associated with organic matter in the environment. Uptake by plants and residues in vegetation as well as by food and feed is well documented (Willet et al. 1998; ATSDR, 2005; EFSA, 2005). Though beta-HCH is not assumed to be very mobile in soil there have been cases of groundwater contamination in the past (HSDB, 2006).

In biota, beta-HCH is selectively accumulated in certain tissues (e.g. liver, muscle, fat) and affects several organs (Willett et al., 1998). It can be concluded that beta-HCH is bioavailable in the environment and in biota.

2.4 Hazard assessment for endpoints of concern

2.4.1 Human Health

Information on the toxicity of beta-HCH is mostly derived from experimental studies in animals. Compared to lindane, the data available are limited, especially concerning human data because occupational exposure occurs mainly with technical-grade HCH and lindane.

Studies of acute/short-term toxicity via the oral route, subchronic and chronic oral toxicity studies and a limited number of studies of reproductive effects are available. No studies of the toxicity of beta HCH via inhalation and dermal application have been conducted. There is a lack of dose-response data after oral exposure in all relevant species. For the present risk profile, the most important findings concerning the hazard assessment have been reviewed. For further studies and details the more comprehensive toxicological profiles should be consulted (IPCS, 1992; ATDSR, 2005; USEPA, 2006).

*Acute Toxicity/ Neurotoxicity:*The concentration range for lethal acute toxic effects is - according to IPCS (1992) - 150 mg/kg to > 16000 mg/kg in mice and 600 mg/kg to > 8000 mg/kg in rats. Symptoms of acute toxicity affect mainly the nervous system: excitation, hunched posture, rough fur, dyspnoea, anorexia, tremors, convulsions and cramps.

*Subchronic toxicity:*In a 13-week study in rats, the effects of oral exposure to beta-HCH (0, 2, 10, 50, 250 mg/kg diet) were investigated. In all dose groups, liver effects were observed. At the highest dose tested (250 mg/kg diet) half of the animals died following ataxia, progressive inactivity, and coma. Observed effects included growth inhibition, decrease of red and white blood cells, increase of liver enzymes and liver effects (increase in organ weight, centrilobular hepatocytic hypertrophy). A decrease in thymus weight (50 and 250 mg/kg) and atrophy of the testes were observed. The females showed atrophy of the ovaries with impaired oogenesis and focal hyperplasiea as well as metaplastic changes of the endometrial epithelium, which was interpreted as a possible estrogenic action of beta-HCH (van Velsen et al., 1986). A NOAEL of 2 mg/kg diet (equivalent to 0.1 mg/kg bw/day) was established (IPCS, 1992; EFSA, 2005).

Chronic Toxicity: A long-term study (52 weeks) in rats with 0, 10, 100 and 800 mg/kg beta-HCH in their diet (i.e. 0.5, 5 and 40 mg/kg bw/day) led to liver enlargement and histological changes. Nearly all animals died. The LOAEL was 10 mg/kg diet (Fitzhugh et al., 1950).

A two-generation reproduction study of rats exposed to 10 mg/kg diet resulted in increased mortality and infertility. The NOAEL was 2 mg beta-HCH/kg diet (equivalent to 0.1 mg/kg bw/day) (van Velsen in IPCS, 1992).

Genotoxicity: Beta-HCH was not mutagenic to bacteria (*Salmonella typhimurium* strains TA 98, TA 100, TA 1535 and TA 1537) with and without metabolic activation and did not induce DNA damage in bacteria. Positive results were seen in an in-vivo rat bone marrow chromosomal aberration study (EFSA, 2005).

Carcinogenicity: Studies of the carcinogenicity of beta-HCH are limited. Several studies in mice were performed, but their value is limited. On the one hand their duration, due to high mortality, was too short; on the other hand histopathological evaluations were missing. Studies in rats have been inadequate due to high mortality and small animal numbers. One study in mice is adequate for an evaluation of the carcinogenicity of beta-HCH. 200 mg/kg beta-HCH in the diet (equivalent to 40 mg/kg bw/day) for 110 weeks led to liver enlargement, hyperplastic changes and an increase in benign and malignant tumours in the exposed mice. In a 32 weeks study where 0, 100, 300, 600 mg/ per kg diet were given to mice, liver toxicity and atypical proliferation was observed in all dose groups (IPCS, 1992). In a 24-week study in mice - given 0, 50, 100, 200, 500 mg beta-HCH /kg diet - liver tumours and nodular hyperplasia in the highest dose group was observed (IPCS, 1992). In a 26-month study, liver cancer in mice was observed at a daily dose of 34 mg/kg (ATSDR, 2005). Based on these data beta-HCH has been classified as possible human carcinogen by IRIS (Integrated Risk Information System). Studies on the mode of action of carcinogenicity showed no clear initiating potential of beta-HCH. In one study the hepatocarcinogenic action of beta-HCH was shown with PCBs as promoting agent (ATSDR, 2005).It was suggested that the neo-plastic response observed with beta-HCH most likely occurs due to a non-genotoxic mechanism (IPCS, 1992). Beta-HCH has been shown to have tumour-promoting activity.

The International Agency for Research on Cancer (IARC) classified beta- HCH in group 2B: limited evidence for carcinogenicity. A positive association has been observed between exposure to beta-HCH and cancer, for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence. USEPA has classified technical HCH and alpha-HCH as probable human carcinogens and beta-HCH as a possible human carcinogen (ATSDR, 2005). The US Department of Health and Human Services (DHHS) has determined that HCH (all isomers) may reasonably be anticipated to cause cancer in humans (ATSDR, 2005).

Endocrine mediated toxicity: Degenerative changes in male reproductive tissues and sperm abnormalities in rats and mice were described (ATSDR, 2005). In a 13-week study, 0, 50, 150 mg beta-HCH/kg diet were given to Wistar rats. At 150 mg/kg diet, atrophy of the testes in males and increase in uterine weights in females and significantly reduced weight gains were reported (IPCS, 1992). Several other studies showed effects such as decrease in sperm counts and sperm abnormalities as well as histological effects on the testes and uterus at high doses of beta-HCH exposure (USEPA, 2006).

Animal studies and a study with MCF-7 cells showed weak estrogenic effects of beta-HCH.

Reproductive toxicity: Adverse reproductive effects after beta-HCH treatment have been observed in laboratory rodents and minks (ovarian atrophy, increased length of estrous cycle, disruption of ovarian cycling, decreased ovulation rate in female, and a decrease in the number of sperm and/or spermatids, degeneration of seminiferous tubules and testicular atrophy in male animals). Also embryotoxic effects were observed (ATSDR, 2005).

Beta-HCH has been shown to increase fetal deaths within 5 days of birth at a dose of 20 mg/kg/day given to rat dams (USEPA, 2006).

Immunotoxicity: Mice, treated with beta-HCH (60 mg/kg/day) orally for 30 days showed decreased lymphoproliferative responses to T-cell mitogens and decreased natural killer cytolytic activity. The NOAEL was 20 mg/kg/day (USEPA, 2006). Cortical atrophy of the thymus was observed at a dose of 22.5-25 mg/kg/day (van Velsen et al., 1986).

Effects in Humans: Adverse effects such as neurophysiological and neuropsychological disorders and gastrointestinal disturbances have been reported in workers exposed to technical HCH during pesticide or fertilizer formulation. Although beta-HCH is only a minor component of technical-grade HCH, it reached higher levels and persisted longer in the serum than either alpha- or gamma-HCH. 60-100 % of the total HCH measured in serum was beta-HCH (0.07-0.72 ppm). Workers suffered from paresthesia of the face and extremities, headache and giddiness, malaise, vomiting, tremors, apprehension, confusion, loss of sleep, impaired memory and loss of libido. Serum enzyme levels were enhanced as well as IgM (ATSDR, 2005). Inhalation of HCH (mixed isomers may lead to irritation of the nose and throat (IPCS, 2006). The observation of serious hepatic effects in animals (e.g., fatty degeneration and necrosis) suggests that the same results could potentially occur in workers following prolonged occupational exposure.

Beta-HCH levels were higher in the blood of women with miscarriages compared to a control group. Several other organochlorine pesticides were also higher in these women, and therefore it was not possible to establish a causal relationship (Gerhard, 1999).

A possible link between human exposure to HCH and breast cancer has been examined in several epidemiological studies. Most studies showed a weak - not statistically significant - correlation. A non-significant trend between beta-HCH in serum and cancer risk was observed during a 17-year follow-up of a Copenhagen cohort study (Hoyer et al., 1998). Blood levels of beta- HCH were higher in women with breast cancer (in the 31-50 age group) when compared to women without breast cancer (Mathur et al., 2002). In one Chinese study (article in chinese) a significant association between high beta-HCH concentrations in blood and breast cancer in premenopausal women was observed (Li et al., 2006).

In another study a possible association between breast milk concentrations of various organochlorine pesticides including beta-HCH and cryptorchidism was investigated. Beta-HCH was measurable, but not statistically significantly higher in case milk than in control milk. A combined statistical analysis of the eight most abundant persistent pesticides, including beta-HCH, showed that pesticide levels in breast milk were significantly higher in boys with cryptorchidism (Damgaard et al., 2006).

2.4.1.1 Risk characterisation

In 2006 the United States Environmental Protection Agency (USEPA) performed a risk assessment that indicated potential risks from dietary exposure to the alpha and beta HCH isomers to communities in Alaska and others in the circumpolar Arctic region who depend on subsistence foods, such as caribou, seal and whale. The dietary profile (intake rates) is based on the subsistence food harvest amounts of nearly 180 communities from the Community Profile Database Version 3.11 dated 3/27/01 from the Alaska Department of Fish and Game Division of Subsistence (data from 1990 to 2001, USEPA, 2006).

USEPA estimated beta-HCH exposures for Alaskan communities in the range of 0.00043-0.0032 mg/kg bw/day for female adults, 0.0014-0.010 mg/kg bw/day for children (age 1-6) and 0.00048-0.0036 mg/kg bw/day for children (age 7-12). The risk is expressed as a percentage of a maximum acceptable dose or reference dose (RfD). A level of concern is reached if the dietary risk exceeds 100 % RfD. The RfD for acute oral toxicity is 0.05 mg/kg/day. The RfD value for intermediate duration is based on a LOAEL of 0.18 mg/kg/day established in a subchronic study in rats and applying an uncertainty factor of 300 (ATSDR, 2005). On this basis USEPA established a chronic RfD of 0.00006 mg/kg/day by assessing another uncertainty factor of 10 for chronic exposure. RIVM calculated a chronic oral RfD of 0.00002 mg/kg/day for beta-HCH based on a NOAEL of 0.02mg/kg/day for observations of infertility in two semi-chronic oral studies on reproduction in rats and applying an uncertainty factor of 1000 (RIVM, 2001 in USEPA, 2006).

Levels of concern are reached if the dietary risk exceeds 100 % RfD. The acute dietary exposure estimates are not of concern according to USEPA (2006). USEPA's dietary risk assessment indicates that the chronic dietary exposure estimates for beta-HCH are above the levels of concern for both low and high end dietary intake estimates. The cancer dietary risk estimates for beta-HCH are also above the level of concern for both low and high-end dietary intake estimates. According to USEPA, the risk values (% cRfD) are 620-4700 for adult males, 720-5300 for adult females, 2 300-17 000 for children (1-6 years) and 800-6000 (7-12 years). The estimated cancer risk for adult males is $6.7x10^{-4}$ to $5.0x10^{-3}$ and $7.7x10^{-4}$ to $5.8x10^{-3}$ for adult females respectively. It should be noted that a general accepted cancer risk is $1x10^{-6}$. Even though this risk estimation is very conservative due to the basic maximum detected levels it can be concluded that the dietary risks are of concern. Additionally, it has to be mentioned that the target organ of chronic toxicity is the liver and it can be expected that HCHs effects might be additive. It has to be considered that the RfD based on effects on fertility (RIVM, 2001 in USEPA, 2006) is remarkably lower and would be exceeded to an even greater extent.

As beta-HCH is present in cord blood and breast milk infants may be exposed to the damaging reproductive effects of HCH inside and outside the womb (USEPA, 2000).

Also, based on the study of Nair et al. (1996), levels of 0.198 mg beta-HCH/l in breast milk would lead to an intake of 0.1386 mg/l (700 ml intake) which is almost 100-fold higher than the safe intake of 0.0015 mg/child (5 kg) and only about three times lower than the LOAEL seen in animal studies (Pohl and Tylenda, 2000). Establishing the chronic RfD value of USEPA, a safe intake for a child with 5 kg would be even lower (0.0003 mg/kg) and would exceed the RfD 462-fold. Also in other regions intake levels with food and especially with breast milk are of high concern.

Anyway the unique social, cultural, spiritual and economic values of traditional foods have to be considered and strong efforts should be taken to minimize beta-HCH levels therein (CACAR, 2003).

2.4.2 Environment

Beta-HCH is acutely toxic to aquatic organisms. Compared to effect concentrations in algae and daphnia (IPCS, 1992), fish is the most sensitive taxon. An LC50 of approximately 1.7 mg/l was determined in an acute test (duration 24 hours) in zebra fish and neon (Oliveira-Filho and Paumgarten, 1997). IPCS (1992) reported an EC50 based on changes in fish behaviour of 47 µg/l (96 hours) and an LC50 in guppy of 0.9 mg/l (48 hours). In a prolonged toxicity study (duration 4 and 12 weeks) including histopathological changes, the NOEC in young guppy was 32 µg/l (Wester and Canton, 1991). Estrogenic activity of beta-HCH occurred in the form of alterations of vitellogenin production, testis atrophy, hermaphroditism in male and pituitary changes.

It seemed that beta-HCH is not very toxic to birds (IPCS, 1992) but that it may affect reproduction. In female birds with high concentrations of various organochlorines including beta-HCH, the body condition of the first and second chicken in the clutch was poorer (AMAP, 2004).

Monitoring data on effects in Svalbard polar bears revealed a significant negative correlation between retinol and HCHs (AMAP, 2004). Retinol is essential as it is required in reproduction, embryonic and foetal development, as well as in vision, growth, differentiation and tissue maintenance.

3 Synthesis of the information

Technical HCH, a mixture of five stable HCH-isomers, contains 5-14 % beta-HCH and was used extensively worldwide as organochlorine pesticide.

Though usage of technical HCH is currently negligible, releases into the environment may still occur. Local sources include hazardous waste sites, contaminated sites, stockpiles, landfills, or dumping grounds. Though no quantitative estimates of these releases exist, the amounts of HCH-residuals in the form of by-products from lindane production were estimated to range between 1.6-1.9 to 4.8 million tonnes. In addition many of local sources are expected to cause environmental pollution and are not maintained or controlled appropriately.

The physico-chemical properties of beta-HCH allow on a global scale for "cold condensation", but pathways of alpha- and beta-HCH diverge in the environment. Reasons are possibly greater physical and metabolic stability, higher water/octanol solubility, a lower Henry's Law Constant and a relatively high octanol-air partition coefficient, which favours partitioning to organic phases.

According to available data beta-HCH can be considered to be persistent in the environment. Though beta-HCH is biodegradable by various microbial strains under favourable conditions degradation rates in field experiments are low indicating very slow decrease under environmental conditions. Residues of beta-HCH remained for years in treated plots in several studies. The only determined DT50 values were 100 and 184 days on cropped and uncropped soil under subtropical conditions. In addition to degradation and plant up-take volatilisation and leaching may also have contributed to the disappearance of beta-HCH in this investigation.

Monitoring data from remote regions far from sources clearly indicate that beta-HCH has undergone long-range environmental transport. It is suggested that beta-HCH enters the Arctic by ocean currents passing through the Bering Strait after wet deposition and partitioning into the North Pacific Ocean.

Beta-HCH has a BCF (whole body) of 1 460 based on a laboratory study in fish. However, there are several field investigations in Arctic marine food webs available that suggest that beta-HCH may accumulate to high concentrations in upper trophic levels (i.e. marine mammals and birds). Thus BMFs as well as FWMFs were greater than 1. It has further been demonstrated that beta-HCH is found in breast milk of highly exposed indigenous mothers who consume a subsistence diet. Thus its high bioaccumulation potential is well documented.

Beta-HCH has been shown to be neurotoxic, hepatotoxic, to cause reproductive and immunosuppressive effects and effects on fertility and reproduction in laboratory animals.

Monitoring data on Arctic polar bears revealed a negative correlation with retinol concentrations and HCHs, which may impact a wide range of biological functions.

The International Agency for Research on Cancer (IARC) has classified beta-HCH in group 2B, possibly carcinogenic to humans. Several epidemiological studies indicate that beta-HCH might play a role in human breast cancer, at least beta-HCH is a known tumour promoting agent. Beta-HCH may adversely affect human health in contaminated areas and as well in Arctic regions. Based on the available toxicity data of beta-HCH it can be concluded that current concentrations of beta-HCH in food and human milk in these regions are of concern. The estimated cancer risk calculated by EPA, though very conservative, seems very high ($5.0x10^{-3}$ to $7.7x10^{-4}$).

It has to be taken into consideration that the Arctic population and wildlife are also exposed against a wide range of other persistent toxic substances, which may act in an additive way. Nevertheless it should be emphasized that traditional foods have unique social, cultural, spiritual and economic value and therefore it is strongly recommended to avoid foods in which beta-HCH levels are of concern.

4 Concluding statement

Though most countries have banned or restricted the use of technical HCH as a pesticide, replacing it in most cases by the use of lindane, the production process creates huge amounts of HCHs residuals. The continued production and existing stockpiles of these waste isomers have been a worldwide problem and contribute to the releases into the environment.

Beta-HCH is persistent and present in all environmental compartments; especially levels in the terrestrial as well as in the aquatic food chain give rise to concern to adversely affect human health. High exposure is expected in polluted areas, which are still present around the globe. High exposure ois also possibly expected as a result of long-range environmental transport.

Based on the inherent properties, together with estimated daily intakes of beta-HCH of Arctic indigenous people that exceeds safe intake reference values, and given the widespread occurrence of beta-HCH in biota, including in remote areas far from likely sources, it is concluded that the substance is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

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別添5

リンデンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 非常に遅い。実験室の好気的条件下の土壌中で半減期は 980 日。嫌気的条件下ではより速く分解が進行。 【光分解性】 光に対しては安定。 【加水分解性】 ・半減期は 92-3090 時間。pH 5、pH 7 において安定であり半減期は 732 日。pH 9 における半減期は 43-182 日。海水中では pH 8（20℃）で 1.1 年。pH 7.6（5℃）のﾋｭｰﾛﾝ湖で 42 年。pH 8（0℃）の北極で 110 年など様々な推定値・算出値が報告されている。 【半減期】 ・大気中：OH ﾗｼﾞｶﾙとの気相反応の速度定数に基づく推定値は 2-3 日。対流圏での寿命は 7 日と推定。熱帯地域での対流圏寿命は 13 日と推定。Brubaker and Hites は大気中での寿命を 96 日と推定。 ・水中：河水では 30-300 日。湖水では 3-30 日。 ・土壌中：2-3 年。	【BCF（経鰓的生物濃縮係数）】 ・水生生物：BCF=10-6000（実験室）。BCF=10-2600（環境中）。BCF=3-36（Berny）。BCF=43-4220（湿重量ﾍﾞｰｽ）。BCF=11,000、1200-2100（脂質ﾍﾞｰｽ） ・ｴﾋﾞ：logBCF=2..26(脂質ﾍﾞｰｽ)。ﾆｼﾞﾏｽ：ogBCF=3.85（脂質ﾍﾞｰｽ）。動物ﾌﾟﾗﾝｸﾄﾝ：logBCF=4.3。無脊椎生物の平均 log BCF=2.28。脊椎生物の平均 log BCF=2.87 【BAF（経鰓及び経口による生物濃縮係数）】 ・ﾆｼﾞﾏｽ：logBAF=4.1 ・無脊椎生物の平均 log BAF=2.94。 ・脊椎生物の平均 log BAF=3.80。肉部分で 780、内臓部分で 2500、全魚体で 1400 という報告がある。 ・海洋哺乳類のﾘﾝﾃﾞﾝの濃度は、より疎水性の PCB や DDT と同等か又はより高ﾚﾍﾞﾙである。	【慢性毒性】 ラット（混餌）：7mg/kg/day で肝臓壊疽（38 週）、肝臓萎縮（104 週） 【生殖毒性】 ウサギ（3 日/週で 12 週）：0.8mg/kg/day で排卵率低下 ラット（5 日）：6mg/kg/day（♂）で精子数減少 ラット（90 日）：75mg/kg/day（♂）で性器萎縮、精子形成能かく乱 ラット（妊娠 15 日単回）：30 mg/kg/day で雄児性行動変化、テストステロン濃度低下 マウス（妊娠 12 日単回）：30 mg/kg/day で胎児の胸腺、胎盤重量低値 ラット（生殖試験：12 週暴露）：1.7uM で成長速度低下、精子数減少、テストステロン濃度低下 【発がん性】 「発がん性を示す科学的根拠が示唆されるが、潜在的人発がん性を評価するには科学的根拠が不十分な物質」に分類（US EPA） 【その他】 リンデン含有殺虫剤摂取で人に発作痙	【慢性毒性】 淡水魚　：NOAEC=0.0029 mg/L（幼魚の生育低下） 水生無脊椎動物　：NOAEC=0.054mg/L（生殖能低下） カエル　：0.0001 mg/Lで統計学的に有意な性比影響（71%雄）、エストロゲン活性の誘導、精子のプロゲステロン応答性変化。試験管内試験において、ビテロゲニン及びエストロゲン受容体の発現誘導。 無脊椎動物　：35日間試験 LOAEL=0.0135 mg/L（生殖能及び個体数への影響） ニワトリ及びニホンウズラ　：それぞれ100及び25 ppmで孵化率低下。

		攣など神経毒性、実験動物で免疫抑制や抗体反応抑制など	

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Persistent Organic Pollutants Review Committee
Second meeting
Geneva, 6–10 November 2006

Report of the Persistent Organic Pollutants Review Committee on the work of its second meeting

Addendum

Risk profile on lindane

At its second meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on lindane, on the basis of the draft contained in document UNEP/POPS/POPRC.2/10. The text of the risk profile, as amended, is provided below. It has not been formally edited.

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LINDANE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its second meeting

November 2006

CONTENTS

Executive summary

Mexico proposed that gamma-hexachlorocyclohexane (lindane) be added to Annex A of the Stockholm Convention. The Review Committee evaluated Annex D information presented by Mexico at its first meeting and concluded that "Lindane meets the screening criteria specified in Annex D".

International initiatives on Lindane include the Protocol on Persistent Organic Pollutants of the Convention on Long Range Transboundary Air Pollution; the Rotterdam Convention; the OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic, the Great Lakes Binational Toxics Strategy between the United States and Canada, and a North American Regional Action Plan on Lindane and Other Hexachlorocyclohexane Isomers under the Commission for Environmental Cooperation between Canada, United States and Mexico.

For each ton of lindane produced, around 6-10 tons of other isomers are also obtained. In the last years the production of lindane has rapidly decreased and it appears that only Romania and India are current producing countries. Lindane has been used as a broad-spectrum insecticide for seed and soil treatment, foliar applications, tree and wood treatment and against ectoparasites in both veterinary and human applications.

Once released into the environment, lindane can partition into all environmental media. Hydrolysis and photolysis are not considered important degradation pathways and reported half-lifes in air, water and soil are: 2.3 days, 3-300 days and up to 2 to 3 years, respectively. A half-life of 96 days in air has also been estimated.

Lindane can bio-accumulate easily in the food chain due to its high lipid solubility and can bio-concentrate rapidly in microorganisms, invertebrates, fish, birds and mammals. The bioconcentration factors in aquatic organisms under laboratory conditions ranged from approximately 10 up to 4220 under field conditions, the bioconcentration factors ranged from 10 up to 2600. Although lindane may bioconcentrate rapidly, bio-transformation, depuration and elimination are also relatively rapid, once exposure is eliminated.

Many studies have reported lindane residues throughout North America, the Arctic, Southern Asia, the Western Pacific, and Antarctica. HCH isomers, including lindane, are the most abundant and persistent organochlorine contaminants in the Arctic where they have not been used, pointing at evidence of their long-range transport.

The hypothesis that isomerization of gamma HCH to alpha HCH in air emerged as a possible explanation for higher than expected alpha HCH/gamma HCH ratios in the Arctic. However no conclusive experimental evidence of isomerization taking place in air has been produced to date. Also, although there is evidence that bioisomerization of lindane can take place through biological degradation, it seems that this process may play an insignificant role in the overall degradation of gamma-HCH.

Lindane can be found in all environmental compartments, and levels in air, water, soil sediment, aquatic and terrestrial organisms and food have been measured worldwide. Humans are therefore being exposed to lindane as demonstrated by detectable levels in human blood, human adipose tissue and human breast milk in different studies in diverse countries. Exposure of children and pregnant women to lindane are of particular concern.

Hepatotoxic, immunotoxic, reproductive and developmental effects have been reported for lindane in laboratory animals. The US EPA has classified lindane in the category of "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". Lindane is highly toxic to aquatic organisms and moderately toxic to birds and mammals following acute exposures. Chronic effects to birds and mammals measured by reproduction studies show adverse effects at low levels such as reductions in egg production, growth and survival parameters in birds, and decreased body weight gain in mammals, with some effects indicative of endocrine disruption.

These findings and the evidence of its long range transport, as well as the fact that lindane is currently the object of local and global action initiatives, that also include thorough analysis and selection procedures, should be sufficient to warrant global action under the Stockholm Convention.

1. Introduction

1.1 Chemical identity

Mexico proposed that gamma-hexachlorocyclohexane (lindane) be added to Annex A of the Stockholm Convention on June 29, 2005. The proposal presented data on the gamma isomer, but mentioned as well that "other isomers of hexachlorocyclohexane should also be considered in this proposal".[1]

Lindane: gamma-hexachlorocyclohexane
Chemical formula: $C_6H_6Cl_6$
CAS number: 58-89-9
Molecular weight: 290.83

Physical and Chemical properties of gamma-HCH

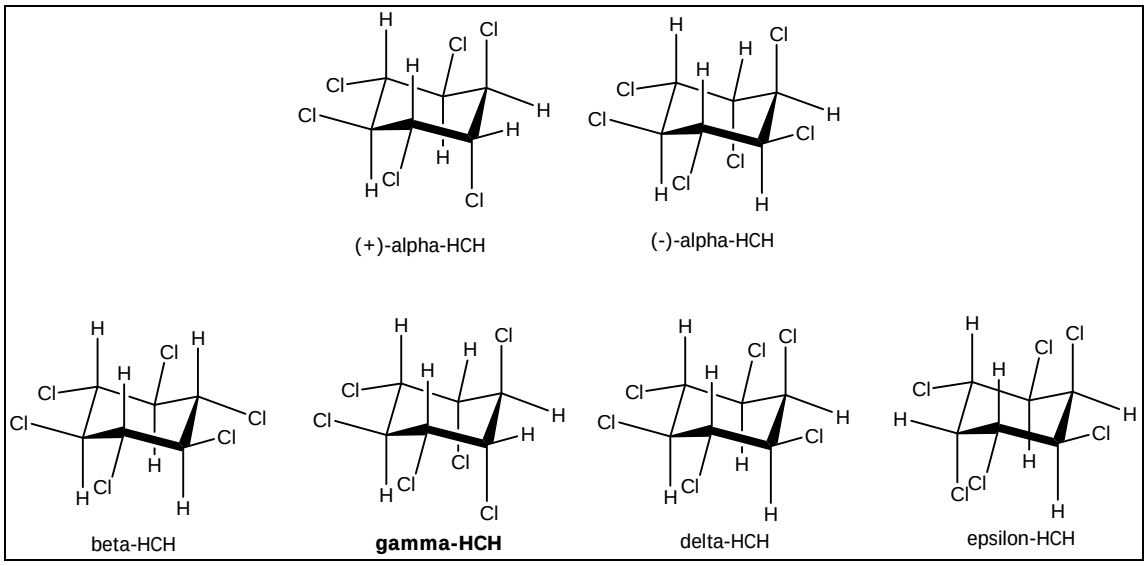
Physical state	Crystalline solid
Melting point	112.5 °C
Boiling point at 760 mmHg	323.4 °C
Vapor pressure at 20°C	4.2×10^{-5} mmHg
Henry's Law constant at 25°C	3.5×10^{-6} atm m^3/mol

ATSDR, 2005

Lindane is the common name for the gamma isomer of 1,2,3,4,5,6-hexachlorocyclohexane (HCH). Technical HCH is an isomeric mixture that contains mainly five forms differing only by the chlorine atoms orientation (axial or equatorial positions) around the cyclohexane ring. The five principal isomers are present in the mixture in the following proportions: alpha-hexachlorocyclohexane (53%–70%) in two enantiomeric forms ((+)alpha-HCH and (-)alpha-HCH), beta-hexachlorocyclohexane (3%–14%), gamma-hexachlorocyclohexane (11%–18%), delta-hexachlorocyclohexane (6%–10%) and epsilon-hexachlorocyclohexane (3%–5%). The gamma isomer is the only isomer showing strong insecticidal properties.

[1] UNEP/POPS/POPRC.1/8 and UNEP/POPS/POPRC.1/INF/8

Structure of alpha, beta, gamma, delta and epsilon HCH isomers



Modified from Buser et al., 1995.

The term "benzene hexachloride (BHC)" is also commonly used for HCH, but according to IUPAC rules this designation is incorrect. Nevertheless the term is used and therefore, gamma-BHC also designates lindane. In the present risk profile document, lindane refers to at least 99% pure gamma-HCH and the BHC term is not used.

1.2 Conclusion of the Review Committee regarding Annex D information

The Committee has evaluated Annex D information at its first meeting held in Geneva, from November 7th to 11th 2005, and has decided that "the screening criteria have been fulfilled for lindane" and concluded that "Lindane meets the screening criteria specified in Annex D." The Committee agreed that the alpha and beta isomers could be included in the discussions, although any decision to propose inclusion of the chemical in the Convention would apply only to lindane, the gamma isomer[2].

1.3 Data sources

Data sources provided by the proposing party, Mexico:

1. ATSDR Toxicological Profile Information Sheet 2001
2. AMAP. 1998. Persistent Organic Pollutants. Arctic Monitoring and Assessment Program (AMAP), 183-373. Oslo, Norway.
3. DeVoto, E., L. 1998. *Arch. Environ. Health* 53:147-55.
4. Extoxnet.1996. USDA/Extension Service/National Agricultural Pesticide Impact Assessment Program.
5. Gregor, 1989. Environ. Sci. technol. 23: 561-565.
6. IARC Monographs, http://monographs.iarc.fr
7. Mössner, S., 1994. Fres. J. Anal Chem. 349: 708-16.
8. Raum, E, A. 1998. *J. Epdiem. Commun. Health* 52 (suppl 1): 50S-5S.

[2] UNEP/POPS/POPRC.1/10

9. U.S Environmental Protection Agency. IRIS.
10. Walker, K., 1999. Environ. Sci. Technol. 33:4373-4378.
11. Wania,F., 1999. Environ. Toxicol. Chem. 18: 1400-1407.
12. WHO. 1991. Environmental Health Criteria 124 Lindane
13. Willett, K., 1998. Environ. Sci. Technol. 32: 2197-207.
14. Yi, F. L., Sci. and Technol. Vol 30, No 12, 1996.

Data sources used by the Committee:

1. UNEP/POPS/POPRC.1/8
2. Nagabe, et al., *Environmental Science and Technology.* 27: 1930–1933. 1993.
3. Harner, T. et al., *Environmental Science and Technology.* 33: 1157–1164. 1999.
4. Harner, T. et al., *Geophysical Research Letters.* 27: 1155–1158. 2000.
5. *Environmental Health Criteria No. 124*: *Lindane*. International Programme on Chemical Safety.
6. UNEP, ILO, WHO. Geneva. 1991. (http://www.inchem.org/documents/ehc/ehc/ehc124.htm).
7. Brock et al., *Alterra Report* 89, Netherlands. 2000.
8. *Guidance document on risk assessment for birds and mammals under Council Directive*
9. *91/414/EEC*. European Union. SANCO/4145/2000 – final, Brussels. 2002.
10. Arctic Monitoring and Assessment Programme. Norway. 2002.
11. Gregor, D., et al., *Environmental Science and Technology.* 23: 561–565, 1989.
12. Brubaker, W. W., and Hites, R.A. 1998. *Environmental Science and Technology* 32: 766–769.

The following parties and observers have answered the request for information specified in Annex E of the Convention: Republic of Macedonia, International HCH & Pesticides Association, Republic of Armenia, Haiti, World Wild Fund for Nature, CropLife International, International POPs Elimination Network, Morocco, Republic of Mauritius, European Community, Brazil, Republic of Lithuania, Canada, United States of America, Australia, Japan, Mexico, Lebanon and Poland. A more elaborated summary of the submissions is provided as separate **UNEP/POPS/POPRC.2/INF.18** document. *Summary of data submitted by Parties and observers for information specified in Annex E of the Convention*.

The following lindane assessment reports are publicly available through the internet:

- Assessment of Lindane and other Hexachlorocyclohexane Isomers. USEPA. February 2006 http://www.epa.gov/fedrgstr/EPA-PEST/2006/February/Day-08/p1103.htm

- Toxicological Profile for Hexachlorocyclohexane, Agency for Toxic Substances and Disease Registry, US Department of Health and Human Services, updated in 2005. http://www.atsdr.cdc.gov/toxprofiles/tp43.html

- USEPA Reregistration Eligibility Decision (RED) for Lindane. 2002. See RED and supporting health and eco assessments included in the docket. http://www.epa.gov/oppsrrd1/REDs/lindane_red.pdf

- The North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane (HCH) Isomers. Draft for Public Comment. October 2005. North

American Commission for Environmental Cooperation http://www.cec.org/files/PDF/POLLUTANTS/Lindane-NARAP-Public-Comment_en.pdf

- Health risks of persistent organic pollutants from long-range transboundary air pollution, Joint WHO/convention task force on the health aspects of air pollution. WHO/Europe. 2003. Chapter 3: Chapter 3/ Hexachlorocyclohexanes http://www.euro.who.int/Document/e78963.pdf

- Technical Review Report on Lindane. Reports on Substances Scheduled for Re-assessments Under the UNECE POPs Protocol. Prepared by Austria in 2004 (available: http://www.unece.org/env/popsxg/docs/2004/Dossier_Lindane.pdf)

- IPCS International Programme on Chemical Safety. Health and Safety Guide No. 54 LINDANE (Gamma-HCH) HEALTH AND SAFETY GUIDE. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva, 1991. http://www.inchem.org/documents/hsg/hsg/hsg054.htm

1.4 Status of the chemical under international conventions

Lindane is listed as a "substance scheduled for restrictions on use" in Annex II of the 1998 **Protocol on Persistent Organic Pollutants of the Convention on Long-Range Transboundary Air Pollution**. This means that products in which at least 99% of the HCH isomer is in the gamma form (i.e. lindane, CAS: 58-89-9) are restricted to the following uses: 1. Seed treatment. 2. Soil applications directly followed by incorporation into the topsoil surface layer 3. Professional remedial and industrial treatment of lumber, timber and logs. 4. Public health and veterinary topical insecticide. 5. Non-aerial application to tree seedlings, small-scale lawn use, and indoor and outdoor use for nursery stock and ornamentals. 6. Indoor industrial and residential applications. All restricted uses of lindane shall be reassessed under the Protocol no later than two years after the date of entry into force. The Protocol entered into force on October 23th, 2003. [3]

Lindane, as well as the mixture of HCH isomers, is listed in Annex III of the **Rotterdam Convention** on the Prior Informed Consent Procedure as "chemicals subject to the prior informed consent procedure". The Rotterdam Convention entered into force 24 February 2004. [4]

Hexachlorocyclohexane isomers, including Lindane, the gamma isomer, are included in the List of Chemicals for Priority Action (Updated 2005) under the **OSPAR Commission for the Protection of the Marine Environment of the Northeast Atlantic**. Under this initiative, the Hazardous Substance Strategy sets the objective of preventing pollution of the maritime area by continuously reducing discharges, emissions and losses of hazardous substances, with the ultimate aim of achieving concentrations in the marine environment near background values for naturally occurring substances and close to zero for man-made synthetic substances. The OSPAR Convention entered into force on 25 March 1998. [5]

[3] Convention on Long-range Transboundary Air Pollution http://www.unece.org/env/lrtap/
[4] Rotterdam Convention http://www.pic.int.
[5] OSPAR Convention for the Protection of the Marine Environment of the Northeast Atlantic. http://www.ospar.org/

HCH (including lindane) is listed as a Level II substance in the **Great Lakes Binational Toxics Strategy** between the United States and Canada, which means that one of the two countries has grounds to indicate its persistence in the environment, potential for bioaccumulation and toxicity. [6]

A North American Regional Action Plan (NARAP) on Lindane and Other Hexachlorocyclohexane Isomers is under development under the Sound Management of Chemicals project, which is an ongoing initiative to reduce the risks of toxic substances to human health and the environment in North America. This program is part of the Pollutants and Health Program of the **Commission for Environmental Cooperation** between the three NAFTA countries: Canada, United States and Mexico. (CEC, 2005)

Lindane is also listed under the **European Waterframework Directive**. This Directive is a piece of water legislation from the European Community. It requires all inland and coastal water bodies to reach at least "good status" by 2015. Lindane is one of the listed priority hazardous substances for which quality standards and emission controls will be set at EU level to end all emissions within 20 years. [7]

2. Summary information relevant to the risk profile

2.1 Sources

a) Production, trade, stockpiles

The manufacture of technical-HCH involves the photochlorination of benzene, which yields a mixture of five main isomers. This mixture of isomers is subject to fractional crystallization and concentration to produce 99% pure lindane, with only a 10-15 percent yield. The production of lindane is therefore inefficient as for each ton of lindane (gamma isomer) obtained, approximately 6-10 tons of other isomers are also obtained (IHPA, 2006). According to the *International HCH & Pesticide Association* (IHPA) (report and Annexes), there have been variations in the production methods for HCH and lindane, as well as for HCH isomers destruction or re-use. However, most of the methods to process or re-use the waste HCH isomers have been given up over the years and consequently, most of the waste products have been dumped over the last 50 years (IHPA, 2006). The lindane industry claims that modern production technology processes the waste isomers into TCB (trichlorobenzene) and HCl (hydrochloric acid) thereby reducing or eliminating environmental contamination from these byproducts (Crop Life, 2006).

Historical production of technical HCH and lindane occurred in many European countries, including the Czech Republic, Spain, France, Germany, United Kingdom, Italy, Romania, Bulgaria, Poland, and Turkey, and took place mainly from 1950 or earlier and stopped in 1970 to the 1990s . According to a research by IHPA, technical HCH and lindane have also been produced in other countries including Albania, Argentina, Austria, Azerbaijan, Brazil, China, Ghana, Hungary, India, Japan, Russia, Slovakia and the United States. Exact information is difficult to obtain, as many countries do not keep records of historical pesticides production, sales and usage or the industry considers this to be proprietary information (IHPA, 2006).

[6] Great Lakes Binational Toxics Strategy http://www.epa.gov/glnpo/gls/index.html

[7] European Union Water Framework Directive http://ec.europa.eu/environment/water/water-framework/index_en.html

It is estimated that global lindane usage from 1950 to 2000 for agricultural, livestock, forestry, human health and other purposes amounts to around 600 000 tons. The next table shows agricultural lindane usage in different continents in the period from 1950 to 2000 (IHPA, 2006).

Continent	Usage (tons)
Europe	287,160
Asia	73,200
America	63,570
Africa	28,540
Oceania	1,032
Total	**435,500**

It appears that in the last years the production of lindane has rapidly decreased leaving only a small number of producing countries. Romania, India, and possibly Russia are the only countries in the world still currently producing Lindane (IHPA, 2006 and USEPA, 2006, CEC, 2005 Annex A). Other sources indicate that Russia (Li et al., 2004) and China (USEPA, 2006) have stopped producing lindane. India produces and uses lindane for the control of mites in sugarcane at 200 tonnes per year.

Global lindane production between 1990 and 1995 was around 3 222 tons per year. In Europe, the top 10 countries with highest lindane usage between 1950 and 2000, representing 96% of the total usage in Europe, were: Czechoslovakia, Germany, Italy, France, Hungary, Spain, Russia, Ukraine, Yugoslavia and Greece (IHPA, 2006).

The 1998 Food and Agriculture Organization Inventory of Obsolete, Unwanted and/or Banned Pesticides found a total of 2785 tons of technical-grade HCH, 304 tons of lindane, and 45 tons of unspecified HCH material scattered in dumpsites in Africa and the Near East (Walker et al., 1999).

According to the information from the Arctic Council's Arctic Contaminants Action Program (ACAP) project on obsolete pesticides, possibly up to 1,000 tonnes of obsolete stockpiles of technical HCH and lindane still exist in the Russian Federation after the ban of production in the beginning of the 1990s.

b) Uses

Lindane has been used as a broad-spectrum insecticide, which acts by contact, for both agricultural and non-agricultural purposes. Lindane has been used for seed and soil treatment, foliar applications, tree and wood treatment and against ectoparasites in both veterinary and human applications (WHO, 1991).

As a consequence of its toxic, suspected carcinogenic, persistent, bioaccumulative and suspected endocrine disrupting properties, lindane became a substance of scrutiny for countries in the European Community. All uses of HCH including lindane have been banned, but Member States may allow technical HCH for use as an intermediate in chemical manufacturing and in products with at least 99% of the isomer content in the gamma form (lindane) for public health and veterinary topical use only, until December 31st 2007 (UNECE, 2004). Currently, the only registered agricultural use for lindane in the United States is for seed treatment and for lice and scabies treatment on humans (CEC, 2005). In Canada the major use of lindane has been on canola

and corn, but the only current allowable use of lindane is for public health purposes, as a lice and scabies treatment (CEC, 2005).

Information on current uses as informed by countries may be found on POPRC/LINDANE/INF.1

c) Releases to the environment

Considering every ton of lindane produced generates approximately 6 - 10 tons of other HCH isomers, a considerable amount of residues was generated during the manufacture of this insecticide. For decades, the waste isomers were generally disposed of in open landfills like fields and other disposal sites near the HCH manufacturing facilities. After disposal, degradation, volatilization, and run off of the waste isomers occurred (USEPA, 2006).

If the estimate of global usage of lindane of 600,000 tons between 1950 and 2000 is accurate, the total amount of possible residuals (if it is assumed that a mean value of 8 tons of waste isomers are obtained per ton of lindane produced) amounts to possibly 4.8 million tons of HCH residuals that could be present worldwide giving an idea of the extent of the environmental contamination problem (IHPA, 2006).

Air releases of lindane can occur during the agricultural use or aerial application of this insecticide, as well as during manufacture or disposal. Also, lindane can be released to air through volatilization after application (Shen et al., 2004). Evaporative loss to air from water is not considered significant due to lindane's relatively high water solubility (WHO/Europe, 2003).

2.2 Environmental fate

Persistence

A half-life for lindane in air of 2.3 days was estimated, based on the rate constant for the vapor-phase reaction with hydroxyl radicals in air; a tropospheric lifetime of 7 days due to gas-phase reaction with hydroxyl radicals was estimated, and a lifetime of 13 days was estimated for atmospheric reaction with OH radicals in the tropics (Mackay, 1997). Brubaker and Hites (1998) estimated a lifetime in air of 96 days for lindane. Lindane has half-lifes of 3-30 days in rivers and 30 to 300 days in lakes. Other studies report calculated or experimental hydrolysis half-lifes ranging from 92 to 3090 hours depending on the study; a persistence of about 2 to 3 years in soil is also reported (Mackay et al., 1997).

Once released into the environment, lindane can partition into all environmental media, but it is demonstrated that evaporation is the most important process in the distribution of lindane in the environment. Several studies focusing on the adsorption-desorption characteristics of lindane have shown that mobility of lindane is very low in soils with a high content of organic material, and higher in soils with little organic matter. The diffusion of lindane has also been investigated, showing it is strongly influenced by the water content of the soil and by temperature. The International Program on Chemical Safety states that when lindane suffers environmental degradation under field conditions, its half-life varies from a few days to three years depending on many factors including climate, type of soil, temperature and humidity (WHO, 1991).

Hydrolysis is not considered an important degradation process for lindane in aquatic environments under neutral pH conditions. Lindane is stable to hydrolysis at pH 5 and 7 with a half-life of 732 days and a half-life of 43 to 182 days at pH 9. Also, different estimated and calculated half-life values for lindane have been reported to be: 1.1 years at pH 8 and 20°C in seawater; 42 years at pH 7.6 and 5°C in Lake Huron, and 110 years in the Arctic Ocean at pH 8 and 0°C (USEPA, 2006).

Lindane is stable to light. Since lindane does not contain chromophores that absorb light, direct photolysis either in air, water or soil is not expected to occur. Even when indirect photolysis could occur with a photosensitizing agent, there is no clear evidence of lindane photodegradation. Lindane degrades very slowly by microbial action with a calculated half-life in soil of 980 days under laboratory aerobic conditions. Degradation takes place faster under anaerobic conditions than in the presence of oxygen. Possible degradation products are pentachlorocyclohexene, 1,2,4,-trichlorobenzene, and 1,2,3-trichlorobenzene (USEPA, 2006).

Bioaccumulation

The bioconcentration factors (BCF) in aquatic organisms under laboratory conditions ranged from approximately 10 up to 6000; under field conditions, the bioconcentration factors ranged from 10 up to 2600 (WHO, 1991). Other studies report bioconcentration factors (log BCF) ranging from 2.26 in shrimp to 3.85 in rainbow trout in early life stages on lipid basis and 4.3 in zooplankton and a bioaccumulation factor (log BAF) up to 4.1 in rainbow trout (Mackay et al., 1997). Also, uptake and elimination rate constants ranging from 180 – 939 h^{-1} and 0.031 – 0.13 h^{-1} respectively have been reported for rainbow trout in early life stages on lipid basis (Mackay et al., 1997).

Lindane can bio-accumulate easily in the food chain due to its high lipid solubility and can bio-concentrate rapidly in microorganisms, invertebrates, fish, birds and mammals. Bioconcentration factors (BCF) within aquatic species vary considerably, with experimental data revealing bioconcentration factors of 3-36 (Berny, 2002); 43-4220 on a wet weight basis, and a mean BCF of 11,000 on a lipid basis (Geyer et al., 1997); and also 1200-2100 (Oliver et al., 1985).

An average log BCF of 2.28 in invertebrate species and an average log BCF of 2.87 in vertebrate species can be calculated from different studies (Donkin et al., 1997, Renberg et al., 1985, Thybaud et al., 1988, Yamamoto et al., 1983, Butte et al., 1991, Carlberg et al., 1986, Kanazawa et al., 1981, Kosian et al., 1981 La Rocca et al., 1991, Oliver et al., 1985, Vigano et al., 1992). In the same way, an average log BAF of 2.94 in invertebrate species, and an average log BAF of 3.80 in vertebrate species can be calculated from other studies (Oliver et al., 1988, Chevreuil et al., 1991, Hartley et al., 1983, Caquet et al., 1992). Bioconcentration factors of 780 for fillet, 2500 for viscera and 1400 for whole fish tissues have also been reported (USEPA, 2002).

In an experiment carried out by Geyer et al. (1997), bioconcentration factors are shown to be dependent on the fish species and their lipid content; additionally, different modes of uptake, metabolism, sources of contamination and even experimental conditions, taken together could explain the significant variation observed for BCF values. Also, most data suggest that, although lindane may bioconcentrate rapidly, bio-transformation, depuration and elimination are relatively rapid once exposure is eliminated. (WHO, 1991).

The bioaccumulation of lindane has been observed for most taxonomic groups, from plants and algae to vertebrates. The environmental consequences of the combination of this bioaccumulation potential with a high toxicity – no-observed-adverse-effect levels (NOAELs) as low as 0.3 mg/kg body weight/day – and ecotoxicity – aquatic ecosystem no-observable-effect concentration (NOEC) below 1 μg/l (*Environmental Health Criteria No. 124, 1991;* and Brock et al., 2000) – should be

considered. For example, when measured field levels in earthworms (0.3 mg/kg for a soil containing 80 μg/kg) are weighed against mammalian toxicity data (*Environmental Health Criteria No. 124, 1991;*) using a realistic food intake ratio of 0.63 (*Guidance document on risk assessment for birds and mammals* 2002.) the comparison indicates an area of ecotoxicological concern which should be further explored.

Lindane has been reported in seabirds, fish and mammals in the Arctic (ATSDR, 2005). Lindane concentrations in marine mammals are found at equivalent or even higher levels than some of the more hydrophobic contaminants such as polychlorinated biphenyls (PCBs) and DDT (ATSDR, 2005). In addition, lindane has been reported in human breast milk among Inuit in the Arctic and in marine mammals (Arctic Monitoring and Assessment Programme, 2002).

Potential for long-range environmental transport

Many studies have reported HCH residues, particularly alpha and gamma isomers throughout North America, the Arctic, Southern Asia, the Western Pacific, and Antarctica. HCH isomers, including lindane, are the most abundant and persistent organochlorine insecticide contaminants in the Arctic, and their presence in the Arctic and Antarctic, where technical HCH and lindane have not been used, is evidence of their long-range transport. HCH isomers, including lindane, are subject to "global distillation" in which warm climates at lower latitudes favor evaporation into the atmosphere where the chemicals can be carried to higher latitudes. At midlatitudes, deposition and evaporation vary with season. At high latitudes, cold temperatures favor deposition (Walker et al., 1999).

Use of lindane in countries such as Canada, where usage was ~ 500 tons in 2000, and certain European countries, such as France, has contributed to gamma-HCH levels present in the Arctic air. Concentrations of lindane were detected at Alert in the Arctic and varied from 10-11 pg/m^3 in 1993 decreasing to 6.4 pg/m^3 in 1997 (CACAR, 2003).

In a study completed by Shen et al. in 2004, 40 passive air sampling stations were located along transects from the Canadian Arctic, down the east coasts of Canada and the U.S., along the Canada - U.S. border and in southern Mexico and Central America for one year. The elevated alpha-HCH levels (sampler volumetric air concentrations between 1.5 and 170 pg/m^3) in eastern Canada were explained by outgassing of alpha-HCH from cold arctic water flowing south, warming, and releasing the alpha-HCH back to the atmosphere. High concentrations of gamma-HCH (sampler volumetric air concentrations between 5 and 400 pg/m^3) were found in the Canadian prairies, north of Lake Ontario, southern Québec, the middle Atlantic states and southern Mexico, reflecting the influence of regional lindane usage (Shen et al., 2004). Transport over the Pacific Ocean of lindane was measured at a sampling site in Yukon and ranged 4-18 pg/m^3 (Bailey et al., 2000). HCH isomers, including lindane, were measured at a mountain site at Tenerife Island from June 1999 to July 2000. Air concentrations of gamma-HCH at this site ranged 18 - 31 (mean 26) pg/m^3 (Van Drooge et al., 2002).

Lindane is very prevalent in the marine environment and soils, and its atmospheric long range transport potential has been demonstrated for the European Union, (WHO/Europe, 2003) especially by the European Monitoring and Evaluation Program (EMEP). High concentrations of gamma-HCH in air occurred in France, Portugal, Spain, the Netherlands and Belgium. These can be explained by the high emission densities of lindane in these countries. Relatively high air concentrations were also found in Germany, Italy, Switzerland and Luxembourg, despite the lower

lindane emission densities in these countries. These elevated air concentrations were probably explained by atmospheric transport from the former high-density emission European countries (Shatalov and Malanichev, 2000; Shatalov et al., 2000).

a) Isomerization

The hypothesis that isomerization of gamma-HCH to alpha-HCH could be taking place in air emerged as a possible explanation for alpha-HCH/ gamma-HCH ratios that were found in the 80's as high as 18, when this ratio was expected to be around 5 according to the fraction of these two isomers found in the technical HCH mixture. (Oehme et al 1984a, Oehme et al., 1984b, Pacyna et al., 1988) However no conclusive experimental evidence of isomerization taking place in air has been produced to date.

In the same line, Walker et al. (1999) noted that if photochemical transformation of gamma-HCH to alpha-HCH in air takes place, one should see significant concentrations of alpha-HCH in the Southern Hemisphere air. However, recent measurements have found alpha-HCH levels are dropping over time in the Southern Hemisphere as well as in the Arctic Ocean, which is not consistent with the isomerization theory and a continued use of lindane. The ratio of alpha-HCH/gamma-HCH in air sampled in the Southern Hemisphere during the 1980s - 1990s was generally 1 to 2.3 (Ballschmiter et al., 1991, Bidleman et al., 1993, Iwata et al., 1993, Kallenborn et al., 1998, Lakaschus et al., 2002; Schreitmüller et al., 1995) and was 0.81 in the most recent study in Antarctica (Dickhut et al., 2005).

Other studies have suggested that differential air-sea gas exchange rates could lead to fractionation of the HCH isomers and preferential accumulation of alpha-HCH in air during long range transport over the oceans. This could account for some portion of the elevated alpha-HCH/gamma-HCH ratios observed during wintertime, but not for the very high ratios found in summer in the early studies. (Pacyna et al., 1988 and Oehme et al., 1991). Walker et al. (1999) concluded that even when the experiments show that photoisomerization is possible, evidence that this process is a substantial contributor to the high alpha/gamma ratios observed in the Arctic is indirect and subject to several interpretations.

Several studies have also reported photolytic isomerization of gamma-HCH to alpha-HCH. However, these studies have demonstrated isomerization in condensed media, but there is no evidence that isomerization takes place in the gas phase under ambient atmospheric conditions. Laboratory evidence shows that gamma-HCH can be transformed into other isomers in soil or sediments through biological degradation, but although the bioisomerization of lindane can take place, it seems that this process may play an insignificant role in the overall degradation of gamma-HCH (Walker et al., 1999 and Shen et al., 2004).

b) Environmental monitoring data

Poland reported concentrations of gamma-HCH in river sediments ranging from 2.4 to 9.4 µg/kg. Results from the National Veterinary Residue Control Programme in Poland indicate that food of animal origin contains levels of gamma-HCH below the level of action of 1000 µg/kg (Annex E information provided by Poland, 2006).

The Ministry of Environment in Japan has monitored Lindane in water finding a concentration of Lindane of 32 to 370 pg/l in 60 surveyed water specimens across the country in 2003. A total of 186 bottom sediment specimens were also surveyed in 2003 and Lindane was detected in all the

specimens, with a concentration of Lindane from traces (1.4) to 4000 pg/g dry, with a geometric mean of 45 pg/g dry. A recent survey in 2003 on shellfish, fish and birds shows that Lindane was detected in all the specimens with concentrations ranging from 5.2 to 130 pg/g-wet for shellfish, 130 pg/g-wet for fish, and 1,800 to 5,900 pg/g-wet for birds. Lindane was detected in all 35 specimens from 35 sites in Japan for ambient air in the warm season in 2003 with a concentration of Lindane ranging from 8.8 to 2,200 pg/m^3 with a geometric mean of 63pg/m^3. The survey on the same sites excluding one site during the cold season in year 2003 indicates a concentration of 3.1 to 330 pg/m^3 with a geometric mean of 14pg/m^3 (Annex E information provided by Japan, 2006).

Australia reported that none of the meat and crop samples monitored for residues in the country contained detectable levels of lindane (Annex E information provided by Australia, 2006).

The United States reported that gamma-HCH, was below the level of detection in all samples analyzed for the Third National Report on Human Exposure to Environmental Chemicals. Lindane was detected in fish tissue from lakes and reservoirs in the US EPA national Lake Fish Tissue Study, with levels ranging from 0.652 to 8.56 ppb. Lindane is being monitored in air and precipitation with the Integrated Atmospheric Deposition Network in the Great Lakes region with average concentration of 15-90 pg/m^3 in the early 90s, decreasing to 5-30 pg/m^3 since 2000. Average concentrations in precipitation (volume-weighted mean) at seven main sites during the years 1997- 2003 were 690-1400 pg/L for lindane. The most recent years of available analytical data in the U.S. EPA's Great Lakes Fish Monitoring Program indicate the concentration of Lindane in sport fish fillets (Chinook and Coho Salmon and Steelhead Trout) have ranged between trace detection and 0.005 ppm between 1982 and 2000. The National Oceanic and Atmospheric Administration's National Status and Trends (NS&T) Program has measured lindane in the tissues of bivalves throughout the coastal US and Great Lakes from 1986 to present. Over the Program's history, a total of 283 sites throughout the contiguous US, Alaska, Hawaii, and Puerto Rico have been sampled, with a total of 4,990 records for the gamma isomer. Median measured concentration for gamma-HCH was 0.56 (range 0-71.0) ng/g dry weight. A trends assessment using data pooled for the entire USA, indicates that there has been a statistically significant decline in lindane levels from 1986 through 2003. (Annex E information provided by the United States of America, 2006).

In Canada, a project was undertaken in 1999-2000 by Alberta Environment to characterize the pesticides found in a number of Alberta locations, and to determine their relative levels and seasonality. Lindane was detected in ambient air at Lethbridge in all samples starting from May to August. Lindane levels peaked on June 15 at 1.15 ng/m^3, while the low level of 0.23 ng/m^3 was present in ambient air on June 22, 1999. As lindane is used on treated seed that is planted in April and early May, lindane is then released into the atmosphere following seeding and hence the higher levels in May followed by a slow decline to low and/or undetectable levels in August and September (Kumar, 2001).

2.3 Exposure

Lindane can be found in all environmental compartments and levels in air, water, soil, sediment, aquatic and terrestrial organisms and food have been measured worldwide. Humans are therefore being exposed to lindane as demonstrated by detectable levels in human blood, human adipose tissue and human breast milk (WHO/Europe, 2003).

A special area of concern is the fact that HCH isomers, including lindane, accumulate in colder climates of the world. High concentrations of HCH isomers, including lindane, are found in the

Beaufort Sea and Canadian Archipelago (CEC, 2005). Through environmental exposure, gamma-HCH can enter the food chain and accumulate in fatty animal tissue constituting an important exposure pathway for Arctic or Antarctic animals as well as for humans who rely on these animals for their subsistence diets (USEPA, 2006)

General population exposure to gamma-HCH can result from food intake, particularly from animal origin products like milk and meat, as well as water containing the pesticide. Lindane was found to be 10 times higher in adipose tissue of cattle than in the feed (ATSDR, 2005) showing that animals may be exposed to the compound through food and even through ectoparasite treatment. Lindane has been detected in cow's milk in countries that still use the chemical as a pesticide. In a study performed in Uganda, Africa, the concentrations of gamma-HCH in cow's milk was 0.006–0.036 mg/kg milk fat, respectively. Mean levels of gamma-HCH analyzed in cow's milk samples from two separate areas in India were 0.002 and 0.015 mg/kg. A monitoring study of 192 samples of cow's milk from Mexico revealed 0.002–0.187 mg/kg of gamma-HCH (ATSDR, 2005).

Determinations of the lindane content in body tissues in the general population have been made in a number of countries. The content in blood in the Netherlands was in the order of < 0.1–0.2 μg/l. In the early 1980s, mean concentrations of gamma-HCH in human adipose tissue in Czechoslovakia, the Federal Republic of Germany and the Netherlands were 0.086, 0.024–0.061 and 0.01–0.02 mg/kg, respectively, on a fat basis. In total-diet and market-basket studies to estimate daily human intake of gamma-HCH, clear differences were observed with time: intake in the period around 1970 was up to 0.05 μg/kg body weight per day, whereas by 1980 intake had decreased to 0.003 μg/kg body weight per day or lower (WHO/Europe, 2003).

Individuals living in rural areas and on a non-vegetarian diet are more likely to be exposed to gamma-HCH as shown by a study performed in India, where women who consumed red meat, eggs and chicken had higher pesticide levels, including lindane, in blood than vegetarian women (ATSDR, 2005). Other sources of direct exposure include facilities at which lindane is still being produced, abandoned pesticide plants, and hazardous waste sites (USEPA, 2006).

Exposure of children to lindane is a particular concern. Gamma-HCH has been found in human maternal adipose tissue, maternal blood, umbilical cord blood and breast milk. Lindane has also been found to pass through the placental barrier. Mean breast milk concentration of lindane was 0.084 mg/l in a study in India. An average level of 6 ppb lindane in breast milk was obtained in a study in Alberta, Canada (ATSDR, 2005). In a study looking at organochlorine pesticides in human breast milk collected from 12 regions in Australia, lindane was detected in all samples with a mean of 0.23 ng/g lipid and a range of 0.08-0.47 ng/g lipid (Annex E information provided by Australia, 2006).

Lindane levels have also been found in human breast milk from different countries including Canada, Germany, the Netherlands and the United Kingdom. Lindane levels ranged from <0.001 to 0.1 mg/kg on a fat basis (WHO/Europe, 2003).

An additional exposure route for children exists in regions where lindane is applied directly to milk and meat producing livestock for pest control. On a body weight basis, children consume more milk per unit body weight than adults, and thus may be exposed to significant concentrations of lindane residues through drinking milk (CEC, 2005). Medical use of products to treat head lice and scabies is also of concern when applied to children, although most adverse effects have been observed after misuse. Another exposure to possibly significant amounts of lindane might occur through household dust in certain conditions, and are also of concern especially for children (ATSDR, 2005).

2.4 Hazard assessment for endpoints of concern

Lindane is the most acutely toxic HCH isomer affecting the central nervous and endocrine systems. In humans, effects from acute exposure at high concentrations to lindane may range from mild skin irritation to dizziness, headaches, diarrhea, nausea, vomiting, and even convulsions and death (CEC, 2005). Respiratory, cardiovascular, hematological, hepatic and endocrine effects have also been reported for humans, following acute or chronic lindane inhalation. Hematological alterations like leukopenia, leukocytosis, granulocytopenia, granulocytosis, eosinophilia, monocytosis, and thrombocytopenia, have been reported, following chronic human occupational exposure to gamma-HCH at production facilities (ATSDR, 2005).

Additionally, gamma-HCH has been detected in the blood serum, adipose tissue and semen of occupationally and environmentally exposed individuals (ATSDR, 2005). Serum luteinizing hormone levels were significantly increased in men occupationally exposed to gamma-HCH. Also, the mean serum concentration of follicle stimulating hormone was increased and testosterone was decreased in exposed individuals, but these trends were not statistically significant compared to unexposed controls (ATSDR, 2005).

The most commonly reported effects associated with oral exposure to gamma-HCH are neurological. Most of the information is from case reports of acute gamma-HCH poisoning. Seizures and convulsions have been observed in individuals who have accidentally or intentionally ingested lindane in insecticide pellets, liquid scabicide or contaminated food (WHO/Europe, 2003).

In India, blood levels of gamma-HCH were significantly higher in 135 breast cancer patients, 41-50 years of age, compared to a control group without the disease. However, in similar studies in other countries, a correlation between breast cancer incidence and elevated levels of gamma-HCH in blood was not observed (ATSDR, 2005).

Rats exposed to various concentrations of gamma-HCH through inhalation for 4 hours exhibited concentration-related neurological effects when observed for up to 22 days after exposure. Slight-to-moderate sedation was observed after exposure to 101 mg/m^3; slight-to severe sedation was noted after exposure to 378 mg/m^3; restlessness, excitation, and ataxia were seen after exposure to 642 and 2,104 mg/m^3; and spasms were also noted at the highest concentration of 2,104 mg/m^3 (ATSDR, 2005).

Hepatotoxic effects of lindane have been demonstrated in laboratory animals by numerous studies. Increases in cytochrome P-450 levels after inhalation of lindane aerosol at 5 mg/m^3 for 90 days and increases in cytochrome P-450 activity cytoplasmic superoxide dismutase, lipid peroxidation in rats after being fed 1.8 mg/kg body weight for 15 and 30 days, have been demonstrated. Chronic studies with a dose of 7-8 mg/kg body weight of lindane in the diet showed liver necrosis and fatty degeneration in rats exposed for 38 to 70 weeks, and hypertophy in Wistar rats exposed for 104 weeks (WHO/Europe, 2003). Rats exposed to 15 mg gamma-HCH/kg/day for 5 days and 2.5 mg gamma-HCH/kg/day for 21 days, showed significant increases in absolute liver weight, P-450 and EROD activity in a dose- and time-dependent manner (ATSDR, 2005).

Some evidence is available for immunotoxic effects, like immunosuppression and suppressed antibodies responses, caused by lindane in laboratory animals. Immunosuppression was observed in rats exposed to 6.25 and 25 mg/kg body weight for 5 weeks. Primary antibody response was

suppressed in albino mice being exposed to 9 mg/kg body weight per day in the diet for 12 weeks, and secondary antibody response suppression was observed after 3 weeks at the same dose (WHO/Europe, 2003).

Reproductive effects of lindane have been recorded in laboratory animals: female rats exposed orally to 10 mg/kg body weight per day for 15 weeks presented anti-estrogenic properties. Female rabbits exposed to gamma-HCH at 0.8 mg/kg body weight per day, 3 days per week for 12 weeks had a reduced ovulation rate (WHO/Europe, 2003). In male rats, reductions in the number of testicular spermatids and epididymal sperms were observed after an oral dose of 6 mg/kg body weight for 5 days, or a single dose of 30 mg/kg body weight of gamma-HCH. Testicular atrophy, seminiferous tubules degeneration and disruption of spermatogenesis were also reported in male rats fed 75 mg/kg body weight per day for 90 days (WHO/Europe, 2003). Lindane has therefore characteristics of an endocrine disrupting compound. Exposure to lindane during gestation with a single dose of 30 mg/kg of body weight at day 15 of pregnancy, induced altered libido and reduced testosterone concentration in male offspring rats (USEPA, 2006).

Developmental effects of lindane have also been reported. Decreased fetal weight, fetal thymic weight, and placental weight were observed in mice treated at 30 and 45 mg/kg by gastric intubation at day 12 of gestation. Fetotoxic effects of lindane were also observed and may be due to induced oxidative stress, enhanced lipid peroxidation and DNA single strand breaks in the fetal and placental tissues (WHO/Europe, 2003). Rats exposed to 1.7, 3.4 and 6.8 µM corresponding to exposure doses that might be encountered in contaminated vegetables (80-250 µg/kg) or contaminated drinking water (0.02 µg/l) for 12 weeks, showed an affected growth rate, decreased spermatozoid count, as well as decreased testosterone levels during gestation, lactation or weaning (WHO/Europe, 2003). Evidence of increased susceptibility of the young animal was noted in a rat multi-generation reproduction study and rat developmental neurotoxicity study (USEPA, 2002).

The available genotoxicity data indicate that gamma-HCH has some genotoxic potential. Gamma-HCH has been shown to increase chromosome clastogeny in bone marrow cells in mice exposed to 1.6 mg per kg body weight per day by gavage for 7 days (ATSDR, 2005). Nevertheless, lindane is not classified as genotoxic by the European Union (WHO/Europe, 2003). DNA damage was observed in cultures of rat nasal and gastric mucosa cells, and human nasal mucosa cells exposed to gamma-HCH and induced unscheduled DNA synthesis in certain types of cells, like human peripheral lymphocytes (ATSDR, 2005).

The International Agency for Research on Cancer (IARC) has classified lindane as possibly carcinogenic to humans; it has also classified technical HCH and alpha-HCH as possible human carcinogens (ATSDR, 2005). The US EPA has recently reclassified lindane in the category "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". USEPA has classified technical-grade HCH and alpha-HCH as probable human carcinogens while beta-HCH is a possible human carcinogen (ATSDR, 2005).

Carcinogenicity of lindane has been tested by oral administration in different experiments. Some studies have shown no significant increases in endocrine, thyroid, pituitary, adrenal gland, liver, or ovary tumors in rats fed 10.8–33 mg/kg/day in the diet for 80 weeks, or 0.07–32 mg gamma-HCH/kg/day in the diet for 104 weeks, but poor survival rates limited the significance of such results (WHO/Europe, 2003). While other studies have reported hepatocellular carcinomas in mice exposed to 13.6–27.2 mg/kg/day in the diet for 80 or 104 weeks, and in mice exposed to 27.2 mg/kg/day in the diet for 96 weeks, these results were obtained in a strain of mouse that has a dominant mutation resulting in an increased susceptibility to formation of strain-specific neoplasms.

Lindane is highly toxic to aquatic organisms and moderately toxic to birds and mammals following acute exposures. Chronic effects to birds and mammals measured by reproduction studies show adverse effects at low levels such as reductions in egg production, growth and survival parameters in birds and decreased body weight gain in mammals, with some effects indicative of endocrine disruption. Acute aquatic toxicity data on lindane indicate that it is highly toxic to both freshwater fish (LC_{50} ranges of 1.7 to 131 ppb) and aquatic invertebrates (LC_{50} ranges of 10.0 to 520 ppb). Chronic aquatic toxicity data for freshwater organisms show reduction in larval growth in freshwater fish at a NOAEC of 2.9 µg/l, and decreased reproduction in aquatic invertebrates at a NOAEC of 54 µg/l (CEC, 2005 and USEPA, 2006).

Lindane produced statistically significant sex ratio effects (71% males) in frogs at a level of 0.1 ppb and estrogenic activity as well as altered sperm responsiveness to progesterone and induced expression of vitellogenin and estrogen receptors in *in vitro* tests (USEPA, 2006). Reproductive and population effects were found at a LOAEL of 13.5 µg/l lindane in invertebrate in a 35 day study. Lindane at 100 ppm and 25 ppm caused reduced hatchability in both laying hens and Japanese quails, respectively (USEPA, 2006).

In 2002, USEPA published a dietary risk assessment for indigenous people in the Arctic for lindane. This dietary risk assessment is based on a number of hazard and exposure assumptions, and estimates risk to communities in Alaska and others in the circumpolar Arctic region who depend on subsistence foods, such as caribou, seal and whale. The total dietary intakes for adults ranged from 0.000055 to 0.00071 mg/kg/day. For non-cancer effects, the Level of Concern was (LOC) =0.0016 mg/kg/day. The dietary risks for lindane did not exceed the LOC (USEPA, 2002).

Although the decision to include lindane in the Stockholm Convention would be based on the gamma isomer alone, the POPRC agreed that discussions could include the alpha and beta isomers. Therefore, information from a 2006 USEPA risk assessment on the alpha and beta isomers is included below.

In February 2006, USEPA published for public comment a risk assessment that discussed risks from lindane and the alpha- and beta-HCH isomers, by-products of the lindane manufacturing process (USEPA, 2006). Total dietary intakes were estimated for adults and children and ranged from 0.00057 to 0.051 mg/kg/day for alpha-HCH, and from 0.00037 to 0.01 mg/kg/day for beta-HCH. These dietary intakes were compared to USEPA's chronic level of concern (LOC). For non-cancer effects, the LOC is cRfD=0.00006 mg/kg/day for beta-HCH and a cRfD=0.001 mg/kg/day for alpha-HCH, based on the dose at which USEPA has concluded will result in no unreasonable adverse health effects. The cancer LOC is when the estimated upper bound cancer risk exceeds one in one million. The dietary risk assessment indicates that the chronic and cancer dietary risk estimates for alpha- and beta-HCH are above the USEPA levels of concern (LOC) for these Arctic populations based on high-end dietary intake estimates.

3. Synthesis of information

Lindane has been shown to be neurotoxic, hepatotoxic, immunotoxic and to have reproductive effects in laboratory animals. Human acute intoxication data show that lindane can cause severe neurological effects, and chronic data suggest possible haematological effects. The International Agency for Research on Cancer (IARC) has classified lindane as possibly carcinogenic to humans

(ATSDR, 2005). The US EPA classified lindane in the category "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential".

Human exposure to lindane, particularly in pregnant women and children, is a concern heightened by the ongoing presence of HCH isomers, including lindane, in human tissues and breast milk. Direct exposure from the use of pharmaceutical products for scabies and lice treatment should be of concern. Exposure from food sources is possibly of concern for high animal lipid content diets and subsistence diets of particular ethnic groups (USEPA, 2006 and CEC, 2005). Occupational exposure at manufacturing facilities should be of concern, because lindane production implies worker exposure to other HCH isomers as well, for example the alpha isomer is considered to be a probable human carcinogen (USEPA, 2006).

Lindane is very prevalent in the marine environment and soils, with higher concentrations often found in colder regions. The atmospheric long range transport potential of lindane has been demonstrated for the European Region (WHO/Europe, 2003).

Although current production of lindane seems to be declining with only a few producing countries remaining, the inefficient production process used to manufacture this insecticide over the years has been a world wide contamination problem which has left, and might still be leaving behind, an enormous legacy of contaminating waste products (IHPA, 2006).

The evaluation of laboratory experimental data of lindane would suggest a lower potential of bioaccumulation and biomagnification than that expected for other organochlorine pesticides. In fact, lindane should be considered a border case in terms of its potential for bioaccumulation. Fortunately, there is a large amount of monitoring data on biota allowing a real estimation of the risk profile of lindane in comparison with other organochlorine pesticides. The information provided by this huge amount of real field data is conclusive: lindane concentrations in biota samples collected far away from use areas is similar to that observed for other organochlorine pesticides, confirming the concern for persistence, bioaccumulation and long-range transport.

As the toxicity of lindane is also similar or even higher than that observed for other organochlorine pesticides, it should be considered that the concern related to the POP characteristics of lindane is equivalent to that observed for other chemicals already included in the Stockholm Convention. For example, Weisbrod et al., (2000) found lindane levels in pilot whales similar or just slightly lower than those found for aldrin, endrin, heptachlor or mirex. Also Sørmo et al. (2003) and Kannan et al. (2004) found equivalent levels for the sum of HCHs and for the sum of chlordanes in gray seal and sea otters respectively.

4. Concluding statement

Lindane has been the subject of numerous risk assessment reports by different agencies, diverse country regulations and international initiatives, indicating the general concern raised by this organochlorine compound and indicating global action has already been undertaken.

The information provided in the present document, as well as the information contained in the numerous risk assessment reports published on lindane, indicate that lindane is persistent, bioccumulative and toxic, and is found in environmental samples all over the world as well as in human blood, human breast milk and human adipose tissue in different studied populations, especially impacting Arctic communities that depend on subsistence foods. These findings indicate

that lindane is likely as a result of its long-range environmental transport to lead to significant adverse human health and environmental effects such that global action is warranted.

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別添6

クロルデコンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性･加水分解性】 水生環境中であるいは土壌中で、生分解又は加水分解するとは予測されない。 【光分解性】 大気中で直接的光分解を受けることは考えられないと結論している。 ･利用可能な全てのﾃﾞｰﾀに基づき、ｸﾛﾙﾃﾞｺﾝは環境中で高い残留性を示すと考えられる。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKow=4.50-5.41 【BCF（経鰓的生物濃縮係数）】 ･藻類：BCF=6000 ･無脊椎生物：BCF=21600 ･魚類：BCF=60200 【BMF（経口的生物濃縮係数）】 ･ほとんど又は全く代謝浄化せず、水生の食物連鎖において生物濃縮の可能性がある。 ･食物連鎖の研究において、藻からｶｷへの移動は非常に低かったが、ｴﾋﾞからｱﾐ、ｱﾐからｽﾎﾟｯﾄへの明白な栄養段階を通じた移動があることが示された。	【反復投与毒性】 ラット（2 年）：NOAEL 0.05mg/kg/day 0.25mg/kg/day で腎臓影響（蛋白尿、重篤な糸球体硬化） ラット（経口 21 ヶ月）：LOAEL 0.07mg/kg/day 肝細胞の病理組織学的変化、甲状腺ろ胞サイズ、コロイド量胞数低下、甲状腺ろ胞上皮細胞厚高値 ラット（経口 3 ヶ月）：LOAEL 1.17mg/kg/day 肝の病巣壊疽、副腎肥大、振戦、多動性、過剰驚愕反応等 【生殖毒性】 ラット（3 ヶ月）：NOAEL 0.25mg/kg/day 精巣萎縮 ラット（90 日）：LOAEL0.83mg/kg/day で精子の運動性･生存率低下、精子数減少、1.67mg/kg/day で性嚢、前立腺重量低下 マウス（160 日）：LOAEL 2mg/kg/day で排卵停止、膣発情持続、ﾗｯﾄ妊娠 14-20 日に母体経由で 15mg/kg/day 投与した雌児動物においても同様の報告	【慢性毒性】 ミジンコ *Daphnia magna* ：21dNOEC=0.0283 mg/L（繁殖）, 21dNOEC=0.025 mg/L（成長） ミシッドシュリンプ *Americamysis bahia* ：28dMATC=0.000026-0.00034 mg/L（成長） ユスリカ *Chironomus tentans* ：14dNOEC=17.9 mg/kg sediment（発達）

		【催奇形性】 ラット(経口):LOAEL 2mg/kg/day で胎児体重低下、骨化度低下、10mg/kg/day で脳水腫、停留精巣、腎盂肥大、脳室肥大 【発がん性】 ラット(80 週):LOAEL 1.2mg/kg/day 肝細胞腺がん及び上皮がん IARC グループ2B (possibly carcinogenic to human) 【その他】 職業ばく露で振戦、情緒不安定、視力障害、筋力低下、歩行運動失調等、実験動物で、脾臓、胸腺重量、好中球数、NK 活性低下、 EU-Strategy for Endocrine Disruptors 優先化学物質(無処置動物の少なくとも一種類において内分泌かく乱活性を示す科学的根拠がある)に分類	

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Persistent Organic Pollutants Review Committee
Third meeting
Geneva, 19–23 November 2007

Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Revised risk profile on chlordecone

At its third meeting, the Persistent Organic Pollutants Review Committee revised and adopted the risk profile on chlordecone, on the basis of the draft contained in document UNEP/POPS/POPRC.2/17/Add.2. The text of the risk profile, as amended, is set out below. It has not been formally edited.

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CHLORDECONE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

TABLE OF CONTENTS

Executive summary

The European Community and its member states being parties to the Stockholm Convention have proposed chlordecone to be listed in the Convention. The Persistent Organic Pollutants Review Committee concluded in its meeting in November 2005 that the substance complies with the screening criteria set out in Annex D of the Convention and that a draft risk profile should be prepared to review the proposal further.

Chlordecone is a synthetic chlorinated organic compound, which has mainly been used as an agricultural insecticide, miticide and fungicide. It was first produced in 1951 and introduced commercially in the United States in 1958 (trade names Kepone® and GC-1189). It was available in the United States until 1976. In France, chlordecone was marketed with a trade name Curlone from 1981 to 1993. Historically, chlordecone has been used in various parts of the world for the control of a wide range of pests. It has been used extensively in banana cultivation against banana root borer, as a fly larvicide, as a fungicide against apple scab and powdery mildew and to control the Colorado potato beetle, rust mite on non-bearing citrus, and potato and tobacco wireworm on gladioli and other plants. Given the specific pesticidal uses of chlordecone, it can be expected that all amounts manufactured are ultimately released to the environment.

Chlordecone is not expected to hydrolyse or biodegrade in aquatic environments, nor in soil. Direct photodegradation is not significant. Therefore, chlordecone is considered to be highly persistent in the environment. With BCF-values in algae up to 6,000, in invertebrates up to 21,600 and in fish up to 60,200 and documented examples of biomagnification, chlordecone is considered to have a high potential for bioaccumulation and biomagnification.

The available data are not conclusive when it comes to long-range atmospheric transport of chlordecone in gaseous form. However, atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents as well as biotic transport could also contribute to long-range environmental transport of chlordecone. Due to lack of monitoring data on chlordecone, the assessment of the potential for long-range transport of chlordecone was based on physico-chemical properties and application of long range transport models.

Chlordecone is readily absorbed into the body and accumulates following prolonged exposure. The pesticide is both acutely and chronically toxic, producing neurotoxicity, immunotoxicity, reproductive, musculoskeletal and liver toxicity at doses between 1 - 10 mg/kg bw/day in experimental animal studies. Liver cancer was induced in rats at a dose of 1 mg/kg body weight per day, and reproductive effects are seen at similar dose levels. The International Agency for Research on Cancer has classified chlordecone as a possible human carcinogen (IARC group 2B). Moreover, chlordecone is very toxic to aquatic organisms, with the most sensitive group being the invertebrates.

Based on the available evidence, chlordecone is likely as a result of its long-range environmental transport to lead to significant adverse human health and environmental effects such that global action is warranted.

1 Introduction

The European Community and its member states being parties to the Stockholm Convention have proposed chlordecone to be listed in Annex A to the Convention (UNEP/POPS/POPRC.1/6).

This risk profile has been prepared following the decision of the Persistent Organic Pollutants Review Committee at its first meeting in November 2005 to establish an ad hoc working group to review the proposal further (UNEP/POPS/POPRC.1/10).

In this document all data are presented according to the International System of Units (SI) and, therefore, many have been recalculated from other units in the data sources. Furthermore, all concentrations are presented based on kg or L (*e. g.* µg/kg or mL/L).

1.1 Chemical Identity of the proposed substance

Chlordecone is a synthetic chlorinated organic compound, which has mainly been used as an agricultural insecticide, miticide and fungicide.

1.1.1 Names and registry numbers

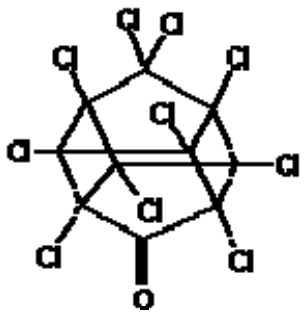
CAS chemical name:
1,1a,3,3a,4,5,5,5a,5b,6-decachloro-octahydro-1,3,4-metheno-2H-cyclobuta-[cd]-pentalen-2-one

Synonyms:
Decachloropentacyclo-[5,2,1,$0^{2,6}$,$0^{3,9}$,$O^{5,8}$]-decan-4-one,
Decachlorooctahydro-1,3,4-metheno-2H,5H-cyclobuta-[cd]-pentalen-2-one
Decachloroketone

Trade names:
GC 1189, Kepone, Merex, ENT 16391, Curlone

CAS registry number:
143-50-0

1.1.2 Structure



Source: **http://webbook.nist.gov**, as quoted in http:// ecb.jrc.it

Chlordecone is chemically closely related to mirex, a pesticide which is already listed under the Stockholm Convention. The chemical structure of chlordecone differs from mirex in that the oxygen of the keto group in chlordecone is replaced by two chlorine atoms in mirex.

1.1.3 Physical and chemical properties

The physical and chemical properties of chlordecone are listed in Table 1.1. It demonstrates that the variation is high between data sources for physical properties like vapour pressure and water solubility. This is confirmed by the fact that the Henry's Law Constant varies by one order of magnitude, depending on the type of data used for the calculation. The source of used data are generally considered to be reliable; the data quality have been assessed in the (inter)national consensus documents (IARC, IPCS HSG, IPCS EHC and US ATSDR) and the quality of the data published by Hansch *et. al.* and Howard has been evaluated (Pedersen *et. al.*, 1995).

Table 1.1 Physical and chemical properties of Chlordecone.

Property	Unit	Value	Reference
Molecular formula		$C_{10}Cl_{10}O$	
Molecular weight	g/mole	490.6	
Appearance at normal temperature and pressure		Tan-white crystalline solid	IARC, 1979[1]
Vapour Pressure	Pa	$3.0x10^{-5}$ (25 °C) $< 4.0x10^{-5}$ (25 °C) $4.0x10^{-5}$ (25 °C)	Kilzer, l *et. al.*, 1979[2] IARC, 1979[1] HSG 41, IPCS, 1990
Water solubility	mg/L	0.35-1.0x 1-2 2.7 (25 °C) 3.0	HSG 41, IPCS, 1990 EHC 43, IPCS, 1990 Kilzer, l *et. al.*, 1979[2] Kenaga, 1980
Melting point	°C	350; (decomposes)	IARC, 1979[1]
Boiling point	°C	No data	
Log K_{OW}		4.50 5.41	Howard, 1991[1] Hansch *et. al.*, 1995[2]
Log K_{aw}		-6.69	Scheringer *et. al* ., 2006
Log K_{oc}		3.38-3.415	Howard, 1991[1]
Henry's Law Constant	Pa m^3/mol	$5.45x10^{-3}$, (25 °C) $2.53x10^{-3}$ (20 °C) $4.9x10^{-3}$ $2.0x10^{-2}$	Calculated[2] Howard, 1991[1] Calculated[3] Calculated[4]
Atmospheric OH Rate Constant	cm^3/molecule-sec	≈ 0 (25 °C)[j]	Meylan & Howard, 1993[2]

* It is likely that the 0.35 number is an outlier. The source (HSG 41 by IPCS) did not provide the reference so it is impossible to track where this number came from. The more robust EHC 43 by IPCS did provide a reference and used 1-2 mg/l. This is in the same range with the other values in peer reviewed articles. ATSDR quotes a value of 3 mg/l from Kenaga.

1: Quoted from US ATSDR, 1995
2: Quoted from http://esc.syrres.com/interkow/webprop.exe
3: Calculated from maximum water solubility and minimum vapour pressure of this table
4: Calculated from minimum reliable water solubility (1 mg/L) and maximum vapour pressure of this table

1.2 Conclusion of the Persistent Organic Pollutants Review Committee on the Annex D information on Chlordecone

The POP Review Committee applied in its first meeting on 7–11 November 2005[1] the screening criteria specified in Annex D to the Stockholm Convention, and decided, in accordance with paragraph 4 (a) of Article 8 of the Convention, that it was satisfied that the screening criteria have been fulfilled for Chlordecone. It decided furthermore, in accordance with paragraph 6 of Article 8 of the Convention and paragraph 29 of decision SC-1/7 of the Conference of the Parties to the Stockholm Convention, to establish an ad hoc working group to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention. It invited, in accordance with paragraph 4 (a) of Article 8 of the Convention, Parties and Observers to submit to the Secretariat the information specified in Annex E of the Convention before 27 January 2006.

[1] See the meeting report at: www.pops.int/documents/meetings/poprc/

1.3 Data sources

This Risk Profile is mainly based on information from the following review reports:

- Environmental Health Criteria (EHC) 43: Chlordecone. IPCS International Programme on Chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1990 (available at: http://www.inchem.org/documents/ehc/ehc/ehc43.htm)
- Health and Safety Guide No. 41, 1990. IPCS International Programme on Chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1990 (available at: http://www.inchem.org/documents/hsg/hsg/hsg041.htm)
- Toxicological profile for Mirex and Chlordecone. U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry (ATSDR) August 1995 (available at: http://www.atsdr.cdc.gov/toxprofiles/tp66-p.pdf).

The above extensive review reports were used as the main source of information on this candidate POP chemical. Prior to the drafting of this risk profile, a detailed literature search was undertaken on Chlordecone which did not uncover any further assessment reports on this chemical, either international or at the level of individual countries. Where the reviews above have been cited, the text quoted (or quoted with modifications) includes the references cited in the original review. These references are not shown individually in the reference list.

Following the request of the POP Review Committee for additional information, as specified in Annex E of the Convention, on Chlordecone, information was provided, which was mainly based on the open literature. However, France provided a report prepared for the Assemblée Nationale describing the history of production and use of Chlordecone in Martinique and Guadeloupe (Beaugendre, 2005).

A search for more recent information included a literature search *via* the Danish Technical University Library and the data base FINDit (search terms: Chlordecone, kepone, merex) as well as a data base search in public data bases. The data bases include "Ecotox" (US-EPA, http://www.epa.gov/ecotox/), "NITE" (Japan, National Institute of Technology and Evaluation http://www.safe.nite.go.jp/english/db.html) BUA Reports (http://www.gdch.de/taetigkeiten/bua/berichte.htm) and Environmental Fate Data Base (http://www.syrres.com/esc/efdb.htm). This search was based on the search terms: Chlordecone, Kepone and the CAS number 143-50-0. In addition, the Arctic Monitoring and Assessment Programme[2] and the UNEP Regionally based assessment of Persistent Toxic Substances Global Report[3] were consulted. Most of these gave no further information regarding Chlordecone.

1.4 Status of the chemical under international conventions

Chlordecone is listed in Annex A of the Protocol to the Convention on Long-Range Transboundary Air Pollution (CLRTAP) on Persistent Organic Pollutants. The provisions of the Protocol oblige Parties (currently 25) to phase out all production and uses of Chlordecone. Chlordecone is included in the OSPAR convention as a substance of possible concern[4].

The proposal to include Chlordecone in the UNEP/FAO Rotterdam Convention was reviewed by the Chemical Review Committee (CRC) at its first meeting in February 2005. The CRC agreed that, on the basis of the information currently available, the notifications from Switzerland and Thailand had met all the criteria of Annex II with the exception of criterion (b) (iii)[5]. Accordingly, the CRC concluded that Chlordecone could not be recommended for inclusion in Annex III of the Rotterdam Convention at the current time.

[2] http://www.amap.no/

[3] http://www.chem.unep.ch/pts/gr/Global_Report.pdf

[4] The chemically related compound mirex is already included in the Stockholm convention. Both mirex and Chlordecone are included in the UNECE 1998 Aarhus Protocol on Persistent Organic Pollutants (POPs). Both are included in OSPAR as substances of possible concern.

[5] This requires that the documentation supplied demonstrates that the final regulatory action is based on a risk evaluation involving prevailing conditions within the Party taking the action.

2 Summary information relevant for the risk profile

2.1 Sources

2.1.1 Production

Chlordecone has been produced by reacting hexachlorocyclopentadiene and sulfur trioxide under heat and pressure in the presence of antimony pentachloride as a catalyst. The reaction product is hydrolyzed with aqueous alkali and neutralized with acid; Chlordecone is recovered *via* centrifugation or filtration and hot air drying (Epstein 1978) (Quoted from US ATSDR, 1995).

Chlordecone was first produced in 1951, patented in 1952, and introduced commercially in the United States by Allied Chemical in 1958 under the trade names Kepone® and GC-1189 (Epstein 1978; Huff and Gerstner 1978). The technical grade of chlordecone, which typically contained 94.5% chlordecone, was available in the United States until 1976 (IARC 1979). Chlordecone was also found to be present in technical grade mirex at concentrations up to 2.58 mg/kg and in mirex bait formulations at concentrations up to 0.25 mg/kg (EPA 1978b; IARC 1979a) (Quoted from US ATSDR, 1995).

2.1.2 Trade and stockpiles

Between 1951 and 1975, approximately 3.6 million pounds (1.6 million kg) of chlordecone were produced in the United States (Epstein 1978). (Quoted from US ATSDR, 1995) Chlordecone production was discontinued in the USA in 1976. However, a year later it was reported that a French company was considering the establishment of production facilities in France (Anonymous, 1978b), but no further information on this proposal is available. (Modified from EHC 43, (IPCS, 1984)).

No current data are available regarding import volumes of chlordecone. By 1976, technical chlordecone was not exported from the United States and the compound was no longer produced there. Diluted technical grade chlordecone (80% active ingredient) was exported to Europe, particularly Germany, in great quantities from 1951 to 1975 by the Allied Chemical Company (Epstein 1978) where the diluted technical product was converted to an adduct, Kelevan. Kelevan is a derivative of chlordecone and used for the same purposes. In the environment, it oxidizes to Chlordecone and could therefore also be considered with Chlordecone for listing in the Stockholm Convention. Approximately 90-99% of the total volume of Chlordecone produced during this time was exported to Europe, Asia, Latin America, and Africa. (DHHS 1985; EPA 1978b) (Modified from US ATSDR, 1995) There is no information, indicating that Kelevan is being produced or used at present.

Chlordecone was marketed in France as a formulation, Curlone, by De Laguarique from 1981 to 1993. The formulation was used in Martinique and Guadeloupe following hurricane Allen in 1979 and David in 1980 which led to considerable pest infestations. Chlordecone for this formulation was synthesised in Brazil. The authorisation for Curlone was withdrawn by the French Ministry of Agriculture in 1990. Use was continued until September, 1993. (Beaugendre, 2005) In Canada, no product containing Chlordecone has been registered as a pest control product since 2000.

2.1.3 Uses

Chlordecone has been used extensively in the tropics for the control of banana root borer (Anonymous, 1978a; Langford, 1978). This was its only registered food use. It is regarded as an effective insecticide against leaf-cutting insects, but less effective against sucking insects (Information Canada, 1973). Historically, Chlordecone has been used in various parts of the world for the control of a wide range of pests. It can be used as a fly larvicide, as a fungicide against apple scab and powdery mildew (Information Canada, 1973), and to control the Colorado potato beetle (Motl, 1977), rust mite on non-bearing citrus, and potato and tobacco wireworm on gladioli and other plants (Suta, 1978). Chlordecone has also been used in household products such as ant and roach traps at concentrations of approximately 0.125% (IARC 1979a). The concentration used in ant and roach bait was approximately 25%. (Epstein 1978) (Modified from EHC 43 (IPCS, 1984) and US ATSDR, 1995).

2.1.4 Releases to the environment

Given the specific pesticidal uses of Chlordecone, it can be expected that all amounts manufactured are ultimately released to the environment. The use of Chlordecone as a pesticide in Martinique and Guadeloupe until 1993 resulted in severe contamination of soil and surface water, which are being monitored at present. (Bocquene & Franco, 2005, Beaugendre, 2005).

Major releases of Chlordecone occurred to the air, surface waters, and soil surrounding a major American manufacturing site in Hopewell, Virginia. Releases from this plant ultimately contaminated the water, sediment, and biota of the James River, a tributary to the Chesapeake Bay (Quoted from US ATSDR, 1995).

2.2 Environmental fate

The partitioning of Chlordecone in the environment will be governed by its high log K_{ow} (5.41 or 4.50) and relatively low water solubility (1-3.0 mg/L) resulting in sorption to particulate matter (dust, soil and sediment) and organic material (living organisms).

The combination of these properties and the vapour pressure (3.0-4.0x10^{-5} Pa) of Chlordecone, results in a relatively low potential for volatilisation as the Henry's Law Constant is between 2.0x10^{-2} and 5.45x10^{-3} Pa m^3/mole (25 °C), depending on the type of data used for the calculation (Table 1.1.).

In the EHC 43 (IPCS, 1984), the volatilisation of Chlordecone is evaluated based on laboratory and field observations that indicate that Chlordecone does not volatilise to any significant extent (Dawson, 1978). However, the release of copious quantities of Chlordecone dust from production facilities has represented a major source of environmental and human contamination. Airborne Chlordecone has been known to spread 60 miles from a point source (Feldmann, 1976), and the potential exists for further dispersion of fine particles (Lewis & Lee, 1976 (Abbreviated from EHC 43 (IPCS, 1984).)

The US ATSDR (1995,), concluded that Chlordecone released to the environment partitions to soil and sediment. Small amounts may remain dissolved in water and Chlordecone released to the atmosphere is eventually deposited on soil or surface waters.

2.2.1 Persistence

In the EHC 43 (IPCS, 1984), early reports that did not include any evidence of Chlordecone degradation in the natural environment (Dawson, 1978; Geer, 1978) were quoted as well as a more recent study, in which microbial action had been shown to transform Chlordecone into monohydro- and possibly dihydrochlordecone (Orndorff & Colwell, 1980a).

EHC 43 (IPCS, 1984), concluded that Chlordecone is an extremely stable compound and is not expected to degrade in the environment to any significant extent. However, there have been reports of trace amounts of monohydrochlordecone being found (Carver *et. al.*, 1978, Orndorff & Colwell, 1980b), but the mechanism of its formation is not clear. Solar irradiation of Chlordecone in the presence of ethylenediamine results in 78% degradation after 10 days (Dawson, 1978) quoted from EHC 43 (IPCS, 1984). However, ethylenediamine is not usually present in the atmosphere, so at the time, there was no information available regarding the photolytic stability of Chlordecone under environmental conditions.

The more recent review (US ATSDR, 1995), concludes that Chlordecone is not expected to be subject to direct photodegradation in the atmosphere. Furthermore, it is concluded that Chlordecone is resistant to aerobic degradation, although some anaerobic biodegradation does occur and that Chlordecone is very persistent in the environment. Chlordecone will strongly bind to organic matter in water, sediment, and soil. When bound to organic-rich soil, Chlordecone is highly immobile; however, when adsorbed to particulate matter in surface water, Chlordecone can be transported great distances before partitioning out to sediment. The primary process for the degradation of Chlordecone in soil or sediments is anaerobic biodegradation (Abbreviated from US ATSDR, 1995) .

Information regarding the persistence of Chlordecone dating after 1995 is scarce, but the use of Chlordecone until 1993 in the Caribbean island of Martinique has resulted in severe contamination and monitoring studies have been initiated. Bocquene & Franco (2005) reported concentrations in samples from 2002 in water (particulate matter) and sediment in rivers of up to 57 µg/kg and 44 µg/kg, respectively. They quoted other investigations for reporting concentrations in river water, sampled in 2000-2001 in the range 1.20 - 2.13 µg/L.

Even though Chlordecone was prohibited from main land France, an exemption was granted that allowed the use of it in the French West Indies until September, 1993. A recent study showed that it is still detected in different ecosystems of Martinique (Coat, S. *et. al.*, 2006). Stocks of Chlordecone may have been used in Martinique after 1993, but it is expected that the use ceased several years ago. However, residues are still measurable in both river water and sediment, where the prevailing anaerobic conditions in the latter allow for the only known biotic degradation of Chlordecone. This is all the more remarkable as the climate in this area is optimal not only for crops and pests but also for biodegradation.

Conclusion

Chlordecone is not expected to hydrolyse or biodegrade in aerobic aquatic environments or in soil; however, there is some evidence of degradation under anaerobic condition. Direct photodegradation is not significant. Based on all available data Chlordecone is considered to be highly persistent in the environment.

2.2.2 Bioaccumulation

Because of the lipophilic nature of this compound (high octanol-water partition coefficient (log K_{ow} 4.50-5.41), Chlordecone has a potential for both bioaccumulation and, with little or no metabolic depuration, also biomagnification in aquatic food chains.

Table 2.1 summarises bioconcentration factors (BCF) selected from the US EPA database Ecotox (US EPA, 2006). The results included are based on measured concentrations and, for organisms different from algae, derived from tests based on flow through exposure. Thereby, the results should reflect the bioconcentration obtained under well defined, constant exposure concentrations. For fish, the results of a series of tests of four days duration were not included, because it is not considered to be likely that equilibrium had been reached[6]. Two additional studies from EHC 43 (IPCS, 1984) are also included.

Table 2.1 BCF values for Chlordecone.

Species	Test Duration	Exposure Concentration µg/L	BCF	Reference[1]
Green algae (*Chlorococcum sp., Dunaliella tertiolecta*)	24 h	100	230-800	Walsh *et. al.*, 1977
Green alga (*Chlorococcum sp.*)	48 h	40	6,000	Bahner *et. al.*, 1977
Diatoms (*Thalassiosira guillardii, Nitzschia sp.*)	24 h	100	410-520	Walsh *et. al.*, 1977
Crustacean (*Callinectes sapidus*)	96 h	110-210	6.2-10.4	Schimmel, 1977
Crustacean (*Palaemonetes pugio*)	96 h	12-121	425-933	Schimmel, 1977
Crustacean (*Palaemonetes pugio, Americamysis bahia*)	21-28 d	0.023-0.4	5,127-13,473	Bahner *et. al.*, 1977
Crustacean (*Palaemonetes pugio*)	16 d	0.041	12,094	Fisher & Clark, 1990
Oyster (*Crassostrea virginica*)	19-21 d	0.03-0.39	9,278-9,354	Bahner *et. al.*, 1977
Midge (*Chironomus tentans*)	14 d	11.8-169.2	21,600	Adams *et. al.*, 1985
Fish (*Brevoortia tyrannus*)	1-18 d	0.14-1.55	2,300-9,750	Roberts & Fisher, 1985
Fish (*Menidia menidia*)	1-28 d	0.08-0.8	21,700-60,200	Roberts & Fisher, 1985
Fish (*Cyprinodon variegatus*)	28 d	< 0.02-1.9	3,100-7,115	Bahner *et. al.*, 1977; Hansen *et. al.*, 1977
Fish (*Leiostomus xanthurus*)	30 d	0.029-0.4	2,340-3,217	Bahner *et. al.*, 1977
Fish (*Pimephales promelas*)	56 d	0.004	16,600	Huckins *et. al.*, 1982[2]
Fish (*Cyprinodon variegatus*)	Life cycle	0.041	1,800-3,900	Goodman *et. al.*, 1982[2]

1: All quoted from the Ecotox database (US EPA, 2006), except for two[2] quoted from EHC 43 (IPCS, 1984)

The information on bioaccumulation from food is limited, but the EHC 43 (IPCS, 1984) report includes two relevant studies; one on food exposure and the other on an estuarine food chain. When chlordecone was fed to juvenile spot for 28 days, the body burden of chlordecone increased additively and equilibrium was not attained (Stehlik & Merriner, 1983). The estuarine food chain study (Bahner *et al*., 1977) was composed of green algae, oysters, mysids, grass shrimps, sheepshead minnows and spot. The transfer from algae to oysters was very low; but a clear transfer from shrimp to mysids

[6] In OECD Test Guideline 305, the prescribed duration of the exposure phase is 28 days.

and from mysids to spot, indicated that much of the chlordecone was being transferred through the trophic levels. Clearance was slow in shrimp and fish, with tissue levels of chlordecone decreasing by 30-50% in 24-28 days.

US ATSDR (1995), described the bioaccumulation of chlordecone together with that of mirex, stating that they are both highly lipophilic and therefore, have a high bioconcentration potential. They bioaccumulate in aquatic food chains with virtually no degradation of the compounds by exposed organisms (de la Cruz and Naqui, 1973; Epstein, 1978; Huckins *et al.*, 1982; Huggett and Bender, 1980; Kenaga, 1980; Lunsford *et al.*, 1987; Naqvi and de la Cruz, 1973; Nichols, 1990; Oliver and Niimi, 1985 and 1988; Roberts and Fisher, 1985)[7].

Only limited information is available on uptake and bioaccumulation of chlordecone in terrestrial food chains (Naqvi and de la Cruz, 1973), and little uptake of chlordecone by plants was observed (Topp *et. al*., 1986).

Conclusion

With BCF-values of up to 6,000 in algae, of up to 21,600 in invertebrates and of up to 60,200 in fish, and with documented examples of biomagnification, chlordecone is considered to have a high potential for bioaccumulation and biomagnification.

2.2.3 Potential for Long-Range Environmental Transport

The potential for long-range environmental transport can be documented through monitoring data from remote regions (*e.g.* the Arctic) and/or through physical-chemical characteristics of the molecule, which are promoting such transport. The most well known mechanism of long-range transport is atmospheric transport of substances in the vapour phase. However, atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents as well as biotic transport could also contribute (*e. g.* AMAP 2004).

One prerequisite for long-range atmospheric transport is persistence to degradation, and Chlordecone is considered to be highly persistent in the environment (see Section 2.2.1). Chlordecone does not volatilise to any significant extent (see section 2.2). The partitioning of Chlordecone in the environment will be governed by its high log K_{ow} (5.41 or 4.50) and relatively low water solubility (1-3.0 mg/L) resulting in sorption to particulate matter (dust, soil and sediment) and organic materials and living organisms. Therefore, the long range transport is expected to take place through these pathways.

The US ATSDR (1995), states that atmospheric transport of dust containing Chlordecone particles was reported during production years based on results from high volume air sample filters from Hopewell: At approximately 200 yards from the Chlordecon production plant, the contents ranged from 3.0-55 micrograms/m^3, depending on weather conditions and date of collection. At more distant sites in May 1975, levels ranged from 1.4-21 ng/m^3. Specifically, in South Richmond, 15.6 miles north west from Hopewell, the level was 1.41 ng/m^3. At Byrd airport, 14.12 miles north of Hopewell, the level was 1.93 ng/m^3. In Petersburg, 8.19 miles south west from Hopewell, the level was 20.7 ng/m^3. (Epstein, 1978). They conclude further, that airborne Chlordecone has been known to spread 60 miles from a point source (Feldmann, 1976), and that the potential exists for further dispersion of fine particles (Lewis & Lee, 1976) (US ATSDR, 1995).

Transport in aquatic environments is illustrated by results of measurements in clams and oysters from the James River at sampling locations from 8-64 miles from Hopewell, Virginia that contained 0.2-0.8 mg/kg of Chlordecone (Epstein, 1978).

However, no records are available regarding concentrations of Chlordecone in areas at long distances from sites of production or use. Therefore, the assessment of the potential for long-range transport of Chlordecone must be based on physical properties. For this - apart from persistence - the vapour pressure and the Henry's Law Constant are considered to be the most relevant properties. For a comprehensive evaluation of the potential for long-range atmospheric transport, knowledge of the vapour pressure at high as well as at low temperatures (*e. g.* 25 °C and 0 °C) is required. This information is, however, available for only a few substances (AMAP, 2004), so the vapour pressure at 25 °C is used as a measure of the volatility of the substance.

As a rule of thumb, substances with vapour pressures $>1.33 \times 10^{-2}$ Pa will be entirely in the vapour phase and substances with vapour pressures $<1.0 \times 10^{-4}$ Pa will be particulate (US ATSDR, 2004).

A way of evaluating the characteristics and effects of a substance for which not enough information exists is to compare it with better known substances of similar characteristics. This approach (known as "the benchmark approach") was proposed by Scheringer (1997) and Beyer *et. al.,* (2000), has been recently used in some recent studies concerning persistence and environmental transport of pollutants (see, *i. e.* Vulykh *et. al.,* 2006, and Klasmeier *et. al.,* 2006). As a measure of values of properties that would qualify for long-range atmospheric transport, the currently listed POPs are used. However,

[7] These references describe both Mirex and Chlordecone.

information regarding physical-chemical properties for chemicals often varies widely between sources and the quality of data cannot be compared without specific review of the individual studies. This is demonstrated by the available data on the physical-chemical properties of Chlordecone presented in Table 1.1. The two values for the vapour pressure are rather uniform (0.3 and $0.4x10^5$ Pa) but the water solubility found in literature varies by an order of magnitude (0.35–3.0 and the lowest value is considered to be unreliable.[8]

The comparison of Chlordecone with already listed POPs is presented in Table 2.2. As a starting point for this comparison, the highest and lowest values for Chlordecone (Table 1.1) were used. For already listed POPs, information was sought on the UNEP-POPs homepage. Among the currently listed POPs, most of the relevant properties were available for aldrin, chlordane, dieldrin, DDT, hexachlorobenzene, mirex, toxaphene, endrin and heptachlor. Missing information (water solubility of mirex) was sought in US ATSDR (1995) and AMAP (2004). The US ATSDR (1995), quotes values of 0.2 and 0.6 mg/L, while the AMAP (2004), quotes Mackay for very low water solubility: $6.5x10^{-5}$ mg/L. In order to avoid introduction of what seems to be an outlier in the comparison, the value for water solubility of mirex from US ATSDR (1995) was used.

The water solubility and vapour pressure as well as Henry's Law Constants calculated from these values of the currently listed POPs are summarised in Table 2.2 together with information on Chlordecone from Table 1.1.

Table 2.2 Water solubility (WS), vapour pressure (VP) and (calculated) Henry's Law Constant (HLC) (at 25°C) for Chlordecone and currently listed POPs.

Substance	WS mg/L	VP Pa	HLC Pa m^3/mol
Chlordecone-min	1.0	0.00003	0.0049[1]
Chlordecone-max	3.0	0.00004	0.02[2]
POP-min	0.0012 (DDT)	0.000025 (DDT)	0.04 (endrin)
POP-max	3.0 (toxaphene)	27 (toxaphene)	3726 (toxaphene)
POP-2nd max	0.5 (dieldrin)	0.04 (heptachlor)	267 (heptachlor)

1: Calculated from maximum water solubility and minimum vapour pressure
2: Calculated from minimum reliable water solubility and maximum vapour pressure

Table 2.2 shows that the water solubility of Chlordecone is at the level of the most water soluble among the currently listed POPs (toxaphene and dieldrin), while the vapour pressure is comparable to that of DDT. The highest of the two Henry's Law Constants that were calculated for Chlordecone is of the same order of magnitude as that of endrin. It should be noted that in presenting the data in table 2.2 it is not inferred that a chemical (in this case Chlordecone) is considered to meet the long range environmental transport criterion just because it fits within the range of values of currently listed POPs.

Further to this, it should be mentioned that the latest AMAP report on POPs (AMAP, 2004) describes the possibilities of particle borne transport for substances, which have Henry's Law Constants (HLC) close to that of Chlordecone (HLC = 0.0049 or 0.056). Based on HLC-values from AMAP (2004), it is concluded that semi-volatile compounds such as lindane (γ-HCH) (HLC = 0.000149) and chlordane (HLC = 0.342) are distributed between airborne particles and the gaseous phase, depending on the temperature. These can be washed out *via* precipitation and temporarily deposited in seawater or soil and can absorb to water, plant and soil surfaces from the gaseous phase. During favourable warm weather conditions, these compounds evaporate again into the atmosphere and undergo further atmospheric transport. This remobilization is also called the 'grasshopper effect'. The role of stormy weather situations in remobilization of semivolatile compounds into the atmosphere is obvious but still scarcely investigated (AMAP, 2004).

Besides, certain physical-chemical properties of Chlordecone, such as the partition coefficients log K_{ow} (octanol-water partition coefficient) and log Kaw (air-water partition coefficient), are similar to those of some toxaphene components which, added to its persistence in air and water, would mean that coupled long range transport in atmosphere and oceans may take place (*i. e.* the substance is exchanging between atmospheric gas phase and oceanic dissolved phase and can be

[8] Availability of high quality data regarding physical-chemical properties could support more firm conclusions.

transported in either phase). (Wania, F. 2006, personal communication). Chlordecone has a very low Henry's law constant and a high mass fraction is found in water, and therefore it can be inferred that transport with ocean currents contributes to the long-range transport of Chlordecone.

In a recent modeling study, Scheringer *et. al*.,(2006), investigated the persistence and long range transport potential of these potential POPs, including chlordecone and hexabromobiphenyl, using an OECD screening tool which based the evaluation of overall environmental persistence and transport potential on the results of several of the currently available multimedia environmental fate models (see also Klasmeier *et. al*., 2006, and Fenner *et. al*., 2005 for a more detailed explanation). They concluded that the four POP candidates have persistence and long range transport potential properties similar to those of several known POPs in this evaluation. Furthermore, they included the uncertainty regarding the data quality in an uncertainty analysis, which indicated that the result is valid although there are considerable uncertainties in the chemical properties of the four POP candidates. It should be noted that environmental fate modeling results strongly depend on the assumptions made, specifically when essential data such as environmental half-lives are not known. In addition, results for substances like Chlordecone, which are strongly bound to particles and are of very low volatility, are highly dependent on the medium to which they are emitted, i.e., to air, to water, or to soil. The emission to air scenario always yields the highest transfer efficiency, and that value is displayed in the Scheringer *et. al.*, (2006) plots. Transfer efficiency will likely differ by several orders of magnitude when evaluated under soil and water emission scenarios.

Conclusion

In summary, the above discussion shows that the available data on Chlordecone are not conclusive when it comes to long-range atmospheric transport in gaseous form. However, atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents, as well as biotic transport, could also contribute to long-range environmental transport of Chlordecone Coupled atmosphere-ocean transport also seems quite possible.

Due to a lack of monitoring data on Chlordecone the assessment of the potential for long-range transport of Chlordecone must be based on physico-chemical properties and modelling data. The modelling study of Scheringer *et. al.*, 2006, shows clearly that long range environmental transport is possible (and possibly more than actually estimated), even considering the uncertainties surrounding the physico-chemical properties.

In accordance with paragraph 7 (a) of Article 8 of the Convention, and taking into account that a lack of full scientific certainty should not prevent a proposal from proceeding, Chlordecone is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects such that global action is warranted.

2.3 Exposure

2.3.1 Environmental concentrations

The available information regarding environmental concentrations of Chlordecone is very limited and includes only areas in the vicinity of production (US) or use (Martinique).

The US ATSDR (1995), illustrates the presence of Chlordecone in the environment following production of the substance. In 1977, 12 years after production of Chlordecone began and 2 years after the production ceased, average concentrations of Chlordecone in estuarine water (dissolved) were <l0 ng/L (ppt) (Nichols 1990). In October 1981, 6 years after production ceased, Chlordecone water concentrations ranged from not detectable to 0.02 µg/L (ppb) (Lunsford *et. al.,* 1987). Groundwater monitoring data are lacking, but because Chlordecone binds tightly to organic matter in soil, leaching into groundwater is not expected to occur extensively (Abbreviated from US ATSDR, 1995).

Recent monitoring data from the United States demonstrate the persistence of Chlordecone, known as Kepone in the United States. The substance is included in the U.S. EPA National Lake Fish Tissue Study to estimate the national distribution of selected residues in fish tissue from lakes and reservoirs in the lower 48 states. There were a total of 881 samples collected and analyzed between 2000 and 2005. For Chlordecone, there were 152 hits (17.25%), ranging from 12.3 and 2008 ppb. (Jensen, 2006).

In Martinique, the widespread use of Chlordecone until 1993 has resulted in contamination of soils and surface water in most of the island (Bocquené & Franco, 2005). These authors reported an investigation from 2002 of the presence of a series of pesticides in the water at the mouth of seven rivers. They measured Chlordecone in particulate matter or sediment of six of the seven rivers at concentrations up to 57 µg/kg in particulate matter, and up to 44 µg/kg in sediment.

Bocquené & Franco (2005), quoted other investigations in which concentrations of Chlordecone in the range 1.20 to 2.13 µg/L were measured in rivers of Martinique in 2002-2001. They also stated that Chlordecone was "ubiquitous" in river water used for drinking water.

Further to this, the report prepared for L'Assemblée Nationale (Beaugendre, June 2005), described the history of the use of Chlordecone in Guadeloupe and Martinique, and mentioned several monitoring programmes which are expected to result in reports at the end of 2005. However, these reports have not been available when drafting this document.

2.3.2 Human exposure

In the US ATSDR (1995), the experience from production of Chlordecone is summarised as follows: Chlordecone has not been detected in human adipose tissue or in blood samples from the general population, although historically it was detected in human milk samples collected in the south-eastern United States (EPA 1978c). Information is available regarding Chlordecone levels in blood of occupationally exposed workers and their families during 1974-1975 employed at the Hopewell, Virginia site. (Cannon *et. al.*, 1978; Epstein 1978; Knishkowy & Baker 1986; Taylor *et. al.*, 1978). (Quoted from US ATSDR, 1995) Further data on human exposure is quoted in section 2.4.1.

Information regarding human exposure resulting from direct use (application) of Chlordecone in the Caribbean Islands is not available. However, monitoring data in agricultural soils, crops, freshwater fish, littoral fish and shellfish indicates that human exposure more than 10 years after the use of chlordecone has ceased in Martinique and Guadeloupe, is still possible In soils having received Chlordecone, residues in crop are proportional to soil contamination and may exceed the recommended national residues limits (50 µg/kg to 200 µg/kg). This concerns mainly root vegetables such as radish (max. measured concentration: 0.055 µg/kg), sweet potatoes (max. measured concentration: 0.300 µg/kg), taro root (max. measured concentration: 0.230 µg/kg), but also aerial part of plants, such as sugar cane (max. measured concentration: 0.690 µg/kg), or pineapple (max. measured concentration: 0.160 µg/kg). In addition, workers are directly exposed to contaminated soils. Concentrations in fisheries products (freshwater and estuarine water) have also been found to exceed in some occasions national residues limits up by a factor of 100 (max. measured concentration: 20 mg/kg). National provisions have been taken in order to prohibit fisheries activities in contaminated area (Cabidoche *et. al*., 2006).

2.4 Hazard assessment for endpoints of concern

2.4.1 Toxicity

Toxicokinetics in experimental animals and in man

The US ATSDR (1995) and EHS 43 (IPCS, 1984) both record that Chlordecone is well absorbed following oral, dermal and inhalation exposure. Toxicokinetic data are mainly available from studies in experimental animals (*e. g.* Blanke *et. al.*, 1978; Boylan *et. al.*, 1979; Cohn *et. al.*, 1978; Egle *et. al.*, 1978; Fujimori *et. al.* 1982a; Guzelian *et. al.*, 1981; Hall *et. al.* 1988; Hewitt *et. al.*, 1986b; Kavlock *et. al.*,1980; Plaa *et. al.*, 1987; Richter *et. al.*, 1979; Shah *et. al.*, 1987; Skalsky *et. al.*, 1980; as reported in IPCS, 1984). Following absorption, it is widely distributed in the body, with accumulation in the liver and to a lesser extent in fat, brain and kidneys, both in experimental animal studies and in humans (as reported in US ATSDR (1995) and EHS 43 (IPCS, 1984). Following administration of a single oral dose to rats at 40 mg/kg body weight, the highest concentrations were found in the adrenal glands and liver, followed by the fat and lung (Egle *et. al.*, 1978, quoted from IPCS, 1984). Chlordecone has been reported to be slowly metabolised *via* reductive biotransformation to Chlordecone alcohol in the rat (Blanke *et. al.*, 1978, as reported in EHS 43). Elimination from the body is slow, with a half-life of the order of several months and Chlordecone disappears more slowly from the liver than from other tissues (Egle *et. al.*, 1978, quoted from IPCS, 1984). Elimination is mainly *via* the faeces, a total of 66% of the dose in the Egle study being removed in the faeces and 2% in the urine in the 84 days following administration (Egle *et. al.*, 1978, quoted from IPCS, 1984).

EHC 43 reports that Chlordecone was detected in high concentrations in the liver (range 13.3-173 mg/kg), whole blood (range 0.6-32 mg/litre), and subcutaneous fat (range 2.2-62 mg/kg) of 32 male workers (Cohn *et. al.*, 1976, adapted from IPCS (1984). In occupationally-exposed workers, serum Chlordecone concentrations ranged from 120 to 2109 µg/litre, and dropped to 37 - 486 µg/litre 6-7 months after exposure had ceased (Adir *et. al.*, 1978, reported in IPCS (1984). The half-life of Chlordecone in these workers was estimated to be 63-148 days. Reductive biotransformation to Chlordecone alcohol has also been reported in humans (Blanke *et. al.*, 1978, as reported in EHS 43). Chlordecone was eliminated, primarily in the faeces, at a mean daily rate of 0.075% of the estimated total store in the body (Cohn *et. al.*, 1976, quoted from IPCS, 1984).

Toxicity of Chlordecone in animal studies

Chlordecone is of high acute toxicity in experimental animal studies, with an LD_{50} of approximately 100 mg/kg in the rat and ranging from 65 mg/kg in the rabbit to 250 mg/kg in the dog (taken from IPCS, 1984, Table 2). Acute toxicity effects include tremors indicative of a neurotoxic effect on the nervous and/or musculoskeletal systems, investigated by many authors as reported in US ATSDR (1995). The neurotoxic effects of Chlordecone have been reported in chickens (Naber & Ware, 1965), quail (McFarland & Lacy, 1969), fish (Couch *et. al.*, 1977), hamsters (Martinez *et. al.*, 1976), mice (End *et. al.*, 1979), rats (Epstein, 1978), and man (Martinez *et. al.*, 1978). Acute oral administration of Chlordecone is also associated with reproductive effects (Khera *et. al.*, 1976; Uzodinma *et. al.*, 1984a; Yarbrough *et. al.*, 1981) and hepatotoxicity in some studies (Fujimori *et. al.*, 1983; Mehendale 1977b, 1981b; Teo & Vore 1991) (quoted from US ATSDR (1995).

Repeated exposure to Chlordecone also causes reproductive, neurological, musculoskeletal and liver toxicity at doses as low as 10 mg/kg bw/day, although effects in other organs including kidney, thyroid, adrenals, and testes have also been reported (US ATSDR, 1995, IPCS, 1984). A Lowest-Observed-Adverse-Effect-Level (LOAEL) of 1.17 mg/kg bw/day was recorded in a 3 month feeding study in rats and signs of toxicity included focal necrosis in liver, enlargement of the adrenal gland, tremor, hyperactivity and exaggerated startle response (Cannon and Kimbrough, 1979, as quoted in US ATSDR, 1995). Histopathological changes in the liver, reduction in thyroid follicular size and colloid content and increase in epithelial cell height were reported in a 21-month gavage study in the rat, with a LOAEL of 0.07 mg/kg bw/day in males (Chu *et al*, 1981, as quoted in US ATSDR, 1995). Renal effects (proteinuria and increased severity of glomerulosclerosis) were seen in a 2-year feeding study in rats, with a NOAEL of 0.05 mg/kg/day (Larson *et. al.*, 1979b, as quoted in US ATSDR, 1995). Oral Chlordecone treatment caused decreased spleen and thymus weights, leukocyte counts, natural killer cell activity, and mitogenic responsiveness (EPA 1986c; Smialowicz *et. al.*, 1985; Swanson and Wooley, 1982); decreased natural killer cell activity (Smialowicz *et. al.*, 1985); and significant increase in plaque-forming cells (Chetty *et. al.*, 1993c) (as reported in ATSDR, 1995). The NOAEL was 5 mg/kg bw/day and the LOAEL was 10 mg/kg bw/day.

Hepatocarcinogenicity (hepatocellular carcinoma) of Chlordecone has been demonstrated in rats and mice (males and females) (NCI 1976, Reuber, 1978, 1979, as quoted in IPCS, 1984 and US ATSDR, 1995). Tumours have been observed at doses as low as 1 mg/kg bw/day in the rat and in mice at a dose of 2.6 mg/kg bw/day (NCI, 1976, as quoted in US ATSDR (1995). The International Agency for Research on Cancer (IARC) concluded in 1987 that there was sufficient evidence that Chlordecone is carcinogenic in mice and rats and possibly carcinogenic to humans (Group 2B). Chlordecone is not genotoxic in *in vitro* microbial and mammalian cell gene mutation assays, in a clastogenicity test and in the dominant lethal assay (Mortelmans *et. al.*, 1986; Probst *et. al.*, 1981; Schoeny *et. al.*, 1979, Tong *et. al.* 1981; Williams 1980, Khera *et. al.*, 1976; Simon *et. al.*, 1986, as reported in ATSDR (1995), although it has been reported to interfere with cell-to-cell communication (Tsushimoto *et. al.*, 1982, Caldwell and Loch-Caruso, 1992, as reported in US ATSDR (1995), suggests that it produces liver tumours by an epigenetic, tumour-promoting mechanism involving both hepatic toxicity and hypertrophy, including cytochrome P-450 induction.

Oral administration of Chlordecone to animals causes decreased fertility or fecundity and litter size, reduced sperm count and testicular atrophy (Khera *et. al.*, 1976; Linder *et. al.* 1983; Uzodinma *et. al.*, 1984a; Yarbrough *et. al.* 1981, as reported in US ATSDR (1995). A LOAEL of 0.83 mg/kg/day was recorded for sperm effects in a 90 day feeding study in rats, while effects on seminal vesicles and prostate were apparent at 1.67 mg/kg bw/day (Linder *et. al.*, 1983) (Quoted from US ATSDR (1995).

Chlordecone is also a developmental toxicant. As reported in US ATSDR (1995) and EHC 43 (IPCS, 1984), gestational exposure of rats and mice to low doses of Chlordecone resulted in increased stillbirths and decreased postnatal viability, reduced fetal or neonatal weight and/or skeletal ossification and a low incidence of malformations such as renal pelvis dilatation, undescended testes, enlarged cerebral ventricles, clubfoot, fused vertebrae or ribs, and encephalocele. Chlordecone administered at levels of 2, 6, and 10 mg/kg bw/day to rats and 2, 4, 8, and 12 mg/kg body weight per day to mice on days 7 - 16 of gestation caused 19% maternal mortality in rats at the highest dose and fetuses exhibited reduced weight, reduced degree of ossification, oedema, undescended testes, enlarged renal pelvis, and enlarged cerebral ventricles. (Chernoff & Rogers, 1976, as reported in IPCS, 1984). Lower dose levels induced reductions in fetal weight and degree of ossification. Male rats born to treated dams did not show any reproductive impairment. The reproductive performance of mice fed 0, 10, 30, or 37.5 mg Chlordecone/kg diet was impaired in terms of offspring and litter size (Huber, 1965, as reported in IPCS, 1984). No litters were produced by females fed 40 mg/kg, but litter production did resume within 7 weeks following withdrawal of the Chlordecone, although litters were still smaller than those of untreated controls (quoted from IPCS (1984)). Anovulation and persistent vaginal estrus were observed in female mice given Chlordecone at a dose level of 2 mg/kg bw/day) (Swartz *et. al.*, 1988, as quoted in US ATSDR, 1995), and similar changes were observed in female offspring of maternal rats given 15 mg/kg/day of Chlordecone on gestation days 14-20 (Gellert and Wilson, 1979, as

quoted in US ATSDR, 1995), although no effects on vaginal patency or fertility were observed in female offspring of maternal mice given 20 mg/kg/day during gestation days 8-12 or 14-18 (Gray and Kavlock 1984, as quoted in US ATSDR, 1995).

Toxicity of Chlordecone in humans

Available human data support the conclusion that Chlordecone has a similar toxicity profile in humans to that seen in experimental animal studies. As reported in US ATSDR (1995), a high incidence of nervous system toxicity was seen in a single group of workers exposed to Chlordecone during its manufacture (Cannon *et. al.*, 1978; Martinez *et. al.*, 1978; Sanbom *et. al.*, 1979; Taylor 1982, 1985; Taylor *et. al.*, 1978, taken from US ATSDR (1995)). Exposure of this population occurred by a combination of inhalation, oral, and dermal exposures, although the dermal route was suggested to be the predominant route. The toxicity was manifested as tremors, visual difficulties, muscle weakness, gait ataxia, in coordination, headache, and increased cerebrospinal fluid pressure (US ATSDR (1995). Prolonged exposure to high concentrations of Chlordecone in the workplace has been suggested to cause oligospermia and decreased sperm motility among male workers, although fertility was not impaired (Guzelian 1982a; Taylor 1982, 1985; Taylor *et. al.,* 1978, taken from US ATSDR (1995). A correlation between blood levels, atmospheric levels and sperm effects has however been difficult to prove conclusively (US ATSDR (1995). Epidemiological evidence for carcinogenicity of Chlordecone in exposed humans following inhalation exposure to Chlordecone is extremely limited (US ATSDR, 1995, IPCS, 1984). Liver biopsy samples taken from 12 workers with hepatomegaly resulting from intermediate- or chronic-duration exposures to high concentrations of Chlordecone showed no evidence of cancer (Guzelian *et. al.,* 1980, taken from US ATSDR (1995). However, conclusions from this study are limited by the very small number of workers sampled (US ATSDR, 1995)

Effects on endocrine systems

The effects of Chlordecone on reproduction indicate that this pesticide has effects on endocrine systems. It has been evaluated under the EU-Strategy for Endocrine Disrupters[9] and has been placed in category 1 (evidence of endocrine-disrupting activity in at least one species using intact animals), in the priority list of chemicals established under the EU-Strategy. This categorisation is based on evidence of ED activity in a number of experimental systems including the mouse uterotropic assay, increased uterine weight in rats given multiple injections of Chlordecone postnatally and receptor binding assays, indicative of an oestrogenic effect (as reported in BKH report, 2000, US ATSDR, 1995).

Conclusion on effects assessment and toxicity of Chlordecone

Chlordecone is readily absorbed into the body and accumulates following prolonged exposure. The pesticide is both acutely and chronically toxic, producing neurotoxicity, immunotoxicity, reproductive, musculoskeletal and liver toxicity at doses between 1 - 10 mg/kg bw/day in experimental animal studies. Liver cancer was induced in rats at a dose of 1 mg/kg body weight per day and in mice at a dose of 2.6 mg/kg bw/day, and reproductive effects are seen at similar dose levels. The International Agency for Research on Cancer has classified Chlordecone as a possible human carcinogen (IARC group 2B).

Table 2.3 summarises the outcomes of key toxicological studies on Chlordecone, including the NOAEL/LOAEL derived in each study. The studies included in this Table have been selected from the very large database on toxicological studies on Chlordecone, on the basis of the importance of the endpoint investigated (*e. g.* reproductive toxicity, carcinogenicity, other key target organ toxicity), robustness of the reported studies and the dose level (NOAEL/LOAEL) at which effects were reported. These studies were considered to be particularly relevant for characterisation of the toxicological risks of these compounds, and some of these studies have been used by US ATSDR to define Minimal Risk Levels (MRLs) for Chlordecone (US ATSDR, 1995).

Table 2.3 Summary of key toxicological studies on Chlordecone.

Species	Study type	Effect	LOAEL/NOAEL (mg/kg bw/day)	Reference
Rat Fischer 344	Short-term/acute toxicity 10 day repeat dose gavage study	65% loss in body weight, changes in clinical chemistry parameters	10 mg/kg bw/day (LOAEL) 5 mg/kg bw/day (NOAEL)	EPA, 1986 (as quoted in US ATSDR, 1995).
Rat Fischer 344	Short-term/acute toxicity 10 day repeat dose	Reductions in spleen and thymus weights, numbers of neutrophils, and natural killer cell activity, secondary to generalized toxicity	10 mg/kg bw/day (LOAEL) 5 mg/kg bw/day	EPA, 1986; Smialowicz *et. al.*, 1985, (as quoted in US ATSDR, 1995).

[9] http://europa.eu.int/comm/environment/endocrine/strategy/substances_en.htm

Species	Study type	Effect	LOAEL/NOAEL (mg/kg bw/day)	Reference
	gavage study		(NOAEL)	
Rat Fischer 344	Short-term/acute toxicity 10 day repeat dose gavage study	Increased startle response	2.5 mg/kg bw/day (LOAEL) 1.25 mg/kg bw/day (NOAEL)	EPA, 1986c (as quoted in US ATSDR, 1995).
Rat (Sherman)	3 month feeding study	Focal necrosis in liver, enlargement of the adrenal gland, hyperplasia and hypertrophy of cortical cells, tremor, hyperactivity, exaggerated startle response	1.17 mg/kg bw/day (LOAEL)	Cannon and Kimbrough 1979 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat, Wistar	2 year feeding study	Renal effects (proteinuria and increased severity of glomerulosclerosis)	0.25 mg/kg bw/day. (LOAEL) 0.05 mg/kg bw/day (NOAEL)	Larson *et. al.*, 1979b (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat Sprague-Dawley	21 month gavage study	Histopathological changes in liver, reduction in follicular size and colloid content and increase in epithelial cell height in thyroid	0.07 mg/kg bw/day (LOAEL), in males	Chu *et. al.*, 1981(as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat, Wistar	3 month feeding study	Testicular atrophy	0.5 mg/kg bw/day. (LOAEL) 0.25 mg/kg bw/day (NOAEL)	Larson *et. al.* , 1979b (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat (Osborne-Mendel) and mouse (B3C6F1)	80 week feeding study	Hepatocellular adenoma and carcinoma	1.2 mg/kg bw/day. (LOAEL, rat) and 2.6 mg/kg bw/day (LOAEL, mouse)	NCI, 1976, Reuber, 1978, 1979(as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat	Multiple injections of Chlordecone to neonatal rats	Uterotrophic response - uterine weights increased in a dose-related manner	10 mg/kg bw/day (LOAEL, Gellert, 1978) $\leq$ 6 mg/kg bw/day (LOAEL, Hammond *et. al.*, 1979)	Gellert 1978; Hammond *et. al.*, 1979 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat, Hotzman strain, ovarectomized immature females	Rats injected x 3 with 0 - 45 mg/kg bw/day Chlordecone $\pm$ 0.01, 0.1, 1 or 10 mg/kg bw/day estradiol benzoate	Uterotrophic response. Effect was additive to that of estradiol benzoate over the dose range studied	Dose of 20 mg/kg bw/day Chlordecone appeared to be threshold for embryo implantation functions	Johnson, 1996
Rat	90-day feeding study	Decrease in sperm motility and viability, decreased sperm, decrease in the weight of seminal vesicles and prostate	0.83 mg/kg bw/day LOAEL for sperm effects 1.67 mg/kg bw/day LOAEL for effects on seminal vesicles and prostate	Linder *et. al.*, 1983 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Mouse, Balbc	130 day feeding study	8% decrease in litter size and 19% increase in pair-days to litter (constant oestrus)	1.3 mg/kg bw/day. (LOAEL)	Huber, 1965 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rats and mice	2, 6, and 10 mg/kg bw/day by gavage to rats and 2, 4, 8, and 12 mg/kg bw/day to mice on days 7 - 16 of gestation.	Reduced foetal weight, reduced degree of ossification, oedema, undescended testes, enlarged renal pelvis, and enlarged cerebral ventricles. Reductions in fetal weight and degree of ossification at lower dose levels. Maternal mortality at top dose. In the mouse, fetotoxicity was observed only at the highest dose level and consisted of increased fetal mortality and clubfoot.	2 mg/kg bw/day. (LOAEL, rat)	Chernoff & Rogers, 1976). (as quoted in IPCS, 1984 and US ATSDR, 1995).
Balbc mice	160 day feeding study	Increased ovulation, persistent oestrus	2 mg/kg bw/day. (LOAEL)	Swartz *et. al.*, 1988 (as quoted in IPCS, 1984 and US ATSDR, 1995).
Rat	Reproductive toxicity	Increased ovulation, persistent oestrus in female offspring of maternal rats given Chlordecone on gestation days 14-20	15 mg/kg/day (LOAEL)	Gellert and Wilson, 1979, as quoted in US ATSDR, 1995)

Species	Study type	Effect	LOAEL/NOAEL (mg/kg bw/day)	Reference
Humans	Occupational exposure	Histories of tremors, unfounded nervousness or anxiety, and visual difficulties. Also skin rashes	Mean blood levels of Chlordecone in workers reporting adverse effects were 2.53 ppm Skin rashes reported in workers with blood Chlordecone levels in excess of 2 µg/L	Cannon *et. al.*, 1978 (as quoted in IPCS, 1984 and US ATSDR, 1995).

2.4.2 Ecotoxicity

A summary of results of aquatic ecotoxicity tests with Chlordecone from the Ecotox database (US EPA, 2006) is given in Table 2.4.

In addition to this, the EHC 43 (IPCS, 1984), summarised a series of experiments investigating the bioavailability of Chlordecone, noting that it is strongly adsorbed on sediment. Exposure of aquatic organisms is therefore partly *via* the water phase and partly *via* sediment. D'Asaro & Wilkes (1982) examined the effects of sediments previously exposed to Chlordecone at a known concentration, and of James River sediments contaminated with Chlordecone, on an estuarine community established in aquaria supplied with non-filtered sea water. Mysid shrimps showed a dose-related mortality rate, when exposed to sediments previously equilibrated at 0.1, 1.0, or 10 µg Chlordecone/L. Mysids were not affected by James River sediment. Put concentration in sediments, if available Oysters showed dose-dependent reduced shell growth when exposed to Chlordecone-equilibrated sediments, and also responded adversely to river sediment. Lugworms *Arenicola cristata* died after 28 days of treatment with sediment exposed to 10 µg Chlordecone/L, though numbers were not affected by lower doses. Both lugworms and oysters concentrated Chlordecone from the sediment. (Quoted from EHC 43, (IPCS, 1984)).

Table 2.4 Summary of key ecotoxicological studies on Chlordecone.

Taxonomic group and species	End point	Duration	Result mg/L	Reference [1]
Algae *Chlorococcum sp., Dunaliella tertiolecta, Nitzschia sp., Thalassiosira pseudonana*	EC_{50} growth inhibition	7 days	0.35 - 0.60 (formulation)	Walsh *et. al.*, 1977
Algae *Chlorococcum sp., Dunaliella tertiolecta, Nitzschia sp., Thalassiosira pseudonana*	EC_{50} growth inhibition	7 days	350 – 600 (formulation)	Hansen *et. al.*, 1977
Crustaceans *Daphnia magna*	EC_{50} immobility	48 hours	0.120 - 0.690	Barera & Adams, 1983; Adams & Heidolph, 1985; Ziegenfuss *et. al.*, 1986
Crustaceans *Americamysis bahia, Callinectes sapidus, Palaemonetes pugio*	LC_{50}	96 hours	0.01 - 0.210	Nimmo *et. al.*, 1977, 1981; Hansen *et. al.*, 1977; Schimmel, 1977; US EPA, 1976
Crustacean *Daphnia magna*	NOEC reproduction	21 days	0.0283	McKee & Knowles, 1986
Crustacean *Daphnia magna*	NOEC growth	21 days	0.025	Adams & Heidolph, 1985
Crustacean *Americamysis bahia*	MATC growth	28 days	0.000026 - 0.00034	Nimmo *et. al.*, 1981
Insect *Chironomus tentans*	LC_{50}	48 hours	0.17 - 2.3	Adams *et. al.*, 1985; Ziegenfuss *et. al.,* 1986
Fish 9 species	LC_{50}	96 hours, flow through	0.0066 - 0.512	Roberts & Bendl, 1982; Roberts & Fisher, 1985; Schimmel, 1977; Hansen *et. al.*, 1977; Mallat & Barron, 1988; Buckler *et. al.*, 1981
Insect *Chironomus tentans*	NOEC development	14 days	17.9 mg/kg sediment	Adams *et. al.*, 1985

1: All are as quoted in Ecotox, US EPA 2006

In a publication from SETAC a collation of critical tissue residues (CTR) was presented and evaluated (Jarvinen *et. al.*, 1999). The database contains 32 entries for Chlordecone, with data originating from different studies (see Table 2.5). Some of the tissue residues were from studies where no effects were observed, so they may not represent the real CTR. Critical tissue residue values obtained in studies where effects were identified represent 15 CTR values for three fish species. For fathead minnow two studies are available with values of 1.7 and of 3.8-5.4 mg/kg ww. For sheepshead minnow 12 CTRs are available, ranging from 0.13 to 17 mg/kg ww with an average of 5.9 mg/kg ww. Furthermore, one CTR of 2.7 mg/kg ww for spot is available.

Conclusion

In summary, Chlordecone is very toxic to aquatic organisms. The most sensitive group is the invertebrates, which is not surprising for a substance with insecticidal properties. Even if the lowest effect concentration (0.000026 mg/L) was considered to be an outlier, the lowest effect concentrations would be well below 1 mg/L with the results of short term tests (mortality) in the range of 0.01 to 0.69 mg/L and those of long term tests (reproduction and growth) at 0.0025 and 0.0028 mg/L.

Table 2.5 Collation of critical tissue residues (CTR)

Species	Life Stage	Exprte	Expo of Concentration	Results □g/g (wet) _)	effect
Cladoceran, Daphnia magna (Fw)	1st instar	Water	175 ng/L	0.133	Survival, Reproduction - No effect
Grass shrimp, Palaemonetes pugio (Sw)	0.09g	Water; Diet	0.04 µg/L; 0.118 µg/g (wet wt)	0.147	Growth - No effect
Blue crab, Callinectes sapidus (Sw)	Juvenile	Diet	2.26 - 2.50 µg/g (wet wt)	2.54 - 4.61	Survival, Growth - No effect
Fathead minnow, Pimephales promelas (Fw)	Larvae-Adult	Water	3.1 µg/L	3.8 - 5.4	Survival, Growth - Reduced
Fathead minnow, Pimephales promelas (Fw)	Larvae-Adult	Water	1.2 µg/L	2.6	Survival, Growth - No effect
Fathead minnow, Pimephales promelas (Fw)	Embryo, 2nd generation	Water; Adult fish	0.31 µg/L; 0.21-0.38 µg/g	1.7	Survival (hatchability) - Reduced
Fathead minnow, Pimephales promelas (Fw)	Embryo, 2nd generation	Water; Adult fish	0.17 µg/L; 0.17-0.46 µg/g	0.26	Survival - No effect
Fathead minnow, Pimephales promelas (Fw)	Larvae, 2nd generation	Water; Adult fish	0.31 µg/L; 0.21- 0.38 µg/g	0.50	Survival, Growth - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Adult	Water	0.8 µg/L	2.5 - 3.6	Survival - Reduced 22%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Adult	Water	1.9 µg/L	11 - 12	Survival - Reduced 80%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Adult	Water	7.8 µg/L	17	Survival - Reduced 100%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Adult	Water	0.16 µg/L	0.65 - 0.90	Survival - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo	Adult fish	11-12 µg/g	11	Survival - Reduced 25%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo	Adult fish	2.5 - 3.6 µg/g	4.7	Survival - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Larvae-Juvenile	Water; Adult fish	1.9 µg/L; 11-12 µg/g	8.4	Survival - Reduced 63%
Sheepshead minnow, Cyprinodon variegatus (Sw)	Larvae-Juvenile	Water	2.0 µg/L	7.8	Survival - Reduced 40%

Species	Life Stage	Exprte	Expo of Concentration	Results □g/g (wet)_)	effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Larvae-Juvenile	Water	0.8 µg/L	2.0	Survival - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Larvae-Juvenile	Adult fish	11-12 µg/g	0.13	Growth - Reduced
Sheepshead minnow, Cyprinodon variegatus (Sw)	Larvae-Juvenile	Water	0.08 µg/L	1.1	Growth – Reduced
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo-Adult	Water	0.78 µg/L	5, 6.8*	Survival - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo-Adult	Water	0.39 µg/L	2.2, 3*	Growth – Reduced
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo-Adult	Water	0.12 µg/L	0.86, 1.2*	Growth - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo-Adult	Water	0.78 µg/L	5, 6.8*	Reproduction – Reduced
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo-Adult	Water	0.39 µg/L	2.2, 3*	Reproduction - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo, 2nd generation	Adult Fish + Water	0.78 µg/L	2.3	Survival – Reduced
Sheepshead minnow, Cyprinodon variegatus (Sw)	Embryo, 2nd generation	Adult Fish + Water	0.39 µg/L	1.3	Survival - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Fry, 2nd generation	Adult Fish + Water	0.78 µg/L	2.3	Survival - No effect
Sheepshead minnow, Cyprinodon variegatus (Sw)	Fry, 2nd generation	Adult Fish + Water	0.12 µg/L	0.41	Growth – Reduced
Sheepshead minnow, Cyprinodon variegatus (Sw)	Fry, 2nd generation	Adult Fish + Water	0.074 µg/L	0.30	Growth - No effect
Spot, Leiostomus xanthurus (Sw)	Juvenile	Diet	3.3 µg/g (wet wt)	2.7	Survival – Reduced
Spot, Leiostomus xanthurus (Sw)	Juvenile	Diet	3.3 µg/g (wet wt)	0.7	Survival - No effect
Spot, Leiostomus xanthurus (Sw)	Juvenile	Water; Diet	0.04 µg/L; 0.101 µg/g (wet wt)	0.144	Growth, No effect

3 Synthesis of the information

Chlordecone is a synthetic chlorinated organic compound, which has mainly been used as an agricultural pesticide. It is closely related chemically to Mirex, a pesticide which is already listed in Annex A of the Stockholm Convention. Chlordecone is already listed in Annex I of the UNECE Protocol on POPs.

According to available data, Chlordecone can be considered to be highly persistent in the environment. Chlordecone is not expected to hydrolyse or biodegrade in aquatic environments, nor in soil. Direct photodegradation is not significant. Chlordecone does not volatilise to any significant extent.

With BCF-values in algae up to 6,000, in invertebrates up to 21,600 and in fish up to 60,200 and documented examples of biomagnification, Chlordecone is considered to have a high potential for bioaccumulation and biomagnification.

Concerning the potential for causing adverse effects, there is a convincing set of data. Chlordecone is readily absorbed into the body and accumulates following prolonged exposure. It is both acutely and chronically toxic, producing neurotoxicity, immunotoxicity, reproductive, musculoskeletal and liver toxicity at doses between 1 - 10 mg/kg bw/day in experimental animal studies. Liver cancer was induced in rats at a dose of 1 mg/kg body weight per day, and reproductive effects are seen at similar dose levels. The International Agency for Research on Cancer has classified Chlordecone as a possible human carcinogen (IARC group 2B). Moreover, Chlordecone is very toxic to aquatic organisms, most sensitive group being the invertebrates.

The available data on Chlordecone are not fully conclusive when it comes to long-range atmospheric transport in gaseous form. It should be noted that atmospheric transport of particle-bound substances and transport of sediment particles in ocean currents as well as biotic transport could also contribute to long-range environmental transport of Chlordecone.

Due to lack of monitoring data on Chlordecone, the assessment of the potential for long-range transport of Chlordecone is based on physico-chemical properties and especially, on modelling data. While the first of these two approaches may seem somehow insufficient, the modelling data state clearly Chlordecone's LRET potential.

Based on the available data, Chlordecone should be considered as a POP warranting global action.

Production and use of Chlordecone has ceased over the last decades in developed countries, but it is assumed that it can still be produced or used as an agricultural pesticide in some developing countries. If it is still used as pesticide, it will be directly released to the environment. Moreover, the high persistency of the substance has caused high contamination of soil and waters in the areas where it has been used and these contaminated sites can serve as a source of pollution for long times.

4 Concluding statement

It has been demonstrated that Chlordecone meets all the criteria laid down in Annex D of the Stockholm Convention. Moreover, it is chemically very similar to Mirex, an organochlorine pesticide which is already listed in the Stockholm Convention. It is very persistent in the environment and has a great potential for bioaccumulation and in addition there is clear evidence of its biomagnification. While there is no monitoring data from areas remote from sources, the physical and chemical properties, as well as the modelling results, suggest that Chlordecone can be transported long distances bound to particles in air and water, and possibly through coupled transport between these two compartments. Chlordecone is associated with a wide range of harmful effects on both mammals and aquatic organisms.

As Chlordecone can travel in the atmosphere far from its sources, neither a single country nor group of countries alone can abate the pollution caused by this substance. Regional action has already been considered necessary and Chlordecone is totally banned under the UNECE Convention on Long-range Transboundary Air Pollution Protocol on Persistent Organic Pollutants. Although the production and use of Chlordecone seems to be ceased in most countries, its reintroduction remains possible. This could lead to increased releases and levels in the environment.

Based on the available evidence, Chlordecone is likely as a result of its long-range environmental transport to lead to significant adverse human health and environmental effects such that global action is warranted.

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別添7

ヘキサブロモビフェニルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 分解度 4%（OECD TG 301C） 【光分解性】 大気中における分解及び変化は、OH ﾗｼﾞｶﾙによる光酸化と光分解である。OH ﾗｼﾞｶﾙとの反応による推定半減期は 182 日。 【半減期】 ・水中：2 ヵ月を超える ・土壌及び底質中：6 ヶ月を超える	【BCF（経鰓的生物濃縮係数）】 ・ﾌｧｯﾄﾍｯﾄﾞﾐﾉｰ：BCF=18100（32 日間暴露） ・ﾌｧｯﾄﾍｯﾄﾞﾐﾉｰの身：BCF=10000 ・ｺｲ：BCF=4700-16000（重量ﾍﾞｰｽ。60 日間暴露） 【BMF（経口的生物濃縮係数）】 ・餌（ﾆｼﾝ）と捕食者（ﾊﾞﾙﾄｱｻﾞﾗｼ）を較べた食物連鎖：BMF=175（脂質ﾍﾞｰｽ）（PCB と同ﾚﾍﾞﾙの値） ・ﾎｯｷｮｸｸﾞﾏ中の濃度がｸﾞﾘｰﾝﾗﾝﾄﾞ東部のﾜﾓﾝｱｻﾞﾗｼの約 100 倍	【反復投与毒性】 ラット（混餌 7 ヶ月）：0.45mg/kg/day で血清中 T4 濃度低下 ラット（混餌 30 日）：LOAEL 0.05mg/kg/day 甲状腺ろ胞数・ろ胞容積増加、血清中 T3、T4 濃度低下 アカゲザル（混餌 25～50 週）：LOAEL 0.73mg/kg/day 主な毒性は、体重低下、潰瘍性大腸炎、脱毛、肝臓の変化等 【発がん性】 マウス（妊娠 0 日～生後 56 日）：NOAEL 0.15mg/kg/day 児の肝細胞腺がん及び上皮がん IARC グループ2 B（possibly carcinogenic to human） 【生殖毒性】 ラット（妊娠 0 日～14 日） 28.6mg/kg/day で未着床、新生児生存率低値 アカゲザル：LOAEL 0.012mg/kg/day 主な毒性は、月経周期遅延、流産、死産等	【慢性毒性】 ニジマス *Oncorhynchus mykiss* ：ELS 試験 LD50=3.910 mg/kg

		【その他】 汚染事故で吐き気、腹痛、食欲減退、関節痛、倦怠感、皮膚障害、 EU-Strategy for Endocrine Disruptors 優先化学物質（無処置動物の少なくとも一種類において内分泌かく乱活性を示す科学的根拠がある）に分類	

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Persistent Organic Pollutants Review Committee
Second meeting
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Report of the Persistent Organic Pollutants Review Committee on the work of its second meeting

Addendum

Risk profile on hexabromobiphenyl

At its second meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on hexabromobiphenyl, on the basis of the draft contained in document UNEP/POPS/POPRC.2/9. The text of the risk profile, as amended, is provided below. It has not been formally edited.

K0653891 151206

HEXABROMOBIPHENYL

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its second meeting

November 2006

CONTENTS

EXECUTIVE SUMMARY

The European Community and its Member States being Parties to the Stockholm Convention have proposed hexabromobiphenyl to be listed in the Convention. The Persistent Organic Pollutants Review Committee concluded in its meeting in November 2005 that the substance comply with the screening criteria set out in Annex D of the Convention and that a draft risk profile should be prepared to review the proposal further.

Hexabromobiphenyl belongs to a wider group of polybrominated biphenyls (PBBs). The term "polybrominated biphenyls" or "polybromobiphenyls" refers to a group of brominated hydrocarbons formed by substituting hydrogen with bromine in biphenyl. The hexabromo congeners exist as 42 possible isomeric forms. According to the available data, production and use of hexabromobiphenyl has ceased in most, if not all, countries. However, it is possible that hexabromobiphenyl is still being produced in some countries.

Hexabromobiphenyl has been used as a fire retardant in acrylonitrile-butadiene-styrene (ABS) thermoplastics for constructing business, machine housings and in industrial and electrical products and in polyurethane foam for auto upholstery. A considerable part of the substance produced will probably reach the environment sooner or later because of the high stability of these compounds.

According to available data, hexabromobiphenyl can be considered to be highly persistent in the environment. There is evidence of low or no degradation in water, soil and sediment, in the laboratory as well as in the field.

Hexabromobiphenyl is less volatile than many of the currently listed POP substances. However, extensive data on monitoring shows that it is found throughout the Arctic wildlife, demonstrating that it does have a high potential for long range environmental transport.

With measured weight-based BCF values in the range 4,700-18,100 and biomagnification factors in the aquatic food chain exceeding 100, hexabromobiphenyl is considered to be highly bioaccumulative and to have a high potential for biomagnification. These properties are demonstrated by several authors to be comparable to those of hexachlorobiphenyl (a PCB compound), for which the bioaccumulative properties are well documented.

Hexabromobiphenyl is readily absorbed into the body and accumulates following prolonged exposure. Although the acute toxicity of hexabromobiphenyl is low, a number of chronic toxic effects including hepatotoxicity have been observed in experimental animals at doses around 1 mg/kg bw/day following long-term exposure, and effects are seen in the rat thyroid at doses as low as 0.05 mg/kg bw/day. The International Agency for Research on Cancer has classified hexabromobiphenyl as a possible human carcinogen (IARC group 2B). The PBBs are endocrine disrupting chemicals, and effects are seen on reproductive capacity in rats, mink and monkeys. There is epidemiological evidence of hypothyroidism in workers exposed to polybrominated biphenyls and of increased incidence of breast cancer in exposed women. Data on toxicity to other species than laboratory mammals is scarce but suggests the environmental toxicity of hexabromobiphenyl is comparable to that of hexachlorobiphenyl.

Based on the available data, hexabromobiphenyl is likely, as result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

1 INTRODUCTION

The European Community and its Member States being Parties to the Stockholm Convention have proposed hexabromobiphenyl to be listed in Annex A to the Convention. The original proposal is contained in document UNEP/POPS/POPRC.1/7.

The acceptance of the original proposal for further consideration by the Persistent Organic Pollutants Review Committee implies that the properties of the substance comply with the screening criteria set out in Annex D of the Convention. Therefore, the screening criteria are not discussed in this document. This draft risk profile has been prepared following the decision of the Committee, at its first meeting in November 2005, to establish an ad hoc working group to review the proposal further.

In this document all data are presented according to the International System of Units (SI) and, therefore, many have been recalculated from other units in the data sources. Furthermore, all concentrations are presented based on kg or L (*e. g.* µg/kg or mL/L).

1.1 Chemical Identity of the proposed substance

1.1.1 Names and registry numbers

Hexabromobiphenyl belongs to a wider group of polybrominated biphenyls (PBBs). The term "polybrominated biphenyls" or "polybromobiphenyls" refers to a group of brominated hydrocarbons formed by substituting hydrogen with bromine in biphenyl. The hexabromo congeners exist as 42 possible isomeric forms, which are listed with CAS and IUPAC numbers in US ATSDR (2004) and in document INF 2.

CAS chemical name:	Hexabromo -1,1'-biphenyl
Synonyms:	Hexabromobiphenyl Biphenyl, hexabromo 1,1'- biphenyl, hexabromo - HBB
Trade names:	FireMaster(R) BP-6 FireMaster(R) FF-1

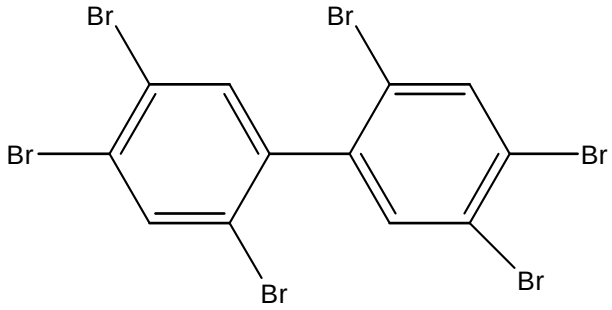
Technical grade PBBs (FireMaster(R)) contain several PBB compounds, isomers and congeners, hexabromobiphenyl being one of the main components. The composition of FireMaster(R) BP-6 changes from batch to batch, but its main constituents are 2,2',4,4',5,5'-hexabromobiphenyl (60-80%), and 2,2',3,4,4',5,5'-heptabromobiphenyl (12-25%) together with lower brominated compounds. Mixed bromochlorobiphenyls and polybrominated naphthalenes have also been observed as minor components of FireMaster(R) (EHC 152 (IPCS, 1994)). FireMaster FF-1 (white powder) is FireMaster BP-6 (brown flakes) to which 2% calcium silicate has been added as an anti-caking agent (EHC 152 (IPCS, 1994)).

Additional data on the composition of identified PBB congeners in FireMaster(R) BP-6 and FireMaster(R) FF-1 is given in US ATSDR (2004).

CAS registry number: 36355-01-8[1] (Common CAS number for hexabromobiphenyl isomers)
59536-65-1 (EHC 192 (IPCS, 1997))[2]
67774-32-7 (EHC 192 (IPCS, 1997))[3]

US ATSDR (2004) provides CAS numbers for a wider number of individual hexabromobiphenyl isomers, as shown in Annex B.

1.1.2 Structure



Structure of 2,2',4,4',5,5'- hexabromobiphenyl (CAS No. 59080-40-9, PBB congener No. 153). (Structural formula source: EHC 192 (IPCS, 1997))

1.1.3 Physical chemical properties

The physical and chemical properties of hexabromobiphenyl are listed in Table 1.1.

Table 1.1 Physical and chemical properties of hexabromobiphenyl.

Property	Unit	Value	Reference
Molecular formula'		$C_{12}H_4Br_6$	
Molecular weight'	g/mol	627.58	
Appearance at normal temperature and pressure		White solid	a)
Vapour Pressure	Pa	$6.9x10^{-6}$ (25° C) $7.5x10^{-4}$ (liquid, sub-cooled)	Jacobs *et. al*., (1976)[a)] Tittlemier *et. al.,* (2002)[a)]
Water solubility	µg/L	11 3	a) Tittlemier *et. al.,* (2002)[a)]
Melting point	°C	72° C	a)
Boiling point		No data	
Log K_{OW}		6.39	Doucette & Andren (1988)[a)]
Log K_{oc}		3.33-3.87	Calculated[a)]
Henry's Law Constant	Pa m^3/mol	$3.95x10^{-1}$ $1.40x10^{-1}$	Waritz *et. al*., 1977[a)] Calculated[a)]

a): Quoted from US ATSDR, 2004

[1] The CAS registry number 36355-01-8 is given as a generic CAS number for PBBs in the 1988 EU Export-Import Regulation and the UNEP Rotterdam Convention.
[2] US ATSDR refers to Firemaster (R) BP-6 as CAS No. 59536-65-1.
[3] US ATSDR refers to FireMaster(R) FF-1as CAS No. 67774-32-7.

Some of the data for the properties listed in Table 1.1 may not be reliable because products of questionable purity were used by earlier investigators to derive them. Therefore, recent physical and chemical property data that have been reported for hexabromobiphenyl in Tittlemier *et. al*., (2002) (Quoted from US ATSDR, 2004) are included in Table 1.1.

1.2 Conclusion of the Persistent Organic Pollutants Review Committee on the Annex D information on Hexabromobiphenyl

The POP Review Committee applied at its first meeting on 7–11 November 2005[4] the screening criteria specified in Annex D to the Stockholm Convention, and decided, in accordance with paragraph 4 (a) of Article 8 of the Convention, that it was satisfied that the screening criteria were fulfilled for hexabromobiphenyl. The Committee decided furthermore, in accordance with paragraph 6 of Article 8 of the Convention and paragraph 29 of decision SC-1/7 of the Conference of the Parties to the Stockholm Convention, to establish an ad hoc working group to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention. It invited, in accordance with paragraph 4 (a) of Article 8 of the Convention, Parties and observers to submit to the Secretariat the information specified in Annex E of the Convention before 27 January 2006.

1.3 Data sources

This Draft Risk Profile is mainly based on information from the following review reports:

- Environmental Health Criteria (EHC) 152: Polybrominated biphenyls. IPCS International Programme on Chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1994. Available at: http://www.inchem.org/documents/ehc/ehc/ehc152.htm.
- Environmental Health Criteria (EHC) 192: Flame Retardants: A General Introduction. IPCS International Programme on Chemical Safety. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva 1994. Available at: http://www.inchem.org/documents/ehc/ehc/ehc192.htm.
- US ATSDR Toxicological Profile for Polybrominated Biphenyls and Polybrominated Diphenyl Ethers (PBBs and PBDEs). 2004. Available at: http://www.atsdr.cdc.gov/toxprofiles/tp68.html

Where the reviews mentioned above have been cited, the text quoted (or quoted with modifications) includes the references cited in the original review. These references are not shown individually in the reference list.

Following the request of the POP Review Committee for additional information, as specified in Annex E of the Convention, information on hexabromobiphenyl was provided by several Parties and observers. This information was mainly based on the open literature or focused on PBDEs.

A search for more recent information included a literature search via the Danish Technical University Library and the data base FINDit (search terms: HBB, hexabromobiphenyl, brominated biphenyls) as well as a data base search in public data bases. The data bases include "Ecotox" (US-EPA, at http://www.epa.gov/ecotox/, "NITE" (Japan, National Institute of Technology and Evaluation at http://www.safe.nite.go.jp/english/db.html, BUA Reports at http://www.gdch.de/taetigkeiten/bua/berichte.htm and Environmental Fate Data Base at http://esc.syrres.com/efdb.htm. This search was based on the search terms: hexabromobiphenyl and CAS numbers 77607091, 36355018, 82865892, 82865905, 59261084, 84303479, 120991482,

[4] See the meeting report at: www.pops.int/documents/meetings/poprc

82865916, 67888997, 84303480, and 60044260. In addition, the Arctic Monitoring and Assessment Programme[5] was consulted.

1.4 Status of the chemical under international conventions

Hexabromobiphenyl is listed in Annex A of the Protocol to the Convention on Long-range Transboundary Air Pollution (CLRTAP) on Persistent Organic Pollutants. The provisions of the Protocol oblige Parties (currently 25) to phase out all production and uses of hexabromobiphenyl. Hexabromobiphenyl, together with other PBBs, is also included in the UNEP/FAO Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade.

2 SUMMARY INFORMATION RELEVANT FOR THE RISK PROFILE

2.1 Sources

2.1.1 Production

The commercial production of polybrominated biphenyls (PBBs) generally involves bromination of biphenyl, a process involving a much more specific reaction and producing a smaller number of product mixtures than chlorination (Sundstrom *et. al*., 1976a) (Quoted from US ATSDR, 2004).

The process of manufacturing PBBs consists of a Friedel-Crafts type reaction in which biphenyl is reacted with bromine in the presence of chloride in an organic solvent, using aluminium chloride, aluminium bromide, or iron as catalyst (Brinkman & de Kok, 1980) (Quoted from EHC 152 (IPCS, 1994)).

2.1.2 Trade and stockpiles

The commercial production of PBBs began in 1970. Approximately 6 million kg of PBBs were produced in the United States from 1970 to 1976. Only three commercial PBB products were manufactured (*i. e.* hexabromobiphenyl, octabromobiphenyl, and hexabromobiphenyl) and these three products were based on a limited number of congeners (Hardy, 2002b). Hexabromobiphenyl constituted about 5.4 million kg (ca 88%) and octa- and decabromobiphenyl constituted ≈ 0.68 million kg together of this total (Neufeld *et. al*., 1977). Michigan Chemical Corporation, St. Louis, Michigan, the sole producer of hexabromobiphenyl in the United States, stopped producing this PBB in 1975. (Quoted from US ATSDR, 2004). Subsequent production of PBBs appears to have been limited to the octa- and decabromobiphenyls.

Production of octa- and decabromobiphenyl continued in the United States until 1979 (IARC 1986; Neufeld *et. al*., 1977). Shortly after the 1973–1974 agriculture contamination accident in Michigan, PBB production in the United States was voluntarily discontinued (Hardy 2000); PBBs are no longer produced in the United States (SRI 2001). Re-initiation of manufacture of PBBs would require approval from the EPA. (Quoted from US ATSDR, 2004)

Two UK companies are reported to have marketed or produced technical-grade decabromobiphenyl in the United Kingdom. In 1977, the production of PBBs in the UK was discontinued. Highly brominated PBBs (Bromkal, 80-9D) were produced in Germany until mid-1985, when the activities concerning bromine-based fire retardants were shifted to the USA. No domestic producer has been identified in the Netherlands. In the early nineties, an Israeli company with two bromine plants in the Netherlands denied the production of PBBs. (Modified from EHC 152 (IPCS, 1994)). There is no information available regarding possible use and production of hexabromobiphenyl in Russia.

[5] See http://www.amap.no/

Until the year 2000, the only PBB in commercial production was decabromobiphenyl, which was manufactured by one company (Atochem) in France (Hardy, 2000). (Modified from US ATSDR, 2004) An author (Darnerud, 2003) has stated that with the closure of the decaBB production in France, the PBB production in the world has ceased.

In the United States, PBBs are not known to be imported or exported anymore except possibly in small quantities for laboratory uses. PBBs have not been imported from other countries into the United States, except in finished products (Neufeld *et. al*., 1977). The two companies that manufactured octa- and decabromobiphenyl in the United States between 1976 (0.805 million pounds) and 1978 exported all of their products to Europe (Neufeld *et. al*., 1977) (Quoted from US ATSDR, 2004) .

EXIDIM, the European Database on the Export Import of Dangerous Chemicals under the Rotterdam Convention has registered a total of 6 export applications for PBBs (which do not however include hexabromobiphenyl) in the years 2003–2006 (1 in 2003 and 2004, 2 each in 2005 and 2006). No imports of PBBs to the European Unions are registered in this period.

Information received by 27 January 2006 as a result of the request for information from Stockholm Convention Parties and observers, included response from Brazil, Australia, Japan, Republic of Lebanon and the USA, all stating that there is no production or use of hexabromobiphenyl in these countries.

In summary, according to the information available, production and use of hexabromobiphenyl has ceased in most, if not all, countries. However, it is possible that hexabromobiphenyl is still being produced in some developing countries or in countries with economies in transition.

2.1.3 Uses

In the United States and Canada, hexabromobiphenyl (FireMaster$^{(R)}$) was the principal PBB product. It was used as a fire retardant in three main commercial products: acrylonitrile-butadiene-styrene (ABS) thermoplastics for constructing business machine housings and in industrial (e.g. motor housing), and electrical (*e. g.* radio and TV parts) products: as a fire retardant in coatings and lacquers, and in polyurethane foam for auto upholstery (Neufeld *et. al*., 1977) (Modified from EHC 152 (IPCS, 1994) and US ATSDR, 2004).

Approximately 5 million tonnes of HBB were produced in the USA from 1970 to 1976; 98 per cent was used as FireMaster BP-6 and the rest as FireMaster FF-1 (Hesse and Powers, 1978). Of the estimated 2,200 tonnes hexabromobiphenyl produced in 1974 (IARC, 1978), about 900 tonnes (Mumma & Wallace, 1975; Neufeld *et. al*., 1977; IARC, 1978) were used in ABS plastic products and an even larger amount in cable coatings (Mumma & Wallace, 1975; Neufeld *et. al*., 1977; IARC, 1978). The exact quantity of FireMaster$^{(R)}$ used in polyurethane foam for automobile upholstery was not published. The two larger consumers ceased using hexabromobiphenyl (one of these in 1972) because PBBs did not decompose in the ultimate incineration of scrapped automobiles (Neufeld *et. al*., 1977) (Quoted from EHC 152 (IPCS, 1994)).

In the EHC 152 (IPCS, 1994), it is stated that at the time, no users of hexabromobiphenyl had been identified (Neufeld *et. al*., 1977; Di Carlo *et. al*., 1978; Brinkman & de Kok, 1980) (Quoted from EHC 152 (IPCS, 1994)) .

2.1.4 Releases to the environment

Data for loss into the environment during normal production are published only for the United States. The following information refers to reviews by Neufeld *et al*., (1977) and Di Carlo *et al*. (1978). Losses of PBBs to the environment at sites of its manufacture can amount to 51 kg/1000 kg of product. These losses occur through:

1) *Emission into the air:*

   In 1977, the maximum air losses as particulate matter at production sites were estimated to total 1.1 kg of PBBs/1000 kg manufactured.

2) *Losses in waste waters* resulting from the quenching and washing of the PBBs as they were recovered from the reaction mass. The losses of PBBs to sewers at manufacturing sites were estimated, in 1977, to be 4.6 µg/kg of product.

3) *Solid losses to landfills* resulting from drying, handling, shipping and transportation. An estimate of PBB losses as solid waste to landfills was 50 g/kg of product.

4) *Losses to the soil*

   Soil samples from the bagging and loading areas of the Michigan Chemical Corp. contained PBBs at concentrations of 3500 and 2500 mg/kg, respectively.

(Abbreviated from EHC 152 (IPCS, 1994))

In 1973, an accidental release of PBBs occurred in Michigan (referred to as the "Michigan disaster" in EHC 152), when two products manufactured by the Michigan Chemical Company were inadvertently confused and 250-500 kg (Di Carlo *et. al*., 1978) of FireMaster(R), instead of NutriMaster(R), a magnesium oxide-based cattle feed supplement, were added to animal feed and distributed to farms within the state. The compound is believed to have been FireMaster(R) FF-1 (*e. g.*, Fries, 1985b), even if in some publications the name FireMaster(R) BP-6 is used (*e. g*., Neufeld *et. al*., 1977; Di Carlo *et. al*., 1978). This accidental mix up resulted in widespread contamination by PBBs. Chronological reports or reviews of the PBB disaster are given by Carter (1976), Getty *et. al*. (1977), Kay (1977), Di Carlo *et. al*., (1978), Damstra *et. al*., (1982), Zabik (1982), and Fries (1985b) (Quoted from EHC 152 (IPCS, 1994)) .

Approximately 5350 tonnes of hexabromobiphenyl were used in commercial and consumer products in the United States, most in the production of plastic products with an estimated use life of 5–10 years (Neufeld *et. al*., 1977). Since the cessation of production, all of these products, such as TV cabinet and business machine housings, are expected to have been disposed of by land filling or incineration (Neufeld *et al*., 1977) (Quoted from US ATSDR, 2004).

Hexabromobiphenyl can enter the environment from the widespread use of flame-retarded products. A considerable part of the substance produced will probably reach the environment sooner or later because of the high stability of these compounds. Furthermore, some of these chemicals may form toxic polybrominated dibenzofurans during combustion processes.

2.2 Environmental fate

2.2.1 Persistence

The EHC review (1994), concludes that polybrominated biphenyls are stable and persistent in the environment. The degradation of PBBs by purely abiotic chemical reactions (excluding photochemical reactions) is considered unlikely.

In air, the two processes that may result in significant degradation or transformation of PBBs are photo-oxidation by hydroxyl (OH) radicals and direct photolysis. Based on a structure-activity relationship for the estimation of half-lives for the gas phase reactions of hydroxyl radicals with organic compounds (Atkinson 1987b), the estimated half-life of hexabromobiphenyl due to reaction with OH radicals is 182 days. The importance of the photochemical reaction under sunlight illumination conditions for the degradation/transformation of PBBs in air cannot be evaluated due to the lack of information. (Abbreviated from US ATSDR, 2004)

The EHC 152 (IPCS, 1994) refers to laboratory experiments in methanol, showing rapid photodegradation of 2,2',4,4',5,5'-hexabromobiphenyl (90% degradation after 9 minutes) and resulting in mainly lower brominated PBBs. However, in the US ATSDR (2004), it is questioned whether this photolysis could take place in water due to the lack of active groups. Therefore it is questionable whether hexabromobiphenyl can be degraded rapidly in air.

Biodegradation in water under aerobic conditions is low, although the lower substituted biphenyls might biodegrade in aerobic water and sediment (Kong and Sayler, 1983; Sugiura, 1992; Yagi, and Sudo, 1980), the higher substituted biphenyls are resistant to aerobic biodegradation (Kawasaki, 1980; Sasaki, 1978; Shelton and Tiedje, 1981) (quoted from US ATSDR, 2004). This is further supported by the measurement (by GC) of negligible biodegradation of hexabromobiphenyl in a four week ready biodegradability test (OECD TG 301C), resulting in 4% reduction in total concentration as measured by GC (Governmental Japanese database NITE, 2006) resulting in an extrapolated half-life in water>2 months.

Under anaerobic conditions, it has been shown that microorganisms in river sediments obtained from populated areas can biodegrade higher substituted PBBs, including FireMaster mixtures (Morris *et al*. 1992) to form lower brominated products (quoted from US ATSDR, 2004). However, the potential of sediment microflora from remote areas has not been investigated, so it cannot be evaluated whether anaerobic debromination may be a considerable cause for degradation under anaerobic conditions.

PBBs have been reported to be persistent under field conditions. The information on the fate of PBBs in soil is limited. Soil samples from a former PBB manufacturing site, analysed several years after accidental release, still contained PBBs. However, the congener composition differed from the original PBB mixture, indicating partial degradation of the PBB residue in the soil samples. According to the 1994 EHC Review, follow-up surveys over a three-year period following the termination of PBB production showed no significant decline in PBB levels in sediments from a river. In laboratory investigations, mixtures of PBBs appear to be fairly resistant to microbial degradation. (Quoted from EHC 152 (IPCS, 1994)) This implies that the degradation half-life in soil and sediment is>6 months.

The US ATSDR (2004), refers to studies in soils with high levels of FireMaster, in which degradation of hexabromobiphenyl was “significant” during a period of several years but it was not complete. However in other soils, in which the concentrations were lower, or to which manure was added, degradation was even slower. The degradation was attributed to photodegradation even if this process will only take place at the soil surface (US ATSDR, 2004).

Conclusion

In spite of photodegradation in methanol, it is questionable whether hexabromobiphenyl can be degraded rapidly in air. There is evidence of low or no degradation in water (DT_{50}>2 months), soil and sediment (DT_{50}>6 months) in the laboratory as well as in the field. Therefore, hexabromobiphenyl is considered to be highly persistent.

2.2.2 Bioaccumulation

The EHC review states that PBBs are lipophilic and able to bioaccumulate. This is also supported by monitoring results from wildlife studies. For example, fathead minnows (*Pimephales promelas*) caged in a river where water levels of PBB remained consistently at less than 0.1 µg/l concentrated these contaminants in their bodies more than 10,000 fold in two weeks of exposure (EHC 152 (IPCS, 1994)).

As expected from their lipophilicity, PBBs show a marked tendency to accumulate in animals. US ATSDR, (2004), states that PBBs may also be transported from water to aquatic organisms in which bioconcentration may take place. Data from different laboratories on the bioconcentration of

PBBs in fish show wide variation. The experimentally determined bioconcentration factor (BCF) for hexabromobiphenyl (mixtures of unspecified congeners) in the whole body of fathead minnows (*Pimephales promelas*) was 18,100 in a 32-day exposure (Veith *et. al*., 1979). In fillet of fathead minnow, the estimated BCF was>10,000 (Hesse and Powers, 1978). Weight-based BCF values in the range 4,700-16,000 were recorded in a 60 day test with the carp *Cyprinus carpio* placed in concentrations of hexabromobiphenyl of 0.1-1 µg/L respectively (Governmental Japanese database NITE, 2006).

Furthermore, a potential for biomagnification has been demonstrated by Jansson *et. al*., (1993), who reported a biomagnification factor (BMF) for 2,2',4,4',5,5'-hexabromobiphenyl (PBB congener 153) of about 175 comparing lipid-based concentrations in prey (herring) and predator (Baltic seal). This BMF was at the same level as that of the PCB congener 153. These findings were supported by Vorkamp *et. al*., (2004)[6], who found lipid-based concentrations of hexabromobiphenyl (PBB 153) in polar bear to be a factor of about 100 higher than in ringed seal from East Greenland. They conclude further, that the PBBs (and PBDEs) seem to biomagnify along the marine food chain in a manner similar to PCBs and that PBBs show indications of a higher biomagnification potential than PBDEs (Vorkamp *et. al*., 2004).

Conclusion

With measured weight-based BCF values in the range 4,700-18,100 (most of which exceed 5,000) and demonstrated biomagnification in the aquatic food chain, hexabromobiphenyl is considered to be highly bioaccumulative and to have a high potential for biomagnification. These properties are demonstrated by several authors to be comparable to those of hexachlorobiphenyl, for which the bioaccumulative properties are well documented. Evidence appears to be satisfactory to conclude high bioaccumulation and biomagnification.

2.2.3 Potential for Long Range Environmental Transport

The partitioning of hexabromobiphenyl in the environment will be governed by its high log K_{ow} (6.39) and low water solubility (3 µg/L) resulting in sorption to particulate matter (dust, soil and sediment) and organic material (including living organisms). Furthermore, the combination of these properties and the relatively low vapour pressure ($6.9x10^{-6}$ to $7.5x10^{-4}$ Pa) of hexabromobiphenyl, results in a low potential for volatilisation. The latter is specified in US ATSDR (2004) as follows: Based on an estimated Henry's law constant of $3.95x10^{-1}$ Pa m^3/mol (where Henry's law constant = vapor pressure/water solubility) and an estimation method (Thomas, 1990), the estimated volatilization half-life of hexabromobiphenyl is 23 days. Therefore, the transport of PBBs from water to the atmosphere by volatilization is not expected to be important.

The assessment of the potential for long-range transport of hexabromobiphenyl could be done by comparing the properties of hexabromobiphenyl to those of the currently listed POPs. As a starting point for the assessment of hexabromobiphenyl, the highest and lowest of the values in Table 1.1 were used (for vapour pressure, only the value at 25 °C) and, for comparison, the information on the UNEP-POPs homepage. Among the currently listed POPs, most of the relevant properties were available for aldrin, chlordane, dieldrin, DDT, hexachlorobenzene, mirex, toxaphene, endrin and heptachlor. Missing information (water solubility of mirex) was sought in US ATSDR (1995), so as not to introduce what seems to be an outlier in the comparison by using the value of $6.5x10^{-5}$ mg/L from AMAP (2004).

[6] These investigations are part of the Arctic Monitoring and Assessment Programme (AMAP).

The water solubility and vapour pressure as well as Henry's Law Constants calculated from these values of the currently listed POPs are summarised in Table 2.1 together with information on hexabromobiphenyl from Table 2.1.

Table 2.1 Water solubility (WS), vapour pressure (VP) and (calculated) Henry's Law Constant (HLC) (at 25 °C) for hexabromobiphenyl and currently listed POPs.

Substance	WS mg/L	VP Pa	HLC Pa m^3/mol
Hexabromobiphenyl-min	0.011	$6.9x10^{-6}$	0.39
Hexabromobiphenyl-max	0.003	$6.9x10^{-6}$	1.44
POP-min	0.0012 (DDT)	$2.5x10^{-5}$ (DDT)	0.04 (endrin)
POP-max	3.0 (toxaphene)	27 (toxaphene)	3726 (toxaphene)
POP-2^{nd} max	0.5 (dieldrin)	0.04 (heptachlor)	267 (heptachlor)

Table 2.1 shows that the water solubility of hexabromobiphenyl is at the level of the least water soluble among the currently listed POPs (DDT), while the vapour pressure of HBB is one order of magnitude lower than that of DDT. The two Henry's Law Constants calculated for hexabromobiphenyl are well inside the range marked by the currently listed POPs, being at least one order of magnitude higher than the lowest (endrin). It should be noted that in presenting the data in table 2.1 it is not inferred that a chemical (in this case hexabromobiphenyl) is considered to meet the long-range environmental transport criterion just because it fits within the range of values of currently listed POPs.

Based on the vapour pressure alone, the potential for long-range airborne transport of hexabromobiphenyl is low compared to most of the currently listed POPs, while a comparison of the Henry's Law Constants places hexabromopbiphenyl in a position close to endrin.

The EHC 152 (1994), argues that the vapour pressure of hexabromobiphenyl is $6.9x10^{-6}$ Pa and, thereby the potential for volatilisation is low. There is no information available about measured half-life of hexabromobiphenyl in the atmosphere. In the laboratory photodegradation of 2,2',4,4',5,5'-hexabromobiphenyl was rapid (90% degradation after 9 minutes) mainly resulting in lower brominated PBBs (EHC 152 (IPCS, 1994)). On the other hand, the rates and extent of photolytic reactions of PBBs in the environment have not been determined in detail. The few field observations available indicate a high persistence of the original PBBs or a partial degradation to less brominated, and often more toxic, photoproducts.

In support of the assessment of the potential for long-range environmental transport, monitoring data demonstrate that this substance has managed to reach remote areas like the Barents Sea and Greenland. In the Arctic, hexabromobiphenyl has been measured in samples of animals in several investigations. The results are summarised in Annex A, Table A.1.

In whitefish from Lapland (North Scandinavia) and ringed seal from Svalbard, concentrations of 0.29 and 0.42 µg/kg lipid, respectively, were reported by Jansson *et. al*., (1993). In another paper, Jansson *et. al*., (1987) reported concentrations of hexabromobiphenyl (Firemaster BP-6) in ringed seal from Svalbard to be 4 µg/kg lipid and concentrations in guillemot muscle of 50 µg/kg lipid. It is not clear whether these results are from different investigations. For comparison, Krüger (1988), measured 0.8 µg/kg of PBB 153 in unspecified seal samples from the same area (Quoted from US ATSDR, 2004).

In samples of large char collected in 1999-2001 from one of two lakes in Bear Island in the Barents Sea, Evenset *et. al*., (2005) measured concentrations of 4.11-51.5 µg/kg lipid of hexabromobiphenyl (PBB 153). These figures should be used with some caution since levels of other POPs are always very high in char from this lake, maybe due to a local biotransfer process through neighbouring bird species. These levels are the same as or higher than levels of PBB 153 (0.2-9.4 µg/kg lipid) in lake trout sampled in 1997 from Lakes Ontario, Erie, Huron and Superior, which were measured by Luross *et al*., (2002) (Table 2.2).

Vorkamp *et. al*. (2004) , measured concentrations of PBDEs in samples from Greenland and the Faroe Islands of sediment and seven species of animals representing different trophic levels of the food chain. As a pilot investigation, analyses for five PBBs including PBB 153 were made in selected samples of blubber or fat from ringed seal, mink whale and polar bear from Greenland as well as pilot whale and fulmar from the Faroe Islands. PBBs were detected in all samples, except sediment samples, shorthorn sculpin samples and samples of ringed seal from West Greenland. In all other samples, PBB 153 was generally the dominant congener. The concentrations measured in samples from (East) Greenland were in the range 0.34–44.26 µg/kg lipid with the lowest values found in the seal and the highest in polar bear. In the Faroese samples, the range of concentrations of PBB 153 was 8.71-25.54 µg/kg lipid weight with the highest values found in fulmar, a fish predator (Vorkamp *et. al*., 2004).

For comparison, concentrations of PBB 153 in grey seal and osprey from the Baltic Sea were 26 and 22 µg/kg lipid weight; respectively (Jansson *et. al*., 1993). Thus, concentrations of PBB 153 as µg/kg lipid weight in seals from the Arctic (0.34-0.74) are considerably lower than in seals from the Baltic Sea (26 µg/kg lipid weight), while concentrations in predatory birds from the two areas (fulmar and osprey) are of the same order of magnitude, being 25 and 22 µg/kg lipid weight; respectively.

Vorkamp *et. al*., (2004), conclude that PBBs and PBDEs seem to biomagnify along the marine food chain in a similar manner to PCBs. PBBs show indications of a higher biomagnification potential than PBDEs. Even though their absolute concentrations are lower than those of PBDEs, the PBDE/PBB ratio increases in the order ringed seal<pilot whale<mink whale<fulmar<polar bear, leading to almost equal concentrations of PBDEs and PBBs in polar bear. Apparently, the compounds follow the same spatial trend as previously observed for organochlorine compounds, with higher concentrations in East Greenland than in West Greenland (Vorkamp *et. al*., 2004). This indicates that the long-range transport of hexabromobiphenyl may be slow.

Monitoring information on PBBs from areas outside the Arctic, Northern Europe and America is scarce, as only one reference has been found. Hexabromobiphenyl (PBB 153) was not detected (LOD between 0.02 and 0.1 µg/kg wet weights) in samples of muscle and liver from several species of fish from the eastern Mediterranean region of Turkey (Erdogrul *et. al*., 2005).

In summary, the 1994 EHC, review concludes that long-range transport of PBBs in the atmosphere has not been proven, but that the presence of these compounds in Arctic seal samples indicates a wide geographical distribution (EHC 152 (IPCS, 1994)). Several authors report levels of hexabromobiphenyl (and other brominated biphenyls) in arctic animals, especially in fish eating predators and predators at higher trophic levels.

In a recent modelling study, Scheringer *et. al.*, (2006), investigated the persistence and long range transport potential of four potential POPs, including chlordecone and hexabromobiphenyl. They concluded that these POP candidates have persistence and long range transport potential properties similar to those of several known POPs. Furthermore, they included the uncertainty regarding the data quality in a Monte Carlo analysis, which indicated that the result is valid although there are considerable uncertainties in the chemical properties of the four POP candidates.

Conclusion

Although hexabromobiphenyl is less volatile than any of the currently listed POPs, it is found throughout the Arctic wildlife, demonstrating that it does have a high potential for long range environmental transport. The potential for long range environmental transport of hexabromobiphenyl is further supported by the modelling study of Scheringer *et. al.*, 2006.

2.3 Exposure

Because production of hexabromobiphenyl is assumed to have ceased (section 2.1.2) the assessment of the exposure will focus on general exposure instead of current production sites.

2.3.1 Concentrations in abiotic environmental media

Recent monitoring data in soil, water and sediments for PBBs are limited. Historical monitoring data from the United States indicate that environmental PBB concentrations are confined to areas near former manufacturing facilities and regions of Michigan affected by the farm accident of the early 1970's (see Section 2.2.3) (US ATSDR, 2004) .

The only available data for environmental concentrations of PBBs in areas outside the vicinity of former production sites are those from sediment samples from Greenland (Vorkamp *et. al*., 2004), where PBBs (including PBB 153) were not detected in any sample (the limits of detection/quantification are, however, not well defined in the paper).

2.3.2 Concentrations in biota

In the vicinity of Michigan

Concentrations in biota in the vicinity of the Michigan production and contamination accident sites were measured in a multitude of samples during the decade following the cessation of production. The US ATSDR (2004) includes the following: In the late 1980's, PBBs were detected in the concentration range of 15–15,000 µg/kg (lipid basis) in fish from embayments and tributaries of Lake Huron, but not from Lake Superior. Recently, Luross *et. al*. (2002) determined the concentrations of several PBB congeners in lake trout from Lakes Huron, Superior, Erie, and Ontario. 2,2',4,4',5,5'-Hexabromobiphenyl (PBB-153) and 2,2',4,5,5'-pentabromobiphenyl (PBB-101) were found at the highest levels at concentrations ranging from 0.189 to 2.083 µg/kg wet weight and from 0.042 to 0.633 µg/kg wet weight, respectively. Several other congeners were also detected in these lake trout samples (Quoted from US ATSDR, 2004). The concentrations of PBBs in eggs of fish-eating birds (common tern, little gull, herring gull, and red-breasted mergansers) collected during 1975–1980 from nesting islands in northwestern Lake Michigan and Green Bay contained PBBs in the concentration range of 0.02–0.25 mg/kg (µg/g) wet weight (Heinz *et al*. 1983, 1985) (quoted from the US ATSDR, 2004).

Other areas

Monitoring data from areas outside the Arctic (see chapter 2.2.3) and the most exposed region of the US are summarised in Table A.2. in Annex A.

EHC 152 (1994) includes the following investigations on residues of (hexa)bromobiphenyl in biota:

- In Europe, 2,2',4,4',5,5'-hexabromobiphenyl (PBB 153) was found in fish from German and Swedish rivers at concentrations ranging from 0.3 to 0.6 µg/kg lipid (Krüger, 1988; Jansson *et. al*., 1992). A trout sample from a breeding farm contained much lower levels of PBBs than the fish samples from the rivers (Krüger, 1988).

- Swedish reindeers (pooled samples) showed PBB 153 levels as low as 0.04 µg/kg lipid (Jansson *et. al*., 1992).
- PBBs (as a group) were not found in otters *(Lutra canadensis)* from a region relatively remote from industrial sites in north eastern Alberta (Canada) (Somers *et. al*., 1987).
- Fish samples (freshwater and marine species) collected in 1983 from an industrial area of Japan (Osaka) did not contain "PBBs" (not specified) (Watanabe & Tatsukawa, 1990).
- In Europe, PBBs have been detected in seals *(Phoca vitulina; Pusa hispida),* guillemots *(Uria aalge; U. lomvi),* and white-tailed sea eagles *(Haliaeetus albicilla).* The concentrations (estimated by comparison with the technical product Firemaster BP-6) ranged from 3 to 280 µg/kg lipid (Jansson *et. al*., 1987). The concentrations of PBBs in comparable samples from the Baltic Ocean were all higher than concentrations in samples from the Arctic Ocean. The same was true for polybrominated biphenyl ethers and PCBs (Jansson *et. al*., 1987).
- Concentrations of PBB 153 determined in marine fish ranged from 0.2 to 2.4 µg/kg lipid (Krüger, 1988; Jansson *et. al*., 1992). PBB 153 levels of 0.4-26 µg/kg lipid were found in seals (Krüger, 1988; Jansson *et. al*., 1992).
- Detailed isomer-specific PBB analyses were carried out by Krüger (1988), in fish (several species) from the Baltic and North Seas and from sections of the Lippe and Rur rivers in North Rhine-Westphalia, Germany. Seal samples from Spitsbergen (Norway) were also included in this investigation. All samples contained PBBs. The smallest number of PBB congeners was found in seals (n=5) from an area remote from industrial sites. The main components were different hexabrominated isomers with 2,2',4,4',5,5'-hexabromobiphenyl reaching a mean concentration of 0.8 µg/kg fat. The mean concentrations of several PBB congeners and isomers (penta- to nonabrominated biphenyls) measured in fish (n=35) ranged, mostly, between 0.01 and 2 µg/kg fat. The pattern of PBB congeners found in fish differed in a characteristic manner, depending on the different capture sites. While relatively high amounts of nona- and octabromobiphenyls (besides polybrominated biphenyl ethers) were present in fish from German rivers (n=17; several species), hexabrominated biphenyls were predominant in fish from the North Sea and the Baltic Sea (n = 17; several species). In all samples from the Baltic Sea (n=6), 3,3',4,4',5,5'-hexabromobiphenyl was found in relatively high concentrations (maximum concentration: 36 µg/kg fat), but it was not detected in samples from the North Sea and from rivers. The concentrations of the other hexabrominated biphenyls were mostly higher in fish from the Baltic Sea than in fish from the North Sea.

(Quoted from EHC 152 (IPCS, 1994))

US ATSDR (2004) supplements with:

- Three bottlenose dolphins (*Tursiops truncatus*) collected during 1987–1988 from the U.S. mid-Atlantic contained PBBs at concentrations of 14–20 µg/kg lipid basis (Kuehl *et. al*., 1991). The source of the PBBs in the dolphins was not given.
- The median concentrations of PBBs in carcass and brain of 10 specimens of bald eagles (*Haliaeetus leucocephalus*) collected from 29 states in 1977 were 0.07 and 0.05 mg/kg (µg/g), respectively (Kaiser *et. al*., 1980). Twenty-two other specimens did not contain detectable levels (<0.03 mg/kg [µg/g]) of PBBs.
- In whitebeaked dolphins from the North Sea, the concentration of hexa-, penta-, and deca-BBs were 13, 8.3, and <0.9 µg/kg (µg/kg) wet weight, respectively. Tetra-, penta-, and deca-BBs concentration ranges were 1.1–1.9, 0.4–0.9, and <0.5 µg/kg wet weight, respectively, in sperm whales from the Atlantic Ocean (de Boer *et. al*., 1999).

The German Baltic fish samples (as the only samples in that investigation) also contained PBB 169 at a concentration of 15.16 µg/kg lipid (EHC 152 (IPCS, 1994)).

In the Belgian samples from corpses of birds of prey, the variation in concentrations of hexabromobiphenyl was high. Thus, the maximum concentrations measured in muscle and liver were 150 and 180 µg/kg lipid; respectively (Jaspers *et. al*., 2006).

Jansson *et al*. (1993), measured hexabromobiphenyl (PBB 153) in samples of reindeer (a herbivore) from northern Sweden at a level of 0.037 µg/kg lipid. In two other herbivores (rabbit and moose) from Southern Sweden, PBBs were not detectable (level of detection not well defined).

2.3.3 Concentrations in human tissues and breast milk

Michigan

The human exposure to hexabromobiphenyl subsequent to the Michigan accident is discussed in EHC 152 (1994) as well as in US ATSDR (2004). The general trends of the findings are described as follows in EHC 152 (1994):

- Nearly 100% of the adipose samples randomly selected throughout the state had detectable PBB concentrations. Thus, statewide exposure of Michigan residents to PBBs can be demonstrated.
- Levels of PBBs in serum (Landrigan, 1980; Wolff *et. al*., 1982), breast-milk (Brilliant *et. al*., 1978; Miller *et. al*., 1984), and adipose tissue (Wolff *et. al*., 1982) were highest in the area of the accident (lower peninsula), and lowest in the upper peninsula, farthest from the source.
- Compared with residents of quarantined farms, direct consumers of products from quarantined farms, and PBB production workers, the tissue burdens among the general population of Michigan were 1-3 orders of magnitude lower. Moreover, for example, only 36% of the general population had serum PBB concentrations greater than 1 µg/L, compared with 78% among farmers (Anderson *et. al*., 1979; Wolff *et. al*., 1982).
- PBB levels appear to be higher in males than females (Meester & McCoy, 1976; Landrigan *e.t al*., 1979; Landrigan, 1980; Wolff *et. al*., 1978; 1980; Kreiss *et. al*., 1982; Eyster *et. al*., 1983) and higher in children (below the age of 10 years) than in adults (Humphrey & Hayner, 1975; Landrigan *et. al*., 1979; Landrigan, 1980; Barr, 1980; Wolff *et. al*., 1982) (Quoted from EHS 152 (IPCS, 1994)).

The subsequent development is described in EHC 152 (1994):

- In most cases, PBB concentrations did not appear to be decreasing significantly over time. Wolff *et. al*. (1979b), did not find any significant variation in the serum PBB levels of nine dairy farm residents during 18 month of observation.
- Paired serum samples, one collected in 1974 and the other in 1977, were also available for 148 members of the Michigan PBB cohort. The data indicate that levels were generally stable over the 3-year period with a mean change of 16 µg/litre (Landrigan *et. al*., 1979). In another study of the Michigan PBB-cohort, the decrements in median serum levels of PBBs between matched pairs over one (1977-78) and two (1977-79) year intervals were both only 1 µg/litre (Kreiss *et. al*., 1982). No significant change in blood plasma PBB levels was observed over a 5-month period in 41 residents of quarantined farms (Humphrey & Hayner, 1975). In contrast, Meester & McCoy (1976) reported a marked decline over 3 years (1974-76) in serum levels of PBBs. These authors also found that the average decrease in PBB concentrations in the fat of 16 individuals was about 40% in a period of 6 months. No changes in PBB levels were seen over an 11-year period (1976-87) in fat samples from a patient with long-term exposure to PBBs from the early 1970s as a result of the Michigan PBBs accident. The average fat level of PBBs was 0.8 mg/kg (Sherman, 1991).

- In 1981, PBBs were found in 13-21% of serum samples from 4-year-old Michigan children. Their mothers belonged to a group that was surveyed either with regard to the consumption of Lake Michigan sport fish (mean PBB level detected in children: 2.4 ng/ml) or with regard to former exposure to quarantined farm products (mean PBB level detected in children: 3.0 ng/ml) (Jacobson *et. al*., 1989) (Quoted from EHC 152 (IPCS, 1994)).

Other areas

The EHC 152 (1994), stresses the lack of available monitoring studies from areas outside Michigan, as few human monitoring data are available for the US population outside of Michigan. One study deals with the population in the vicinity of industrial areas involved in PBB production or use (Stratton & Whitlock, 1979), the other with farmers of the state of Wisconsin who were examined as control group in connection with the Michigan PBB studies (Wolff *et. al*., 1978).

PBBs were found in all studies, but, because of the limited data, the significance is unclear. The highest PBB levels were found in the hair of humans living near PBB industry. Of the nine samples analysed, five had detectable PBB levels. Both male and female hair samples contained PBBs (Stratton & Whitlock, 1979).

There is very little human monitoring data on PBBs in the populations of countries other than the United States. Krüger *et. al*., (1988) reported PBB contamination of breast-milk from women in Europe in a survey from North Rhine-Westphalia, Germany. The milk samples (n=25) contained a typical pattern of certain PBB congeners. It included penta- to octabromobiphenyls in concentrations ranging from 0.002 to 28 µg/kg, based on milk fat. The most abundant component was 2,2'4,4',5,5'-hexabromobiphenyl (PBB 153) followed by a peak consisting of two heptabromobiphenyl isomers (2,2',3,4',5,5',6- and 2,2',3,4,4',5,6'-heptabromobiphenyl, PBB 187 and 182 respectively). Differences in the pattern were only found in the milk given by a Chinese woman and in that given by a woman having been exposed to several fires in industry.

Concentrations of PBB 153 in human and cow's milk, both collected from the same region (North Rhine-Westphalia), were 1 µg/kg and 0.03 µg/kg, respectively, measured on a lipid basis (Krüger, 1988). (Quoted from EHC 152 (IPCS, 1994))

2.3.4 Human exposure

The US ATSDR (2004), considers the current human exposure to PBBs to be very low, because PBBs are no longer produced or used. Thus, the general population exposure to PBBs will only be from historical releases. For people residing in the lower peninsula of Michigan, especially in the immediate vicinity of the PBB contaminated areas of this region, exposure to PBBs may still be occurring today. However, environmental levels have decreased since the 1970s and current exposure, if any, will be at low levels. For other regions of the United States, the levels of exposure will either be very low or none (Quoted from US ATSDR, 2004) .

In Arctic and North Atlantic regions, where the traditional diet includes top predators (*e. g.* seal in Greenland and pilot whale in the Faroe Islands), exposure has not ceased. Especially the level of PBBs in pilot whale blubber of up to 17 µg/kg lipid indicate the presence of hexabromobiphenyl in food. Pilot whale blubber is consumed as a delicacy in the Faroe Islands.

2.4 Hazard assessment for endpoints of concern

2.4.1 Toxicity

As described in Section 1.1.1, the descriptor “hexabromobiphenyl” covers 42 different hexabrominated biphenyls or congeners, as individually listed in Annex B. The EHC review (IPCS, 1994) indicates that the hexabrominated biphenyls are the most toxic of the chemical class

of polybrominated biphenyls (PBBs) and that the higher homologues (hepta-, octa-, nona- and decabrominated biphenyls) are of progressively lower toxicity. Toxicological studies on hexabromobiphenyl have been carried out mainly on the congener 2,2',4,4',5,5'-hexabromobiphenyl (PBB 153), which is the major component of the PBB mixture FireMaster®, and on FireMaster® itself. The toxicity of FireMaster® appears to be primarily associated with the minor components 2,3,3',4,4',5-hexabromobiphenyl, 2,3',4,4',5,5'-hexabromobiphenyl, 3,3',4,4',5,5'-hexabromobiphenyl (PBB 169) and 2,3',4,4',5-pentabromobiphenyl (IPCS, 1994). The predominant congeners in FireMaster® (2,2',4,4',5,5'-hexabromobiphenyl and 2,2',3,4,4',5,5'-heptabromobiphenyl), are less toxic (IPCS, 1994). Other toxic contaminants in technical PBB mixtures include the polybrominated naphthalenes (HBNs). Hexabromonapthalene has been identified as a toxic contaminant of Firemaster BP-6 or FF-1 at levels of approximately 150 ppm (Birnbaum *et. al.*, 1983, as reported in US ATSDR, 2004). The toxicological effects of the PBBs in humans and in animal studies, as described in the scientific literature, are considered to be attributable mainly to exposure to hexabromobiphenyl congeners (EHC 152 (IPCS, 1994) and US ATSDR, 2004)), although a possible contribution of the HBNs to toxicity cannot be ignored.

Mechanism of action

Hexabromobiphenyl, in common with all PBBs, is a potent inducer of hepatic cytochrome P-450 metabolizing enzymes in the liver. The mechanism of action underlying a number of the toxicological effects of some of these compounds, including induction of metabolising enzymes, immunotoxicity, hepatotoxicity and reproductive toxicity, is considered to be due to interaction with the cellular Ah receptor (also the target of the polychlorinated dioxins, furans and dioxin-like PCBs), causing altered gene expression (Poland & Glover, 1977, 1980; Poland *et. al*., 1979; Goldstein, 1980; Moore *et al*., 1980; McKinney & Singh, 1981; Parkinson & Safe, 1981; Bandiera *et. al*., 1982, 1983; McKinney & McConnell, 1982; Nebert *et. al*., 1982; Poland & Knutson, 1982; Robertson *et. al*., 1982b, 1984c,d; Safe *et. al*., 1982, 1985; Aust *et. al*., 1983; Dannan *et. al*., 1983; Lai, 1984; Safe, 1984, as quoted in IPCS, 1994).

Toxicokinetics

Hexabromobiphenyl is readily absorbed into the body, the primary route of human exposure being via food, due to accumulation and biomagnification in the food chain (IPCS, 1994; US ATSDR, 2004). The majority of animal toxicology studies have used the oral route of exposure and little information is available on exposure via the inhalation and dermal routes, although worker exposure is likely to occur mainly via these routes (Wolff *et. al*., 1979a, as quoted in IPCS, 1994). Following absorption, hexabromobiphenyl is widely distributed in the body and accumulates, with the highest concentrations found in adipose tissue and to a lesser extent the liver (IPCS, 1994).

Exposure *in utero* occurs via transfer of PBBs to offspring by placental transfer and infants are also exposed via milk. Human milk has been found to contain levels of 2,2',4,4',5,5'-hexabromobiphenyl 100 times higher than those found in maternal blood (Brilliant *et. al*., 1978; Landrigan *et. al*. 1979; Eyster, 1983, as reported in IPCS, 1994).

Metabolism and excretion of the hexabromobiphenyls is low (IPCS, 1994; US ATSDR, 2004), and the compounds therefore show marked bioaccumulation and persistence in all species. Average half-lives for 2,2',4,4',5,5'-hexabromobiphenyl in humans have been estimated to be between 8 and 12 years (IPCS, 1994), while shorter half-lives have been reported in rats, monkeys, and other species (see Table 68 in IPCS, 1994). It has been suggested that humans may retain certain congeners to a greater degree than experimental animals (*e. g.* Fries (1985b, as quoted in IPCS, 1994), a phenomenon that is also found with the polychlorinated dioxins and furans.

Darnerud (2003), argues that the pattern of toxicity of PBBs should be similar to that of PCBs apart from the change in effects brought about by the chlorine-bromine substitution. Consequently, the planar PBBs are expected to be most toxic (as they bind to the Ah receptor) and toxicity to decrease through mono-ortho congeners to di-ortho congeners. This should be supported by experimental evidence, as 3,3',4,4',5,5' hexabromobiphenyl was found to be the most toxic PBB congener in several systems (Darnerud, 2003).

Toxicity of hexabromobiphenyl in animal studies

In experimental animal studies, hexabromobiphenyl shows relatively low acute toxicity (LD_{50}>1 g/kg body weight) (see Table 70, IPCS, 1994). Toxicity is higher following repeated exposure (IPCS, 1994), due to progressive accumulation of the compounds and a characteristic delay in lethality after exposure is seen (Di Carlo *et. al*., 1978; Gupta & Moore, 1979, (as quoted in IPCS, 1994). At lethal doses, death is reported to be due to a "wasting syndrome" with marked loss in body weight rather than to specific organ pathology (Hutzinger *et. al*., 1985a; McConnell, 1985, as quoted in IPCS, 1994). However, prolonged exposure of laboratory animals to doses in the range of<1 mg/kg bw/day to 100 mg/kg bw/day results in liver, kidney and thyroid changes, accompanied by effects in the nervous and immune systems, porphyria and skin disorders (IPCS, 1994).

A summary of outcomes of a number of the key toxicological studies on hexabromobiphenyl, including the NOAEL/LOAEL derived in each study is provided in Annex A, Table A.3 to this document. The studies included in Annex A, Table A.3 have been selected from the very large database on toxicological studies on hexabromobiphenyl, on the basis of the importance of the endpoint investigated (*e. g.* reproductive toxicity, carcinogenicity, other key target organ toxicity), robustness of the reported studies and the dose level (NOAEL/LOAEL) at which effects were reported. Table 2.2 below provides information on pivotal toxicological studies (also included in Annex A Table A.3) that provide information on the toxicity of hexabromobiphenyl at low levels of exposure, considered to be particularly relevant for characterisation of the toxicological risks of these compounds. Some of these studies have been used by US ATSDR to define Minimal Risk Levels (MRLs) for hexabromobiphenyl (US ATSDR, 2004).

Effects in toxicological studies included decreased circulating thyroid hormones in a 10-day gavage study in rats with a NOAEL of 1 mg/kg bw/day (Allen-Rowlands *et. al*., 1981, as quoted in US ATSDR, 2004), decreased lymphoproliferative responses in rats at a dose level of 3 mg/kg/day (LOAEL) (Luster *et. al*., 1980, as quoted in US ATSDR, 2004), and generalised toxicity in male Rhesus monkeys at 0.73 mg/kg bw/day (LOAEL) (Allen *et. al*., 1978; Lambrecht *et. al*. 1978 (as quoted in US ATSDR, 2004)). PBBs produced porphyria in rats and male mice at doses as low as 0.3 mg/kg bw/day. The no-effect level was 0.1 mg/kg bw/day.

These results show that hexabromobiphenyl produced long-term toxicity in experimental animals at very low doses, a critical effect for the purposes of risk characterization being the effects seen in the thyroid in rats at doses as low as 0.05 mg/kg bw/day, comprising increased number and decreased size of follicles, accompanied by changes in levels of circulating T_3 and T_4 hormone (Akoso *et al*., 1982, as quoted in US ATSDR, 2004).

Hepatocarcinogenicity of hexachlorobiphenyl has been demonstrated in a number of studies including repeated dose studies in Fischer-344/N rats and B6C3F1 mice (males and females) administered FireMaster$^{(R)}$ FF-1 at dosages of 0, 0.1, 0.3, 1, 3, or 10 mg/kg bw/day (NTP 1983, NTP, 1992, as quoted in US ATSDR, 2004). Tumors included hepatocellular adenoma and carcinoma and, in female rats, cholangiocarcinoma. The lowest dose of FireMaster$^{(R)}$ that produced tumors (primarily adenomas rather than carcinomas) in rats was 3.0 mg/kg bw/day for 2 years, and in mice the dose was10 mg/kg bw/day (NTP 1983, as quoted in US ATSDR, 2004). Mice receiving 0.15 mg/kg bw/day in a study involving pre- and perinatal exposure in addition to lifetime exposure

did not suffer any adverse effects (NTP, 1992, as quoted in US ATSDR, 2004). The International Agency for Research on Cancer (IARC) in 1987 concluded that there was sufficient evidence that hexabromobiphenyl is carcinogenic in mice and rats and possibly carcinogenic to humans (Group 2B). Hexabromobiphenyl is not genotoxic in *in vitro* microbial and mammalian cell gene mutation assays (see Table 88 in IPCS, 1994), although it has been reported to interfere with cell-to-cell communication (Sleight, 1985 as quoted in IPCS, 1994). These results, coupled with the results of tumor promotion studies (*e. g*. Schwartz *et. al*., 1980; Jensen *et. al*., 1982, 1983, 1984; Jensen & Sleight, 1986; Rezabek *et. al*., 1987; Dixon *et. al*., 1988, as quoted in IPCS, 1994) indicate that these chemicals cause cancer by epigenetic mechanisms, involving both hepatic toxicity and hypertrophy, including cytochrome P-450 induction (IPCS, 1994).

Oral administration of hexabromobiphenyl was associated with adverse effects on reproductive parameters in a range of experimental animals (see Table 86 and 87 in IPCS, 1994). The most common adverse effects on reproduction were failure in implantation and decreases in pup viability of offspring. These effects were seen at a dose level of 28.6 mg/kg bw/day in a 15-day reproductive toxicity study in rats, with dosing between gestational day 0-14 (Beaudoin, 1979, as quoted in US ATSDR, 2004) and in mink at concentrations of 1 mg/kg diet (Aulerich and Ringer, 1979 as quoted in IPCS, 1994). Increased menstrual cycle duration and prolonged implantation bleeding were observed in female monkeys fed approximate daily dose levels of 0.012 mg/kg bw/day for 7 months before breeding and during pregnancy. Fetal deaths were also observed after approximately 1 year of exposure. Effects were attributed to decreases in serum progesterone (Lambrecht *et, al*., 1978; Allen *et, al*., 1978; 1979, (as quoted in US ATSDR, 2004).

Table 2.2 Pivotal toxicological studies on the toxicity of hexabromobiphenyl.

Species	Study type	Effect	LOAEL/ NOAEL
Rat	Short-term/acute toxicity 10 day repeat dose gavage study	decreased thyroid serum T4 hormones	3 mg/kg bw/day (LOAEL) 1 mg/kg bw/day (NOAEL)
Rat, Sprague Dawley	30-day dietary feeding study	increased number and decreased size of thyroid follicles	0.05 mg/kg bw/day (LOAEL)
Mice B6C3F1	In utero and post partum exposure from Gd 0-ppd 56	hepatocellular adenoma and carcinoma in offspring	1.5 mg/kg bw/day (LOAEL) 0.15 mg/kg bw/day (NOAEL)
Rhesus Monkey	25-50 wk dietary feeding study	34% weight loss in adult male, 0% weight gain in juvenile, proliferation of mucosal cells, chronic inflammation, severe ulcerative colitis, alopecia, keratinization of hair follicles and sebaceous glands, clinical chemical and hepatic changes	0.73 mg/kg bw/day (LOAEL, males)
Rat, Sprague Dawley	7 month dietary feeding study	decreased thyroid serum T3 and T4 hormones	0.45 mg/kg bw/day (LOAEL)
Monkey, Rhesus		increased menstrual cycle duration in 4/7;implantation bleeding in 2/7). 1/7 fetuses were aborted, 1/7 fetuses stillborn, 12% decreased birth weight and 22% decreased postnatal weight gain in 4/7 survivors	0.012 mg/kg bw/day (LOAEL)

Toxicity of hexabromobiphenyl in humans

Information on toxicological effects of PBBs (and by inference, hexabromobiphenyl) in humans has mainly been derived from the Michigan accident described in Section 2.1.4 of this draft Risk Profile (Carter (1976), Getty *et. al*., (1977), Kay (1977), Di Carlo *et. al*., (1978), Damstra *et. al*., (1982), Zabik (1982), and Fries (1985b), as quoted in EHC 152 (IPCS, 1994)). This accident resulted in widespread exposure of consumers for periods approaching 1 year, before the contamination of food by PBBs was identified and affected foodstuffs were removed from the food chain.

Adverse health effects reported included changes in liver enzymes, nausea, abdominal pain, loss of appetite, joint pain and fatigue (Anderson *et. al.*, 1978b, 1979, as reported in IPCS, 1994), together with reports of skin disorders, including acne and hair loss, in the period following the contamination. (IPCS, 1994). Similar skin disorders have also been reported in workers with occupational exposure to PBBs (Anderson *et. al.*, 1978a, as reported in IPCS, 1994), and also following exposure to the polychlorinated dioxins and furans.

Detailed epidemiological studies have been carried out on the health status of exposed individuals including immunological status, cancer incidence, reproductive effects and effects on development of young children. These studies have in the main failed to establish a definite link between any of these effects and exposure to PCBs, although some studies have reported decreased immune function in Michigan farm residents (Bekesi *et. al.*, 1979, 1987) and effects have also been reported on pubertal development in young females (see endocrine-disrupting effects below).

There are no reports of acute hexabromobiphenyl intoxication in humans, and there is also no consistent epidemiological evidence for hepatocarcinogenicity in exposed humans. A relationship between increasing serum levels (>2 ppb) of PBBs and increasing risk of breast cancer was indicated in case-control studies of women exposed during the Michigan contamination episode (Henderson *et. al.*, 1995; Hoque *et. al.*, 1998), but according to US ATSDR, 2004 (and quoted from this source) the results are only suggestive due to factors such as the small number of cases, insufficient information on known breast cancer risk factors, and confounding exposures to other organochlorine chemicals.

Effects on endocrine systems

The PBBs (and by inference, hexabromobiphenyl) are considered to have effects on endocrine systems. They have been evaluated under the EU-Strategy for Endocrine Disrupters[7] and have been placed in category 1 (evidence of endocrine-disrupting activity in at least one species using intact animals) in the priority list of chemicals established under the EU-Strategy. This categorisation is based on evidence of delayed vaginal opening in new-born rats, epidemiological evidence of hypothyroidism in workers exposed to polybrominated biphenyls and of increased incidence of breast cancer among women exposed to polybrominated biphenyls (as reported in BKH report, 2000). In an assessment (Blanck *et. al.*, 2000) of pubertal development in girls and young women exposed in utero and via breast milk to high levels of PBBs (>7pbb), it was found that this population had an earlier age to menarche than a similar breastfed population exposed to lower levels of PBBs, or than a highly-exposed population who were not breastfed. Earlier pubic hair development was also seen in the more highly exposed population, suggesting an effect of PBBs on pubertal events (Blanck *et. al.*, 2000).

[7] http://europa.eu.int/comm/environment/endocrine/strategy/substances_en.htm

Conclusion on effects assessment and toxicity of hexabromobiphenyl

Hexabromobiphenyl is readily absorbed into the body and accumulates following prolonged exposure. Although the acute toxicity of hexabromobiphenyl is low, a number of chronic toxic effects including hepatoxicity have been observed in experimental animals at doses around 1 mg/kg bw/day following long-term exposure, and effects are seen in the rat thyroid at doses as low as 0.05 mg/kg bw/day. Cancer was induced in animal studies at a dose of 0.5 mg/kg bw/day and the no-observed-effect level was 0.15 mg/kg bw/day. The International Agency for Research on Cancer has classified hexabromobiphenyl as a possible human carcinogen (IARC group 2B). The PBBs (and by inference, hexabromobiphenyl) are endocrine disrupting (ED) chemicals, and effects are seen on reproductive capacity in rats, mink and monkeys. Effects were seen in monkeys fed 0.012 mg/kg bw/day for 7 months before breeding and during pregnancy, the lowest effect level reported for hexabromobiphenyl in toxicology studies. There is epidemiological evidence of hypothyroidism in workers exposed to polybrominated biphenyls and of increased incidence of breast cancer in exposed women.

It can be concluded that hexabromobiphenyl is a bioaccumulative chemical with a range of potentially adverse effects on health, including carcinogenicity, reproductive toxicity, endocrine and other hormone-disrupting effects, at very low levels of exposure.

2.4.2 Ecotoxicity

Only few data are available on effects of PBBs on other organisms than mammals. Toxicity tests with technical decabromobiphenyl (Adine 0102) and bacteria (*Pseudomonas putida)* and the water flea *Daphnia magna* are quoted in EHS 152 (1994). The results were an EC10 of 53 mg/L for *Pseudomonas putida* (cell multiplication) and an EC50>66 mg/liter for *Daphnia magna* (immobilization, 24 hours). Because these concentrations exceed the solubility of HBB in water, the data may be of limited relevance to evaluating the environmental effects. However, the fact that the NOEC is reported to be <2 mg/L indicates that the water fleas were affected at the lowest concentration tested.

MacPhee & Ruelle (1969) and Applegate *et. al*., (1957), report results from short term tests with hexabromobiphenyl (CAS No. 36355-01-8) and several species of fish in the range 5-10 mg/L (Quoted from the Ecotox data base (US EPA, 2006)). These concentrations are also above the water solubility and may also be of limited environmental relevance.

In a field study on water birds, correlations between behavioural effects and reproductive success were not unambiguously correlated to body burdens of PBBs. (EHS 152 (IPCS, 1994)).

In an untraditional fish early life stage test, Hornung *et al*., (1996), injected halogenated organic contaminants into rainbow trout eggs. For 3,3',4,4',5,5'- hexabromobiphenyl they found an LD_{50} of 3,910 µg/kg. This result is not comparable to those of traditional fish tests, where exposure is via the water but it is comparable to results of other test with similar exposure. Hornung *et. al*. (1996), made such experiments to compare the toxicity of PBBs and PCBs and found that both 3,3',4,4'-tetrabromobiphenyl and 3,3',4,4',5,5'-hexabromobiphenyl were 10-fold more potent than identically substituted polychlorinated biphenyls.

Based on this, it seems to be relevant to expect the environmental toxicity of hexabromobiphenyl to be comparable to that of hexachlorobiphenyl.

3 SYNTHESIS OF THE INFORMATION

Hexabromobiphenyl belongs to a wider group of polybrominated biphenyls (PBBs). It has mainly been used as a fire retardant. Hexabromobiphenyl is already listed in Annex I of the UNECE Protocol on POPs.

According to available data, hexabromobiphenyl can be considered to be highly persistent in the environment. There is evidence of low or no degradation in water, soil and sediment, in the laboratory as well as in the field. Therefore, hexabromobiphenyl is considered to be highly persistent.

Hexabromobiphenyl is less volatile than many POP substances. However, extensive data on monitoring shows that it is found throughout the Arctic wildlife, demonstrating that it does have a high potential for long range environmental transport.

With measured weight-based BCF values in the range 4,700 - 18,100 and biomagnification factors in the aquatic food chain exceeding 100, hexabromobiphenyl is considered to be highly bioaccumulative and to have a high potential for biomagnification. These properties are demonstrated by several authors to be comparable to those of hexachlorobiphenyl (a PCB compound), for which the bioaccumulative properties are well documented.

Hexabromobiphenyl is readily absorbed into the body and accumulates following prolonged exposure. Although the acute toxicity of hexabromobiphenyl is low, a number of chronic toxic effects including hepatotoxicity have been observed in experimental animals at doses around 1 mg/kg bw/day following long-term exposure, and effects are seen in the rat thyroid at doses as low as 0.05 mg/kg bw/day. The International Agency for Research on Cancer has classified hexabromobiphenyl as a possible human carcinogen (IARC group 2B). The PBBs are endocrine disrupting chemicals, and effects are seen on reproductive capacity in rats, mink and monkeys. There is epidemiological evidence of hypothyroidism in workers exposed to polybrominated biphenyls and of increased incidence of breast cancer in exposed women. Data on toxicity to other species than laboratory mammals is scarce but suggests the environmental toxicity of hexabromobiphenyl is comparable to that of hexachlorobiphenyl.

Based on the available data, hexabromobiphenyl should be considered as a POP warranting global action.

Production and use of hexabromobiphenyl has ceased over the last decades but it cannot be excluded that it is still produced or used in some countries. In addition to emissions during manufacture or use, hexabromobiphenyl can enter the environment from the widespread use of flame-retarded products. A considerable part of the substance produced will probably reach the environment sooner or later because of the high stability of these compounds. Furthermore, some of these chemicals may form toxic polybrominated dibenzofurans during combustion processes.

4 CONCLUDING STATEMENT

It has been demonstrated that hexabromobiphenyl clearly meets all the criteria laid down in Annex D of the Stockholm Convention: It is very persistent in the environment. It has a great potential for bioaccumulation and in addition there is clear evidence of its biomagnification. Due to its physical and chemical properties and based on findings in environmental samples, it is verified that hexabromobiphenyl can be transported long distances in air, far from its sources. Hexabromobiphenyl is a possible human carcinogen and can also be regarded as a substance capable of disrupting the endocrine system.

As hexabromobiphenyl can travel in the atmosphere far from its sources, neither a single country nor group of countries alone can abate the pollution caused by this substance. Regional action has already been considered necessary and hexabromobiphenyl is totally banned under the Convention on Long-range Transboundary Air Pollution Protocol on Persistent Organic Pollutants. Although the production and use of hexabromobiphenyl seems to be ceased in most countries, its reintroduction remains possible. This could lead to increased releases and levels in the environment.

Based on the available data, hexabromobiphenyl is likely, as result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

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ANNEX A

Table A.1 Concentrations of hexabromobiphenyl (PBB 153) in Arctic predators.

Year of sampling	Location	Species	Tissue	Concentration µg/kg lipid
1999-2002	East Greenland	Polar bear (*Ursus maritimus)* [1]	Blubber	33-44
1998	Faroe Islands	Fulmar (*Fulmarus glacialis*) [1]	Fat	16-26
2001	Faroe Islands	Pilot whale (*Globicephala melas*) [1]	Blubber	8.7-17
< 1987	Arctic Ocean	Guillemot (*Uria aalge*) [2]	Muscle	50 [6]
2002	East Greenland	Ringed seal (*Phoca hispida*) [1]	Blubber	0.34-0.42
1998-2002	West Greenland	Ringed seal (*Phoca hispida*) [1]	Blubber	n.d.
< 1987	Svalbard	Ringed seal (*Phoca hispida*) [2]	Blubber	4 [6]
1981	Svalbard	Ringed seal (*Phoca hispida*) [3]	Blubber	0.42
< 1988	Svalbard	Seal sp. [4]	? (mean)	0.8
1998	East Greenland	Minke whale (*Balaenoptera acutorostrata*) [1]	Blubber	0.56-1.2
1999-2001	Barents Sea	Arctic char (*Salvelinus alpinus*) [5]	Muscle	n.d.-52
1986	Lapland	Whitefish (*Coregonus sp.*) [2]	Muscle	0.29
2002	East Greenland	Shorthorn sculpin (*Myoxocephalus scorpius*) [1]	Liver	n.d.
2002	West Greenland	Shorthorn sculpin (*Myoxocephalus scorpius*) [1]	Liver	n.d.

n.d. = Not detected. Limits of detection are not well described in the references.

1: Vorkamp *et al*., 2004,
2: Jansson *et al*., 1987,
3: Jansson *et al*., 1993,
4: Krüger, 1988 (Quoted from EHC 152),
5: Evenset *et al*. 2005.
6: FireMaster(R) BP-6

Table A.2 Concentrations of hexabromobiphenyl (PBB 153) in biota, collected in subarctic and temperate regions outside the vicinity of Michigan.

Year of sampling	Location	Species	Tissue	Concentration µg/kg lipid
Aquatic species				
1979-85	Baltic Sea	Grey seal (*Halichoerus grypus*) [2]	Blubber	26
< 1987	Baltic Sea	Harbour seal (*Phoca vitulina*) [7]	Blubber	20
< 1987	~North Sea	Harbour seal (*Phoca vitulina*) [7]	Blubber	3
< 1987	Baltic Sea	Guillemot (*Uria aalge*) [7]	Muscle	160
1987-88	US mid Atlantic	Bottlenose dolphin (*Tursiops truncatus*) [8]	?	14-20
< 1999	North Sea	Whitebeaked dolphin (*Lage-norhynchus albirostris*) [10]	?	13 (wwt)
1987	S. Sweden	Arctic char (*Salvelinus alpinus*) [2]	Muscle	0.42
1986	Bothnian Bay	Herring (*Clupea harengus*) [2]	Muscle	0.092
1987	Baltic Proper	Herring (*Clupea harengus*) [2]	Muscle	0.16
1987	Skagerak	Herring (*Clupea harengus*) [2]	Muscle	0.27
< 1988	Germany	River fish (average) [1]	?	0.60
< 1988	Baltic Sea	Fish [1]	?	2.39
< 1988	North Sea	Fish [1]	?	1.31
1997	USA, Great Lakes	Lake trout (*Salvelinus nanay-cush*) (range of means) [6]	Whole fish	0.19-2.08
Predatory birds				
< 1987	Baltic Sea	White tailed sea eagle (*Hali-aeetus albicilla*) [7]	Muscle	280
1977	USA, 29 states	Bald eagle (*Haliaeetus leuco-cephalus*) [9]	Carcass	< 0.03 – 0.07 (wwt?)
1977	USA, 29 states	Bald eagle (*Haliaeetus leuco-cephalus*) [9]	Brain	< 0.03 – 0.05 (wwt?)
1982-86	S. Sweden	Osprey (*Pandion haliaeetus*), corpses [2]	Muscle	22
2003-2004	Belgium	7 species of predatory birds, corpses (range of medians) [3]	Muscle	2-35
2003-2004	Belgium	7 species of predatory birds, corpses (range of medians) [3]	Liver	2-43
1998-2000	Belgium	Little owl (*Athene noctua*) [5]	Unhatched eggs	1-6
1991-2002	Norway	6 species of predatory birds (range of medians) [4]	Unhatched eggs	0.2-9.4 µg/kg wwt
Terrestrial herbivores				
1986	S. Sweden	Rabbit (*Oryctlagus cuniculus*) [2]	Muscle	n.d.
1985-86	S. Sweden	Moose (*Alces alces*) [2]	Muscle	n.d.
1986	N. Sweden	Reindeer (*Rangifer tarandus*) [2]	Suet (fat)	0.037

n.d. = Not detected. Limits of detection are not well described in the references.

1: EHC 152 (IPCS, 1994), 2: Jansson *et al*. 1993, 3: Jaspers *et al*., 2006, 4: Herzke *et al*., 2005, 5: Jaspers *et al*., 2006, 6: Luross *et al*., 2002, 7: Jansson *et al*. 1987, 8: Kuehl *et al*. 1991 (quoted from US ATDSR, 2004), 9:Kaiser *et al*., 1980 (quoted from US ATSDR, 2004), 10: de Boer *et al*., 1999 (quoted from US ATSDR, 2004).

Table A.3. Summary of key toxicological studies on hexabromobiphenyl.

Species (test material)	Study type	Effect	LOAEL/ NOAEL	Ref.
Rat Fischer 344/N (FF-1)	Short-term/acute toxicity, 14-day repeat dose, 5 single daily doses per week	Body weight loss, emaciation, hepatotoxicity, renal & adrenal changes, atrophy of thymus; necrosis of splenic lymphoblasts)	1000 mg/kg/day (LOAEL)	Gupta and Moore 1979 (as quoted in US ATSDR, 2004).
Rat	Short-term/acute toxicity10 day repeat dose gavage study	decreased thyroid serum T4 hormones	3 mg/kg bw/day (LOAEL) 1 mg/kg bw/day (NOAEL)	Allen-Rowlands *et al*. 1981(as quoted in US ATSDR, 2004).
Rat, Sprague Dawley (BP-6)	30-day dietary feeding study	increased number and decreased size of thyroid follicles	0.05 mg/kg/day (LOAEL)	Akoso *et al*. 1982 (as quoted in US ATSDR, 2004).
Mouse B6C3F1 (FF-1)	Short-term/acute toxicity, 14-day repeat dose, 5 single daily doses per week	Hepatocyte enlargement and single-cell necrosis	0.3 mg/kg bw/day (NOAEL)	Gupta *et al*. 1981 (as quoted in US ATSDR, 2004).
Guinea Pig (PBB not specified)	30-day dietary feeding study	vacuolation and fatty changes in liver	0.04 mg/kg bw/day	Sleight and Sanger 1976, (as quoted in US ATSDR,2004).
Balb/c) Mouse (BP-6)	Short-term/acute toxicit, 10 day oral dietary study	suppressed antibody-mediated response to SRBC, thymic atrophy)	130 mg/kg bw/day (LOAEL)	Fraker and Aust 1978, (as quoted in US ATSDR, 2004).
Rat Fischer 344/N (FF-1)	6 month gavage study, 5 single daily doses per week	decreased lymphoproliferative responses and decreased delayed hypersensitivity responses)	3 mg/kg bw/day (LOAEL)	Luster *et al*. 1980 (as quoted in US ATSDR, 2004).
Rhesus Monkey (FF-1)	25-50 wk dietary feeding study	34% weight loss in adult male, 0% weight gain in juvenile, proliferation of mucosal cells, chronic inflammation, severe ulcerative colitis, alopecia, keratinization of hair follicles and sebaceous glands, clinical chemical and hepatic changes	0.73 mg/kg bw/day (LOAEL, males)	Allen *et al*. 1978; Lambrecht *et al*. 1978 (as quoted in US ATSDR, 2004).
Rat, Sprague Dawley (BP-6)	7 month dietary feeding study	decreased thyroid serum T3 and T4 hormones	0.45 mg/kg bw/day (LOAEL)	Byrne *et al*. 1987, (as quoted in US ATSDR, 2004).

Note: FF-1 and BP-6 in column 1 refer to FireMaster(R) FF-1 and FireMaster(R) BP-6, the PBBs used in the toxicity study described.

Table A.3 (continued) Summary of key toxicological studies on hexabromobiphenyl.

Species (test material)	Study type	Effect	LOAEL/ NOAEL	Ref.
Rat Fischer 344/N (FF-1)	25 wk gavage study, 5 single daily doses per week	gastric ulcers, decreased serum thyroid T4 hormone) hepatic, haematological disorders, thymic atrophy, progressive nephropathy	0.3 mg/kg bw/day (LOAEL) 0.1 mg/kg bw/day (NOAEL)	NTP 1983, (as quoted in US ATSDR, 2004).
Rat Sprague-Dawley Holtzman (FF-1)	4 week gavage study, 5 single daily doses per week	decreased motor activity	6 mg/kg bw/day (LOAEL) 3 mg/kg bw/day (LOAEL	Geller *et al*. 1979, (as quoted in US ATSDR, 2004).
Rat, Sprague Dawley (BP-6)	6 month gavage study, 5 single daily doses per week	delayed acquisition of locomotion and reduced open field activity in offspring).	2 mg/kg bw/day (LOAEL) 0.2 mg/kg bw/day (NOAEL)	Henck *et al*. 1994, (as quoted in US ATSDR, 2004).
Monkey, Rhesus (FF-1)		increased menstrual cycle duration in 4/7; implantation bleeding in 2/7). 1/7 fetuses were aborted, 1/7 fetuses stillborn, 12% decreased birth weight and 22% decreased postnatal weight gain in 4/7 survivors	0.012 mg/kg bw/day (LOAEL)	Lambrecht *et al*. 1978; Allen *et al*. 1978; 1979, (as quoted in US ATSDR, 2004).
Rat, Wistar (BP-6)	15-day reproductive toxicity study, dosing between gestational day 0-14	no implantations in 2/5 rats	28.6 mg/kg bw/day (LOAEL) 14.3 mg/kg bw/day (NOAEL)	Beaudoin 1979, (as quoted in US ATSDR, 2004).
Rat, Sprague Dawley	Gavage study in pregnant rats, dosing between gestional day 7-15	Reproductive: Delayed vaginal opening in pups	0.04 mg/kg bw/day (NOAEL)	Harris *et al*. (1978) (as quoted in BKH Final Report 2000)
Rat, Sprague Dawley (BP-6)	40 day dietary feeding study	Reproductive deficits in learning behavior in offspring, 6 months after prenatal and lactational exposure)	0.2 mg/kg bw/day (LOAEL)	Henck and Rech 1986, (as quoted in US ATSDR, 2004).

Note: FF-1 and BP-6 in column 1 refer to FireMaster(R) FF-1 and FireMaster(R) BP-6, the PBBs used in the toxicity study described.

Table A.3 (continued) Summary of key toxicological studies on hexabromobiphenyl.

Species (test material)	Study type	Effect	LOAEL/ NOAEL	Ref.
Rat, Fischer 344/N (FF-1)	6 month gavage study, 5 single daily doses per week dosages of 0, 0.1, 0.3, 1, 3, or 10 mg/kg/day	hepatocellular adenoma and carcinoma, cholangiocarcinoma (females only	3 mg/kg bw/day (LOAEL)	NTP 1983, (as quoted in US ATSDR, 2004).
Mice B6C3F1 (FF-1)	6 month gavage study, 5 single daily doses per week dosages of 0, 0.1, 0.3, 1, 3, or 10 mg/kg/day	hepatocellular adenoma and carcinoma	10 mg/kg bw/day (LOAEL)	NTP 1983, (as quoted in US ATSDR, 2004
Mice B6C3F1 (FF-1)	In utero and post partum exposure from Gd 0-ppd 56	hepatocellular adenoma and carcinoma in offspring	1.5 mg/kg bw/day (LOAEL) 0.15 mg/kg bw/day (NOAEL)	NTP 1992, (as quoted in US ATSDR, 2004).
Humans	Females accidentally exposed in the Michigan incident	relationship between serum PBBs and risk of breast cancer	relationship between serum PBBs of > 2 pbb and risk of breast cancer when compared with the reference group (<2 ppb),	Henderson *et al*. 1995, (as quoted in US ATSDR, 2004).
Humans	Michigan farm residents accidentally exposed in the Michigan incident	Significant reduction of in vitro immunological function		Bekesi *et at*. 1979, 1985 (as quoted in US ATSDR, 2004) Bekesi *et al*, 1987
Humans	Females accidentally exposed in the Michigan incident	Possible disturbance in ovarian function as indicated by menstrual cycle length and bleed length		Davis *et al*., 2005
Humans	Offspring of females accidentally exposed in the Michigan incident	breastfed girls exposed to high levels of PBB in utero had an earlier age at menarche	Effects at > or =7 ppb in breast milk	Blanck *et al*., 2000, (as quoted in US ATSDR, 2004)

Note: FF-1 and BP-6 in column 1 refer to FireMaster(R) FF-1 and FireMaster(R) BP-6, the PBBs used in the toxicity study described.

ANNEX B
HEXABROMOBIPHENYL ISOMERS

IUPAC Number[8]	Name	CAS Registry number[9].
	Hexabromobiphenyl	36355-01-8
128	2,2',3,3',4,4' hexabromobiphenyl	82865-89-2
129	2,2'3,3',4,5 hexabromobiphenyl	
130	2,2',3,3',4,5' hexabromobiphenyl	82865-90-5
131	2,2',3,3',4,6 hexabromobiphenyl	
132	2,2',3,3',4,6' hexabromobiphenyl	119264-50-5
133	2,2',3,3',5,5' hexabromobiphenyl	55066-76-7
134	2,2',3,3',5,6 hexabromobiphenyl	
135	2,2',3,3',5,6' hexabromobiphenyl	119264-51-6
136	2,2',3,3',6,6' hexabromobiphenyl	
137	2,2',3,4,4',5 hexabromobiphenyl	81381-52-4
138	2,2',3,4,4',5' hexabromobiphenyl	67888-98-6
139	2,2',3,4,4',6 hexabromobiphenyl	
140	2,2',3,4,4',6' hexabromobiphenyl	
141	2,2',3,4,5,5' hexabromobiphenyl	120991-47-1
142	2,2',3,4,5,6 hexabromobiphenyl	
143	2,2',3,4,5,6' hexabromobiphenyl	
144	2,2',3,4,5',6 hexabromobiphenyl	119264-52-7
145	2,2',3,4,6,6' hexabromobiphenyl	
146	2,2',3,4',5,5' hexabromobiphenyl	
147	2,2',3,4',5,6 hexabromobiphenyl	
148	2,2',3,4',5,6' hexabromobiphenyl	
149	2,2',3,4',5',6 hexabromobiphenyl	69278-59-7
150	2,2',3,4',5,6' hexabromobiphenyl	93261-83-7
151	2,2',3,5,5',6 hexabromobiphenyl	119264-53-8
152	2,2',3,5,6,6' hexabromobiphenyl	
153	2,2',4,4',5,5' hexabromobiphenyl	59080-40-9
154	2,2',4,4',5,6' hexabromobiphenyl	36402-15-0
155	2,2',4,4',6,6' hexabromobiphenyl	59261-08-4
156	2,3,3',4,4',5 hexabromobiphenyl	77607-09-1
157	2,3,3',4,4',5' hexabromobiphenyl	84303-47-9
158	2,3,3',4,4',6 hexabromobiphenyl	
159	2,3,3',4,5,5' hexabromobiphenyl	120991-48-2
160	2,3,3',4,5,6 hexabromobiphenyl	
161	2,3,3',4,5',6 hexabromobiphenyl	
162	2,3,3',4',5,5' hexabromobiphenyl	
163	2,3,3',4',5,6 hexabromobiphenyl	
164	2,3,3',4',5',6 hexabromobiphenyl	82865-91-5
165	2,3,3',5,5',6 hexabromobiphenyl	
166	2,3,4,4',5,6 hexabromobiphenyl	
167	2,3',4,4',5,5' hexabromobiphenyl	67888-99-7
168	2,3',4,4',5',6 hexabromobiphenyl	84303-48-0
169	3,3',4,4',5,5' hexabromobiphenyl	60044-26-0

(US ATSDR (2004)[10])

[8] Ballschmiter and Zell 1980
[9] From EHC 152 (IPCS, 1994).
[10] Note: the US ATSDR List does not include the two CAS numbers included in EHC 192 1997

別添8

商業用ペンタブロモジフェニルエーテルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 ・（Tetra, Penta, HexaBDE）難分解性（BIOWIN） ・（PentaBDE） 分解せず（OECD TG 301B で CO_2 発生なし） 【半減期】 ・大気中：11-19 日（EPIWIN） ・水中： 150 日（EPIWIN） ・土壌中：半減期 150 日（EPIWIN） ・好気性底質中： 600 日（EPIWIN） ・1970 年代初期にﾖｰﾛｯﾊﾟの海洋の底質に沈降した PentaBDE 同属体が現在も相当量存在しており、底質中での残留性が高いことが示されている。	【ｵｸﾀﾉｰﾙ/水分配係数】 log KOW=6.5-7.4 【BAF（経鰓及び経口による生物濃縮係数）】 ｾﾞﾌﾞﾗｶﾞｲ：BAF=1.8 【BMF（経口的生物濃縮係数）】 ・ｳﾐﾊﾞﾄ/ﾆｼﾝ：BMF=17 ・ﾊｲｲﾛｱｻﾞﾗｼ/ﾆｼﾝ：BMF=4.3 ・ｻｹ/ﾆｼﾝ：BMF=3.8 ・動物ﾌﾟﾗﾝｸﾄﾝ/底生生物：BMF=7.1 ・ﾎｯｷｮｸﾀﾞﾗ/動物ﾌﾟﾗﾝｸﾄﾝ：BMF=0.04-3.4 ・ﾜﾓﾝｱｻﾞﾗｼ/ﾎｯｷｮｸﾀﾞﾗ：BMF=13.7 ・ﾎｯｷｮｸｸﾞﾏ/ﾜﾓﾝｱｻﾞﾗｼ：BMF=0.3-11 ・多数の調査から、上位捕食者において懸念される濃度の PentaBDE が存在することが示されている。北極圏では、ﾜｼｶﾓﾒ、ﾎｯｷｮｸｸﾞﾏ、ﾜﾓﾝｱｻﾞﾗｼ、ｼﾛｲﾙｶなどの上位捕食鳥類および哺乳類中から高ﾚﾍﾞﾙの PentaBDE が検出されている ・土壌又は底質中のPentaBDEは、容易に食物連鎖に取り込まれ、人など食物連鎖上位者の脂肪組織中に生物濃縮する。	【反復投与毒性】 ラット（90 日）：NOEL 2mg/kg/day 未満 主な毒性は、肝臓肥大等（DE71） 【生殖毒性】 ラット（妊娠♀単回）：0.06mg/kg で児に自発行動変化（多動性） 0.3mg/kg で児に精巣体積・精子数の低値 （BDE99） 【催奇形性】 ラット（妊娠 6 日単回）：0.3mg/kg でばく露の母動物（F1）2 個体から得られた F2 児で、外観・骨格異常 （BDE99） 【その他】 実験動物で甲状腺ホルモン系への影響	【慢性毒性】 ミジンコ *Daphnia magna* ：繁殖阻害が認められた。

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Report of the Persistent Organic Pollutants Review Committee on the work of its second meeting

Addendum

Risk profile on commercial pentabromodiphenyl ether

At its second meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on commercial pentabromodiphenyl ether, on the basis of the draft contained in document UNEP/POPS/POPRC.2/7. The text of the risk profile, as amended, is provided below. It has not been formally edited.

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PENTABROMODIPHENYL ETHER

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its second meeting

November 2006

CONTENTS

Executive Summary

A substantial range of studies on pentabromodiphenyl ether has been identified and the findings summarised in this risk profile. The new findings reported here support the conclusion reached by the Persistent Organic Pollutants Review Committee in 2005 that PentaBDE's properties fulfill the screening criteria in Annex D of the Stockholm Convention.

Commercial pentabromodiphenyl ether (C-PentaBDE) refers to mixtures of bromodiphenyl ether congeners in which the main components are 2,2', 4,4'- tetrabromodiphenyl ether (BDE-47 CAS No. 40088-47-9) and 2,2',4,4',5-pentabromodiphenyl ether (BDE-99 CAS No. 32534-81-9), which have the highest concentration by weight with respect to the other components of the mixture.

Commercial pentabromodiphenyl ether mixtures (C-PentaBDE) are used for flame retardant purposes as additives in consumer products. The commercial mixtures contain brominated diphenyl ether congeners with three to seven bromines in the molecule, but molecules with four and five bromines predominate. The proportion of the different polybromodiphenyl ether (PBDE) congeners in C-PentaBDE varies in different regions of the world.

PentaBDE is released into the environment during the manufacture of the commercial product, in the manufacture of products containing PentaBDE, during their use and after they have been discarded as waste. Even though production of C-PentaBDE is phased out or being phased out worldwide, different products containing it will still be in use in several years to come, resulting in continuing releases to the environment. The products will in the end of their lifetime become wastes with the potential of additional releases.

The main source in North America and Western Europe has been the C-PentaBDE incorporated in polyurethane foam, used in domestic and public furniture. This use is now mainly phased out. The information is too limited to draw conclusions on the importance of other uses, like textiles, electrical and electronic products, building materials, vehicles, trains and aeroplanes, packaging, drilling oil fluid and rubber products. While some representative examples are covered, detailed information on use is lacking for many regions of the world.

Major releases to air are emissions from products during use, through volatilization of PentaBDE and dust-borne PentaBDE. Emissions of PentaBDE can also occur from recycling and dismantling activities such as dismantling of vehicles, buildings and constructions. Emissions can occur from electronic waste recycling plants and shredder plants. Potentially toxic products such as brominated dibenzo-*p*-dioxins and furans might be generated during incineration of articles containing C-PentaBDE.

The releases of PentaBDE are to air, water and soil, but the major part ends up in soil. The distribution between the environmental compartments is: soil>>>water>air. Several studies using sediment cores show that PentaBDE is very persistent in marine sediments, still occurring after 30 years. In the main, PentaBDE in the environment is bound to particles; only a small amount is transported in its gaseous phase or diluted in water but such transport over long periods can be effective in distributing the PentaBDE widely in the environment, especially into Arctic regions. Occurrence in the Arctic environment is demonstrated in several monitoring studies in air and biota.

Due to its high persistency in air, the main route for long-range transport of PentaBDE - as with so many substances that are sufficiently volatile, persistent and bioaccumulative - is through the atmosphere. Modelling and environmental studies indicate that the transport is through a series of deposition/volatilization hops towards the poles but particulate transport is known to be important, too. Long-range transport through water and emigrating animals is also likely.

Several studies show that PentaBDE in soil and sediments is bioavailable, enters the food chain and that it bioaccumulates and biomagnifies in the food webs, ending up in high levels in top predators.

PentaBDE is widespread in the global environment. Levels of components of C-PentaBDE have been found in humans in all UN regions. Most trend analyses show a rapid increase in concentrations of PentaBDE in the environment and in humans from the early 1970s to the middle or end of the 1990s, reaching plateau levels in some regions in the late 1990s, but continuing to increase in others. The levels in North America and the Arctic are still rising. Vulnerable ecosystems and species are affected, among them several endangered species. Some individuals of endangered species show levels high enough to be of concern. Toxicological studies have demonstrated reproductive toxicity, neurodevelopmental toxicity and effects on thyroid hormones in aquatic organisms and in mammals. The potential for the toxic effects in wildlife, including mammals, is evident.

Potential exposure to humans is through food, and through use of products and contact with indoor air and dust. PentaBDE transfers from mothers to embryos and lactating infants. A Canadian assessment of risk quotients suggests that the highest risks accrue to species high in the food chain. Information is lacking on the effects in humans of short-term and long-term exposure, although it is to be expected that vulnerable groups can be pregnant women, embryos and infants. Considerably higher levels are found in humans from North America in general. About 5% of general populations have been found to be subjected to elevated exposure. This, together with the estimates of the long half-life of PentaBDE congeners in humans, raises concern for long-term effects on human health.

Based on the information in this risk profile, PentaBDE, due to the characteristics of its components, is likely, as a result of long-range environmental transport and demonstrated toxicity in a range of non-human species, to cause significant adverse effects on human health or the environment, such that global action is warranted.

1. Introduction

The Stockholm Convention is a global treaty to protect human health and the environment from persistent organic pollutants (POPs), of which twelve are currently listed under the Convention. POPs are chemicals that remain intact in the environment for long periods, become widely distributed geographically, accumulate in living organisms and can cause harm to humans and the environment. Norway, which is a Party to the Stockholm Convention, submitted a proposal in January 2005 to list pentabromodiphenyl ether in Annex A to the Stockholm Convention, and the POPRC agreed that the commercial product 'pentabromodiphenyl ether' ('PentaBDE') – actually a mixture as described below - met the screening criteria of Annex D to the Convention.

1.1 Chemical identity of the proposed substance

Commercial pentabromodiphenyl ether (C-PentaBDE) refers to mixtures of bromodiphenyl ether congeners in which the main components are 2,2', 4,4'- tetrabromodiphenyl ether (BDE-47 CAS No. 40088-47-9) and 2,2',4,4',5-pentabromodiphenyl ether (BDE-99 CAS No. 32534-81-9), which have the highest concentration by weight with respect to the other components of the mixture.

The numbering system for the PBDEs is the same as that used for polychlorobiphenyls (PCBs) (Ballschmiter *et al.* 1993).

The acronym PBDE is used for the generic term polybromodiphenyl ether, covering all congeners of the family of brominated diphenyl ethers. It is sometimes abbreviated to BDE.

1.2 Conclusion of the Review Committee regarding Annex D information

The Committee has evaluated Annex D information at its first meeting in Geneva in November 2005 (UNEP/POPS/POPRC.1/10) and has concluded that the screening criteria have been fulfilled for C-PentaBDE (Decision POPRC-1/3).

1.3 Data sources

This risk profile is elaborated using Annex E information submitted by countries and nongovernmental organizations, national reports from web sites for environment protection agencies in different countries, contact and submissions from Norwegian research institutes, the bromine industry, EMEP and AMAP.

Eleven countries have submitted information (Australia, Brazil, Canada, Japan, Norway, Mexico, Poland, Republic of Lebanon, Spain, Switzerland and United States of America). Seven countries submitted information on production and use. Only one country submitted information on releases; another reported that they did not have release data. All except one country provided monitoring data. There was no information on stock-piles from submitting countries and only a few have submitted information on trade. Two observers submitted information - World Wide Fund for Nature (WWF) and the International POPs Elimination Network (IPEN).

1.4 Status of the chemical under other international conventions

1.4.1 The OSPAR Convention

The Convention for the Protection of the Marine Environment of the North-East Atlantic (the OSPAR Convention) is guiding international cooperation on the protection of the marine environment of the North-East Atlantic. The OSPAR Convention was signed in Paris in 1992 and entered into force on 25 March 1998. The OSPAR Commission is made up of representatives of the Governments of 17 Contracting Parties and the European Commission, representing the European Community. In 1998, the OSPAR Commission placed PBDEs on its “List of Chemicals for Priority Action.” An OSPAR

Commission background document on PBDEs was reviewed by Sweden in 2001. The next full review of this document is not planned before 2008. At the 4th North Sea Conference, it was decided to phase out the use of brominated flame retardants by 2020.

1.4.2 The UNECE Convention on Long-range Transboundary Air Pollution

United Nations Economic Commission for Europe (UNECE) works for sustainable economic growth among its 55 member countries. The UNECE Convention on Long-range Transboundary Air Pollution was signed by 34 Governments and the European Community in 1979 in Geneva. Under it, Parties shall endeavour to limit and, as far as possible, gradually reduce and prevent air pollution including long-range transboundary air pollution. It entered into force in 1983 and has been extended by eight specific protocols. There are today 50 countries that are parties to the Convention. The Protocol for persistent organic pollutants (POPs) was adopted on 24 June 1998 in Aarhus (Denmark). It focuses on a list of 16 substances that have been singled out according to agreed risk criteria, for total ban, elimination at a later stage or restrictive use. C-PentaBDE was nominated as a new POP to the Convention in 2004 by Norway. In December 2005 it was considered by the Executive Body of the Convention to meet the screening criteria for POPs, set out in EB decision 1998/2. They requested that the UNECE Task Force on POPs continue with the review and fuether explore management strategies..

1.4.3. The Rotterdam Convention

The Rotterdam Convention is a multilateral environmental agreement designed to promote shared responsibility and cooperative efforts among Parties in the international trade of certain hazardous chemicals. It is an instrument to provide importing Parties with the power to make informed decisions on which chemicals they want to receive and to exclude those they cannot manage safely.

The text of the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade was adopted at the Diplomatic Conference held in Rotterdam on 10 September 1998. The Convention entered into force on 24 February 2004 and became legally binding for its Parties. Today there are 102 states that are parties to the Convention. The EU notified PentaBDE to the Rotterdam Convention in 2003. For it to become a candidate, bans of the substance must be notified by two parties under the Convention.

1.4.4 Other international forums of relevance

The Arctic Council is a high-level intergovernmental forum that provides a mechanism for addressing the common concerns and challenges faced by the Arctic governments and the people of the Arctic. Member states are Canada, Denmark (including Greenland and the Faeroe Islands), Finland, Iceland, Norway, Russia, Sweden and United States of America. Six international organizations representing many Arctic indigenous communities have the status of Permanent Participants of the Arctic Council.

Significant monitoring and assessment of pollution in the Arctic is performed under the auspices of the Arctic Council (The Arctic Monitoring and Assessment Programme, AMAP). This work is important in identifying pollution risks, their impact on Arctic ecosystems and in assessing the effectiveness of international agreements on pollution control, such as the Stockholm Convention on Persistent Organic Pollutants (POPs). AMAP has shown that PentaBDE is one of the important pollutants of the Arctic.

In the autumn of 2004, the Arctic Council adopted a new Arctic project concerning the reduction of brominated flame retardants. The project will be managed by Norway.

2. Summary information relevant to the risk profile

2.1 Sources

2.1.1. Production and use

Based on the last information on total market demand of C-PentaBDE presented at the Bromine Science and Environmental Forum (BSEF), the estimated cumulative use of C-PentaBDE since 1970 was 100 000 metric tons (tones). The total market demand decreased during the later years of this period, for example from 8,500 tons in 1999 to 7,500 tons in 2001 (BSEF, 2001).

Table 2.1. C-PentaBDE volume estimates: Total market demand by region in metric tons (BSEF, 2001).

	America	Europe	Asia	Rest of the world	Total
1999	8,290	210	-	-	8,500
2001	7,100	150	150	100	7,500

These consumption figures need to be seen in the context of the global demand for polybrominated flame retardants of all types, which vastly outweighs the demand for C-PentaBDE. Thus, world totals of PBDE were 204,325 (1999), 203,740 (2001), 237,727 (2002) and 223, 482 (2003) tonnes (BSEF 2006).

C-PentaBDE has been produced in Israel, Japan, U.S. and EU (Peltola *et al.* 2001 and van der Goon *et al.* 2005). Since 2001 actions to regulate or voluntarily phase-out C-PentaBDE have been conducted in several countries.

Production in EU ceased in the former EU (15) in 1997 (EU 2000). Usage in the EU (15) has been declining during the second half of the 1990s and is estimated to be 300 metric tonnes in 2000 (used solely for polyurethane production) (EU 2000). The use of PentaBDE was banned in the EU (25) in 2004. Use in electrical and electronic appliances ceased on 1 July 2006.

In the United States of America, in June 2006, the U.S. Environmental Protection Agency (EPA) issued a significant new use rule on tetra-octaBDE and any combinations of these chemicals resulting from a chemical reaction, which requires persons to notify EPA before commencing manufacture or import for any use. C-PentaBDE will be banned in the state of California from 2008. The sole US manufacturer voluntarily ceased production, but use may be continuing and will cease only when stocks are fully exhausted. Although a patent on production of C-PentaBDE was taken out in China as recently as 1999 for a PBDE mixture that differs from the traditional penta-mix, the substance is being phased out in that country. Remaining production in China is estimated as less than 100 MT/year and will cease in 2007 when the substance is banned in that country.

A major bromine producer in Israel, Israel Chemicals and Industrial Products (formerly the Dead Sea Bromine Group), declares in a public statement on its web site that their products do not contain PentaBDE. This aligns the producer with the ban in the EU, which is an important market for the company's flame retardants.

There is today no production in Japan. The use of C-PentaBDE was voluntarily withdrawn from the Japanese market in 1990 (Kajiwara et al. 2004). Some developing countries around the East China Sea are potential "hot spots" releasing PentaBDE into the marine environment (Ueno *et al.* 2004). Many industrial manufacturers of computers, television sets and other electric household equipment are situated in the coastal areas of Asian developing countries (Ueno *et al.* 2004). There are indications on a phase-out of C-PentaBDE in manufacture of new electrical and electronic products in the Asian

region, although uses there were always subsidiary to the major uses in polyurethane foams. The extent of this is uncertain. Waste electric products used in developed countries have been exported to Asian developing countries, such as China, India and Pakistan. This waste material has been recycled for recovery of valuable metals (Ueno *et al.* 2004) and continuation of this trade can remain a source to PentaBDE releases. No restrictions have so far been implemented in developing countries in the Asia Pacific and the southern hemisphere.

The release of 'banked' PentaBDE during recycling of foam products has its parallel in the release of CFCs and other ozone depleting substances which have similarly remained in the foam during its useful lifetime.

Results from a survey of Canadian industries regarding certain substances on the country's Domestic Substances List conducted for the year 2000 indicated that no PBDEs were manufactured in Canada, but approximately 1300 tonnes of C-PentaBDE (for incorporation into finished articles) was imported into the country (Environment Canada 2003). Based on quantities reported, C-PentaBDE was the PBDE imported in greatest volume, followed by the commercial decabromodiphenyl ether product. A very small amount of octabromodiphenyl ether was imported in 2000. The volumes reported do not include quantities imported in finished articles. In 2004, it was proposed that PentaBDE be added to the Virtual Elimination list in Canada.

In the U.S. the sole producer voluntarily ended their production of C-PentaBDE in 2004. In 2001 alone, almost 70,000 metric tons of PBDEs were produced globally, almost half of which was used in products sold in the US and Canada. Before the phase-out in U.S. the majority of C-PentaBDE formulation produced globally was used in North America (>97 %). At the end of 2004 in the US, approximately 7.5% of the more than 2.1 billion pounds of flexible polyurethane foam produced each year in the US contained the C-PentaBDE formulation (Washington State 2005).

In Australia in 2004, the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) advised that all importers were phasing out imports of PentaBDE by the end of 2005, and this was reconfirmed by the major importers in mid-2005.

C-PentaBDE is used or has been used in the following sectors (Alaee *et al.* 2003, Danish EPA 1999, EU 2000, Prevedouros *et al.* 2004b, Swiss Agency for the Environment 2002, Birnbaum and Staskel, 2004):

- Electrical and electronic appliances (EE appliances) – computers, home electronics, office equipment, household appliances and other items containing printed circuit laminates, plastic outer casings and internal plastic parts such as small run components with rigid polyurethane elastomer instrument casings.
- Traffic and transport – cars, trains, aircraft and ships containing textile and plastic interiors and electrical components.
- Building materials – foam fillers, insulation boards, foam insulation, piples, wall and floor panels, plastic sheeting, resins etc.
- Furniture – upholstered furniture, furniture covers, mattresses, flexible foam components.
- Textiles – curtains, carpets, foam sheeting under carpets, tents, tarpaulins, work clothes and protective clothing.
- Packaging – polyurethane foam based packaging materials.

The most common use, accounting for 95-98% of C-PentaBDE since 1999, has been in polyurethane foam (Hale *et al.* 2002). This foam may contain between 10 and 18% of the C-PentaBDE formulation. Polyurethane foam is mainly used for furniture and upholstery in domestic furnishing, automotive and

aviation industry. Other uses are in rigid polyurethane elastomers in instrument casings, in epoxy resins and phenolic resins in electrical and electronic appliances, and construction materials. For some years now, the more highly brominated Deca-BDE has been preferred in these applications. C-PentaBDE has also been incorporated in minor amounts in textiles, paints, lacquers, in rubber goods (conveyer belt, coating and floor panels) and in oil drilling fluids. Levels range from 5-30% by weight. Up to the early 1990s, C-PentaBDE was used in printed circuit boards, usually FR2 laminates (phenolic resins) in Asia. Such FR2 laminates are used in household electronics (television, radio, video), vehicle electronics, white goods (washing machines, kitchen appliances, for example). In the early 1990s the amount C-PentaBDE used in textile treatment was 60 % of total use in the EU, but this application is now banned.

C-PentaBDE has been identified as an additive flame retardant in textiles in national substance flow analyses in the ECE region (Danish EPA 1999). Manufacturers of furniture textiles have stated that the textile contained 0.45% PentaBDE in a Norwegian flow analysis reported in 2003. Stringent rules on flammability apply to textiles used in the public sector, the transport sector and business sector, but rules for domestic use are less consistent.

According to information obtained from the bromine industry the use of C-PentaBDE as hydraulic fluid (as a component of a mixture) in petroleum borings and mining was discontinued 10-20 years ago.

Australia has reported uses in manufacture of polyurethane foams for refrigerators and packaging, and in epoxy resin formulations supplied into aerospace market and for use as potting agents, laminating systems and adhesive systems. The US has reported use of C-PentaBDE in the aircraft industry. There is no use of C-PentaBDE in newer aircraft, and thus no exposure of the public, but C-PentaBDE is still used in military aircraft.

2.1.2 Global demands for brominated flame retardants in the future

According to a market analyst consulting company, the global demand for flame retardants is expected to grow at 4.4% per year, reaching 2.1 million metric tons in 2009, valued at $4.3 billion. Growth will largely be driven by gains in developing countries in Asia (China, in particular), Latin America and Eastern Europe. Strong increases are forecast for most of the flame retardants. Globally, demand will be greatest for bromine compounds, due mainly to strong growth in China. Electrical and electronic uses will grow fastest. Higher value products will continue to make inroads as substitutes for less environmentally friendly compounds, especially in Western Europe, and chlorine compounds will begin to be replaced in China by bromine- and phosphate-based and other flame retardants (Fredonia Group 2005).

After a severe falloff in demand in 2001, electrical and electronic applications will continue to recover. Demand growth for flame retardants will be strongest in such applications. As electronic circuits become smaller, and more densely packed electronics are subjected to ever higher temperatures, the need for flame retardants will increase. Construction markets will be the second fastest growing globally, but in China second place will be held by motor vehicles, followed by textiles, both of which industries are growing rapidly in that country. Plastics will continue to replace other materials such as metals and glass in a wide range of products, in order to lower both cost and weight and to allow improved design and more flexible production. Plastic usage is already widespread and growing in fields such as transportation, building products and electronics. Plastics must be made flame retardant for many applications, and as a result some 75% of all flame retardants are used in plastics (Fredonia Group 2005).

Environmental restrictions vary by region. In Western Europe, Japan and to a lesser extent in North America, such restrictions will especially limit growth of chlorinated compounds. A ban on some brominated flame retardants in Western Europe is not expected to spread substantially to other regions, but it will drive the development of alternatives in electrical and electronic equipment for sale on the world market. Dozens of Asian, European and US companies announced in 2005 that they have

developed or are developing electrical and electronic equipment that does not contain C-PentaBDE. In Asia, 51% of electronic manufacturers already make products compliant with the ban on PentaBDE in the EU, and 42% expected to have products that are compliant by 1 July 2006. Officials from electronics companies and industry consultants expected that the difficulty of keeping product streams separate would ensure that most electronic equipment sold on the world market would be compliant by 2005 (International Environment Reporter 2006).

2.1.3 Releases to the environment during production

PentaBDE is released into the environment during the manufacturing process, in the manufacture of products, during their use and after they have been discarded as waste. In addition to working towards a manufacturing process that does not cause emissions, it is also important to consider the contributions of emissions from products during use as well as after they have been discarded. Most of the PentaBDE is released as diffuse pollution during and after the service life of articles incorporating C-PentaBDE and as small-scale point source pollution from the waste management chain of the end products.

PentaBDE is synthesised from diphenyl ether by brominating it with elemental bromine in the presence of a powdered iron Friedel-Craft catalyst. The producers of PentaBDE have reported that the major routes of PentaBDE from this process to the environment are filter waste and rejected material, both of which are disposed of in landfills. Waste water releases of PentaBDE may also occur from spent scrubber solutions (Peltola *et al.* 2001).

According to the EU risk assessment of PentaBDE, the emissions in polyurethane production are assumed to occur prior to the foaming process, when handling the additives (discharges to water) and during the curing (emissions to air). Releases to air may occur during the curing phase of foam production, during which the foam stays at elevated temperature for many hours, depending on the production block size. Emission to air at this stage is estimated to be 1 kg/tonne PentaBDE, but it is assumed that some of the volatilized PentaBDE condenses in the production room and ends up in the waste water. The EU risk assessment concludes that 0.6 kg of PentaBDE is released in this way, and 0.5 kg into air, for each tonne of C-PentaBDE used in polyurethane foam production.

Table 2.2 Global production and use of C-PentaBDE in polyurethane foam production, and estimation of associated releases in 2000 (foam containing 10-18% PentaBDE).

Polyurethane foam production	**Quantity of PentaBDE**	**Release of PentaBDE into waste water**	**Emissions of PentaBDE to air during production**
150,000 tonnes/year	15,000-27,000 tonnes/year	9,000-16,200 kg/year	7,500-13,500 kg/year

An important source of release has been associated with the use of liquid flame retardant additives such as C-PentaBDE in production of polymer foams. Approximately 0.01% (that is, 100 g /tonne) of the raw material handled during mixing is estimated to be released to wastewater. There is also potential for release due to volatilization during the curing phase as described above, since foam reaches temperatures of 160^{o}C for several hours. Wong *et al.* (2001) examined the atmospheric partitioning characteristics of BDEs 47, 99 and 153, and predicted that tetra- and pentabromo-congeners will become gaseous at warmer air temperatures. Therefore, although the low measured vapour pressure values for the PBDEs indicate that volatilization is minimal at normal air temperatures, there is potential for release to air at the elevated temperatures reached during curing (European Communities 2001). The European Communities (2001) study estimates the overall release of PentaBDE to be approximately 0.11%, with about one half of this going to air and the other half to wastewater.

2.1.4 Releases to the environment during product use

C-PentaBDE is used solely as an additive in physical admixture with the host polymer, and can thus migrate within the solid matrix and volatilize from the surface of articles during their life cycle (EU 2000). Approximately 3.9 % of the PentaBDE present in articles was estimated to be released each year through volatilization during their assumed service life of 10 years in the EU risk assessment, but each congener will have its own characteristic migration and volatility coefficients. Based on the quantities of shown in Table 2.2, and the 3.9% loss rate, it can estimated that 585-1053 tonnes of PentaBDE enters the environment in this way each year.

Wilford *et al.* (2003) conducted controlled chamber experiments in which they passed air through samples of C-PentaBDE -treated foam products containing 12% PBDE w/w. They found that PBDEs volatilized from polyurethane foam at measurable levels. Average total PBDE levels of 500 ng/m^3/g foam were released from the chamber. For BDE-47, BDE-99 and BDE-100 (4,5 and 5 bromines, respectively), the loss rates were 360, 85 and 30 ng/m^3/g foam, respectively. The average temperature range during sampling was 30-34^{o}C.

Given the use of C-PentaBDE in domestic items such as furniture, carpeting and appliances, exposure to indoor air house dust containing PentaBDE has been examined in a number of studies (Shoeib *et al.* 2004, Wilford *et al.* 2005). US researchers (Stapleton *et al.* 2005) report results for a study conducted in 2004 in the Washington, DC, metropolitan area and one home in Charleston, South Carolina. The concentrations of PBDEs in house dust from sixteen homes ranged from 780 ng/g dry mass to 30,100 ng/g dry mass. The dominant congeners were those associated with C-PentaBDE and DecaBDE. It was estimated that young children (1-4 years) would ingest 120-6000 ng/day of PBDEs. For five of the homes, clothes dryer lint was also analyzed, showing PBDE concentrations of 480-3080 ng/g dry mass. The exposures are higher than those observed in Europe, a fact that the researchers attribute to the fact that most markets for C-PentaDBE has been in the United States.

The information in the preceding paragraph highlights the fact that while PentaBDE can volatilize from the products in which it is incorporated, as well as during their whole life-cycle, and during recycling or after disposal, a major route for dissemination of this chemical into the environment will be in the form of particles on which it is absorbed or adsorbed. When emitted from products, the flame retardants are likely to adsorb to particles, and these may adhere to surfaces within appliances or on other surfaces in the indoor environment, or they may spread to the outdoor environment during airing of rooms. Industrial environments where equipment is dismantled may suffer much higher exposures (Danish EPA 1999). There are also releases from products due to weathering, wearing, leaching and volatilization at the end of their service life during disposal or recycling operations (dismantling, grinding or other handling of waste, transport and storage, for example). The annual releases in the EU region from the product life-cycle of polyurethane products were estimated to be distributed among the different compartments as follows: 75% to soil, 0.1% to air and 24.9% to surface water (EU 2000).

The inclusion of C-PentaBDE in materials used for car undercoating, roofing material, coil coating, fabric coating, cables, wires and profiles, and shoe soles can result in slow release to the environment. Emission factors for such releases in the EU risk assessment were judged to be 2-10% during the lifetime of the product, with the higher factors applying to uses with high wear rates such as car undercoating and shoe soles. A further 2% was assumed to be emitted during disposal operations. Taking these into account, the losses in the EU region were estimated to be 15.86 tonnes/year to soil, 5.26 tonnes/year to surface water, and 0.021 tonnes/year to air. No actual measurements were found in the literature with which one might compare these estimates.

Hale *et al.* (2002) demonstrated that flame-retardant treated polyurethane foam exposed to direct sunlight and typical Virginia summer conditions with temperatures up to 30-35^{o}C and humidity of 80% or greater, became brittle and showed evidence of disintegration within four weeks. The authors postulate that the resulting small, low density foam particles would be readily transportable by

stormwater runoff or air currents. Such degradation processes may provide an exposure route to organisms via inhalation or ingestion of the foam particles and their associated PentaBDE.

2.1.5 Emissions from waste containing C-PentaBDE

Waste can be generated from production of C-PentaBDE, from processes for manufacture of C-PentaBDE -containing materials, and from end-of-service-life management of products containing PentaBDE.

In production, the C-PentaBDE producers have stated that the major source of release was from filter waste and reject material, but quantities are small to negligible. In general, the waste was disposed of to landfill (EU 2000), although it is noted that waste containing more than 0.25% PentaBDE is classified as 'hazardous waste'.

After curing and cooling, blocks of polyurethane foam generally have to be cut to the required size, although for some applications the foam is produced in a mould of the desired shape so cutting is not required. Some flame retardant is lost in the scrap foam that results from the cutting process. Such foam scrap is often recycled into carpet underlay (rebond), particularly in the United States. Interestingly, the EU exports about 40,000 tonnes/year of scrap foam to the US for such use (EU 2000). In other uses, scrap foam is ground and used as filler in a number of applications such as cars eats or used for addition to virgin polyol in slab foam production. It is also possible that some foam scrap will be disposed of to landfill, or even incinerated.

During the production of printed circuit boards a substantial part of the laminate is cut off and becomes solid waste. In most countries, however, C-PentaBDE is no longer used in this application. There is limited information about waste generated in other applications of C-PentaBDE, such as its use in electrical and electronic appliances. While some such appliances are recycled on account of their metal content, many are burned in municipal waste incinerators and this often the fate of non-metallic portions of this waste stream. In the EU, from December 2006, plastics containing brominated flame retardants must be separated from such waste prior to recovery and recycling.

Used vehicles, often containing solid or foam components with C-PentaBDE are stored outdoors and then dismantled in shredder plants. In some countries, restrictions require that components containing substances like PentaBDE be treated as hazardous waste. Wastes generated from production of building materials, textiles and furniture are disposed of in landfills, or incinerated. This is easy enough for small, easily dismounted components, but most material containing flame retardants is harder to segregate and so these materials end up in the waste from shredder plants and are usually landfilled.

Movement of polymer foam particles containing PentaBDE within the landfill could provide a mechanism for transport of the brominated material to leachate or groundwater. It is not currently possible to assess the significance of such processes. However, given the physico-chemical properties of the substance, it is considered unlikely that significant amounts of PentaBDE will leach from landfills, since it has low water solubility, high octanol-water partition coefficient, and adsorbs strongly to soils (EU 2000). Norwegian screening studies have found levels of PentaBDE of concern in landfill leachates (Fjeld *et al.* 2003, Fjeld *et al.* 2004, Fjeld *et al.* 2005). The quantity of PentaBDE disposed of annually in the EU, and going to landfill or incineration, is estimated to be approximately 1,036 tonnes (EU 2000).

In a Dutch project, the emissions of PentaBDE in the EMEP region were estimated and distribution between sources was as follows: 0.33 tonnes/year from industrial combustion and processes, 9.45 tonnes/year from solvent and product use and 0.05 tonnes/year from waste incineration (van der Gon *et al*. 2005).

At the operating temperatures of municipal waste incinerators almost all flame retardants will be destroyed, but based on experience with other organic compounds, trace amounts could be passing the combustion chamber (Danish EPA 1999). Studies of recipients to municipal solid waste incinerators have detected above-background levels of PentaBDE in both gaseous and particulate fractions in the air in the vicinity of the facility (Agrell *et al.* 2004, Law 2005, ter Schure *et al.* 2004b). Potentially toxic products like brominated dibenzo-*p*-dioxins and dibenzofurans may be produced during incineration of articles containing C-PentaBDE (Danish EPA 1999, Ebert and Bahadir 2003, Weber and Kuch 2003, Birnbaum and Staskel 2004) and possibly released to the environment.

Analyses of dismantled FR2 circuit boards in electrical scrap show that about 35% of the PBDE used was PentaBDE, and for estimation purposes it was assumed that 25% of FR2 laminates in older appliances had been treated with the C-PentaBDE (Swiss agency 2002). Prevedouros *et al.* (2004) estimated production, consumption, and atmospheric emissions of PentaBDE in Europe between 1970 and 2000 based on literature data. According to that study, the flow of PentaBDE in discarded electrical and electronic appliances in Europe is in the range 17-60 metric tons per year for the period 2000-2005. However, a Swiss experimental study of such flow in a modern recycling plant showed values higher than expected on the basis of the literature study. This could mean that the literature has under-estimated the PBDE content of such appliances, and the study acknowledges that companies seldom provide all the information necessary to make accurate estimates (Swiss agency 2002). This same study reported a flow analysis for the life cycles of Penta-, Octa- and Deca-BDE as well as tetrabromobisphenol A (TBBPA). Waste electrical and electronic equipment was the biggest contributor, ahead of automotive shredder residues and construction waste. The plastics in vehicles produced in 1980 contained 0.089 g/kg of PentaBDE (excluding that contained in electrical and electronic components), whereas plastic in those built in 1998 had 0.044 g/kg. At the beginning of this period, almost all unsaturated polyurethane resins were treated with brominated flame retardants, primarily DecaBDE and TBBPA, but also PentaBDE. Even larger quantities, up to 50 g PentaBDE/kg of resin, were used in rail vehicles produced in 1980.

The average concentration of PentaBDE in appliances is estimated to be 34 mg/kg, with the highest concentration – 125 mg/kg – in the plastic fraction (Morf *et al.* 2005). In plants with off-gas filtering, a large proportion of the PentaBDE will be found in the collected fraction (Morf *et al.* 2005). On the other hand, in a facility without an efficient air pollution control device such as that in the modern facility studied, a significant flow of dust-borne PentaBDE may be released to the environment. A case in point was presented by Wang *et al.* (2005), who detected levels of PentaBDE in soil and sediment collected in the vicinity of an open electronic waste disposal and recycling facility located in Guiyu, Guandong, China.

The Swiss study showed that 5% of polyurethane foams produced in 1990 were used in the building industry, and contained up to 220 g/kg of C-PentaBDE. About 10-20% of the thermoplastic sheeting used in construction was treated with brominated flame retardants at levels of 1.3-5% by weight (Danish EPA) but no information about C-PentaBDE content is available. Some polyvinyl chloride sheeting would also have been treated with C-PentaBDE, typically at 49 g/kg. PentaBDE can be assumed to be emitted during dismantling activities but no information is available about the extent of such emissions.

2.2 Environmental fate

2.2.1 Persistence

Estimated half-life values of PDBE in different environmental compartments are scarce in the literature. In table 2.3 half-life estimates found in literature are summarized.

*Table 2.3 Half-lives of PentaBDE (**BDE-99**) in different environmental compartments, estimated with the use of Syracus Corporation's EPIWIN program.*

Environmental compartment	Half-life estimate (d)	References
Soil	150	Palm 2001, Palm *et al.* 2002
Aerobic sediment	600	Palm 2001, Palm *et al.* 2002
Water	150	Palm 2001, Palm *et al.* 2002
Air	19 11	Palm *et al.* 2002 Vulykh *et al.* 2004

It is noted that caution should be used in relying on half-life estimates derived from this program, now called EPI Suite (http://www.epa.gov/opptintr/exposure/docs/episuite.htm). The EPI Suite's intended use is chemical screening only and may not be appropriate for consideration of substances for global control. Because of interest in this matter, it is likely that half-life data from new studies will be published but the picture provided by existing data seems unlikely to change substantially. The nature of degradation products of the PBDEs is also likely to be elucidated in future, leading to consideration of their toxicity.

With respect to biodegradation, Tetra-, Penta- and Hexa-BDE are predicted to be "recalcitrant" by the BIOWIN program. Using the EPIWIN program, estimated half-lives for PentaBDE are 600 days in aerobic sediment, 150 days in soil, and 150 days in water (Palm 2001). This degree of persistence is supported by the fact that no degradation (as CO_2 evolution) was seen in 29 days in an OECD 301B ready biodegradation test using PentaBDE (Schaefer and Haberlein 1997).

Schaefer and Flaggs (2001) carried out a 32-week anaerobic degradation study using a mixture of ^{14}C-labelled and unlabelled BDE-47 (a TetraBDE) incorporated into sediments. The study showed that <1% of the total radioactivity was recovered as $^{14}CO_2$ and $^{14}CH_4$, indicating that essentially no mineralization had occurred. Overall, the study found that levels of degradation were not statistically significant; however, the HPLC analytical method with radiometric detection indicated that some products had been formed in the 32-week samples. Between one and three such peaks were identified in 26 of 42 samples analyzed. Work is underway to identify these products. It is likely that BDE-47 has the potential to degrade very slowly under anaerobic conditions.

Several studies using sediment cores show that PentaBDE congeners deposited in European marine sediments at the beginning of 1970s are still present in significant amounts, indicating high persistency in sediments (Covaci *et al.* 2002a, Nylund *et al.* 1992, Zegers *et al.* 2000, Zegers *et al.* 2003). The industrial production and use in Europe started in the beginning of the 1970s, with a reduction in more recent years. This is reflected in the sediment core profiles, with no occurrence before this date, and an increase in levels after, with a levelling off in more recent years. In the most recent studies (Zegers *et al.* 2003) sediment cores from Norway, the Netherlands and Germany
were studied. Concentrations of PBDEs, normalized to total organic carbon content, were in the range 10-20 µg/g total carbon.

2.2.2 Bioaccumulation

2.2.2.1 Studies on bioaccumulation and biomagnification in local food webs

Several studies have focused on PentaBDE's potential for bioaccumulation and biomagnification. The studies show an increase of concentrations in biota with increasing trophic level in pelagic and Arctic food webs. The calculated bioconcentration factors (BCFs), bioaccumulation factors (BAFs) and biomagnification factors (BMFs) indicate PentaBDE's potential for bioaccumulation and biomagnification. In Table 2.4 the calculated values in the literature are summarized. The octanol/water

partition coefficient (log K_{OW}) for PentaBDE in those studies is 6.5 – 7.4. The more recent studies are described in the following text.

Table 2.4 Calculated bioaccumulation factors (BAFs) and biomagnification factors (BMFs) for one PentaBDE (BDE-99) in the literature from environmental studies in pelagic and Arctic food webs. The data are calculated using the mean lipid weight concentrations, except for the study performed by Sørmo et al. 2006, in which the values in brackets are BMFs calculated from mean whole body concentrations.

Variable	Organism	Area	Value	Reference
BAF	*Dreissena polymorpha*	Lake Mälaren, Sweden	1.8	Lithner et al. 2003
BMF	Guillemot egg/herring	Baltic sea	17	Sellström 1996
	Grey seal/herring	Baltic sea	4.3	Sellström 1996
	Salmon/sprat	Baltic sea	10	Burreau *et al.* 1999
	Salmon/sprat	Baltic sea	5.9	Burreau *et al.* 2000
	Atlantic Salmon/Small Herring	The Northern Atlantic Sea	3.8	Burreau *et al.* 2000
	Net plankton/Benthic organisms	Lake Ontario, Canada	7.1	Alaee *et al.* 2002
	Benthic organisms/Forage fish	Lake Ontario, Canada	0.8	Alaee *et al.* 2002
	T. libellula/Copepods	Svalbard, Arctic Norway	0.65 (1.3)	Sørmo *et al.* 2006
	G.wilkitzkii/Copepods	Svalbard, Arctic Norway	47.6 (19.0)	Sørmo *et al.* 2006
	Polar cod/Copepods	Svalbard, Arctic Norway	2.1 (1.6)	Sørmo *et al.* 2006
	Polar cod/*T. inermis*	Svalbard, Arctic Norway	1.9 (1.2)	Sørmo *et al.* 2006
	Polar cod/*T. libellula*	Svalbard, Arctic Norway	3.4 (1.3)	Sørmo *et al.* 2006
	Polar cod/*G.wilkitzkii*	Svalbard, Arctic Norway	0.04 (0.1)	Sørmo *et al.* 2006
	Ringed seal/*T. inermis*	Svalbard, Arctic Norway	26.8 (54.5)	Sørmo *et al.* 2006
	Ringed seal/*T. libellula*	Svalbard, Arctic Norway	43.1 (60.0)	Sørmo *et al.* 2006
	Ringed seal/*G.wilkitzkii*	Svalbard, Arctic Norway	0.6 (3.9)	Sørmo *et al.* 2006
	Ringed seal/Polar cod	Svalbard, Arctic Norway	13.7 (56.6)	Sørmo *et al.* 2006
	Polar bear/Ringed seal	Svalbard, Arctic Norway	0.3 (0.29)	Sørmo *et al.* 2006
	Polar bear/Ringed seal	Arctic Canada	3.4	Muir *et al.* 2006
	Polar bear/Ringed seal	Arctic Canada	11	Muir *et al.* 2006
	Polar bear/Ringed seal	Arctic Canada	8.0	Muir *et al.* 2006
	Polar bear/Ringed seal	Greenland	1.0	Muir *et al.* 2006
	Polar bear/Ringed seal	Svalbard, Arctic Norway	5.9	Muir *et al.* 2006

PBDE analyses of zebra mussels (*Dreissena polymorpha*) were included in a larger study undertaken in and around the city of Stockholm, Sweden (Lithner *et al.*, 2003). Mussels were collected from a background site and transplanted in baskets to other downstream sites in Lake Mälaren, Saltsjön and in several small lakes. Freshwater flows from Lake Mälaren, through the middle of Stockholm, then out into the brackish Baltic Sea via Saltsjön. Five PBDE congeners (BDE-47, BDE-99, BDE-100, BDE-153 and BDE-154) were determined. The congener pattern was dominated by BDE-47 and BDE-99 (four and five bromines, respectively) and was similar to the C-PentaBDE. Bioaccumulation factors (BAFs) for the various compounds studied were estimated using data from suspended particulate matter (SPM) collected in sediment traps in 1998-99 at the same sites in Riddarfjärden and Saltsjön (Broman *et al.*, 2001). The concentrations on SPM were assumed to reflect water concentrations. BAFs were calculated using lipid weight concentrations in mussels and organic carbon based concentrations in the SPM.

When compared to other compounds (PCBs, DDTs, HCB), the BDEs had the highest BAFs, ranging from 1 to 2. The BAF (= level in mussel/level in SPM) for PentaBDE was 1.8.

Concentrations of BDE-47 and BDE-99 in Lake Ontario pelagic food web show increasing concentrations with increasing trophic position (Alaee *et al.* 2002). In this study, concentrations of PBDEs in archived plankton, *Mysis*, *Diporeia*, alewife, smelt, sculpin and lake trout samples collected in 1993 were determined. The trophodynamics of PBDEs in the Lake Ontario pelagic food web were also investigated. Lake Ontario pelagic food web consists of three trophic levels. The lake trout (*Salvelinus namaycush*) is a top predator fish species in Lake Ontario, feeding on forage fish including alewife (*Alosa pseudoharengus*), rainbow smelt (*Osmerus mordax*) and slimy sculpin (*Cottus cognatus*); in turn these fish feed on *Mysis* and *Diporeia*, which feed on phytoplankton, and zooplankton sampled as net plankton. Concentrations were increasing at each step up the food chain. The exception to this trend was the biomagnification of BDE-99 from benthic organisms to forage fish, which had a biomagnification factor of 0.8. This is an indication of the breakdown of BDE-99. In fact, the PBDE profile in the plankton; *Mysis* and *Diporeia* resembled the C-PentaBDE formulation, which indicates that BDE-99 bioaccumulates in the invertebrates and starts to be metabolized by forage fish.

Further studies of metabolism involving reductive debromination are discussed in Section 2.3.5.

Whittle *et al.* (2004) conducted surveys of PBDE levels in fish communities of Lake Ontario and Lake Michigan in 2001 and 2002 and evaluated biomagnification in the local pelagic food web (net plankton/*Mysis*/*Diporeia* → forage fish (smelt/sculpin/alewife) → lake trout). Their analysis, which included a total of forty one PBDE congeners, showed that BDE 47, 99 and 100 were prominent at each trophic level. The biomagnification factors (BMFs) representing total PBDEs for forage fish to lake trout ranged from 3.71 to 21.01 in Lake Michigan and from 3.48 to 15.35 in Lake Ontario. The BMF for plankton to alewife as 22.34 in Lake Ontario.

A recent study of an Arctic food chain shows the same result (Sørmo *et al.* 2006) as Alaee´s study. Concentrations of PBDEs were investigated in an Arctic marine food chain, consisting of four invertebrate species, polar cod (*Boreogadus saida*), ringed seals (*Pusa hispida*) and polar bears (*Ursus maritimus*). The most abundant PBDEs, BDE-47 and BDE-99, were found in detectable concentrations even in zooplankton, the lowest trophic level examined in this study. Most of the investigated PBDEs biomagnified as a function of tropic level in the food chain. A noticeable exception occurred at the highest trophic level, the polar bear, in which only BDE-153 was found to increase from its main prey, the ringed seal, indicating that polar bears appear to be able to metabolize and biodegrade most PBDEs. The authors suggested that this discrepancy in the fate of PBDEs among the different species may be related to greater induction of oxidative detoxification activities in the polar bear. Absorption and debromination rates may be more important for bioaccumulation rates of PBDEs in zooplankton, polar cod and ringed seals. BDE-99 showed no biomagnification from pelagic zooplankton to polar cod, probably as a consequence of intestinal or tissue metabolism of BDE-99 in the fish. Also among pelagic zooplankton, there was no increase in concentrations from calanoid copepods to *T. libellula*. Lipid-weight based concentrations (LWCs) and whole-body based concentrations (WBCs) of PBDEs were used to assess biomagnification factors (BMFs). Whole body concentrations gave the most realistic BMFs, as BMFs derived from LWCs seem to be confounded by the large variability in lipid content of tissues from the investigated species. This study demonstrates that PentaBDEs have reached measurable concentrations even in the lower trophic levels (invertebrates and fish) in the Arctic and biomagnifies in the polar bear food chain.

Polybrominated diphenyl ethers (PBDEs) were determined in adipose tissue of adult and sub-adult female polar bears sampled between 1999 and 2002 from sub-populations in Arctic Canada, eastern Greenland, and Svalbard, and in males and females collected from 1994 to 2002 in northwestern Alaska (Muir et al. 2006). Only four congeners (BDE-47, BDE-99, BDE-100, and BDE-153) were consistently identified in all samples. BDE-47 was the major PBDE congener representing from 65% to 82% of the

ΣPBDEs. Age was not a significant covariate for individual PBDEs or ΣPBDE. Higher proportions of BDE-99, BDE-100, and BDE-153 were generally found in samples from the Canadian Arctic than from Svalbard or the Bering- Chukchi Sea area of Alaska. All four major PBDE congeners were found to biomagnify from ringed seals to polar bears. The polar bear-seal BMFs were relatively consistent despite the large distances among sites. The exceptions were the BMFs for BDE-99, BDE-100, and BDE-153 in East Greenland which had lower BMFs than those at all other sites. This may imply differences in the transformation of PBDEs in the marine food web leading to polar bears or to food web differences. Species differences in bioaccumulation and biotransformation of PBDEs have been noted for fish and this could lead to differences in congener patterns in fish-eating mammals and their predators.

Studies of the biomagnification of Tri- to DecaBDEs were carried out in three different food chains, two in the Baltic Sea and one in the Atlantic Ocean (Law 2005). All of Tri- to HeptaBDE congeners biomagnified, but the maximum biomagnification was for the PentaBDEs.

Matscheko *et al.* (2002) investigated the accumulation of seven PBDEs, eight PCBs and polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCCD/Fs) by earth worms collected from Swedish soils in spring and autumn 2000. The selected sampling sites were agricultural lands receiving applications of sewage sludge, and a field flooded by a river known to contain the target substances in its sediment. Reference sites were rural and urban soils with no known sources of the target substances other than background. Earthworms (primarily *Lumbricus terrestris*, *Lumbricus spp*, *Aporrectodea caliginosa, A. rosea* and *Allolobophora chlorrotic*) were collected from all field sites, starved for 24 h to clear gut contents, and then analyzed for the presence of the target substances. Biota-soil accumulation factors (BSAFs) were calculated as the ratio of concentration of target substance in worm lipids to that in soil organic matter. BSAFs for BDE-47, BDE-66, BDE-99 and BDE-100 ranged from 1 to 10. They were comparable to those determined for the PCBs but higher than those for PCCD/Fs. BSAFs of greater than 10 were determined at one agricultural site, where factors of 11, 18 and 34 were calculated for BDE 99, 47 and 100 respectively. Data collected for BDE-153, BDE-154 and BDE-183 were not used, as levels in the earthworm blanks were deemed to be unacceptable high.

2.2.2.2 Monitoring results indicating bioaccumulation

A large range of studies show concentrations of concern in top predators. High levels in top predators are usually an indication on the potential of a compound to bioaccumulate in the top predator food chain.

Several studies (Jaspers *et al.* 2004, Herzke *et al.* 2005, Lindberg *et al.* 2004, D`Silva *et al.* 2004, Law *et al.* 2005, Sinkkonen *et al.* 2004, Sellström *et al.* 2003) indicate that PentaBDE is widespread in top predatory birds in Europe, such as peregrine falcon (*Falco pereg*rine), merlin (*Falco columbarius*), goshawk (*Accipiter gentiles*), golden eagle (*Aquila chrysaetos*), and buzzard (*Buteo buteo*). High levels are detected in top predatory eggs of white-tailed sea eagle, peregrine falcon, osprey, and golden eagle (Herzke et al. 2005, Lindberg *et al.* 2004). High levels have also been detected in European harbour porpoises (*Phocoena phocoena*) (Thron *et al*. 2004 and Covaci *et al.* 2002).

In the Arctic, C-PentaBDE is detected in high levels in top predatory birds and mammals (Verrault *et al.* 2005, Verrault *et al.* 2004, Norström *et al.* 2002, Herzke *et al.* 2003, Vorkamp *et al.* 2004a and b, Wolkers *et al.* 2004, Thron *et al.* 2004, Thomas *et al.* 2005, Ikonomou *et al.* 2002), such as glaucous gulls (*Larus hyperboreus*), polar bears (*Ursus maritimus*), ringed seals (*Phoca hispida*) and beluga whales (*Delphinapterus leucas*).

2.2.3 Long-range environmental transport

2.2.3.1 Environmental studies on transport and distribution

There are several factors indicating long-range transboundary transport of PentaBDE in the environment. It has a high persistency in air, with a half-life of 11-19 days (Palm *et al.* 2002, Vulykh *et al.* 2004)). Monitoring studies have detected a widespread occurrence in the European atmosphere (ter Shure *et al.* 2004, Lee *et al.* 2004, Jaward *et al.* 2004, Harrad and Hunter 2004, Harrad *et al.* 2004) and Arctic (AMAP 2002 and AMAP 2005, Peltola *et al.* 2001).

Sampling of air in the Great Lakes region of North America was undertaken in 1997-1999 and reported by Strandberg *et al.* (2001). PBDEs, mainly BDE-47 and BDE-99, were detected in all samples from four locations, and there was little variation over the time period. PBDE concentrations ranged from 5 pg/m^3 near Lake Superior to about 52 pg/m^3 in Chicago. At the temperatures of collection, 20±3^{o}C, approximately 80% of the tetrabromo congeners were in the gas phase, but 70% of the hexabromo congeners were associated with particles.

Results for the far-northern Pacific covered particulate matter collected in July-September 2003 from the Bohai Sea to the high Arctic, 37^o – 80^o N (Xin-Ming Wang *et al.* 2005). The dominant congeners were BDE-47, BDE-99, BDE-100 (all present in the commercial pentamix) and BDE-209, with concentrations falling from mid- to high-latitudes, probably resulting (according to the authors) from dilution, deposition and decomposition of the PBDEs during long-range transport. Total PBDE concentrations were in the range 2.25 – 198.9 pg/m^3 with a mean of 58.3 pg/m^3. The source of the PBDEs is believed to be the North American continent from which they distill to an Arctic 'cold trap'.

The emphasis on any assessment of the dispersal of PentaBDE into the environment has to be on long-range transport, specially to Arctic regions, but there also is a growing body of data on dispersal of the substance and related congeners within regions. Air sampling in Southern Ontario in the Spring of 2000, before bud burst, showed PBDE concentrations of 88-1250 pg/m^3, with the lighter congeners (DBE-17, -28 and -47) dominating (Gouin *et al.* 2002). The concentrations fell to 10-20 pg/m^3, a change that the researchers attributed to, firstly, enhanced levels caused by expiration from the winter snowpack, followed by possible sorption by emergent foliage. Other studies in Ontario (Harner *et al.* 2002) found air levels of total PBDE in the range 3.4-46 pg/m^3. In later work, organic films on indoor and outdoor windows in Southern Ontario were examined for their content of PBDEs by Butt *et al.* (2004). While the PBDE content was dominated by BDE-209 from the decabromo mixture, there were significant quantities of congeners deriving from the C-PentaBDE. Back calculation gave total PBDE concentrations in outdoor air of 4.8 pg/m^3 and 42.1 pg/m^3 for indoor air.

Jaward *et al.* (2004a) studied a total of 71 passive air samples using semi permeable membrane devices (SPMDs) for eight BDE congeners (BDE-28, BDE-47, BDE-49, BDE-75, BDE-99, BDE-100, BDE-153 and BDE-154) during a six week period in 2002 at remote/rural/urban locations across 22 countries in Europe. BDEs were detected in approximately 50% of the samples, and the equivalent ΣBDE air concentrations estimated from the passive sampler data ranged from 0.5 to 250 pg m^3. The focus of the most elevated concentrations was the UK, which has a history of PBDE production and has also been a major user of PBDE formulations due to stringent fire regulations within the country. The UK is clearly a regional source for BDEs to the European atmosphere and, in contrast, levels reaching Europe from the west (over the Atlantic Ocean) are low. Other high values were detected in urban centres in mainland Europe – samples from Athens, Bilthoven (Netherlands), Geneva, Milan and Seville, for example. Non-detectable/very low values occurred in remote/background sites, especially in Iceland, Ireland, Norway and Sweden, and values in Eastern Europe were generally low. BDE-47 and BDE-99 contributed ca. 75% to ΣBDE, similar to their proportion in the Bromkal 70-5DE C-PentaBDE.

In the US, high-volume samplers were used to examine concentrations of gaseous and particulate PBDEs at five sites (urban, semi-urban, agricultural and remote) from the Midwest to the Gulf of Mexico, every twelve days during 2002-2003 (Hoh and Hites 2005). The mean concentration of total PBDEs at the Chicago site was 100±35 pg/m^3, some 3-6 times higher than those at other sites and significantly higher than measurements made in 1997-1999 (Strandberg *et al.* 2001). The mean concentration of PentaBDE was 31 pg/m^3 at the Chicago site, some 2-4 times the values for other sites.

Fugacity model results indicate that PBDEs will largely partition to organic carbon in soil and sediment and that their persistence will be strongly influenced by degradation rates in these media (although these are not well known). Only a small proportion of PBDEs exist in air and water. If this is the case, it suggests that these compounds have limited LRAT potential (Prevedouros *et al.* 2004a, Gouin and Harner 2003). This corresponds with PentaBDE's affinity for carbon, low solubility in water (1.0 µg/L) and low vapour pressure (7.6 x 10^{-6} Pa). However, Gouin and Harner (2003) suggest that because of their physical–chemical properties, PBDEs may experience active surface–air exchange as a result of seasonally and diurnally fluctuating temperatures. Subsequently, this may result in the potential for LRAT of the PBDEs through a series of deposition/volatilization hops, otherwise known as the ‘‘grasshopper’’ effect. This assumption is supported by environmental data. Lee et al. (2004) detected atmospheric concentrations of BDEs at two rural/semirural sites in England, and one remote site on the west coast of Ireland in 2001 and in 2000, respectively. ΣBDE concentrations at Mace Head, Ireland, were 0.22 to 5.0 pg/m^3 with a mean of 2.6 pg/m^3 and were controlled primarily by advection. ΣBDE concentrations at Hazelrigg (NW England) were 2.8 to 37 pg/m^3 with a mean of 12 pg/m^3, and at Chilton (SW England) were 3.4 to 33 pg/m^3 with a mean of 11 pg/m^3. The congener profile was, on average, similar to that of the C-PentaBDE. At the two English sites in the summer, PBDE concentrations were strongly influenced by temperature, indicating that land/air exchange processes play an important role in determining atmospheric concentrations.

The concentrations of PBDEs were determined in soil samples collected along a latitudinal transect through the UK and Norway, at remote/rural woodland (both coniferous and deciduous) and grassland sites (Hassanin *et al.* 2004). Concentrations for ΣBDE ranged from 65 to 12,000 ng/kg dry weight. BDE congeners BDE-47, BDE-99, BDE-100, BDE-153 and BDE-154, covering the major constituents of the C-PentaBDE, dominated the average congener pattern in the soils. This was interpreted as evidence that transfer of the congeners from materials treated with the commercial product from source to air to soil occurs with broadly similar efficiency, and that there is little degradation of the congeners by processes acting either during atmospheric transport or within the soils themselves. There was evidence of latitudinal fractionation of the BDE congeners, with the relative amounts of BDE-47 and the lighter congeners increasing to the north (with increasing distance from source areas) while the proportion of BDE-99 and the heavier congeners decreased. Plots of BDE congener concentrations against percentage soil organic matter yielded different slopes for different congeners. Steeper slopes were generally observed for lighter congeners such as BDE-47, indicating that they have undergone some air-surface exchange (“hopping”), whilst those of heavier congeners such as BDE-153 were close to zero, indicating that they are retained more effectively by soil following deposition. A Japanese study detected seasonal variations in the partitioning of PBDEs between the gas and particulate phase. The fraction of particulate PBDEs was higher in samples collected in winter than those in the summer (Hayakawa *et al.* 2004). PentaBDE is expected to be transported in the environment mostly by being absorbed onto particles due to its low volatility, low solubility and high affinity for carbon compounds. There are results from environmental studies which indicate that PBDEs are transported on air borne particles, and that they are susceptible to wet deposition (ter Schure *et al.* 2004a, ter Schure and Larsson 2002). Further transport depends on the fate of the particles. Fate after depositions on land depends on the level of wind erosion, that can vary with the season. Fate after deposition into the sea depends on oceanographic processes, such as water layering and transport by currents in the surface layers.

Ter Schure *et al.* (2004a) collected air and atmospheric bulk deposition samples on the island of Gotska Sandön in the Baltic Proper during a 10 week period in autumn 2001. The sampling site was chosen because of its central position in the Baltic Sea, and because of the absence of local point sources of

pollution. Ten PBDE congeners were determined (BDE-17, BDE-28, BDE-47, BDE-85, BDE-99, BDE-100, BDE-153, BDE-154, BDE-183 and BDE-209). The median ΣBDE concentration (ΣBDE is the sum of the concentrations of the congeners determined in each study) was 8.6 pg/m^3, and the BDEs were mainly associated with particles. A comparison to levels of PCB in the atmosphere indicated that, as PCB concentrations in Baltic air have been declining, the input of BDEs by atmospheric deposition to the Baltic Proper now exceeds that of the PCBs by a factor of almost 40 times.

BDEs were determined in precipitation falling in southern Sweden during a two week period in 2000 (ter Schure and Larsson, 2002). The particle-associated and "dissolved" phases were separated during sampling and 65 ± 18% of ΣBDE was found to be particle-associated. The volume weighted mean concentration of ΣBDE (nine congeners) in rain was 209 pg/l, and the total deposition rate was 2 ± 1 ng ΣBDE/m^2/day. The congener profile in both phases of the total deposition was dominated by BDE-209, and thereafter BDE-47, BDE-99 and BDE-183, representing inputs from all three commercial PBDE formulations. The authors found that particle associated BDEs are effectively removed during small precipitation episodes, and that particle scavenging was an important mechanism for the wet deposition of BDEs.

A model assessment of potential for long-range transboundary atmospheric transport and persistence of PentaBDE have been carried out by EMEP (Co-operative programme for monitoring and evaluation of the long-range transmission of air pollutants in Europe). The values of LRTP were considered to be strongly influenced by environmental processes, such as degradation, deposition, gas/particle partitioning, and gaseous exchange with underlying surface. The main process of removal from the atmosphere for the two congeners BDE-47 and BDE-99 was found to be deposition to land and seawater, 78% to land and 15% to sea for BDE-47 and 77% to land and 21% to sea for BDE-99. Only 7% of BDE-47 and 2% of BDE-99 was degraded. The calculated half-life in air was 7 days for BDE-47 and 11 for BDE-99. The findings showed a spatial distribution of BDE-47 that covers the Arctic, Europe, the Mediterranean Sea and northern Africa. BDE-99 spreads over longer distances and spreads to the Arctic, Atlantic Ocean, Asia and Africa. Transport distances (TD) were calculated for the two congeners. The TD was 2300 km for BDE-47 and 2800 km for BDE-99 (EMEP 2004).

Wania and Dugani (2003) examined the long-range transport potential of PBDEs using a number of models – TaPL3-2.10, ELPOS-1.1.1, Chemrange-2, and Globo-POP-1.1 – and various physical and chemical properties – for example, solubility in water, vapour pressure, log K_{OW}, log K_{oa}, log K_{aw}, and estimated half-lives in various media. They found that all models yielded comparable results, with tetrabromodiphenyl ether showing the greatest atmospheric transport potential and decabromodiphenylether the lowest. The researchers estimated a characteristic transport distance (CTD) ranging from 1113 to 2483 km for the tetrabromo, 608 to 1349 for the pentabromo, 525 to 854 for the hexabromo, and 480 to 735 for the decabromo congener. The CTD was defined as the distance a parcel of air has travelled until 1/*e* (approximately 63%) of the chemical has been removed by degradation or deposition processes (Gouin and Mackay 2002).

The EU risk assessment (EU 2000) concluded that the major part of releases end up in soil. From soil, PentaBDE can be expected to be moved mainly through leaching with water in the suspended solids fraction or through wind erosion where it occurs. A small part in the soil can be volatilized, especially in the warm season, and so may be considered a plausible alternative mechanism for transport in addition to volatilization and advective transport of vapor identified in the literature. Although PentaBDE has low water solubility, it has been detected in lakes and seas, and can be transported with water in the soluble and particle phases (Peltola *et al.* 2001). Occurrence in migratory birds and fish indicate the possibility of transport by migration of animals, but the main route seems to be through the atmosphere.

2.2.3.2. Levels in remote areas

The detected levels in the Arctic atmosphere, biota and environment are strong indicators of the PentaBDEs potential for long-range transport (Verreault *et al.* 2005, Verreault *et al.* 2004, Norstrøm *et al.* 2002, Herzke *et al.* 2003, Vorkamp *et al.* 2004a and b, Wolkers *et al.* 2004, Thron *et al.* 2004, Thomas *et al.* 2004, Ikomomou *et al.* 2002, Christensen *et al.* 2002, de Wit *et a*l. 2004, AMAP 2002 and AMAP 2005).

There are several studies showing the occurrence of PentaBDE in remote areas in Europe as well (Vives *et al.* 2004, Hassanin *et al.* 2004 and Zenegg *et al.* 2003). Levels in remote regions are considered to be an indication on long-range transport.

PentaBDE (as total BDE) has been detected in Canadian and Russian Arctic air at concentrations up to 28 pg/m^3 (Alaee *et al.* 2002). Strandberg *et al.* (2001) reported concentrations of total PBDE (BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, BDE-190 and BDE-209) in air from the Great Lakes area during the period 1997-1999. Average concentrations based on four samples from each of four locations ranged from 4.4 pg/m^3 near Lake Superior in 1997 to 77 pg/m^3 in Chicago in 1998. The average air concentration of total PBDEs (1997, 1998 and 1999) for the sampling sites ranged from 5.5 to 52 pg/m^3. Tetra- and pentabromo congeners accounted for approximately 90% of the total mass of PBDE in this study. At 20±3^{o}C, about 80% of the tetrabromo congeners and 55-65% of the pentabromo congeners were in the vapour phase while about 70% of the hexabromo congeners were associated with the particulate phase.

A larger study was performed detecting BDEs in trout (three species) from eleven high mountain lakes in Europe (566 to 2,485m altitude) (Vives *et al.*, 2004). These lakes were selected as being far from local pollution emission sources, and it was considered that the only source of BDEs to these lakes was as a result of atmospheric transport and deposition. The major congeners identified (of 39 determined) were BDE-47 and BDE-99, followed by BDE-100, BDE-153, BDE-154 and BDE-28, and these congeners were found in all samples analysed. The highest concentrations of ΣBDE in fish muscle and liver were found in Lochnagar, Scotland, 1.2 and 11 μg/kg wet weight, respectively (177 and 366 μg/kg on a lipid basis). No correlation was observed between the occurrence of these compounds and altitude, latitude or temperature, and the authors inferred that the environmental distribution of the BDEs has not, as yet, reached a steady-state.

2.3 Exposure

2.3.1 Levels

PentaBDE has spread widely in the global environment. A large quantity of monitoring data exist with detected levels in marine and terrestrial birds, sea and terrestrial mammals, sediments, soil, seafood and fish. A global study by Ueno *et al.* (2004) of PentaBDE in skipjack tuna (*Katsuwonus pelamis*) shows a wide spread occurrence in the offshore waters of various regions in the world. Table 2.5 gives an overview over the levels found in different parts of the world.

Contamination of the environment and biota in remote regions can be a threat to vulnerable species and ecosystems. In the Arctic, together with other pollutants of concern, PentaBDE is detected in high levels in top predatory birds and mammals (Verreault *et al.* 2005, Verreault *et al.* 2004, Norstrøm *et al.* 2002, Herzke *et al.* 2003, Vorkamp *et al.* 2004a and b, Wolkers *et al.* 2004, Thron *et al.* 2004, Thomas *et al.* 2004, Ikomomou *et al.* 2002) showing that the Arctic food webs are seriously affected. Wolkers *et al.* (2004) detected levels of PentaBDE in beluga whales (*Delphinapterus leucas*) in the Arctic, a species protected by the Convention on migratory species (the Bonn convention). ΣBDE concentrations (geometric mean; 22 congeners) were 234, 161 and 29 μg/kg in juvenile, adult male and adult female beluga.

In fact, there are detected high levels of PentaBDE in several species, with populations of concern protected by the Bonn convention. Several studies (Jaspers *et al.* 2004, Herzke *et al.* 2005, Lindberg *et al.* 2004, D`Silva *et al.* 2004, Law *et al.* 2005, Sinkkonen *et al.* 2004, Sellström *et al.* 2003, Kannan *et al.* 2005, Ramu *et al.* 2005 and Wolkers *et al.* 2004) indicate that PentaBDE is widespread in peregrine falcon (*Falco pereg*rine), merlin (*Falco columbarius*), goshawk (*Accipiter gentiles*), golden eagle (*Aquila chrysaetos*), buzzard (*Buteo buteo)*, beluga whales (*Delphinapterus leucas*), irrawaddy dophins (*Orcaella brevirostris*), and Indo-Pacific humpback dolphin (*Sousa chinensis*), all protected by the Bonn convention. High levels of PBDEs are also detected in peregrine falcon eggs in Sweden (Lindberg *et al.* 2004), for which individual ΣBDE concentrations were as high as 39,000 µg kg^{-1} lipid weight, some of the highest concentrations seen in wildlife so far.

The populations of harbour porpoises (*Phocoena phocoena*) in the North and Baltic seas are protected through the Bonn Convention. Studies have detected high levels in those populations (Thron *et al*. 2004 and Covaci *et al.* 2002). In a study by Thron *et al.* (2004) animals with poor body condition (lower mean blubber thickness) had much higher concentrations than other individuals. Only females showed decreasing concentrations with age, indicating elimination via transfer from mother to offspring.

The harbour porpoise is, together with peregrine falcon and merlin, also on the list for strictly protected (endangered) species in the convention on the conservation of European wildlife and natural habitats (the Bern Convention). The white-tale sea eagle is on the list for endangered species in the Bern Convention. Levels of concern are detected in both individuals and eggs (Herzke *et al.* 2005). Beluga whales and irrawaddy dolphins are on list for protected (vulnerable) species. High levels are found in white-beaked dolphin (*Lagenorhyncus albirostris*), another endangered species. The parties of this convention undertake to take appropriate measures to ensure the conservation of endangered and vulnerable species and their habitats.

*Table 2.5 Levels of PentaBDE (**BDE-99**) in different parts of the world (LW=Lipid weight, DW=Dry weight).*

Country/Region	Organism/compartment	Levels of PentaBDE	References	Comments
Europe	Atmosphere Gas phase	10-120 pg/m^3	Jaward *et al.* 2004	22 countries
Japan	Atmosphere Particulate Gas phase	0.05-0.9 pg/m^3 0.05-19' pg/m3	Hayakawa *et al.* 2004	Measured in the summer
Sweden	Sediments	<0.7-51.4 ng/g DW	Palm *et al*. 2002	Rivers at point source
United Kingdom	Soil	78 – 3200 pg/g DW	Hassanin *et al.* 2004	
Western Europe	Sediments	<0.2-6.9 ng/g DW	Palm *et al*. 2002	Estuaries
Japan, Osaka	Sediments	9-28 ng/g DW	Palm *et al*. 2002	
North Pacific Ocean	Skipjack tuna	0.18-2.1 ng/g LW	Ueno *et al.* 2005	
Japan	Skipjack tuna	1.1-1.7 ng/g LW	Ueno *et al.* 2005	Offshore waters
East China Sea	Skipjack tuna	2.4-4.7 ng/g LW	Ueno *et al.* 2005	
Philippines	Skipjack tuna	2.1 ng/g LW	Ueno *et al.* 2005	Offshore waters
Brazil	Skipjack tuna	1.9 ng/g LW	Ueno *et al.* 2005	Offshore waters
Canada	Atlantic tomcod	77 ng/g LW	Law *et al.* 2003	
Chilika Lake, India	Irrawaddy dolphin	0.12-0.78 ng/g LW	Kannan *et al.* 2005	Endangered species
Hong Kong, China	Indo-Pacific humpback dolphin	33.6-720 ng/g LW	Ramu *et al.* 2005	Coastal waters 12% of ΣPBDEs
United Kingdom	White beaked dolphin	1480 ng/g LW	Law *et al.* 2003	Endangered species
Hong Kong, China	Finless porpoises	27.6-117.6 ng/g LW	Ramu *et al.* 2005	Coastal waters 12% of ΣPBDEs
Japan	Northern fur seal	2.64-4.56 ng/g LW	Kajiwara *et al.* 2004	Pacific coast 12% of ΣPBDEs

Svalbard, Arctic Norway	Polar bear	0.7-4.7 ng/g LW	Gabrielsen *et al.* 2004	
Canadian Arctic	Polar bear	1.04-11.3 ng/g LW	Muir *et al.* 2006	
Bjørnøya, Arctic Norway	Glacous gulls	0-7.9 ng/g LW	Herzke *et al.* 2003	
Norway	White-tailed sea eagle	6-184 ng/g LW	Herzke *et al.* 2005	In eggs. Endangered Species
Sweden	Peregrine falcons	110-9200 ng/g LW	Lindberg *et al.* 2004	Endangered species
Australia	Melon-headed whale	4.8 ng/g LW	Law *et al.* 2003	
Canada	Beluga whale	108 ng/g LW	Law *et al.* 2003	Vulnerable species
Netherlands	Mussels	0.3-11 ng/g LW	Law *et al.* 2003	Marine+freshwater
Sweden	Frog	5.6 ng/g LW	De Wit *et al.* 2004	
Canada	Zooplankton	0.46 ng/g LW	Law *et al.* 2003	

2.3.2 Trends

Most trend analysis show an increase in concentrations of PBDEs in the environment and in humans from the beginning of the 1970s, with a peak around the mid-1990s and a stabilisation or subsequent levelling off in Europe (Covaci *et al.* 2002, Fängström *et al.* 2005, Thomsen *et al.* 2005 and Knudsen *et al.* 2005), but with a continuous increase in the Arctic (Vorkamp *et al.* 2005, AMAP 2002 and AMAP 2005). PentaBDEs are reported in the studies to follow the same trend as ΣPBDEs. This increase has also been seen in North America, in air, soil and sediment, and wildlife, but insufficient data exist to allow comment on trends in the human population.

In the Asia-Pacific region a study on northern fur seals on the Pacific coast of Japan shows an increase of PBDEs to about 150 times between 1972 and 1994, and then levels decreased to about 50% in 1998 (Kajiwara *et al.* 2004). The reduction in PBDEs values was assumed to be due to the voluntary phase out of C-PentaBDE in Japan in 1990. BDE-99 levels showed the same pattern as ΣPBDEs.

Analysis of archived herring gull eggs (sampled in 1981, 1983, 1987, 1989, 1990, 1992, 1993, 1996, 1998, 1999 and 2000) enabled Norstrom *et al.* (2002) to establish temporal trends in PBDE concentrations over the period 1981-2000. At Lake Michigan, Lake Huron and Lake Ontario sampling sites, concentrations of tetra- and pentabromodiphenyl ethers (that is, BDE-47, BDE-99 and BDE-100) increased by 71-112-fold over these two decades (from 4.7 to 400.5 µg/kg ww at Lake Ontario; from 8.3 to 927.3 µg/kg ww at Lake Michigan; from 7.6 to 541.5 µg/kg ww at Lake Huron). These increases were found to be exponential at all three locations ($r^2 = 0.903 – 0.964$, $p < 0.00001$).

Wakeford *et al.* (2002) undertook sampling of eggs of the great blue heron in 1983, 1987, 1991, 1996, 1998 and 2000 in southern British Columbia and found that total PBDE concentrations (sum of tetra-, penta- and hexabromo-congeners) increased from 1.31 to 287 µg/kg ww between 1983 and 1996, but then dropped slightly to 193 µg/kg ww in 2000. They also undertook sampling of the eggs of thick billed murre in the Canadian North in 1975, 1987, 1993 and 1998, and observed a trend of gradually increasing PBDE concentrations (sum of tetra-, penta- and hexabromo-congeners) in these eggs from 0.43-0.89 µg/kg ww in 1975, to 1.83-3.06 µg/kg ww in 1998.

PBDEs have been detected in a variety of marine mammals. Alaee *et al.* (1999) reported average PBDE (di-to hexaBDE) concentrations in the blubber of marine mammals from the Canadian Arctic as 25.8 µg/kg lipid in female ringed seals (*Phoca hispida*), 50.0 µg/kg lipid in male ringed seals, 81.2 µg/kg lipid in female beluga (*Delphinapterus leucus*) and 160 µg/kg lipid in male beluga. BDE-47, a tetrabromodiphenyl ether, was the predominant congener, followed by the pentabromo BDE-99. Ikonomou *et al.* (2000, 2000b) reported PBDE concentrations in biota samples from the west coast and Northwest Territories of Canada. The highest concentration of of total PBDE residues, 2269 µg/kg lipid, was found in the blubber of a harbour porpoise form the Vancouver area. With a concentration of about

1200 µg/kg, one congener, BDE-47, accounted for slightly more than half of the total PBDE in the sample. Ikonomou *et al.* (2002a) analyzed temporal trends in Arctic marine mammals by measuring PBDE levels in the blubber of Arctic male ringed seals over the period 1981-2000. The mean total concentrations increased exponentially, from 0.572 µg/kg lipid in 1981 to 4.622 µg/kg in 2000, a greater than eightfold increase. They determined that Penta- and HexaBDEs are increasing at approximately the same rate (doubling time 4.7 and 4.3 years, respectively), more rapidly than TetraBDEs, for which the doubling time was 8.6 years. Once again, BDE-47 was predominant, followed by BDE-99 and BDE-100.

A marked increase in tissue PBDE levels was also evident in blubber samples collected from San Francisco Bay harbour seals over the period 1989 to 1998 (She *et al.* 2002). Total PBDEs (the sum of BDEs 47, 99, 100, 153 and 154) rose from 88 µg/kg lipid to a maximum of 8325 µg/kg lipid over this short period. Stern and Ikonomou (2000) examined PBDE levels in the blubber of make SE Baffin Bay beluga whales over the period 1982-1997, and found that the levels of total PBDEs (tri-to hexa-congeners) increased significantly, Mean total PBDE concentrations were about 2 µg/kg lipid in 1982, and reached a maximum value of about 15 µg/kg lipid in 1997. BDE-47 was the dominant congener, with a mean concentration of approximately 10 µg/kg lipid in 1997. Total PBDE residues (concentrations for individual congeners not provided) in the blubber of St Lawrence estuary belugas sampled in 1997-1999 amounted to 466 (±230) µg/kg ww blubber in adult males, and 655 (±457) µg/kg ww blubber in adult females. These values were approximately twenty times higher than concentrations in beluga samples collected in 1988-1990 (Lebeuf *et al.* 2001).

The results from a modelling exercise utilizing the European variant (EVn) BETR multimedia environmental fate model were presented for the C-PentaBDE product by Prevedouros *et al.* (2004). To predict future atmospheric concentration trends, the model was used in its fully dynamic mode over the period 1970-2010. It predicted that atmospheric concentrations would have peaked around 1997, and then declined with an overall "disappearance" half-life of 4.8 years. The model steady state simulations gave generally good agreement with measured data for BDE- 47 and BDE-99. The empirical data for North America presented above, however, show continuing increases in concentrations, at least up the year 2000, and so while the model results match some European data with fair agreement, they are not in accord with data from North America.

Three dated sediment cores from locations in Western Europe were analyzed for 14 BDE congeners (Zegers *et al.*, 2003). Cores from the Drammenfjord (Norway), the western Wadden Sea (The Netherlands) and Lake Woserin (Germany) showed a time dependent pattern in the distribution of BDEs since the start of production of PBDE formulations. Two of the three commercial formulations could be distinguished. The penta-mix formulation is clearly present from the beginning of the 1970s. This is in agreement with data for the industrial production of this formulation. In the cores from the Netherlands and Germany, concentrations of BDE congeners associated with the C-PentaBDE were levelling off in the most recent layers (1995 & 1997), whereas those in the Drammenfjord were still increasing in 1999. The absence of all BDE congeners in the older (deeper) layers of all three cores, as well as in several 100 to 150 million year old layers of clay from Kimmeridge, UK, indicated that these BDE congeners are not produced naturally.

Human exposure to polychlorobiphenyls and PBDEs in Japan in 1980 and 1995 showed that levels of the latter had increased substantially over the twenty-year period, although there was great variation between regions. The main congeners detected in serum were BDE-47 and BDE-99. Most total PBDE levels had more than doubled, and in one area increased twenty-fold, with 1995 values falling in the range 0.6 – 41.4 ng/g lipid Koizumi *et al.* 2006).

2.3.3. Bioavailability

Environmental studies on bioavailability have detected uptake of PentaBDE in soil organisms (Matscheko *et al.* 2002), sediment dwelling organisms (Magnusson *et al.* 2003) and aquatic organisms (Lithner *et al.* 2003, Voorspoels *et al.* 2003, Marsch *et al*. 2004, Kierkegaard *et al*. 2004, and Sinkkonen *et al.* 2004), making PentaBDE's way into the food webs evident. Subsequent bioaccumulation and biomagnification of the compound has been detected and described in Section 2.2.2.

Soil exposed to PBDEs in various ways was analyzed for BDE-47, BDE-66, BDE-99, BDE-100, BDE-153, BDE-154 and BDE-183 (Matscheko *et al.*, 2002). Earthworms collected at all soil sampling sites were analyzed as well. The BDE congener profile in all soil samples was dominated by BDE-47 and BDE-99. Accumulation of the compounds in earthworms from the sites yielded a direct relationship between the concentrations in the soil and concentrations in the worms. The biota-soil accumulation factors (BSAFs) of BDE congeners BDE-47, BDE-99 and BDE-100 were around 5 (organic matter/lipids). Thus, earthworms living in contaminated soils will accumulate tissue BDE concentrations and, as these animals represent the base of the terrestrial food chain for many organisms, this form a pathway for the accumulation of BDEs in organisms at higher trophic levels.

The western Scheldt estuary is subject to a variety of suspected PBDE sources, such as a brominated flame retardant manufacturing plant, Antwerp harbour, and the textile industry located further upstream. PBDE concentrations in samples of biota, including crab, shrimp, starfish, benthic fish (such as dab, goby, plaice and sole) and gadoid fish (such as bib and whiting) from the estuary were compared to those in samples from the Belgian North Sea beyond the mouth of the estuary (Voorspoels *et al.*, 2003). Eight BDE congeners (BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, BDE-183 and BDE-209) were determined. Concentrations observed in the estuarine samples were up to 30 times higher than in those from the Belgian North Sea, with an increasing gradient towards Antwerp. Concentrations in the North Sea ranged from 0.02 to 1.5 µg/kg wet weight in benthic invertebrates and goby, from 0.06 to 0.94 µg/kg wet weight in fish muscle, and from 0.84 to 128 µg/kg wet weight in fish liver. The corresponding ranges in samples from the estuary were from 0.2 to 30, 0.08 to 6.9, and from 15 to 984 µg/kg wet weight, respectively. The ratio BDE-99/BDE-100 was found to be highly location- and species-dependent, possibly relating to differences in metabolism. In shrimp, the value of this ratio (4:1) was very similar to that observed in the Bromkal formulation and in estuarine sediment, and was similar in shrimp from both the North Sea and the estuary, implying both that these congeners are readily bioavailable and that shrimp lack the ability to metabolize either congener. On a lipid weight basis, concentrations of BDE-47 ranged from 3 to 108 µg/kg lipid weight in samples from the North Sea, and from 8 to 1,550 µg/kg lipid weight in estuarine samples. BDE-47 was the most abundant congener in all samples, comprising 43 to 75% of ΣBDE.

Thomas *et al*. (2004) conducted an input-output balance study of BDEs on three captive, juvenile grey seals. The animals were fed a diet of herring for six months, and the study was performed during the last three months of this period. BDE analysis was undertaken using GC-ECNIMS. Consistently high absorption (89 - 99%) was observed for all PBDE congeners studied (BDE-28, BDE-47, BDE-49, BDE-99, BDE-100, BDE-153, BDE-154 and BDE-209).

2.3.4 Human exposure

Studies, assessments and reviews referred to in this section have shown that the main routes for human exposure are food, and exposure to dust in indoor air at home and workplaces due to levels in products like furniture and electronic devices. Fish and agriculture products are the main food sources of PentaBDE for humans, and mother's milk for the nursing child. Fatty fish from contaminated areas are a major source (Sjödin *et al.* 2003). PentaBDE has been detected in various foods (VKM 2005, Burniston *et al.* 2003 and Bocio *et al.* 2003) as well as in indoor dust (Shoeib *et al.* 2004 and Wilford *et al.* 2005). Levels in foods in the US have been reported by Schecter *et al.* (2004), Schecter *et al* 2006, and Huwe *et al.* (2005). There are several hazard assessments in EU and US, looking into the exposure of humans

(VCCEP 2003, COT 2004, VKM 2005). They conclude that the available hazard or exposure information is inadequate to fully characterize the risks.

About 5% of the individuals in general populations have been found to be subjected to elevated exposure (Thomsen *et al.* 2005 b). This, together with estimates of the half life of C-PentaBDE congeners in humans, raises concern for long-term effects on human health. The half-lives for these congeners in humans have been estimated to be 1,040 days (BDE-99) and 573 days (BDE-100) (Geyer *et al.* 2004).

Domestic house dust is likely to be a significant source where furniture, carpet or appliances contain C-PentaBDE. This has been discussed in Section 2.1.1. It is not clear which sources are the greatest, and there could be wide variations depending on lifestyle and diet.

Several studies have detected levels of PentaBDE in sewage sludge (Matscheko *et al.* 2002, Fabrellas *et al.* 2004, Motche and Tanner 2004 and Sjödin *et al.* 2003, Hale 2002). Sewage sludge is considered to be one of the main sinks for PBDEs. The application of sewage sludge to agricultural land is one of the reasons for detected levels of PentaBDE in food products. This can explain the detected levels in vegetables and root crops in experimental studies. Levels in fish and root crops can be the source of exposure to domestic animals like chickens and pigs, and the source of PBDEs in meat products for human nourishment.

A Canadian global study showed that PentaBDE is widespread in human milk in populations all over the world (Ryan 2004). There are data on levels in human blood serum and milk from USA, Canada, Mexico, Japan, the EU region, the Arctic region and Scandinavia. A meta-analysis by Hites (2004), using data published up to mid-2003, showed that serum and milk levels in the US were much higher than those in Europe - ~35 ng/g *vs* ~ 2 ng/g lipid – and were doubling on average every 4-6 years. BDE-47 and BDE-99 were the major congeners detected. Considerably higher levels are found in humans from North America in general. About 5% of general populations have been found to be subjected to elevated exposure. Thus, together with estimates of the half-life of PentaBDE congeners in humans, raiss concern for long-term effects on human health (Thomsen *et al.* 2005b).

Levels increasing from the 1980s to the 2000s have been observed in mother's milk from Sweden as well as in blood from Germany and Norway (Sjödin *et al.* 2003). A more recent study in Sweden (Fängström *et al.* 2005) assessed the temporal trends of polybrominated diphenyl ethers (PBDEs), in mothers' milk in the Stockholm area. The pooled samples were covering the time period 1980 to 2004, with emphasis on samples from the last ten years. Concentrations of BDE-47, BDE-99 and BDE-100 reached a peak in the mid-1990s and are now clearly showing decreasing levels. The concentrations are however still much higher than in 1980.

The objective of a recent Norwegian study was to complete and extend a previous study on time trends of PBDEs in Norwegian pooled serum samples (Thomsen *et al.* 2005a) and put together an overview of the PBDE body burden in the general population from 1977 to 2004. The temporal trend of the sum of seven PBDEs (BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154 and BDE-183) in the pooled serum from the present study are in close agreement with the levels found in a previous study by the same authors. In general, for similar time periods the levels in breast milk seem to be somewhat lower than in the serum, but the same overall trend is observed. This confirms that the PBDE body burdens in these regions have risen rapidly from 1977 to about 1997, but now seem to have stabilized or even to have decreased. This is in accordance with the trends observed in Swedish breast milk, as an indicator of the European situation, but may not be true of levels in North America. The PBDE level was previously found to be about twice as high in a serum pool from infants up to four years of age compared to serum pools from elderly persons. This finding was confirmed in the Norwegian study. However, in 2002, children between the ages of 5 and 14 years showed higher levels of PBDEs than the average adult.

Contemporary PBDE concentrations in Europe and Asia are remarkably similar, with low median values on a lipid basis for all countries and relatively small variations. The situation in North America is completely different with median values for individual studies in the range of 20-50 ng/g LW (Ryan 2004). However, in parallel with the regional differences that were reported above for biota, the levels in breast adipose tissue taken from women living in San Francisco Bay area in 2000 were almost two orders of magnitude higher than what has been reported in human milk from Sweden (Sjödin *et al.* 2003). A more recent study of levels in human adipose tissue in New York was published by Johnson-Restrepo *et al.* (2005). The study of 40 males and 12 females of a range of ages and ethnicities showed wide variations in lipid PBDE concentrations, with mean values substantially higher than the medians. Median concentrations were: BDE-47, 29.3 ng/g lipid; BDE-99, 10.3 ng/g lipid; BDE-100, 12.0 ng/g lipid.

In a preliminary screening of PBDEs in plasma and milk samples from Mexican women, the levels were well above European levels of PBDEs reported so far (López *et al.* 2004). The mean level of PBDEs (with BDE-209 excluded) in Mexican women living in urban areas was approx. 20 ng/g LW in plasma. The levels in women living in rural areas in Mexico were however comparable with women living in rural areas in Sweden. (BDE-209 levels were only detected in women living in the Mexican city).

Ryan (2004) detected a big individual variation in levels in the general population in a study from Canada. The values span more than three orders of magnitude, with a few values showing a much greater level. Levels detected in the Canadian Arctic in Ryan's study (2004) were increasing. Values in human milk from the Faroe Islands showed the same trend (Fängström *et al.* 2004).

Two studies in Australia indicated that levels of PBDEs in Australian breast milk and blood serum are higher than those in Europe but lower than those found in North America (Harden *et al.* 2004 and 2005).

*Table 2.6 Data on mean levels of PentaBDE (**BDE-99**) (ng/g LW) in humans from different parts of the world.*

Data	Country/region	Levels	References	Year	Comments
blood	The Netherlands	0.8	Weiss *et al.* 2004	unknown	
blood	Norway	1.0	Thomsen *et al.* 2004	1999	
blood	Mexico	2.0	López *et al.* 2004	2003	Urban population
blood	Australia	2.3	Harden *et al.* 2004	2003	
milk	Germany	0.2	Harden *et al.* 2004	2000	
milk	Sweden	0.3	Fängström *et al.* 2005	2003	Urban population
milk	Mexico	0.6	López *et al.* 2004	2003	Rural population
milk	Sweden	0.5	López *et al.* 2004	2003	Rural population
milk	United Kingdom	0.9	Harden *et al.* 2004	?	median
milk	Faroe Islands	1.0	Fängström *et al.* 2004	1999	Rural population
milk	Australia	1.9	Harden et al. 2005	2002/2003	
milk	Canada	4	Ryan *et al.* 2002	2002	Rural population
milk	USA	28	Päpke *et al.* 2001	2000	Urban population

Although they are less relevant that environmental data, results from occupational studies bear out the facility with which the PBDEs are taken up by human bodies. In Sweden, occupational exposure to PBDE has been identified among electronics recycling personnel (Sjødin *et al.*, 1999) and in technicians responsible for repair and maintenance of computers (Jacobsson *et al.,* 2002) as well as in nearby soil and sediment (Wang *et al.* 2005). Also workers in industry manufacturing C-PentaBDE, or polyurethane foam and electronic equipment containing it can be exposed to PentaBDE. There is an extensive literature on such exposures.

2.3.5 Debromination

There is growing interest in the fate of PBDEs in the environment. In experiments reported by Stapleton *et al.* (2004), carp were fed food spiked with individual BDE congeners for 62 days, and tissue and excreta were examined. At least 9.5±0.8% of BDE-99 in the gut was reductively debrominated to BDE-47 (one less bromine) and assimilated in carp tissues. Similarly, 17% of the heptabromo congener BDE-183 was reductively debrominated to hexabromo congeners. The authors noted that body burdens of PBDEs may thus reflect direct uptake from exposure as well as debromination of more highly brominated congeners. Highly selective reductive microbial debrominations were observed in experiments reported by He *et al.* (2006). Hepta- and Octa-BDEs were produced in cultures of *Sulfurospirillum multivorans* to which DecaBDE had been added, but OctaBDE was not attacked in a similar system. Cultures of an alternative organism, *Dehalococcoides sp.*, failed to attack the DecaBDE but an OctaDBE mixture was extensively changed, yielding a mixture of Hepta- through Di-BDEs which included the PentaBDE, BDE-99. The authors draw attention to the potential for conversion of higher congeners in the environment to more toxic congeners with fewer bromine substituents. Further studies particularly environmental monitoring studies focussing on congeners for which the primary source is likely to be debromination reactions, are required to clarify the role of debromination in determining the final mix of PBDE congeners in the environment.

Hydroxylated BDEs (OH-BDEs) have been detected and identified as metabolites in several species after exposure to specific BDE congeners but have also been found to occur as natural products in marine sponges and ascidians (Marsch *et al.* 2004). Methoxylated BDEs (MeO-BDEs) have also been reported as natural products present in marine sponges and green algae. It would seem that the origin of these substances can be natural, anthropogenic or both. Nine OH-BDEs and six MeO-BDEs were identified in blood of Baltic Sea salmon (*Salmo salar*) using newly synthesized standards (Marsch *et al.*, 2004). All of the identified OH- and MeO-BDEs were substituted with four or five bromine atoms and five of them also had one chlorine substituent. Fourteen have the methoxy or hydroxy group substituted in the position *ortho*-to the diphenyl ether bond. The structures of several of the compounds support natural rather than anthropogenic origins. However, at least one of the OH-BDEs (4'-OH-BDE-49) may be a hydroxylated metabolite of BDE-47. Estrogenic activity of some hydroxylated PBDEs has been reported by Meerts *et al.* (2001).

Other studies of metabolism of PBDEs are summarized in Section 2.2.2.1.

2.4 Hazard assessment for endpoints of concern

Evidence to date suggests that the major congeners of the C-PentaBDE formulation, BDE-47 and BDE-99, are likely to be more toxic and bioaccumulative than other PBDE congeners. Although the toxicology of PBDEs is not completely understood, some studies on PentaBDE have demonstrated reproductive toxicity, neurodevelopmental toxicity and effects on thyroid hormones. The neurotoxic effects of PBDEs are similar to those observed for PCBs and so children exposed to PBDEs are likely to be prone to subtle but measurable developmental problems. It is presumed that PBDEs are endocrine disrupters, but research results in this area are scant (Siddiqi *et al.* 2003).

While further studies follow internationally-accepted guidelines might be needed to make a full risk assessment of the situations of children, there are sufficient data for development of the present risk profile.

It is acknowledged that these conclusions rest to some extent on examination of reviews, rather than reanalysis of primary data, but in general the studies under review have followed internationally accepted experimental protocols. Nonetheless, there is no significant disagreement between some reported results and later analyses, such as that of the US Voluntary Children's Chemical Evaluation Program (VCCEP) (2005).

2.4.1 Ecotoxicity

Recent studies show that exposure to BDE-47 can cause growth inhibition in colonies of the plankton algae (*Skeletonema costatum*) and a depression on reproductive output of the zooplankton *Daphnia magna* (Källqvist *et al.* 2006).

A recent paper by Timme-Laragy *et al.* (2006) showed adverse effects on fish development at low concentrations. However, the endpoints that were affected in this report (behavioural learning) are not usually accepted risk assessment endpoints. Other endpoints that would be acceptable, such as growth or survival, were not affected.

Canada was able to perform a risk quotient analysis for each congener, integrating known or potential exposures with known or potential adverse effects. In its simplest form, the risk quotient may be described by the equation:

$$\text{Risk quotient} = \frac{\text{exposure reference value}}{\text{toxicity reference value}}$$

and it is customary to use conservative values in order to highlight the worst case.

Exposures were estimated local to emission sources including areas receiving urban drainage (wildlife consumers) and downstream of a polymer processing facility (benthic organisms). Adjustment factots of 100-1000-fold were applied to critical toxicity values to reflect extrapolation from laboratory to fielod conditions, intraspecies and interspecies variations in sensitivity, and because compounds are bioaccumulative and persistent.

A risk quotient value >1 signifies the likelihood or potential for adverse effects to occur, while those <1 imply no danger to organisms. The Canadian results shown in Table 3.1 are based partly on Canadian empirical data and partly on surrogate data from Swedish and US sources.

Table 3.1 Risk quotient values for PentaBDE (Environment Canada 2006, Canadian Wildlife Table 8).

Commercial Product	**Pelagic organisms**	**Benthic organisms**	**Soil organisms**	**Wildlife consumers**
C-PentaBDE	$4x10^{-3}$	45.2	0.13-0.26	149

These values reflect the bioaccumulation of PentaBDE which causes organisms higher in the food chain to be exposed to greater risk.

2.4.2 Effects in mammals

In a review article on toxic effects of brominated flame retardants, Darnerud (2003) drew on a range of primary literature to conclude that exposure to PBDEs gives rise to adverse effects in experimental *in vivo* models, and depending on type of product different effects are seen, occurring at varying dose levels. Generally, the C-PentaBDE products cause effects at the lower dosages. The critical effects of PentaBDE are those on neurobehavioral development and, although somewhat less sensitive, thyroid hormones in offspring (from 0.6 to 0.8 and 6 to 10 mg/kg body wt., respectively) (Darnerud 2003). Note that some data reported in Table 2.7 show levels below these. More recent information, especially for North America, is available in Birnbaum and Staskal (2004).

Blubber biopsy and blood samples were collected from weaned grey seal (*Halichoerus grypus*) pups and juveniles during 1998 and 1999 (Hall *et al.*, 2003). Fifty four post-weaned pups and fifty five first year juveniles (of which thirteen were recaptured post- weaned pups) were studied. The median concentrations of ΣBDE (14 congeners) were 0.17 and 0.46 µg/kg lipid weight in the blubber of the pups and the juveniles, respectively. The study indicated that thyroid hormone levels in the blood of grey seals during their first year of life were significantly, and positively, related to ΣBDE concentrations in blubber, after accounting for the effects of possible confounding variables. Such an association is not, in itself, sufficient evidence for a causal relationship, but is in accordance with the hypothesis that these compounds can act as endocrine disrupters in grey seal pups.

Darnerud (2003) concluded in his review that for PentaBDEs, the critical effects among the available studies seem to be developmental neurotoxicity and, although generally at somewhat higher doses, altered thyroid hormone homeostasis. Regarding the neurotoxicity in mice, no clear mechanism could be defined but effects of the PentaBDEs both via thyroid hormone disruption and directly on signal transmission in brain have been discussed. For example, a number of PBDEs were capable of inducing cell death of cerebellar granule cells in culture (Reistad *et al.*, 2002, Reistad and Mariussen 2005). The LOAEL value for PentaBDE could be set to 0.6–0.8 mg/kg body wt., based on the most sensitive effect observed, neurobehavioral effects during early development (Darnerud 2003, although it is not the task of the POPRC to set a regulatory level, for construction of which resort would need to be made a wider range of data.

In a hazard assessment by the Committee on Food Safety in Norway (VKM 2005) the following toxic effects of exposure to BDE-99 or the C-PentaBDE formulation was reported: neurotoxicity, effects on neurobehavioral development, effects on the thyroid hormone system and hispatological alterations in the tyroid and liver.

*Table 2.7 Overview of No Observed Effect level (NOEL) and Lowest Observed Effect Level (LOEL) after oral administration of **BDE-99** congener or C-PentaBDE formulations. Bold values are the lowest LOEL or NOEL detected.**

PentaBDE	**Duration**	**Dose**	**NOEL mg/kg/ day**	**LOEL mg/kg/day**	**Endpoint**	**Species**	**Reference**
BDE-99	s.d	0.8 or 12.0 mg/kg	n.d.	0.8	Neurotoxicity Behaviour, motor activity level and learning	mouse	Eriksson *et al.* 2001
BDE-99	s.d	0.6, 6, or 30 mg/kg	n.d.	0.6	Developmental- and neurotoxicity Behaviour - hypoactive	mouse	Branchi *et al.* 2002
BDE-99	s.d	0.4, 0.8, 4.0, 8.0, or 16 mg/kg	**0.4**	**0.8**	Developmental- and neurotoxicity Behaviour	mouse	Viberg *et al.* 2004 Sand *et al*. 2004
BDE-99	s.d.	0,06 and 0,3 mg/kg to pregnant female	**n.d.**	**0,06**	Developmental- and neurotoxicity Behaviour (increased activity)	rat, F1 gen.	Kuriyama *et al.* 2005
BDE-99	s.d.	0,06 and 0,3 mg/kg to pregnant female	**0,06**	**0,3**	Reduced testis size and number of sperms	rat, F1 gen.	Kuriyama *et al.* 2005

Penta mix DE-71	30 d	0.01, 0.05, 0.1, 0.5, or 1.0 mg/kg/day	**1**	n.d.	Growth, food intake, hematology, histopatology Clinical chemistry	rat	Great lakes Chemical Corporation 1985
Penta mix DE-71	30 d	0, 3, 30, or 60 mg/kg/day	3	30	Liver weight, puberty, reproduction, liver enzymes, T_4-reduction	Male rat	Stoker *et al.* 2004
Penta mix DE-71	30 d	0, 3, 30, or 60 mg/kg/day	n.d.	3	T_4-reduction	Female rat	Stoker *et al.* 2004
Penta mix DE-71	35 d	0, 1, 10 or 30 mg/kg/day	1	10	T_4-reduction Liver enzymes	pregnant rat	Zhou *et al.* 2002, Zhou *et al.* 2001
Penta mix DE-71	90 d	0-0.44 mg/kg/day	n.d.	0.44	Liver enzymes	rat	Carlson 1980
Penta mix DE-71	90 d	0, 2,10, or 100 mg/kg/day	0-2	2-10	Hepatocyto-megali Tyreoidea hyperplasi	rat	Great lakes Chemical Corporation 1984

n.d. = not defined, s.d. = single dose

* Most of the studies are in line with the OECD test guidelines and for those are not, the quality of the study is assessed to be adequate.

The PBDE mixture known as DE-71 (71% bromine by mass, and containing BDE-47, BDE-99, BDE-100, BDE-153, BDE-154) delays the puberty and suppresses the growth of androgen-dependent tissues in male Wistar rat following a peri-pubertal exposure. These effects suggest that DE-71 may be either inducing steroid hormone metabolism or acting as an androgen receptor (AR) antagonist (Stoker *et al.* 2005).

Talsness *et al.* (2005) evaluated the effects of environmentally relevant concentrations (low doses) of BDE-99 on the female reproductive system in rats. Ultra structural changes compatible with altered mitochondrial morphology were observed in the ovaries of the F1 offspring. No statistically significant changes in ovarian follicle counts were observed. External and skeletal anomalies were detected in offspring (F2) from two different dams (F1) with early developmental exposure to 300 µg BDE-99/Ikg BW. Exposure to BDE-99 resulted in female reproductive tract changes in the F1 generation which were apparent at adulthood.

In utero exposure to a single low dose of BDE-99 disrupts neurobehavioral development and causes permanent effects on the rat male reproductive system apparent in adulthood (Kuriyama *et al.* 2005). Also in this study, the effects of developmental exposure to BDE-99 on juvenile basal motor activity levels and adult male reproductive health were assessed. The exposure to low-dose BDE-99 during development caused hyperactivity in the offspring at both time points (postnatal days 36 and 71) and permanently impaired spermatogenesis by the means of reduced sperm and spermatid counts. The doses used in this study of 60 and 300 µg/kg BW are relevant to human exposure levels, being approximately 6 and 29 times, respectively, higher than the highest level reported in human breast adipose tissue. This is the lowest dose of PBDE reported to date to have an *in vivo* toxic effect in rodents and supports the premise that low-dose studies should be encouraged for hazard identification of persistent environmental pollutants. The study by Viberg *et al.* (2004) shows that neonatal exposure to BDE-99 can induce developmental neurotoxic effects, such as changes in spontaneous behaviour (hyperactivity), effects that are dose-response related and worsen with age. The changes are seen in C57/B1 mice of both sexes. Spontaneous behaviour (locomotion, rearing, and total activity) was observed in two-, five- and eight-month-old mice.

2.4.3 Toxicity to humans

Several hazard assessments have been produced in EU and in US. The conclusions in the hazard assessments elaborated are qualified by the lack of sufficient knowledge of the toxicology of PentaBDE to enable assessment of the risk to humans (COT 2004, VKM 2005 and VCCEP 2003). The toxicological importance for humans of detected effects in laboratory animals is not clear. There is still not enough knowledge of the mechanisms, half-life and metabolism of PentaBDE in experimental animals and humans (VKM 2005).

The conclusion in the hazard assessment by the Committee on Food Safety in Norway was that the exposure through food and mother's milk is considerably lower than the observed NOEL in laboratory mammals (VKM 2005). It is believed that long-time exposure to lower doses of PentaBDE can cause health effects, since PentaBDE accumulates in the human body. Since the half-life of PentaBDE in humans is not known it is not possible today to conclude on long-time exposure effects. This is true even for the US situation, where levels may be 10-20 times those observed in Europe, but pharmacokinetics, toxicology, exposure and other critical data are lacking.

Vulnerable groups could however be pregnant women, embryos and infants, because of effects on the thyroid hormone balance, and the embryo's development of the central nervous system. During pregnancy, maintenance of the thyroid hormone balance is a physiological challenge. Embryos and infants are particularly vulnerable for reductions in thyroid hormone levels (VKM 2005). Infants are exposed to PentaBDE through the diets of their mothers' milk, since PentaBDE is lipophilic and accumulates in the milk (VKM 2005).

3. Synthesis of information

3.1 Summary

PentaBDE meets all of the Annex D screening criteria, and details are included (for the sake of completeness) in Table 3.2, below.

In the absence of production controls, the levels detected in humans, other species and the environment have been observed to rise steeply and this increase is observed in remote locations as well as closer to sites of production and use. In the US, where C-PentaBDE was in high use until recently and where it remains in such materials as polyurethane foam incorporated into consumer products, there has been a build-up in human tissue.

PentaBDE in soil or sediment is readily incorporated into the food chain and bioaccumulates in the fatty tissues of top predators, including humans.

There are toxicological studies of concern that demonstrate neurodevelopmental impacts in animals at low tissue levels that are of relevance to levels observed in populations. Such body burdens remain under close review.

An assessment of the impact of PBDEs on the environment was recently concluded by Environment Canada (2006), taking into account critical studies and lines of evidence that support the conclusion that these commercial substances entering the environment have or may have an immediate or long-term harmful effect on the environment or its biodiversity.

4. Concluding statement

Pentabromodiphenyl ether (C-PentaBDE) is a synthetic mixture of anthropogenic origin with no known natural occurrence. It can be concluded therefore that the presence of components of PFOS in the environment is the result of anthropogenic activities. Long range transport must be responsible for its presence in areas such as the Arctic region, remote from sites of production and release. PentaBDE degrades slowly in the environmernt and can bioaccumulate and biomagnify in mammals and piscivorous birds.

The phase out of C-PentaBDE production and use has led to a reduction in current use but many materials in use, such as polyurethane foams and plastics in electronic equipment, contain PentaBDE which is slowly released to the environment. This release will be accelerated at end-of-life of such materials, especially during recovery and recycling operations.

Although levels of PentaBDE in human blood and milk, and in other environmental species, are falling in Europe, they continue to increase in North America and the Arctic region.

Based on the information in this risk profile, C-PentaBDE, due to the characteristics of its components, is likely, as a result of long-range environmental transport and demonstrated toxicity in a range of non-human species, to cause significant adverse effects on human health and the environment, such that global action is warranted.

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別添9

商業用オクタブロモジフェニルエーテルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 分解せず（OECD TG 301D） 【半減期】 ・大気中：（Hexa-Nona BDE）30.4-161.0 日（OH ﾗｼﾞｶﾙとの反応）（AOPWIN）	【BCF（経鰓的生物濃縮係数）】 ・ｺｲ：（HexaBDPE）BCF=2580-5640 ・ｺｲ：（HeptaBDE）BCF＜1.1-3.8 ・ｺｲ：（OctaBDE）BCF＜9.5 ・ｺｲ：（c-OctaBDE）BCF）＜10-36 【BMF（経口的生物濃縮係数）】 ・飼育中のﾀｲｾｲﾖｳｻｹの餌に含まれる HeptaBDE 183 をﾓﾆﾀ-した結果、95%がｻｹに蓄積。 【BSAF（生物相-底質濃縮係数）】 ・2 種の淡水魚：（HexaBDE）BSAF =1,（HeptaBDE）BSAF =2 ・（BDE 154） BSAF =9.1±1.1	【反復投与毒性】 ラット（28 日）：10mg/kg/day で T4 濃度減少（octa-BDE:30.7%, hepta-BDE:45.1%,） 【催奇形性・発生毒性】 ウサギ（経口 妊娠 7～19 日）：5mg/kg/day で胎児毒性、15mg/kg/day で児の肝重量増加、体重増加量減少、骨形成遅延 マウス（生後 10 日目単回）：0.45mg/kg で 2、4 及び 6 月齢での異常行動並びに成長後の空間認識能・記憶の影響（BDE153）	アメリカチョウゲンボウ*Falco sparverius*：18.7μg PBDEs/egg 及び15.6±0.3 ng PBDEs/g bw/dayで29日間曝露した雛鳥において、PHA応答（T細胞媒介性免疫）が増大し、抗体媒介性反応が減少した。脾臓（胚中心の減少）、滑液嚢（アポトーシスの減少）、胸腺（マクロファージの増大）に構造的変化あり。脾臓の体細胞指標とPBDEs間及び滑液嚢の体細胞指標とBDE-47間に負の相関性あり。

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Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Third meeting
Geneva, 19–23 November 2007

Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Risk profile on commercial octabromodiphenyl ether

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on commercial octabromodiphenyl ether, on the basis of the draft contained in document UNEP/POPS/POPRC.3/14. The text of the risk profile, as amended, is set out below. It has not been formally edited.

K0763734 171207

COMMERCIAL OCTABROMODIPHENYL ETHER

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

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Executive summary

The European Union and its Member States, which are Parties to the Stockholm Convention, submitted a proposal in July 2006 for listing octabromodiphenyl ether in Annex A of the Stockholm Convention pursuant to paragraph 1 of Article 8 of the Convention, and the POPRC agreed that the commercial product Commercial octabromodiphenyl ether (c-OctaBDE) – actually a mixture as described below - met the screening criteria of Annex D to the Convention. This risk profile reviews the available information on the commercial mixture and its main components: Hexa, Hepta, Octa and NonaBDE.

The polybrominated diphenyl ethers in general are used as flame retardants of the additive type. They are physically combined with the material being treated rather than chemically combined (as in reactive flame retardants). The commercial products cover several congeners and bromination levels. The information provided by the bromine industry indicates that (c-OctaBDE) has been produced in The Netherlands, France, USA, Japan, UK and Israel, but since 2004, it is no longer produced in the EU, USA and the Pacific Rim and there is no information that indicates it is being produced in developing countries. According to the Bromine Science and Environmental Forum (BSEF), OctaBDE was commercialized sometime in the mid 70's. By the early 2000's global production was <4000 tonnes/year and by the time production ceased, demand was <500 tonnes; assuming 30 years of production at 6000 tonnes per year total production volume would be around 180,000 tonnes.

Although the commercial OctaBDE seems to be not longer produced, releases during the service life of articles containing the commercial mixtures and at the end of article service life during disposal operations are still relevant. Switzerland reported for this country diffuse emission from the use of products containing OctaBDE of about 0.37 t/a (based on worst-case estimations) for a total stock of 680 tons.

The persistence of c-OctaBDE components in the environment is well documented. The only relevant degradation pathways identified until now are photolysis, anaerobic degradation and metabolism in biota, acting through debromination and producing other BDE which may have higher toxicity and bioaccumulation potential.

Assessing the bioaccumulation potential of c-OctaBDE components constitutes a main challenge in this risk profile. A high potential for bioaccumulation (including a moderate potential for bioconcentration) and food-web biomagnification has been demonstrated for HexaBDE; and it is fully in line with the reported elimination rates. The food-web biomagnification has been reported for HeptaBDE, although at a lower extend than expected from the Kow; this fact can be explained by metabolism resulting in a relatively short half-life (experimentally demonstrated and explained by the authors by debromination). The presence of Octa and NonaBDE in biota is well document but its potential for bioaccumulation from water and food is much lower than expected from their Kow. Reduced availability, metabolisms or both can justify this fact. The number of scientific papers demonstrating debromination of Octa to DecaBDE to other PBDEs is continuously increasing; this is critical for the assessment as would indicate that the supposed low bioaccumulation potential could be in reality the consequence of metabolism to bioaccumulative PBDEs. A quantitative estimation cannot be presented yet, but the debromination process has been already reported for aquatic organisms, mammals and birds. This is an active research field, and new results will need to be assessed by the POPRC as they appear in refereed literature.

Biota monitoring data in remote areas offer the best demonstration on the potential for long range transport of the c-OctaBDE components, Hexa and HeptaBDE. The role of atmospheric transport is confirmed based on its detection in alpine lakes. The potential for long range transport has been observed for DecaBDE. The lack of confirmation for Octa and NonaBDE may be related to the lower relative contribution and/or metabolism via debromination.

No relevant effects have been observed in aquatic, sediment and soil laboratory studies; however, the measured endpoints and the exposure conditions employed in these assays are clearly insufficient for a proper assessment of chemicals such as Hexa to NonaBDE.

The available information on mammals and birds offer relevant information. The lowest reported NOAEL for traditional endpoints is 2-5 mg/kg bw/d. The effects are relevant for the health and the ecological assessments and therefore useful for assessing risks for humans and wildlife. In addition, immuno-toxicological effects and particularly delayed neurotoxic effects observed after a single dose require specific attention. A critical body burden for HexaBDE 153 of 2000 µg/kg lipid has been estimated based on a NOEL of 0.45 mg/kg; it should be noted that HexaBDE 153 concentrations close to these value have been found in several species and geographic sites and total PBDE concentrations frequently exceed this threshold by a large margin.

The evaluation of the human and environmental risk of commercial OctaBDE associated to its potential for long range transport must consider that the commercial product is a mixture of components with different properties and profiles, which may also be released to the environment due to its presence as components of other PBDE commercial products and also produced in the environment by debromination of commercial DecaBDE.

The greatest difficulty appears for the estimation of the potential hazard of the commercial mixture and its components. There are traditional ecotoxicological and toxicological studies where no effects have been observed even at unrealistically high concentrations. However, an in-depth assessment of these studies considering in particular the properties and toxicokinetic of PBDE indicates that the test design, exposure conditions and measured endpoints are not appropriate for a sound assessment of these types of chemicals. Thus, the lack of effects reported in those tests should be considered with care. Specific studies have reported particular hazards such as delayed neurotoxicity and immunotoxicity which may be particularly relevant in the assessment of both human health and ecosystem risks; although a quantitative evaluation of these effects in terms of hazard for human health and ecosystem is not possible based on the current level of information, it may become feasible soon if additional scientifically sound information is produced at a similar rate than in recent years.

Based on the existing evidence, it is concluded that the Hexa and HeptaBDE components of the octabromodiphenyl ether are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

The increasing evidence related to debromination of Octa and Nona BDE into BDEs with POPs properties and considering that under Article 8, paragraph 7(a) of the Convention states that the lack of full scientific certainty shall not prevent a proposal from proceeding, it is concluded that the Octa and NonaBDE components of the octabromodiphenyl ether are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

1. Introduction

The Stockholm Convention is a global treaty to protect human health and the environment from persistent organic pollutants (POPs), of which twelve are currently listed under the Convention. POPs are chemicals that remain intact in the environment for long periods, become widely distributed geographically, accumulate in living organisms and can cause harm to humans and the environment. The European Union and its Member States, which are Parties to the Stockholm Convention, submitted a proposal in July 2006 for listing octabromodiphenyl ether in Annex A of the Stockholm Convention pursuant to paragraph 1 of Article 8 of the Convention, and the POPRC agreed that the commercial product Commercial octabromodiphenyl ether – actually a mixture as described below - met the screening criteria of Annex D to the Convention.

1.1 Chemical identity of the proposed substance

This proposal concerns the c-OctaBDE. There are several components in the commercial product, with different properties and potential risks. Thus this risk profile focuses on the assessment of individual components of the commercial product, and the final compilation for an overall assessment of the commercial product itself.

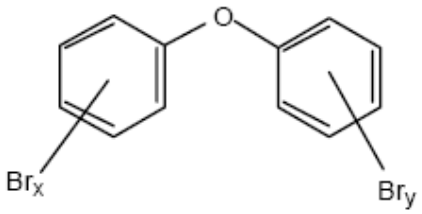
It is believed that little if any c-OctaBDE is produced since the major supplier located in North America stopped production in 2004. The commercially supplied OctaBDE was complex mixture consisting (as of 2001 within the EU Member States) typically of ≤0.5% Pentabromodiphenyl ether isomers, ≤12% Hexabromodiphenyl ether isomers, ≤45% Heptabromodiphenyl ether isomers, ≤33% OctaBDE isomers, ≤10% Nonabromodiphenyl ether isomers and ≤0.7% Decabromodiphenyl ether. The composition of older products or products from non-EU countries may be different from this.

The c-OctaBDE is sold as a technical grade under the Chemical Abstracts Service (CAS) Registry number for the OctaBDE isomer.

IUPAC Name: Diphenyl ether, octabromo derivative (octabromodiphenyl ether, OctaBDE)

Synonyms: octabromobiphenyl oxide; octabromodiphenyl oxide; octabromo phenoxybenzene and benzene; 1,1' oxybis-, octabromo derivative
CAS Number: 32536-52-0
Molecular formula: $C_{12}H_2Br_8O$
Molecular weight: 801.38

Chemical structure: (x+y=8)



Three polybrominated diphenyl ether flame retardants were historically available commercially. They are referred to as penta, octa and decabromodiphenyl ether, but each product is a mixture of diphenyl ethers with varying degrees of bromination. Several synonyms and abbreviations for polybrominated diphenyl ethers exist and these are shown below:

polybrominated biphenyl ethers ≡ polybromobiphenyl ethers – PBBEs
polybrominated biphenyl oxides ≡ polybromobiphenyl oxides - PBBOs
polybrominated diphenyl ethers ≡ polybromodiphenyl ethers - PBDPEs
polybrominated diphenyl oxides ≡ polybromodiphenyl oxides – PBDPOs

The abbreviations PBDE and BDE preceded by the number of bromine atoms (e.g. HeptaBDE) will be used in this document. The commercial mixtures will be identified by a c- (e.g. c-OctaBDE).

The compositions of the commercial polybrominated diphenyl ethers based on composite samples from the EU suppliers are shown in Table 1-1below. These are the substances that have been used in the recent tests and used as a basis for the EU risk assessment reports (RAR) for the three commercial substances. La Guardia et al (2006) have recently reported additional information on the composition of commercial mixtures.

The commercial mixture covered by this entry is therefore a complex combination of isomers and congeners, as defined at POPRC. This risk profile will focus on the series of Hexa, Hepta, Octa and Nona homologues, as the Penta and Deca homologues are covered by their respective commercial mixtures. There is a tendency in scientific literature to present the identities of polybrominated diphenyl ether congeners using the numbering system based on the polychlorinated biphenyl system:

- Hexabromodiphenyl ethers (benzene, 1,1'-oxybis-, hexabromo derivative; HexaBDE) (CAS No. 36483-60-0; IUPAC Nº between BDE-128 and BDE-169)
- Heptabromodiphenyl ethers (benzene, 1,1'-oxybis-, heptabromo derivative; HeptaBDE) (CAS No. 68928-80-3; IUPAC Nº between BDE-170 and BDE-193)
- octabromodiphenyl ethers (benzene, 1,1'-oxybis-, octabromo derivative; OctaBDE) (CAS No. 32536-52-0; IUPAC Nº between BDE-194 and BDE-205)
- Nonabromodiphenyl ethers (benzene, 1,1'-oxybis-, nonabromo derivative; NonaBDE) (CAS No. 63936-56-1; IUPAC Nº between BDE-206 and BDE-208)

Table 1-1. Composition of commercial polybrominated diphenyl ethers as described in the EU RAR.

Component	% Composition of commercial product			
	Penta-		Octa-	Deca-
	1997	2000	1997	1997
Tribromodiphenyl ether		0.23		
Tetrabromodiphenyl ether	33.7	36.02		
Pentabromodiphenyl ether	54.6	55.10		
Hexabromodiphenyl ether	11.7	8.58	5.5	
Heptabromodiphenyl ether			42.3	
Octabromodiphenyl ether			36.1	0.04
Nonabromodiphenyl ether			13.9	2.5
Decabromodiphenyl ether			2.1	97.4

The complexity for setting a risk profile for a complex mixture has been already discussed by the POPRC with reference to the commercial mixture of pentabromodiphenyl ether. A full data set for conducting a risk profile is not available for the commercial mixture or for the individual components. Thus the available pieces of information have been combined in this risk profile. The information was particularly scarce for Hepta- to NonaBDEs but there is an increasing interest in the scientific community for covering these congeners. A quantitative assessment is still not possible nowadays, but may become feasible soon if additional scientifically sound information is produced at a similar rate than in recent years,

1.2 Conclusion of the POP Review Committee of Annex D informat*ion*

The POPRC has evaluated Annex D information and has concluded that proposal fulfils the requirements of Article 8 and Annex D of the Convention (POPRC-2/6)

1.3 Data sources

The EU risk assessment report (EC, 2003), the Canadian assessment (Environment Canada, 2004), and references from the WHO (1994) report were the main source of information used by the POP RC in Annex D screening. Additional information has been submitted by Canada, the Czech Republic, Germany, Japan, Lithuania, Norway, Switzerland, Turkey, UK, USA, the NGO Environmental Health Fund on behalf of the International POPs Elimination Network (IPEN), and the industry organization Bromine Science and Environmental Forum (BSEF), as well as during the consultation period. Considering the large amount of new scientific information produced nowadays, a review of recent scientific literature has also been conducted and used as an essential data source in this report.

1.4 Status of the chemical under international conventions

- OSPAR Convention: OctaBDE is included in the list of selected substances for the OSPAR lists (no 236). Under the reviewed list, OctaBDE is put under section C – about the substances put on hold because they are not produced and/or used in the OSPAR catchment or are used in sufficiently contained systems making a threat to the marine environment unlikely.
- UNECE, Convention on Long-range Transboundary Air Pollution (LRTAP) and its Protocol on Persistent Organic Pollutants (POPs): c-OctaBDE is being considered under Protocol procedures for inclusion.

2. Summary information relevant for the risk profile

2.1 Sources

The information provided by the bromide industry indicates that the commercial product has been produced in The Netherlands, France, USA, Japan, UK and Israel, but since 2004, it is no longer produced in the EU, USA and the Pacific Rim and there is no information that indicates it is being produced in developing countries.

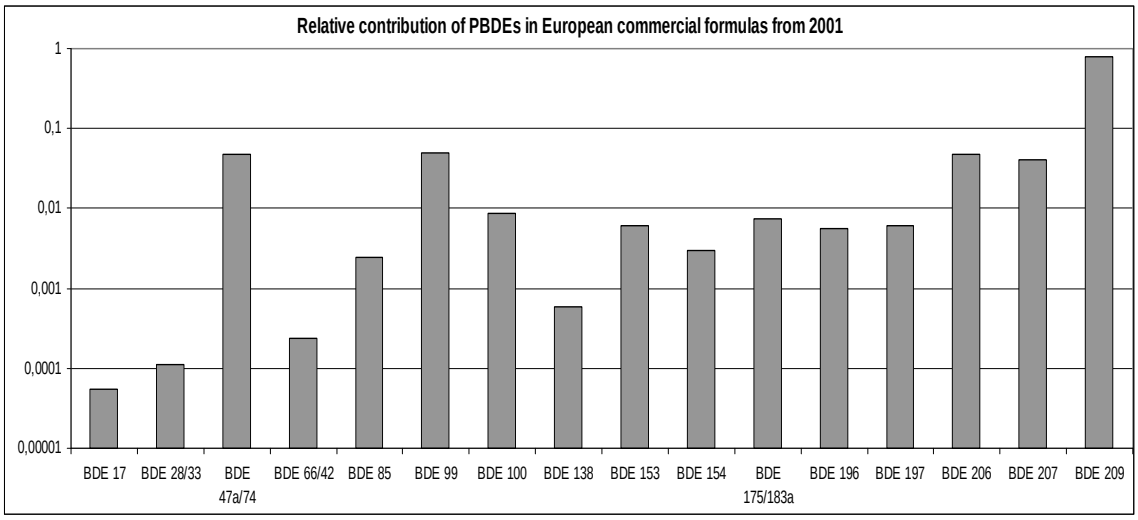
The polybrominated diphenyl ethers in general are used as flame retardants of the additive type. They are physically combined with the material being treated rather than chemically combined (as in reactive flame retardants). This means that there is the possibility that the flame retardant may diffuse out of the treated material to some extent. Industry indicates that octabromodiphenyl ether is always used in conjunction with antimony trioxide. In Europe, it is primarily used in acrylonitrile-butadiene-styrene (ABS) polymers at 12-18% weight loadings in the final product. Around 95% of the total octabromodiphenyl ether supplied in the EU is used in ABS. Other minor uses, accounting for the remaining 5% use, include high impact polystyrene (HIPS), polybutylene terephthalate (PBT) and polyamide polymers, at typical loadings of 12-15% weight in the final product. In some applications, the flame retardant is compounded with the polymer to produce pellets (masterbatch) with slightly higher loadings of flame retardant. These are then used in the polymer processing step to produce products with similar loadings as given above.

The flame retarded polymer products are typically used for the housings of office equipment and business machines. Other uses that have been reported for octabromodiphenyl ether include nylon and low density polyethylene (WHO, 1994), polycarbonate, phenol-formaldehyde resins and unsaturated polyesters (OECD, 1994) and in adhesives and coatings (WHO, 1994).

Assuming that the commercial OctaBDE is not longer produced, the releases to the environment must be associated to historical processes, as well as to releases during the service life of articles containing the commercial mixtures and at the end of article service life during disposal operations. The information review by La Guardia et al (2006) allows estimations of the relative contribution of each congener in different markets and time periods. As an example, Figure 1-1 presents the calculations for European commercial products in 2001.

Although there are some figures on annual production of this mixture, there are no accurate values on the amount of the commercial Octa and/or the individual homologues in articles in service and disposed at the world-wide level, but considering the estimated figure of 6 000 tonnes/year (WHO, 1994) the total amount should be expected in the $10^5 – 10^6$ tonnes range. According to the BSEF, OctaBDE was commercialized sometime in the mid 70's. By the early 2000's global production was <4000 tonnes/year and by the time production ceased, demand was <500 tonnes. While thus, assuming 30 years of production at 6000 tonnes per year gives 180,000 tonnes, a figure within the proposed range.

Figure 1-1. Estimated relative contribution for the different BDE congeners in products in the European market in 2001. Calculated from data published by La Guardia et al., 2006. Note the logarithmic scale.



Morf et al., (2002) reported for Switzerland diffuse emission from the use of products containing OctaBDE of about 0.37 t/a (based on worst-case estimations) for a total stock of 680 tons.

2.2 Environmental fate

2.2.1 Persistence

No aerobic biodegradation of the Hexa- to NonaBDEs is expected based on BIOWIN estimates as recalcitrant with respect to biodegradation, and no degradation, based on oxygen uptake, occurred in a 28-day closed bottle test OECD 301D (EC, 2003).

Gerecke et al. (2005) reported the degradation of NonaBDE 206 and 207 and DecaBDE to OctaBDEs under anaerobic conditions using sewage sludge innoculum; and this degradation has been confirmed in other studies (Gaul et al, 2006; He et al, 2006).

AOPWIN predicts half-lives for reaction with atmospheric hydroxyl radicals ranging from 30.4 to 161.0 d for Hexa- to NonaBDEs, respectively. However, in the atmosphere, Hexa to NonaBDEs are expected to strongly adsorb to suspended particles in the air and be removed via wet and/or dry deposition. Note that predicted half-lives have not been empirically substantiated, but are provided for reference purposes.

The photodecomposition of several BDEs has been studied in different matrices such as sealed polyethylene tube exposed to natural sunlight for up to 120 min (Peterman et al. 2003); or water (Sanchez-Prado et al., 2006); in general degradation was faster for the higher brominated DEs than for the lower brominated congeners. Rayne et al. (2006) suggest a short photochemical half-life for the Hexa BDE153 in aquatic systems, with rapid photohydrodebromination to some of the most prevalent Penta- and Tetra-brominated diphenyl ether congeners.

2.2.2 Bioaccumulation

The bioaccumulation potential differs strongly among the components of the commercial mixture. For facilitating, the assessment, the different bioaccumulation processes will be presented independently.

2.2.2.1. Bioconcentration from water

Bioconcentration from water is considered relevant only for HexaBDE. The UK has re-analyzed the CITI (1982) bioconcentration data and suggests BCFs of up to ~5,640 l/kg and ~ 2,580 l/kg for components D and E (both HexaBDE).

Bioconcentration factors were reported (EC, 2003) for carp. Assuming that the actual concentrations of the c-OctaBDE components were at or around the reported water solubility for the substance of 0.5 µg/L, then the BCF for OctaBDE would be <9.5; for HeptaBDE about <1.1-3.8 and for c-OctaBDE about <10-36. These BCF values are lower

than would be expected from the substance's octanol-water partition coefficients. This can be explained by a reduced bioavailability, metabolisms or both.

2.2.2.2 Bioaccumulation and biomagnification from food exposures.

Oral exposure is expected to be the most relevant exposure pathway for these chemicals. Van Beusekom et al. (2006) reported biota-sediment accumulation factors between 1 and 3 for Hexa and HeptaBDE on two freshwater fish species in Spain and concluded that 100% of the exposure was associated to food or food plus sediment for bleak (Alburnus alburnus) and barbel (Barbus graellsii), respectively.

A controlled feeding trial assessed transfer and accumulation of PBDEs from feed to farmed Atlantic salmon (Salmo salar). On average, 95% of the total PBDE content in the feed accumulated in whole salmon including HeptaBDE 183 (Isosaari, et al. 2005).

The potential for biomagnification has been demonstrated for Hexa and HeptaBDE (Burreau et al., 2004; 2006; Sormo et al., 2006; Tomy et al., 2004), and more recently suggested for the DecaBDE (Law et al., 2006).

Food-web biomagnification was not been observed for Octa and NonaBDE in an aquatic ecosystem, but the congeners were detected in biota from zooplanckton to fish species (Burreau et al. 2006).

2.2.2.3. Bioaccumulation from sediment exposures

Ciparis and Hale (2005) have reported a rapid bioaccumulation of HexaBDE in the aquatic oligochaete, *Lumbriculus variegates*, exposed via sediment, with differences between isomers and in the contamination pathway. A biota-sediment accumulation factor of 9.1± 1.1 was observed for BDE 154, the highest concentration was found on day 15 and the depuration rate constant was 0.032 ± 0.016 $days^{-1}$.

2.2.2.4. Toxicokinetics and relevance of metabolisms

The potential for bioaccumulation and biomagnification of these types of molecules can be calculated using toxicokinetic models, based on metabolism and elimination. Differences among isomers and the reported debromination processes introduce additional uncertainty when reviewing field data.

Stapleton et al. (2004) in a dietary study on carps found depuration rates of 0.051± 0.036 $days^{-1}$ and assimilation efficiencies of 4% ± 3 for the HexaBDE 153. Stapleton and Baker (2003) and Stapleton et al. (2004b) in dietary studies on common carp (*Cyprinus carpio*) found significant and rapid debromination of HeptaBDE183 to HexaBDE154 and to another unidentified HexaBDE congener within the intestinal tissues of the carp after consuming its food. I*n vitro* studies have demonstrated the microsomal debromination in fish (Stapleton et al. (2006).

Tomy et al (2004) exposed juvenile lake trout (*Salvelinus namaycush*) to three dietary concentrations of 13 BDE congeners (3-10 Br atoms) in the laboratory for 56 days, followed by 112 days of clean food. Half-lives (t1/2's) for some BDE congeners (e.g., BDE-85 and -190) were much lower than expected based on their Kow, whereas t1/2's of other BDE congeners (e.g., BDE-66, -77, -153, and -154) were much longer than anticipated based on Kow. This was explained by debromination. The detection of three BDE congeners (an unknown PentaBDE, BDE-140, and an unknown HexaBDE) in the fish that were not present in the food or in the control fish provided further evidence for the debromination of BDEs.

The role of exposure levels in the elimination rate of several chemicals including HexaBDE 153 has been studied by the LPTC). Université Bordeaux I and the INIA's Laboratory for Ecotoxicology within the context of LRI-Cefic Research Project ECO-1AINIA-1100. Depuration rates of 0.03-0.05 for *Sparus aurata* and *Mytilus edulis,* were obtained (Alonso et al., 2006).

The debromination of PBDEs has also indicated in mammals, e.g. for a c-PentaBDE formulation in mice (Qiu et al., 2007) and for DecaBDE in cows (Kierkegaard et al., 2007).

A recent study (Drouillard et al., 2007) has reported a depuration rate constant for the HexaBDE 0.016 $days^{-1}$ in juvenile American kestrels (*Falco sparverius*), with a retention of about 50% of the administered dose in a 36 days study.

Van den Steen et al. (2007) used silastic implants to expose European starlings (Sturnus vulgaris) to DecaBDE209 and found Octa- (BDE196, BDE197) and NonaBDEs (BDE206, BDE207, BDE208) in muscle and liver in addition to DecaBDE209, resulting in the first indications of debromination in birds.

2.2.2.5 Integrated assessment of the bioaccumulation potential.

A high potential for bioaccumulation (including a moderate potential for bioconcentration) and food-web biomagnification has been demonstrated for HexaBDE; and it is fully in line with the reported elimination rates.

The food-web biomagnification has been also demonstrated for HeptaBDE, although at a lower extend than expected from the Kow; this fact can be explained by metabolism resulting in a relatively short half-life (experimentally demonstrated and explained by the authors by debromination).

The presence of Octa and NonaBDE in biota is well document but its potential for bioaccumulation from water and food is much lower than expected from their Kow. Reduced availability, metabolisms or both can justify this fact. The number of scientific papers demonstrating debromination of Deca-, Nona, and Octa- BDE to other PBDEs is continuously increasing; this is critical for the assessment as would indicate that the supposed low bioaccumulation potential could be in reality the consequence of metabolism to bioaccumulative PBDEs. A quantitative estimation cannot be presented yet, but the debromination process has been already reported for aquatic organisms, mammals and birds.

2.2.3 Long range environmental transport

The presence of components of commercial Octa BDE in remote areas (e.g. Norway info, Norway Info 2; Canada info 2; Switzerland info2, Japan info) is considered the best demonstration for the potential for long range transport of these chemicals. As debromination in biota has been demonstrated, hypothetically, the presence of Hexa to NonaBDEs could be explained by a long range transport of DecaBDE and its subsequent debromination, however, since Hexa to Deca congeners have similar atmospheric transport characteristics in terms of gas-partitioning and reactivity it is evidence of long range transport for DecaBDE and is indirect evidence of long range transport for the Nona to Hexa congeners.

Previous model predictions suggested a low potential for long-range atmospheric transport for highly brominated BDEs (e.g. Wania and Dugani, 2003). However, in a recent paper on DecaBDE, Breivik et al., (2006) have reported that chemicals that are both sorbed to particles and potentially persistent in the atmosphere, such as BDE-209, may have a larger potential for LRT than anticipated on the basis of earlier model evaluations. This explanation could be also applied to c-OctaBDE components.

Recently Wegmann, et al, (2007) applied the OECD Pov and LRTP Screening Tool to the current POPs candidates, including c-OctaBDE. The authors noted that they believed that the substance property values for c-OctaBDE in Wania and Dugani (2003) were more accurate than the values in the POPRC document and therefore included the Wania and Dugani values in their Monte Carlo uncertainty analysis. Although there were considerable uncertainties, the results indicated that c-OctaBDE has Pov and LRTP properties similar to those of several known POPs.

2.3 Exposure

2.3.1 Atmosphere

Strandberg et al. (2001) analyzed air samples from urban, rural and remote sites in the United States near the Great Lakes. The average total c-OctaBDE-related congeners (i.e., sum of BDEs 153, 154 and 190) present in the samples ranged from approximately 0.2 to 0.9 pg/m3.

Bergander et al. (1995) analyzed air samples from two areas of Sweden remote from industry, HexaBDE and HeptaBDE were found in the particulate phase samples.

In a monitoring study carried out in coastal areas of Korea over one-year period, twenty individual PBDE congeners were found in atmospheric samples collected from urban, suburban and rural sites. DecaBDE (BDE 209) was the predominant congener (<93%) The depositional fluxes ranged from 10.1 to 89.0 µg/m2/year (Moon et al., 2007a). In northwest China, the measurements of total PBDEs (8.3 ± 4.0 pg/m3) in the samples collected at the Waliguan Baseline Observatory (April to May, 2005) were at comparable concentration levels with other remote areas (Cheng et al., 2007).

PBDEs have also been detected over the Indian Ocean (mean concentration of 2.5 pg/m3) and along the coastal line of Java, Indonesia (values of 15 pg/m3). Air back trajectory analysis is suggested in relation to the potential of PBDEs for long-range atmospheric transport from remote regions of areas more industrialized (Wurl et al. 2006).

Wang et al. (2005,) report atmospheric concentrations for c-OctaBDE components for a large number of remote locations, and additional information about the presence of Penta to HeptaBDE congeners in air at several locations can be found in the review paper by de Wit et al. (2006).

2.3.2 Water

Luckey et al. (2002) measured total PBDE (mono- to HeptaBDE congeners) concentrations of approximately 6 pg/L in Lake Ontario surface waters in 1999, with HexaBDE congeners BDE153 and BDE154 each contributing approximately 5 to 8% of the total.

C-OctaBDE was not detected in 1987 in 75 surface water samples taken in Japan at a detection limit of 0.1µg/L or in 1988 in 147 water samples at a detection limit of 0.07 µg/L (Environment Agency Japan 1991). According to EC (2003), the concentrations are considered to be representative of industrial, urban and rural areas of Japan, but it is not known whether any of the sampling sites were in the vicinity of a polybrominated diphenyl ether production site or a polymer processing site.

There is additional information on concentrations of c-OctaBDE components (HexaBDEs 153 and 154) in the dissolved phase in water in a study by Law et al. (2006).

2.3.3 Sediments

Concentrations of c-OctaBDE in UK sediments ranged from <0.44 to 3030 µg/kg dw (Allchin et al. 1999; Law et al. 1996; Environment Agency UK, 1997)). The highest levels were in sediments downstream from a warehouse where c-DecaBDE was stored. C-OctaBDE was detected in 3 of 51 sediment samples from Japan in 1987 at concentrations from 8 to 21 µg/kg (detection limit 7 µg/kg; ww or dw not specified), and in 3 of 135 samples collected in 1988 at concentrations of 15 to 22 µg/kg (detection limit 5 µg/kg; ww or dw not specified) (Environment Agency Japan 1991).

Kolic et al. (2004) presented levels of PBDEs in sediments from tributaries flowing to Lake Ontario, and area biosolids in southern Ontario. Total Hexa- and HeptaBDEs (i.e., BDE 138, 153, 154 and 183) measured in sediment samples taken from fourteen tributary sites (only 6 sites were reported) ranged from approximately 0.5 to 4.0 µg/kg dw.

Historical trends of PBDEs in sediments have been determined in the Lake of Ellasjøen, Norwegian Arctic, where contamination is due to both atmospheric and biological transport. Maximum level of PBDEs was detected in 2001 (0.73 ng/g dw) (Evenset et al., 2007). Marvin et al. 2007, have reported temporal trends in PBDEs in Niagara river suspended sediments from 1988 to 2004. Prior to 1988, PBDEs (sum of 16 congeners including DecaBDE) were generally detected at low-ppb concentrations, but showed a trend toward increasing concentrations over the period 1980–1988. After 1988, PBDE concentrations in the Niagara River showed a more rapidly increasing trend (maximum of approximately 35 ng/g in 1995). DecaBDE was the predominant congener detected, and a similar situation has been observed in Europe (Eljarrat et al., 2005), and Asia (Moon et al. 2007b).

The study by Law et al. (2006) provides additional information on concentrations of c-OctaBDE components (HexaBDEs 153 and 154) for sediments at a background location.

2.3.4 Soil

Hassanin et al. (2004) determined PBDEs in undisturbed surface soils (0-5 cm) and subsurface soils from remote/rural woodland and grassland sites on a latitudinal transect through the United Kingdom and Norway. In total, 66 surface soils were analyzed for 22 tri- to HeptaBDEs. Concentrations of total PBDEs in the surface soils ranged from 0.065 to 12.0 µg/kg dw. Median PBDE concentrations in the surface soils ranged from 0.61 to 2.5 µg/kg dw, with BDEs 47, 99, 100, 153 and 154 dominating the total concentrations. The median concentration of the sum of these five congeners ranged from 0.44 to 1.8 µg/kg dw. The researchers noted that the congener patterns in the European background soils closely matched that reported for the c-PentaBDE mixture. Northward along the latitudinal transect, there was an increasing relative contribution of BDE 47 and other lighter PBDEs in comparison to the heavier PBDEs measured in the samples.

2.3.5 Waste Effluent and Biosolids

Kolic et al. (2004) presented levels of PBDEs in sediments from tributaries flowing to Lake Ontario, and of biosolids from nearby wastewater treatment facilities in southern Ontario. Total Hexa- and HeptaBDEs (i.e., BDEs 138, 153, 154 and 183) measured in biosolids ranged from approximately 111 to 178 µg/kg dw.

La Guardia (2001) analyzed 11 sewage sludge samples before land application from Canada and the United States and found that total Hexa- to OctaBDE congener concentrations ranged from 40 to 2080 µg/kg dw. Kolic et al. (2003) investigated PBDE levels in sewage sludge from 12 sites in southern Ontario and found Hexa- to OctaBDE congener concentrations totaled 124 to 705 µg/kg dw. Hexa- to OctaBDE congeners were not detected in manure samples, and were at very low levels in pulp mill biosolids (up to approximately 3 µg/kg dw).

Martinez et al. (2006) have recently reported concentrations of sum of Hexa to NonaBDE in the range of 15.5 to 160 µg/kg dw in sludge from municipal wastewater treatment facilities in Spain, and up to 268 µg/kg dw in industrial facilities.

Gevao et al. (2006) measured PBDEs in coastal sediments receiving industrial and municipal effluents in Kuwait. Total concentrations varied from 80 to 3800 pg/g dw with HeptaBDE183 dominating the congener distribution which resembled the commercial formulation, Bromkal 79-8DE. Wastewater discharge from industrial activities appeared to be the primary source of the compounds.

2.3.6 Biota

Concentrations of components found in c-OctaBDEs in biota were reviewed in Law et al. (2003). The concentration of c-OctaBDE (reported as the commercial mixture DE-79) in various biota found in aquatic environments in the UK ranged up to 325 µg/kg ww in the liver of dab (Allchin et al. 1999). Concentrations of OctaBDE in muscle tissue from UK fish ranged from <1 to 12 µg/kg ww (Allchin et al. 1999). In Japan, OctaBDE was not detected in 75 fish samples taken in 1987 (detection limit 5 µg/kg ww), nor was it detected in 144 fish samples taken from 48 locations in 1988-89 (detection limit 4 µg/kg; ww or dw not specified) (Environment Agency Japan 1991). HeptaBDE, along with other PBDE congeners, was detected in eggs of peregrine falcons, *Falco peregrinus*, from Sweden, at concentrations from 56 to 1300 µg/kg lipid (Lindberg et al. 2004).

Alaee et al. (1999) sampled lake trout from Lakes Superior, Huron and Ontario and found that the total of HexaBDE and HeptaBDE congeners ranged from an estimated 11 to 53 µg/kg lipid.

Rice et al. (2002) compared PBDE levels and congener patterns in carp and bass sampled from two industrialized regions in the eastern U.S. The fish were collected from the Detroit River, MI. and the Des Plaines River, IL. in May and June of 1999, and analyzed for the presence of BDEs 47, 99, 100, 153, 154, 181, 183 and 190. Both river systems are considered to receive high contributions from municipal and industrial effluents. BDE47 dominated in fish taken from the Detroit River, comprising an average of 53 to 56% of the total PBDEs by wet weight. BDEs 99, 100, 153 and 154 each contributed between 8 and 9%, and BDEs 181 and 183 each comprised about 5% of the total PBDEs. BDE190 was not detected in either fish species. Only carp were sampled from the Des Plaines River, and these exhibited a markedly different PBDE profile from that seen in the Detroit River fish. HeptaBDEs 181 and 183 were predominant, contributing about 21% and 19%, respectively. BDE47 was third in prevalence, comprising about 17% of the total PBDEs. Levels of the two HexaBDE congeners, BDEs 153 and 154 were 8 to 13%, compared with about 5% for each of the Penta- congeners, BDEs 99 and 100. BDE190, not detected in the Detroit River fish, was present at about 12% of total PBDE.

Norstrom et al. (2002) evaluated the geographical distribution and temporal trends (during the 1981 to 2000 period) of PBDEs in herring gull (*Larus argentatus*) eggs from a network of colonies scattered throughout the Great Lakes and their connecting channels in 2000 (see Section 2.1.6.6 and Appendix D). Although samples were analyzed for Octa- to DecaBDE, these were not found at their respective limits of detection (0.01-0.05 µg/kg ww). However, total concentrations of Hexa- and HeptaBDE congeners (i.e., BDEs 153,154 and 183) increased 6 to 30 fold over the 1981 to 2000 period at the Lake Michigan (from 6.7 to 195.6 µg/kg ww), Lake Huron (from 13.8 to 87.6 µg/kg ww) and Lake Ontario (3.8 to 112.1 µg/kg ww) sites. This increase was not as dramatic as that found for the tetra- and PentaBDE congeners.

Wakeford et al. (2002) conducted sampling of wild bird eggs in western and northern Canada between 1983 and 2000. They determined that the total of Hexa- and HeptaBDE congeners ranged from 0.148 to 52.9 µg/kg ww in Great Blue Heron (*Ardea herodias*) eggs (on Canada's west coast), 0.03 to 0.68 µg/kg ww in Northern Fulmer (*Fulmarus glacialis*) eggs (in the Canadian arctic) and 0.009 to 0.499 µg/kg ww in Thick Billed Murre (*Uria lomvia*) eggs (in the Canadian arctic). OctaBDE, NonaBDE and DecaBDE congeners were subject to analysis by the researchers, but were not detected (detection limit was not specified) in the any of the samples.

Temporal, spatial, and interspecific trends in PBDEs were determined in eggs of marine and freshwater bird species from the province of British Columbia, Canada. Temporal trends in the Fraser River estuary, 1983-2002, were examined by analysis of eggs of great blue herons (Ardea herodias) and from the Strait of Georgia marine ecosystem, 1979-2002, in eggs of double-crested cormorants (Phalacrocorax auritus). PBDEs increased exponentially with a doubling time of 5.7 years in eggs of both herons and cormorants. The PBDE pattern was relatively consistent in most years and sites, with BDEs 47 > 100 > 99 > 153 > 154 > 28 > 183. This was interpreted as evidence of technical PentaBDE formulations as primary sources of the contamination, with the OctaBDE formulations as secondary. Higher resolution analysis of a subsample of the eggs revealed the presence of up to nine other congeners, including BDE209 (range: 0.9-1.8 microg/kg), indicating exposure and uptake of DecaBDE sourced congeners in North American foodchains (Elliot et al., 2005)

A recent study (Burreau et al., 2006) has demonstrated the presence of Hexa to NonaBDE in biota (zooplankton, sprat, herring and salmon) from the Baltic Sea and Northern Atlantic.

2.3.7 Humans

EC (2003) presents some information on the levels of components of c-OctaBDE measured in human samples including human milk, blood, and adipose tissue. Large variations among individuals were generally observed, but significant differences between the control population and occupationally exposed groups were also reported.

In a recent study (Toms et al., 2007) the concentrations of PBDEs (18 congeners from BDE17 to BDE-183) found in Australian human milk were lower than those reported from North America but higher than those reported from Europe and Asia

Thomsen et al., 2007, investigated the levels of PBDEs in 21 pooled serum samples archived from the general Norwegian population (from 1977 to 2003). In serum from men (age 40–50 years) the sum of seven PBDE congeners (28, 47, 99, 100, 153, 154 and 183) increased from 1977 (0.5 ng/g lipids) to 1998 (4.8 ng/g lipids). From 1999 to 2003 the concentration of PBDEs seems to have stabilised.

Fernandez et al., 2007, have reported a study of the detection of PBDEs in the adipose tissue of women from Spain. Mean ∑PBDE (BDE 28, 75, 71, 47, 66, 77, 100, 119, 99, 85, 154, 153, 138, and 183) levels were 3.85 and 0.36 ng/g of lipid, respectively. Among PBDEs, congeners 153, 47, 183, 99, and 100 were the most frequent and abundant and together constituted 96% of the total amount of PBDEs in adipose tissue. Concentrations of PBDEs in this population were similar to those reported in other parts of Spain and in Swedish and Belgium populations but lower than those found in other Western countries.

PBDEs were measured in samples of human blood serum taken from 23 donors in Wellington, New Zealand. Concentrations expressed as the sum of congeners 47, 99, 100, 153, 154, and 183 (∑PBDE) were – at an average of 7.17 ng ∑PBDE g $(\text{lipid})^{-1}$ – within the range reported for human tissues in Europe, but lower than in Australia and North America (Harrad et al., 2007).

Based on the measured PBDE levels detected in various meat, fish and dairy food products, an average daily dietary intake estimate of PBDEs was calculated in a study carried out in Belgium. PBDE intake calculations were estimated between 23 and 48 ng/day of total PBDEs. Fish is the major contributor to the total daily PBDE-intake (around 40%) due to the high PBDE levels in this type of food, although it is only a minor constituent of the Belgian diet. Meat products account for around 30% of the total dietary intake of PBDEs. Dairy products and eggs contribute to a lesser degree (less than 30%, Voorspoels et al., 2007).

Schuhmacher et al., 2007 have carried out an study to compare levels of PBDEs due to dietary intake and population living near a hazardous waste incinerator (HWI), in Spain. This study suggests that dietary intake is more relevant for human exposure to PBDEs than living near the HWI. Dietary intake of PBDEs for standard adult women were 72 and 63 ng/day for PBDEs, for residents in urban and industrials areas, respectively. Mean PBDE concentrations were 2.2 and 2.5 ng/g fat for women living in urban and industrial zones, respectively. Similar results have also been reported in a study carried out in Korea (Lee et al., 2007)

Exposure to components of c-OctaBDE in remote areas is confirmed and based on the available information should be attributed to a combination of releases and transport of c-OctaBDE, c-PentaBDE (for HexaBDE) and c-DecaBDE (for NonaBDE), and to the debromination of DecaBDE in the environment including biota. There is no sufficient information for assessing these processes in quantified terms. The exposure route is mainly via food. In addition to the feeding strategy, several additional confounding factors are associated to the species to specific differences observed in the isomer distribution pattern of PBDE in wildlife. These factors include, among others, species-specific differences in assimilation, metabolism and depuration of different isomers, even with the same level of bromination.

Measured levels of Hexa and Hepta components of c-OctaBDE in biota from remote areas seem to be the best available information for estimating exposure as result of LRET for these chemicals. Knudsen et al (2005) have recently review temporal trends of PBDE in eggs from three bird species, three locations and three sampling times (from 1983 to 2003) from Northern Norway. Spatial differences were only observed for HexaBDE 153, and increases in the measured concentration from 1983 to 2003 were observed for the HexaBDE 153 and 154 and the HeptaBDE 183. Mean values were around 1 µg/kg ww for each isomer and maximum values above 10 µg/kg ww were observed for BDE 154 and 183. Inter-species differences could be associated to feeding behavior and migration. In general the concentrations were lower than those reported for similar species in industrialized areas and those observed in terrestrial predatory birds. The presence of Hexa and HeptaBDE in fish from remote alpine lakes in Switzerland (Schmid et al., 2007) reported to be related to atmospheric deposition confirms the potential for atmospheric long-range transport. Hexa to NonaBDE have been found in salmon in the Atlantic Ocean west of Iceland (Burreau et al. 2006).

Despite its large molecular size, the evidence demonstrates the capability of c-OctaBDE components to cross the cellular membranes and to accumulate in biota. Although the information is limited, the assimilation and metabolisms of each isomer may vary significantly among species, but also in relation to the administered dose. As a consequence, it is essential to understand the toxicokinetics of these chemicals at environmentally relevant concentrations. These differences would justify the disparities observed in the assessment of biomagnification potential for different trophic chains.

Like for other chemicals with similar properties, aging processes are expected to reduce the bioavailability, and the experiments conducted on sediment dwelling organisms comparing the bioaccumulation in spiked sediments and from contaminated biosolids offer and indirect support for this hypothesis.

2.4 Hazard assessment for endpoints of concern

2.4.1. Experimental studies

2.4.1.1. Aquatic Organisms

The EU Risk Assessment report (EC, 2003), presents a set of studies on the commercial mixture and concludes that for water it seems sensible to assume that no adverse effects on aquatic organisms are likely to occur at concentrations up to the substance's water solubility. However it must be noted, first, that aquatic organisms are also exposed from food and/or sediment; and second, that setting this strong conclusion on chemicals such as PBDEs requires multigenerational or at least full life-cycle assays on the three taxonomic groups covering a large list of sublethal effects, information which is unavailable at this time.

2.4.1.2. Benthic Organisms

There are two available 28 day spiked sediment studies on *Lumbriculus variegatus* using the c-OctaBDE product (Great Lakes Chemical Corporation 2001a, b). These studies found no statistically significant effects relevant to survival, reproduction or growth at the highest tested concentration (1272 mg/kg dw and 1340 mg/kg dw measured for sediments with 2.4% and 5.9% OC, respectively). Kinetic data from Ciparis and Hale (2005) confirms the expected exposure and bioaccumulation under these conditions.

2.4.1.3. Soil Organisms

Survival and growth of earthworms, *Eisenia fetida,* were not affected by a 56 day exposure to a commercial OctaBDE formulation in an artificial soil at concentrations up to 1470 mg/kg dw (measured concentration in sediments with 4.7% OC) (Great Lakes Chemical Corporation 2001c).

The toxicity of c-OctaBDE to corn (*Zea mays*), onion (*Allium cepa*), ryegrass (*Lolium perenne*), cucumber (*Cucumis sativa*), soybean (*Glycine max*), and tomato (*Lycopersicon esculentum*) was evaluated in a 21-day emergence and growth study using an artificial sandy loam soil (Great Lakes Chemical Corporation 2001d). No statistically significant effects were observed for any plant species between the controls and the treatments for emergence, survival or growth at any of the tested concentrations (up to 1190 mg/kg dw, measured concentration).

2.4.1.4. Mammals and Birds

The lowest reported NOAEL for traditional endpoints is a NOAEL of 2 mg/kg/d based on slight fetotoxicity at 5 mg/kg/d (considered relevant in the EU report) or 5 mg/kg bw/d based on increased liver weights and decreased body weight gain among the maternal treatment group and delayed fetal skeletal ossification at 15 mg/kg bw/d (for those reviewers that do not consider relevant the slight fetotoxicity effects) described by Breslin et al. (1989) in a developmental toxicity study with Saytex 111 on New Zealand White rabbits exposed orally via gavage over days 7 to 19 of gestation.

Effects on other endpoints have been described at lower concentrations, including:

- A significant increase in EPN detoxification and *p*-nitroanEROD and isole demethylation in male Sprague-Dawley rats at an oral dose of 0.60 mg/kg bw/day OBDE formulation for 14-days.
- dose-dependent depletion of serum total thyroxine T4 and induced pentoxyresorufin *O*-deethylase (PROD) activities in rats receiving 10 or more mg/kg bw/day of commercial OctaBDE (Zhou et al. 2001)
- Delayed neurotoxic effects. Neonatal mice exposed to a single dose of 0.45 mg BDE153/kg bw on postnatal day 10 showed when tested at 2, 4 and 6 months of age altered motor behavior. Spatial learning ability and memory function in the adult mice were also affected (Viberg et al.,2001)
- Eriksson et al. (2002) confirmed neurotoxic effects (aberrant behavioral responses) on developing male mice exposed to 0.45 to 9.0 mg/kg bw of BDE153 on day 10 of development. The effects were comparable to those

observed for PCB153 leading the authors to speculate that interactive neurotoxic action may be possible between the two compounds.

- These neurotoxic effects have also been observed after a single oral dose of NonaBDE 206 or OctaBDE 203 administered on postnatal day 3 or 10 to, or PBDE 183; with disturbances in spontaneous behavior, leading to disrupted habituation and a hyperactive condition in adults at the age of 2 months. (Viberg et al., 2006).
- Immunomodulation effects in captive nestling American kestrels (*Falco sparverius*) have been reported by Fernie et al. (2005). Eggs within each clutch, divided by laying sequence, were injected with safflower oil or PentaBDE congeners-47, -99, -100, and -153 dissolved in safflower oil (18.7 µg PBDEs/egg). For 29 days, nestlings consumed the same PBDE mixture (15.6+/-0.3 ng/g body weight per day), reaching PBDE body burden concentrations that were 120x higher in the treatment birds (86.1+/-29.1 ng/g ww) than controls (0.73+/-0.5 ng/g ww). PBDE-exposed birds had a greater PHA response (T-cell-mediated immunity), which was negatively associated with increasing BDE-47 concentrations, but a reduced antibody-mediated response that was positively associated with increasing BDE-183 concentrations. There were also structural changes in the spleen (fewer germinal centers), bursa (reduced apoptosis) and thymus (increased macrophages), and negative associations between the spleen somatic index and PBDEs, and the bursa somatic index and BDE-47. Immunomodulation from PBDE exposure may be exacerbated in wild birds experiencing greater environmental stresses.
- Fernie et al., 2006 also reported for the same species and test conditions that exposure did not affect hatching or fledging success. PBDE-exposed nestlings were larger (weight, bones, feathers) as they gained weight more quickly and ate more food, the latter in association with their PBDE body burdens. BDE-100 was most influential on nestling growth, being positively associated with size, weight gain, and food consumption. Increasing concentrations of BDE-183 and -153 were related to longer bones and BDE-99 to longer feathers. The larger size of the PBDE-exposed birds may be detrimental to their bone structure and have excessive energetic costs.
- In vitro studies indicates that BDE (including the HexaBDE 153) affected protein kinase C (PKC) and calcium homeostasis in cerebellar granule neuronal cultures in a similar way to those of a structurally-related polychlorinated biphenyl (PCB) (Kodavanti et al., 2005).

Although these studies do not allow a quantitative assessment, they indicate the need for addressing long-term and delayed effects, as well as specific mechanisms of action, in the evaluation of potential health and ecosystem adverse effects.

2.4.2. Monitoring data on effects

There are several scientific papers comparing population effects observed in the field with measured concentrations of POP like chemicals, including Hexa to NonaBDE in individuals from different species.

Unfortunately, wild populations are co-exposed to a mixture of PBDEs as well as to other related brominated and chlorinated persistent pollutants, and with the current level of knowledge epidemiological investigations can just present associations but no cause-effect relationships between the exposure/accumulation of the components of the commercial OctaBDE mixtures and potential adverse effects observed in wildlife.

A similar situation is observed regarding human health data, and no studies offering conclusive evidence on the hazards of Hexa to NonaBDE for humans at environmentally relevant exposure levels have been found.

3. Synthesis of the information

A quantitative evaluation of the specific risks of c-OctaBDE is not possible due to the presence of its components in commercial Penta- and Deca mixtures, and the lack of information; this include the absence of information for supporting quantitative assessments of the role on debromination and the lack of a solid body of toxicological and ecotoxicological information for the mixture and its components; covering the long-term low level exposure conditions and the sublethal endpoints considered relevant for assessing the risk of a POP candidate. Australia and Canada have reported quantitative risk assessments for health and for the environment based on risk quotients and margins of safety suggesting a potential risk. The evaluations do not cover expected conditions in remote areas but are useful in the overall assessment (Environment Canada, 2006; NICNAS, 2007).

In this risk profile, Hexa to NonaBDE have been considered the relevant components in c-OctaBDE. It should be noted that other BDE are also found in commercial mixtures, including those present in c-PentaBDE and c-DecaBDE..

The persistence of these PBDE in the environment is well documented. The only relevant degradation pathways identified until now are photolysis, anaerobic degradation and metabolism in biota, acting through debromination and producing other BDE which may have higher toxicity and bioaccumulation potential.

The bioaccumulation potential depends on the level of bromination. HexaBDE shows a significant potential for bioconcentration and biomagnification; HeptaBDE biomagnifies through the food web but at a lower extend than that expected from the Kow. Octa and NonaBDE have been found in biota but no food-web biomagnification has been observed. Metabolisms and/or reduced bioavailability explain the divergences between observations and Kow predictions. The contribution of metabolism through debromination into other BDEs is supported by and increasingly amount of scientific evidence.

Biota monitoring data in remote areas cover Hexa and HeptaBDE and offer the best demonstration on the potential for long range transport of c-OctaBDE components. Theoretically this presence could also be explained by the transport of DecaBDE and its subsequent debromination. However, it is not realistic to assume that DecaBDE debromination may explain the process without additional transport from other congeners. The role of atmospheric transport is confirmed for Hexa and HeptaBDE based on its detection in alpine lakes.

Unfortunately, the available information on the toxicity and ecotoxicity of Hexa to NonaBDE is very limited and does not offer enough information for presenting sound toxicological and ecotoxicological profiles for each isomer, mixtures of isomers and commercial mixtures.

No relevant effects have been observed in aquatic, sediment and soil laboratory studies; but the measured endpoints and the exposure conditions, employed in these assays are clearly insufficient for a proper assessment of chemicals such as Hexa to NonaBDE. Ecotoxicity tests on these types of chemicals should cover if possible several generations or at least a full life cycle, and the measured endpoints must include sublethal effects associated to the accumulation and re-mobilization of the PBDEs during critical periods of development and reproduction, as well as the ecologically relevant consequences of metabolic changes. In addition, all environmentally relevant exposure routes must be addressed. The available tests do not fulfill these conditions,.

The available information on mammals and birds offer relevant information. The lowest reported NOAEL for traditional endpoints is 2-5 mg/kg bw/d based on slight fetotoxicity or increased liver weights and decreased body weight gain among the maternal treatment group and delayed fetal skeletal ossification. These effects are relevant for the health and the ecological assessment and therefore useful for assessing risks for humans and wildlife. Nevertheless, the additional available information also creates concerns on the capability of these traditional endpoints for assessing the toxicological profile of Hexa to NonaBDE in mammals and other vertebrates.

The immuno-toxicological effects and particularly the delayed neurotoxic effects observed after a single dose require specific attention. Although a quantitative evaluation of these effects in terms of its potential risk for human health and ecosystem is not possible based on the current level of information, the reported observations must be analyzed with care. Certainly, the doses at which the effect have been observed are well above exposure levels in remote areas estimated from current monitoring data for a single congener. However, the effects have been observed for different congeners, and realistic environmental exposure occurs for a mixture of PBDEs. There is not enough information for considering if these effects may be additive or even more than additive in synergistic exposures. The margins between effects observed in the lab and estimated oral exposure levels in the field (based on monitoring data) are not so high when the different isomers/homologues are summed. McDonald (2005) estimated a critical body burden for HexaBDE 153 of 2000 µg/kg lipid based on the NOEL of 0.45 mg/kg reported by Viberg et al 2003 and gives a margin of safety of 7 between this level and the 95 percentile of total PBDE levels in US human populations. It should be noted that HexaBDE 153 concentrations close to these value have been found in several species and geographic sites (see Canada info 2 for a review) and total PBDE concentrations frequently exceed largely this threshold.

The degradation of PBDEs in the environment and biota is a key issue as higher congeners are converted to lower, and possibly more toxic, congeners. This possibility has been demonstrated for debromination of DecaBDE and several c-OctaBDE components (see references above) but the extent to which different PBDEs can be degraded under various conditions, the role of metabolism in addressing the bioaccumulation potential, and the identity of any lower congeners that may be produced, is an active research field. New results will need to be assessed by the POPRC as they appear in refereed literature.

There is an increasing evidence suggesting similar toxicological profiles and therefore, equivalent hazards and concerns, between PBDEs and PCBs, although the mode of action seems to be better categorized by AhR-independent mechanisms, as PBDEs do bind but not activate the AhR-AhR nuclear translocator protein-XRE complex (Peters et al., 2006) and appear capable of up-regulating CYP2B and CYP3A in rats at doses similar to that for non-dioxin-like

PCB153 (Sanders et al., 2005). As the persistence, bioaccumulation potential and long range transport of the c-OctaBDE components are well documented, the confirmation of an equivalent level of hazard for these two groups should be sufficient for confirming a long-range transport associated risk

4. Concluding statement

The evaluation of the human and environmental risk of commercial OctaBDE associated to its potential for long range transport must consider that the commercial product is a mixture of components with different properties and profiles, which may also be released to the environment due to its presence as components of other PBDE commercial products and also produced in the environment by debromination of commercial DecaBDE.

Although the production of c-OctaBDE has ceased in developed countries and there is no information suggesting that the chemical is produced elsewhere; it must be noticed that the product is still present and released from articles in use and during their disposal. Model estimations and measured levels in sewage sludge suggest that current emissions are still significant.

The persistence of the Hexa to NonaBDE is well documented. The main route of degradation is debromination forming other BDEs, also of concern. The potential for certain components in c-OctaBDE to bioaccumulate and also for biomagnification in some trophic chains is also sufficiently documented and confirmed by the good agreement between field observations in monitoring programmes and toxicokinetic studies. Monitoring data in remote areas confirm the potential for long-range transport and at least for some congeners the relevance of atmospheric distribution in this process.

The highest difficulty appears for the estimation of the potential hazard of the commercial mixture and its components. There are traditional ecotoxicological and toxicological studies where no effects have been observed even at unrealistically high concentrations. However, an in-depth assessment of these studies considering in particular the properties and toxicokinetic of PBDE indicates that the test design, exposure conditions and measured endpoints are not appropriate for a sound assessment of these types of chemicals. Thus, the lack of effects reported in those tests should be considered with care. In addition, specific studies have reported particular hazards such as delayed neurotoxicity and immunotoxicity which may be particularly relevant in the assessment of both human health and ecosystem risks.

Based on the existing evidence, it is concluded that the Hexa and HeptaBDE components of the commercial octabromodiphenyl ether are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

The increasing evidence related to debromination of Octa and Nona BDE into BDEs with POPs properties and considering that under Article 8, paragraph 7(a) of the Convention states that the lack of full scientific certainty shall not prevent a proposal from proceeding, it is concluded that the Octa and NonaBDE components of the commercial octabromodiphenyl ether are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

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資料２－２

残留性有機汚染物質に関するストックホルム条約の附属書改正に係る化学物質の審査及び製造等の規制に関する法律に基づく追加措置について（第一次報告案）

１．経緯

「残留性有機汚染物質に関するストックホルム条約」（平成 16 年 5 月発効。以下「POPs 条約」という。）においては、本年５月に第 4 回締約国会議が開催され、新たに 9 種類の物質（群）を附属書 A、附属書 B 又は附属書 C に追加することが決定された。これらの物質について、製造、使用等の廃絶・制限に係る国際上の義務を履行するため、国内担保措置を講ずる必要がある。

このため、POPs 条約の附属書に追加されることとなった物質（群）について、別表１の通り１２の物質名に整理した上で、化審法に基づく措置について中央環境審議会への諮問がなされたところ、審議の結果を第１次報告としてとりまとめた。

２．化審法に基づく措置について

別表１の物質については、以下の理由により、化審法第 2 条第 2 項による第一種特定化学物質に該当すると考えられる。

（理由）

別表１の化学物質は、残留性有機汚染物質検討委員会により科学的な評価が行われ、別表２のとおり、難分解性、高蓄積性、毒性を含む性状を有するとの結論が得られており、同委員会の結論は妥当なものと考えられる。

(別表１)

CAS 番号	官報公示番号	物質名
1763-23-1 2795-39-3* 4021-47-0* 29457-72-5* 29081-56-9* 70225-14-8* 56773-42-3* 251099-16-8*	2-1595 2-2810	ペルフルオロ(オクタン－１－スルホン酸)（別名ＰＦＯＳ）又はその塩
307-35-7	2-2803	ペルフルオロ（オクタン－１－スルホニル）＝フルオリド（別名ＰＦＯＳＦ）
608-93-5	3-76	ペンタクロロベンゼン
319-84-6	3-2250 9-1652	ｒ－１，ｃ－２，ｔ－３，ｃ－４，ｔ－５，ｔ－６－ヘキサクロロシクロヘキサン（別名α－ヘキサクロロシクロヘキサン）
319-85-7	3-2250 9-1652	ｒ－１，ｔ－２，ｃ－３，ｔ－４，ｃ－５，ｔ－６－ヘキサクロロシクロヘキサン（別名β－ヘキサクロロシクロヘキサン）
58-89-9	3-2250 9-1652	ｒ－１，ｃ－２，ｔ－３，ｃ－４，ｃ－５，ｔ－６－ヘキサクロロシクロヘキサン（別名γ－ヘキサクロロシクロヘキサン又はリンデン）
143-50-0	－	デカクロロペンタシクロ［５．３．０．$0^{2,6}$．$0^{3,9}$．$0^{4,8}$］デカン－５－オン（別名クロルデコン）
36355-01-8	－	ヘキサブロモビフェニル
40088-47-9**	3-61	テトラブロモ（フェノキシベンゼン）（別名テトラブロモジフェニルエーテル）
32534-81-9**	－	ペンタブロモ（フェノキシベンゼン）（別名ペンタブロモジフェニルエーテル）
68631-49-2*** 207122-15-4***	3-2845	ヘキサブロモ（フェノキシベンゼン）（別名ヘキサブロモジフェニルエーテル）
446255-22-7*** 207122-16-5***	3-3716****	ヘプタブロモ（フェノキシベンゼン）（別名ヘプタブロモジフェニルエーテル）

*ペルフルオロオクタンスルホン酸塩の例

**商業用ペンタブロモジフェニルエーテルに含まれる代表的な異性体

***商業用オクタブロモジフェニルエーテルに含まれる代表的な異性体

****ジフェニル=エーテルの臭素化物(Br=7~9)として

別表2

ペルフルオロオクタンスルホン酸の危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 活性汚泥、底質培養物、土壌培養物中での好気的生分解試験及び下水汚泥での嫌気的生分解試験では、分解の兆候はまったく示されなかった。 【光分解性】 ・直接または間接光分解の証拠は見られなかった（EPA OPPTS ﾌﾟﾛﾄｺﾙ 835.5270）。 ・25℃における間接光分解の半減期は3.7年以上と算出された。 【加水分解性】 ・分解はまったく示されなかった（EPA OPPTS ﾌﾟﾛﾄｺﾙ 835.2210） ・半減期は41年以上とされた。 ※ＰＦＯＳＦは水中で速やかに加水分解されＰＦＯＳを生成する知見が別途得られている。	【BCF（経鰓的生物濃縮係数）】 ・ﾆｼﾞﾏｽ： BCF =2900（肝臓），3100（血漿） ・丸ﾊｾﾞ：BCF =約2400（全魚体） ・ﾌﾞﾙｰｷﾞﾙｻﾝﾌｨｯｼｭ：BCFk =2796 ※上記の値は、POPs条約付属書Dの基準値（BCF＜5000）以下であるが、PFOSの物性の一つである非脂肪組織中の蛋白質親和性を考慮すると、脂溶性物質を対象に設定されているBCF基準値のPFOSへの適用は不適切な可能性がある。 【BMF（経口的生物濃縮係数）】 ・ﾐﾝｸ：BMF=22（魚中の濃度から推計） ・ﾎｯｷｮｸｸﾞﾏ：BMF＞160（ﾎｯｷｮｸｱｻﾞﾗｼ中の濃度から推計） ※人為的発生源から最も遠く離れた北極圏の動物において高濃度のPFOSが検出されていることに留意。魚類･魚食性鳥類など食物連鎖上の低位種においてもPFOSが検出。また、ﾜｼなど捕食生物種は、低位にある鳥類よりも高濃度のPFOSを蓄積することが認められている。このことは、PFOSの残留性と長期蓄積性によるものである。	【反復投与毒性】 アカゲザル（強制経口90日）： 4.5mg/kg/dayで全数死亡、 0.5mg/kg/dayで消化管毒性 （カリウム塩） ラット（経口90日）：18mg/kg/dayで全数死亡、6mg/kg/dayで半数死亡、 2mg/kg/dayで体重及び臓器重量変化 （カリウム塩） カニクイサル（26週）：LOEL 0.03mg/kg/day 主な毒性は、胸腺萎縮（♀）、HDL、コレステロール、T3低下 ラット（混餌2年）：0.06（♂）、 0.07mg/kg/day（♀）で肝細胞の病理組織的変化 【発生毒性】 ラット（二世代経口）： NOAEL:0.1mg/kg/day 0.4mg/kg/dayでF1児体重増加量低下、 1.6mg/kg/dayでF1世代生存率低下、母体体重低下等（カリウム塩） ラット（♀）：妊娠17-20日目の 25mg/kgで全児死亡	【慢性毒性】 ユスリカ *Chironomus tentans* ： 10dNOEC=0.0491 mg/L（成長･生存）

	・PFOS は疎水性・疎油性であるため POPs に特有な脂肪組織に蓄積するという典型的パターンに該当しない。また、PFOS は物理化学的特性が特異なため、生物蓄積のﾒｶﾆｽﾞﾑは他の POPs と異なる。		

ペンタクロロベンゼンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 分解しない（OECD TG 301C） 【光分解性】 大気中で、主として OH ﾗｼﾞｶﾙとの反応により光酸化される。日光照射下の表層水での分解は早く、4 時間で 41%が消失。 【半減期】 ・大気中：推定値は 45-467 日。OH ﾗｼﾞｶﾙとの反応による半減期の計算値は 277 日。ﾓﾃﾞﾙﾃﾞｰﾀに基づく半減期は 65 日。分解ﾌﾟﾛｾｽのみを考慮した場合の推定半減期は 155 日 ・水中：表層水中の推定半減期は 194-1250 日。更に深いところでの嫌気性生分解による推定半減期は 776-1380 日。 ・土壌中：ｽﾊﾟｲｸした下水汚泥改良土壌中で半量は揮発により素早く消失し、残り半量の半減期は 187-1550 日。好気性のﾛｰﾑ砂質土壌中の半減期は 194-345 日。湖水の砂状底質中で 150 日後に 75%が分解し、これに続く一次代謝物の半減期は 50 日。温帯地域の有機土壌と底質中の推定半減期は 6 年。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKOW=4.88-6.12（推奨値 5.17-5.18） 【BCF（経鰓的生物濃縮係数）】 ・魚：BCF=1085-23000 ・軟体動物：BCF=833-4300 ・甲殻類：BCF=577-2258	【反復投与毒性】 ［ラット　混餌：100 日］ NOEL：18.2mg/kg/day（♀） LOEL：8.3mg/kg/day（♂） 8.3mg/kg/day 以上（♂）で腎重量増加、腎硝子滴 37.5mg/kg/day 以上（♀）で肝重量増加及び肝細胞肥大 81.1mg/kg/day（♂）及び 78.7mg/kg/day（♀）でヘモグロビン減少、白血球増加等 ［ラット　混餌：13 週］**(NTP)** NOEL：2.4mg/kg/day（♂）、 24mg/kg/day（♀） 2.4mg/kg/day 以上（♂）で絶対・相対肝重量増加、2.4mg/kg/day 以上（♀）で体重減少、7.2mg/kg/day 以上（♂）で組織学的所見を伴う腎重量増加、 24mg/kg/day（♂）以上で精子異常、小葉中心性肝細胞肥大、72mg/kg/day（♀）で腎毒性 【催奇形性】 ラット：50mg/kg/day の母体暴露で肋骨数過剰、胸骨異常の報告	【慢性毒性】 カダヤシ *Gambusia affinis* ： 42dEC10=0.002 mg/L（成長） タイワンガザミ *Portunus pelagicus* ： 40dEC10=0.014 mg/L（成長）

α－ヘキサクロロシクロヘキサンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 生分解は嫌気的条件で起こる。 【光分解性】 日光照射下での水溶液中の半減期は 4-6 日。固い表面上では半減期は 91 時間。 【加水分解性】 ・半減期は温度依存性を示し、pH 8 (20℃) で 0.8 年。pH 7.8 (5℃) で 26 年。北極海で 63 年 【半減期】 ・水中：高緯度北極圏湖沼で 0.6 年-1.4 年と推定。東部北極海ではｴﾅﾝﾁｵ選択性の分解により、(＋)異性体は 5.9 年、(-)異性体が 23.1 年。加水分解が考慮される場合は、(＋)異性体は 5.4 年、(-)異性体が 16.9 年。 ・土壌中：亜熱帯地域のｲﾝﾄﾞの砂質ﾛｰﾑで 55 日。温帯地域では 161 日。ｶﾅﾀﾞの砂質ﾛｰﾑでの長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 15 年後に 4%が残留。高緯度北極圏湖沼堆積物で 2 年と推定。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKOW=3.8 【BCF (経鰓的生物濃縮係数)】 ・単細胞緑藻類：BCF=200-2700 (乾重量ﾍﾞｰｽ) ・鞭毛藻：BCF=13000(脂質ﾍﾞｰｽ) ・無脊椎動物：BCF=60(脂質ﾍﾞｰｽ 8000)-2750 ・ｾﾞﾌﾞﾗﾌｨｼｭ：BCF=1100(OECD TG 305E) ・ﾆｼﾞﾏｽ：BCF=1100-2800 【BMF (経口的生物濃縮係数)】 ・動物ﾌﾟﾗﾝｸﾄﾝ、ﾎｯｷｮｸﾀﾞﾗ：BMFs＞1 ・海鳥 (ﾋﾒｳﾐｽｽﾞﾒとﾊｼﾞﾛｳﾐﾊﾞﾄを除く) BMFs＜1 (alphaHCH は新陳代謝されるため) ・ﾜﾓﾝｱｻﾞﾗｼ：BMF= 2.5 (脂肪組織) ・ﾎｯｷｮｸｸｼﾞﾗ：BMF=9.85 ・結論として、北極の生態系において、効果的な蓄積性が見られる。 【FWMF (食物連鎖による経口的生物濃縮係数)】 ・FWMFs＞1 (北極海の食物連鎖の研究)	【反復投与毒性】 ラット (混餌 107 週)：NOAEL 50mg/kg 主な毒性は、100mg/kg で肝肥大及び肝細胞の病理組織学的変化、800mg/kg で成長遅延、死亡率増加及び腎障害 ラット (混餌 90 日)：NOAEL 0.1mg/kg/day 主な毒性は、0.5mg/kg/day で肝重量増加及び白血球数減少、2.5mg/kg/day で肝実質細胞肥大等、 12.5mg/kg/day で肝、心、腎及び副腎相対重量増加、成長遅延 【発がん性】 肝腫瘍 IARC グループ 2B (possibly carcinogenic to human) 【その他】 農薬、肥料の HCH 暴露により、感覚異常、頭痛、倦怠、嘔吐、振戦等 急性毒性試験において、背弯姿勢、呼吸困難、振戦、痙攣等神経症状 マウス：0.5mg/kg/day で血清中 IgG、IgM 減少	

β－ヘキサクロロシクロヘキサンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【光分解性･加水分解性】 非生物的な分解ﾌﾟﾛｾｽ（光分解や加水分解）では分解しない。 【半減期】 ･大気中：56 日(計算値) ･水中：水及び底質中の半減期のﾃﾞｰﾀはないものの、ﾓﾆﾀﾘﾝｸﾞに基づき残留性があり、容易に分解しないと推定される。 ･土壌中：亜熱帯地域のｲﾝﾄﾞの砂質ﾛｰﾑで 100 及び 184 日。温帯地域では嫌気性条件下で分解せず。ｶﾅﾀﾞの砂質ﾛｰﾑでの長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 15 年後に 44%が残留。日本の農地での長期ﾌｨｰﾙﾄﾞｽﾀﾃﾞｨでは 570 日後に 30%が残留。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKow=3.78 【BCF（経鰓的生物濃縮係数）】 ｾﾞﾌﾞﾗﾌｨｼｭ：BCF=1460 【FWMF（食物連鎖による経口的生物濃縮係数）】 ･FWMFs＞1（北極海の食物連鎖の研究） ･FWMF=7.2（高塩素処理された PCB に相当） ･FWMF=2.9（ﾎﾞｰﾌｫｰﾄ･ﾁｭﾄｺ海の食物連鎖の研究による計算値） 【BMF（経口的生物濃縮係数）】 ･ｶﾀﾂﾑﾘに高い蓄積性が見られ、その捕食者（小さいｼﾗｻｷﾞなど）の BMF は 1 を超える。 ･ﾛｼｱのﾁｭｺﾄ半島の先住民の母乳含まれる betaHCH のﾚﾍﾞﾙが高い。	【反復投与毒性】 ラット（混餌　52 週）：LOAEL 0.5mg/kg/day 肝肥大、肝細胞の組織学的変化、ほぼ全動物死亡 ラット（混餌　13 週）：NOAEL 0.1mg/kg/day 主な毒性は、0.1mg/kg/day 以上で肝臓影響、2.5mg/kg/day 以上で胸腺重量減少、精巣萎縮、卵巣萎縮等、12.5mg/kg/day で死亡（運動失調、昏睡）、成長遅延、白血球･赤血球減少等 【発がん性】 マウス（26 週）：34mg/kg/day で肝腫瘍 IARC グループ2 B（possibly carcinogenic to human） 【生殖毒性】 ラット（2世代繁殖試験）：NOAEL 0.1mg/kg/day 死亡率増加、不妊 ラット：20mg/kg/day を母胎投与で児死亡率増加 ミンク等で性周期かく乱、生殖器萎縮等の報告 【その他】	【慢性毒性】 グッピー　*Poecilia reticulata*　：4-12週間試験　NOEC=0.032 mg/L（組織学的変化）。エストロゲン活性により、雄魚において、ビテロゲニン生成の変化、精巣の萎縮、雌雄同体現象、下垂体の変質が起こった。 ニワトリ：β -HCHを含む様々な有機塩素化合物に高濃度に曝露された雌が1回目及び2回目に産卵した雛鳥の身体状況が劣っていた。

		農薬、肥料の HCH 暴露により、感覚異常、頭痛、倦怠、嘔吐、振戦等 急性毒性試験において、背弯姿勢、呼吸困難、振戦、痙攣等神経症状 マウス（経口　30 日）：60mg/kg/day でリンパ球増殖、NK 活性減少	

リンデンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 非常に遅い。実験室の好気的条件下の土壌中で半減期は 980 日。嫌気的条件下ではより速く分解が進行。 【光分解性】 光に対しては安定。 【加水分解性】 ・半減期は 92-3090 時間。pH 5、pH 7 において安定であり半減期は 732 日。pH 9 における半減期は 43-182 日。海水中では pH 8（20℃）で 1.1 年。pH 7.6（5℃）のﾋｭｰﾛﾝ湖で 42 年。pH 8（0℃）の北極で 110 年など様々な推定値・算出値が報告されている。 【半減期】 ・大気中：OH ﾗｼﾞｶﾙとの気相反応の速度定数に基づく推定値は 2-3 日。対流圏での寿命は 7 日と推定。熱帯地域での対流圏寿命は 13 日と推定。Brubaker and Hites は大気中での寿命を 96 日と推定。 ・水中：河水では 30-300 日。湖水では 3-30 日。 ・土壌中：2-3 年。	【BCF（経鰓的生物濃縮係数）】 ・水生生物：BCF=10-6000（実験室）。BCF=10-2600（環境中）。BCF=3-36（Berny）。BCF=43-4220（湿重量ﾍﾞｰｽ）。BCF=11,000、1200-2100（脂質ﾍﾞｰｽ） ・ｴﾋﾞ：logBCF=2..26(脂質ﾍﾞｰｽ)。ﾆｼﾞﾏｽ：ogBCF=3.85（脂質ﾍﾞｰｽ）。動物ﾌﾟﾗﾝｸﾄﾝ：logBCF=4.3。無脊椎生物の平均 log BCF=2.28。脊椎生物の平均 log BCF=2.87 【BAF（経鰓及び経口による生物濃縮係数）】 ・ﾆｼﾞﾏｽ：logBAF=4.1 ・無脊椎生物の平均 log BAF=2.94。 ・脊椎生物の平均 log BAF=3.80。肉部分で 780、内臓部分で 2500、全魚体で 1400 という報告がある。 ・海洋哺乳類のﾘﾝﾃﾞﾝの濃度は、より疎水性の PCB や DDT と同等か又はより高ﾚﾍﾞﾙである。	【慢性毒性】 ラット（混餌）：7mg/kg/day で肝臓壊疽（38 週）、肝臓萎縮（104 週） 【生殖毒性】 ウサギ（3 日/週で 12 週）：0.8mg/kg/day で排卵率低下 ラット（5 日）：6mg/kg/day（♂）で精子数減少 ラット（90 日）：75mg/kg/day（♂）で性器萎縮、精子形成能かく乱 ラット（妊娠 15 日単回）：30 mg/kg/day で雄児性行動変化、テストステロン濃度低下 マウス（妊娠 12 日単回）：30 mg/kg/day で胎児の胸腺、胎盤重量低値 ラット（生殖試験：12 週暴露）：1.7uM で成長速度低下、精子数減少、テストステロン濃度低下 【発がん性】 「発がん性を示す科学的根拠が示唆されるが、潜在的人発がん性を評価するには科学的根拠が不十分な物質」に分類（US EPA） 【その他】 リンデン含有殺虫剤摂取で人に発作痙	【慢性毒性】 淡水魚 ：NOAEC=0.0029 mg/L（幼魚の生育低下） 水生無脊椎動物 ：NOAEC=0.054mg/L（生殖能低下） カエル ：0.0001 mg/Lで統計学的に有意な性比影響（71%雄）、エストロゲン活性の誘導、精子のプロゲステロン応答性変化。試験管内試験において、ビテロゲニン及びエストロゲン受容体の発現誘導。 無脊椎動物 ：35日間試験 LOAEL=0.0135 mg/L（生殖能及び個体数への影響） ニワトリ及びニホンウズラ ：それぞれ100及び25 ppmで孵化率低下。

		攣など神経毒性、実験動物で免疫抑制や抗体反応抑制など	

クロルデコンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性･加水分解性】 水生環境中であるいは土壌中で、生分解又は加水分解するとは予測されない。 【光分解性】 大気中で直接的光分解を受けることは考えられないと結論している。 ･利用可能な全てのﾃﾞｰﾀに基づき、ｸﾛﾙﾃﾞｺﾝは環境中で高い残留性を示すと考えられる。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKow=4.50-5.41 【BCF（経鰓的生物濃縮係数）】 ･藻類：BCF=6000 ･無脊椎生物：BCF=21600 ･魚類：BCF=60200 【BMF（経口的生物濃縮係数）】 ･ほとんど又は全く代謝浄化せず、水生の食物連鎖において生物濃縮の可能性がある。 ･食物連鎖の研究において、藻からｶｷへの移動は非常に低かったが、ｴﾋﾞからｱﾐ、ｱﾐからｽﾎﾟｯﾄへの明白な栄養段階を通じた移動があることが示された。	【反復投与毒性】 ラット（2 年）：NOAEL 0.05mg/kg/day 0.25mg/kg/day で腎臓影響（蛋白尿、重篤な糸球体硬化） ラット（経口 21 ヶ月）：LOAEL 0.07mg/kg/day 肝細胞の病理組織学的変化、甲状腺ろ胞サイズ、コロイド量胞数低下、甲状腺ろ胞上皮細胞厚高値 ラット（経口 3 ヶ月）：LOAEL 1.17mg/kg/day 肝の病巣壊疽、副腎肥大、振戦、多動性、過剰驚愕反応等 【生殖毒性】 ラット（3 ヶ月）：NOAEL 0.25mg/kg/day 精巣萎縮 ラット（90 日）：LOAEL0.83mg/kg/day で精子の運動性･生存率低下、精子数減少、1.67mg/kg/day で性嚢、前立腺重量低下 マウス（160 日）：LOAEL 2mg/kg/day で排卵停止、膣発情持続、ﾗｯﾄ妊娠 14-20 日に母体経由で 15mg/kg/day 投与した雌児動物においても同様の報告	【慢性毒性】 ミジンコ *Daphnia magna* ：21dNOEC=0.0283 mg/L（繁殖）, 21dNOEC=0.025 mg/L（成長） ミシッドシュリンプ *Americamysis bahia* ：28dMATC=0.000026-0.00034 mg/L（成長） ユスリカ *Chironomus tentans* ：14dNOEC=17.9 mg/kg sediment（発達）

		【催奇形性】 ラット(経口):LOAEL 2mg/kg/day で胎児体重低下、骨化度低下、10mg/kg/day で脳水腫、停留精巣、腎盂肥大、脳室肥大 【発がん性】 ラット(80 週):LOAEL 1.2mg/kg/day 肝細胞腺がん及び上皮がん IARC グループ2B (possibly carcinogenic to human) 【その他】 職業ばく露で振戦、情緒不安定、視力障害、筋力低下、歩行運動失調等、実験動物で、脾臓、胸腺重量、好中球数、NK 活性低下、 EU-Strategy for Endocrine Disruptors 優先化学物質(無処置動物の少なくとも一種類において内分泌かく乱活性を示す科学的根拠がある)に分類	

ヘキサブロモビフェニルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 分解度 4% (OECD TG 301C) 【光分解性】 大気中における分解及び変化は、OH ﾗｼﾞｶﾙによる光酸化と光分解である。OH ﾗｼﾞｶﾙとの反応による推定半減期は 182 日。 【半減期】 ･水中:2 ヵ月を超える ･土壌及び底質中:6 ヶ月を超える	【BCF (経鰓的生物濃縮係数)】 ･ﾌｧｯﾄﾍｯﾄﾞﾐﾉｰ:BCF=18100 (32 日間暴露) ･ﾌｧｯﾄﾍｯﾄﾞﾐﾉｰの身:BCF=10000 ･ｺｲ:BCF=4700-16000 (重量ﾍﾞｰｽ。60 日間暴露) 【BMF (経口的生物濃縮係数)】 ･餌 (ﾆｼﾝ) と捕食者 (ﾊﾞﾙﾄｱｻﾞﾗｼ) を較べた食物連鎖:BMF=175 (脂質ﾍﾞｰｽ) (PCB と同ﾚﾍﾞﾙの値) ･ﾎｯｷｮｸｸﾞﾏ中の濃度がｸﾞﾘｰﾝﾗﾝﾄﾞ東部のﾜﾓﾝｱｻﾞﾗｼの約 100 倍	【反復投与毒性】 ラット (混餌 7 ヶ月):0.45mg/kg/day で血清中 T4 濃度低下 ラット (混餌 30 日):LOAEL 0.05mg/kg/day 甲状腺ろ胞数･ろ胞容積増加、血清中 T3、T4 濃度低下 アカゲザル (混餌 25～50 週):LOAEL 0.73mg/kg/day 主な毒性は、体重低下、潰瘍性大腸炎、脱毛、肝臓の変化等 【発がん性】 マウス (妊娠 0 日～生後 56 日): NOAEL 0.15mg/kg/day 児の肝細胞腺がん及び上皮がん IARC グループ2 B (possibly carcinogenic to human) 【生殖毒性】 ラット (妊娠 0 日～14 日) 28.6mg/kg/day で未着床、新生児生存率低値 アカゲザル:LOAEL 0.012mg/kg/day 主な毒性は、月経周期遅延、流産、死産等	【慢性毒性】 ニジマス *Oncorhynchus mykiss* :ELS 試験 LD50=3.910 mg/kg

		【その他】 汚染事故で吐き気、腹痛、食欲減退、関節痛、倦怠感、皮膚障害、 EU-Strategy for Endocrine Disruptors 優先化学物質（無処置動物の少なくとも一種類において内分泌かく乱活性を示す科学的根拠がある）に分類	

商業用ペンタブロモジフェニルエーテルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 ・（Tetra, Penta, HexaBDE）難分解性（BIOWIN） ・（PentaBDE） 分解せず（OECD TG 301B で CO_2 発生なし） 【半減期】 ・大気中：11-19 日（EPIWIN） ・水中： 150 日（EPIWIN） ・土壌中：半減期 150 日（EPIWIN） ・好気性底質中： 600 日（EPIWIN） ・1970 年代初期にﾖｰﾛｯﾊﾟの海洋の底質に沈降した PentaBDE 同属体が現在も相当量存在しており、底質中での残留性が高いことが示されている。	【ｵｸﾀﾉｰﾙ/水分配係数】 log KOW=6.5-7.4 【BAF（経鰓及び経口による生物濃縮係数）】 ｾﾞﾌﾞﾗｶﾞｲ：BAF=1.8 【BMF（経口的生物濃縮係数）】 ・ｳﾐﾊﾞﾄ/ﾆｼﾝ：BMF=17 ・ﾊｲｲﾛｱｻﾞﾗｼ/ﾆｼﾝ：BMF=4.3 ・ｻｹ/ﾆｼﾝ：BMF=3.8 ・動物ﾌﾟﾗﾝｸﾄﾝ/底生生物：BMF=7.1 ・ﾎｯｷｮｸﾀﾞﾗ/動物ﾌﾟﾗﾝｸﾄﾝ：BMF=0.04-3.4 ・ﾜﾓﾝｱｻﾞﾗｼ/ﾎｯｷｮｸﾀﾞﾗ：BMF=13.7 ・ﾎｯｷｮｸｸﾞﾏ/ﾜﾓﾝｱｻﾞﾗｼ：BMF=0.3-11 ・多数の調査から、上位捕食者において懸念される濃度の PentaBDE が存在することが示されている。北極圏では、ﾜｼｶﾓﾒ、ﾎｯｷｮｸｸﾞﾏ、ﾜﾓﾝｱｻﾞﾗｼ、ｼﾛｲﾙｶなどの上位捕食鳥類および哺乳類中から高ﾚﾍﾞﾙの PentaBDE が検出されている ・土壌又は底質中のPentaBDEは、容易に食物連鎖に取り込まれ、人など食物連鎖上位者の脂肪組織中に生物濃縮する。	【反復投与毒性】 ラット（90 日）：NOEL 2mg/kg/day 未満 主な毒性は、肝臓肥大等（DE71） 【生殖毒性】 ラット（妊娠♀単回）：0.06mg/kg で児に自発行動変化（多動性） 0.3mg/kg で児に精巣体積・精子数の低値 （BDE99） 【催奇形性】 ラット（妊娠 6 日単回）：0.3mg/kg でばく露の母動物（F1）2 個体から得られた F2 児で、外観・骨格異常 （BDE99） 【その他】 実験動物で甲状腺ホルモン系への影響	【慢性毒性】 ミジンコ *Daphnia magna* ：繁殖阻害が認められた。

商業用オクタブロモジフェニルエーテルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 分解せず（OECD TG 301D） 【半減期】 ・大気中：（Hexa-Nona BDE）30.4-161.0 日（OH ﾗｼﾞｶﾙとの反応）（AOPWIN）	【BCF（経鰓的生物濃縮係数）】 ・ｺｲ：（HexaBDPE）BCF=2580-5640 ・ｺｲ：（HeptaBDE）BCF＜1.1-3.8 ・ｺｲ：（OctaBDE）BCF＜9.5 ・ｺｲ：（c-OctaBDE）BCF）＜10-36 【BMF（経口的生物濃縮係数）】 ・飼育中のﾀｲｾｲﾖｳｻｹの餌に含まれる HeptaBDE 183 をﾓﾆﾀ-した結果、95%がｻｹに蓄積。 【BSAF（生物相-底質濃縮係数）】 ・2 種の淡水魚：（HexaBDE）BSAF =1,（HeptaBDE）BSAF =2 ・（BDE 154） BSAF =9.1±1.1	【反復投与毒性】 ラット（28 日）：10mg/kg/day で T4 濃度減少（octa-BDE:30.7%, hepta-BDE:45.1%,） 【催奇形性・発生毒性】 ウサギ（経口 妊娠 7～19 日）：5mg/kg/day で胎児毒性、15mg/kg/day で児の肝重量増加、体重増加量減少、骨形成遅延 マウス（生後 10 日目単回）：0.45mg/kg で 2、4 及び 6 月齢での異常行動並びに成長後の空間認識能・記憶の影響（BDE153）	アメリカチョウゲンボウ*Falco sparverius*：18.7μg PBDEs/egg 及び15.6±0.3 ng PBDEs/g bw/dayで29日間曝露した雛鳥において、PHA応答（T細胞媒介性免疫）が増大し、抗体媒介性反応が減少した。脾臓（胚中心の減少）、滑液嚢（アポトーシスの減少）、胸腺（マクロファージの増大）に構造的変化あり。脾臓の体細胞指標とPBDEs間及び滑液嚢の体細胞指標とBDE-47間に負の相関性あり。

（参考１）ストックホルム条約第４回締約国会議において決定された事項（概要）

○附属書Aへの追加

物質名	主な用途	決定された主な規制内容
テトラブロモジフェニルエーテル、ペンタブロモジフェニルエーテル	プラスチック難燃剤	・製造・使用等の禁止 （以下の用途を除外する規定あり） -当該物質を含有する製品のリサイクル
クロルデコン CAS No:143-50-0	農薬	・製造・使用等の禁止
ヘキサブロモビフェニル CAS No:36355-01-8	プラスチック難燃剤	・製造・使用等の禁止
リンデン（γ－ＨＣＨ） CAS No:58-89-9	農薬	・製造・使用等の禁止 （以下の用途を除外する規定あり） -アタマジラミ、疥癬の医薬品用の製造と使用
α－ヘキサクロロシクロヘキサン CAS No:319-84-6	リンデンの副生物	・製造・使用等の禁止
β－ヘキサクロロシクロヘキサン CAS No:319-85-7	リンデンの副生物	・製造・使用等の禁止
ヘキサブロモジフェニルエーテル、ヘプタブロモジフェニルエーテル	プラスチック難燃剤	・製造・使用等の禁止 （以下の用途を除外する規定あり） -当該物質を含有する製品のリサイクル

○附属書Bへの追加

物質名	主な用途	決定された主な規制内容
ペルフルオロオクタンスルホン酸（PFOS）とその塩、ペルフルオロオクタンスルホン酸フルオリド（PFOSF） CAS No: 1763-23-1 CAS No: 307-35-7	撥水撥油剤、界面活性剤	・製造・使用等の禁止 （以下の目的・用途を除外する規定あり） -写真感光材料 -半導体用途 -フォトマスク -医療機器 -金属メッキ -泡消火剤 -カラープリンター用電気電子部品 -医療用 CCD カラーフィルター　など

○附属書A及びCへの追加

物質名	主な用途	決定された主な規制内容
ペンタクロロベンゼン CAS No: 608-93-5	農薬	・製造・使用等の禁止 ・非意図的生成による排出の削減

（参考２）ＰＯＰｓ条約附属書Ｄに規定されている情報の要件及び選別のための基準

ＰＯＰＲＣでは、締約国から提案のあった化学物質ごとに、附属書Ｄに定められた選別のための基準（下記を参照）に基づき審査を実施後、附属書Ｅに沿って、これら情報を更に考慮、評価した上で、当該化学物質が、長距離にわたる自然の作用による移動の結果として、世界的規模の行動を正当化するようなヒトの健康又は環境に対する重大な悪影響をもたらすかどうかの評価を行うため、危険性の概要（Risk Profile）の作成が行われる。

化学物質の特定	商品名、商業上の名称、別名、ケミカル・アブストラクツ・サービス（ＣＡＳ）登録番号、国際純正・応用化学連合（ＩＵＰＡＣ）の名称その他の名称
	構造（可能な場合には異性体の特定を含む。）及び化学物質の分類上の構造
残留性 （次のいずれか）	化学物質の水中における半減期が２ヶ月を超えること、土中における半減期が６ヶ月を超えること又は堆積物中における半減期が６ヶ月を越えることの証拠
	この条約の対象とすることについての検討を正当とする十分な残留性を化学物質が有することの証拠
生物蓄積性 （次のいずれか）	化学物質の水生種の生物濃縮係数若しくは生物蓄積係数が五千を超えること又はこれらの資料がない場合にはオクタノール／水分配係数の常用対数値が五を越えることの証拠
	化学物質に他に懸念される理由（例えば、他の種における高い生物蓄積性、高い毒性、生態毒性）があることの証拠
	化学物質の生物蓄積の可能性がこの条約の対象とすることについての検討を正当とするのに十分であることを示す生物相における監視に基づく資料
長距離にわたる自然の作用による移動の可能性 （次のいずれか）	化学物質の放出源から離れた地点における当該化学物質の潜在的に懸念すべき測定の水準
	化学物質が別の環境に移動した可能性とともに、大気、水又は移動性の種を介して長距離にわたり自然の作用により移動した可能性を示す監視に基づく資料
	化学物質がその放出源から離れた地点における別の環境に移動する可能性とともに、大気、水又は移動性の種を介して長距離にわたり自然の作用により移動する可能性を示す環境運命の性質又はモデルによる予測結果。主に大気中を移動する化学物質については、大気中における半減期が二日を超えるべきである。
悪影響 （次のいずれか）	この条約の対象となる化学物質とすることについての検討を正当とする人の健康又は環境に対する悪影響を示す証拠
	人の健康又は環境に対する損害の可能性を示す毒性又は生態毒性の資料

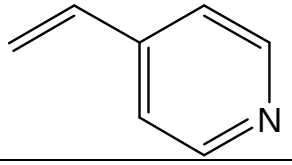
資料2－3

既存化学物質審査シート(生態影響)

(平成21年6月26日開催)

官報公示整理番号	CAS No.	物質名称	判定案		頁
			人健康影響	生態影響	
5-717	100-43-6	4－ビニルピリジン		三監相当	1
5-1060	40220-08-4	トリス(2－ヒドロキシエチル)イソシアヌル酸アクリル酸エステル		三監相当	2
3-521 4-57	95-87-4	2，5－キシレノール		三監相当	7
4-643	86-73-7	フルオレン		三監相当	9

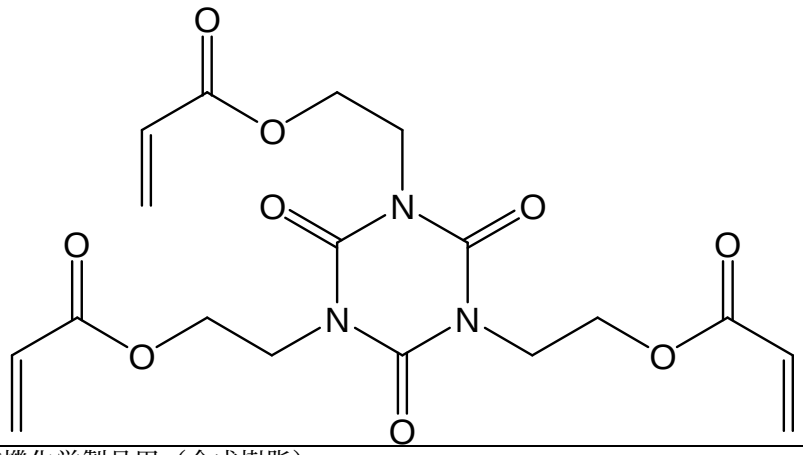
既存化学物質審査シート

官報公示整理番号	5-717	CAS No.	100-43-6
判定案	生 態 影 響　第三種監視化学物質相当		
名称 構造式等	名　称：４－ビニルピリジン 		
用途	－		
外観	無色～うすい黄色　透明液体		
分解性	難分解性		
蓄積性	高濃縮性でない		
藻類生長阻害試験	生物種：*Pseudokirchneriella subcapitata* 試験法：化審法 TG（2006） 培養方式：振とう培養 純度：96.1%（不純物 4-tert-ﾌﾞﾁﾙｶﾃｺｰﾙ 含有率不明） 試験濃度：設定濃度　1.0、2.1、4.5、9.5、20 mg/L 実測濃度　0.86、1.9、3.8、8.2、17 mg/L（時間加重平均値） 助剤：なし 72hEC50（実測値に基づく）＝4.6 mg/L 72hNOEC（実測値に基づく）＝0.86 mg/L		
ミジンコ急性遊泳阻害試験	生物種：オオミジンコ *Daphnia magna* 試験法：化審法 TG 試験方式：半止水式、24 時間後に換水 純度：96.1%（不純物 4-tert-ﾌﾞﾁﾙｶﾃｺｰﾙ 含有率不明） 試験濃度：設定濃度　0.50、0.89、1.6、2.8、5.0 mg/L 実測濃度　0.45、0.80、1.4、2.6、4.5 mg/L（時間加重平均値） 助剤：なし 48hEC50（実測値に基づく）＝1.2 mg/L		
魚類急性毒性試験	生物種：ヒメダカ *Oryzias latipes* 試験法：化審法 TG 試験方式：半止水式、24 時間毎に換水 純度：96.1%（不純物 4-tert-ﾌﾞﾁﾙｶﾃｺｰﾙ 含有率不明） 試験濃度：設定濃度　0.50、0.89、1.6、2.8、5.0 mg/L 実測濃度　0.44、0.78、1.4、2.5、4.4 mg/L（時間加重平均値） 助剤：なし 96hLC50（実測値に基づく）＝1.0 mg/L 以下の濃度群において以下のような毒性症状が認められた。 0.78 mg/L 群：遊泳異常（72h 4/10、96h 10/10）		
生態影響判定根拠	藻類生長阻害試験において 72hEC50＝4.6 mg/L、72hNOEC＝0.86 mg/L、ミジンコ急性遊泳阻害試験において 48hEC50＝1.2 mg/L であるが、魚類急性毒性試験において 96hLC50＝1.0 mg/L であることから第三種監視化学物質相当。		
備考	試験用水溶解度： 藻類培地：>100mg/L、Elendt M4 medium：>100mg/L、脱塩素水道水：>100mg/L		

既存化学物質審査シート

官報公示整理番号	5-1060	CAS No.	40220-08-4

判定案	総合判定　生 態 影 響　第三種監視化学物質相当

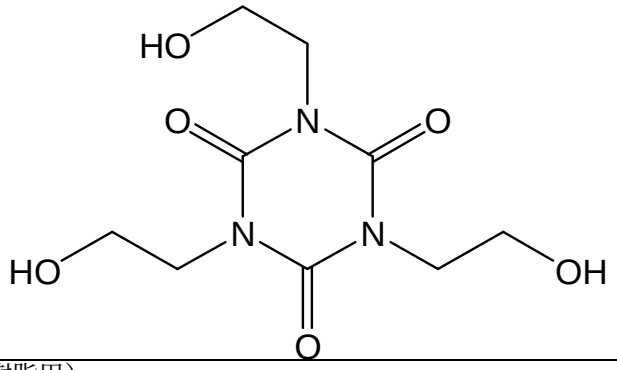
名称 構造式等	名　称：トリス（２－ヒドロキシエチル）イソシアヌル酸アクリル酸エステル 
用途	中間物、有機化学製品用（合成樹脂） ※化学物質の製造・輸入量に関する実態調査（平成１６年実績）
外観	白色固体
分解性	難分解性
蓄積性	高濃縮性でない

藻類生長阻害試験	生物種：*Pseudokirchneriella subcapitata* 試験法：化審法 TG（2006） 培養方式：振とう培養 純度：不明（分解度試験に用いた試料の純度：79.7%） 試験濃度：設定濃度　1.0、2.2、4.7、10、22、47、100 mg/L 実測濃度　0.82、1.8、4.2、8.6、20、42、90 mg/L（時間加重平均値） 助剤：なし 72hEC50（実測値に基づく）＝26 mg/L 72hNOEC（実測値に基づく）＝0.82 mg/L
ミジンコ急性遊泳阻害試験	生物種：オオミジンコ *Daphnia magna* 試験法：化審法 TG 試験方式：半止水式、24 時間後に換水 純度：不明（分解度試験に用いた試料の純度：79.7%） 試験濃度：設定濃度　25、38、57、86、130 mg/L 実測濃度　21、34、50、77、120 mg/L（時間加重平均値） 助剤：なし 48hEC50（実測値に基づく）＝87 mg/L
魚類急性毒性試験	生物種：ヒメダカ *Oryzias latipes* 試験法：化審法 TG 試験方式：半止水式、24 時間毎に換水 純度：不明（分解度試験に用いた試料の純度：79.7%） 試験濃度：設定濃度　1.0、1.8、3.2、5.6、10 mg/L 実測濃度　0.87、1.6、2.7、4.7、8.6 mg/L（時間加重平均値） 助剤：なし 96hLC50（実測値に基づく）＝6.8 mg/L

生態影響判定根拠	変化物が第三種監視化学物質相当でなく、藻類生長阻害試験において 72hEC50=26 mg/L、72hNOEC=0.82 mg/L、ミジンコ急性遊泳阻害試験において 48hEC50=87 mg/L であるが、魚類急性毒性試験において 96hLC50=6.8 mg/L であることから第三種監視化学物質相当。
備考	試験用水溶解度： 藻類培地：700mg/L、Elendt M4 medium：680mg/L、脱塩素水道水 820mg/L 変化物あり（分解度試験において、被験物質は一部分解し、トリス（２－ヒドロキシエチル）イソシアヌル酸、トリス（２－ヒドロキシエチル）イソシアヌル酸モノアクリル酸エステル及びトリス（２－ヒドロキシエチル）イソシアヌル酸ジアクリル酸エステルが残留した。トリス（２－ヒドロキシエチル）イソシアヌル酸モノアクリル酸エステル及びトリス（２－ヒドロキシエチル）イソシアヌル酸ジアクリル酸エステルについては標品の入手が困難であった。）

既存化学物質審査シート

官報公示 整理番号	5-1051 5-1058	CAS No.	839-90-7

判定案	人健康影響　収集された情報からは第二種監視化学物質相当に該当するとは判断されない。【平成 17 年 9 月に審議済み】 生 態 影 響　収集された情報からは第三種監視化学物質相当に該当するとは判断されない。【平成 17 年 9 月に審議済み】
名称 構造式等	名　称：１，３，５－トリス（２－ヒドロキシエチル）イソシアヌル酸 
用途	中間物、添加剤（樹脂用） ※化学物質の製造・輸入量に関する実態調査（平成１６年実績）
外観	白色結晶性粉末
分解性	難分解性
蓄積性	高濃縮性でない

Ames 【平成 17 年 9 月に審議済み】	陰性 純度 99.0%．溶媒（注射用水－溶解）. TA98，TA100，TA1535，TA1537，WP2 uvrA. －S9mix 群：5000μg/plate ＋S9mix 群：5000μg/plate
染色体異常 【平成 17 年 9 月に審議済み】	陰性 純度 99.0%．溶媒（生理食塩液－溶解）．CHL/IU. 2.612 mg/mL(10mM)まで実施した細胞増殖抑制試験の結果を参考に、以下の濃度まで実施. －S9mix 群：2.612 mg/mL ＋S9mix 群：2.612 mg/mL 24 時間処理群：2.612 mg/mL

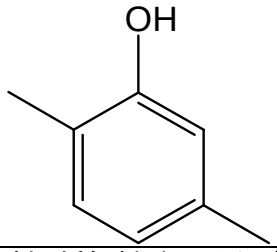
反復経口投与毒性・生殖発生毒性併合試験(ReproTox) 【平成 17 年 9 月に審議済み】	投与方法	強制経口投与　溶媒：注射用水
	純度	99.0 %.
	用量	４投与群（30，100，300，1000mg/kg）
	死亡	なし
	NOEL	反復投与毒性：300 mg/kg/day 生殖発生毒性：1000 mg/kg/day
	推定根拠	反復投与毒性： 組織学的所見（肝－髄外造血：1000♀） 生殖発生毒性： 全群で特に毒性学的影響は認められていない
	他の毒性	－
	回復性	実施せず

他の毒性情報 【平成 17 年 9 月に審議済み】	［SIAR（OECD/HPV プログラム）より引用］ 変異原性： Ames 試験（TA97, TA98, TA100, TA1535, TA1537）：陰性 - (With and without metabolic activation) 染色体異常試験（CHO cells）：陰性 - (With and without metabolic activation)
人健康影響判定根拠	Ames 試験及び染色体異常試験は陰性、NOEL 300 mg/kg/day であることから第二種監視化学物質相当でない。
藻類生長阻害試験 【平成 17 年 9 月に審議済み】	生物種：*Pseudokirchneriella subcapitata* 試験法：OECD-TG201（1984） 培養方式：振とう培養 純度：99.7% 試験濃度：設定濃度　1000 mg/L（限度試験） 実測濃度　940 mg/L（幾何平均値） 助剤：なし 試験上限濃度（1000 mg/L）で影響が認められなかった。
ミジンコ急性遊泳阻害試験 【平成 17 年 9 月に審議済み】	生物種：オオミジンコ *Daphnia magna* 試験法：OECD-TG202（1984） 試験方式：止水式 純度：99.7% 試験濃度：設定濃度　1000 mg/L（限度試験） 実測濃度　930 mg/L（幾何平均値） 助剤：なし 試験上限濃度（1000 mg/L）で影響が認められなかった。
ミジンコ繁殖阻害試験 【平成 17 年 9 月に審議済み】	生物種：オオミジンコ *Daphnia magna* 試験法：OECD-TG211（1998） 試験方式：半止水式、48 時間毎に換水 純度：99.7% 試験濃度：設定濃度　100 mg/L（限度試験） 実測濃度　94 mg/L（時間加重平均値） 助剤：なし 試験上限濃度（100 mg/L）で影響が認められなかった。
魚類急性毒性試験 【平成 17 年 9 月に審議済み】	生物種：ヒメダカ *Oryzias latipes* 試験法：OECD-TG203（1992） 試験方式：半止水式、24 時間毎に換水 純度：99.7% 試験濃度：設定濃度　100 mg/L（限度試験） 実測濃度　92 mg/L（幾何平均値） 助剤：なし 96hLC50（設定値に基づく）＞100 mg/L（100 mg/L 区で 10%の影響が認められた。）
生態影響判定根拠	藻類生長阻害試験、ミジンコ急性遊泳阻害試験及びミジンコ繁殖阻害試験において試験上限濃度で影響が認められず、魚類急性毒性試験において 96hLC50＞100 mg/L であることから第三種監視化学物質相当でない。

環境調査※1	媒体	実施年度	検体	検出範囲	検出下限値
	水質	S54	0/18	－	(5～10) μg/L
	底質	S54	0/18	－	(0.002～0.07) μg/g-dry

	魚類				
	大気				
	その他				
備考	※１　S55 版「化学物質と環境」（環境省環境保健部環境安全課） 対水溶解度(20℃)：　820 g/L（14th SIAM）				

既存化学物質審査シート

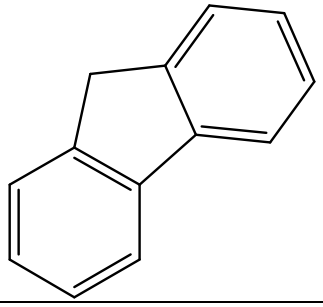
官報公示 整理番号	3-521 4-57	CAS No.	95-87-4
判定案	生 態 影 響　第三種監視化学物質相当		
名称 構造式等	名　称：２，５－キシレノール 		
用途	３－５２１として合成樹脂用、溶剤、添加剤（ゴム用、樹脂用、油用） ４－５７として接着剤、殺虫剤殺菌剤等、添加剤（樹脂用）、電気材料等（半導体） ※化学物質の製造・輸入量に関する実態調査（平成１６年実績）		
外観	白色微細結晶		
分解性	難分解性		
蓄積性	高濃縮性でない		
藻類生長阻害試験	生物種：*Pseudokirchneriella subcapitata* 試験法：化審法 TG（2006） 培養方式：振とう培養 純度：99.6% 試験濃度：設定濃度　5.0、10、20、40、80 mg/L 実測濃度　4.8、9.6、18、38、75 mg/L（幾何平均値） 助剤：なし 72hEC50（設定値に基づく）＝29 mg/L 72hNOEC（設定値に基づく）＝5.0 mg/L		
ミジンコ急性遊泳阻害試験	生物種：オオミジンコ *Daphnia magna* 試験法：化審法 TG 試験方式：止水式 純度：99.6% 試験濃度：設定濃度　1.0、2.0、4.0、8.0、16 mg/L 実測濃度　0.97、2.0、3.9、8.0、16 mg/L（幾何平均値） 助剤：なし 48hEC50（設定値に基づく）＝5.2 mg/L		
魚類急性毒性試験	生物種：ヒメダカ *Oryzias latipes* 試験法：化審法 TG 試験方式：半止水式、24 時間毎に換水 純度：99.6% 試験濃度：設定濃度　1.0、2.0、4.0、8.0、16 mg/L 実測濃度　0.94、1.9、4.0、7.9、16 mg/L（幾何平均値） 助剤：なし 96hLC50（設定値に基づく）＝5.7 mg/L 以下の濃度群において以下のような毒性症状が認められた。 2.0 mg/L 群：遊泳異常（96h 3/10） 4.0 mg/L 群：遊泳異常（96h 1/9）		

生態影響判定根拠	藻類生長阻害試験において 72hEC50=29 mg/L、72hNOEC=5.0 mg/L、ミジンコ急性遊泳阻害試験において 48hEC50=5.2 mg/L であるが、魚類急性毒性試験において 96hLC50=5.7 mg/L であることから第三種監視化学物質相当。

環境調査※1	媒体	実施年度	検体	検出範囲	検出下限値
	水質	S57	0/33	－	(0.04～0.5) μg/L
	底質	S57	0/33	－	(0.0002～0.02) μg/g-dry
	魚類				
	大気				
	その他				

備考	※1　S58 版「化学物質と環境」（環境省環境保健部環境安全課） 試験用水溶解度：藻類培地：≧100mg/L、脱塩素水道水：≧100mg/L

既存化学物質審査シート

官報公示整理番号	4-643	CAS No.	86-73-7
判定案	生 態 影 響　第三種監視化学物質相当		
名称 構造式等	名　称：フルオレン 		
用途	－		
外観	うすい黄色、結晶性粉末		
分解性	難分解性		
蓄積性	高濃縮性でない		
藻類生長阻害試験	生物種：*Pseudokirchneriella subcapitata* 試験法：化審法 TG（2006） 培養方式：振とう培養（密閉系） 純度：95.5% 試験濃度：設定濃度　0.050、0.095、0.18、0.34、0.64、1.2 mg/L 実測濃度　0.043、0.074、0.17、0.32、0.60、1.1 mg/L（時間加重平均値） 助剤：DMF 99 μL/L 72hEC50（実測値に基づく）＝0.76 mg/L 72hNOEC（実測値に基づく）＝0.074 mg/L ①対照区等で pH が 1.5 以上変動しているが、密閉系で試験を実施しており、pH の上昇は避けられなかったものと考えられる。		
ミジンコ急性遊泳阻害試験	生物種：オオミジンコ *Daphnia magna* 試験法：化審法 TG 試験方式：半止水式、24 時間後に換水 純度：95.5% 試験濃度：設定濃度 0.10、0.18、0.32、0.56、1.0 mg/L 実測濃度 0.085、0.16、0.29、0.49、0.90 mg/L（時間加重平均値） 助剤：DMF 99 μL/L 48hEC50（実測値に基づく）＝0.49 mg/L		

魚類急性毒性試験	生物種：ヒメダカ *Oryzias latipes* 試験法：化審法 TG 試験方式：半止水式、24 時間毎に換水 純度：95.5% 試験濃度：設定濃度 0.13、0.23、0.41、0.73、1.3 mg/L 実測濃度 0.12、0.20、0.37、0.67、1.2 mg/L（時間加重平均値） 助剤：DMF 99 μL/L 96hLC50（実測値に基づく）＞1.2 mg/L（0.67 及び 1.2 mg/L 区で 10%の影響が認められた。） 以下の濃度群において以下のような毒性症状が認められた。 0.37 mg/L 群：遊泳異常（48h 1/10、72h 4/10） 0.67 mg/L 群：遊泳異常（24h 3/10、48h 6/10、72h 8/10、96h 9/9） 1.2 mg/L 群：遊泳異常（24h 10/10、48h 10/10、72h 8/9、96h 9/9） 遊泳不能（72h 1/9）
生態影響判定根拠	魚類急性毒性試験において 96hLC50＞1.2 mg/L（溶解限度）であるが、藻類生長阻害試験において 72hEC50=0.76 mg/L、72hNOEC=0.074 mg/L、ミジンコ急性遊泳阻害試験において 48hEC50=0.49 mg/L であることから第三種監視化学物質相当。

環境調査 ※1	媒体	実施年度	検体	検出範囲	検出下限値
	水質	S58 S59	0/33 8/138	－ 0.07～2.5	(0.03～0.4) μg/L (0.006～1) μg/L
	底質	S58 S59	27/33 94/138	0.003～0.091 0.0010～0.13	(0.003～0.041) μg/g-dry (0.0001～0.088) μg/g-dry
	魚類	S58 S59	 魚 26/138	 魚 0.001～0.37	 (魚 0.0003～0.05) μg/g-wet
	大気				
	その他				

備考	※1　S59、S60 版「化学物質と環境」（環境省環境保健部環境安全課） 対水溶解度（25℃）：1.69 mg/L（Howard P.H. and W.M.Meylan ed.:Handbook of Physical Properties of Organic Chemicals） 試験用水溶解度： 藻類培地：1.2mg/L、Elendt M4 medium：1.0mg/L、脱塩素水道水：1.3mg/L

資料2－4

既存化学物質の生態影響に関する情報

平成21年6月26日　化審法3省合同会議

官報公示整理番号	CAS No.	物質名称	頁
5-717	100-43-6	4－ビニルピリジン	1
5-1060	40220-08-4	トリス（2－ヒドロキシエチル）イソシアヌル酸アクリル酸エステル	12
3-521 4-57	95-87-4	2，5－キシレノール	23
4-643	86-73-7	フルオレン	40

要　約

試験委託者　：環境省

表　　題　：4-ビニルピリジンの藻類（*Pseudokirchneriella subcapitata*）に対する生長阻害試験

試験番号：A070391

試験方法：本試験は，「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成15年11月21日 薬食発第 1121002号，平成15・11・13製局第2号，環保企発第031121002号，最終改正：平成18年11月20日）に準拠して実施した。

1)供試生物：　単細胞緑藻類（*Pseudokirchneriella subcapitata*）

2)試験用水：　試験ガイドライン推奨培地

3)暴露期間：　72時間

4)培養方式：　止水式（開放系），振とう培養（100 rpm）

5)初期生物量：　前培養した藻類　5×10^{3} cells/mL
（指数増殖期の藻類乾燥重量：1.7×10^{-8} mg/cell，n=7）

6)試験温度：　22 ℃（暴露期間中の変動範囲は±2 ℃以内）

7)照明：　65～75 μE/m²/s，白色蛍光灯で連続照明（液面付近）

8)試験濃度（設定値）：

試験区	濃度（mg/L）
対照区	—
濃度区1	1.0
濃度区2	2.1
濃度区3	4.5
濃度区4	9.5
濃度区5	20

公比：2.1

9)分析法：　高速液体クロマトグラフ（ＨＰＬＣ）法

結　果：

1)試験液および試験培養液中の被験物質濃度

被験物質濃度測定値の時間加重平均値は，それぞれ低濃度区側から 0.860，1.86，3.83，8.24，17.0 mg/L であり，ほぼ設定値通りであった。

2) 生長速度の比較による阻害濃度

阻害濃度の算出には測定値の時間加重平均値を用いた。

半数生長阻害濃度 ErC50(0-72h)：　4.55 mg/L（95%信頼区間：4.14～5.01 mg/L）

最大無影響濃度 NOECr(0-72h)：　0.860 mg/L

3)藻類の形態観察

暴露開始後 72時間の顕微鏡下での細胞形態観察の結果，対照区と比較して9.5 および 20 mg/L濃度区では，細胞色調の退色化が認められた。その他の濃度区では，細胞形態の変化（収縮，膨張，破裂等）や細胞凝集は認められず，また，対照区との相違もなかった。

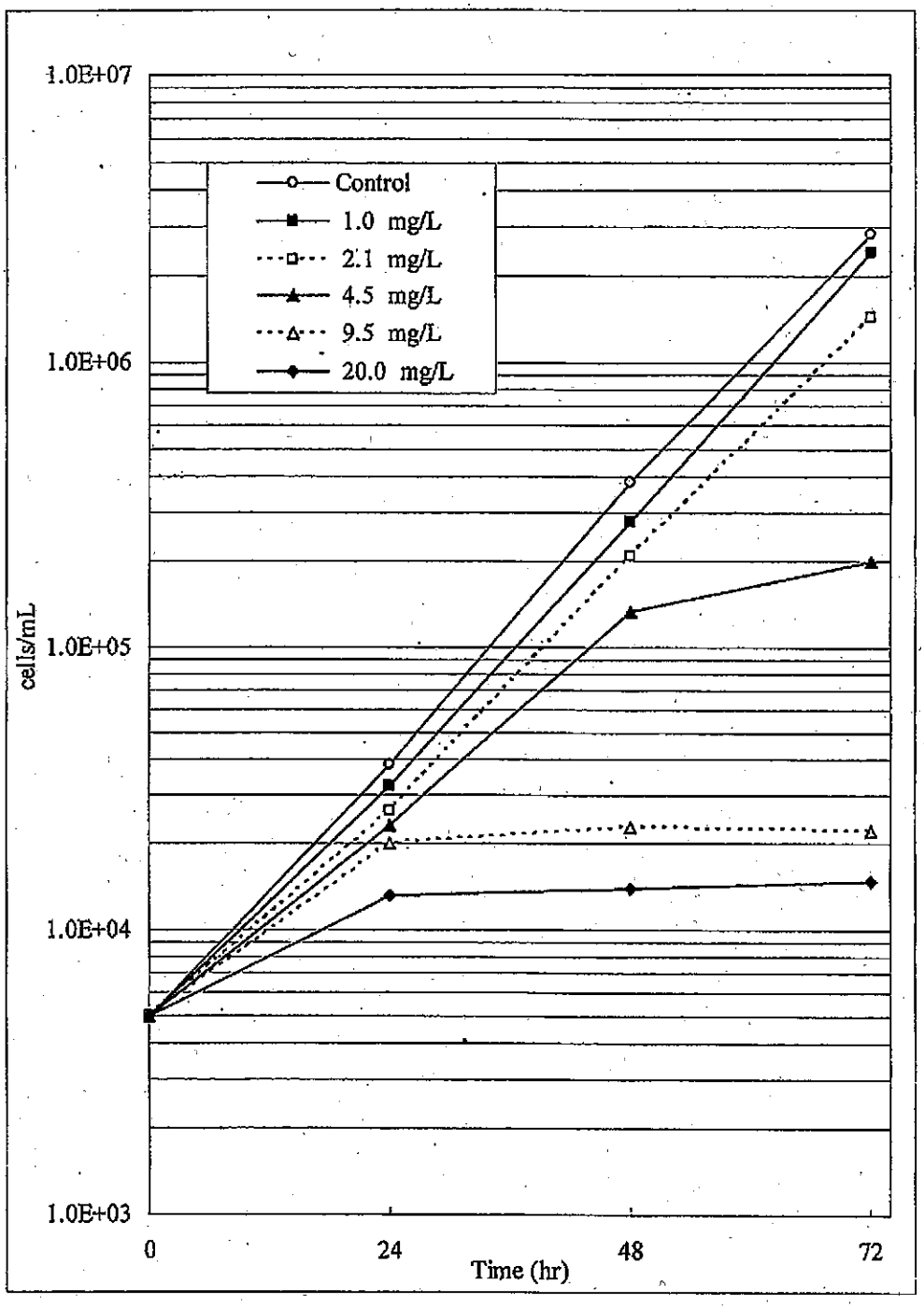
Table 4 Measured Concentration of the Test Substance in Test Cultures

Test Group	Nominal Concentration (mg/L)	Measured Concentration (mg/L) (Percent of Nominal)		Mean[a] Measured Concentration (mg/L) (Percent of Nominal)
		0 Hour	72 Hours	
Control	--	<0.01	<0.01	---
Conc.1	1.0	0.921 (92)	0.801 (80)	0.860 (86)
Conc.2	2.1	1.97 (94)	1.75 (83)	1.86 (89)
Conc.3	4.5	4.11 (91)	3.57 (79)	3.83 (85)
Conc.4	9.5	8.67 (91)	7.83 (82)	8.24 (87)
Conc.5	20	17.9 (90)	16.2 (81)	17.0 (85)

a : Time weighted mean

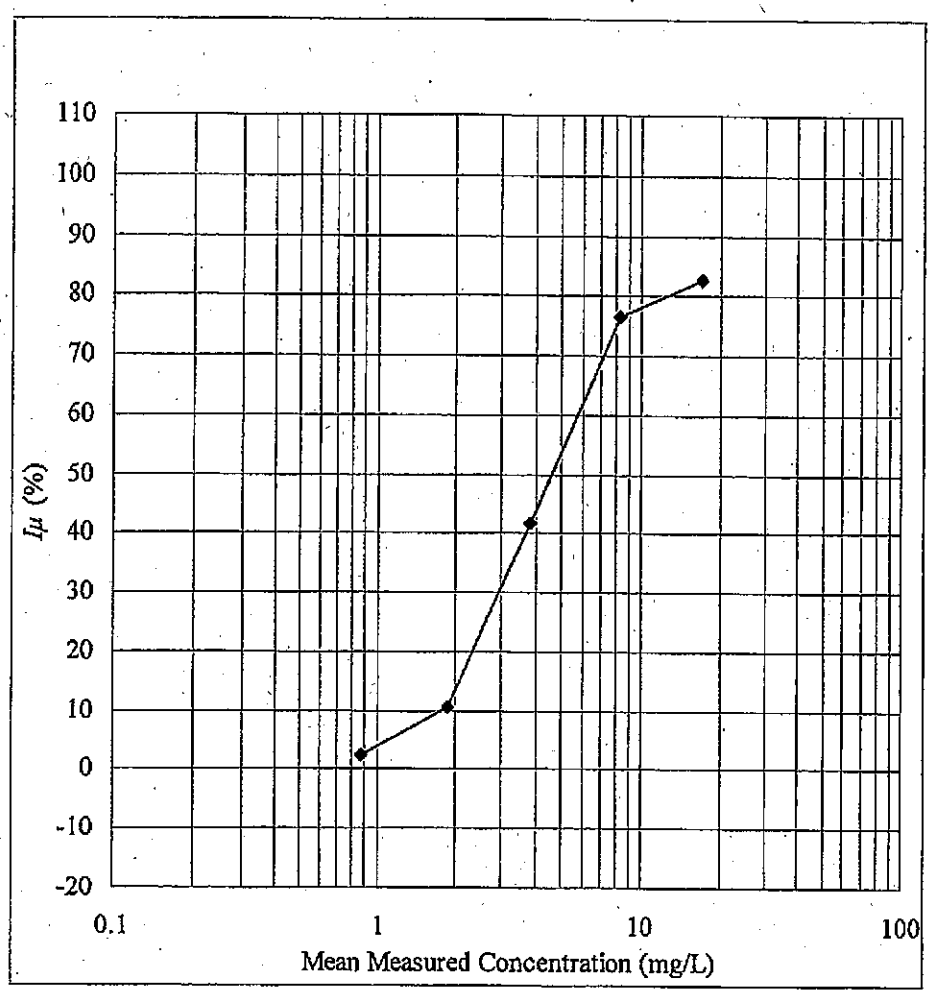
Figure 1 Growth Curve of *Pseudokirchneriella subcapitata*

(Mean biomass *vs* time during the 72-hour exposure)



Values in legend are given in the nominal concentration.

Figure 2 Concentration-Inhibition Curve Based on I_μ values Calculated from the Growth Rates



要 約

試験委託者： 環境省

表　　題： 4-ビニルピリジンのオオミジンコ（*Daphnia magna*）に対する急性遊泳阻害試験

試験番号： A070390

試験方法： 本試験は，「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成 15 年 11 月 21 日 薬食発第 1121002 号，平成 15･11･13 製局第 2 号，環保企発第 031121002 号，最終改正：平成 18 年 11 月 20 日）に準拠して実施した。

1) 供試生物： オオミジンコ（*Daphnia magna*）

2) 試験用水： Elendt M4 medium

3) 暴露期間： 48 時間

4) 暴露方式： 半止水式（24 時間後に試験液の全量を交換）

5) 供試生物数： 20 頭／試験区（5 頭／容器）

6) 試験温度： 20±1℃

7) 照明： 室内光，16 時間明（800 lux 以下）／8 時間暗

8) 試験濃度（設定値）：

試験区	濃度（mg/L）
対照区	―
濃度区 1	0.50
濃度区 2	0.89
濃度区 3	1.6
濃度区 4	2.8
濃度区 5	5.0

公比 1.8

9) 分析方法： 高速液体クロマトグラフ（ＨＰＬＣ）法

結　　果： 以下の結果は，測定値をもとに算出した。

48 時間 半数遊泳阻害濃度（EC50）： 1.17 mg/L（95%信頼限界 0.802～1.44 mg/L）

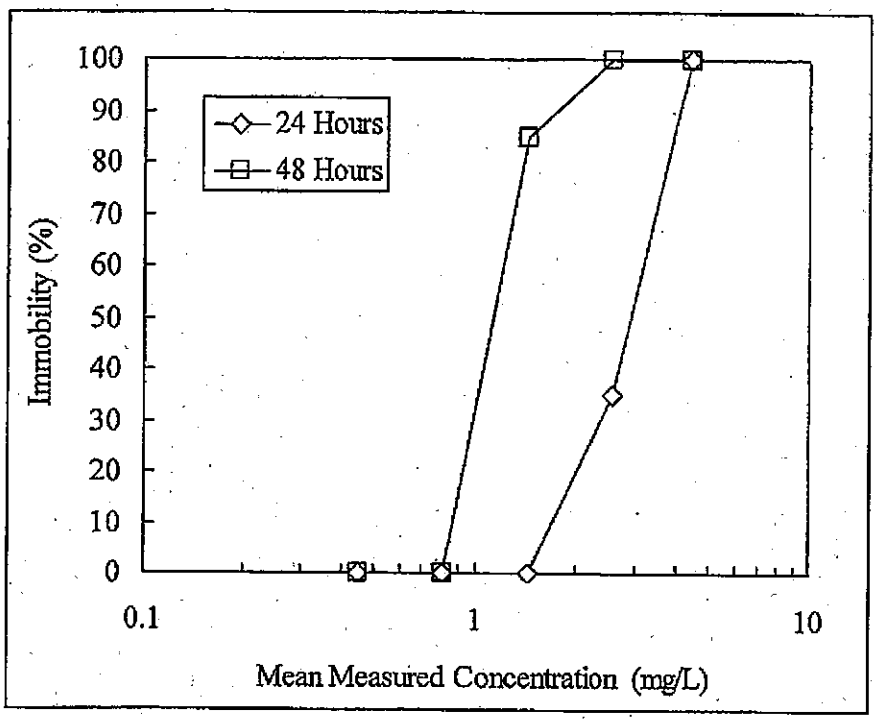
Table 5 Measured Concentrations of the Test Substance in Test Solutions

(Semi-Static Condition)

Test Group	Nominal Concentration (mg/L)	Measured Concentration (mg/L)				
		0 Hour New	24 Hours Old	24 Hours New	48 Hours Old	Mean[a]
		(Percent of Nominal, %)				
Control	--	<0.01	<0.01	<0.01	<0.01	--
Conc.1	0.50	0.465 (93)	0.453 (91)	0.458 (92)	0.439 (88)	0.454 (91)
Conc.2	0.89	0.821 (92)	0.796 (89)	0.814 (91)	0.778 (87)	0.802 (90)
Conc.3	1.6	1.47 (92)	1.43 (89)	1.45 (91)	1.40 (88)	1.44 (90)
Conc.4	2.8	2.62 (94)	2.52 (90)	2.61 (93)	2.50 (89)	2.56 (91)
Conc.5	5.0	4.57 (91)	4.39 (88)	4.53 (91)	4.32 (86)	4.45 (89)

a: Time-weighted mean
New: New test water freshly prepared
Old: Old test water immediately prior to renewal or at the end of the exposure

Figure 1 Concentration-Immobility Curve



8

要　　約

試験委託者：　環境省

表題：　4-ビニルピリジンのヒメダカ（*Oryzias latipes*）に対する急性毒性試験

試験番号：　Ａ０７０３８９

試験方法：　本試験は「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成 15 年 11 月 21 日薬食発第 1121002 号，平成 15･11･13 製局第 2 号，環保企発第 031121002 号，最終改正：平成 18 年 11 月 20 日）に準拠して実施した。

1）供試生物：　ヒメダカ（*Oryzias latipes*）
2）試験用水：　脱塩素水道水
3）暴露期間：　96 時間
4）暴露方式：　半止水式（24 時間毎に試験液の全量を交換）
5）供試生物数：　10 尾／試験区
6）水温：　24±1℃
7）照明：　室内光，16 時間明（1000 lux 以下）／8 時間暗
8）試験濃度（設定値）：

試験区	濃度（mg/L）
対照区	－
濃度区１	0.50
濃度区２	0.89
濃度区３	1.6
濃度区４	2.8
濃度区５	5.0

公比：1.8

9）分析方法：　高速液体クロマトグラフ（ＨＰＬＣ）法

結果：

以下の結果は，被験物質濃度の測定値をもとに算出した。

96 時間半数致死濃度（LC50）：　1.04 mg/L　（95%信頼限界 0.784 ～ 1.39 mg/L）

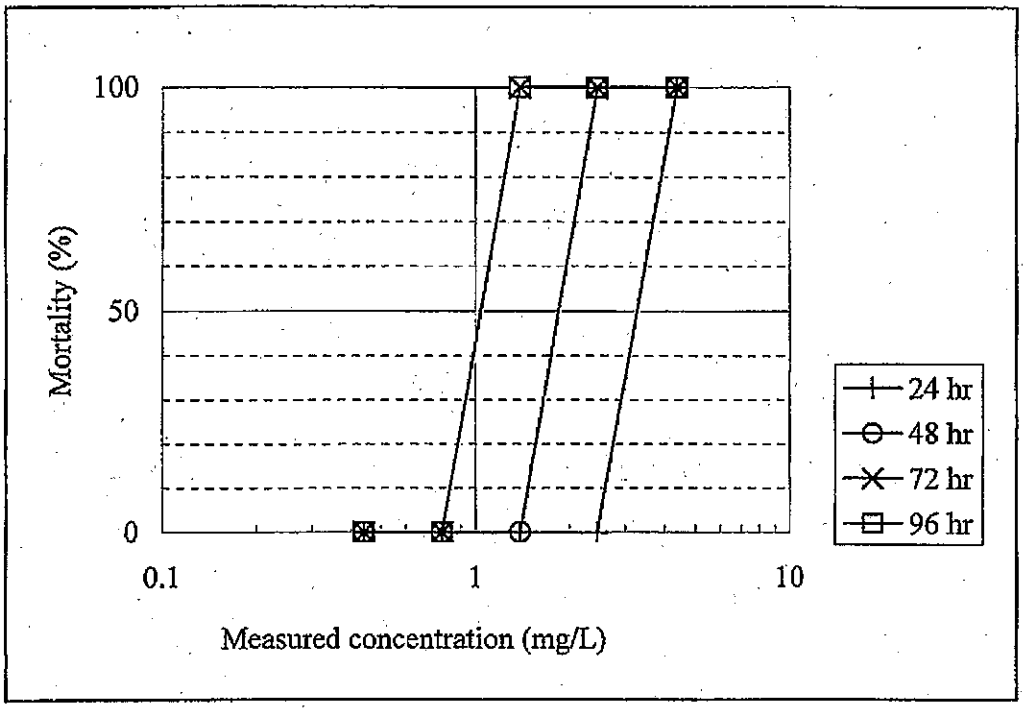
Table 5 Measured Concentrations of the Test Substance in Test Water

Test group	Nominal conc. (mg/L)		Measured concentration (mg/L)				
			0 - 24 hr	24 - 48 hr	48 - 72 hr	72 - 96 hr	Mean
Control		New	<0.01	<0.01	<0.01	<0.01	
		Old	<0.01	<0.01	<0.01	<0.01	
Conc.1	0.50	New	0.452	0.446	0.443	0.445	0.441
		Old	0.432	0.428	0.438	0.443	[88%]
			(96%)	(96%)	(99%)	(100%)	
Conc.2	0.89	New	0.783	0.789	0.797	0.772	0.784
		Old	0.761	0.779	0.797	0.793	[88%]
			(97%)	(99%)	(100%)	(103%)	
Conc.3	1.6	New	1.40	1.41	1.42	--	1.39
		Old	1.34	1.40	1.40	--	[87%]
			(96%)	(99%)	(99%)	--	
Conc.4	2.8	New	2.50	2.51	--	--	2.46
		Old	2.35	2.47	--	--	[88%]
			(94%)	(98%)	--	--	
Conc.5	5.0	New	4.47	--	--	--	4.38
		Old	4.30	--	--	--	[88%]
			(96%)	--	--	--	

New: New test water freshly prepared
Old: Old test water immediately prior to renewal or at the end of exposure
(Percent of New)
Mean: Time weighted mean
[Percent of Nominal]

--: Not measured because all fish were dead.

Figure 1 Concentration-Mortality Curve



要　約

試験委託者 ： 環境省

表　　題 ： トリス(2-ヒドロキシエチル)イソシアヌル酸アクリル酸エステルの藻類（*Pseudokirchneriella subcapitata*）に対する生長阻害試験

試験番号 ： A060500

試験方法 ： 本試験は，「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成15年11月21日 薬食発第 1121002号，平成15・11・13製局第2号，環保企発第031121002号，最終改正：平成18年11月20日）に準拠して実施した。

1)供試生物　　：単細胞緑藻類（*Pseudokirchneriella subcapitata*）

2)試験用水　　：試験ガイドライン推奨培地

3)暴露期間　　：72時間

4)培養方式　　：止水式（開放系），振とう培養（100 rpm）

5)初期生物量　　：前培養した藻類　5×10^3 cells/mL

（指数増殖期の藻類乾燥重量：1.7×10^{-8} mg/cell，n=7）

6)試験温度　　：22℃（暴露期間中の変動範囲は±2℃以内）

7)照明　　：65～75 μE/m²/s，白色蛍光灯で連続照明（液面付近）

8)試験濃度（設定値）：

試験区	濃度（mg/L）
対照区	－
濃度区１	1.0
濃度区２	2.2
濃度区３	4.7
濃度区４	10
濃度区５	22
濃度区６	47
濃度区７*	100

公比：2.2

*：試験ガイドライン上限濃度

9)分析法　　：高速液体クロマトグラフ質量分析（ＬＣ／ＭＳ）法

結　果

1)試験液および試験培養液中の被験物質濃度

被験物質濃度測定値の時間加重平均値は，それぞれ低濃度区側から 0.823，1.82，4.19，8.63，20.1，42.4 および 90.2 mg/L であった。低濃度区側で被験物質のわずかな減少が認められたが，この原因として被験物質の藻類への移行が考えられた。

2)生長速度の比較による阻害濃度

阻害濃度の算出には測定値の時間加重平均値を用いた。

半数生長阻害濃度 ErC50(0-72h)：　26.0 mg/L (95%信頼区間：18.1～37.5 mg/L)

最大無影響濃度 NOECr(0-72h)：　0.823 mg/L

3)藻類の形態観察

暴露開始後 72時間の顕微鏡下での細胞形態観察の結果，対照区と比較して 22 および 47 mg/L 濃度区では一部の細胞で，100 mg/L 濃度区ではほとんど全ての細胞で容積の拡大が認められた。その他の濃度区では，細胞形態の変化（収縮，膨張，破裂等）や細胞凝集は認められず，また，対照区との相違もなかった。

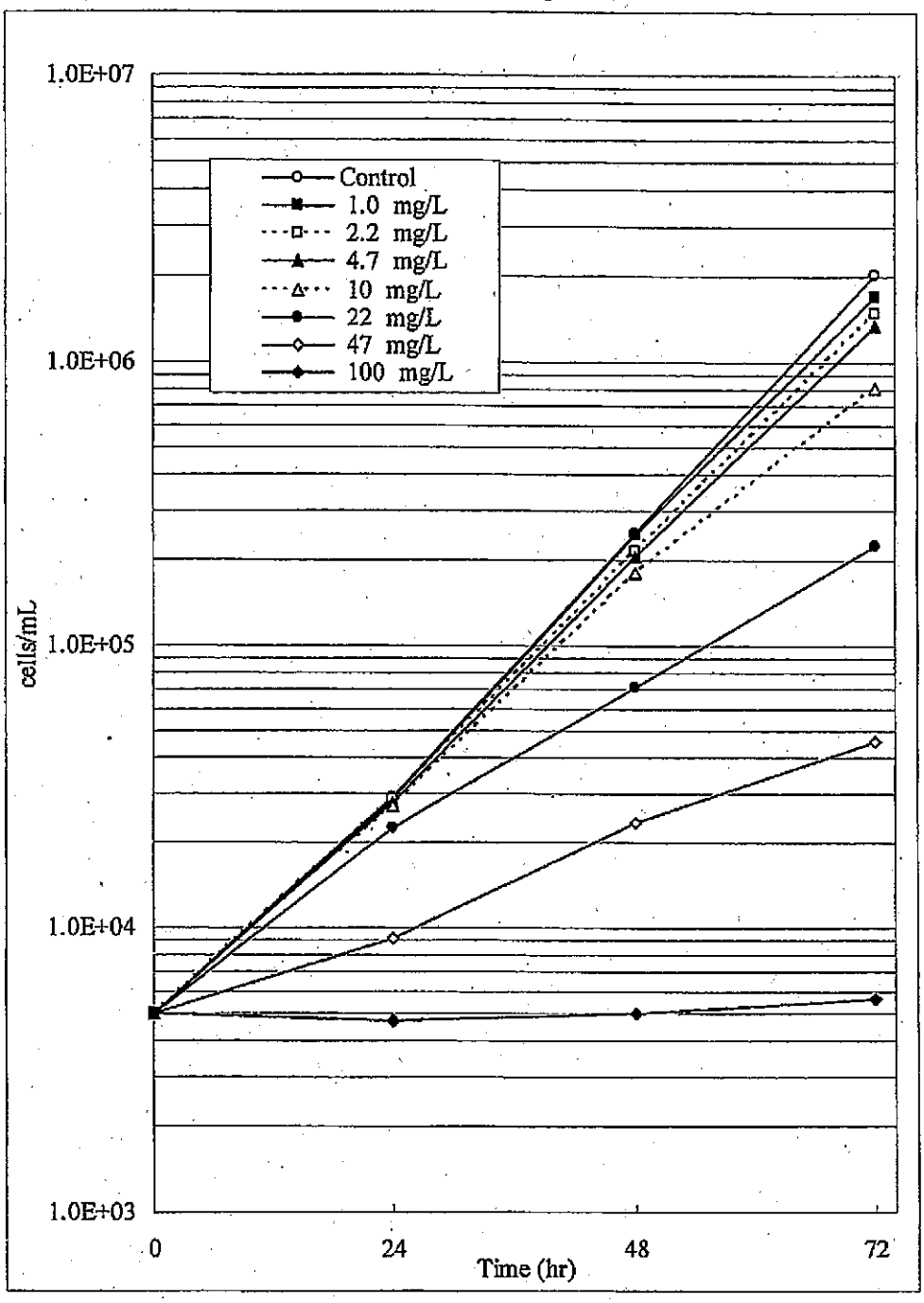
Table 4 Measured Concentrations of the Test Substance in Test Cultures

Test Group	Nominal Concentration (mg/L)	Measured Concentration (mg/L) (Percent of Nominal)		Mean[a] Measured Concentration (mg/L) (Percent of Nominal)
		0 Hour	72 Hours	
Control	--	<0.005	<0.005	----
Conc.1	1.0	0.906 (91)	0.746 (75)	0.823 (82)
Conc.2	2.2	2.01 (91)	1.64 (75)	1.82 (83)
Conc.3	4.7	4.50 (96)	3.90 (83)	4.19 (89)
Conc.4	10	8.83 (88)	8.43 (84)	8.63 (86)
Conc.5	22	20.1 (91)	20.2 (92)	20.1 (91)
Conc.6	47	43.1 (92)	41.7 (89)	42.4 (90)
Conc.7	100	91.2 (91)	89.2 (89)	90.2 (90)

a : Time weighted mean

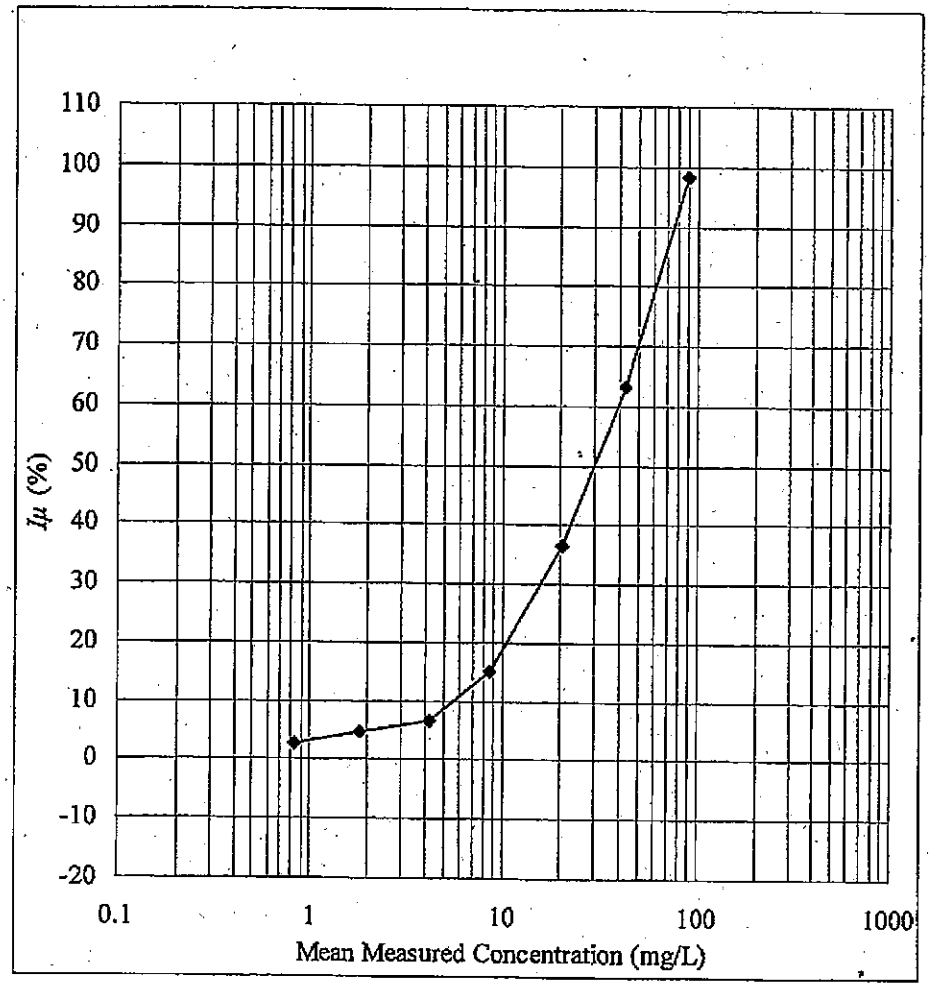
Figure 1 Growth Curve of *Pseudokirchneriella subcapitata*

(Mean biomass *vs* time during the 72-hour exposure)



Values in legend are given in the nominal concentration.

Figure 2 Concentration-Inhibition Curve Based on I_μ values Calculated from the Growth Rates



要 約

試験委託者： 環境省

表　　題： トリス(2-ヒドロキシエチル)イソシアヌル酸アクリル酸エステルのオオミジンコ（*Daphnia magna*）に対する急性遊泳阻害試験

試験番号： A060501

試験方法： 本試験は，「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成 15 年 11 月 21 日薬食発第 1121002 号，平成 15･11･13 製局第 2 号，環保企発第 031121002 号，最終改正：平成 18 年 11 月 20 日）に準拠して実施した。

1) 供試生物： オオミジンコ（*Daphnia magna*）

2) 試験用水： Elendt M4 medium

3) 暴露期間： 48 時間

4) 暴露方式： 半止水式（24 時間後に試験液の全量を交換）

5) 供試生物数： 20 頭／試験区（5 頭／容器）

6) 試験温度： 20±1℃

7) 照明： 室内光，16 時間明（800 lux 以下）／8 時間暗

8) 試験濃度（設定値）：

試験区	濃度（mg/L）
対照区	−
濃度区 1	25
濃度区 2	38
濃度区 3	57
濃度区 4	86
濃度区 5*	130

公比 1.5

*：分析濃度が試験ガイドライン上限濃度付近になるよう設定

9) 分析方法： 高速液体クロマトグラフ質量分析（ＬＣ／ＭＳ）法

結　　果： 以下の結果は，測定値をもとに算出した。

48 時間 半数遊泳阻害濃度（EC50）： 86.9 mg/L（95%信頼限界 79.1～97.0 mg/L）

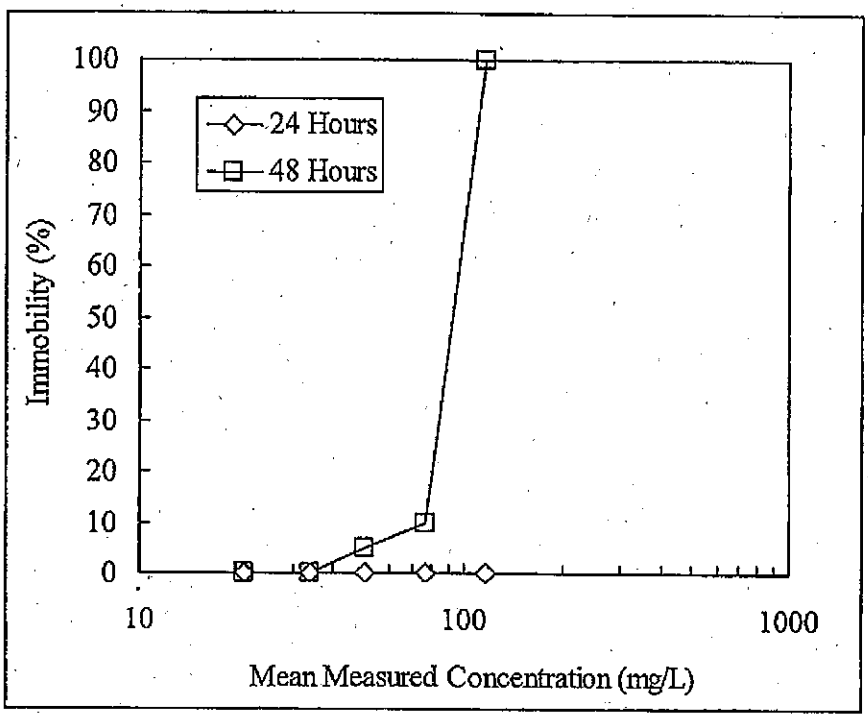
Table 5 Measured Concentrations of the Test Substance in Test Solutions

(Semi-Static Condition)

Test Group	Nominal Concentration (mg/L)	Measured Concentration (mg/L) (Percent of Nominal, %)				
		0 Hour New	24 Hours Old	24 Hours New	48 Hours Old	Mean[a]
Control	--	<0.008	<0.008	<0.008	<0.008	--
Conc.1	25	21.6 (86)	20.9 (84)	21.3 (85)	20.8 (83)	21.1 (84)
Conc.2	38	35.4 (93)	33.6 (88)	32.8 (86)	34.8 (92)	34.1 (90)
Conc.3	57	52.7 (92)	49.7 (87)	48.7 (85)	49.6 (87)	50.2 (88)
Conc.4	86	80.0 (93)	75.8 (88)	74.9 (87)	77.3 (90)	77.0 (90)
Conc.5	130	125 (96)	114 (88)	110 (85)	117 (90)	116 (89)

a: Time-weighted mean
New: New test water freshly prepared
Old: Old test water immediately prior to renewal or at the end of the exposure

Figure 1 Concentration-Immobility Curve



要　　約

試験委託者：　環境省

表題：　トリス(2-ヒドロキシエチル)イソシアヌル酸アクリル酸エステル
のヒメダカ（*Oryzias latipes*）に対する急性毒性試験

試験番号：　Ａ０６０５０２

試験方法：　本試験は「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成15年11月21日薬食発第1121002号，平成15･11･13製局第2号，環保企発第031121002号，最終改正：平成18年11月20日）に準拠して実施した。

1）供試生物：　ヒメダカ（*Oryzias latipes*）
2）試験用水：　脱塩素水道水
3）暴露期間：　96時間
4）暴露方式：　半止水式（24時間毎に試験液の全量を交換）
5）供試生物数：　10尾／試験区
6）水温：　24±1℃
7）照明：　室内光，16時間明（1000 lux 以下）／8時間暗
8）試験濃度（設定値）：

試験区	濃度（mg/L）
対照区	－
濃度区1	1.0
濃度区2	1.8
濃度区3	3.2
濃度区4	5.6
濃度区5	10

公比：1.8

9）分析方法：　高速液体クロマトグラフ質量分析（ＬＣ／ＭＳ）法

結果：

以下の結果は，被験物質濃度の測定値をもとに算出した。

96時間半数致死濃度（LC50）：　6.79 mg/L　(95%信頼限界 4.70 ～ 8.63 mg/L)

Table 5 Measured Concentrations of the Test Substance in Test Water

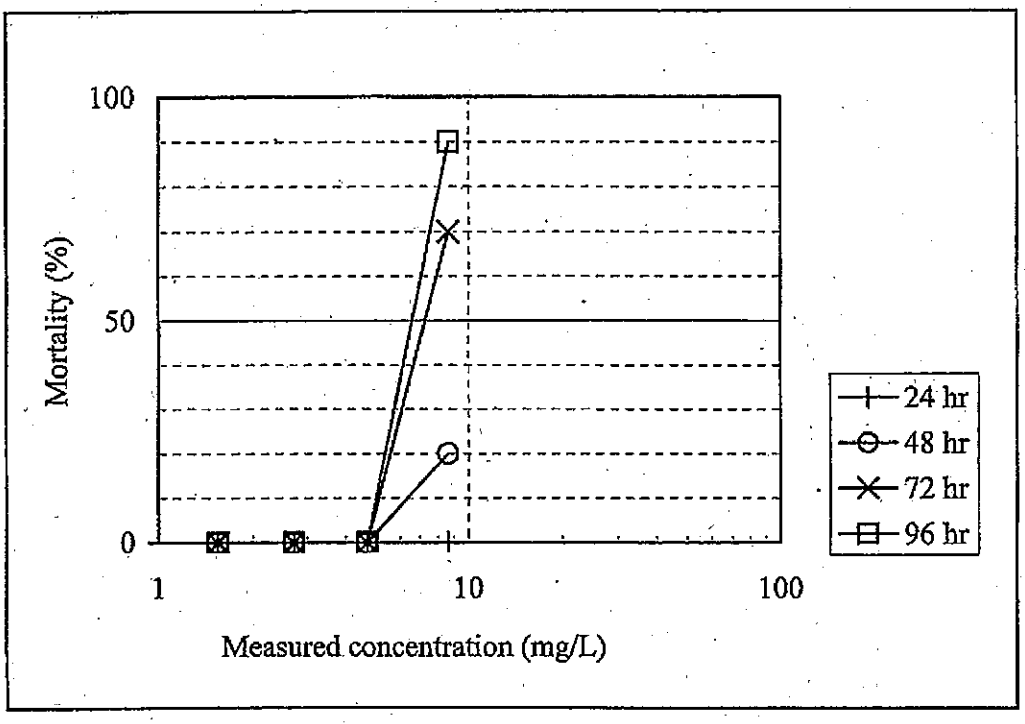
Test group	Nominal conc. (mg/L)	Measured concentration (mg/L)					
			0 - 24 hr	24 - 48 hr	48 - 72 hr	72 - 96 hr	Mean
Control		New	<0.01	<0.01	<0.01	<0.01	
		Old	<0.01	<0.01	<0.01	<0.01	
Conc.1	1.0	New	0.911	0.908	0.813	0.847	0.865 [87%]
		Old	0.877 (96%)	0.884 (97%)	0.821 (101%)	0.863 (102%)	
Conc.2	1.8	New	1.63	1.62	1.52	1.48	1.55 [86%]
		Old	1.55 (95%)	1.59 (98%)	1.47 (97%)	1.57 (106%)	
Conc.3	3.2	New	2.83	2.85	2.60	2.62	2.72 [85%]
		Old	2.84 (100%)	2.85 (100%)	2.67 (103%)	2.54 (97%)	
Conc.4	5.6	New	4.55	5.13	4.58	4.66	4.70 [84%]
		Old	4.45 (98%)	4.93 (96%)	4.43 (97%)	4.85 (104%)	
Conc.5	10	New	8.79	8.90	8.17	8.18	8.63 [86%]
		Old	8.87 (101%)	8.67 (97%)	8.66 (106%)	8.78 (107%)	

New: New test water freshly prepared

Old: Old test water immediately prior to renewal or at the end of exposure
(Percent of New)

Mean: Time weighted mean
[Percent of Nominal]

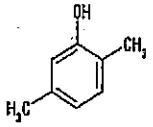
Figure 1 Concentration-Mortality Curve



[様式 7]

藻類生長阻害試験結果報告書

1. 一般的事項

新規化学物質等の名称(IUPAC 命名法による)	2，5－キシレノール		
別名	－		
CAS 番号	95-87-4		
構造式又は示性式(いずれも不明な場合は、その製法の概要)			
分子量	122.16		
試験に供した新規化学物質の純度（%）	99.6%		
試験に供した新規化学物質のロット番号	LTR3669		
不純物の名称及び含有率	情報なし		
蒸気圧	情報なし		
対水溶解度	100 mg/L 以上 (脱塩素水道水、日曹分析センター 報告書番号 NCAS08-026)		
1-ｵｸﾀﾉｰﾙ/水分配係数	情報なし		
融点	情報なし		
沸点	情報なし		
常温における性状	白色微細結晶		
安定性	情報なし		
溶媒に対する溶解度等	溶媒	溶解度	溶媒中の安定性
	OECD 培地	100 mg/L 以上	情報なし

[備 考] 物理化学的性状は、可能な限り記入すること。

1. 「蒸気圧」の欄には、被験物質の蒸気圧を記入すること。
2. 「安定性」の欄には、温度、光等に対する安定性を記入すること。
3. 「溶媒に対する溶解度等」の欄には、被験物質の溶媒に対する溶解度及びその溶媒中での安定性を記入すること。

2. 試験溶液の被験物質濃度の分析方法

項　目	方　　法
分析方法	高速液体クロマトグラフィー（HPLC）
前処理法	試験溶液を遠沈管に採取後、等量のアセトニトリルを加えてよく混合し、遠心分離（10000 rpm（8000×*g*）、5分間、設定温度20℃）を行った。得られた上澄み液をHPLCにより分析した。
定量条件	HPLC条件： カ ラ ム：CAPCELL PAK C18 UG120、5 μm、4.6 mm I.D.×150 mm 移動相：アセトニトリル／20m リン酸二水素ナトリウム(pH2.5)*＝50/50 (v/v) *20mM リン酸二水素ナトリウム溶液をリン酸でpH2.5に調整した溶液 流　速：1.0 mL/min カラム温度：40℃ 検出波長：218 nm 注 入 量：10 μL

[備 考]

1. 「分析方法」の欄には、実測した分析法を具体的に記入すること。
2. 「前処理法」の欄には、分析を行う前に実施した処理の概要を記入すること。藻類においては細胞の分離手法を明記すること。
3. 「定量条件」の欄には、分析に用いた機器や温度･溶離液等の分析の条件を記入すること。

3. 試験材料及び方法

項目			内容
試験生物	種（学名・株名）		*Pseudokirchneriella subcapitata*
	入手先		American Type Culture Collection (ATCC) Manassas,VA20108.USA を住商ファーマ インターナショナルより 2001 年 8 月 2 日に入手し、当事業所において継代培養したもの
	対照物質への感受性（EC_{50}）（対照物質名）		対照物質名：重クロム酸カリウム（試薬特級、和光純薬工業） 72 時間 ErC_{50} の背景データ：0.84 (n=1、2008 年 8 月実施)
前培養	前培養の期間		3 日間
	培地名		OECD 培地
	環境条件（水温、光強度）		22.6℃、76～77 μE/m²/s（フラスコ液面付近）で連続照明
試験条件	試験容器		アルミキャップ付 300 mL ガラス製三角フラスコ
	培地名		OECD 培地
	暴露期間		2008 年 8 月 4 日～2008 年 8 月 7 日
	試験濃度（設定値）		5.00、10.0、20.0、40.0、80.0 mg/L (公比 2.0) および対照区
	初期生物量		5,005 cells/mL (計算値)
	連数	試験濃度区	3 連
		対照区	6 連
	試験溶液量		100 mL/試験容器
	助剤	助剤の有無	無し
		種類	－
		濃度	－
		助剤対照区の連数	－
	培養方式（振とう培養、静置培養、連続培養等）		止水式（開放系）、振とう培養
	水温または培養温度		試験溶液温度：22.0～22.8℃
	照明（光強度・時間等）		65～71 μE/m²/s（フラスコ液面付近）で連続照明
結果の算出方法	速度法		ErC_{50}： Probit 法 NOECr：Bartlett test、1-way ANOVA および Dunnett 法

[備 考]

1. 「対照物質への感受性」の欄には、試験生物の感受性検定の結果を記入（対照物質を明記した上で EC_{50} を記入）すること。
2. 「試験濃度（設定値）」の欄には、試験に用いた被験物質の濃度をすべて掲げ、その公比も記入すること。
3. 「試験条件」の「試験容器」の欄には、材質及び容量を記入すること。なお、被験物質が揮発性を有する場合は「密閉の有無」を記載すること。
4. 「結果の算出方法」の欄には、毒性値（EC_{50} 及び NOEC）の算出に用いた統計解析手法（例えば、probit 法、ANOVA 等）を記入すること。

4. 試験結果及び考察

項目	内容
毒性値	0-72 h ErC_{50} = 29 mg/L 0-72 h NOECr = 5.00 mg/L
試験濃度	(1.) 設定値　　2. 実測値
考察及び特記事項	暴露開始時および暴露終了時の被験物質濃度について、設定濃度に対する変動は±20%未満であったため、設定濃度を被験物質濃度とした。 対照区の細胞濃度は、72時間の培養で平均79倍に増加し、規定の16倍を上回った。対照区の生長速度について、毎日の生長速度の変動係数の平均値は31.6%、各繰り返し間の変動係数は2.35%であり、いずれの値も規定の範囲内に収まった。以上のことから試験は有効と判断した。 試験計画書からの逸脱事項:前培養は本試験と同じ条件で行うと記載されているが、規定よりも約10倍多い細胞濃度で前培養を開始した。本試験の結果、前述のとおり試験の有効性の判断基準は満たされた。また、暴露終了後に測定した対照区試験溶液の乾燥重量の結果から、本試験開始時の細胞濃度(5005 cells/mL、計算値)ではガイドライン記載の初期生物量の規定(乾燥重量0.5 mg/L以内)を満たすことを確認した。前培養中、対照区と同様の生長曲線と増加倍率が認められ、藻類の状態は外観上良好であった。以上のことから、指数増殖期の藻類が供試できたものと判断し、試験結果に影響を及ぼした可能性は無かったと判断した。

[備 考]

1. 「試験濃度」の欄には、毒性値(EC_{50}及びNOEC)を算出するために用いた濃度が「設定値」か、あるいは「実測値」かを明記すること。
2. 「考察及び特記事項」の欄には、被験物質の物理的化学的特性を踏まえて、毒性値の特徴や試験の有効性に関して考察すること。また、試験における異常な事項や本試験法から逸脱した事項等については、試験結果への影響等を記載すること。

5. 藻類の生長曲線及び濃度―生長阻害率曲線

暴露期間中の①生長曲線及び②各試験濃度での生長阻害率を示した図を添付すること。

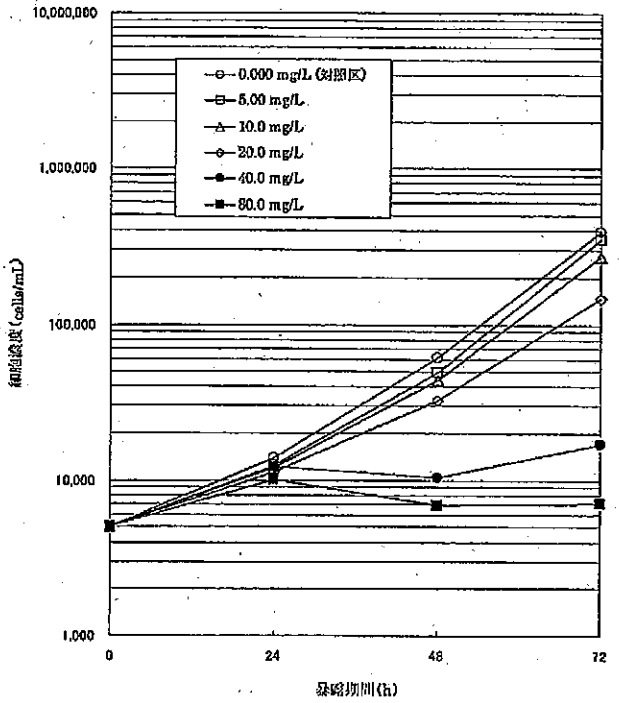


図１　藻類の生長曲線

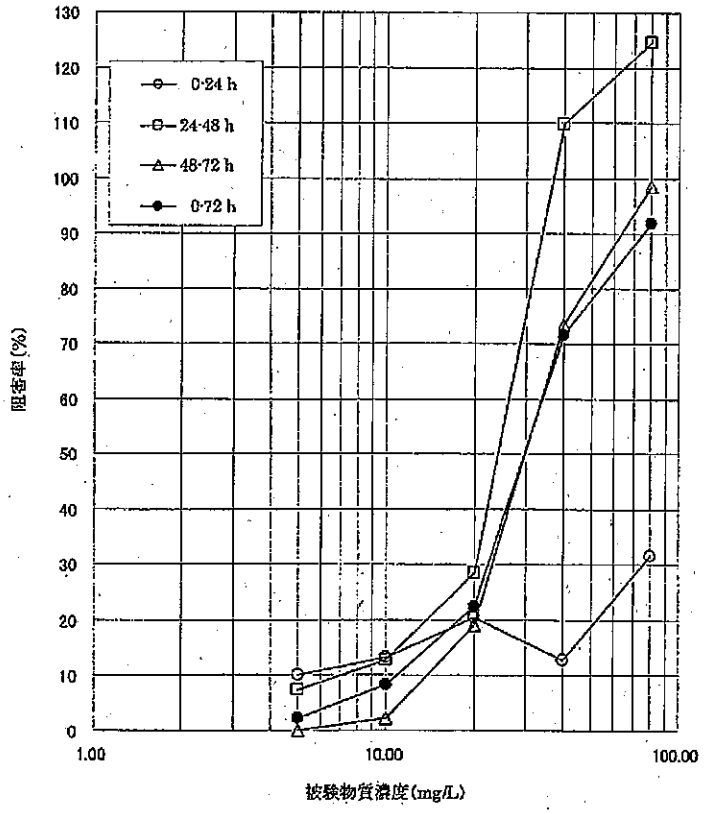


図２　藻類の濃度－生長阻害率曲線（生長速度）

表1　繰り返し精度の確認

設定濃度(mg/L)	検出濃度(mg/L)	平均濃度(mg/L)	変動係数(%)
5.00	4.60	4.61	0.452
	4.63		
	4.59		
80.0	76.2	76.4	0.496
	76.8		
	76.1		

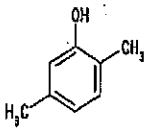
表2　試験溶液中の被験物質濃度

設定濃度 (mg/L)	0時間		72時間	
	検出濃度 (mg/L)	設定濃度に対する割合(%)	検出濃度 (mg/L)	設定濃度に対する割合(%)
対照区	—	—	—	—
5.00	4.75	95.0	4.78	95.6
10.0	9.62	96.2	9.54	95.4
20.0	18.6	93.0	17.9	89.5
40.0	38.0	95.0	37.6	94.0
80.0	76.3	95.4	74.4	93.0

[様式 8]

ミジンコ急性遊泳阻害試験結果報告書

1. 一般的事項

新規化学物質等の名称（IUPAC 命名法による）	2，5－キシレノール		
別名	－		
CAS 番号	95-87-4		
構造式又は示性式（いずれも不明な場合は、その製法の概要）			
分子量	122.16		
試験に供した新規化学物質の純度（%）	99.6%		
試験に供した新規化学物質のロット番号	LTR3669		
不純物の名称及び含有率	情報なし		
蒸気圧	情報なし		
対水溶解度	100 mg/L 以上 (脱塩素水道水、日曹分析センター 報告書番号 NCAS08-026)		
1-ｵｸﾀﾉｰﾙ/水分配係数	情報なし		
融点	情報なし		
沸点	情報なし		
常温における性状	白色微細結晶		
安定性	情報なし		
溶媒に対する溶解度等	溶媒	溶解度	溶媒中の安定性
	情報なし	情報なし	情報なし

[備 考] 物理化学的性状は、可能な限り記入すること。

1. 「蒸気圧」の欄には、被験物質の蒸気圧を記入すること。
2. 「安定性」の欄には、温度、光等に対する安定性を記入すること。
3. 「溶媒に対する溶解度等」の欄には、被験物質の溶媒に対する溶解度及びその溶媒中での安定性を記入すること。

2. 試験溶液の被験物質濃度の分析方法

項　目	方　　法
分析方法	高速液体クロマトグラフィー（HPLC）
前処理法	試験溶液を遠沈管に採取後、等量のアセトニトリルを加えてよく混合し、遠心分離（10000 rpm（8000×*g*）、5 分間、設定温度 20℃）を行った。得られた上澄み液をHPLC により分析した。
定量条件	HPLC 条件： カ ラ ム：CAPCELL PAK CI8 UG120、5 μm、4.6 mm I.D.×150 mm 移動相：アセトニトリル／20mM リン酸二水素ナトリウム(pH2.5)*＝50/50 (v/v) *20mM リン酸二水素ナトリウム溶液をリン酸で pH2.5 に調整した溶液 流　速：1.0 mL/min カラム温度：40℃ 検出波長：218 nm 注 入 量：10 μL

[備 考]

1. 「分析方法」の欄には、実測した分析法を具体的に記入すること。
2. 「前処理法」の欄には、分析を行う前に実施した処理の概要を記入すること。藻類においては細胞の分離手法を明記すること。
3. 「定量条件」の欄には、分析に用いた機器や温度･溶離液等の分析の条件を記入すること。

3. 試験材料及び方法

項目			内容
試験生物	種（学名・系統・時間齢）		*Daphnia magna*、24 時間齢未満
	入手先		国立環境研究所より 2005 年 5 月 25 日に入手したものを当事業所において継代したもの
	対照物質への感受性（EC_{50}）（対照物質名）		対照物質名：重クロム酸カリウム（試薬特級、和光純薬工業） 48 時間 EC_{50} の背景データ：0.20～0.36 mg/L（n=6、2005 年 7 月～2007 年 12 月）
飼育	飼育水の種類		脱塩素水道水
	環境条件（水温、明暗周期）		20.0℃、16 時間明/8 時間暗
試験条件	試験容器		100 mL 容ガラス製ビーカー
	試験用水	種類（天然水、脱塩素水道水、人工調製水等）	脱塩素水道水
		硬度	69 mg/L（$CaCO_3$ 換算）
		pH	7.8～7.9
	暴露期間		2008 年 3 月 4 日～2008 年 3 月 6 日
	試験濃度（設定値）		1.00、2.00、4.00、8.00 および 16.0 mg/L（公比 2.0）および対照区
	供試数		20 頭（5 頭/試験容器）
	連数	試験濃度区	4 連
		対照区	4 連
	試験溶液量		100 mL/試験容器
	助剤	助剤の有無	無し
		種類	－
		濃度	－
		助剤対照区の連数	－
	試験方法（止水、半止水、流水等）		止水式（開放系）
	換水又は流水条件		なし
	水温		20.2℃
	溶存酸素濃度（DO）		8.6～8.7 mg/L
	明暗周期		16 時間明/8 時間暗
結果の算出方法	EC_{50}		Probit 法

[備 考]

1. 「対照物質への感受性」の欄には、試験生物の感受性検定の結果を記入（対照物質を明記した上で EC_{50} を記入）すること。
2. 「試験濃度（設定値）」の欄には、試験に用いた被験物質の濃度をすべて掲げ、その公比も記入すること。
3. 「試験条件」の「試験容器」の欄には、材質及び容量を記入すること。なお、被験物質が揮発性を有する場合は「密封の有無」を記載すること。
4. 「結果の算出方法」の欄には、毒性値（EC_{50}）の算出に用いた統計解析手法（例えば、probit 法等）を記入すること。

4. 試験結果及び考察

項目	内容
毒性値	48h EC_{50} ＝ 5.2 mg/L
試験濃度	(1.) 設定値　2. 実測値
考察及び特記事項	暴露 24 時間後の遊泳阻害率は対照区、1.00、2.00 および 4.00 mg/L 区で 0%、8.00 mg/L 区で 40%、16.0 mg/L 区では 100%であった。暴露 48 時間後の遊泳阻害率は、対照区および 1.00 mg/L 区で 0%、2.00 mg/L 区で 10%、4.00 mg/L 区で 25%、8.00 mg/L 区で 75%、16.0 mg/L 区で 100%であった。 暴露 48 時間の EC_{50} は、Probit 法で算出した結果 5.2 mg/L となり、95%信頼限界は 4.2～6.4 mg/L と算出された。 対照区のミジンコについて、暴露期間中に遊泳阻害および行動や外見の異常は観察されなかった。また、暴露終了時において、溶存酸素濃度は対照区も含めた全ての試験区で規定の 3 mg/L 以上の濃度であり、試験は有効とみなされた。

［備 考］

1. 「毒性値」の欄には、48 時間での遊泳阻害における EC_{50} を記入すること。
2. 「試験濃度」の欄には、毒性値（EC_{50}）を算出するために用いた濃度が「設定値」か、あるいは「実測値」かを明記すること。
3. 「考察及び特記事項」の欄には、被験物質の物理的化学的特性を踏まえて、毒性値の特徴や試験の有効性に関して考察すること。また、試験における異常な事項や本試験法から逸脱した事項等については、試験結果への影響等を記載すること。

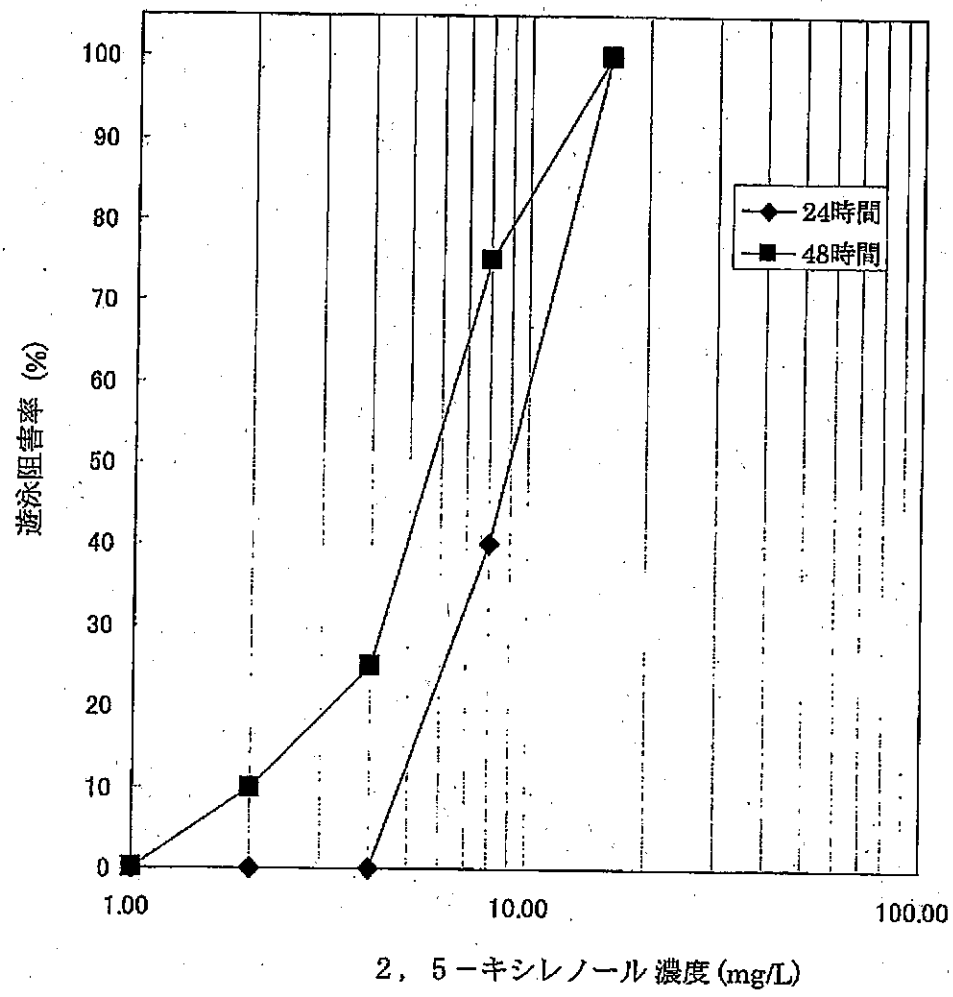


図10　2，5－キシレノール濃度と遊泳阻害率

表 1 繰り返し精度の測定結果

設定濃度 (mg/L)	反復	検出濃度 (mg/L)	平均濃度 (mg/L) (n=3)	変動係数 (%) (n=3)
1.00	1	1.00	1.00	1.05
	2	0.989		
	3	1.01		
16.0	1	15.5	15.9	3.68
	2	15.7		
	3	16.6		

表 2 試験溶液中の被験物質濃度

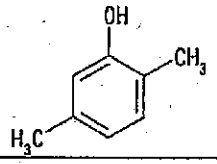
設定濃度 (mg/L)	測定濃度 (mg/L) *	
	暴露開始時	48 時間後
対照区	検出せず	検出せず
1.00	1.00 (100)	0.935 (93.5)
2.00	2.10 (105)	1.95 (97.5)
4.00	3.96 (99.0)	3.91 (97.8)
8.00	8.08 (101)	7.91 (98.9)
16.0	15.6 (97.5)	15.8 (98.8)

* : ( )内は設定濃度に対する割合(%)を示した。

［様式９］

魚類急性毒性試験結果報告書

1．一般的事項

新規化学物質等の名称（IUPAC命名法による）	2，5－キシレノール		
別名	－		
CAS番号	95-87-4		
構造式又は示性式（いずれも不明な場合は、その製法の概要）			
分子量	122.16		
試験に供した化学物質の純度（%）	99.6%		
試験に供した化学物質のロット番号	LTR3669		
不純物の名称及び含有率	情報なし		
蒸気圧	情報なし		
対水溶解度	100 mg/L 以上 （脱塩素水道水、日曹分析センター 報告書番号 NCAS 08-026）		
1-ｵｸﾀﾉｰﾙ/水分配係数	情報なし		
融点	情報なし		
沸点	情報なし		
常温における性状	白色微細結晶		
安定性	情報なし		
溶媒に対する溶解度等	溶媒	溶解度	溶媒中の安定性
	情報なし	情報なし	情報なし

［備 考］物理化学的性状は、可能な限り記入すること。

1. 「蒸気圧」の欄には、被験物質の蒸気圧を記入すること。
2. 「安定性」の欄には、温度、光等に対する安定性を記入すること。
3. 「溶媒に対する溶解度等」の欄には、被験物質の溶媒に対する溶解度及びその溶媒中での安定性を記入すること。

2. 試験溶液の被験物質濃度の分析方法

項　目	方　　法
分析方法	高速液体クロマトグラフィー（HPLC）
前処理法	試験溶液を遠沈管に採取後、等量のアセトニトリルを加えてよく混合し、遠心分離（10000 rpm (8000×*g*)、5 分間、設定温度 20℃）を行った。得られた上澄み液を HPLC により分析した。
定量条件	HPLC 条件 カ ラ ム：CAPCELL PAK C18 UG120、5μm、4.6 mm I.D.×150 mm 移動相：アセトニトリル/20mM リン酸二水素ナトリウム(pH2.5)*=50/50(V/V) *20mM リン酸二水素ナトリウム溶液をリン酸で pH2.5 に調整した溶液 流　速：1.0 mL/min カラム温度：40℃ 検出波長：218 nm 注 入 量：10 μL

[備 考]

1. 「分析方法」の欄には、実測した分析法を具体的に記入すること。
2. 「前処理法」の欄には、分析を行う前に実施した処理の概要を記入すること。藻類においては細胞の分離手法を明記すること。
3. 「定量条件」の欄には、分析に用いた機器や温度･溶離液等の分析の条件を記入すること。

3. 試験材料及び方法

項目			内容
試験生物	種（和名・学名・系統）		ヒメダカ・*Oryzias latipes*
	入手先		the Fish 湘南
	大きさ（体長、体重）・月齢		3.3 cm、0.23 g・10 ケ月齢
	対照物質への感受性（LC_{50}）（対照物質名）		0.75 mg/L（硫酸銅(Ⅱ)の無水物として）
じゅん化	じゅん化期間		10 日間（2008 年 2 月 22 日～3 月 3 日）
	飼育水の種類		脱塩素水道水
	じゅん化前の薬浴の有無		なし
	じゅん化方式（止水、半止水、流水等）		止水式
	環境条件（水温、明暗周期）		22.8～23.0℃、16 時間明/8 時間暗
	餌料（種類・量・頻度等）		メダカのえさ（テトラジャパン製）魚体重の 1.5%相当量・1 日 1 回
試験条件	試験容器		3 L ガラス製ビーカー、密閉なし
	試験用水	種類（天然水、脱塩素水道水、人工調製水等）	脱塩素水道水
		硬度	51～53 mg/L
		pH	7.3～7.7
	曝露期間		2008 年 3 月 3 日 ～ 2008 年 3 月 7 日
	試験濃度（設定値）		1.00、2.00、4.00、8.00、16.0 mg/L（公比 2.0）および対照区
	供試数		10 尾/試験容器
	試験溶液量		3 L
	助剤	助剤の有無	無し
		種類	－
		濃度	－
	試験方法（止水、半止水、流水等）		半止水式（開放系）
	換水または流水条件		24 時間換水
	水温		22.8～23.0℃
	溶存酸素濃度（DO）		6.4～8.4 mg/L
	明暗周期		16 時間明/8 時間暗
結果の算出方法	LC_{50}		プロビット法

[備 考]

1. 「対照物質への感受性」の欄には、試験生物の感受性検定の結果を記入（対照物質を明記した上で LC_{50} を記入）すること。
2. 「じゅん化」の「じゅん化前の薬浴の有無」の欄には、じゅん化前に行った薬浴の有無を記入し、薬浴を実施した場合は薬剤の種類も記載すること
3. 「試験濃度（設定値）」の欄には、試験に用いた被験物質の濃度をすべて掲げ、その公比も記入すること。
4. 「試験条件」の「試験容器」の欄には、材質及び容量を記入すること。なお、被験物質が揮発性を有する場合は「密封の有無」を記載すること。
5. 「結果の算出方法」の欄には、毒性値の（LC_{50}）算出に用いた統計解析手法（例えば、probit 法等）を記入すること。

4. 試験結果及び考察

項目	内容
毒性値	96hLC$_{50}$ = 5.7 mg/L
試験濃度	(1.) 設定値　2. 実測値
考察及び特記事項	予備検討（報告書番号 NCAS 07-223NG）の結果、設定濃度 1.00 および 10.0 mg/L 区でそれぞれ 0%および 100%の死亡が確認された。これより、設定濃度 1.00、2.00、4.00、8.00 および 16.0 mg/L の 5 濃度（公比 2.0）で試験を実施した。対照区では、全ての暴露時間において死亡は観察されなかった。暴露期間中、溶存酸素濃度は 76～100%であり、飽和濃度の 60%以上が維持された。

［備 考］

1. 「毒性値」の欄には、96 時間での LC$_{50}$ を記入すること。
2. 「試験濃度」の欄には、毒性値（LC$_{50}$）を算出するために用いた濃度が「設定値」か、あるいは「実測値」かを明記すること。
3. 「考察及び特記事項」の欄には、被験物質の物理的化学的特性を踏まえて、毒性値の特徴や試験の有効性に関して考察すること。また、試験における異常な事項や本試験法から逸脱した事項等については、試験結果への影響等を記載すること。

5. 魚類の濃度 — 死亡率曲線

曝露期間中における各試験濃度での魚類に対する死亡率を示した図を添付すること。

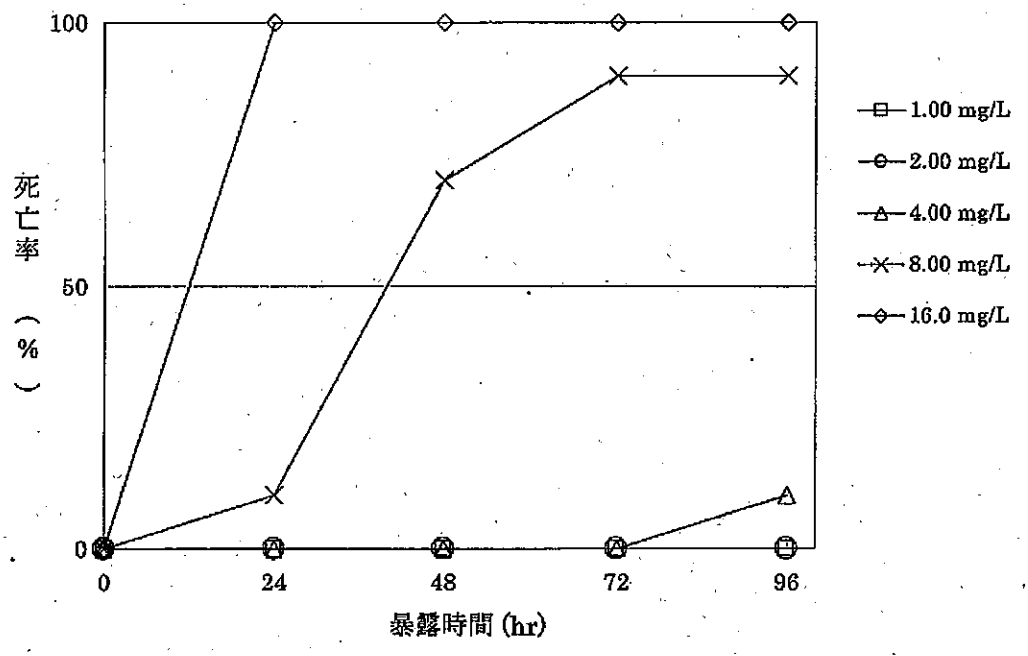


表 1 繰り返し精度の測定結果

設定濃度 (mg/L)	反復	検出濃度 (mg/L)	平均濃度 (mg/L) (n=3)	変動係数 (%) (n=3)
1.00	1	0.896	0.901	1.16
	2	0.913		
	3	0.894		
16.0	1	16.0	16.3	1.55
	2	16.5		
	3	16.3		

表 2 試験溶液中の被験物質濃度

設定濃度 (mg/L)	各暴露時間の被験物質濃度 (mg/L)			
	0 時間	24 時間 換水前	72 時間 換水後	96 時間
対照区	検出されず	検出されず	検出されず	検出されず
1.00	0.900 (90.0)	0.956 (95.6)	0.997 (99.7)	0.926 (92.6)
2.00	1.99 (99.5)	1.92 (96.0)	1.96 (98.0)	1.90 (95.0)
4.00	4.07 (102)	4.00 (100)	3.99 (99.8)	3.87 (96.8)
8.00	8.30 (104)	7.72 (96.5)	8.00 (100)	7.76 (97.0)
16.0	16.1 (101)	15.2 (95.0)	−*	−*

( )内は設定濃度に対する割合 (%)

＊：生存無しのため測定せず。

要　約

試験委託者　：　環境省

表　　題　：　フルオレンの藻類（*Pseudokirchneriella subcapitata*）に対する生長阻害試験

試験番号：　A080326

試験方法：　本試験は，「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成15年11月21日 薬食発第 1121002号，平成15・11・13製局第2号，環保企発第031121002号，最終改正：平成18年11月20日）に準拠して実施した。

1)供試生物：　単細胞緑藻類（*Pseudokirchneriella subcapitata*）

2)試験用水：　試験ガイドライン推奨培地

3)暴露期間：　72時間

4)培養方式：　止水式（密閉系），振とう培養（100 rpm）

5)初期生物量：　前培養した藻類　5×10^3 cells/mL
（指数増殖期の藻類乾燥重量：1.7×10^{-8} mg/cell，n=8）

6)試験温度：　22 ℃（暴露期間中の変動範囲は±2 ℃以内）

7)照明：　60～65 μE/m²/s，白色蛍光灯で連続照明（液面付近）

8)試験濃度（設定値）：

試験区	濃度（mg/L）
対照区	—
助剤対照区	—
濃度区1	0.050
濃度区2	0.095
濃度区3	0.18
濃度区4	0.34
濃度区5	0.64
濃度区6*	1.2

公比：1.9

助剤：*N,N*-ジメチルホルムアミド，99μL/L（濃度一定，ただし対照区は未使用）

*：試験液調製可能最高濃度

9)分析法：　高速液体クロマトグラフ（ＨＰＬＣ）法

結　果：

1)試験液および試験培養液中の被験物質濃度

被験物質濃度測定値の時間加重平均値は，それぞれ低濃度区側から 0.0434，0.0744，0.166，0.322，0.603，1.08 mg/L であった。暴露開始後 72 時間の測定値は，全ての濃度区において暴露開始時測定値の 80%以上であり，暴露期間中被験物質濃度を維持した。

2) 生長速度の比較による阻害濃度

阻害濃度の算出には，測定値の時間加重平均値を用いた。

半数生長阻害濃度 ErC50(0-72h)：　0.759 mg/L (95%信頼区間：算出不可)

最大無影響濃度 NOECr(0-72h)：　0.0744 mg/L

3)藻類の形態観察

暴露開始後 72時間の顕微鏡下での細胞形態観察の結果，0.64 mg/L濃度区 で，一部に細胞凝集が認められたが，その他の濃度区では，細胞形態の変化（収縮，膨張，破裂等）や細胞凝集は認められず，また，対照区および助剤対照区との相違もなかった。なお，1.2 mg/L濃度区は細胞数が少なく，十分に観察できなかった。

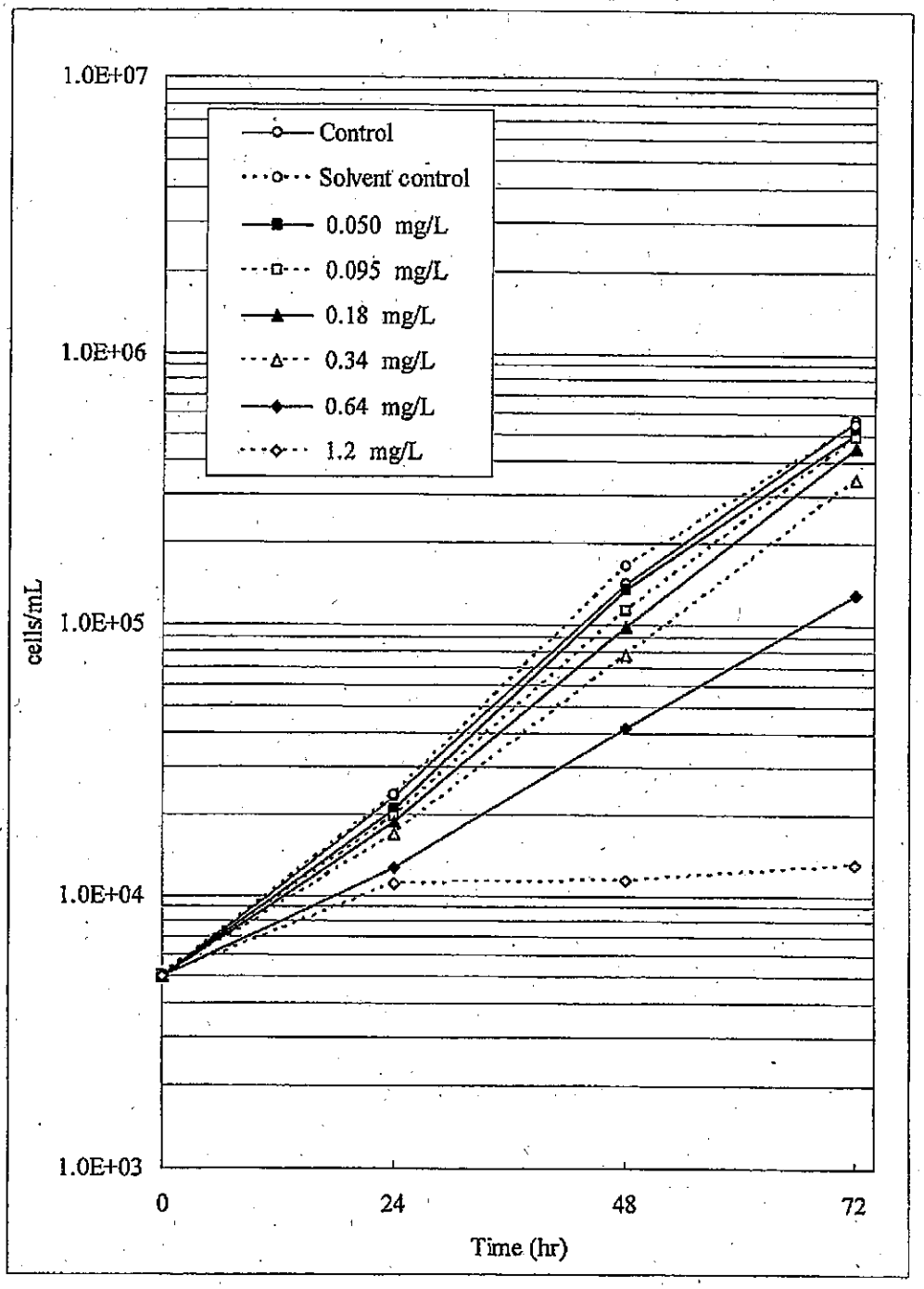
Table 4 Measured Concentration of the Test Substance in Test Cultures

Test Group	Nominal Concentration (mg/L)	Measured Concentration (mg/L) (Percent of Nominal)				Mean[a] Measured Concentration (mg/L) (Percent of Nominal) [Percent of 0hr Conc.]
		0 Hour	24 Hours	48 Hours	72 Hours	
Control	--	<0.002	<0.002	<0.002	<0.002	----
Solvent control	--	<0.002	<0.002	<0.002	<0.002	----
Conc.1	0.050	0.0436 (87)	0.0443 (89)	0.0438 (88)	0.0409 (82)	0.0434 (87), [100]
Conc.2	0.095	0.0788 (83)	0.0761 (80)	0.0738 (78)	0.0681 (72)	0.0744 (78), [94]
Conc.3	0.18	0.176 (98)	0.171 (95)	0.165 (92)	0.148 (82)	0.166 (92), [94]
Conc.4	0.34	0.337 (99)	0.339 (100)	0.315 (93)	0.286 (84)	0.322 (95), [96]
Conc.5	0.64	0.597 (93)	0.634 (99)	0.597 (93)	0.560 (88)	0.603 (94), [101]
Conc.6	1.2	1.12 (93)	1.08 (90)	1.08 (90)	1.07 (89)	1.08 (91), [96]

a : Time weighted mean

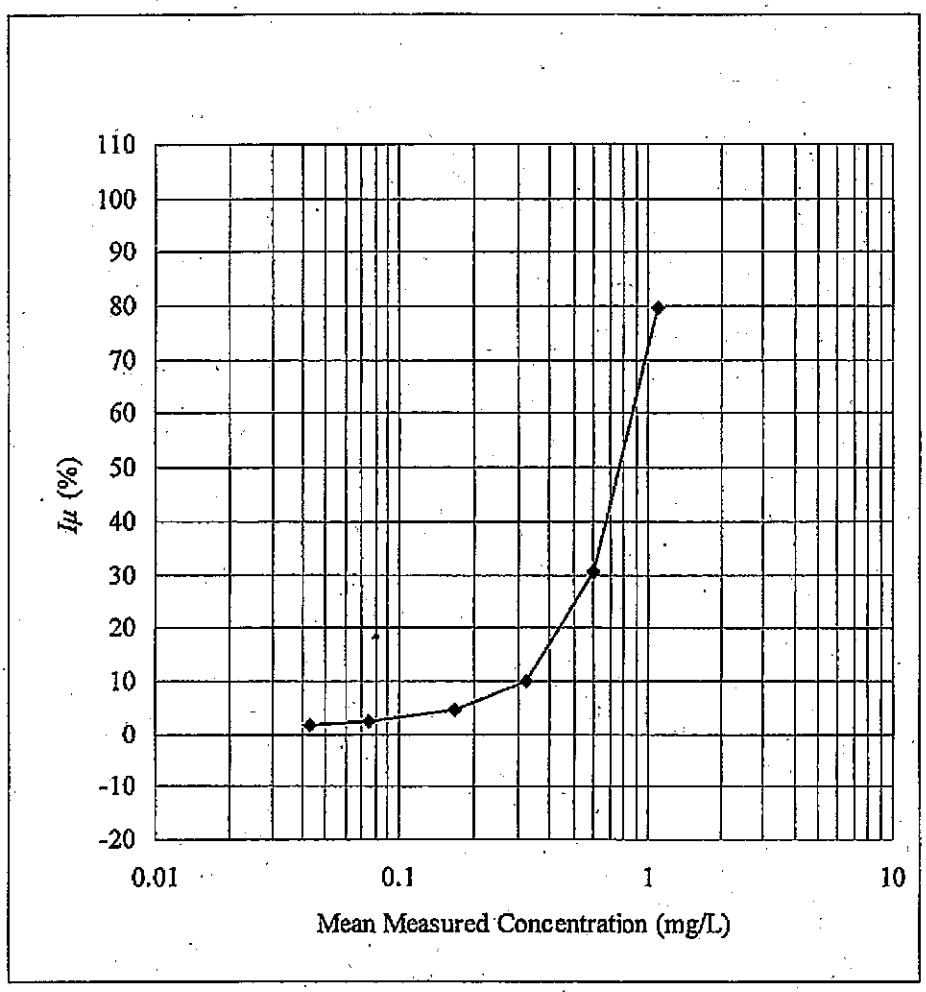
Figure 1 Growth Curve of *Pseudokirchneriella subcapitata*

(Mean biomass *vs* time during the 72-hour exposure)



Values in legend are given in the nominal concentration.

Figure 2 Concentration-Inhibition Curve Based on I_μ values Calculated from the Growth Rates



要 約

試験委託者： 環境省

表　　題： フルオレンのオオミジンコ（*Daphnia magna*）に対する急性遊泳阻害試験

試 験 番 号： A 0 8 0 3 2 7

試 験 方 法： 本試験は，「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成 15 年 11 月 21 日 薬食発第 1121002 号，平成 15･11･13 製局第 2 号，環保企発第 031121002 号，最終改正：平成 18 年 11 月 20 日）に準拠して実施した。

1) 供試生物： オオミジンコ（*Daphnia magna*）

2) 試験用水： Elendt M4 medium

3) 暴露期間： 48 時間

4) 暴露方式： 半止水式（24 時間後に試験液の全量を交換）

5) 供試生物数： 20 頭／試験区（5 頭／容器）

6) 試験温度： 20±1℃

7) 照明： 室内光，16 時間明（800 lux 以下）／8 時間暗

8) 試験濃度（設定値）：

試験区	濃度（mg/L）
対照区	−
助剤対照区	−
濃度区 1	0.10
濃度区 2	0.18
濃度区 3	0.32
濃度区 4	0.56
濃度区 5	1.0

公比 1.8
助剤：*N,N*-ジメチルホルムアミド，99 μL/L
（濃度一定，ただし対照区は使用せず）

9) 分析方法： 高速液体クロマトグラフ（ＨＰＬＣ）法

結　　果： 以下の結果は，測定値をもとに算出した。

48 時間 半数遊泳阻害濃度（EC50） ： 0.490 mg/L（95%信頼限界 0.422～0.575 mg/L）

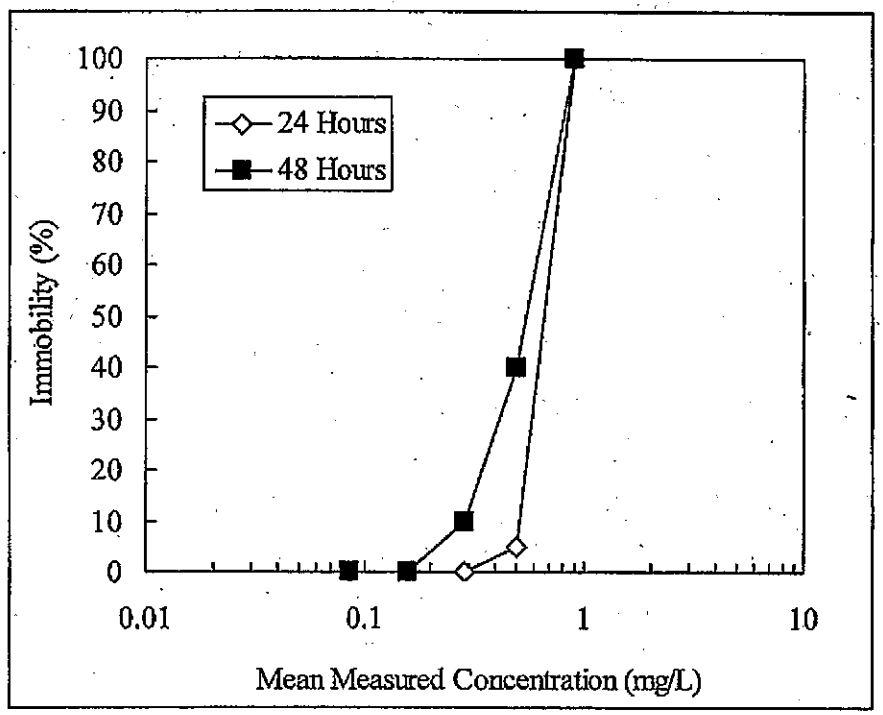
Table 5 Measured Concentrations of the Test Substance in Test Solutions

(Semi-Static Condition)

Test Group	Nominal Concentration (mg/L)	Measured Concentration (mg/L)				
		0 Hour New	24 Hours Old	24 Hours New	48 Hours Old	Mean[a]
		(Percent of Nominal, %)				
Control	--	<0.002	<0.002	<0.002	<0.002	--
Solvent Control	--	<0.002	<0.002	<0.002	<0.002	--
Conc.1	0.10	0.0908 (91)	0.0755 (76)	0.0941 (94)	0.0784 (78)	0.0845 (85)
Conc.2	0.18	0.170 (94)	0.148 (82)	0.169 (94)	0.153 (85)	0.160 (89)
Conc.3	0.32	0.307 (96)	0.268 (84)	0.301 (94)	0.281 (88)	0.289 (90)
Conc.4	0.56	0.532 (95)	0.455 (81)	0.524 (94)	0.466 (83)	0.493 (88)
Conc.5	1.0	0.967 (97)	0.817 (82)	0.958 (96)	0.867 (87)	0.901 (90)

a: Time-weighted mean
New: New test water freshly prepared
Old: Old test water immediately prior to renewal or at the end of the exposure

Figure 1 Concentration-Immobility Curve



要　　約

試験委託者：　環境省

表題：　フルオレンのヒメダカ（*Oryzias latipes*）に対する急性毒性試験

試験番号：　Ａ０８０３２８

試験方法：　本試験は「新規化学物質等に係る試験の方法について＜藻類生長阻害試験，ミジンコ急性遊泳阻害試験及び魚類急性毒性試験＞」（平成 15 年 11 月 21 日 薬食発第 1121002 号，平成 15･11･13 製局第 2 号，環保企発第 031121002 号，最終改正：平成 18 年 11 月 20 日）に準拠して実施した。

1) 供試生物：　ヒメダカ（*Oryzias latipes*）
2) 試験用水：　脱塩素水道水
3) 暴露期間：　96 時間
4) 暴露方式：　半止水式（24 時間毎に試験液の全量を交換）
5) 供試生物数：　10 尾／試験区
6) 水温：　24±1℃
7) 照明：　室内光，16 時間明（1000 lux 以下）／8 時間暗
8) 試験濃度（設定値）：

試験区	濃度（mg/L）	
対照区	—	
助剤対照区	—	
濃度区１	0.13	
濃度区２	0.23	
濃度区３	0.41	
濃度区４	0.73	
濃度区５	1.3	（試験用水に対する溶解度）

公比：1.8

助剤：*N,N*-ジメチルホルムアミド，99 μL/L（濃度一定，ただし対照区は使用せず）

9) 分析方法：　高速液体クロマトグラフ（ＨＰＬＣ）法

結果：

以下の結果は，被験物質濃度の測定値をもとに算出した。

96 時間半数致死濃度（LC50）：　>1.17 mg/L（95%信頼限界 算出不可）

Table 5 Measured Concentrations of the Test Substance in Test Water

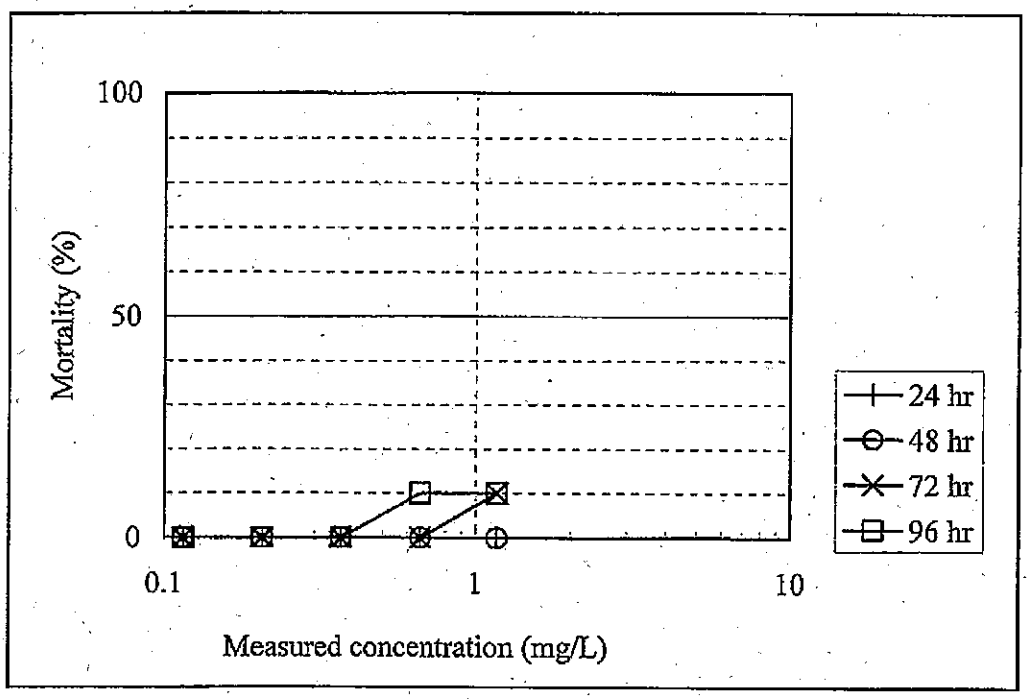
Test group	Nominal conc. (mg/L)		Measured concentration (mg/L)				
			0 - 24 hr	24 - 48 hr	48 - 72 hr	72 - 96 hr	Mean
Control		New	<0.002	<0.002	<0.002	<0.002	
		Old	<0.002	<0.002	<0.002	<0.002	
Solvent control		New	<0.002	<0.002	<0.002	<0.002	
		Old	<0.002	<0.002	<0.002	<0.002	
Conc.1	0.13	New	0.117	0.125	0.121	0.115	0.115 [88%]
		Old	0.100 (85%)	0.116 (93%)	0.115 (95%)	0.113 (98%)	
Conc.2	0.23	New	0.207	0.229	0.215	0.201	0.204 [89%]
		Old	0.179 (86%)	0.205 (90%)	0.199 (93%)	0.202 (100%)	
Conc.3	0.41	New	0.377	0.383	0.399	0.370	0.366 [89%]
		Old	0.319 (85%)	0.364 (95%)	0.360 (90%)	0.360 (97%)	
Conc.4	0.73	New	0.739	0.717	0.656	0.697	0.665 [91%]
		Old	0.569 (77%)	0.659 (92%)	0.630 (96%)	0.664 (95%)	
Conc.5	1.3	New	1.20	1.23	1.20	1.19	1.17 [90%]
		Old	1.07 (89%)	1.17 (95%)	1.17 (98%)	1.13 (95%)	

New: New test water freshly prepared

Old: Old test water immediately prior to renewal or at the end of exposure
(Percent of New)

Mean: Time weighted mean
[Percent of Nominal]

Figure 1 Concentration-Mortality Curve



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参考1

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参考２

諮　問　第　２５８　号
環保企発第 090623003 号
平成２１年　６月２３日

中央環境審議会会長
　　鈴木　基之　殿

環境大臣
斉藤　鉄夫

残留性有機汚染物質に関するストックホルム条約の附属書改正に係る化学物質の審査及び製造等の規制に関する法律に基づく追加措置について（諮問）

標記について、環境基本法（平成５年法律第９１号）第４１条第４項の規定に基づき、次のとおり諮問する。

「残留性有機汚染物質に関するストックホルム条約の附属書改正に係る化学物質の審査及び製造等の規制に関する法律に基づく追加措置について、貴審議会の意見を求める。」

（諮問理由）

平成 13 年５月に採択された「残留性有機汚染物質に関するストックホルム条約」（以下「ストックホルム条約」という。）は、残留性有機汚染物質から人の健康及び環境を保護することを目的として、残留性有機汚染物質の製造及び輸出入、使用等に係る規制等について規定した条約である。我が国は、平成 14 年８月、本条約を締結した。これまで、本条約で意図的な製造及び使用から生ずる放出を削減し、又は廃絶するための措置が必要な残留性有機汚染物質として規定されている物質については、化学物質の審査及び製造等の規制に関する法律（昭和４８年法律第１１７号。以下「化審法」という。）において、第一種特定化学物質に指定し、製造、輸入、使用及びこれらを含む製品の輸入を禁止する措置を講じてきたところである。

本年５月に開催されたストックホルム条約第４回締約国会合において、附属書の改

正が決定され、新たに１２物質が意図的な製造及び使用から生ずる放出の削減又は廃絶の対象となった。ついては、我が国として条約の遵守に不可欠な措置を講じるため、化審法の第一種特定化学物質に指定すること、並びにペルフルオロ（オクタン－1－スルホン酸）又はその塩及びペルフルオロ（オクタン－1－スルホニル）=フルオリドについては本条約に基づく例外的用途について指定すること、これらの物質を含有し輸入禁止の対象となる製品、技術上の指針の遵守義務及び表示義務の対象となる製品を指定することについて、貴審議会の意見を求める。

（ストックホルム条約の附属書改正により規制対象に追加された９物質(群)及び第一種特定化学物質への指定候補である１２物質）

物質名
ペルフルオロ（オクタン－１－スルホン酸）（別名ＰＦＯＳ）又はその塩
ペルフルオロ（オクタン－１－スルホニル）＝フルオリド（別名ＰＦＯＳＦ）
ペンタクロロベンゼン
r－1，*c*－2，*t*－3，*c*－4，*t*－5，*t*－6－ヘキサクロロシクロヘキサン（別名α－ヘキサクロロシクロヘキサン）
r－1，*t*－2，*c*－3，*t*－4，*c*－5，*t*－6－ヘキサクロロシクロヘキサン（別名β－ヘキサクロロシクロヘキサン）
r－1，*c*－2，*t*－3，*c*－4，*c*－5，*t*－6－ヘキサクロロシクロヘキサン（別名γ－ヘキサクロロシクロヘキサン又はリンデン）
デカクロロペンタシクロ［5．3．0．$0^{2,6}$．$0^{3,9}$．$0^{4,8}$］デカン－５－オン（別名クロルデコン）
ヘキサブロモビフェニル
テトラブロモ（フェノキシベンゼン）（別名テトラブロモジフェニルエーテル）
ペンタブロモ（フェノキシベンゼン）（別名ペンタブロモジフェニルエーテル）
ヘキサブロモ（フェノキシベンゼン）（別名ヘキサブロモジフェニルエーテル）
ヘプタブロモ（フェノキシベンゼン）（別名ヘプタブロモジフェニルエーテル）

既存の第一種特定化学物質に関する毒性評価一覧

参考３

物質名	ﾎﾟﾘ塩化ﾋﾞﾌｪﾆﾙ(PCB)	ﾎﾟﾘ塩化ﾅﾌﾀﾚﾝ	ﾍｷｻｸﾛﾛﾍﾞﾝｾﾞﾝ	ｱﾙﾄﾞﾘﾝ	ﾃﾞｨﾙﾄﾞﾘﾝ	ｴﾝﾄﾞﾘﾝ	DDT	ｸﾛﾙﾃﾞﾝ(ｸﾛﾙﾃﾞﾝ類)	ﾍﾌﾟﾀｸﾛﾙ(ｸﾛﾙﾃﾞﾝ類)	ﾋﾞｽ(ﾄﾘﾌﾞﾁﾙｽｽﾞ)=ｵｷｼﾄﾞ
指定年月日	S49.6.7	S54.8.14	S54.8.14	S56.10.2	S56.10.2	S56.10.2	S56.10.2	S61.9.17	S61.9.17	H1.12.27
慢性毒性	［ラット雄　混餌］ 100ppm　肝重量増加	［マウス］ 肝細胞の壊死、変性等、間質の線維化等の肝障害 肝硬変様の非可逆的変化の可能性				［ラット　混餌］ 雄50ppm,雌25ppm以上で死亡率の上昇 50ppm以上で外部刺激に対する感受性の亢進、時に痙攣 25ppm以上の死亡動物には脳、肝、腎及び副腎に、50ppm以上の生存動物には肝臓に、それぞれ瀰漫性変性	［ラット　混餌］ 400ppm以上で神経症状、用量相関性のある死亡率の上昇 すべての投与群（100～800ppm）で肝障害を示す病理所見	［マウス　経口］ 12.5ppmでGOT,GPTの異常 5,12.5ppmで肝腫大、雄で肝細胞変性、壊死 ［ラット　経口］ 25ppmで肝腫大、雄では肝細胞壊死 ［イヌ　経口］ 15,30ppmでTTT,Alpの異常、用量依存の肝重量増加 30ppmで肝相対重量増加と肝細胞の変化 他に甲状腺への影響	［ラット　混餌］ 45ppmで肝障害と認められる肝細胞の組織学的変化 ［ラット　経口］ 5mg/kgで肝、腎及び脾臓に病理所見他に甲状腺への影響	［ラット　経口］ 3～12mg/kgで胸腺重量低下。 6mg/kg以上で副腎重量の増加 ［ラット　混餌］ 80mg/kgで貧血症状、甲状腺重量の低下 100ppm以上で出血傾向胸腺相対重量減少、副腎相対重量の増加 300ppmで死亡率増加、るい痩、貧血症状 50ppmで体重減少、貧血症状、甲状腺重量減少、副腎重量増加、ﾘﾝﾊﾟ球減少等 25ppm以上で体重増加抑制、出血傾向、血液凝固時間の延長 80ppmでﾘﾝﾊﾟ球数減少、胸腺重量減少、血清IgGの減少とIgMの増加
生殖能及び後世代に及ぼす影響	［マウス　混餌］ 500ppmで、F2で催奇形作用は否定できず		［ラット］ 妊娠率低下､児動物生存率及び体重の低下		［ラット　混餌］ 0.24ppm以上で妊娠率低下					
催奇形性	［ラット　混餌］ 50ppm催奇形作用認めず				［ラット　混餌］ 0.08ppmで児動物に脳浮腫や水頭などの病理所見					［ラット　経口］ 11.7mg/kg以上で母動物の体重増加抑制、児動物の口蓋裂や骨格形態異常の発生頻度増加 ［ラット　経口］ 10mg/kgで母動物体重増加抑制、一腹児数減少､出生児成長抑制､児動物の膣開口遅延､脳重量低下等 ［マウス］ 胎児前肢芽培養液中への添加で発育阻害作用 催奇形性とは断定不可
がん原性	［ラット　混餌］ 154～616ppm 肝良性腫瘍		[ハムスタ-混餌] 50ppm 肝、血管、甲状腺等への腫瘍	［マウス雄 混餌］ 4,8ppm 用量相関性のある肝腫瘍 ﾌﾟﾛﾓｰﾀｰ作用有	［マウス雄 混餌］ 2.5,5ppm 用量相関性のある肝腫瘍 ﾌﾟﾛﾓｰﾀｰ作用有		［マウス　混餌］ 雄2ppm,雌10ppm以上で肝腫瘍 ［ラット］ 500ppmで肝腫瘍ﾌﾟﾛﾓｰﾀｰ作用有	［マウス］ 肝腫瘍の発生増加 ［ラット］ 催腫瘍性認めず催腫瘍性の有無は結論に至らず	［マウス］ 肝腫瘍の発生増加 ［ラット］ 催腫瘍性認めず催腫瘍性の有無は結論に至らず	［ラット　混餌］ 0.5～50ppmで下垂体腺腫､副腎褐色細胞腫・上皮小体腺腫発生増加 膵腺癌の発生(頻度が低く、用量相関認めず)
生体内運命	［マウス　経口］ 100μg/day ４ヶ月で150μg程度蓄積						ヒト体内でDDEに変化して長期間残留 DDEの250ppm混餌投与で肝腫瘍	動物における排泄は遅く、動物体内に蓄積ﾁﾄｸﾛｰﾑP-450の顕著な誘導	体内で代謝されて毒性の強いﾍﾌﾟﾀｸﾛﾙ･ｴﾎﾟｷｼﾄﾞに変化 この化合物の排泄は遅く、脂肪組織等に蓄積	ﾗｯﾄ経口の吸収率20～50%。消化管吸収不良。３日後までに約70%が糞便中に排泄。腸肝循環の可能性。尿中排泄は代謝物。 肝､腎に多く分布。脂肪､脳にも分布 血漿中濃度は低い 血中半減期:14時間 脳中半減期:6.6日
変異原性								ﾌﾟﾛﾓｰﾀｰ試験(+) Ames,染色体:弱い(+)	ﾌﾟﾛﾓｰﾀｰ試験(+) 染色体：弱い(+)	Ames,染色体,小核で一部(＋)。弱い変異原性
その他	PCB混入食用油の摂取により、眼脂の増加、爪の変色、嘔吐等		ﾍｷｻｸﾛﾛﾍﾞﾝｾﾞﾝにて殺菌した種子用小麦の誤食により、晩発性皮膚ﾎﾟﾙﾌｨﾘﾝ症の発症			ｴﾝﾄﾞﾘﾝ汚染小麦粉原料のﾊﾟﾝ摂取で悪心、嘔吐､頭痛､腹部不快感､痙攣､意識喪失等 含量:48～1807ppm		ﾋﾄで嘔吐、痙攣等の急性中毒症状ｼｽｸﾛﾙﾃﾞﾝ、ﾄﾗﾝｽｸﾛﾙﾃﾞﾝ、ﾍﾌﾟﾀｸﾛﾙ、ﾉﾅｸﾛﾙ等を含む混合物	ﾍﾌﾟﾀｸﾛﾙはｸﾛﾙﾃﾞﾝの一成分。毒性ﾃﾞｰﾀもｸﾛﾙﾃﾞﾝと同様の傾向	ﾐﾄｺﾝﾄﾞﾘｱでの酸化的ﾘﾝ酸化の阻害等と推定 皮膚等に刺激作用 ﾄﾘﾌﾞﾁﾙｽｽﾞ化合物はﾋﾄ赤血球を溶血
ADI	5μg/kg/day			0.1μg/kg/day	0.1μg/kg/day	0.2μg/kg/day	5μg/kg/day	1μg/kg/day	0.5μg/kg/day	

既存の第一種特定化学物質に関する毒性評価一覧　（続）

物質名	N,N'-ｼﾞﾄﾘﾙ-p-ﾌｪﾆﾚﾝｼﾞｱﾐﾝ N-ﾄﾘﾙ-N'-ｷｼﾘﾙ-p-ﾌｪﾆﾚﾝｼﾞｱﾐﾝ N,N'-ｼﾞｷｼﾘﾙ-p-ﾌｪﾆﾚﾝｼﾞｱﾐﾝ	2,4,6-ﾄﾘ-tert-ﾌﾞﾁﾙﾌｪﾉｰﾙ	トキサフェン	マイレックス	2,2,2-トリクロロ-1,1-ビス（4-クロロフェニル）エタノール（別名ケルセン又はジコホル）	ヘキサクロロブタ-1,3-ジエン	2-（2H-1,2,3-ベンゾトリアゾール-2-イル）-4,6-ジ-ｔｅｒｔ-ブチルフェノール
指定年月日	H12.6.7	H12.8.14	H14.9.4	H14.9.4	H17.4.1	H17.4.1	H19.10.31
慢性毒性	［ラット　混餌］ 0.02%以上で （♀♂） 肝臓の絶対重量、脾臓の絶対及び相対重量並びに副腎の絶対重量の増加、副腎皮質のコレステリン様物質を含む貪食細胞増加及び血小板数の減少 （♂） アスパラギン酸アミノトランスフェラーゼ活性の上昇 （♀） 体重増加抑制、摂餌量の減少、血清中鉄濃度の低下、副腎の相対重量の増加及び脾臓の繊維化 0.1%以上で （♀♂） 血清中銅濃度、アルカリフォスファターゼ活性及びロイシンアミノペプチダーゼ活性の上昇、肝臓及び腎臓の相対重量の増加並びに肝臓の髄外造血 （♂） 血清中鉄濃度の低下、ｺﾘﾝエステラーゼ活性の上昇、トリグリセリド並びに副腎の相対重量及び腎臓の絶対重量の増加（♀） アルブミン及びリン脂質の減少、A/G比の低下 以上よりNOELは0.004%（♂：約1.8mg/kg/day,♀：約1.28mg/kg/day）と推定	［マウス］ 肝細胞の壊死、変性等､間質の線維化等の肝障害 肝硬変様の非可逆的変化の可能性	[ラット] 2.5mg/kgで肝細胞の組織学的変化 50mg/kgで肝細胞肥大	マウス　経口] １mg/kgで肝肥大	［ラット　混餌］ 2.2mg/kgで肝細胞肥大・副腎皮質細胞空胞化	［ラット　混餌］ 2mg/kg/day以上で、腎の組織学的変化	[ラット経口] 0.5mg/kg雄で肝の組織学的変化（変異肝細胞等）
生殖能及び後世代に及ぼす影響	［ラット　経口］ 8mg/kgで、生存児数の減少及び胚胎児死亡率の増加		行動への影響、免疫抑制	[マウス] 5mg/kgで同腹児数減少 1.8mg/kgで繁殖停止 [ラット] 25mg/kgで同腹児数減少、生存率低下	[ラット] 2世代生殖毒性試験において250ppm(P1),25ppm(P2)で卵巣間質細胞空胞化 250ppm(F1),125ppm(F2)で新生児体重、生存率低下	［ラット］ 20あるいは7.5mg/kg/day以上で、それぞれ出生児及び新生児の体重の低下。 75mg/kg/dayで受胎率低下及び着床阻害	
催奇形性	［ラット　経口］ NOEL:（親）8mg/kg/day （児）4mg/kg/day		[マウス] 35mg/kgで児動物に脳瘤	[ラット] 6mg/kgで内臓異常			
がん原性	［ラット　混餌］ 慢性毒性試験２４ヶ月目に屠殺した♀において、卵巣の顆粒膜夾膜細胞腫の発生が0、0.004、0.02、0.1%の各投与群において、それぞれ２０匹中０例、１９匹中０例、１８匹中０例及び１９匹中５例に認められ、また0.1%投与群の死亡例においても１例の卵巣黄体腫が認められた		[マウス] 肝腫瘍 [ラット] 甲状腺濾胞細胞癌・甲状腺腺腫（雄） 甲状腺癌（雌）	[マウス及びラット] 肝腫瘍		［ラット］ 腎尿細管の腺腫・腺癌	
生体内運命	［ラット　混餌］ 主として糞中に排泄、代謝物の構造確認できず。 尿中への排泄は１%以下で主要な尿中排泄物はメチル基の水酸化体と思われる代謝物。 脂肪組織中濃度は血中濃度に対して♂：109～2493倍、♀：140～7972倍 肝臓中濃度は血中濃度に対して♂：7～168倍、♀：7～467倍			動物における半減期は遅く、数カ月	ラットにおける半減期は、雄で1.5～4日、雌においては4～7日。	放射標識されたHCBDを投与した場合、マウス及びラットにおける放射活性の半減期は72時間以内 腎においてHCBDの活性代謝物が蓄積し、腎毒性を示す	
変異原性			Ames陽性	優性致死試験　陰性（ラット） Ames陰性	in vitro及び in vivo系において陰性	グルタチオン添加及び腎Ｓ9存在下でAmes陽性、SCE陽性	Ames　陰性 染色体　陰性
その他	PCB混入食用油の摂取により、眼脂の増加、爪の変色、嘔吐等				農薬事故による暴露により悪心、めまい、嘔吐等 急性毒性試験において自発運動低下、運動失調、傾眠傾向、振戦等の神経症状		
ADI	5μg/kg/day		1.25μg/kg/day	RfD: 0.2μg/kg/day	2μg/kg/day (RfD: 0.4μg/kg/day)	MRL:0.2μg/kg/day	

特定化学物質及び監視化学物質の要件及び評価のための試験項目について

参考４

	要　　件　　※（）内は法律上の規定	評価のための試験項目
第一種特定化学物質 （注）人及び高次補食動物への長期毒性を有することがいずれも明らかでない場合には第一種監視化学物質として判定される。	難分解性である （自然的作用による化学的変化を生じにくいもの）	微生物等による化学物質の分解度試験
	高濃縮性である （生物の体内に蓄積されやすいもの）	魚介類の体内における化学物質の濃縮度試験 又は 1-オクタノールと水との間の分配係数測定試験
	人への長期毒性を有する （継続的に摂取される場合には、人の健康を損なうおそれがあるもの） 又は　高次捕食動物への長期毒性を有する （継続的に摂取される場合には、高次捕食動物の生息又は生育に支障を及ぼすおそれがあるもの）	化学物質の慢性毒性試験、生殖能及び後世代に及ぼす影響に関する試験、催奇形性試験、変異原性試験、がん原性試験、生体内運命に関する試験及び薬理学的試験 ほ乳類の生殖能及び後世代に及ぼす影響に関する試験並びに鳥類の繁殖に及ぼす影響に関する試験
第一種監視化学物質	難分解性である （自然的作用による化学的変化を生じにくいもの）	微生物等による化学物質の分解度試験
	高濃縮性である （生物の体内に蓄積されやすいもの）	魚介類の体内における化学物質の濃縮度試験 又は 1-オクタノールと水との間の分配係数測定試験
	人への長期毒性を有するか不明 （継続的に摂取される場合には、人の健康を損なうおそれがあるかどうか明らかでない） かつ　高次捕食動物への長期毒性を有するか不明 （継続的に摂取される場合には、高次捕食動物の生息又は生育に支障を及ぼすおそれがあるかどうか明らかでない）	
第二種監視化学物質 ｏｒ **第三種監視化学物質**	難分解性である （自然的作用による化学的変化を生じにくいもの）	微生物等による化学物質の分解度試験
	高濃縮性ではない* （生物の体内に蓄積されにくいもの）	魚介類の体内における化学物質の濃縮度試験 又は 1-オクタノールと水との間の分配係数測定試験
	人への長期毒性の疑いを有する（第二種監視化学物質） （継続的に摂取される場合には、人の健康を損なうおそれがあるものに該当する疑いがあるもの）	ほ乳類を用いる28日間の反復投与毒性試験並びに細菌を用いる復帰突然変異試験及びほ乳類培養細胞を用いる染色体異常試験による変異原性試験
	生態毒性を有する（第三種監視化学物質） （動植物の生息又は生育に支障を及ぼすおそれがあるもの）	藻類生長阻害試験、ミジンコ急性遊泳阻害試験及び魚類急性毒性試験

＊「難分解性」、「高濃縮性」及び「生態毒性あり」（高次捕食動物への毒性なし）の化学物質も第三種監視化学物質に該当することもあり得る。

参考５

平成２１年６月３省合同審議会

既存化学物質審査物質
（生態影響）
に係る分解性・蓄積性データ

既存化学物質安全性点検データ

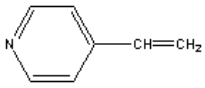
データの説明 分解性 濃縮性

経済産業公報（平成13年1月5日以前は通産省公報）公表内容

公表名称	公表年月日	点検結果
4－ビニルピリジン	昭和60年12月28日	濃縮性がない又は低いと判断される化学物質

物質情報

構造式



CAS番号	100-43-6
点検対象物質名称	4－ビニルピリジン

官報公示整理番号	官報公示名称
5-717	4－ビニルピリジン

分解性

判定	難分解性
試験方法	標準法

試験装置	試験期間	試験物質濃度	活性汚泥濃度
標準	4週間	100ppm	30ppm

間接測定	BOD
	0%

直接測定	TOC	HPLC
	1%	4%

濃縮性

判定	低濃縮性
試験方法	濃縮度試験

48TLm値(48hr)	魚種
1.57mg/L	ヒメダカ

試験装置	試験期間	魚種	脂質含量(%)
揮発	8週間	コイ	5

	濃度設定	濃縮倍率
第1濃度区	20μg/L	58 ～ 96
第2濃度区	2μg/L	48 ～ 96

総合検索システムへ
100-43-6

前画面に戻る

National Institute of Technology and Evaluation 独立行政法人 製品評価技術基盤機構

既存化学物質安全性点検データ

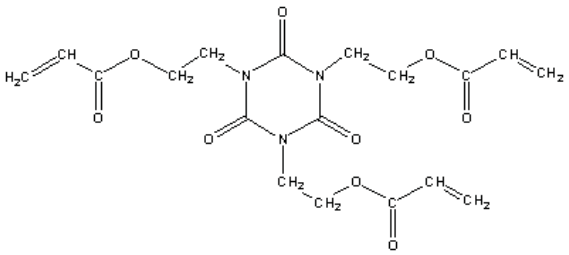
データの説明 分解性 濃縮性

経済産業公報（平成13年1月5日以前は通産省公報）公表内容

公表名称	公表年月日	点検結果
2，2'，2''－(2，4，6－トリオキソ－1，3，5－トリアジナン－1，3，5－トリイル)トリエチル＝トリアクリラート [官報公示整理番号：5-1060] [CAS番号：40220-08-4]	平成14年11月8日	難分解性と判断される物質
2，2'，2''－(2，4，6－トリオキソ－1，3，5－トリアジナン－1，3，5－トリイル)トリエチル＝トリアクリラート [官報公示整理番号：5-1060] [CAS番号：40220-08-4]	平成17年12月22日	難分解性であるが高濃縮性ではないと判断される物質

物質情報

構造式



CAS番号	40220-08-4
点検対象物質名称	トリス（2－ヒドロキシエチル）イソシアヌル酸アクリル酸エステル

官報公示整理番号	官報公示名称
5-1060	トリス（2－ヒドロキシエチル）イソシアヌル酸アクリル酸エステル

備考

・HPLC分析（逆相系）における保持時間から、分解度試験において生成した変化物は、点検対象物質より極性が高い。このため、濃縮性については点検対象物質で確認した。

分解性

判定	難分解性
試験方法	標準法

試験装置	試験期間	試験物質濃度	活性汚泥濃度
標準	4週間	100mg/L	30mg/L

間接測定	BOD
	24, 0, 12 (12)%

直接測定	TOC	HPLC
	44, 16, 49 (36)%	100, 53, 100 (84)%

備考

・TODは組成式から算出した。
・被験物質は試験液中で変化し、被験物質より極性が高いトリス（2－ヒドロキシエチル）イソシアヌル酸（86,27及び106%生成）、トリス（2－ヒドロキシエチル）イソシアヌル酸モノアクリル酸エステル（13,7及び0%生成）及びトリス（2－ヒドロキシエチル）イソシアヌル酸ジアクリル酸エステル（0,32及び0%生成）を生成した。

濃縮性

判定	低濃縮性
試験方法	分配係数試験

n－オクタノール／水分配係数

log Pow	試験方法
1.9	HPLC法

備考

・溶離液：メタノール／精製水（60/40 V/V）

総合検索システムへ
40220-08-4

前画面に戻る

既存化学物質安全性点検データ

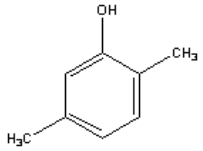
データの説明 分解性 濃縮性

経済産業公報（平成13年1月5日以前は通産省公報）公表内容

公表名称	公表年月日	点検結果
2，5－ジメチルフェノール ［官報公示整理番号：3-521］ ［CAS番号：95-87-4］	平成17年12月22日	難分解性と判断される物質
2，5－ジメチルフェノール ［官報公示整理番号：3-521，4-57］ ［CAS番号：95-87-4］	平成20年8月12日	難分解性であるが高濃縮性ではないと判断される物質

物質情報

構造式



CAS番号	95-87-4
点検対象物質名称	2，5－キシレノール

官報公示整理番号	官報公示名称
3-521	ジアルキル（C＝1～5）フェノール
4-57	ポリ（1～3）アルキル（C＝1～3）ポリ（1～3）ヒドロキシポリ（1～5）フェニル

分解性

判定	難分解性
試験方法	標準法

試験装置	試験期間	試験物質濃度	活性汚泥濃度
標準	4週間	100mg/L	30mg/L

間接測定	BOD
	0，-1，0%

直接測定	TOC	HPLC
	2，3，1%	3，2，1%

濃縮性

判定	低濃縮性
試験方法	分配係数試験

n－オクタノール／水分配係数

log Pow	試験方法
2.6	HPLC法

備考

・溶離液：メタノール／リン酸緩衝液（pH3.0）（6/4 V/V）

総合検索システムへ
95-87-4
前画面に戻る

National Institute of Technology and Evaluation 独立行政法人 製品評価技術基盤機構

既存化学物質安全性点検データ

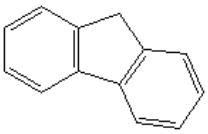
データの説明 分解性 濃縮性

経済産業公報（平成13年1月5日以前は通産省公報）公表内容

公表名称	公表年月日	点検結果
フルオレン	平成2年12月28日	蓄積性がない又は低いと判断される化学物質

物質情報

構造式



CAS番号	86-73-7
点検対象物質名称	フルオレン

官報公示整理番号	官報公示名称
4-643	フルオレン

分解性

判定	難分解性
試験方法	標準法

試験装置	試験期間	試験物質濃度	活性汚泥濃度
標準	4週間	100ppm	30ppm

間接測定	BOD
	0%

直接測定	GC
	1%

濃縮性

判定	低濃縮性
試験方法	濃縮度試験

48TLm値(48hr)	魚種
51.5mg/L	ヒメダカ

試験装置	試験期間	魚種	脂質含量(%)
標準	8週間	コイ	3.9

	濃度設定	濃縮倍率
第1濃度区	20μg/L	396 ～ 821
第2濃度区	2μg/L	219 ～ 830

総合検索システムへ
86-73-7

前画面に戻る

参考6－1

監視化学物質への該当性の判定等に係る試験方法及び判定基準

最終改正　平成１８年７月２１日

厚生労働省医薬食品局審査管理課化学物質安全対策室
経済産業省製造産業局化学物質管理課化学物質安全室
環境省総合環境政策局環境保健部企画課化学物質審査室

化学物質の審査及び製造等の規制に関する法律に基づく化学物質の審査に係る厚生労働省、経済産業省及び環境省の関係審議会を合同で開催するに当たり、第一種監視化学物質、第二種監視化学物質及び第三種監視化学物質への該当性の判定を行うために必要とされる試験の試験成績に係る現在の判定基準等について、下記のとおりとする。

下記の基準を基本としつつ、関係審議会における専門的知見に基づく意見を踏まえ、各監視化学物質への該当性の判定を行うこととする。

記

Ⅰ．試験方法

（１）新規化学物質及び既存化学物質が監視化学物質に該当するかどうかの判断は、当該新規化学物質及び既存化学物質について既に得られている知見の他、「新規化学物質に係る試験並びに第一種監視化学物質及び第二種監視化学物質に係る有害性の調査の項目等を定める省令」第２条第１項から第３項まで及び第２条の２の規定による以下の試験の試験成績に基づき行うものとされている。

①微生物等による化学物質の分解度試験（分解度試験）

②魚介類の体内における化学物質の濃縮度試験（濃縮度試験）又は１－オクタノールと水との間の分配係数測定試験（Pow 測定試験）

③ほ乳類を用いる２８日間の反復投与毒性試験（２８日間反復投与毒性試験）又はほ乳類を用いる９０日間の反復投与毒性試験（９０日間反復投与毒性試験）

④細菌を用いる復帰突然変異試験及びほ乳類培養細胞を用いる染色体異常試験又はマウスリンフォーマ TK 試験（変異原性試験）

（以下、③及び④を「スクリーニング毒性に関する試験」という。）

⑤藻類生長阻害試験、ミジンコ急性遊泳阻害試験及び魚類急性毒性試験（生態毒性試験）

（２）これらの試験は、原則として「新規化学物質等に係る試験の方法について（平成１５年１１月２１日薬食発第１１２１００２号・平成１５・１１・１３製局第２号・環保企発第０３１１２１００２号）」（以下「通知」という。）に沿って実施することとされているが、通知に定められていない試験方法（ＯＥＣＤテストガイドライン等）に基づく試験成績については、上記(1)の試験方法と同等の取扱いが可能である

と考えられ当該試験成績の信頼性が確保されていると認められる場合には、判定の際に用いることとしている。

Ⅱ．試験成績に係る判定基準

上記Ⅰ．（１）に掲げる試験の試験成績に基づき判定を行う場合には、原則として以下の基準によることとしている。

（１）分解度試験

①良分解性

・３つの試験容器のうち２つ以上でBODによる分解度が６０％以上であり、かつ３つの平均が６０％以上であること。

：あわせて HPLC、GC 等の直接分析法により分解生成物が生成していないことが確認されること。

：なお、通知で定められた試験方法による試験成績が上記の基準を満たさない場合であって、BOD 曲線等から試験終了後も引き続き生分解していることが示唆される場合（上昇傾向等）には、ＯＥＣＤテストガイドライン 302Cによる試験成績に基づいて判定を行うことができる。

②難分解性

・良分解性でないこと。

（２）濃縮度試験又はPow測定試験

①高濃縮性

・濃縮倍率が5000倍以上であること。

②高濃縮性でない

以下のいずれかであること。

・濃縮倍率が1000倍未満であること

・１－オクタノール／水分配係数（Pow）の対数が３．５未満であること。ただし、界面活性のある物質、分子量分布を有する混合物、有機金属化合物、純度の低い物質（HPLC法を除く）及び無機化合物には適用しない。

③濃縮倍率が1000倍以上、5000倍未満の場合には、必要に応じ、以下の成績を考慮して高濃縮性かどうかを総合的に判断する。

・排泄試験

・部位別（可食部）の濃縮倍率

なお、上記の判定に当たっては、原則として、定常状態における濃縮倍率を用いることとし、定常状態での数値が得られない場合には、総合的に判断をする。また、濃縮倍率に濃度依存性が認められる場合には、必要に応じてより低濃度区での試験を行い、その成績を踏まえ判断する。

（３）スクリーニング毒性に関する試験

①細菌を用いる復帰突然変異試験

a)陽性

・いずれかの試験系で溶媒対照の２倍を超えて復帰変異誘発コロニー数が増加し、その作用に再現性又は用量依存性が認められること。

・比活性値が概ね 1000rev/mg 以上である場合には、原則として、強い陽性と判断する。

・陽性の場合にあって、再現性や用量依存性に乏しい場合等には、原則として、軽微な陽性と判断する。

b)陰性

・陽性でないこと。

②ほ乳類培養細胞を用いる染色体異常試験又はマウスリンフォーマ TK 試験

a) ほ乳類培養細胞を用いる染色体異常試験

［1］陽性

・染色体異常を持つ細胞の出現率が陰性対照に比べ概ね１０％以上であり、その作用に再現性又は用量依存性が認められること。

・D_{20} 値が 10^{-2}mg/ml 以下である場合には、原則として、強い陽性と判断する。

・陽性の場合にあって、再現性や用量依存性に乏しい場合等、又は概ね 50%あるいはそれ以上の細胞増殖阻害が起こる濃度でのみの陽性反応等は、原則として、軽微な陽性と判断する。

［2］陰性

・陽性でないこと。

b) マウスリンフォーマ TK 試験

［1］陽性

・いずれかの試験系で突然変異頻度が統計学的に有意な増加を示し、その作用に再現性又は用量依存性が認められること。

・いずれかの試験系で突然変異頻度が陰性対照の 4 倍、又は陰性対照より 400 $\times 10^{-6}$ を超えて増加している場合には、原則として、強い陽性と判断する。

・陽性の場合にあって、再現性や用量依存性に乏しい場合、若しくは突然変異頻度が陰性対照の２倍未満である場合等、又は概ね 80%あるいはそれ以上の細胞毒性が認められる濃度でのみの陽性反応等は、原則として、軽微な陽性と判断する。

［2］陰性

・ 陽性でないこと。

③２８日間反復投与毒性試験（以下、OECD テストガイドライン４２２で定められた方法に準じて実施された試験を含む。）又は９０日間反復投与毒性試験

a)NOEL 及び発現した毒性の程度から以下の３段階に分類する。

［１］：・NOEL が概ね 25mg/kg/day 未満のもの（NOEL の推定根拠において非特異的な変化等、毒性学的に軽微な変化のみが発現した場合を除く。）

・NOEL が概ね 25mg/kg/day 以上 250mg/kg/day 未満のものであって、NOEL の推定根拠又はその他の発現した毒性において、神経行動毒性や重篤な病理組織学的な変化等、毒性学的に重要な変化（回復期の影

響については、b）Ａ又はＢに該当するものとする。）が発現したもの。

［２］：NOEL が概ね 250mg/kg/day 未満のもの（［１］に該当するものを除く。）

［３］：NOEL が概ね 250mg/kg/day 以上のもの。

なお、９０日間反復投与毒性試験においては、２８日間反復投与毒性試験に比べて投与期間が長いこと等を考慮しつつ、判断することとする。

b)回復試験中に見られる影響の程度から以下の３段階に分類する。なお、分類に当たっては、可逆性の程度、回復期における毒性の残存状況、遅発毒性の有無、組織学的変化に起因する生化学的な変化かどうか等を考慮する。

Ａ：回復試験期間内に回復しない病理組織学的な変化を生じさせるもの、又は遅発毒性を生じさせるもの

Ｂ：回復試験期間内に回復しない生化学的な変化を生じさせるもの

Ｃ：回復試験の期間において回復する、又は回復途上であることが示される可逆的変化

（４）生態毒性試験

藻類生長阻害試験、ミジンコ急性遊泳阻害試験及び魚類急性毒性試験の結果から以下の３段階に分類する。（藻類生長阻害試験に基づく毒性値は、原則として速度法により算出したものを用いる。以下同じ。）

［１］：３種の試験結果から得られる L(E)C50 値の最小値が概ね 1mg/l 以下のもの。

［２］：３種の試験結果から得られる L(E)C50 値のいずれかが概ね 1mg/l 超、10mg/l 以下のもの。（［１］に該当する場合を除く。）

［３］：３種の試験結果から得られる L(E)C50 値の最小値が概ね 10mg/l 超のもの。

（５）第一種監視化学物質の判定

既存化学物質について、（１）が難分解性であり、（２）が高濃縮性であると判断された場合であって、人及び高次捕食動物への長期毒性を有することがいずれも明らかでない場合には第一種監視化学物質として判定する。

（６）第二種監視化学物質の判定

（１）が難分解性であり、（２）が高濃縮性ではないと判断された場合であって、（３）の結果、次のいずれかに該当する場合には第二種監視化学物質として判定する。

①２８日間反復投与毒性試験又は９０日間反復投与毒性試験（以下「反復投与毒性試験等」という。）において強い毒性が示唆されるもの

（（３）③［１］に該当する場合）

②変異原性試験において強い陽性が示唆されるもの

（（３）①又は②が強い陽性の場合）

③反復投与毒性試験等において中程度の毒性を示すとともに、変異原性試験で強い陽性ではないものの陽性であるもの

（（３）③［２］に分類され、かつ、（３）①又は②が陽性（但し、軽微な陽性

である場合を除く。）の場合）

ただし、通知に規定する慢性毒性試験、生殖能及び後世代に及ぼす影響に関する試験、催奇形性試験、変異原性試験（小核試験等）、がん原性試験、生体内運命に関する試験、薬理学的試験又はこれらと試験の目的が合致している試験において、死亡、がん、長期にわたる障害、生殖能又は後世代の発生に及ぼす影響その他これらに準じて毒性学的に重要な影響が認められた知見がある場合には、必要に応じ、これらの試験成績を考慮して第二種監視化学物質に該当するか判定する。

（７）第三種監視化学物質の判定

（１）が難分解性であり、第一種特定化学物質ではないと判断された場合、以下の［１］、［２］のいずれかにより第三種監視化学物質に該当する場合には、第三種監視化学物質として判定する。

［１］（４）の結果から以下のように判定する。

①３種の試験結果から得られる L(E)C50 値の最小値が概ね 1mg/l 以下である場合（（４）［１］に該当する場合）には、第三種監視化学物質として判定する。

②３種の試験結果から得られる L(E)C50 値のいずれかが概ね 1mg/l 超、10mg/l 以下である場合（（４）［２］に該当する場合）には、以下のとおり判断する。なお、下記ａ）～ｃ）に複数該当する場合であって、第三種監視化学物質に該当するかの判定が分かれた場合においては、第三種監視化学物質として判定する。

ａ）魚類急性毒性試験の結果が該当する場合には、第三種監視化学物質として判定する。

ｂ）ミジンコ急性遊泳阻害試験の結果が該当する場合には、物質の化学構造等を考慮して個別に判断する。

ｃ）藻類生長阻害試験の結果が該当する場合には、以下のように判定する。

（ｉ）EC50 の値が 1mg/l 超、2mg/l 以下である場合には、第三種監視化学物質として判定する。

（ii）EC50 の値が 2mg/l 超、10mg/l 以下である場合には、第三種監視化学物質として判定しない。

③３種の試験結果から得られる L(E)C50 値の最小値が概ね 10mg/l 超である場合（（４）［３］に該当する場合）には、第三種監視化学物質とは判定しない。

［２］「第三種監視化学物質に係る有害性調査のための試験の方法について（平成１６年３月２５日平成１６・３・１９製局第６号・環保企発第０４０３２５００４号）」に定める藻類生長阻害試験、ミジンコ繁殖試験又は魚類初期生活段階毒性試験の試験結果において、少なくとも、NOEC が 0.1mg/l 以下となる場合には第三種監視化学物質として判定する。また、これらの試験以外の水生生物に対する慢性毒性を示唆する試験結果が得られた場合には、個別に判断する。

なお、上記に基づき判定が困難な物質については、類似の物質の評価及び判定の例を参考にしつつ、安全側に立脚した観点から判定する。

Ⅲ．高分子フロースキームに基づく判定

高分子フロースキームに基づき判定を行う場合には、原則として以下の基準によることとしている。

（１）以下の安定性試験の結果及び溶解性試験の結果に係る基準を満たす場合には、難分解性であり、かつ、高濃縮性ではないと判定する。

①安定性試験

・重量変化の基準

：試験前後で変化がないこと（2%以下の変化は変化とは見なさない）。

・DOC 変化の基準

：試験前後で変化がないこと（5ppm 以下の変化は変化とは見なさない）。

・ＩＲスペクトルの基準

：試験前後で変化がないこと。

・分子量変化の基準

：試験前後で変化がないこと。

②溶解性試験

a)以下の９種類の溶媒のいずれにも溶けない場合であって、特定の構造特性（架橋構造、高結晶性等）を有するか、又は酸・アルカリに不溶であること。

水、n-ｵｸﾀﾉｰﾙ、n-ﾍﾌﾟﾀﾝ、ﾄﾙｴﾝ、1,2-ｼﾞｸﾛﾛｴﾀﾝ、ｲｿﾌﾟﾛﾋﾟﾙｱﾙｺｰﾙ、ﾃﾄﾗﾋﾄﾞﾛﾌﾗﾝ（THF）、ﾒﾁﾙｲｿﾌﾞﾁﾙｹﾄﾝ（MIBK）、ｼﾞﾒﾁﾙﾎﾙﾑｱﾐﾄﾞ（DMF）

b)上記 a)以外の場合は、分子量 1000 未満の成分含有量が１%以下であること。

なお、上記①及び②の基準を満たさない場合には、分解性試験、濃縮度試験、スクリーニング毒性に関する試験、生態毒性試験の試験成績に基づき判定を行う。

（２）Ⅲ．（１）①及び②の基準を満たす場合には、以下のとおり判定を行う。

a)重金属を含まず、化学構造と長期毒性との関連性に関する知見等から判断して人への長期毒性を有することが示唆されない場合には、第二種監視化学物質に該当しないと判定する。

b) a)以外の場合には、スクリーニング毒性に関する試験の試験成績に基づき第二種監視化学物質への該当性の判定を行う。

c)以下のいずれかの場合には、第三種監視化学物質に該当しないと判定する。

（ｉ）重金属を含まず、水、酸及びアルカリに対する溶解性が確認されない場合であって、次のいずれかに該当する場合

・水への自己分散性*が確認されない場合

・水への自己分散性が確認された場合であって、カチオン性を示さない場合

＊　分散剤を含まない条件下で分散する性状を有するもの

（ⅱ）重金属を含まず、水、酸及びアルカリに対する溶解性が確認された場合にカチオン性を示さないものであって、化学構造と動植物への毒性との関連性に関する知見等から判断して、動植物の生息又は生育に支障を及ぼすおそれを有すると示唆されない場合

d)c)以外の場合には、生態毒性試験の試験成績に基づき第三種監視化学物質への該当性の判定を行う。

「監視化学物質（指定化学物質）への該当性の判定等に係る試験方法及び判定基準」の改正履歴

制定：平成１５年４月１８日

改正：平成１６年４月３０日（指定化学物質から監視化学物質への名称変更、生態毒性試験の追加、第一種監視化学物質及び第三種監視化学物質の判定基準の追加）

改正：平成１６年６月１８日（Pow 測定試験における判定基準を 3.0 未満から 3.5 未満に変更及び Pow 測定試験における除外規定を追加）

改正：平成１７年１月１４日（高分子フロースキームに基づく第三種監視化学物質判定基準において水への自己分散性が確認された場合の基準を追加及び Pow 測定試験に HPLC 法を採用したことに伴う変更を追記）

改正：平成１７年６月２４日（マウスリンフォーマＴＫ試験、90 日間反復投与毒性試験及び慢性毒性試験等の記載を追加）

改正：平成１７年９月３０日（第三種監視化学物質において３種生物における生態毒性試験の判定基準及び水生生物に対する慢性毒性における判定基準等の記載を追記）

改正：平成１８年７月２１日（第三種監視化学物質判定基準中の藻類生長阻害試験に関し、毒性値の計算に原則として速度法を用いることを追記及び判定基準を変更）

水溶性ポリマーの生態毒性について

米国ＴＳＣＡ（Toxic Substances Control Act）では、製造前届出（PMN）を免除するポリマーの要件を定めているが、このポリマー免除の設定基準については「Ecological Assessment of POLYMER (Strategies for Product Stewardship and Regulatory Program)」(1997)において示されているところである。

この中で、水溶性ポリマーの生態毒性については、ポリマーの持つ電荷によって評価を行うことが可能であるとされ、以下のとおり整理されている。

電荷の種類	生態毒性（一般論）	備　　考
カチオン性	高い	米国 TSCA では免除対象から除外されている。
アニオン性	中程度	・ Poly(aromatic acids)（スルホン酸、カルボン酸によるもの）の多くは、水生生物に中程度の毒性を示し、その作用機作は不明。 ・ Poly(aliphatic acids)は藻類にのみ中程度の毒性を示すが、その作用は水中の必須金属をキレートすることによるものであり、カルシウムイオンの濃度を上げることなどで毒性を打ち消すことができる。
非イオン性	低い	非イオン性ポリマーは一般には毒性は弱いが、界面活性作用のあるものは水生生物に有毒。
両性イオン性	カチオン・アニオン比率による	両性イオン性ポリマーの毒性は、正電荷密度とカチオン・アニオン比率による。