Annex XV report

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name(s): 1,6,7,8,9,14,15,16,17,17,18,18-Dodecachloropentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene ("Dechlorane Plus"™) [covering any of its individual anti- and syn-isomers or any combination thereof]

EC Number(s): 236-948-9; -; -

CAS Number(s): 13560-89-9; 135821-74-8; 135821-03-3

Submitted by: United Kingdom

Date: 29 August 2017

CONTENTS

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57 IV

PART I 1

JUSTIFICATION 1

1. IDENTITY OF THE SUBSTANCE AND PHYSICAL AND CHEMICAL PROPERTIES 2

1.1 Name and other identifiers of the substance 2
1.2 Composition of the substance 2
1.3 Identity and composition of degradation products/metabolites relevant for the SVHC assessment 3
1.4 Identity and composition of structurally related substances (used in a benchmarking or read-across approach) 7
1.5 Physicochemical properties 12

2. HARMONISED CLASSIFICATION AND LABELLING 16

3. ENVIRONMENTAL FATE PROPERTIES 17

3.1 Degradation 17
3.1.1 Abiotic degradation 17
3.1.2 Biodegradation 18
3.1.3 Other data 23
3.1.4 Summary and discussion of degradation 23
3.2 Environmental distribution 24
3.2.1 Adsorption/desorption 24
3.2.2 Volatilisation 24
3.2.3 Distribution modelling 25
3.3 Data indicating potential for long-range transport 26
3.4 Bioaccumulation 30
3.4.1 Bioaccumulation in aquatic organisms (pelagic & sediment organisms) 30
3.4.2 Bioaccumulation in terrestrial organisms (soil dwelling organisms, vertebrates) 44
3.4.4 Summary and discussion of bioaccumulation 52

4. HUMAN HEALTH HAZARD ASSESSMENT 55

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination) 55

5. ENVIRONMENTAL HAZARD ASSESSMENT 57

6. CONCLUSIONS ON THE SVHC PROPERTIES 58

6.1 CMR assessment 58
6.2 PBT and vPvB assessment 58
6.2.1 Assessment of PBT/vPvB properties 58
6.2.1.3.1 Fulfilment of the T criterion based on human health classification 63
6.2.1.3.2 Fulfilment of the T criterion based on ecotoxicity data 63
6.2.2 Summary and overall conclusions on the PBT and vPvB properties 65

PART II 67

7. REGISTRATION AND C&L NOTIFICATION STATUS 67

7.1 Registration status 67
7.2 CLP notification status 67

8. TOTAL TONNAGE OF THE SUBSTANCE 67

9. INFORMATION ON USES OF THE SUBSTANCE....68
Quantities....71
10. INFORMATION ON STRUCTURE OF THE SUPPLY CHAIN....73
11. ADDITIONAL INFORMATION....73
11.1 Substances with similar hazard and use profiles on the Candidate List....73
11.2 Alternatives....73
11.3 Existing EU legislation....73
11.4 Previous assessments by other authorities....73
REFERENCES FOR MAIN REPORT AND APPENDICES....75
LIST OF APPENDICES....90

TABLES

Table 1: Substance identity of 1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo-[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene, Dechlorane Plus [1]. 2
Table 2: Substance identity of (1S,2S,5S,6S,9R,10R,13R,14R)-1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene, anti- (or exo) Dechlorane Plus [2, see structural formula below] 3
Table 3: Substance identity of (1S,2S,5R,6R,9S,10S,13R,14R)-1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene, syn- (or endo) Dechlorane Plus [3, , see structural formula below] 4
Table 4: Constituents other than impurities/additives 2
Table 5: Identity of 1,3-DPMA 4
Table 6: Identity of 1,5-DPMA 5
Table 7: Identity of DP-1Cl....6
Table 8: Identity of DP-2Cl....6
Table 9: Identity of selected analogues....8
Table 10: Overview of physicochemical properties 12
Table 11: Summary of predicted and measured degradation data for Dechlorane Plus analogues....21
Table 12: Input properties used in assessing long range transport potential....28
Table 13: Depuration half-lives and BCF values for chemicals meeting the vB criteria 39
Table 14: Registration status....67
Table 15: CLP notifications 67
Table 16: EU and global tonnage status 67
Table 17: Use of Dechlorane Plus and total number of preparations containing Dechlorane Plus in Sweden....69
Table 18: Uses according to the REACH registration(s) 70
Table 19: Non-confidential descriptor codes used in registration....71

FIGURES

Figure 1: Geometric isomers of Dechlorane Plus....2
Figure 2: Potential dechlorinated transformation products of Dechlorane Plus...3
Figure 3: Potential mono-adduct transformation products of Dechlorane Plus ...4
Figure 4: Dechlorane Plus levels in chicken tissues 48

PROPOSAL FOR IDENTIFICATION OF A SUBSTANCE OF VERY HIGH CONCERN ON THE BASIS OF THE CRITERIA SET OUT IN REACH ARTICLE 57

Substance Name(s): 1,6,7,8,9,14,15,16,17,17,18,18-Dodecachloropentacyclo-[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene

("Dechlorane Plus"™)

[covering any of its individual anti- and syn-isomers or any combination thereof]

EC Number(s): 236-948-9; -; -

CAS number(s): 13560-89-9; 135821-74-8; 135821-03-3

- It is proposed to identify the substance(s) as very persistent and very bioaccumulative (vPvB) according to Article 57(e) of Regulation (EC) No 1907/2006 (REACH).

Summary of how the substance meets the criteria set out in Article 57 of the REACH Regulation

Persistence

Based on the weight of evidence of the data available, it is concluded that Dechlorane Plus meets the criteria for vP in Annex XIII of REACH. This is based on:

- modelling of degradation potential and microbial metabolic pathways which suggests that biodegradation is likely to be very slow; and

- a low probability that it will degrade any faster than structural analogues that are considered to be very persistent under the Stockholm Convention.

This conclusion is also supported by the very low water solubility (suggesting limited bioavailability to micro-organisms once bound to solid matrices), monitoring data indicating that the substance can persist in sediments (a major sink) for many years, lack of evidence of biotransformation in fish (supporting the premise that the molecule is metabolically recalcitrant) and widespread occurrence in remote regions.

Bioaccumulation

Using a weight of evidence assessment of the data available, Dechlorane Plus meets the vB criteria in Annex XIII of REACH. This is based on:

- the long-depuration half-life determined in fish feeding studies which is indicative of a BCF above 5 000 L/kg, by comparison with other substances (supported by a long depuration half-life in mammalian liver);

- numerous studies that show that the substance is widely dispersed in freshwater, marine and terrestrial food chains, including top predators; and

- evidence that the substance can exceed levels in biota that are of concern based on critical body burden considerations related to baseline narcosis.

This conclusion is supported by the detection of the substance in human blood, placenta and breast milk.

Toxicity

Based on the available ecotoxicity and mammalian data, Dechlorane Plus does not currently meet the T criterion. Long-term toxicity studies using relevant life stages of fish (via diet), sediment or soil organisms, and/or birds could be performed to clarify whether adverse effects can occur via these exposure routes. However, as the substance meets both the vP and vB criteria, these are not scientifically necessary for environmental risk management purposes.

Other concerns

The substances 1,3- and 1,5-Dechlorane Plus monoadduct (DPMA) have been detected in the environment, sometimes at higher concentrations than Dechlorane Plus in the same samples. DPMA might be under-reported because destructive sample preparation methods may degrade it. Dechlorane Plus is the only likely source of these two substances, although there is no information on reaction rates or amounts that can be formed under relevant environmental conditions. Based on predictive models, DPMA screens as being potentially PBT and vPvB on the basis of QSAR (although some of the predictions are uncertain). No information is available on its mammalian toxicity, but due to structural similarities to aldrin or heptachlor it might be epoxidised in the environment to form a substance that could be neurotoxic and/or cause hepatotoxicity. Experimental data would be needed to confirm these properties. However, as a degradation product of Dechlorane Plus, any concerns about DPMA would be alleviated by the identification of Dechlorane Plus as a substance of very high concern.

In conclusion, despite the lack of definitive data, Dechlorane Plus is proposed to be identified as a vPvB substance according to Art. 57(e) of REACH by comparing all relevant and available information listed in Annex XIII of REACH with the criteria set out in the same Annex, in a weight-of-evidence determination.

Registration dossiers submitted for the substance? Yes

PART I

Justification

The data described in this dossier were taken from public sources unless stated otherwise, including robust study summaries from the REACH registration dossier available on the ECHA dissemination website in May 2015 (http://www.echa.europa.eu/) and submitted to the U.S. EPA by the Occidental Chemical Company (2003). Studies that are not formal regulatory test reports or published in peer reviewed journals (e.g. conference posters) are indicated as abstracts only [ABST]. Original test reports have not been reviewed (unless stated), although the information in the robust study summaries is considered sufficient. Published literature articles have been reviewed in detail.

The number of published papers is growing at a fast rate and it is not considered proportionate to attempt to summarise all available studies that refer to this substance. Detailed study descriptions for the major end points relevant to this dossier are provided in Appendix 1, which also includes a list of references that are not considered relevant, and another list of references that might be relevant but are likely to be of relatively low significance.

1. Identity of the substance and physical and chemical properties

1.1 Name and other identifiers of the substance

The substance 1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo-[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene has two isomers, named anti- [2] and syn- [3]. This dossier covers the individual anti- and syn- isomers (mono-constituent substances) and all possible combinations of the syn- and anti- isomers [1] (see structural formula below).

Table 1: Substance identity of 1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo-[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene, Dechlorane Plus [1].

EC number:	236-948-9
EC name:	1,6,7,8,9,14,15,16,17,17,18,18-Dodecachloro-pentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene
CAS number (in the EC inventory):	13560-89-9
CAS number: Deleted CAS numbers:	13560-89-9 -
CAS name:	1,4:7,10-Dimethanodibenzo[*a*,*e*]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-
IUPAC name:	1,6,7,8,9,14,15,16,17,17,18,18-Dodecachloropentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene
Index number in Annex VI of the CLP Regulation	Not applicable
Molecular formula:	$C_{18}H_{12}Cl_{12}$
Molecular weight range:	653.73 g/mole
Synonyms:	Bis(hexachlorocyclopentadieno)cyclooctane; 1,2,3,4,7,8,9,10,13,13,14,14-Dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodechydro-1,4:7,10-dimethanodibenzo[a,e]cyclooctene; Dodecachlorododecahydrodimethanodibenzocyclooctene; Dechlorane Plus 25 (Dech Plus); Dechlorane Plus 35 (Dech Plus-2); DP-515; Dechlorane 605; DP; DDC-CO

Note: The academic literature usually refers to this substance by a registered trade name “Dechlorane Plus” (often abbreviated as DP, but sometimes DDC-CO), and this is the name used throughout this report for convenience.

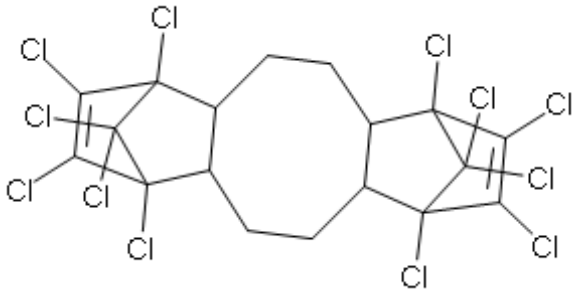
Table 2: Substance identity of (1S,2S,5S,6S,9R,10R,13R,14R)-1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo[12.2.1.$1^{6,9}$.$0^{2,13}$.$0^{5,10}$]octadeca-7,15-diene, anti- (or exo) Dechlorane Plus [2, see structural formula below]

EC number:	-
EC name:	-
CAS number: Deleted CAS numbers:	135821-74-8 -
CAS name:	1,4:7,10-Dimethanodibenzo[*a*,*e*]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6, 6a,7,10,10a,11,12,12a-dodecahydro-, (1*R*,4*S*,4a*S*,6a*S*,7*S*,10*R*,10a*R*,12a*R*)-*rel*-
IUPAC name:	(1S,2S,5S,6S,9R,10R,13R,14R)-1,6,7,8,9,14,15,16,17,17,18,18-Dodecachloropentacyclo[12.2.1.$1^{6,9}$.$0^{2,13}$.$0^{5,10}$]octadeca-7,15-diene
Index number in Annex VI of the CLP Regulation	Not applicable
Molecular formula:	$C_{18}H_{12}Cl_{12}$
Molecular weight range:	653.73 g/mole
Synonyms:	anti-DP, anti-Dechlorane plus, anti-Dodecachloropentacyclooctadecadiene

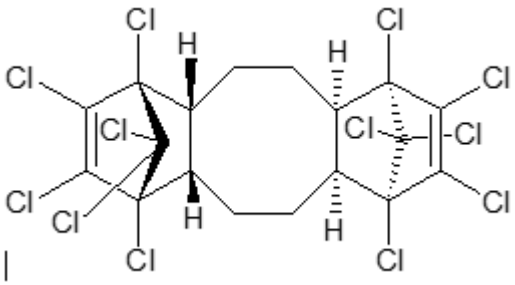
Table 3: Substance identity of (1S,2S,5R,6R,9S,10S,13R,14R)-1,6,7,8,9,14,15,16,17,17,18,18-dodecachloropentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene, syn- (or endo) Dechlorane Plus [3, , see structural formula below]

EC number:	-
EC name:	-
CAS number: Deleted CAS numbers:	135821-03-3 -
CAS name:	1,4:7,10-Dimethanodibenzo[a,e]cyclooctene, 1,2,3,4,7,8,9,10,13,13,14,14-dodecachloro-1,4,4a,5,6,6a,7,10,10a,11,12,12a-dodecahydro-, (1*R*,4*S*,4a*S*,6a*R*,7*R*,10*S*,10a*S*,12a*R*)-*rel*-
IUPAC name:	(1S,2S,5R,6R,9S,10S,13R,14R)-1,6,7,8,9,14,15,16,17,17,18,18-Dodecachloropentacyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene
Index number in Annex VI of the CLP Regulation	Not applicable
Molecular formula:	$C_{18}H_{12}Cl_{12}$
Molecular weight range:	653.73 g/mole
Synonyms:	syn-DP, syn-Dechlorane plus, syn-Dodecachloropentacyclooctadecadiene

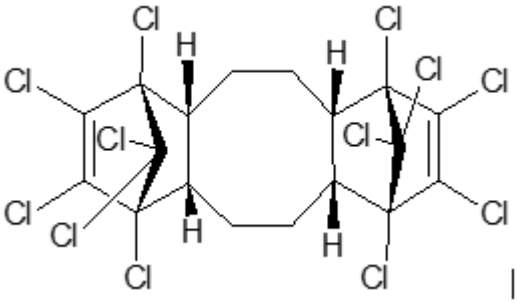
Structural formula:



anti- (or exo) Dechlorane Plus [2]



syn- (or endo) Dechlorane Plus [3]



1.2 Composition of the substance

Name: Dechlorane Plus™

Substance type: not applicable (group entry)

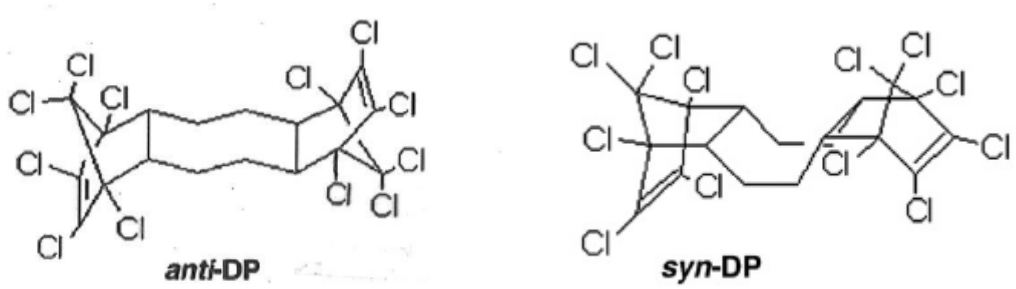
The information in this section is for the substance containing both the anti- and the syn- isomers as main constituents.

Table 4: Constituents other than impurities/additives

Constituents	Typical concentration	Concentration range (w/w)	Reference
anti- (or exo-)Dechlorane Plus (CAS no. 135821-74-8)	-	60-80 %	Ben *et al.* (2013)
syn- (or endo-)Dechlorane Plus (CAS no. 135821-03-3)	-	20-40 %	Ben *et al.* (2013)

The substance is described as mono-constituent by the lead Registrant. However, two geometric isomers are present in the commercial substance (e.g. Chou *et al.*, 1979; Occidental, 2013). This means that it is multi-constituent. The structures of the two isomers are provided in Figure 1.

Figure 1: Geometric isomers of Dechlorane Plus



(reprinted from Muñoz-Arnanz *et al.* (2010). Copyright 2010: International Symposium on Halogenated Persistent Organic Pollutants)

Ben *et al.* (2013) reported that the anti- isomer fractional abundance (f_{anti}) value (defined as [anti- isomer]/([anti- isomer] + [syn- isomer])) is not constant in Chinese commercial products, and varies from 0.60 to 0.80. The f_{anti} value of OxyChem commercial products has also been reported by several authors to be in the range 0.64 to 0.80 (e.g. see references in Wang *et al.*, 2010).

The substance is made by a Diels-Alder reaction between 1,5-cyclooctadiene and hexachlorocyclopentadiene in a molar ratio of 2:1. Cyclooctadiene can also exist as 1,4- and 1,3- isomers, and both these, 4-vinylcyclohexene and 1,2-divinylcyclobutane might be present as impurities in, or formed via thermal rearrangement of, the starting materials (Sverko *et al.*, 2010b). Consequently, they can produce Diels-Alder reaction products with the same molecular weight as Dechlorane Plus. Sverko *et al.* (2010b) analysed a technical Dechlorane Plus product and detected four minor chromatographic peaks that are potentially related to these other substances.

Compounds with a smaller number of chlorine atoms may also be impurities in the commercial substance. For example, Li *et al.* (2013b) found a mono-dechlorinated substance (DP-1Cl; see Section 1.3) in the commercial substance produced by

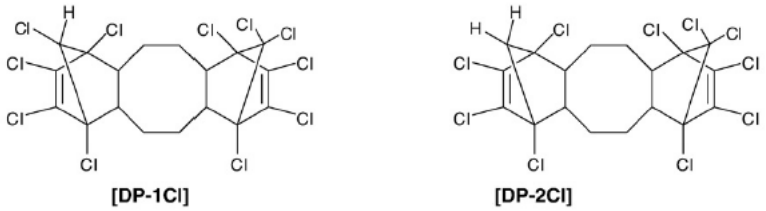
Jiangsu Anpon Co. Ltd., China; in contrast, Peng *et al*. (2014) could not detect DP-1Cl in samples from the same source (although this might reflect differences in detection limits).

Based on the variation of isomer-specific properties and the available test results, the study outcomes reported in Sections 3 can be considered to reflect with sufficient certainty the P and B properties of this group entry. The Annex XV entry covers the identity of the assessed substance to the level possible.

1.3 Identity and composition of degradation products / metabolites relevant for the SVHC assessment

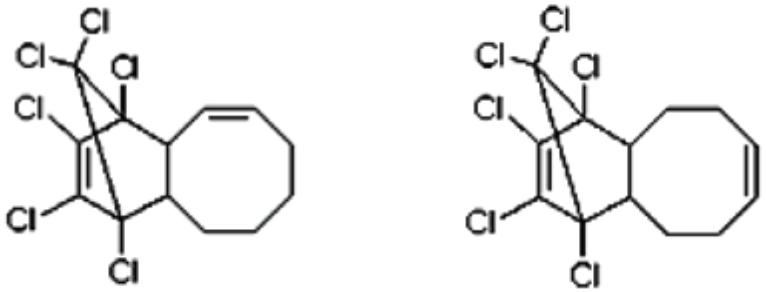
Three substances are relevant to this evaluation because they have been detected in various monitoring studies (e.g. Sverko *et al*., 2008 & 2010b; Muñoz-Arnanz *et al*., 2010; Möller *et al*., 2010; Guerra *et al*., 2011; Sun *et al*., 2012; Chen *et al*., 2013b; Yu *et al*., 2013; Ben *et al*., 2013 & 2014; Zheng *et al*., 2014a; Wang *et al*., 2015). These are 1,3-Dechlorane Plus monoadduct (1,3-DPMA), 1,5-Dechlorane Plus monoadduct (1,5-DPMA) and two substances formed through dehalogenation: one that has a single chlorine atom replaced by hydrogen (DP-1Cl or Cl_{11}-DP) and another in which two adjacent chlorine atoms are replaced by hydrogen (DP-2Cl or Cl_{10}-DP). The structures of these three substances are provided in Figure 2. Other substances could include hydroxyl or other substituents in place of the hydrogen atoms.

Figure 2: Potential dechlorinated transformation products of Dechlorane Plus



(reprinted from Muñoz-Arnanz *et al*. (2010). Copyright 2010: International Symposium on Halogenated Persistent Organic Pollutants)

Figure 3: Potential mono-adduct transformation products of Dechlorane Plus



1,3-DPMA 1,5-DPMA

(adapted with permission from Sverko *et al*. (2010). Copyright 2010: American Chemical Society)

There is no information about their rates of formation or the conditions under which they are formed. They might also be impurities in the commercial substance (see Section 1.2). Their properties have been estimated for the purposes of this document (see Appendix 2).

Table 5: Identity of 1,3-DPMA

EC number:	Not available
EC name:	Not available
SMILES:	C32(Cl)C(Cl)(Cl)C(Cl)(C(Cl)=C3Cl)C1C2CCCCC=C1
CAS number (in the EC inventory):	Not available
CAS number:	Not available
CAS name:	Not available
IUPAC name:	1,10,11,12,13,-13-Hexachlorotricyclo[8.21.$0^{2,9}$]-trideca-3,11-diene
Index number in Annex VI of the CLP Regulation	Not applicable
Molecular formula:	$C_{13}H_{12}Cl_6$
Molecular weight range:	380.96 g/mole
Synonyms:	1,3-DPMA, 1,3-Dechlorane Plus mono-adduct

Table 6: Identity of 1,5-DPMA

EC number:	Not available
EC name:	Not available
SMILES:	C32(Cl)C(Cl)(Cl)C(Cl)(C(Cl)=C3Cl)C1C2CCC=CCC1
CAS number (in the EC inventory):	Not available
CAS number:	Not available
CAS name:	Not available
IUPAC name:	1,10,11,12,13,-13-Hexachlorotricyclo[8.21.$0^{2,9}$]-trideca-5,11-diene
Index number in Annex VI of the CLP Regulation	Not applicable
Molecular formula:	$C_{13}H_{12}Cl_6$
Molecular weight range:	380.96 g/mole
Synonyms:	1,5-DPMA, 1,5-Dechlorane Plus mono-adduct

Table 7: Identity of DP-1Cl

EC number:	Not available
EC name:	Not available
SMILES:	C(=C(C(C1(CL)CL)(C(C2CCC(C(C(=C(C34CL)CL)CL)(C3(H)CL)CL)C4C5)C5)CL)CL)(C12CL)CL
CAS number (in the EC inventory):	Not available
CAS number:	Not available
CAS name:	Not available
IUPAC name:	1,6,7,8,9,14,15,16,17,17,18-Undecachloropenta-cyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene
Index number in Annex VI of the CLP Regulation	Not applicable
Molecular formula:	$C_{18}H_{13}Cl_{11}$
Molecular weight range:	619.29 g/mole
Synonyms:	DP-1Cl or Cl_{11}-DP

Table 8: Identity of DP-2Cl

EC number:	Not available
EC name:	Not available
SMILES:	C(=C(C(C1(CL)CL)(C(C2CCC(C(C(=C(C34CL)CL)CL)(C3(H)H)CL)C4C5)C5)CL)CL)(C12CL)CL
CAS number (in the EC inventory):	Not available
CAS number:	Not available
CAS name:	Not available
IUPAC name:	1,6,7,8,9,14,15,16,17,17-Decachloropenta-cyclo[12.2.1.1^{6,9}.0^{2,13}.0^{5,10}]octadeca-7,15-diene
Index number in Annex VI of the CLP Regulation	Not applicable
Molecular formula:	$C_{18}H_{14}Cl_{10}$
Molecular weight range:	584.84 g/mole
Synonyms:	DP-2Cl or Cl_{10}-DP

1.4 Identity and composition of structurally related substances (used in a benchmarking or read-across approach)

Ten substances sharing the hexachlorinated norbornene moiety are listed in Table 5 along with data for key physico-chemical end points.[1] The measured data are taken from the 13th (Budavari, 2001) and 15th (O'Neil, 2013) editions of *The Merck Index* (and subsequently https://www.rsc.org/Merck-Index/) and the experimental database within *EPI Suite v4.11* (U.S. EPA, 2012). Data were estimated using *EPI Suite v4.11* for consistency reasons.

Dechlorane Plus contains two chlorinated norbornene groups, whereas seven of the potential analogues only contain one such group. Whilst they tend to share limited water solubility, high n-octanol-water partition coefficients (log K_{OW} values) and very low vapour pressures, they are not a homogeneous group:

- Compared to Dechlorane Plus, six of the substances (dieldrin/endrin, aldrin, endosulfan, chlorendic acid[2], Dechlorane 602 and Dechlorane 604) contain additional functional groups (i.e. epoxide, alkene, sulfite, carboxylic acid, furan or brominated benzene) that affect polarity and reactivity, and are likely to influence their (eco)toxicological and environmental fate properties. With the exception of Dechlorane 602 and Dechlorane 604, they also have a lower molecular weight and higher water solubility than Dechlorane Plus. Therefore, these substances are not suitable analogues for Dechlorane Plus in terms of bioaccumulation or (eco)toxicity assessment, but they may offer a 'best case' comparison in terms of persistence.

- Chlordane and heptachlor do not contain reactive functional groups but do have additional chlorine atoms, so are closer structural analogues to Dechlorane Plus. However, they have much lower molecular weights (410 and 370 g/mole, respectively, compared to 650 g/mole for Dechlorane Plus), significantly higher water solubility (0.06 and 0.2 mg/L, respectively, compared to <0.00000167 mg/L for Dechlorane Plus), and lower log K_{OW} values (6.3 and 5.9, respectively, compared to ≥9 for Dechlorane Plus). Their bioavailability and toxicokinetic profile are likely to be quite different to Dechlorane Plus and so direct read-across of bioaccumulation and (eco)toxicity end points is not appropriate. Read-across for persistence is likely to be more reliable than for the previous six substances.

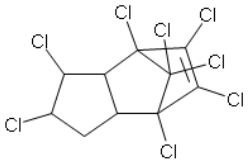
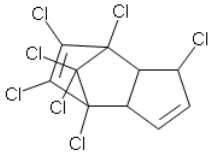
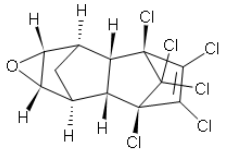
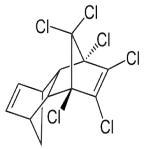
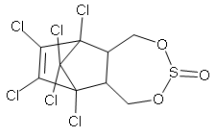
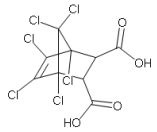
- Dechlorane 603 and Chlordene Plus have two chlorinated norbornene groups like Dechlorane Plus and no additional reactive functional groups. They have lower conformational flexibility, which could affect reactivity. They have similar molecular weights to Dechlorane Plus (611 – 638 g/mole), and very similar predicted water solubility and log K_{OW} values. They are therefore its closest structural analogues. They appear to have been impurities in some pesticide active substances rather than commercial products as such, and no experimental data seem to be available.

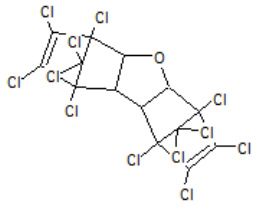
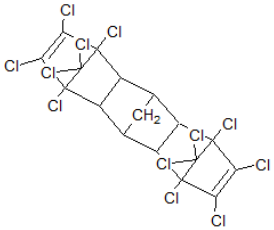
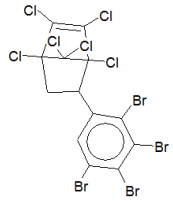
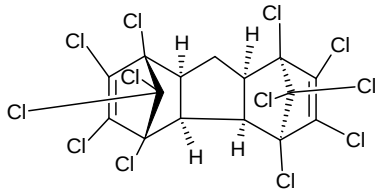
[1] Mirex (EC no. 219-196-6, CAS no. 2385-85-5) [also known as Dechlorane and perchloropentacyclodecane] is made using similar starting materials, but has a much more compact carbon skeleton and is fully chlorinated (molecular formula: $C_{10}Cl12$; SMILES: C12(C3(C4(C5(C3(C(C1(C5(C2(C4(Cl)Cl)Cl)Cl)Cl)(Cl)Cl)Cl)Cl)Cl)Cl)Cl). It is therefore not a suitable analogue for the purposes of this assessment. Further information can be found in WHO (1984b & 1995).

[2] Chlorendic anhydride (EC no. 204-077-3, CAS no. 115-27-5) is another analogue but as it rapidly forms chlorendic acid in contact with water it is not directly relevant for this analysis. The acid was considered as part of an EU Substance Evaluation of chlorendic anhydride. A decision requesting further information was sent to the Registrant(s) and the data submission deadline was 26 September 2016. The follow-up evaluation is not yet available.

Table 9: Identity of selected analogues

Substance name	Chlordane[a]	Heptachlor[b]	Dieldrin[c]	Aldrin[d]	Endosulfan	Chlorendic acid
EC number:	200-349-0	200-962-3	200-484-5	206-215-8	204-079-4	
EC name:	Chlordane , pur	Heptachlor	Dieldrin	Aldrin	Endosulfan	1,4,5,6,7,7-hexachloro-8,9,10-trinorborn-5-ene-2,3-dicarboxylic acid
Canonical SMILES	ClC1CC2C(C1Cl)C1(C(C2(Cl)C(=C1Cl)Cl)(Cl)Cl)Cl	ClC1C=CC2C1C1(Cl)C(Cl)=C(Cl)C2(Cl)C1(Cl)Cl	ClC1=C(Cl)[C@]2(Cl)[C@@H]3[C@@H]4C[C@@H]([C@H]5O[C@@H]45)[C@@H]3[C@@]1(Cl)C2(Cl)Cl	ClC3=C(Cl)C4(Cl)C2C1CC(C=C1)C2C3(Cl)C4(Cl)Cl	O=S1OCC2C(CO1)C1(C(C2(Cl)C(=C1Cl)Cl)(Cl)Cl)Cl	OC(=O)C1C(C(=O)O)C2(C(C1(Cl)C(=C2Cl)Cl)(Cl)Cl)Cl
CAS number (in the EC inventory):	57-74-9	76-44-8	60-57-1	309-00-2	115-29-7	115-28-6
CAS no.	57-74-9	76-44-8	60-57-1	309-00-2	115-29-7	115-28-6
CAS name:	4,7-Methano-1H-indene, 1,2,4,5,6,7,8,8-octachloro-2,3,3ª,4,7,7ª-hexahydro-	4,7-Methano-1H-indene, 1,4,5,6,7,8,8-heptachloro-3ª,4,7,7ª-tetrahydro-	2,7:3,6-Dimethanonaphth[2,3-b]oxirene, 3,4,5,6,9,9-hexachloro-1ª,2,2ª,3,6,6ª,7,7ª-octahydro-, (1ªR,2R,2ªS,3S,6R,6ªR,7S,7ªS)-rel-	1,4:5,8-Dimethanonaphthalene, 1,2,3,4,10,10-hexachloro-1,4,4ª,5,8,8ª-hexahydro-, (1R,4S,4ªS,5S,8R,8ªR)-rel-	6,9-Methano-2,4,3-benzodioxathiepin, 6,7,8,9,10,10-hexachloro-1,5,5ª,6,9,9ª-hexahydro-, 3-oxide	Bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid, 1,4,5,6,7,7-hexachloro-
IUPAC name:	1,2,4,5,6,7,8,8-Octachloro-3ª,4,7,7ª-tetrahydro-4,7-methanoindane	1,4,5,6,7,8,8-Heptachloro-3ª,4,7,7a-tetrahydro-4,7-methano-1*H*-indene	(1S,2R,3R,6S,7S,8R,9R,11S)-3,4,5,6,13,13-hexachloro-10-oxapentacyclo[6.3.1.1^{3},^{6}.0^{2},^{7}.0^{9},^{11}]tridec-4-ene	(1R,2R,3R,6S,7S,8S)-1,8,9,10,11,11-hexachlorotetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene	1,2,3,4,7,7-hexachloro-8,9,10-trinorborn-2-en-5,6-ylenedimethylene sulfite|1,4,5,6,7,7-hexachloro-8,9,10-trinorborn-5-en-2,3-ylenedimethylene sulfite	1,4,5,6,7,7-hexachloro-5-norbornene-2,3-dicarboxylic acid
Index no. in CLP Annex VI	602-047-00-8	602-046-00-2	602-049-00-9	602-048-00-3	602-052-00-5	-
Molecular formula:	$C_{10}H_6Cl_8$	$C_{10}H_5Cl_7$	$C_{12}H_8Cl_6O$	$C_{12}H_8Cl_6$	$C_9H_6Cl_6O_3S$	$C_9H_4Cl_6O_4$

Structural formula						
Molecular weight, g/mole	409.78	373.32	380.91	364.92	406.93	388.85
Melting point (experimental)	106 °C	95.5 °C	226-230 °C	104 °C, 240°C	106 °C	209 °C
Boiling point (experimental)	175 °C at 2 mm Hg	310 °C	-	-	-	-
Vapour pressure	0.0013 Pa at 25 °C (experimental) 0.003 Pa at 25 °C (estimated)	0.053 Pa at 25 °C (experimental) 0.03 Pa at 25 °C (estimated)	4.0E-04 Pa at 20 °C (experimental) 3.7 E-04 Pa at 25 °C (estimated)	0.016 Pa at 25 °C (experimental) 2.5 E-04 Pa at 25 °C (estimated)	8.0E-05 Pa at 25 °C (experimental) 1.7E-04 Pa at 25 °C (estimated)	1.9E-06 Pa at 25 °C (estimated)
Water solubility	0.056 mg/L at 25 °C (experimental) 0.013 mg/L at 25 °C (estimated)	0.18 mg/L at 25 °C (experimental) 0.095 mg/L at 25 °C (estimated)	0.195 - 0.25 mg/L at 25 °C (experimental) 0.15 mg/L at 25 °C (estimated)	0.017 mg/L at 25 °C (experimental) 0.002 - 0.014 mg/L at 25 °C (estimated)	0.325 mg/L at 22 °C (experimental) 1.5 mg/L at 25 °C (estimated)	3,500 mg/L at 25 °C (experimental) 18 mg/L at 25 °C (estimated)
log K_{OW}	6.1-6.2 (experimental) 6.3 (estimated)	5.5-6.1 (experimental) 5.9 (estimated)	5.2-5.4 (experimental) 5.4 (estimated)	6.5 (experimental) 6.8 (estimated)	3.8 (experimental) 2.25 (estimated)	3.1 (estimated)

Substance name	Dechlorane 602	Dechlorane 603	Dechlorane 604	Chlordene Plus
EC number:	250-472-9	-	252-097-6	-
EC name:	1,2,3,4,6,7,8,9,10,10,11,11-Dodecachloro-1,4,4a,5a,6,9,9a,9b-octahydro-1,4:6,9-dimethanodibenzofuran		1,2,3,4,7,7-Hexachloro-5-(tetrabromophenyl)bicyclo[2.2.1]hept-2-ene	
Canonical SMILES	C12C3C(C4(C(=C(C3(C4(Cl)Cl)Cl)Cl)Cl)Cl)OC1C5(C(=C(C2(C5(Cl)Cl)Cl)Cl)Cl)Cl	C62(Cl)C(Cl)(Cl)C(Cl)(C(Cl)=C6Cl)C1C3C4C5(Cl)C(Cl)(Cl)C(Cl)(C(Cl)=C5Cl)C4C(C21)C3	C1C(C2(C(=C(C1(C2(Cl)Cl)Cl)Cl)Cl)Cl)C3=CC(=C(C(=C3Br)Br)Br)Br	ClC4=C(Cl)[C@@]5(Cl)[C@@H]1[C@@H](C[C@H]2[C@@H]1[C@]3(Cl)C(Cl)=C(Cl)[C@@]2(Cl)C3(Cl)Cl)[C@]4(Cl)C5(Cl)Cl
CAS number (in the EC inventory):	31107-44-5	13560-92-4	34571-16-9	13560-91-3
CAS no.	31107-44-5	13560-92-4	34571-16-9	13560-91-3
CAS name:				
IUPAC name:	1,4,5,6,7,11,12,13,14,14,15,15-dodecachloro-9-oxapentacyclo[9.2.1.1⁴,⁷.0²,¹⁰.0³,⁸]pentadeca-5,12-diene	1,2,3,4,5,6,7,8,12,12,13,13-dodecachloro-1,4,4a,5,8,8a,9,9a,10,10a-decahydro-1,4:5,8:9,10-trimethanoanthracene	1,2,3,4,7,7-hexachloro-5-(2,3,4,5-tetrabromophenyl)bicyclo[2.2.1]hept-2-ene	(1*R*,4*S*,4a*R*,4b*S*,5*S*,8*R*,8a*S*,9a*R*)-1,2,3,4,5,6,7,8,10,10,11,11-dodecachloro-4,4a,4b,5,8,8a,9,9a-octahydro-1H-1,4:5,8-dimethanofluorene
Index number in CLP Annex VI	-	-	-	-
Molecular formula:	$C_{14}H_4Cl_{12}O$	$C_{17}H_8Cl_{12}$	$C_{13}H_4Br_4Cl_6$	$C_{15}H_6Cl_{12}$
Structural formula				
Molecular weight, g/mole	613.62	637.69	692.49	611.61
Melting point	190 °C (estimated)	198 °C (estimated)	203 °C (estimated)	189 °C (estimated)
Boiling point	-	-	-	-
Vapour pressure	1.1E-06 Pa at 25 °C (estimated)	3.2E-07 Pa at 25 °C (estimated)	1.7E-07 Pa at 25 °C (estimated)	1.3E-06 Pa at 25 °C (estimated)
Water solubility	≤1.7E-05 mg/L at 25 °C (estimated)	≤6.4E-07 mg/L at 25 °C (estimated)	≤4.7E-06 mg/L at 25 °C (estimated)	6E-07 mg/L at 25 °C (estimated)
log K_{OW}	8.0 (estimated)	11.2 (estimated)	10.6 (estimated)	9.8 (estimated)

Note: a – Chlordane consists of more than 140 compounds, of which trans-chlordane, cis-chlordane and trans-nonachlor are present in the highest amounts (Dearth & Hites, 1991; Liu et al., 2009).

b – Technical heptachlor usually contains about 72 % (±)-heptachlor and 28 % related compounds including about 18 % trans-chlordane (EFSA, 2007).

c – A stereoisomer of dieldrin called endrin (CAS no. 72-20-8) was also made commercially. It has effectively the same physico-chemical properties as dieldrin.

d – A stereoisomer of aldrin called isodrin (CAS no. 465-73-6) was also made commercially. It has effectively the same physico-chemical properties as aldrin.

1.5 Physicochemical properties

Unless otherwise stated, the data are taken from the REACH registration on the ECHA public dissemination website. There is no information available for the individual syn- and anti- isomers. Therefore it is not possible to conclude whether there are physicochemical differences between these or not.

Table 10: Overview of physicochemical properties

Property	Value [Unit]	Reference/source of information/remarks
Physical state at 20°C and 101.3 kPa	The substance is a free flowing solid	
Melting/freezing point	Decomposition from 340 – 382 °C (no melting observed)	
Boiling point	*Data waived on the basis of a melting point > 300 °C*	
Vapour pressure	*Data waived on the basis of a melting point > 300 °C*	A vapour pressure of approximately 9.4E-08 Pa at 25 °C is predicted using MPBPVP v1.43 (U.S. EPA, 2012, modified Grain method, recommended for solids). This is highly uncertain (approximately ±1 log unit) as it is close to the lower limit of the range of the model, where there is some scatter in the training set. However, the molecular weight of the substance is within the range of the model's training set. Also, structural analogues are part of the MPBPVP training and test sets. A measured vapour pressure of approximately 0.008 hPa (0.8 Pa) at 200 °C was reported by Occidental Chemical Company (2003). An extrapolated vapour pressure of 4.6E-04 Pa at 25 °C can be estimated from this result using EUSES v2.1.2, and this is preferred for assessment purposes. There is some uncertainty due to the extrapolation from very high temperature, and the unknown reliability of the underlying result. The substance has a very low vapour pressure at environmentally relevant temperatures.
Surface tension	*Data waived on the basis of low water solubility (<1 mg/L).*	
Dissociation constant	*Data waived on the basis of low solubility in water.*	The substance does not contain any acidic or basic functional groups.

Property	Value [Unit]	Reference/source of information/remarks
Water solubility	< 1.67 ng/L at 20 °C (below the limit of quantitation)	Reliability 1: OECD Test Guideline 105 (column elution method) and GLP (ECHA website, 2017)). Dechlorane Plus (>99 % purity) was coated onto the column using dichloromethane. HPLC grade reagent water was pumped through the column at two different flow rates, and analysed using gas chromatography with micro electron capture detection (GC-ECD). There is some uncertainty in the precise value for water solubility. However, all available measurements and predictions[3] are in agreement that the substance is very poorly water soluble.
Partition coefficient n-octanol/water (log value)	*Waived by Registrant due to low water solubility.*	Chou *et al*. (1979) reported a log K_{OW} of 9.3 (also reported by the U.S. EPA, 2012). This is a calculated value; its validity has not been assessed. A log K_{OW} of 11.3 is predicted using KOWWIN (U.S. EPA, 2012). This result was also reported in the U.S. EPA (2001) review. The predicted result is considered to be within the validity range of the model because the molecular weight of the substance is within the range for this parameter for both the training and test sets. The number of aliphatic chlorines exceeds the maximum occurrences of this fragment in a single compound in the training set (8 in Dechlorane Plus, maximum 6 in the training set). The value is above the log K_{OW} values used in the training and tests sets and above the normal experimental range, but is indicative of the expected lipophilic character of the substance. It would be unusual to expect to quantify values above approximately 9 experimentally. The log of the ratio of n-octanol and water solubilities is >8.4, using a solubility of < 2 ng/L at 20 °C for water (ECHA website, 2017) and 470 mg/L at 25 °C for n-octanol (see below). Additional estimation methods give similar values. For example, the ACD/Percepta platform gives the following results: LogP Classic: 9.51±0.67; LogP GALAS: 9.16 (Reliability: Borderline; RI = 0.41. Chlordene and different chlordane isomers are in the training set). Whilst there is clearly uncertainty in the value of log K_{OW}, the value is assumed to be ≥9.

[3] Chou *et al*. (1979) reported mean water solubilities of 207 and 572 ng/L for the two isomers at 22±2.5°C using radiolabelled substance in equilibration with water by slow stirring for six weeks. This is considered unreliable by the Registrant. No reason is provided, but the report concluded that samples in the solubility experiment may have contained particulates, and so estimated a solubility of 44.1±2 ng/L at 22 °C (total for both isomers).

Water solubilities estimated based on a log K_{OW} range of 7 to 9 using WSKOWWIN v.1.42 (U.S. EPA, 2012) are 7.5E-05 – 1.5E-06 mg/L [75 – 1.5 ng/L]. The substance is outside the estimation domain of the model because both molecular weight and log K_{OW} are outside the ranges of these parameters in the training and test sets for the method. A water solubility of 6.5E-07 mg/L [0.65 ng/L] can be estimated using the WaterNT v1.01 fragment method (U.S. EPA, 2012), which does not use log K_{OW} as an input. The molecular weight is outside the range of this parameter in the training set, but not the test set. The number of aliphatic attached chlorines exceeds the maximum occurrences of this fragment in a single compound in the training set (8 in Dechlorane Plus, maximum 6 in the training set). Therefore, the substance is not considered to be within the estimation domain of the model.

U.S. EPA (2011) reported another measured value of 2.49E-04 mg/L [240 ng/L] at 25 °C (Scharf, 1978). In EPI Suite (U.S. EPA, 2012), a measured water solubility of 4.4E-08 mg/L at 25 °C is reported citing a HPV Robust Summary as the source; this result is discounted given the discrepancy between the value quoted and the original source (4.4E-05 mg/L, Chou *et al*., 1979).

Property	Value [Unit]	Reference/source of information/remarks
Partition coefficient air/water (log value) [log K_{AW}]	*No data were provided by the Registrant.*	The following log K_{AW} values at 25 °C are estimated based on the Henry's Law constant: -3.2 (from measured water solubility and estimated vapour pressure) 0.44 (from measured water solubility and vapour pressure) -2.8 (from EPIWIN predicted water solubility using log K_{OW} of 9 and vapour pressure) -3.5 (from HENRYWIN v.3.20, predicted from structure using Bond Method). See discussion of Henry's Law Constant (Section 3.2.2 of Appendix 1) for further details.
Partition coefficient n-octanol/air (log value) [log K_{OA}]	*No data were provided by the Registrant.*	A log K_{OA} of 14.8 is estimated using KOAWIN (U.S. EPA 2012). This is a simple ratio of the octanol-water (log K_{OW} 11.3) and air-water (log K_{AW} -3.5) partition coefficients calculated within EPI Suite. There is uncertainty in this value resulting from uncertainty in the estimated K_{OW} and K_{AW} (see above). Using a log K_{OW} of 9, a log K_{OA} of 12.5 is estimated with a log K_{AW} of -3.5, or 8.6 with a log K_{AW} = 0.44.
Henry's Law Constant	*No data were provided by the Registrant.*	The following values were obtained using a range of estimation methods (including a structural fragment based QSAR method) in light of the uncertainty in vapour pressure and solubility measurements and predictions: 1.4 Pa.m^3/mol at 25 °C (from measured water solubility and estimated vapour pressure) 6800 Pa.m^3/mol at 25 °C (from measured water solubility and extrapolated vapour pressure) 41 Pa.m^3/mol at 25 °C (from EPIWIN predicted water solubility using log K_{OW} of 9 and vapour pressure) 0.75 Pa.m^3/mol at 25 °C (from HENRYWIN v.3.20, predicted from structure using Bond Method). The Bond method training set comprises much smaller molecules than Dechlorane Plus, which are generally much more soluble and of higher vapour pressure than the substance, although the predicted Henry's Law constant is mid-range for the method. It is therefore difficult to estimate the uncertainty of the predicted values. See also Section 3.2.2 of Appendix 1 for further discussion.
Solubility in organic solvent[4]	n-Octanol solubility: 470 mg/L (to the nearest 10 mg/L) at 25 °C	Reliability 1: non-guideline study conducted in a GLP facility but not formally to GLP (reference not provided, but it appears to have been conducted in the UK in 2013) Approximately 2 g sample was weighed into a 125 mL conical flask and 20 mL n-octanol was added. A magnetic stirrer was placed on a thermostatic water bath overnight followed by slow stirring. Stirring was stopped and test solutions containing insoluble test substance were allowed to settle for 30 minutes before filtration under gravity. Clear colourless filtrates were

[4] Occidental Chemical Company (2004) refers to a study from 1978 that mentions a solubility in n-octanol of 264 - 346 (average 305) ppb (µg/L) at 25 °C. No further details are available, but the result was obtained "after partitioning" (presumably with water, as the data entry is for the water solubility end point) so this is probably not a true solubility value.

Product literature (OxyChem, 2007) provides further values (all in units of g/100 g solvent at 25 °C) as follows: benzene 2.0, xylene 1.0, styrene 1.8, trichloroethylene 1.4, methyl ethyl ketone 0.7, n-butyl acetate 0.7, hexane 0.1, methyl alcohol [methanol] 0.1. The analytical information provided in the REACH registration dossier mentions that the substance is "insoluble" in methanol, but "soluble" in tetrachloroethane, dichloromethane and tetrahydrofuran.

Property	Value [Unit]	Reference/source of information/remarks
		obtained and test solution was analysed using GC-ECD without further dilution. The solubility in octanol is used as part of the assessment of octanol-water partitioning and also bioaccumulation. Although the test solution was filtered, it is not known whether the reported result represents truly dissolved substance.

2. Harmonised classification and labelling

No harmonised classification is reported for Dechlorane Plus (CAS 13560-89-9) in Annex VI of Regulation (EC) No. 1272/2008 (CLP Regulation).

There are no proposals for new or amended harmonised classification of Dechlorane Plus (CAS 13560-89-9) on the Registry of Intention.

The Registrant has not proposed classification for any hazard.

The European Chemical Agency (ECHA) online Classification & Labelling (C&L) Inventory database, which was checked on 13 July 2017, reports a joint submission (consisting of 92 notifiers) indicating no classification according to the CLP criteria. In addition, 78 notifiers have classified the substance as Acute Toxicity Category 4, H332 Harmful if inhaled.

3. Environmental fate properties

3.1 Degradation

3.1.1 Abiotic degradation

3.1.1.2 Hydrolysis

The Registrant waived the hydrolysis endpoint in accordance with Column 2 of REACH Annex VIII because the substance is highly insoluble in water. Dechlorane Plus does not contain any hydrolysable groups. Hydrolysis is not expected to be a relevant fate process.

3.1.1.3 Oxidation

The Registrant considers that an estimated first-order rate constant of 1/10 000 000 000 s^{-1} (corresponding to a half-life of 2 100 years) for oxidation in water by Chou *et al*. (1979) is unreliable as the calculation method was not described.

The potential for phototransformation in air has been predicted using the AOPWIN Program (v1.92). Under standard atmospheric conditions, the half-life is predicted to be 17 hours at 25 °C, based on reaction with hydroxyl radicals in the vapour phase. Complete information on training set development for this well-established predictive method is not publicly available, although hydroxyl radical rate constants for numerous polycyclic and highly chlorinated or brominated substances are represented in the training set. The molecular weight of Dechlorane Plus is high relative to substances in the training set, so the predicted half-life may be misleading. However, given the very low vapour pressure of this substance (see Section 1.5), the relevance of this estimate is low.

3.1.1.3 Phototransformation/photolysis

3.1.1.3.1 Phototransformation in air

Details of available studies are summarised in Appendix 1 (Sverko *et al*., 2008; Wang *et al.*, 2011; Li *et al*., 2013b; Wang *et al.*, 2013b; Tao *et al*., 2015). These suggest that significant photodegradation can potentially occur (with the formation of at least mono-dechlorinated substances), and that the anti- isomer might be more photodegradable than the syn- isomer. However, these studies cannot be directly related to natural conditions. The light intensity might not be comparable, and the use of organic solvents could promote the generation of hydrogen radicals (especially as the substance itself does not show any significant light absorption above 260 nm).

Dechlorane Plus will be mainly adsorbed on particulates in air (see Section 3.2.1). Particulates will shield the substance from light and inhibit radical reactions.

Nevertheless, monitoring studies provide some evidence of changes in isomer ratios with increasing distance from the source (further details are provided in Section 3.1.1.3.1 in Appendix 1). For example, Möller *et al.* (2010) found that the f_{anti} value decreased with decreasing northern latitude ($r = 0.974$, $p < 0.01$) from 0.63 to around 0.33 southwards of the equator. Yang *et al*. (2012) also found that the mean f_{anti} value was highest in spring and lowest in the autumn, although the

differences were not statistically significant (p > 0.05). These observations are often explained as being due to the effects of UV light (i.e. the anti- isomer degrading more rapidly than the syn- isomer), although Sverko *et al*. (2011) point out that it may reflect isomerisation of the anti- isomer to the syn- isomer.

Overall, atmospheric phototransformation/photolysis is likely to be of relatively low relevance to the overall fate of the substance, but may account of some of the changes in isomer fractional abundance that are observed in some matrices compared to the commercial products.

3.1.1.3.2 Phototransformation in water

Details of available studies are summarised in Appendix 1 (Chou *et al.*, 1979). In general, aquatic photolysis is unlikely to be a significant fate process in natural waters, since light is attenuated with increasing water depth and shading. Radical reactions may also be inhibited by humic substances. The available information suggests that phototransformation in water is a potential but insignificant removal process for Dechlorane Plus.

3.1.1.3.3 Phototransformation in soil

No data were reported by the Registrant. Similar to water, this is unlikely to be a significant removal pathway.

3.1.2 Biodegradation

3.1.2.1 Biodegradation in water

3.1.2.1.1 Estimated data

The aerobic biodegradation potential of the substance can be assessed using BIOWIN v4.10 (U.S. EPA, 2012). It has six different models which have been developed based on expert judgment. The program outputs for the non-linear model (BIOWIN 2), ultimate biodegradation (BIOWIN 3) and the MITI non-linear model (BIOWIN 6) can be used as a screening assessment of persistence (P) in accordance with the REACH Guidance R.7b (ECHA, 2017b). The following results indicate that a substance may be persistent:

BIOWIN 2: Does not biodegrade fast (<0.5) or
BIOWIN 3: ≥months (< 2.25 (to 2.75)[5])
BIOWIN 6: Not readily biodegradable (<0.5) and

Inputting the structural details of Dechlorane Plus results in a BIOWIN 2 value of 0, a BIOWIN 3 value of -1.60 and a BIOWIN 6 value of 0. These values are all significantly below the cut-offs, indicating that Dechlorane Plus is not expected to be aerobically biodegradable.

With regard to validity, the BIOWIN models are based on structural group contributions and there is no defined estimation domain as such. The software providers acknowledge that multiple occurrences of a contributing positive fragment group can sometimes lead to incorrect prediction of rapid degradation. In

[5] For substances fulfilling this but BIOWIN 3 indicates a value between 2.25 and 2.75 more degradation relevant information is generally warranted.

view of the group fragment values present in Dechlorane Plus, and the prediction of “not biodegradable”, this is unlikely to be a problem for the substance.

The BIOWIN model validity is considered in detail in the appendix (section 3.1.2.1.1). In summary the BIOWIN 2 and 3 model estimates have a degree of uncertainty due to (i) the lack of fragment coefficients to represent the whole Dechlorane Plus structure and, (ii) the number of identified fragments exceeding the maximum of occurrence in training set substances. The latter issue does not appear to affect the prediction that Dechlorane Plus is not biodegradable. For BIOWIN 6, the Dechlorane Plus structure is fully represented by the model fragments. The number of each fragment in the Dechlorane Plus structure is also within the range of the training set. The training set substances include two chemicals, which contain the hexchloronorbornene moiety of Dechlorane Plus. The model predictions for those substances do agree with the measured data. Overall BIOWIN 6 is considered to be a relevant and reliable model for Dechlorane Plus. The model provides support to the BIOWIN 2 and 3 predictions as all three models are consistent in predicting that Dechlorane Plus does not biodegrade fast.

It is concluded that based on the estimated data associated uncertainties, that Dechlorane Plus is unlikely to be biodegradable.

Overall it can therefore be concluded, based on estimated data, that Dechlorane Plus is unlikely to be biodegradable.

3.1.2.1.2 Screening tests

Two old biodegradation screening studies were included in the registration dossier as key studies, and further details are provided in Appendix 1 (Boudreau, 1973; Chou *et al.*, 1979). Neither was performed according to a standard test guideline method, and neither assessed biodegradation using biological oxygen demand or carbon dioxide evolution, which would be appropriate for such an insoluble substance. No biodegradation was observed over 21 days in the first test (based on analysis of the test substance). In the second, degradation was determined as loss of radioactivity; significant loss was observed after 6 weeks’ [42 days’] incubation under aerobic conditions, but no mass balance was performed, no metabolites were detected, adsorption to sludge or bacteria cannot be excluded and the position of radiolabelling in the molecule was not described. Consequently the Registrant concluded that Dechlorane Plus is non-biodegradable.

In view of the inappropriate test methods used, these screening studies provide no reliable information on the biodegradation potential of the substance.

A modified MITI (OECD TG 301C) study using an activated sludge inoculum was conducted in 1974, and the limited details are summarised in Appendix 1. Dechlorane Plus achieved 0.6 % of its theoretical biochemical oxygen demand (BOD) over two weeks and 0.3 % degradation was determined by gas chromatography. The reliability of this study cannot be assessed.

3.1.2.1.3 Simulation tests (water)

No simulation data were presented by the Registrant. A test would be technically very challenging given the reported solubility in pure water.

3.1.2.2 Biodegradation in sediment

No data are available in the registration dossier.

Qiu *et al*. (2007) measured Dechlorane Plus in a sediment core from central Lake Ontario, Canada. There was a linear trend (r^2 = 0.739) of increasing f_{anti} values with time, from an average of 0.76 in surficial (recent) sediments to >0.90 in the deeper layers corresponding to around 1980. This suggests that the anti- isomer could be more persistent than the syn- isomer in sediment (although the variation of f_{anti} in commercial batches over this time period is not known, and it could also reflect the isomerisation of the syn- isomer to the anti-).

Wang *et al*. (2010) measured f_{anti} values in two freshwater sediment samples collected from a canal close to the Chinese manufacturing facility. An f_{anti} value of 0.76 in the surficial layer (0-5 cm) contrasted with a value of 0.70 in a deeper layer (15-20 cm). The study authors contrast these with the measured f_{anti} value of the Chinese commercial product (0.60) and speculate that this implies a stereoselective depletion of the syn- isomer in sediment.

Fang *et al*. (2014) investigated the distribution of Dechlorane Plus in marine sediments from South Korea. The highest concentrations (451.2 and 149.9 µg/kg dw for the two bays studied) were detected in the finest grain size (< 10 µm). The f_{anti} in the two fractionated samples increased with reduced grain size and significantly correlated with organic carbon content. The study authors hypothesised that the enrichment of the anti- isomer was likely to be due to preferential biodegradation of the syn- isomer in the sediment.

Discussion

Dechlorane Plus is very hydrophobic, so it is not surprising that these three academic studies indicate that it accumulates in sediments. The study of Qiu *et al*. (2007) suggests that it can still be present over thirty years after initial deposition. However, it is not possible to estimate sediment degradation half-lives. This is because the initial amount of substance deposited in the sediment is unknown, and the nature of the sediment (e.g. in terms of heavy metal content and presence of other substances, which may inhibit micro-organisms) is not described.

3.1.2.3 Biodegradation in soil

No standard simulation data are available. The registration dossier summarises a monitoring study by Wang *et al*. (2010) which indicates that the substance can be detected in layers up to one metre deep (see Appendix 1), but it cannot be used to estimate soil degradation half-lives for similar reasons to the sediment studies.

3.1.2.4 Analogue data

In view of the lack of definitive degradation half-life data in water, sediment and soil it is appropriate to consider information from analogues. As discussed in Section 1.4 there are ten potential analogues to Dechlorane Plus based on a common hexachlorinated norbornene moiety: chlordane, heptachlor, dieldrin/endrin, aldrin, endosulfan, chlorendic acid, Dechlorane 602, Dechlorane 603, Dechlorane 604 and Chlordene Plus.

The closest structural analogues are Dechlorane 603 and Chlordene Plus. No standardised degradation data appear to be available for these (they are not registered under REACH and there are no data available from a search of the OECD eChemPortal[6] (accessed 13 July 2017)).

Five of the substances (chlordane, heptachlor, dieldrin/endrin, aldrin and

[6] https://www.echemportal.org/echemportal/index.action

endosulfan) are identified as Persistent Organic Pollutants (POPs) under the Stockholm Convention. The persistence of many of the early POPs was determined based on their favourable chemical properties for long-range transport and their detection in compartments and biota in the Arctic. Measured property data are presented in Appendix 1. There are few measured environmental half-lives, which is not surprising as many were banned before formal test guidelines or requirements for these existed.

Simulation data for endosulfan indicate that the α isomer is not persistent (P) within the meaning of the Annex XIII criteria, but the β isomer would be considered very persistent (vP) in some soils. In addition, the primary degradant (a sulfate) would meet the vP criterion in a number of soils. In sediment, the metabolites would be at least P (with an unbounded DT_{50} value of 120 days). None of the data for endosulfan indicate rapid breakdown of the chlorinated norbornene moiety, and very little mineralisation were observed in the studies (<5 %).

The use of the five POPs as pesticide active substances implies that they are reasonably bioavailable, which is confirmed by their high aquatic toxicity (not reported here). A comparison of the physico-chemical data of Dechlorane Plus with the POPs (summarised in Section 1.4) suggests that it is likely to be much less bioavailable as it is considerably less water soluble, and has a much higher log K_{OW} value. In addition, those POPs that do show signs of degrading have functional groups (e.g. dichlorocyclopentyl for chlordane, monochlorocyclopentenyl for heptachlor and sulfite for endosulfan) that are not present in Dechlorane Plus (which is a less polar molecule as a result). The POPs are all agreed to be environmentally persistent (within the meaning of the Stockholm Convention[7]). These provide a "best case" indication of persistence for Dechlorane Plus, i.e. it is expected to be at least as persistent as POPs with higher bioavailability and polarity.

There are no simulation data for chlorendic acid despite its relatively high water solubility (168 mg/L). Although it appears to rapidly degrade under UV light in water (half-life 5 days) and on solid surfaces (half-life 16 days), the half-life is much longer in soil (140 d at 1 mg/kg; 280 d at 10 mg/kg). No degradation was observed in a test for ready biodegradation after 31 days (based on removal of dissolved organic carbon). It therefore screens as being potentially P/vP. This is a much more polar and hydrophilic molecule than Dechlorane Plus, i.e. Dechlorane Plus is likely to degrade much more slowly than this substance.

In view of the lack of reliable environmental half-life data for most of the POPs, BIOWIN (v4.10) predictions for each of them and chlorendic acid are included in Table 7. As described in Section 3.1.2.1.1, conclusions about aerobic biodegradation potential can be drawn based on predictions from three of the models (BIOWIN 2, 3 and 6). The applicability of BIOWIN to these substances will be the same as for Dechlorane Plus (i.e. they are within the prediction domain).

Table 11: Summary of predicted and measured degradation data for Dechlorane Plus analogues[8]

Substance	CAS no.	BIOWIN prediction	Measured half-life data
Chlordane	57-74-9	BIOWIN 2 = 0 BIOWIN 3 = 0.27 BIOWIN 6 = 0	Sediment study suggests reduction in concentration by 70 % in 414 days
Heptachlor	76-44-8	BIOWIN 2 = 0 BIOWIN 3 = 0.53	Rapid hydrolysis

[7] That is, the half-life in water is greater than two months, or the half-life in soil is greater than six months, or the half-life in sediment is greater than six months; or the chemical is otherwise sufficiently persistent to justify its consideration within the scope of the Convention.

[8] Note that only the POP analogues and chlorendic acid are included here as these have measured (as well as predicted) degradation data available. Aldrin transforms to dieldrin.

Substance	CAS no.	BIOWIN prediction	Measured half-life data
		BIOWIN 6 = 0	Soil DT_{50} = 9-10 months or 2 years (shorter half-lives lack supporting information)
Dieldrin	60-57-1	BIOWIN 2 = 0 BIOWIN 3 = 0.67 BIOWIN 6 = 0	Very little degradation detected in soil
Aldrin	309-00-2	BIOWIN 2 = 0 BIOWIN 3 = 0.72 BIOWIN 6 = 0	No quantitative information
Endosulfan (α and β isomer)	115-29-7	BIOWIN 2 = 0 BIOWIN 3 = 0.62 BIOWIN 6 = 0	Soil DT_{50} = 25-128 days Metabolite: soil DT_{50} = 123 - 391 days Water/sediment DT_{50} >120 days
Chlorendic acid	115-28-6	BIOWIN 2 = 0 BIOWIN 3 = 1.39 BIOWIN 6 = 0	0 % mineralisation in 31 days

The results for BIOWIN 2 and 6 are zero for all substances, indicating a similarly low potential for biodegradation as Dechlorane Plus. The results for BIOWIN 3 indicate that Dechlorane Plus (-1.60, see Section 3.1.2.1.1) may resist biodegradation more than all of the POPs. This appears to be due to the factor added for each chlorine atom in the model. While the same atom addition applies to the BIOWIN 2 and 6 models, these structure-activity relationships appear to only return zero or positive values. As a minimum, Dechlorane Plus is not predicted to be more rapidly biodegraded than the analogues. Chlorendic acid appears to provide a "best-case", as it is the most water soluble of the group, yet it fails to undergo ready biodegradation.

Fragment considerations

Dechlorane Plus differs from all of the analogues by virtue of its cyclooctane ring which links the two chlorinated norbornene fragments. If this ring could be opened by biotic or abiotic degradation, chlorendic acid (see above) could be formed as a stable metabolite. Whilst likely to be persistent, the negative log K_{OW} of this substance suggests that it is not bioaccumulative. Cyclooctane (CAS no. 292-64-8) is not currently registered under REACH, and a literature search[9] has not located any degradation data for the substance.

Cyclooctane is a relatively simple alkane. Although predicted to be of moderate water solubility and log K_{OW}, EPIWEB v4.1[10] predicts that it can be rapidly degraded. However, in Dechlorane Plus, the two chlorinated norbornene rings constrain the flexibility of the cycloalkane structure (there are two structural isomers). Hoh *et al*. (2006) suggested that because of the configuration of the pendant chlorocyclopentene moieties, the anti- isomer would be more susceptible to biological attack than the syn- isomer.

Biodegradation pathway considerations

The EAWAG-BBD Pathway Prediction tool[11] for biodegradation can be used to explore the possible aerobic degradation pathways for Dechlorane Plus. The model suggests two possible pathways: hydroxylation of a secondary carbon (on the cyclooctane ring) and hydroxylation of a tertiary carbon (the carbon atom common

[9] Including the draft voluntary assessment of gasoline under the Existing Substances Regulation, and recent assessments submitted to the OECD.

[10] Relevant predicted results for cyclooctane, C1CCCCCCC1, are: log Kow = 4.16, water solubility = 4.9 mg/L and 14.1 mg/L using WSKOW and WATERNT respectively. BIOWIN predictions: BIOWIN2 = 0.80 (Biodegrades Fast); BIOWIN3 = 2.95(weeks); BIOWIN6 = 0.76 (Biodegrades Fast).

[11] http://eawag-bbd.ethz.ch/predict/

to the cyclooctane and norbornene rings)[12]. Both pathways are predicted to be of neutral likelihood, which is an assessment of the general pathway rather than specific to the substance. As noted in Section 1.3, dechlorinated substances have been detected in the environment. These may be reductive transformation products, but might also be impurities in the commercial substance. None of the substances are predicted to be formed using this tool.

Similar to Dechlorane Plus, prediction for cyclooctane also suggests degradation via hydroxylation of a secondary carbon on the ring. Both cyclooctane attached to a single norbornene ring, and chlordane (the only analogue that contains a secondary carbon, in a pentyl ring) are predicted to degrade via both the tertiary or secondary carbon. Heptachlor and chlorendic acid are indicated to have the same tertiary carbon biodegradation pathways as Dechlorane Plus.

The prediction for endosulfan suggests that conversion to the sulfate is favoured over the hydroxylation of the tertiary carbon which agrees with the experimental observation described in the POPs dossier. The epoxidation of dieldrin is favoured over the hydroxylation of the tertiary carbon.

The predictions suggest that the pathways available for Dechlorane Plus are no different to those for the analogues. However, the tool does not provide a prediction of rates for any part of the pathway, and it is not possible to determine how degradation rates will vary between the chemicals. The two degradation pathways predicted to exist for Dechlorane Plus do not appear to be rapid where these occur for the other analogues (e.g. dieldrin). For dieldrin one pathway is suggested to be more likely than the other. However, the persistence of the substance suggests that both are slow.

As a further indication of the limited biotransformation potential of Dechlorane Plus, Tomy *et al*. (2008) were unable to identify any Dechlorane Plus metabolites in a 161-day dietary exposure study with juvenile Rainbow Trout (*Oncorhynchus mykiss*) (see Section 3.4.1.2.2).

3.1.3 Other data

A study investigating changes in sewage sludge concentrations is briefly summarised in Appendix 1 (de la Torre *et al*., 2011), but does not provide any information to enable an environmental half-life to be estimated.

3.1.4 Summary and discussion of degradation

No degradation studies are available that meet modern regulatory standards. Key studies cited in the registration dossier cannot be considered reliable. However, it is possible to conclude that Dechlorane Plus is unlikely to undergo significant abiotic degradation. There are no environmental simulation studies, but evidence from quantitative structure-activity relationships (QSARs), analogue read-across and biodegradation pathway considerations all indicate that the rate of biodegradation is likely to be very slow in the environment. In particular, BIOWIN predictions suggest that Dechlorane Plus has a biodegradation potential similar to – or possibly lower than – analogues that are POPs. The much more water soluble chlorendic acid provides the “best case” analogue in terms of persistence, and even this is not readily biodegradable. Two potential biodegradation pathways are predicted for

[12] Secondary aliphatic → secondary alcohol (bt0242), tertiary aliphatic → tertiary alcohol (bt0241).

Dechlorane Plus. One of these is common to all of the POP analogues, and both are common to chlordane. Neither of the pathways is predicted to be “likely” or “very likely”, suggesting they are not favourable ways for the molecule to degrade. This agrees with sediment degradation data for chlordane, which suggest slow degradation. Overall, the non-test information provides a strong signal that Dechlorane Plus will degrade slowly and so have a long half-life in sediments and/or soils.

Field studies (e.g. Qiu *et al.*, 2007) provide some limited evidence of high persistence (in that Dechlorane Plus was found in a sediment core layer corresponding to around 1980). A fish bioaccumulation study (Tomy *et al.*, 2008) also suggests a limited potential for rapid biotransformation.

The same limited field data provides the only information for the fate of the two isomers of Dechlorane Plus. At present there is no strong evidence to contradict the assumption that both isomers have a similar level of persistence based on the conclusion drawn for the registered substance.

3.2 Environmental distribution

3.2.1 Adsorption/desorption

No reliable information on the organic carbon-water partition coefficient (K_{OC}) is included in the registration dossier, but a non-standard study investigating adsorption to sediment is summarised in Appendix 1 (Chou *et al.*, 1979).

In view of the fact that Dechlorane Plus is a highly insoluble substance with a high log K_{OW} and (relatively) high solubility in n-octanol, it is expected to have a high potential for adsorption. KOCWIN v2.00 (U.S. EPA, 2012) can be used to predict log K_{OC} values of 7.7 (Molecular Connectivity Index estimation method) and ≥7.8 (log K_{OW}-based estimation method; using the log K_{OW} value ≥9). The substance is within the domain of the method because the molecular weight is within the molecular weight range of the training set, and no fragment corrections are applied. The Registrant assumes a log K_{OC} of 8 in their Chemical Safety Report (CSR).

These predicted values indicate a high adsorption potential for Dechlorane Plus, suggesting that sediment and soil are more relevant environmental compartments than water (i.e. they are likely to be major sinks).

3.2.2 Volatilisation

No information on volatilisation was reported in the registration dossier.

The volatilisation potential of the substance from water can be estimated based on the available vapour pressure and water solubility data for the substance, and also by reference to QSAR-estimated values (see Appendix 1). Whilst there is some uncertainty in the values of water solubility and vapour pressure (see Section 1.5), the calculated HLC based on measured input data is ≥1.39×10^{5} Pa.m^3/mol at 25 °C, suggesting that Dechlorane Plus could be volatilised from water. However, strong adsorption to organic matter is likely to make this fate pathway less important in natural waters.

Given the very low vapour pressure and high K_{OW} of the substance (i.e. a high K_{OA}), Dechlorane Plus will be mainly adsorbed on particulates in air. This has been demonstrated by monitoring studies, with mean fractions on particulates of 97 % or more (e.g. Hoh *et al.*, 2006; Ren *et al.*, 2008; Wang *et al.*, 2010), although

Möller *et al.* (2010) measured it as around 80 ± 30 % and Yang *et al*. (2012) only detected Dechlorane Plus in the particulate phase.

3.2.3 Distribution modelling

No information on distribution modelling was reported in the registration dossier.

The CEMC Level III Fugacity Model v 2.80 (CEMC, 2004) can be used to model the distribution of Dechlorane Plus. The physico-chemical property values used in the model are those selected in Table 7: water solubility 2.0×10^{-6} mg/L; vapour pressure 4.6×10^{-4} Pa; log K_{OW} 9. The degradation half-lives used in the model environment are: air 16.8 hours; water 1.8×10^{4} hours (assuming photodegradation) or 8.4×10^{6} hours (assuming no photodegradation); soil 8.4×10^{6} hours.

If Dechlorane Plus is assumed to be released at equal rates to air, water and soil, the model predicts the following distribution: air 3.7×10^{-3} %, water 0.087 %, soil 96.5 % and sediment 3.45 % (the two half-lives in water give the same result). The substance has a very low vapour pressure. If it is released only to water (with no application to soil, including WWTP sludge), the calculated distribution is very different: air 9.0×10^{-5} %, water 2.46 %, soil 1.9×10^{-3} % and sediment 97.5 %. It should be noted that there is uncertainty in the property values used in the modelling and hence uncertainty in the results. More than 97 % of the Dechlorane Plus in the atmosphere is likely to reside in the particulate phase (see Section 3.2.1).

Using the OECD P_{ov} and LRTP Screening Tool v2.2 (Wegmann *et al*., 2009), the results obtained for Dechlorane Plus (see Section 3.3) suggest that it has a relatively low transfer efficiency from air to surface media[13] of 3×10^{-4} %.

Sverko *et al*. (2011) studied air-water exchange using the data measured by Möller *et al*. (2010) in the marine environment. The mean concentrations in air (gas phase) and seawater (dissolved phase) were 0.12 pg/m^3 and 0.009 pg/L, respectively, in the East Greenland Sea and 0.028 pg/m^3 and 0.044 pg/L, respectively, along the Atlantic transect. The resulting fugacity fraction[14] is near unity, suggesting net gaseous deposition of Dechlorane Plus to seawater.

Sverko *et al*. (2011) also compared the ratio of concentrations in air and soil reported by Wang *et al*. (2010) with an estimate based on the log K_{OA} value. The good agreement suggested that Dechlorane Plus in the gas phase originated from soil volatilization. However, they did not perform a similar analysis to compare gas phase with particulate concentrations.

[13] Transfer efficiency in this model is defined as "the ratio of the deposition mass flux from air to surface media in a region adjacent to the region to which the chemical is released and the mass flux of the chemical emitted to air in the release region"

[14] This is used to assess equilibrium status of a chemical between two interacting phases, in this case air and water:

Fugacity fraction = C_A / (C_A + $K_{AW}C_W$)

where C_A is the air concentration (in pg/m^3), C_W is the water concentration (in pg/L)

Values equal to 0.5 indicate air–water equilibrium and no net gas exchange. Values < 0.5 indicate net volatilization from water, and values > 0.5 indicate net gaseous deposition to water.

3.3 Data indicating potential for long-range transport

No information on long range transport potential was reported by the Registrant. However, a summary of Xian *et al*. (2011) given as supporting monitoring information in the IUCLID file states that “long-range atmospheric transportation of Dechlorane Plus has been observed in remote regions, indicating a global presence of Dechlorane Plus.”

The potential for long range transport (LRTP) can be modelled using the OECD P_{ov} and LRTP Screening Tool (Wegmann *et al*., 2009).

Table 8 shows a summary of input data for Dechlorane Plus and context for the model. Uncertainties in the values of vapour pressure, water solubility and log K_{OW} for Dechlorane Plus (see Section 1.5) all affect the input parameters for the calculation.

Table 12: Input properties used in assessing long range transport potential

Input property	Value	Context in terms of property input data for reference POPs in the model
Log K_{AW}	1.75	Above the range (i.e. relatively volatile)
Log K_{OW}	9	Above the upper limit (i.e. relatively lipophilic)
Half-life in air	16.8 h	Within range, relatively short half-life
Half-life in water	Variable inputs used to explore range: 8.4×10^{6} h (assuming no photodegradation); 1.8×10^{4} h (assuming photodegradation)	Relatively persistent (unless photodegradation assumed)
Half-life in soil	8.4×10^{6} h	Relatively persistent

Whilst no absolute criteria for classifying chemicals as compounds with high or low overall persistence (P_{ov}) and LRTP have been established, the threshold values established by Klasmeier *et al*. (2006), based on limit values for reference POPs, can be applied (P_{ov} = 195 days, Characteristic Travel Distance = 5 097 km, and Transfer Efficiency = 2.248 %):

- If no degradation in water or soil is assumed for Dechlorane Plus, the conclusion is that the potential for long range transport is low, with a characteristic travel distance of 350 km. The overall half-life (P_{ov}) for Dechlorane Plus is predicted to be long, at 5 900 days, and it is predicted to have relatively low transfer efficiency from air to surface media of 3×10^{-4} %. In this model, the fraction of Dechlorane Plus in air present in aerosols is 0.01 %.

- Taking photodegradation as a potentially relevant degradation pathway into account, the overall half-life (P_{ov}) for Dechlorane Plus remains high, at 4 100 days. The characteristic travel distance and transfer efficiency are unchanged.

Although there are significant uncertainties in the physico-chemical data set, the predicted log K_{OA} (>7.25 to >12) and log K_{AW} (1.75) values for Dechlorane Plus also suggest a low potential to reach the Arctic according to the criteria cited by Wania (2006) and Brown and Wania (2008).

The results from this modelling are uncertain, largely because most of the input parameters are estimated. In the context of the input properties for reference chemicals in the OECD model, the properties of Dechlorane Plus show that it has comparable or higher hydrophobicity than reference POPs, is comparatively more volatile (based on log K_{OA} and log K_{AW} values) and has relatively rapid degradation in the atmosphere (due to photodegradation, although this is still a slow process – see also Section 3.1.1.3.1).

Nevertheless, modelling may be of limited value for substances that have low vapour pressure and adsorb strongly to particulates in the air. Atmospheric transport for such substances is likely to be governed by the fate of these particulates. This can result in long-range transport to remote regions when atmospheric conditions permit (e.g. during dry periods). This is confirmed for Dechlorane Plus by monitoring evidence: Appendix 1 summarises several studies that demonstrate detection in the Polar regions as well as high mountains (Kaj *et al*., 2010; Möller *et al*., 2010; Sverko *et al*., 2010a [ABST]; Möller *et al*., 2011; Möller *et al*., 2012; Xiao *et al*., 2012; Arinaitwe *et al*., 2014; Newton *et al*., 2014;

Salamova *et al*., 2014; Vorkamp *et al*., 2014; Ma *et al*., 2015; Na *et al.,* 2015; Vorkamp *et al*., 2015), and also a study by Okonski *et al*. (2014) that investigated the presence of Dechlorane Plus on different sizes of particulate. Several of the studies measured Dechlorane Plus in seawater (Möller *et al*., 2010; Möller *et al*., 2011; Möller *et al*., 2012). The authors of these papers suggest that this reflects either riverine emission or atmospheric deposition (rather than long range transport via particles in water).

In summary, although the modelling data give mixed results, possibly as a consequence of the physicochemical characteristics of the substance, the monitoring data indicate that Dechlorane Plus can undergo long range transport, most probably as a result of adsorption to particulates in the atmosphere.

3.4 Bioaccumulation

3.4.1 Bioaccumulation in aquatic organisms (pelagic & sediment organisms)

3.4.1.1 Screening information

The log K_{OW} of Dechlorane Plus is estimated to be ≥9 (see Section 1.5). It therefore screens as potentially very bioaccumulative (vB). The log K_{OA} above 5 together with high log K_{OW} also suggest it may have a high bioaccumulation potential in air-breathing wildlife.

The bioconcentration factor (BCF) of an organic chemical can often be predicted using QSAR correlations with log K_{OW}, especially if the substance is not metabolised very readily. For the purposes of this assessment, some standard methods have been used to predict the following fish BCF values assuming a log K_{OW} of 9 as the lower limit (further details are provided in Appendix 1; this also includes published predictions by Chou *et al.* (1979) which appear unreliable):

i) Non-linear equation from REACH Guidance R.7c (ECHA, 2017c): ≤5 500 L/kg (unreliable)

ii) log K_{OW} >7 regression equation from BCFBAF v3.01 (U.S. EPA, 2012): ≤1 400 L/kg

iii) Arnot and Gobas (2003) method in BCFBAF v3.01: 1 200 L/kg (lower trophic level); bioaccumulation factor (BAF) 7.5 × 10^5 L/kg wet weight (ww)[15]

Given the uncertainty in the actual log K_{OW} value, all of these predictions should be considered with caution. In addition, the QSARs themselves are based on assumptions and in some cases very small data sets (see Appendix 1 for further comment). It is also relevant to note that the BCFBAF program estimates the BCF (and BAF) on the basis of the total concentration in water rather than the dissolved concentration in water (EA, 2013). The freely dissolved concentration of Dechlorane Plus would be significantly lower than the total concentration and hence the actual BCF based on dissolved concentrations may be higher than predicted above.

The REACH guidance (ECHA, 2017a) suggests several chemical properties that may limit the absorption and distribution of a chemical via passive transport. In summary, the fish BCF is unlikely to be above 2 000 L/kg if a substance has:

- an average maximum diameter greater than 17 Å (1.7 nm)[16], plus a molecular weight greater than 1 100 g/mol; or
- a measured octanol solubility (in mg/L) below 0.002 times the molecular weight, as an indicator of lipid solubility (in the case of Dechlorane Plus, this would be 1.3 mg/L) (without observed toxicity or other indicators of bioaccumulation).

The molecular weight of Dechlorane Plus is 654 g/mol. Using the OECD QSAR Toolbox v2.1, the maximum molecular diameter can be estimated as 1.43 nm (the minimum and effective diameters are 0.85 and 0.9 nm, respectively). Using the BCF_{max} model with mitigating factors (Dimitrov *et al.*, 2005), Environment Canada estimated a maximum diameter of 1.35 – 1.48 nm (pers. comm.). Fang *et al.* (2014) performed molecular characterization of both isomers using Gaussian 03 (Revision C.02) software, showing that the syn- isomer has a higher dipole moment, slightly larger Van der Waals volume, but smaller maximal cross-sectional diameter than the

[15] Sverko *et al.* (2011) included estimated biotransformation rate constants with this model to derive BAFs of 5.9 × 10^4 L/kg for the anti- isomer and 1.1 × 10^5 L/kg for the syn- isomer, based on total water concentrations. BAFs at the middle and upper trophic levels were higher.

[16] A maximum molecular length greater than 43 Å (4.3 nm) is also mentioned, but EA (2009c) found that the basis for this value was highly dubious so it is not considered further here.

anti- isomer (1.24 nm compared to 1.42 nm).[17] On the basis of these estimates, the first criterion is not fulfilled.

The registration dossier reports the n-octanol solubility of Dechlorane Plus to be 470 mg/L at 25 °C. It therefore appears that neither of the two criteria are fulfilled (i.e. the molecular size and n-octanol solubilities do not suggest that the substance is incapable of accumulation). An n-octanol solubility of around 0.5 g/L suggests that lipid solubility might be relatively high.

Fang *et al*. (2014) performed experiments using activated charcarbon to adsorb Dechlorane Plus dissolved in methanol. The adsorption results revealed that the syn- isomer was preferentially adsorbed, suggesting that it is more hydrophobic than the anti- isomer. Tomy *et al*. (2008) used a reverse-phase C18 liquid chromatography column as a surrogate for lipid, where the retentiveness of chemicals on the column is driven by the intrinsic polarity of the compound. Under isocratic conditions, the anti- isomer eluted before the syn- isomer (retention time 28.5 and 31.1 minutes, respectively) indicating that the syn- isomer is more lipophilic. These observations are consistent with measured bioaccumulation data and strongly suggests that polarity is an important factor for the differential bioaccumulation of the two isomers.

3.4.1.2 Laboratory studies

3.4.1.2.1 Aqueous exposure

The combined solubility of both Dechlorane Plus geometric isomers in pure water is below 2 ng/L (0.002 µg/L) at 20 °C (see Section 1.5). It is a very hydrophobic substance, with a presumed log K_{OW} value of ≥9. These properties make aqueous laboratory studies very difficult to carry out reliably owing to the potential difficulties in maintaining stable exposure levels at such low concentrations.

Five fish bioconcentration studies are available in the registration dossier and grey literature, which are summarised in detail in Appendix 1 (Boudreau & Rausina, 1973; Gara & Rawisina, 1975; Chou *et al*., 1979; Zitko, 1980; U.S. EPA, 2011 (citing an unpublished Japanese study)). All were carried out at concentrations significantly above the solubility limit in pure water, and only one followed a regulatory test guideline (this study is forty years old, key data are missing, and it did not achieve steady state). None of these studies is reliable. However, the longer duration studies do indicate that the substance can be taken up into fish tissues. If it is assumed that the fish were exposed to the substance at its water solubility limit (<2 ng/L), tentative BCFs are estimated to be well above 10 000 L/kg, although the likely oral exposure of the fish to particulates means that these values might be a misleading indication of bioaccumulation potential. The maximum fish concentrations measured in the aqueous BCF studies were 0.385 – 8.72 mg/kg after 30 days for *Lepomis macrochirus* (Gara & Rawisina, 1975; Boudreau & Rausina, 1973) and 0.327 mg/kg after 56 days for *Cyprinus carpio* (Japanese BCF study cited by U.S. EPA, 2011). The wide range for *L. macrochirus* could be due to experimental variation (especially as the exposure conditions were variable) or could perhaps be linked to differences in lipid content and age of the test fish. It is not known if these measurements would have included any substance adsorbed to the skin or present in the gut. As steady state had not been reached it is possible that the concentrations could become higher with longer exposures.

A sixth study is summarised in Appendix 1, suggesting a BCF for plants (Sea Lettuce *Ulva pertusa*) below 100 L/kg (Zhao *et al.*, 2014). There are a number of uncertainties with this study that mean the results should be treated with caution, including variable exposure concentrations (significantly exceeding the reported water solubility limit), presence of Dechlorane Plus in controls, potential growth inhibition during the test (which may or may not be related to the test

[17] Tomy *et al*. (2008) performed molecular modelling for the global minimum energy conformer of the Dechlorane Plus structure using semi-empirical AM1 calculations in the Spartan ES program. However, as the modelling resulted in the chair conformation for the cyclooctane moiety for both isomers, the calculations may have been unreliable, and so the values for molecular volume and dipole moments are not reported.

substance), and issues around the way that growth was calculated and kinetics fitted.

In summary, aqueous exposure is expected to be of limited importance in terms of bioaccumulation potential, and whilst significant uptake has been shown to occur in fish, there are no reliable measured fish BCF data.

3.4.1.2.2 Dietary exposure

OECD TG 305 advises that dietary exposure is more suitable than aqueous exposure for substances with log K_{OW} >6. Five dietary studies for fish are available and four are summarised in Appendix 1 (Zitko, 1980; Xiao *et al*., 2013; Zeng *et al*., 2014a; Hang et al., 2013 [ABST]). The key study is Tomy *et al*. (2008), which is summarised in full here.

Tomy *et al*. (2008) report a dietary bioaccumulation laboratory test using juvenile Rainbow Trout (*Oncorhynchus mykiss*). The fish were exposed to doses of syn- and anti- isomers of Dechlorane Plus via their diet for 49 days (uptake phase), followed by 112 days of untreated food (depuration phase) to examine bioaccumulation parameters and possible metabolic products. Each treatment group consisted of 60 fish held in 200 L aquaria. Two groups of fish (initial mean weight 50 ± 5 g) were exposed separately to food dosed with 0.79 ± 0.03 µg/g (lipid weight) of syn- isomer and 1.17 ± 0.12 µg/g (lipid weight) of anti- isomer, while a third control group was fed unfortified food. Commercial fish food was blended for 20 minutes with corn oil spiked with known amounts of each isomer, followed by a further 20 minutes stirring with an aqueous gelatin binder. The food was air-dried for 40 minutes then extruded through a 4-mm-diameter noodler, dried at 10 °C for 48 hours, and crushed into pellets that were stored in the dark at -4 °C to limit the possibility of light-induced degradation. The concentrations of both Dechlorane Plus isomers did not decline in the food from the start of the exposure to the end of the depuration. Small amounts of the syn- isomer were detectable in the unfortified food (1.5 ng/g). The average lipid content of the food was 14.3 ± 0.3 per cent. Feed was presented by sprinkling at the surface of the water and was generally consumed by each group of fish within one minute. The daily feeding rate was 1.0 % of the mean weight of fish, adjusted after each sampling period based on the mean weight of the subsample of fish that were sacrificed. Flow-through conditions were used. The influent water was at 12 °C, pH 7.9-9.1 and dissolved oxygen was always at the level of saturation. A 12 h light:12 h dark photoperiod was maintained throughout the experiment.

Four fish were sampled from each tank on days 0, 7, 14, 21, 35, and 49 of the uptake period and on days 7, 22, 35, 49, 70, and 112 days of the depuration period. Fish were always sampled 24 hours after the previous feeding. Samples were homogenized and weighed prior to accelerated solvent extraction and purification (carcass only) by Florisil chromatography. Analysis was by both high and low resolution gas chromatography-mass spectrometry analysis (GC-MS) and also liquid chromatography-UV analysis. Quality control procedures included injections of hexane after every five samples and method (procedural) blanks. Method detection limits were estimated to be 0.02 pg/g (0.6 fmoles) for both isomers. When detected, concentrations of the Dechlorane Plus isomers in tissue of control fish were subtracted from that in fish exposed to treated food. Concentrations in fish were also corrected for lipid percent and recovery corrected using BDE-77, -126, -197, and -207.

Dechlorane Plus had no effect on growth rate, liver somatic index or mortality at the concentrations used.

Fish lipid content on days 49 and 161 were 6.9 ± 0.5 % and 7.3 ± 0.6 % for the anti- isomer treatment, 7.5 ± 0.3 % and 7.3 ± 0.7 % for the syn- isomer treatment and 8.6 ± 0.4 % and 7.1 ± 0.7 % for the untreated control group (which could indicate some variation in feeding rate in the controls), respectively (average of four fish per sample point). The growth rates of the fish were stated to be 0.0308±0.0020, 0.0316±0.0018 and 0.0353±0.0022 mass/d for the anti- isomer, syn- isomer and control fish treatments, respectively (based on a fitted linear growth model; see later discussion).

After the 49-day exposure period, neither isomer had reached a steady-state concentration in the fish. The data in the paper are shown graphically in terms of the amount of substance per fish rather than the more normal concentration units. The maximum arithmetic mean fish whole body (minus liver) mass of the syn- isomer (control- and lipid- corrected) present at the end of the uptake period was 2.2 nmole, or 1.44 µg (value read from a graph). The mass of the anti- isomer was 1.7 nmole, or 1.11 µg (value read from a graph). The presentation of data in this way is unusual; it would normally be expressed in terms of a wet weight concentration. As the lipid correction method is unclear, no attempt has been made to estimate what the concentration in fish would be at the end of the uptake phase (see also below).

The syn- isomer accumulated in the fish linearly with time (whole body minus liver) during the exposure phase with a calculated uptake rate of 0.045 ± 0.005 nmol/d. This rate corresponds to the initial slope of the plot of the amount of substance in fish against time. A similar uptake rate was also observed for this isomer in the liver. The uptake rate for the anti- isomer was calculated to be 0.018 ± 0.002 nmol/d over days 7 to 49, as there was a large increase in the amount of this isomer accumulated during the first seven days, after which time the uptake was linear. This was statistically different to the syn- isomer at the 95 % confidence level. These rates of uptake are considered further later.

The elimination of both isomers from the fish (whole minus liver) followed first order depuration kinetics according to the paper, with reported rate constants of 0.013 ± 0.003 d^{-1} (syn- isomer)[18] and 0.023 ± 0.004 d^{-1} (anti- isomer), reported assimilation efficiencies of 6.0 % (syn- isomer) and 3.9 % (anti- isomer) and calculated half-lives of 53.3 ± 13.1 days (syn- isomer) and 30.4 ± 5.7 days (anti- isomer).[19] However, Figure 1 in the paper shows that following an initial steep decrease in concentration of the syn- isomer over the first ten days of depuration, the concentration increased by a factor of two between days 59 and 100, after which the concentration declined once more. The paper does not discuss this pattern specifically. This is considered below.

Liver-specific uptake kinetics were similar to those observed in the carcass suggesting that uptake rates of the isomers are not tissue-specific. Depuration from the liver did not follow first order kinetics for either isomer. Elimination of the isomers from the liver was difficult to interpret because of suspected enterohepatic circulation and redistribution of the isomers in the liver during clearance from other tissues.

The biomagnification factor (BMF) values were reported to be 5.2 for the syn- isomer and 1.9 for the anti- isomer (whole fish minus liver), suggesting that the syn- isomer is more bioaccumulative. However, it is not clear how these values were obtained and they appear too high when compared to methods of calculation more in line with the methods recommended in the OECD 305 test guideline (see further discussion below).

None of the possible metabolic products of Dechlorane Plus (including dechlorinated, hydroxylated, methoxylated and methyl sulfone derivatives) were detected in the liver.

Discussion

Dietary studies provide a more environmentally realistic exposure route for very hydrophobic substances than aqueous exposure studies, and also provide a means to dose fish to see if

[18] Table 2 in the paper reports a depuration rate constant with units of "/d $\times 10^{-2}$" in the header, whereas the main text uses the unit of "/d". If the value inferred from Table 2 for the *syn*- isomer were 0.00013 d^{-1}, the half-life would be about 5,300 days. Arnot & Quinn (2015) (supporting information) show that "$\times 10^{-2}$" is an error.

[19] Sverko *et al*. (2011) applied the method to estimate *in vivo* biotransformation rates in fish developed by Arnot *et al*. (2008) to the dietary test data reported by Tomy *et al*. (2008). The estimated biotransformation rate constants (normalized to a 10 g fish at 15 ºC) were 0.015 d^{-1} and 0.0083 d^{-1} for the anti- and syn- isomer, respectively. An uncertainty analysis indicated that 95 % of the expected values are approximately within an order of magnitude of the estimates. The equivalent biotransformation half-life is 47 and 84 days for the anti- and syn- isomer, respectively. Such biotransformation half-lives are slow, and comparable to biotransformation half-lives associated with chemicals that are known to biomagnify and bioaccumulate in aquatic food webs (Arnot *et al*., 2009).

uptake can occur and to follow depuration kinetics. Nevertheless, studies with other highly hydrophobic substances such as decabromodiphenyl ether (ECHA, 2012a) suggest that the presence of undissolved microcrystals can affect the degree of absorption across the gut and the nature of the food may also have an influence.

The Registrant describes the Tomy *et al*. (2008) study as reliable with restrictions. Based on the information available in the paper, the study method is broadly in accordance with the OECD TG 305-III (Dietary Exposure Bioaccumulation Fish Test). Minor deviations include the use of slightly fewer fish (e.g. five fish per sampling point is recommended) and lack of information on spiked feed homogeneity and total organic carbon content of the test water. The most important missing information is the actual wet weight fish concentrations at each time point (this is not provided in the supporting information either).

The BMF calculation in the paper was based on a method described in a previous paper by the same authors (Tomy *et al*., 2004a). There are a number of differences between this method and that recommended in the OECD TG 305-III. In particular, Tomy *et al*. (2004a) report rates for certain processes rather than the equivalent rate constant that is required for calculations by the OECD TG 305 methods[20]:

- Growth rate was calculated by fitting fish and liver weight data to a linear growth model, whereas the OECD TG recommends that a growth rate constant is obtained from the slope of a plot of natural logarithm of fish wet weights against time, separately for the uptake and depuration phases. This cannot be done precisely in the absence of the raw data. However, if it is assumed that the initial fish weight was 50 g, and that the growth rate (rate of change of fish weight with time) was fitted using an equation of the form (1 + b × time), the expected fish concentrations at each time point during the study can be estimated approximately using the growth rates given in the paper (0.0308 mass/day for anti-DP and 0.0316 mass/day for syn-DP). Using these back-calculated fish weights it is then possible to estimate the rate constant for growth dilution from the slopes of plots of ln [back-calculated fish weight] versus time. Using this approach the rate constant for growth dilution (k_g) can be tentatively estimated to be around 0.01 d^{-1} for both anti-DP and syn-DP, although it should be noted that the plots show a slight deviation from linearity.

- Fish concentrations were lipid-corrected and corrected for growth dilution by multiplying them by a factor of (1 + b × time), where b is the growth rate. The method used for lipid correction is not clear, but it is possible that the data have been corrected to give them on a lipid weight basis prior to correcting for growth (although this cannot be ascertained). The OECD TG recommends that correction for growth is done separately. However, the method used by Tomy *et al*. (2008) effectively estimates the amount of substance present in the fish (rather than the concentration). Such data can be used directly to estimate the growth-corrected depuration rate constant from the slope of a plot of ln [amount per fish] versus time. This is the “alternative” method for estimating the growth corrected depuration rate constant that is discussed in the OECD TG 305. Unfortunately the raw concentration/amount data are not provided in the Tomy *et al*. (2008) paper and are only presented graphically. The amounts per fish during the depuration phase for both anti-DP and syn-DP from can be estimated the plots in the original paper and estimated the approximate value for the growth-corrected depuration rate

[20] It is important to distinguish clearly between rates (or more correctly the rate of change) of a process and the rate constant for a process. For example, OECD TG 305 assumes that the rates of uptake, depuration and growth dilution are all first order processes, i.e. the rate of change in concentration is a result of a constant (rate constant) multiplied by the appropriate concentration. Thus, as the accumulation proceeds, the rate of the uptake and depuration changes but the rate constant remains constant. In several places Tomy *et al*. (2008) reported the rate rather than the rate constant. Typically, the rate for the initial phases of a first order process can be approximated to the initial slope of the concentration-versus-time curve. Thus it is possible to estimate approximately the required rate constant from the rate data presented in the Tomy *et al*. (2008) paper in some instances.

constant (k_{2g}) to be 0.019 d^{-1} for anti-DP and 0.012 d^{-1} for syn-DP. These are reasonably consistent with the depuration rate constants of 0.023 d^{-1} for anti-DP and 0.013 d^{-1} for syn-DP reported by Tomy *et al*. (2008).

- It is also possible to estimate the overall depuration rate constant, and hence growth-corrected depuration rate constant, using the back-calculated fish weight data estimated above to convert the data on the amount per fish to a concentration in fish (µg/g (lipid?)[21]). The overall depuration rate constant (k_2) can be obtained from plots of ln [concentration (µg/g (lipid?))] versus time. Such plots have been constructed for the purposes of this assessment using the amounts per fish read from the graphs in the Tomy *et al*. (2008) paper and these give estimates for the k_2 values as 0.027 d^{-1} for anti-DP and 0.020 d^{-1} for syn-DP. Using the k_g value estimated above of 0.01 d^{-1}, results in growth-corrected depuration rate constants (k_{2g}) of approximately 0.017 d^{-1} for anti-DP and 0.010 d^{-1} for syn-DP. Given the assumptions made in estimating these values, agreement with the values of k_{2g} determined above using the amounts per fish data directly is good.

- It is also important to note that the above depuration rate constants are obtained by including the value for day 49 of uptake in the depuration plot. As noted earlier, for both anti-DP and syn-DP there was a relatively rapid decrease from the value on day 49 of uptake to that on day 7 of depuration. The inclusion of the day 49 of uptake value for the estimation of the depuration rate constant could be questioned as the fish were still being exposed on day 49. When the day 49 of uptake value is omitted, the growth-corrected depuration rate constant (k_{2g}) obtained from the amount per fish data is lower than the above values, around 0.017 d^{-1} for anti-DP and 0.0099 d^{-1} for syn-DP. Again these values are reasonably consistent with the above estimates.

- The assimilation efficiency was calculated with the equation:

$$\frac{\text{(control-corrected concentration in fish} \times \text{mass of fish)}}{\text{(control-corrected concentration in food} \times \text{mass of food eaten)}}$$

In contrast, the OECD TG recommends that it is calculated using the equation:

(derived concentration in fish at time zero of the depuration phase × overall (not growth-corrected) depuration rate constant) / (food ingestion rate constant × concentration in food × $(1 - e^{-(\text{overall depuration constant} \times \text{uptake duration})})$

This calculation cannot be performed precisely due to the lack of raw data, but it is possible to use the estimates for the k_2 value obtained above to estimate a value for the assimilation efficiency. The value of the concentration in fish at time zero of the depuration phase (C_0) can be estimated to be around 0.0059 µg/g (lipid?) for anti-DP, and around 0.0075 µg/g (lipid?) for syn-DP, from the plot of ln [back-calculated concentration] versus time. As mentioned above it is not clear if these are lipid-normalised concentrations or not. Using the known concentrations in food (1.17 µg/g (lipid weight) for the anti- isomer and 0.79 µg/g (lipid weight) of the syn- isomer), the values of the overall depuration rate constants estimated above (0.027 d^{-1} for anti-DP and 0.020 d^{-1} for syn-DP) and the feeding rate[22], the assimilation efficiency can be roughly estimated as 0.008 (0.8 %) for anti-DP and 0.016 (1.6 %) for syn-DP. These values are significantly lower than estimated by Tomy *et al*. (2008).

[21] As noted earlier, it is not clear how the concentrations have been lipid-corrected in this study.

[22] The feeding rate was 0.01 kg food/kg fish (1 % of body weight); if the concentrations are on a lipid basis then the feeding rate on a lipid basis is needed for the calculation. Using the food lipid content of 14.3 % and the lipid content of fish on day 49 of uptake of 6.9 % for anti-DP and 7.5 % for syn-DP the equivalent feeding rate on a kg lipid food/kg lipid fish can be estimated to be around 0.021 for anti-DP and 0.019 for syn-DP.

- Depuration half-life was calculated by the formula ln(2)/depuration rate constant. This is the same as OECD 305, except that for the latter, the growth-corrected depuration rate constant can be used. As the authors seem to have corrected the data for growth prior to analysis, then presumably the derived half-life is effectively already growth-corrected (see above and as also assumed by Arnot & Quinn, 2015).

- The equilibrium biomagnification factor (BMF) was predicted from the equation (assimilation efficiency × feeding rate) / depuration rate constant, where the feeding rate is "corrected for the lipid percentage of the food". The OECD TG 305 uses the same equation, with lipid correction for the feeding rate where lipid-corrected concentration data have been used. As the authors seem to have corrected the data for lipid prior to analysis, then presumably the reported BMFs can be considered to be lipid-normalised. However, as noted above the method used by Tomy *et al*. (2008) to estimate the assimilation efficiency is different to that recommended in OECD TG 305. This may be important when comparing the data with the results of other substances.

- For the uptake phase, Tomy *et al.* (2008) appear to report rates (in units of nmoles/day) rather than the rate constant (which has units of g/g/day). It is, however, possible to estimate an approximate rate constant for the uptake (k_1) from the initial rate of uptake[23]. Using the reported initial rates of uptake of 0.018 nmol/day for anti-DP and 0.045 nmol/day for syn-DP, the equivalent values of k_1 can be estimated as 0.0002 g/g/day for anti-DP and 0.00075 g/g/day for syn-DP. These values of k_1 correspond to an assimilation efficiency of approximately 0.02 (2 %) for anti-DP and 0.075 (7.5 % for syn-DP). Assuming the growth-corrected depuration rate constant (k_{2g}) is around 0.019 d^{-1} for anti-DP and 0.012 d^{-1} for syn-DP, the kinetic, growth-corrected BMF_{kg} can be estimated to be around 0.01 for anti-DP and 0.062 for syn-DP. Normalising these values to the lipid contents in fish at day 49 and the lipid concentration in food, gives the growth-corrected and lipid normalised BMF_{kgL} as around 0.022 for anti-DP and 0.12 for syn-DP. However, it should be noted that it is not clear how the raw data were lipid-normalised in the original study and so these lipid-normalised values should be treated with caution.

Whilst the study is considered to be reliable with restrictions by the Registrant, access to the original raw data is required for proper interpretation. An attempt to contact the lead author was unsuccessful, and so a number of assumptions and approximations have had to be made in order to attempt to calculate the appropriate kinetic parameters from the data. This has necessarily introduced some uncertainty into the analysis but the results of re-analysis suggests that the actual BMF from the study is much lower than originally reported by Tomy *et al.* (2008). The main findings of the re-analysis are summarised below:

	Anti-DP	Syn-DP
Growth-corrected depuration rate constant	~0.019 d^{-1}	~0.012 d^{-1}
Growth-corrected depuration half-life	~36 days	~58 days
Assimilation efficiency	~0.8-2 %	~1.6-7.5 %
Growth-corrected BMF	~0.01	~0.062
Growth-corrected and lipid-normalised BMF	~0.022	~0.12

[23] The rate of uptake = $k_1 \times [C_{food}]$ - $k_2 \times [C_{fish}]$. At the early stages of the uptake where the concentrations in fish are low the term $k_2 \times [C_{fish}]$ is small compared with the term $k_1 \times [C_{food}]$ and so the intial rate of uptake approximates to $k_1 \times [C_{food}]$.

This study has also been analysed in depth by Arnot & Quinn (2015) who critically reviewed a large number of published dietary feeding studies (based on information in the original publications rather than primary data). Arnot & Quinn (2015) state that the BMFs derived by Tomy *et al*. (2008) are not reproducible: by reading the depuration data from Figures 1 and 2 of the original paper (which plot the (control- and lipid-corrected) concentration of each isomer in nanomoles for whole body (minus liver) tissues against time in days), and transforming them (using natural logarithms) to re-calculate the depuration rate constant, growth-corrected kinetic BMFs of 0.046 and 0.023 were estimated for the syn- and anti- isomers, respectively. These are reasonably consistent with the values estimated above. The re-estimated growth-corrected depuration rate constant and half-life for the syn- isomer were consistent with those provided in Tomy *et al*. (2008), but the re-estimated growth-corrected depuration rate constant for the anti- isomer was slightly lower at 0.017 d^{-1}, with a higher growth corrected depuration half-life of about 40 days (again these values are reasonably consistent with the values estimated above). Arnot & Quinn (2015) also estimated lipid-normalised growth-corrected BMFs, but given the uncertainty in how the lipid normalisation was done in the original paper, these values are not indicated here (they are slightly higher than the BMFs without lipid normalisation).

Tomy *et al*. (2008) noted that in view of the high log K_{OW} of Dechlorane Plus and a BMF greater than 1, it is anticipated that Dechlorane Plus isomers will biomagnify in aquatic food webs. In contrast, the analysis presented in this report indicates that the BMFs actually derived by Tomy *et al.* (2008) are unreliable and so they are not considered further in this dossier.

Conclusions

Overall the Dossier Submitter agrees with the Registrant's assignment of the Tomy *et al*. (2008) study as "reliable with restrictions". Unfortunately it is not possible to fully analyse the study in line with the recommendations of OECD TG 305-III since the raw data are not available. Nevertheless, the calculations made in this dossier and by Arnot & Quinn (2015) indicate estimated growth-corrected BMFs of 0.01 – 0.023 for the anti- isomer and 0.046 – 0.062 for the syn- isomer. Lipid normalisation of these data is uncertain but it is possible that the lipid-normalised values would be around a factor of two higher than these values. Another factor that should be considered is that the study used a feeding rate of 1 % of body weight per day. OECD TG 305 recommends a feeding rate of 1-2 % of body weight. In theory, the BMF obtained in an OECD TG 305 study should be directly proportional to the feeding rate[24], but even if a higher feeding rate of 2 % of body weight had been used, the BMF would still likely be below 1 (i.e. around 0.12 for syn-DP, which has the higher BMF).

The following points are important:

- Neither isomer had reached a steady-state concentration in the fish after 49 days of uptake, implying that concentrations could become higher given sufficient exposure time. However, the kinetic approach used above (and presumably by Arnot & Quinn, 2015) would approximate to the steady-state situation. Using the overall depuration rate constants (k_2) of 0.027 d^{-1} for anti-DP and 0.02 d^{-1} for syn-DP, it can be estimated that it would take approximately 110-150 days to achieve 95 % steady state.

- The growth-corrected depuration half-lives are around 30 – 40 days for the anti- isomer and 50 – 70 days for the syn- isomer for juvenile Rainbow Trout (*O. mykiss*).

- The maximum arithmetic mean fish whole body (minus liver) (control- and lipid- corrected) mass of the syn- isomer present at the end of the uptake period was 2.2 nmole, or 1.44 µg (value read from a graph). The mean mass of the anti- isomer was 1.7 nmole, or 1.11 µg per fish (value read from a graph). Fish weight was around 51.5 g, but a wet weight concentration cannot be estimated as the lipid correction method is unclear.

[24] The BMF = feeding rate × assimilation efficiency/depuration rate constant. Thus assuming the assimilation efficiency and depuration rate constant do not vary much with feeding rate, doubling the feeding rate should double the BMF.

Turning to the other studies summarised in Appendix 1, the non-guideline study by Zitko (1980) with Atlantic Salmon *Salmo salar* is not valid for a variety of reasons. It does, however, indicate that uptake and elimination can occur in fish. The highest reported fish concentration was 176 µg/kg ww after 15 days, although it is not clear whether this included substance present in the gut or adsorbed to skin (whole fish were analysed). A depuration half-life of 58 days was estimated by the study authors, but this did not take any account of fish growth or lipid content changes. The fish growth rate for this part of the study was 0.19 d^{-1} (based on a plot of fish weight against time from day 16 of depuration). If the results are expressed in terms of mass of Dechlorane Plus, there was effectively *no change in the amount of Dechlorane Plus present in the fish during the 72-day depuration phase* (the range was 290-370 ng, with the lower value occurring after 16 days of depuration). Arnot & Quinn (2015; supporting information) estimated a growth-corrected depuration half-life of about 100 days for ca. 15 g, 5 % lipid content fish using the results of this study. It therefore supports the findings of a long elimination half-life by Tomy *et al*. (2008).

Xiao *et al*. (2013) found that juvenile Rainbow Trout *O. mykiss* appear to absorb at least 16 % of the dose from a single feed (a single exposure to 1 270 µg/kg in food led to a whole body concentration of around 12 µg/kg), although there are analytical uncertainties with this study. The study of Zeng *et al*. (2014a) showed that a steady state was not achieved over 50 days' exposure in Common Carp *Cyprinus carpio* muscle, serum or liver tissue, with the highest concentrations being detected at the end of the 50-day uptake period (when the total concentration in liver was ~615 µg/kg ww). This further supports the findings of the Tomy *et al*. (2008) study. The substance also accumulated in gonad tissue. This study suggests that factors other than lipid solubility (e.g. hepatic binding enzymes) could play important roles in determining deposition. Whole body concentrations were not reported and the small number of samples and variable depuration results also prevent any calculations of an overall depuration half-life. A BMF therefore cannot be derived from the data. However, residues remained in all tissues after 45 days of depuration (e.g. the total concentration in liver was ~250 µg/kg ww at the end of the study) which is consistent with the relatively long depuration half-life seen in other studies.

Benchmarking the fish bioaccumulation data

- Inoue *et al.* (2012) investigated the correlation of dietary BMF with BCF in Common Carp *Cyprinus carpio* for eight aromatic compounds with log K_{OW} values in the range 4.3 – 9.0. This indicated that a BMF (growth-corrected and lipid-normalised) above 0.31 can correspond to a (lipid normalised) BCF above 5 000 L/kg. A theoretical analysis by MacKay *et al*. (2013) provides information to suggest that BCF values of 5 000 and 2 000 L/kg correspond approximately to BMF values of 0.25 and 0.1, respectively. This assumes that chemicals partition to the lipid fraction of the fish with no metabolism or growth dilution, and "sets" values for respiration rate and absorption efficiency that may not be typical for all species. Although a simplification, this supports the empirical relationship reported by Inoue *et al*. (2012). The re-estimated BMFs from the Tomy *et al*. (2008) study do not correlate with a BCF above 5 000 L/kg. A theoretical BMF of around 0.092 – 0.12 for the syn- isomer (if the feeding rate had been 2 % of body weight rather than 1 %) would just about correlate with a BCF of 2 000 L/kg. Whilst it is possible that lipid normalisation could increase the BMF still further (perhaps up to about 0.24), this cannot be established with any certainty.
- In the absence of a reliable aqueous fish BCF value to compare to the REACH Annex XIII criteria, the depuration half-life is considered further. There may be significant variability between and within species (e.g. due to differences in lipid content and metabolic profiles). However, advantages of using this metric as a key indicator for bioaccumulation assessment are that it is relatively easy to determine and not so dependent on other variables within a particular study. The achievement of a high level of bioaccumulation is obviously related to uptake as well as depuration kinetics, since this affects body burdens. Nevertheless, in terms of the aims of protecting organisms from unpredictable adverse

effects, a long depuration half-life is a key determinant of bioaccumulation potential and is directly related to one of the protection aims of the PBT assessment, i.e. concentrations for a PBT substance may take a long time to decline once emissions cease.

Two benchmarking approaches have been used to compare the depuration half-life of Dechlorane Plus with other relevant substances:

(a) An Environment Agency report (EA, 2012) analysed depuration rate constants (k_2) from a large number of available BCF studies. A k_2 value ≤ 0.065 d^{-1} (95 % CI: 0.062 – 0.068) or a lipid-normalised k_2 ≤0.085 d^{-1} 95 % CI: 0.083 – 0.086)[25] was found to be consistent with a BCF of ≥5 000 L/kg (normalised to a 5 % lipid content)[26]. The 'growth-corrected lipid-normalised' k_2 values for Dechlorane Plus from Tomy *et al*. (2008) were 0.010 – 0.013 d^{-1} (syn- isomer) and 0.017 – 0.023 d^{-1} (anti- isomer). Thus the low rate of depuration seen in the feeding study with *O. mykiss* is consistent with a BCF above 5 000 L/kg.

(b) It is relevant to compare the data for Dechlorane Plus with polychlorobiphenyls (PCBs) and other substances previously assessed to be vB under REACH. In particular, PCB data were used to support the identification of perfluorohexane-1-sulfonic acid and its salts (PFHxS, CAS no. 355-46-4) as vB (the data are summarised in Appendix 7). There are nine studies, although only four provide useable depuration half-lives for this analysis. Twelve further substances had been determined as meeting the vB criteria up to May 2015. Seven studies covering four of those substances report a depuration half-life (see Appendix 6). The information is summarised in Table 13.

Table 13: Depuration half-lives and BCF values for chemicals meeting the vB criteria

Depuration half-life, days	BCF value, L/kg	Source
39 – 77	7 273	SCCPs (REACH vB)
77 – 87		
2.8 – 4.2	3 730 – 10 500	Musk xylene (REACH vB)
3.8, 105	≥11 495	D4 (REACH vB)
24 – 39	≥ 5 860	D5 (REACH vB)
19 – 22	12 600	
>28	>>5 000	Arochlor 1248 (commercial PCB mixture)
>42, 50		Arochlor 1260 (commercial PCB mixture)
>974		PCB-52

Therefore with one exception (musk xylene), substances already agreed to meet the vB criterion or identified as POPs based on BCF values generally have relatively long depuration half-lives of 20 days or more in at least one fish species. A depuration half-life above around 8-10 days is also suggestive of a lipid-normalised and growth-corrected BCF above 5 000 L/kg according to the analysis in EA (2012). The depuration half-life for Dechlorane Plus was around 30-40 days for the anti- isomer and 50-70 days for the syn- isomer in the dietary study of Tomy *et al*. (2008) with juvenile Rainbow Trout *O. mykiss*.[27]

[25] Equivalent to depuration half-lives above around 8-10 days, assuming first order kinetics.

[26] Goss *et al*. (2013) also consider the use of elimination half-life data in bioaccumulation assessment, taking a first principles approach without considering actual data. The proposed half-life corresponding to a BMF of 1 is 70 days assuming 100 % assimilation efficiency (longer if the assimilation rate goes down).

[27] Arnot & Quinn (2015) estimated a growth-corrected depuration half-life of about 100 days for a ca. 15 g fish with 5 % lipid content using the results of the Zitko (1980) study with Atlantic Salmon *S. salar*. However, this study is not valid for a variety of reasons: in particular co-exposure to other related substances might have affected the uptake or

> Zeng *et al*. (2014a) found that residues remained in all tissues in a study using Common Carp *C. carpio* after 45 days of depuration. The long depuration half-life for Dechlorane Plus in fish is therefore highly indicative of a very bioaccumulative substance.

As noted above depuration half-life can be influenced by a number of experimental factors such as species differences, age of fish, etc. Therefore it may be difficult to reach clear conclusions for borderline cases. Sufficient uptake of a chemical by an organism is also required, so depuration half-life alone may not be indicative of a very bioaccumulative substance. However, field monitoring data (see following sections) suggest that Dechlorane Plus is bioavailable, and can achieve a relatively high body burden in some cases that may be expected to be associated with toxic effects due to baseline narcosis (see Appendix 3, 4 and 6). Therefore the use of depuration half-life to guide decision-making is considered to be reasonable for Dechlorane Plus, and its very long depuration half-life is given a high weighting in the bioaccumulation assessment.

3.4.1.2.3 Sediment exposure

Li *et al.* (2014a) determined the bioaccumulation of Dechlorane Plus in the oligochaete *Lumbriculus variegatus*. The study was carried out using both laboratory-spiked sediment and field-collected sediment from an electronics recycling site in South China. The test was carried out in triplicate beakers containing approximately 120 g of wet sediment and 300 mL of moderately hard water, with each beaker containing 30 worms. The mean measured concentrations of anti-DP and syn-DP in the field sediments were 8.8 and 3.54 mg/kg organic carbon, respectively. For the laboratory-spiked sediments two exposure concentrations (high and low) were used for each of anti-DP and syn-DP. The mean measured anti-DP concentrations were 83.1 mg/kg organic carbon (high) and 24.3 mg/kg organic carbon (low). The mean measured syn-DP concentrations were 27.3 mg/kg organic carbon (high) and 7.66 mg/kg organic carbon (low). An uncontaminated sediment was used as a control. The organic carbon contents of the sediments were 2.75 % for the control and 1.80 % for the field sediment. The organic carbon content of the laboratory soil is not clear.

The test consisted of a 28-day uptake period followed by a 28-day (laboratory sediment) or 21-day (field sediment) depuration period. The test was carried out at 23 °C and the worms were not fed during the test. Approximately 150 mL of the overlying water was changed twice daily. The dissolved oxygen content of the water was 5.4±0.4 mg/L and the pH was 7.6. The sediment concentrations were found to remain constant during the uptake phase of the test.

The exposed worms behaved similarly to the control worms, with no overt avoidance of the sediment and no significant reproduction of the worms occurred.

The concentrations of anti-DP and syn-DP in the worms increased during the first 14 days and then reached a plateau (steady-state) between days 14 and 28. The biota-sediment accumulation factor (BSAF) was determined as the ratio of the uptake rate constant and the depuration rate constant obtained using a first order kinetic model. No obvious growth of the worms was reported to occur in the test (worm weights per replicate were similar before and after the test).

The uptake rate constants for anti-DP were determined to be between 0.027 and 0.037 g organic carbon/g lipid/day in the laboratory sediments and 0.037 g organic carbon/g lipid/day in the field sediment. The depuration rate constants for anti-DP were determined to be 0.092-0.095 d^{-1} in laboratory sediment and 0.18 d^{-1} in the field sediment and the BSAF was determined to be 0.29-0.39 g organic carbon/g lipid in laboratory sediment and 0.21 g organic carbon/g lipid in the field

metabolism of Dechlorane Plus, as well as the health of the fish.

sediment. For syn-DP the uptake rate constant was between 0.0298 and 0.0698 g organic carbon/g lipid/day in the laboratory sediments and 0.044 g organic carbon/g lipid/day in the field sediment, and the depuration rate constant was 0.063-0.15 d^{-1} in the laboratory sediments and 0.13 d^{-1} in the field sediment. The BSAF values for syn-DP were therefore 0.47-0.48 g organic carbon/g lipid in the laboratory sediments and 0.34 g organic carbon/g lipid in the field sediment.

All of the BSAF values determined were <1. The BSAF value for syn-DP was greater than for anti-DP and this difference was statistically significant ($p<0.05$) for the low-level laboratory sediment and the field sediment.

Discussion

The BSAF determined with *Lumbriculus variegatus* is in the range 0.21-0.39 g organic carbon/g lipid for anti-DP and 0.34-0.48 g organic carbon/g lipid for syn-DP. The BSAF for syn-DP was found to be higher than for anti-DP. The values obtained in the laboratory study are discussed further in Section 3.4.1.2.4 alongside the available BSAF values from field studies.

3.4.1.2.4 Field studies

Twenty-two biota monitoring studies that report some measure of bioaccumulation potential have been summarised in detail in Appendix 1 (Wu *et al*., 2010; Tomy *et al*., 2007; Mo *et al*., 2013; Klosterhaus *et al*., 2012; Peng *et al.*, 2012; He *et al*., 2014; Zhang *et al*., 2011b; Peng *et al*., 2014; Wang *et al*., 2015; Barón *et al*., 2013; She *et al*., 2013; Jia *et al*., 2011; Shen *et al*., 2011a; Wang *et al.*, 2012; Chen *et al*., 2012b; Muñoz-Arnanz *et al*., 2012; Zhang *et al.*, 2010b; Kim *et al.*, 2015; Wu *et al.*, 2013; Li *et al.,* 2014b; Sühring *et al*., 2015; Sun *et al.*, 2015). Other biota monitoring data are reported in Appendix 3.

In general, monitoring studies are of limited usefulness for bioaccumulation assessment because the concentrations that the organisms were exposed to are unknown. Some species are highly migratory, so exposure at the sampling location might not be very relevant (i.e. the body burden may result from exposures some distance away). The studies are often screening exercises, with several substances investigated in the same samples, and often only include relatively low numbers of samples. The lack of a suitably ring-tested analytical method means that the results should be treated with caution, especially when comparing studies undertaken by different laboratories and at different times. Comparisons are also limited by the expression of the concentration in terms of either wet or lipid weight (rarely both), the use of different tissues and potentially the age/size and health of the organism when it was collected (particularly dead or injured individuals that may have depleted fat reserves). This is important if the accumulation of Dechlorane Plus is linked to more factors than lipid content alone, as suggested by the studies of Zeng *et al*. (2014a), de la Torre *et al*. (2012), Zhang *et al*. (2011a), Li *et al*. (2013a), Chen *et al*. (2013b) and Zheng *et al*. (2014a) (summarised in Section 3.4.1).

Nevertheless, the available monitoring studies show that the two isomers of Dechlorane Plus are widely dispersed in the European environment. Evidence from around the world shows that uptake can clearly occur in a wide range of wildlife species throughout freshwater and marine aquatic food webs, from invertebrates and fish to piscivorous top predators such as Bald Eagle *Haliaeetus leucocephalus*, Double-crested Cormorant *Phalacrocorax auritus*, Eurasian Otter *Lutra lutra* and cetaceans (e.g. *Delphinus delphis*). Dechlorane Plus is also found in bird- and mammal-eating predators associated with aquatic environments (such as Peregrine Falcon *Falco peregrinus* and Polar Bear *Ursus maritimus*). From the small number of studies available, maximum levels in top predators in Europe are broadly in the range 0.1 – 1 µg/kg ww, although there are many non-detects.

Most European samples have been collected from relatively unpolluted environments, where the substance is more likely to be present at very low concentrations due to long range transport rather than (in)direct local releases. Such studies show that Dechlorane Plus can be present in wildlife (including top predators) in regions relatively remote from human activity, although the

levels are typically very low (<0.1 µg/kg ww). In contrast, studies in more polluted environments in China and near the U.S. manufacturing facility show higher levels, indicating that organisms have the potential to accumulate in the region of 1 – 10 µg/kg ww, and up to 1 mg/kg ww [97 mg/kg lw] in fish muscle in the vicinity of point sources (Wang *et al*., 2015) (whole body concentrations are not available). This suggests that if exposure in the European environment were to increase, levels in wildlife might also increase. The higher levels that have been found in wildlife exceed concentrations that are considered to be of concern within a bioaccumulation context (e.g. a "critical concentration" of 0.065 or 0.65 mg/kg ww [1.3 or 13 mg/kg lw] can be estimated for Dechlorane Plus based on a critical body burden of 0.001 mmol/kg ww recommended in the REACH PBT Guidance (ECHA, 2017a); see Appendix 7).

According to equilibrium partitioning theory, BSAF values should be in the range 1–2 when the partitioning of a non-ionic organic chemical is at equilibrium between the organic carbon in the sediment and lipids of an organism (e.g. Burkhard *et al*., 2004). Lower BSAFs imply that the partitioning of an organic compound into lipids is lower than expected, i.e. that the partitioning between the fish or invertebrate species and the sediment is not in equilibrium (which may be due to chemical disequilibrium between the water and sediment, limited bioavailability due to the amount and type of sediment organic carbon and/or dietary uptake efficiencies, and/or metabolism in the organism or its food items). In contrast, higher BSAFs suggest that the substance can accumulate to a greater extent than by simple partitioning alone. The available data for Dechlorane Plus are as follows:

- For fish, reported average BSAFs[28] for total isomers were below 1 in four studies (Zhang *et al*. (2011c): three species; Shen *et al*. (2011a): one fish species; Wang *et al.* (2012): one fish species; He *et al*. (2014): three species). However, another study (Wang *et al*., 2015) reported BSAFs above 1 for three fish species, with values up to 3.2 and 9.0 for the anti- and syn- isomers, respectively.
- For invertebrates, one study reported BSAFs below 1.7 (Wang *et al.* (2015): river snail & shrimp) whereas another reported BSAFs above 2 (Jia *et al*. (2011): oysters).
- BSAF values below 1 (in the range 0.2-0.5 g organic carbon/g lipid) have been determined for *Lumbriculus variegatus* in a laboratory study (Li *et al*. (2014a); see Section 3.4.1.2.3).

This conflicting information is difficult to interpret. The studies tend to be based on small sample sizes, with sediment and biota sometimes collected at different time points and/or locations in the same general area, so their reliability is uncertain. In addition, the ECHA PBT guidance R.11 (Appendix R.11-4) states that it is often difficult to distinguish between real uptake and adsorption to the organisms or interference of gut content in the determination of the BSAF values for highly hydrophobic substances. BSAF values of 0.1 and below may give an incomplete indication of bioaccumulation potential based on pore water concentrations. However, one study for fish and one for invertebrates suggest that BSAFs might exceed 2, suggesting an enhanced level of bioaccumulation. For two studies where the BSAF is below 1, the BSAF values for BDE-183 (a heptabromodiphenyl ether) are similar to those for Dechlorane Plus in the same samples. In the support document for bis(pentabromophenyl)ether, heptaBDE congeners were concluded to meet the B criterion of Annex XIII (ECHA, 2012a).

Detection of Dechlorane Plus (and anti-[DP-1Cl]) in eggs shows that maternal uptake and transfer to eggs can occur in birds. Similar maternal uptake and transfer has also been seen in fish (e.g. Wu *et al.* (2013) and Sühring *et al.* (2015)). The studies of Zhang *et al*. (2011a) and Zeng *et al*. (2014a) also show that the substance can cross the blood-brain barrier and be passed from females to eggs in fish. Li *et al.* (2014b) showed that the substance can cross the blood-

[28] Fish BSAFs are defined as the lipid normalized concentration in the fish divided by the organic carbon normalized sediment concentration.

brain barrier in frogs. Sensitive life stages and tissues are therefore exposed to the substance.

Of particular relevance to this assessment are field studies that indicate biomagnification between trophic levels. The interpretation of such studies is evolving and it is clear that they can be complicated by a range of factors such as migratory behaviour of the species sampled, difficulties in establishing trophic position and feeding relationships, concentration gradients in water and/or sediment, and measurement limitations (e.g. in terms of temporal and spatial coverage, sample numbers (especially for larger species), specific tissue versus whole body, contamination during sampling, processing and analysis, etc.). These findings should therefore be treated with caution. Whilst some studies do not provide convincing evidence of biomagnification (e.g. Barón *et al*. (2013), Peng *et al*. (2014) and Klosterhaus *et al*. (2012)), four independent studies of aquatic food webs provide some evidence of trophic magnification:

- Wu *et al*. (2010) calculated a TMF above 1 for both Dechlorane Plus isomers in a Chinese aquatic food web. The value for both isomers together was approximately five times higher than that of total PBDEs and similar to polychlorinated biphenyls in the same web (although the overall Dechlorane Plus concentrations were 1 – 2 orders of magnitude lower). Sample numbers were low. The TMF depends on the assignment of one species (a water snake) to the highest trophic position; inclusion of a top predatory fish (Northern Snakehead) results in a lack of biomagnification (and even biodilution for the anti- isomer). Levels in three benthic-feeding carp species are consistently higher than potential invertebrate prey, suggesting that biomagnification may occur for some feeding relationships although this might also be influenced by sediment ingestion. This study provides evidence of biomagnification for some feeding relationships in an aquatic food web, though this is not unequivocal.

- Tomy *et al*. (2007) investigated food web samples from Lake Ontario and Lake Winnipeg, Canada. In Lake Winnipeg, trophic level-adjusted BMFs (based on the ratio of lipid-corrected concentrations) for four feeding relationships were all below 1 for both syn- and anti- isomers, with the exception of the Walleye/Whitefish predator-prey relationship for the anti- isomer only (BMF of 11). In Lake Ontario, trophic level-adjusted BMFs for three of four feeding relationships were below 1 for both isomers. The exception was the Lake Trout/Smelt predator-prey relationship, with a BMF of 12 for the syn- isomer and 11 for the anti- isomer. These calculations assume that a predator consumes one prey species only, and as this is unlikely to be the case in reality, the BMFs should be treated with caution.

  A TMF value above 1 was calculated for the anti- isomer in Lake Winnipeg (TMF = 2.5, r^2 = 0.12, p = 0.04), but not for the syn- isomer, or either isomer in Lake Ontario. The positioning of some of the species in the food web is open to question, and the Lake Winnipeg results were based on fish muscle only, which introduces uncertainty. Low concentrations, the very small sample sizes and possibility of variable exposure raise additional concerns about the representivity of the data for these food chains.

  Whilst the study suggests that interspecies differences in bioaccumulation/ biotransformation are likely, and that biomagnification may be taking place in some aquatic food webs and feeding relationships, the evidence is equivocal.

- Wang *et al*. (2015) investigated trophic magnification in an aquatic food chain that receives discharges from the Dechlorane Plus production facility in China. Sample numbers were low, but the TMF was 1.9 (95 % CI: 1.1–3.4) for anti-Dechlorane Plus, and this was statistically significant. Total Dechlorane Plus concentrations were in the range 0.8 – 1.1 mg/kg ww for four of the five fish species sampled, including the species at the highest trophic level.

  In addition, the log-normalized concentration ratios of anti-DP-1Cl to anti-DP showed a significant relationship with trophic level (p < 0.001), implying that anti-DP-1Cl may have a higher trophic magnification potential than anti-DP.

  A significant negative correlation was found between f_{anti} and trophic level for the sampled

species (p < 0.01), suggesting that the organisms have lower uptake efficiencies and higher depuration rates for the anti- isomer compared to the syn-isomer.

- Sun *et al.* (2015) investigated the bioaccumulation of Dechlorane Plus in biota from the Island Mangrove Nature Reserve, Pearl River estuary, South China. A total of 22 samples from four species were analysed in the study and anti-DP was detectable in 100 % of the samples and syn-DP was detectable in 54 % of the samples. The TMF for total Dechlorane Plus was determined to be 2.31, although the regression was not statistically significant (p = 0.07). Estimated BMFs for various predator-prey combinations were in the range 1.27 to 11.8. These calculations assume that a predator consumes one prey species only, and as this is unlikely to be the case in reality, the BMFs should be treated with caution.

The interpretation of trophic transfer studies involving waterbirds is complicated by the fact that sample sizes are small, and a single tissue (usually egg, muscle or liver) is typically analysed. Zheng *et al*. (2014a) (summarised in Section 3.4.2) showed that fat tissue is an important compartment for Dechlorane Plus accumulation in the Domestic Chicken (*Gallus gallus*), so whole body burdens might be significantly different from those implied by measured concentrations in a single tissue (particularly muscle). Coupled with the uncertainties about the relevance of lipid normalisation, firm conclusions about trophic transfer in birds cannot be drawn from the available data.

3.4.2 Bioaccumulation in terrestrial organisms (soil dwelling organisms, vertebrates)

3.4.2.1 Screening information

Although there are significant uncertainties in the physicochemical data set, the combination of a predicted log K_{OW} >2 and log K_{OA} >5 indicate that Dechlorane Plus has the potential to bioaccumulate in terrestrial food webs if the rate of chemical transformation or metabolism is low, as suggested by Gobas *et al*. (2003) and Kelly *et al*. (2007). In particular, bioaccumulation of very hydrophobic substances (log K_{OW} >7) in terrestrial biota does not necessarily fall off with increasing K_{OW}. It is therefore important not to overlook the potential for terrestrial bioaccumulation for Dechlorane Plus.

It is not useful to estimate an earthworm BCF using QSAR approaches given the uncertainty in the log K_{OW} value and limitations of the QSAR equations themselves.

3.4.2.2 Laboratory studies

Short-term and *in vitro* studies are summarised in Appendix 1 (Zhang *et al*., 2014; Chabot-Giguère *et al*., 2013; Peng *et al*., 2014; Zhang *et al*., 2015). Due to limitations in terms of duration or experimental set up, these do not provide any relevant information for the assessment of bioaccumulation.

Mammalian studies are reported in Section 4.1.

Three studies involving birds are available and are summarised below:

- Li *et al*. (2013a) exposed male Common Quail (*Coturnix coturnix*) (6–8 weeks' old, with an average weight of 125 g) to commercial Dechlorane Plus mixed in corn oil by oral gavage for 90 days at different doses (0, 1, 10, and 100 mg/kg/d). Sixty animals were used in all. Liver, muscle and serum samples were analysed using GC-MS at the end of the exposure period. The LoDs for the anti- and syn- isomers were 46.12 and 27.85 µg/kg lw in muscle/liver, and 0.054 and 0.20 ng/mL in serum, respectively.

  Both isomers were detected in all of the tissues measured in the control group at the end of the 90-day exposure period (average concentrations in liver were 15 ± 8.1 and 10 ± 5.9 mg/kg lw for the anti- and syn- isomer, respectively), indicating a background level of exposure (e.g. from feed or air-borne dust). DP-1Cl was also detected in the control group (e.g. 0.131 mg/kg lw in liver).

In the exposure groups, the highest concentrations were detected in liver. For the 10 mg/kg/d dose group, the total liver concentration was ~1 750 mg/kg lw (260 ± 39 mg/kg lw for the anti- isomer and 1 500 ± 69 mg/kg lw for the syn- isomer). These levels were around ten times greater than in the lower dose group, and three times greater than in the highest dose group (although the levels of the anti- isomer were greatest in liver in the 1 mg/kg/d group, at 300 ± 120 mg/kg lw). The syn- isomer tended to accumulate more in the two highest dose groups, whereas the anti- isomer was dominant in the low-dose group (the isomer ratio was similar to the commercial product at this dose).

The highest average total concentration of the mono-dechlorination products syn-DP-1Cl and anti-DP-1Cl occurred in the 10 mg/kg/d group, reaching 1.2 mg/kg lw in liver. Two additional unidentified substances were detected in the tissue samples as well as in the commercial substance.

In conclusion, both isomers preferentially accumulate in liver rather than muscle or blood in Common Quail, but accumulation was not dose-dependent (with lower levels observed in the top dose group compared to the mid-dose group). There appeared to be enrichment of the syn- isomer at higher exposures. It is not known how long it would take to achieve a steady state.

- Zheng *et al*. (2014a) investigated dietary accumulation and tissue distribution in Domestic Chickens (*Gallus gallus domesticus*). Birds purchased from a market (several weeks old; n=12: 1 male, 11 females) were raised for seven months in a farmer's yard surrounded by e-waste recycling workshops in Qingyuan county, Guangdong province, China. Atmospheric particles (n=10, collected using a high-volume air sampler), chicken food (mixture of rice, wheat and other types of grain, n=9) and soil (n=10) samples were collected from the yard. After sacrifice, eight tissues (liver, muscle, heart, gonad, brain, lung, and fat from all birds, and kidney from ten) and digestive tract contents (n=12 for chyme[29], intestinal contents and faeces) were sampled, weighed and then stored at –20 °C until further analysis.

  After being spiked with surrogate standards (BDE-77, -181 & -205), approximately 2 g of lyophilized tissue sample were extracted with solvents, then spiked with known amounts of internal standards (BDE-118 & -128, 4-F-BDE-67 and 3-F-BDE-153) prior to instrumental analysis via GC-MS using electron capture negative ionization operated in the selected ion monitoring mode.

  Regular analysis of procedural blanks (n=17), spiking blanks, blind triplicate samples, and regular injection of solvent blanks and standard solutions were performed for quality control purposes. Trace amounts of the anti- isomer were detected in procedural blanks with median concentrations of 0.46 ng/mL (accounting for 15 % of the sample with the lowest Dechlorane Plus level), so this was subtracted from the sample results. The recoveries in the spiking blanks were 90 ± 6.5 %. No surrogate correction was made to the final concentrations. Target chemicals detected in the triplicate samples were consistent (RSD <15 %). LoQs for syn-DP, anti-DP, anti-DP-2Cl, and anti-DP-1Cl were 0.04, 0.12, < 0.01, < 0.01 µg/kg dw/ww in environment matrices; 0.21, 0.61, 0.01, 0.01 µg/kg dw/ww in digestive tract; and 0.11, 0.13, 0.01 and 0.01 µg/kg dw/ww in chicken tissues, respectively.

  The median (and range) concentrations of Dechlorane Plus (total isomers) in chicken food, atmospheric particulates and soil were 0.2 (not detected – 0.98), 1 500 (360–8 700), and 7 600 (5 900–10 000) µg/kg dw, respectively.

  The median (and range) concentrations of Dechlorane Plus (total isomers) in chyme, intestinal contents and faeces were 7.6 (3.7–1 100), 35 (14–580), and 31 (not detected–1 300) µg/kg dw, respectively. Mass balance calculations indicated that there was 52 % "absorption" [transfer?] from chyme to intestinal contents and 50 % "absorption" [transfer?] from intestinal contents to faeces. No significant differences in Dechlorane Plus levels were found between the intestinal contents and faeces (p > 0.05); while levels in chyme were

[29] Chyme is partly digested food that is expelled by the stomach into the duodenum.

significantly lower (p < 0.05).

The substance was detected in all tissues. Since there was only one male, gender differences in accumulation behaviour were not considered. Median Dechlorane Plus (total isomers) concentrations (and range) were in the order of fat (10 (3.4–72) µg/kg ww) > gonad (7.9 (0.82–417) µg/kg ww) > kidney (6.8 (1.07–460) µg/kg ww) > heart (6.3 (1.0–21) µg/kg ww) > liver (4.4 (0.79–320) µg/kg ww) > lung (2.8 (1.3–126) µg/kg ww) > brain (1.4 (0.43–5.2) µg/kg ww) > muscle (0.92 (not detected–124) µg/kg ww). The range for all tissues was 17 – 140 µg/kg lw.

The mass deposition percentage of Dechlorane Plus in individual tissues indicated that fat was the most important reservoir (accounting for 56 % of the residues), followed by liver (12 %) and gonad (12 %). No significant differences were found amongst the tissues levels (p > 0.05), except muscle contained significantly lower concentrations than those in liver, gonad, fat, and kidney (p < 0.05). This was thought to relate to the lower lipid content of muscle.

The lipid content of fat tissue was significantly higher than other tissues (p < 0.05) although fat did not show significantly elevated substance concentrations compared with other tissues (expect for muscle). This suggests that lipid content was not the only factor that influenced tissue distribution, and it was speculated that blood perfusion and sequestration by proteins could be additional factors (Government of Canada (2016) reports that the OECD QSAR Toolbox (2012) profile suggests a high level of protein binding for this substance).

Brain concentrations were not significantly different to those in other tissues, but as it has the lowest lipid content, the lipid-normalized concentration in brain was the highest among all tissues. The study suggested transfer to and retention of Dechlorane Plus in chicken brain, despite its high molecular weight and hydrophobicity.

The f_{anti} values varied from 0.39 to 0.79 in chicken tissues. Fat (0.65), brain (0.64), and liver (0.64) had higher f_{anti} values than the other tissues (p < 0.01), as well as soil (0.52). The f_{anti} value for the whole chicken was calculated as 0.57 ± 0.07, which was significantly higher than those in soil (t-test, p = 0.048). However, the f_{anti} values ranged from 0.39 to 0.73 in chyme, intestinal contents and faeces, respectively, and these were not statistically significantly different, suggesting that gastrointestinal absorption was not stereoselective. It was estimated that soil contributed 94–100 % of the substance in chyme. These results suggest a preferential accumulation of the anti- isomer in chicken compared with soil, which is not due to differences in gastro-intestinal absorption efficiencies.

Anti-DP-1Cl was detected in most samples of atmospheric particulates and soil at concentrations of 2.2–7.5 and 16–51 µg/kg dw, respectively, but not in chicken food. It was detected in three chyme samples at concentrations from 0.07 to 0.96 µg/kg dw and one faeces sample (1.12 µg/kg dw). In chicken tissues, concentrations of anti-DP-1Cl were in the range of 'not detected' to 4.7 µg/kg ww. It was detected in 67 % of heart and 83.3 % of liver samples (the detection frequency in other tissues was below 34 %). Anti-DP-2Cl was not detected.

Significant correlation was found between anti-DP-1Cl and anti-DP (p < 0.01) in both atmospheric particulates (r^2 = 0.98) and soil samples (r^2 = 0.79), and in both liver (r^2 = 0.99, p < 0.01) and heart (r^2 = 0.31, p < 0.05).

The ratio of anti-DP-1Cl to anti-DP was lower in soil (0.005 ± 0.002) than atmospheric particulates (0.010 ± 0.003). The ratios in heart and liver varied from 0.0017 to 0.01 and 0.001 to 0.009, respectively. No significant differences were found in the ratios between soil and chicken tissues (p > 0.05), implying that anti-DP-1Cl mainly derives from the dietary uptake rather than *in vivo* dechlorination. This study is considered by to be reliable with restrictions, because the birds were not dosed in a standardised manner, and the variability in individual tissue concentrations was high. The validity of comparisons based on median concentrations only is therefore open to question. Since the birds appear to have been only around one year old at sacrifice, it is also possible that higher concentrations might have been achieved had the exposure duration been longer. However, the study is important

because it shows that the anti- isomer is preferentially accumulated in chicken, which is presumably due to differences in metabolism and/or elimination. In addition, most trophic transfer studies in birds use measured concentrations in either liver or muscle only (see Section 5.5.1 of Appendix 1), and since these are not necessarily the main compartments for accumulation, whole body burdens might be significantly different.

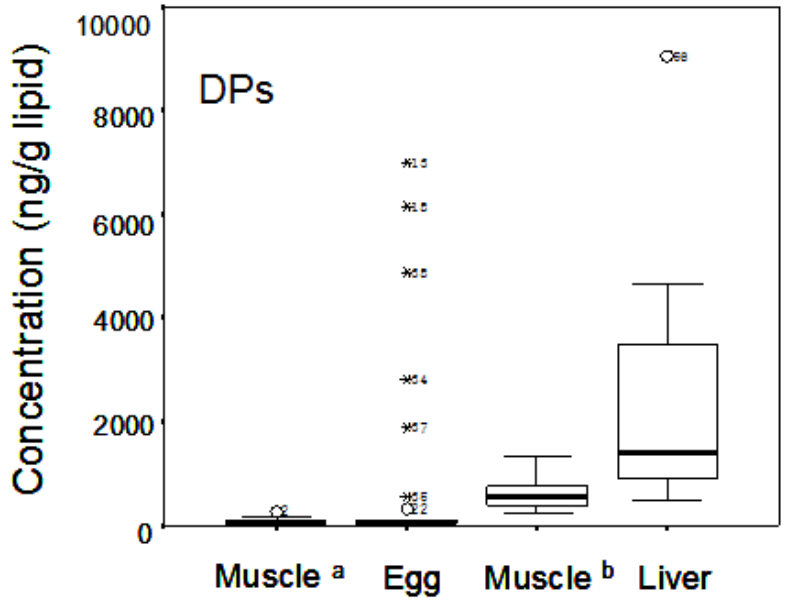
- Zheng *et al*. (2014b) investigated maternal transfer, potential metabolism and tissue distribution of Dechlorane Plus (and other flame retardants) during egg formation and embryo development in Domestic Chickens (*Gallus gallus domesticus*), apparently using the same birds as described in the study of Zheng *et al*. (2014a). Eggs were collected every day after the hens began laying, between March and April 2012 (n=79). The collected eggs were stored at ambient temperature in the yard. Nine chicks were hatched from ten collected eggs in an electric incubator and then sacrificed on the day of hatching, with liver and muscle tissues excised.[30] The hens were sacrificed in May 2012, and muscle samples (n=11) were collected. All samples were weighed and stored at -20 °C until further analysis, which followed the same procedures as Zheng *et al*. (2014a).

Dechlorane Plus (total isomers) was found in all of the samples, covering a wide range of concentrations from 0.77 to 9 034 µg/kg lw. The highest concentration was reported for a liver sample, but eggs also had a wide range of concentrations, some of which were around 7 000 µg/kg lw. The results are summarised in

Figure 4. The horizontal lines represents 5th, median and 95th percentiles, and the box represents 25th and 75th percentiles. Outliers exceeding 1.5 and 3 times of the height of box are shown as individual circles and asterisks, respectively. Unfortunately, the data for the two isomers and two potential transformation products are lumped together in the data table and figure in the original paper. Anti-DP-2Cl was not detected in any sample, but anti-DP-1Cl was found in 79 % of samples at concentrations between ‘not detectable’ and 30.7 µg/kg lw.

[30] Nine eggs that had not been incubated were also divided into albumin and yolk for analysis. However, no significant differences were found between levels in eggs from 0 d after the onset of incubation and these nine eggs (*t* test, $p > 0.05$) so their results are not provided in the paper.

Figure 4: Dechlorane Plus levels in chicken tissues



a: adult; b: chicken

(reprinted with permission from Zheng *et al.* (2014b). Copyright 2014: SETAC)

Eggs were analysed in three groups (collected at 0, 7 and 14 d of incubation, n=10 for each). No significant difference in concentration was found once extremes were removed (one-way ANOVA, $p>0.05$), with median levels of 16, 24 and 30 µg/kg lw, respectively. With the outliers included, the means (±standard error) were 1 336±878, 58±29 and 1 032±529 µg/kg lw (total concentration of Dechlorane Plus isomers and anti-DP-1Cl).

The mean (±standard error) concentration in hen muscle was 82±32 µg/kg lw (total concentration of Dechlorane Plus isomers and anti-DP-1Cl). The ratios of median concentrations in eggs to hen muscle for the syn- (0.40) and anti- isomer (0.67) were less than 1, indicating that these substances were more selectively retained by mothers. The maternal transfer potential of syn-Dechlorane Plus was lower than that of the anti- isomer. Consequently, the f_{anti} values in eggs (median 0.65, range 0.37 – 0.77; higher in albumin (0.89) than in yolk (0.59)) were significantly higher than those in hen muscle (median 0.56) ($p < 0.05$). The study therefore provides strong evidence for the stereoselective maternal transfer of Dechlorane Plus isomers to eggs.

The mean (±standard error) concentration in chick muscle and liver samples was 673±124 and 2 595±928 µg/kg lw, respectively (total concentration of Dechlorane Plus isomers and anti-DP-1Cl). The difference in levels in chick tissues compared with mid-incubation eggs was likely caused by lipid consumption during the last days of incubation[31]. Egg weights also decreased (by 10 % at 14 days after the onset of incubation) because of water loss and energy consumption during incubation.

With the assumption that the levels in eggs during incubation represented the initial level in eggs from which chicks were successfully hatched, the residual percentage of pollutants after incubation was roughly estimated by dividing the amount of substance in chicks (a summation of muscle and liver) by that in eggs (median levels were used for the calculation). The ratio for Dechlorane Plus was in the range 9 – 14 %. Although this estimation is crude (uncertainty exists due to data heterogeneity and underestimations of whole-body

[31] The lipid contents in chick muscle and liver (6.3±1.7 % and 13.1±2.8 %, respectively) were significantly lower than that in eggs (14.3±2.9 %) ($p < 0.05$).

amounts), the result suggests that there might have been significant metabolism by chicken embryos.

The f_{anti} values (0.68±0.02 in liver and 0.72±0.03 in muscle) in chick tissues were higher than those in eggs (0.65±0.07). The difference was statistically significantly different for muscle and eggs (p < 0.01). This suggests that stereoselective metabolism of the syn-isomer occurred during chicken embryo development.

This study is considered to be reliable with restrictions, because the birds were not dosed in a standardised manner, and the variability in individual tissue concentrations was high. The validity of comparisons based on median concentrations only is therefore open to question. However, the study shows that when exposure is sufficiently high, chicken eggs can accumulate up to around 7 mg/kg of Dechlorane Plus on a lipid weight basis [around 1 mg/kg ww[32]]. It also implies selective maternal transfer of the anti- isomer to eggs and stereoselective metabolism of the syn- isomer during chicken embryo development. In addition, it suggests that caution is needed in the interpretation of trophic transfer studies involving concentrations in bird eggs (see Sections 3.4.1.3 and 3.4.2.2), since they do not necessarily reflect parental whole body burdens.

Discussion

Studies with other highly hydrophobic substances such as decabromodiphenyl ether (ECHA, 2012a) suggest that achieving truly dissolved concentrations in many standard solvent vehicles is very difficult. The presence of undissolved microcrystals can mean that the degree of absorption across the gut can actually be higher at lower doses and solvent choice may also have an influence. This could confound conclusions drawn from any apparent dose-response relationship, since the nominal concentrations might not represent the actual dissolved concentrations. Dechlorane Plus does seem to have a reasonable degree of solubility in several organic solvents (see Section 1.5), so the variation seen might perhaps be more related to saturation of various pathways at different doses. The studies by Zheng *et al*. (2014a&b) involved birds contaminated from their local environment, so at least represent concentrations that can actually be achieved in nature.

The main conclusions that can be drawn from these bird studies is that uptake, distribution and elimination kinetics are complex. Zheng *et al*. (2014a) detected the substance in all tissues examined in a sample of Domestic Chickens (*Gallus gallus domesticus*): concentrations were variable, but the data suggest that concentrations were typically highest in fat (median: 10 µg/kg ww), with liver (median: 4.4 µg/kg ww) and muscle (median: 0.92 µg/kg ww) having lower concentrations. Fat was the most important reservoir (accounting for 56 % of the residues), followed by liver (12 %) and gonad (12 %). Muscle contained significantly lower concentrations than other tissues (p < 0.05). The comparable concentrations in these other tissues suggests that lipid content was not the only factor that influenced tissue distribution, and it was speculated that blood perfusion and sequestration by proteins could be additional factors. Wet weight brain concentrations were not significantly different to those in other tissues, but as it has the lowest lipid content, the lipid-normalized concentration in brain was the highest among all tissues. There was some evidence of preferential accumulation of the anti- isomer in chicken compared with soil. In contrast, the Zheng *et al*. (2014b) study found that liver had the highest levels in chicks of this species (up to 9 034 µg/kg lw). Similarly, Li *et al*. (2013a) found the highest concentrations in liver in Common Quail *Coturnix coturnix* (~1 750 mg/kg lw in the 10 mg/kg/d dose group after 90 days; lower total levels were found at the 100 mg/kg/d dose group, and there appeared to be enrichment of the syn- isomer as exposure increased).

Like fish, residues increased with longer exposure times and a steady state was not achieved. It is not known how long it would take to achieve a steady state in chicken or quail, and none of the studies investigated depuration kinetics.

Zheng *et al*. (2014b) reported a wide range of concentrations in Domestic Chicken eggs and

[32] The lipid content of the eggs was 15 ± 4, 14 ± 2 and 15 ± 4 per cent on days 0, 7 and 14 of incubation, respectively.

chicks. Concentrations in the mother birds were higher than in the eggs and chicks, and the maternal transfer potential of the syn- isomer was lower than that of the anti- isomer. There could also have been stereoselective metabolism of the syn- isomer during chicken embryo development. The study also showed that when natural exposure is sufficiently high, birds' eggs can accumulate up to around 7 mg/kg of Dechlorane Plus on a lipid weight basis [around 1 mg/kg ww].

3.4.2.3 Field studies

Six biota monitoring studies that report some measure of bioaccumulation potential have been summarised in detail in Appendix 1 (Sun *et al*., 2012; Yu *et al*., 2013; Barón *et al*., 2014a; Yu *et al*., 2014; Muir *et al.,* 2014 [ABST]; Peng *et al.*, 2015). Other terrestrial wildlife monitoring results from the open literature are reported in Appendix 5.

Monitoring studies for terrestrial wildlife face the same problems and limitations as those involving aquatic species (see Section 3.4.1.3). The available data show that European terrestrial wildlife is contaminated with Dechlorane Plus, so uptake is clearly occurring. Many European samples have been collected from relatively unpolluted environments, where the substance is more likely to be present due to long range transport rather than (in)direct local releases. Levels therefore tend to be lower than in more polluted environments close to the U.S. manufacturing site and in China (e.g. by two orders of magnitude in the study of Guerra *et al*., 2011).

The highest concentration in terrestrial bird eggs reported to date is around 7 mg/kg lw [around 1 mg/kg ww] (Zheng *et al*., 2014b) for Domestic Chicken (*Gallus gallus domesticus*) from an e-waste recycling region in southern China (Zheng *et al*. (2012) reported a slightly lower maximum concentration of just over 3 mg/kg lw). Sun *et al*. (2012) and Chen *et al*. (2013b) found that other terrestrial bird tissues (e.g. liver and muscle) may accumulate Dechlorane Plus up to 3 820 µg/kg [3.82 mg/kg] lw (approximately 500 µg/kg [0.5 mg/kg] ww). In addition, the latter study suggests that Dechlorane Plus burdens in terrestrial organisms could be driven by the accumulation of the anti- isomer, and factors other than lipid solubility (e.g. hepatic binding enzymes) could play important roles in determining deposition in terrestrial bird tissues (based on the ratio of muscle and liver levels). Similar findings apply to other highly hydrophobic halogenated substances, such as decabromodiphenyl ether (ECHA, 2012a).

Four studies have attempted to investigate biomagnification potential in terrestrial food chains involving birds:

- Yu *et al*. (2013) investigated the biomagnification of Dechlorane Plus in two terrestrial food chains in China. BMFs based on median lipid normalized concentrations were 2 in a rat–owl food chain, indicating biomagnification, and 0.3 for a sparrow–kestrel food chain, indicating biodilution. As previously noted, lipid normalisation might not be appropriate for this substance, and when wet weight is considered, the BMFs become 0.9 and 0.4, respectively. No significant differences were found for the BMF values of the two isomers in either feeding relationship. Other studies have found significantly higher concentrations of Dechlorane Plus in some of the same species from the same general area, which raises some doubts about the reliability of the BMFs, although they could be higher.

- Barón *et al*. (2014a) investigated biomagnification potential for terrestrial birds of prey in a Spanish national park using egg concentrations (total isomers) and stable isotope analysis. Although the paper did not find a clear linear correlation with trophic position, a strongly positive trend would result if the species in the highest trophic position is discounted (only a single egg was collected for that species).

- Sun *et al*. (2012) found a positive correlation between log normalized median muscle concentrations (syn- and anti- isomer separately) and $\delta^{15}N$ values at both rural and urban sites for three terrestrial passerine bird species: Light-vented Bulbul (*Pycnonotus*

sinensis), Long-tailed Shrike (*Lanius schach*), and Oriental Magpie-robin (*Copsychus saularis*) collected from southern China. Whilst this could imply biomagnification, comparisons of trophic position between locations based on raw $\delta^{15}N$ data are inappropriate since the baseline $\delta^{15}N$ values for each site are unknown. It is also unclear how the calculations would be affected if the concentrations were expressed as a geometric mean rather than median concentration. The variation in trophic status is also surprisingly wide for each species. The actual level of accumulation from the diet cannot be assessed. This study therefore only provides equivocal evidence that contamination levels increase with trophic position in terrestrial passerines.

- Peng *et al.* (2015) investigated the accumulation of Dechlorane Plus in terrestrial passerines from a national nature reserve in South China. The levels of total Dechlorane Plus ranged from 1.2 to 104 µg/kg lipid and the levels were found to be significantly (p=0.03) higher in insectivorous birds (mean 16.9 µg/kg lipid; n-=27) than in omnivorous birds (mean 6.4 µg/kg lipid; n-17). As insectivorous birds generally occupy a higher trophic level than omnivorous birds Peng *et al*. (2015) considered that this could be an indication of biomagnification. Unfortunately the trophic levels of the birds in the study were not determined.

The interpretation of trophic transfer studies involving terrestrial birds is complicated by the fact that sample sizes are small, and a single tissue (usually egg, muscle or liver) is typically analysed. Zheng *et al*. (2014a) showed that fat tissue is an important compartment for Dechlorane Plus accumulation in the Domestic Chicken (*Gallus gallus*), so whole body burdens might be significantly different from those implied by measured concentrations in a single tissue (particularly muscle). Coupled with the uncertainties about the relevance of lipid normalisation, firm conclusions about trophic transfer in birds cannot be drawn from the available data.

Guerra *et al*. (2011) found that the concentration of total Dechlorane Plus isomers in Peregrine Falcon *Falco peregrinus* eggs from birds with a known terrestrial diet was slightly lower than those with an aquatic-based diet in Spain, but of a similar order of magnitude in Canada. This study suggested differences in uptake in the two isomers, with the relative concentration of the anti- isomer in eggs from birds with a known terrestrial diet being significantly higher in Spanish samples compared to their Canadian counterparts.

Detection of Dechlorane Plus and anti-[DP-1Cl] in birds' eggs shows that maternal uptake and transfer to eggs can occur. Similarly, detection of these substances in human cord serum indicates transfer across the placenta and exposure of foetuses. Presence in human breast milk also means that exposure can continue prior to weaning. Sensitive life stages are therefore exposed to the substance. Concentrations in maternal sera imply that elevated concentrations may arise following prolonged exposure.

In addition, a number of studies have examined contamination of human tissues (Ren *et al*. (2009); Yan *et al*. (2012); Ben *et al*. (2013); Ben *et al*. (2014); Zhang *et al*. (2013); He *et al*. (2013); Wang *et al*. (2014); Chen *et al*. (2015); Cequier *et al*. (2013); Sahlström *et al*. (2014); Brasseur *et al*. (2014); Siddique *et al*. (2012); and Zhou *et al*. (2014)) and these are briefly summarised in Appendix 1. Studies involving humans are complicated by exposure in occupational and consumer settings. It is therefore difficult to interpret these data in terms of bioaccumulation assessment. Most of the studies are from China, and reflect local sources that presumably include exposure to Dechlorane Plus as vapour or in/on particulates at higher levels than might be expected under 'normal' environmental conditions (including exposure to contaminated indoor dust). However, the substance has also been detected in breast milk samples from North America, and is present in blood serum in the European population. The distribution of concentrations in various tissues is often skewed, with some high values but many lower ones. However, the studies clearly show that Dechlorane Plus is bioavailable to humans and frequently detected in general populations (with higher levels in workers). The Zhang *et al*. (2013) study is interesting because it showed an increase in blood levels with presumed exposure time (working life). Exposure to developing foetuses and new born children can occur due to its

presence in placenta and breast milk. Concentrations in non-occupationally exposed people appear to be typically in the region of 1-10 µg/kg lw depending on the tissue. The highest reported concentration in human blood is around 3 000 µg/kg [3 mg/kg] lw (Zhang *et al*., 2013), although given the low lipid content of blood, the wet weight concentration would be much lower. Anti-DP-1Cl is also frequently detected at lower concentrations.

In addition, Dechlorane Plus has been detected in terrestrial plants. For example, Wang *et al*. (2013a) detected mean total isomer concentrations of 1 038 µg/kg ww for vegetables and 877 µg/kg ww for grains collected at a site close to the Chinese manufacturing facility[33]. The maximum (for one vegetable type) was 2 720 µg/kg [2.72 mg/kg] ww.

3.4.4 Summary and discussion of bioaccumulation

Dechlorane Plus is very hydrophobic, but its molecular dimensions and relatively high n-octanol solubility indicate potential for bioaccumulation. Uncertainties in the physico-chemical data set make QSAR predictions based on log K_{OW} difficult to interpret, but a fish BCF of ≤5 500 L/kg is suggested. Aqueous exposure is likely to be of limited importance in terms of bioaccumulation potential. There are no reliable measured fish BCF data. Based on the apparent water solubility limit and reported concentrations in fish in the available aquatic exposure studies, BCFs above 10 000 L/kg can be estimated, but these are confounded by likely oral ingestion of the substance as a precipitate and/or adsorbed to food. The maximum wet weight fish concentrations measured in the aqueous BCF studies were 0.385 – 8.72 mg/kg after 30 days for Bluegill Sunfish *L. macrochirus* and 0.327 mg/kg after 56 days for Common Carp *C. carpio*, although this does not necessarily represent the concentration at steady state (it might also include the substance adsorbed to skin or present in the gut).

Dietary studies provide a more environmentally realistic exposure route for very hydrophobic substances. Whilst none of the available laboratory studies suggest a BMF > 1, they indicate that that it takes a long time to reach steady-state conditions (beyond 50 days), and that Dechlorane Plus has a long depuration half-life (around 50 days or more in fish). Tomy *et al*. (2008) is the best dietary study available, but the raw data are not available for analysis. Based on correlations and theoretical considerations, the long depuration half-lives for Dechlorane Plus observed in fish by Tomy *et al*. (2008) (supported by the findings of Zeng *et al*., 2014a) are considered highly indicative that the fish BCF could exceed 5 000 L/kg. Other dietary studies show that juvenile *O. mykiss* can absorb at least 16 % of the dose from a single feed, and the substance has been shown to distribute throughout the body in *C. carpio*, including gonadal tissue.

Studies with mammals and birds show complex uptake, distribution and elimination kinetics with preferential accumulation in liver rather than muscle or blood in some species. The substance can be found in gonads and brain tissue, and can be transferred from mothers to eggs. There are similar findings in amphibians (Li *et al.*, 2014b). The comparable concentrations in most tissues suggests that lipid content may not be the only factor that influences tissue distribution; blood perfusion and sequestration by proteins could be additional factors. Like fish, residues in birds and mammals appear to increase with longer exposure times and steady state was not achieved in the laboratory tests. Also like fish, Dechlorane Plus has a long elimination half-life from rat liver, in the region of 180 days or more (Li *et al*. (2013b), discussed in Section 4.1).

There is conflicting information available on BSAFs although they can be difficult to interpret for highly hydrophobic substances. Four studies suggest BSAFs below 1 and one laboratory study also gave BSAF values below 1 for *Lumbriculus variegatus*. However, one field study reported

[33] Wang *et al*. (2010) reported soil concentrations in the range 377 – 13,400 µg/kg dw from sampling sites within 0.5 km of the Chinese manufacturing site (decreasing by an order of magnitude within 7.5 km).

BSAFs above 1 for three fish species, with values up to 3.2 and 9.0 for the anti- and syn- isomers, respectively and another reported BSAFs above 2 for molluscs. A BSAF above 2 suggests that the substance can accumulate to a greater extent than by simple partitioning alone. For two studies where the BSAF was below 1, the BSAF values for Dechlorane Plus were similar to those for BDE-183 (a heptabromodiphenyl ether) in the same samples.

Several field studies have attempted to measure biomagnification between trophic levels, in both aquatic and terrestrial environments. Some studies suggest trophic dilution, whereas others suggest trophic magnification. The lack of a standardised approach to the assessment of trophic magnification and other confounding factors (including variable exposure across concentration gradients in the sampled environment, small sample sizes, analysis of single tissues, and reliance on specific feeding relationships) mean that none of the studies is fully reliable.

Monitoring studies show that the two isomers of Dechlorane Plus are widely dispersed in the European aquatic and terrestrial environment. Evidence from around the world shows that uptake occurs in a wide range of wildlife species throughout freshwater and marine aquatic food webs, from invertebrates and fish to piscivorous top predators such as Bald Eagle *Haliaeetus leucocephalus*, Double-crested Cormorant *Phalacrocorax auritus*, Eurasian Otter *Lutra lutra* and cetaceans (e.g. *Delphinus delphis*). Dechlorane Plus is also found in bird- and mammal-eating predators associated with both aquatic and terrestrial environments (such as Peregrine Falcon *Falco peregrinus* and Polar Bear *Ursus maritimus*). From the small number of studies available, maximum levels in top predators in Europe are broadly in the range 0.1 – 1 µg/kg ww, although there are many non-detects.

Many European samples have been collected from relatively unpolluted environments, where the substance is more likely to be present due to long range transport rather than (in)direct local releases. Such studies show that Dechlorane Plus can be present in wildlife (including top predators) in regions relatively remote from human activity, although the levels are typically very low (<0.1 µg/kg ww). In contrast, studies in more polluted environments in China and North America show higher levels, indicating that organisms have the potential to accumulate in the region of 1 – 10 µg/kg ww. The highest concentrations have been observed in China, at up to 1 mg/kg ww [97 mg/kg lw] in fish muscle in the vicinity of point sources (whole body concentrations are not available), and around 0.5 – 1 mg/kg ww [3 – 7 mg/kg lw] in terrestrial bird tissues, including up to around 7 mg/kg lw [~1 mg/kg ww] in birds' eggs. This suggests that if exposure in the European environment were to increase, levels in wildlife might also increase. The higher levels that have been found in wildlife exceed those that are considered to be of concern within a bioaccumulation context (e.g. a "critical concentration" of 0.065 or 0.65 mg/kg ww [1.3 or 13 mg/kg lw] can be estimated for Dechlorane Plus based on a critical body burden of 0.001 mmol/kg ww recommended in the REACH PBT Guidance (ECHA, 2017a); see Appendix 7).

Differences in bioaccumulation patterns in terrestrial environments compared to aquatic are difficult to distinguish based on the available information. The concentration of total Dechlorane Plus isomers in Peregrine Falcon *Falco peregrinus* eggs from birds with a known terrestrial diet was slightly lower than those with an aquatic-based diet in Spain, but of a similar order of magnitude in Canada. Dechlorane Plus has also been detected in terrestrial plants at mean concentrations of 1 mg/kg ww for vegetables and 0.9 mg/kg ww for grains collected at a site close to the Chinese manufacturing facility (with a maximum for one vegetable type of 2.72 mg/kg ww). Uptake and translocation in plants has also been shown in a laboratory study although the results may have been affected by toxicity caused by other substances.

Although not easily interpretable in the context of bioaccumulation potential, studies of human exposure also suggest an increase in blood levels with presumed exposure time (working life). Concentrations in non-occupationally exposed people appear to be typically in the region of 1-10 µg/kg lw depending on the tissue. The highest reported concentration in human blood is around 3 000 µg/kg [3 mg/kg] lw, although given the low lipid content of blood, the wet weight concentration would be much lower. Detection in human cord serum indicates transfer across the placenta and exposure of human foetuses, and presence in human breast milk also means that exposure can continue prior to weaning.

The amount of information available for the anti- and syn- isomers varies amongst the studies. Where the information is available, the syn- isomer appears to be somewhat more bioaccumulative as it reaches slightly higher body concentrations or has a longer depuration half-life. However, the results for the anti- isomer remain of concern. For instance, the depuration half-life in the key fish bioaccumulation study is around three times the bench-marked value for other vB substances. Without a better understanding of what might affect bioaccumulation behaviour of the two isomers (for example metabolic pathways and/or switches between isomers *in vivo*), the two isomers are assumed to have the same bioaccumulation potential in the absence of further information.

4. Human health hazard assessment

Mammalian toxicity data are summarised in detail in Appendix 1. They are not included in the main part of this report because the proposal is to identify Dechlorane Plus as vPvB only. This section includes relevant information for the bioaccumulation assessment.

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

A toxicokinetic study conforming to OECD TG 417 is not available.

The registration dossier includes two robust study summaries for toxicokinetics assessment:

- The first unreferenced study, considered reliable with restrictions by the Registrant (due to the small number of animals) was performed in 1983. No guideline was followed and the study was not subject to GLP. ^{14}C-Radiolabelled Dechlorane Plus (31.5 mCi/mmol) was administered in corn oil once by oral gavage at a dose of 1 mg/kg bw (corresponding to 4.8 µCi) or 113 mg/kg bw (corresponding to 3.8 µCi) to Sprague-Dawley rats (*Rattus norvegicus*). The composition of the substance was stated to be the same as the commercial substance (the ratio of isomers was 5.4:1). The low dose group consisted of three females and two males, and the high dose group consisted of two females. Another group of two females was fed non-labelled Dechlorane Plus at 1 % in the diet for 14 days before gavage administration. No control animals were used. Excretion via urine, faeces, and expired air and residual concentrations in organs and carcass were determined.

  One rat was used for monitoring radioactivity in expired air and one rat was used for monitoring the time course of blood levels for 48 hours after administration of 1 mg/kg bw. Urine and faeces were collected from all remaining rats for 4 days, then the animals were killed and radioactivity in 17 different organs/tissues and carcass were determined.

  At four days after a single oral administration of 1 mg/kg bw, the percentage of the dose excreted in faeces was 83.5 % for females and 92.7 % for males (0.07 % and 0.01 % in urine, respectively). This indicates a maximum absorption of 16.5 % in females and 7.3 % in males.

  The percentage of the dose excreted in faeces in the higher dose (113 mg/kg bw) group was 96.5 % for females (0.009 % in urine). This indicates a maximum absorption of 3.5 % in females.

  Four days after single oral administration of 1 mg/kg bw to rats pre-treated with the non-labelled substance at 1 % in diet for 14 days, 102 % of the dose was excreted in faeces (0.03 % in urine) indicating almost no absorption.

  Excretion in expired air amounted to 0.004 % of the administered dose within 4 days.

  The concentrations in all organs and tissues investigated, besides liver and residual carcass, were below 1 ppm. At the high dose, the liver of females contained 1.66 ppm and the residual carcass contained 1.25 ppm. All organs and tissues besides liver and residual carcass contained well below 1 % of the dose. The livers of males and females at the low dose contained 1.60 and 2.29 % of the dose, respectively. The residual carcass of males and females at the low dose contained 5.09 and 5.05 % of the dose, respectively. The residual carcass of females at the high dose contained 0.90 % of the dose. The carcass of pre-treated females contained 4.44 % of the dose.

  Metabolites were not investigated.

  The Registrant concludes that “almost no” absorption occurs after oral administration to a single dose.

- The second unreferenced study, considered reliable with restrictions by the Registrant (due to the small number of animals and detection of more than 100 % of the administered dose in the faeces) was performed in 1979. No guideline was followed and the study was not subject to GLP. Two groups of three Sprague-Dawley rats (*R. norvegicus*) each were given a single oral dose of 0.57 mg of ^{14}C-radiolabeled Dechlorane Plus (27.6 µCi in 0.5 mL) (purity stated to be the same as the commercial substance) suspended in water with 5 % Tween 80 and 5 % gum arabic. Three rats were killed 4 hours after administration and the remainder after 24 hours, and Dechlorane Plus was determined by liquid scintillation in blood, kidneys, liver, urine, and faeces.

  Within 4 hours after oral administration, less than 0.1 % was excreted in urine. At 24 hours, less than 1 % had been excreted in urine, and a mean of 94.6 % (range: 76.1 – 104.8 %) of the administered dose was excreted in faeces, indicating a maximum absorption of around 5.4 %. The sum of total radioactivity detected in blood, kidneys, liver, and urine was at or below 6 % of the total dose.

  Blood (total blood volume) contained less than 2 %, kidneys contained less than 1 %, and liver contained less than 5 % of the administered dose.

  One metabolite was found in the liver but its identity and concentration was not reported.

  The Registrant concludes that Dechlorane Plus is poorly absorbed after oral administration, at a maximum of 6 % of the administered dose. Highest concentrations are found in the liver.

- A third study missing from the registration dossier is Li *et al*. (2013b), who exposed male Sprague–Dawley rats (*R. norvegicus*) (35 days' old with an average weight of 110 g) to commercial Dechlorane Plus mixed in corn oil by oral gavage for 90 days at different doses (0, 1, 10, and 100 mg/kg/d). Another group was exposed to 100 mg/kg/d of the substance for 45 days followed by 45 days' depuration, together with a control group that was fed uncontaminated food. Forty-two animals were used in all. Liver, muscle and serum samples were analysed using GC-MS. The LoDs for the anti- and syn- isomers were 70.44 and 108.31 µg/kg lw in muscle/liver, and 0.054 and 0.20 ng/mL in serum, respectively.

  Both isomers were detected in all of the tissues measured in the control group at the end of the 90-day exposure period (average concentrations in liver were 2.8 ± 1.2 and 0.9 ± 0.4 mg/kg lw for the anti- and syn- isomer, respectively according to the paper, but the supplementary data give slightly different values), indicating a background level of exposure (e.g. from feed or air-borne dust). DP-1Cl and DP-2Cl were not detected in the control group (LoDs for anti-DP-1Cl were 0.98 µg/kg lw in muscle and liver, and 0.042 ng/mL in serum, respectively).

  In the exposure groups, the highest concentrations of both isomers were detected in liver from the 100 mg/kg/d dose group, at 320 ± 49 mg/kg lw for the anti- isomer and 750 ± 120 mg/kg lw for the syn- isomer (i.e. total concentration ~1 000 mg/kg lw). These levels were 12–15 times higher than in muscle and around 5 times higher than in serum from the same group. In liver, the concentration of both isomers increased with the dose. However, in muscle, the highest concentration of the syn- isomer occurred in the 10 mg/kg/d group (~85 mg/kg lw). Some of the statements in the paper about highest concentrations of the anti- isomer and in other tissues do not seem to match the information provided in the supplementary data.

  The concentration ratio of the anti- isomer to total isomers was similar to the commercial substance in the 1 mg/kg/d group, but significantly decreased in the two higher dose groups, suggesting enrichment of the syn- isomer with increasing dose.

  The highest average concentration of syn-DP-1Cl and anti-DP-1Cl occurred in liver in the 100 mg/kg/d group, reaching 140 ± 51 and 480 ± 170 µg/kg lw, respectively. Average concentrations were 5-8 times lower in muscle in the same group, but whereas levels in

liver increased with dose, levels in muscle remained fairly constant. Two additional unidentified substances were detected in liver as well as in the commercial substance.

The treatment group that was exposed to 100 mg/kg/d for 45 days accumulated a lower amount of total isomers in the liver compared to the animals exposed for 90 days (achieving an average total liver concentration of ~310 mg/kg lw). This suggests that residues increase with longer exposure times. The amounts of both isomers in muscle and liver showed no statistically significant change during depuration, although levels in serum decreased significantly. The content ratio of syn- and anti- isomers in liver to those in liver plus muscle significantly increased after depuration compared with the end of the uptake phase. These data suggest that Dechlorane Plus is more prone to accumulate in liver or that the elimination rate in liver is lower than that in muscle. The content of both syn- and anti-DP-1Cl in the liver decreased significantly after depuration and neither was detected in serum after depuration. The elimination half-life of the syn- isomer was about 179 days in liver, 44 days in muscle and 24 days in serum. The elimination half-life of the anti- isomer was 54 days in muscle and 25 days in serum (the figure for liver is not provided as the concentration increased during the depuration phase, although not significantly).

In conclusion, both isomers preferentially accumulate in liver rather than muscle or blood, and have a long elimination half-life in rats. Residues appear to increase with longer exposure times – it is not known how long it would take to achieve a steady state.

Discussion

Based on the two studies summarised in the registration dossier, a single oral dose of 1 mg/kg bw in rats may lead to a maximum absorption of between 5 and 20 %. Higher doses, or dosing following 14 days' prior exposure suggest a lower level of absorption, although if the substance was present as microcrystals in the vehicle, the nominal concentrations might not reflect actual exposure to dissolved substance. About 90 % of the substance is excreted unchanged in faeces (excretion in urine and expired air is below 0.1 %). The absorbed substance is widely distributed in the body, with the highest concentration in liver. Four days after administration, between 1 % and 10 % of the administered dose was found in the carcass. Levels of around 1 – 2 ppm [mg/kg] may be reached in both liver and the residual carcass.

The main conclusion that can be drawn from the Li *et al*. (2013b) study is that uptake, distribution and elimination kinetics are complex, with preferential accumulation in liver rather than muscle or blood. Dechlorane Plus achieved levels of ~1 000 mg/kg lw in rat liver when dosed at 100 mg/kg/d via oral gavage for 90 days (the paper does not provide the lipid content so a wet weight concentration cannot be estimated). Like fish, residues increased with longer exposure times and a steady state was not achieved. Also like fish, Dechlorane Plus has a long elimination half-life from rat liver, in the region of 180 days or more.

None of the studies permit firm conclusions to be drawn about the level of accumulation or tissue distribution following exposure to low concentrations over long time periods.

5. Environmental hazard assessment

Aquatic and terrestrial organism toxicity data are summarised in detail in Appendix 1. They are not included in the main part of this report because the proposal is to identify Dechlorane Plus as vPvB only.

6. Conclusions on the SVHC Properties

6.1 CMR assessment

Not relevant for the identification of the substance as SVHC in accordance with Article 57(e) of REACH.

6.2 PBT and vPvB assessment

6.2.1 Assessment of PBT/vPvB properties

A weight-of-evidence determination according to the provisions of Annex XIII of REACH is used to identify the substance as vPvB. All available information (such as the results of standard tests, monitoring and modelling, information from the application of the analogue approach (read-across) and (Q)SAR results) was considered together in a weight-of-evidence approach.

6.2.1.1 Persistence

The available data on persistence have been considered in terms of unequivocal, equivocal and negative evidence that the substance is very persistent.

Unequivocal evidence

- There are no measured half-life data for degradation of Dechlorane Plus in surface water, sediment or soil. Therefore there is no unequivocal evidence that the half-life of the substance in these media is sufficiently long to meet the Annex XIII criteria for P or vP.

Equivocal evidence

- Predictions using the BIOWIN model suggest that biodegradation of Dechlorane Plus will be very slow. The BIOWIN results are the same as a number of hexachloro-norbornene-containing analogue chemicals that have been agreed to be persistent organic pollutants (POPs) under the Stockholm Convention. These POPs are considered to have long environmental half-lives consistent with the vP criteria of Annex XIII. For example, heptachlor has a half-life of up to two years in soil, whereas the half-life of chlordane in soil is around one year. These two substances are the closest analogues to Dechlorane Plus with measured data. Soil and sediment simulation studies for endosulfan (a much more polar substance) indicate that the hexachloro-norbornene part of the molecule is very stable: the water-sediment half-life was >120 days and the soil half-life of metabolites was between 123 and 391 days.

  In addition, the two possible microbial degradation pathways predicted for Dechlorane Plus are the same as the POP analogues. It is unlikely that metabolic rates for these pathways will be more rapid for Dechlorane Plus, which is significantly less water soluble than the POPs.

  This information is assigned a high weighting in the persistence evaluation.

- The water solubility data for Dechlorane Plus (<2 ng/L), together with a likely log K_{OW} value above 9, suggests that it will be strongly bound to organic carbon in sediment/soil particles and therefore likely to be of low bioavailability to micro-organisms for biodegradation. In addition, studies with fish do not suggest a high potential for

biotransformation (e.g. Tomy *et al.*, 2008). This supports the premise that the molecule is metabolically recalcitrant.

- Dechlorane Plus was detected in a lake sediment core layer corresponding to around 1980 (Qiu *et al*., 2007). Whilst this does not provide any information about half-life, it shows that the substance can persist in sediments for over 20 years.

- Dechlorane Plus has been detected in remote locations such as the Arctic and Antarctic in air, sediment and in wildlife such as Arctic Char (*Salvelinus alpinus*), Glaucous Gull (*Larus hyperboreus*), Black Guillemot (*Cepphus grylle*), Common Guillemot (*Uria aalge*), Ringed Seal (*Phoca hispida*) and Polar Bear (*Ursus maritimus*). This indicates long range transport of Dechlorane Plus, probably as a result of adsorption to particulates in the atmosphere.

Negative evidence

- None of the available data clearly show that Dechlorane Plus is rapidly degraded in water, sediment or soil. One biodegradation screening study (Chou *et al*., 1979) reports low recoveries of radioactivity under aerobic conditions after six weeks' incubation. However, as discussed in Section 3.1.2.1.2 of Appendix 1, there are significant deficiencies in the methodology. It was not performed according to a standard test guideline and the analytical method was inappropriate to assess the degradation of such a poorly water soluble substance as Dechlorane Plus. It is not considered to be valid.

In summary, although there are no environmental simulation studies available for Dechlorane Plus that provide an unequivocal measurement of the half-life in water, sediment or soil, several lines of evidence indicate that it meets the vP criteria[34] in Annex XIII of REACH. In particular, the predicted low level of biodegradability and structural similarity to chemicals that have been agreed to meet the Stockholm Convention definition of a POP, and lack of any predicted degradation pathways that are different to the POPs strongly point to the high probability that it will not degrade any faster than them. This conclusion is supported by its very low water solubility (suggesting limited bioavailability to micro-organisms once bound to solid matrices), lack of evidence of biotransformation in fish (supporting the premise that the molecule is metabolically recalcitrant) and field evidence suggesting persistence in sediment as well as widespread presence in remote regions.

6.2.1.2 Bioaccumulation

The available data on bioaccumulation have been considered in terms of unequivocal, equivocal and negative evidence that the substance is very bioaccumulative.

Unequivocal evidence

- None of the available BCF studies is valid, so it is not possible to unequivocally demonstrate that the substance has a BCF value above 2 000 L/kg (B) or 5 000 L/kg (vB). Based on the apparent water solubility limit and reported fish concentrations in the available aquatic exposure studies, BCFs above 10 000 L/kg can be estimated, but these are confounded by likely oral ingestion of the substance as a precipitate and/or adsorbed to food. They are therefore assigned a low weighting for the purposes of this analysis.

[34] A substance fulfils the vP criterion when the half-life is higher than:

- 60 days in marine, fresh- or estuarine water, or
- 180 days in marine, fresh- or estuarine water sediment, or
- 180 days in soil.

These are the same as the Stockholm Convention criteria.

Dietary exposure is more relevant, so the lack of a valid BCF study is not a hindrance for the evaluation of bioaccumulation.

Equivocal evidence

- Dechlorane Plus is a very hydrophobic substance, with a measured solubility in pure water below 2 ng/L (0.002 µg/L) at 20 °C and estimated log K_{OW} value ≥9. This meets the screening vB criterion (log K_{OW} ≥5). QSAR predictions based on log K_{OW} are uncertain, but a fish BCF of up to 5 500 L/kg is suggested, and one model predicts a BAF of 7.5 × 10^5 L/kg ww. Its molecular weight of 654 g/mole, estimated maximum diameter of around 1.4 nm and n-octanol solubility of 470 mg/L at 25 °C mean that significant uptake via passive transport cannot be ruled out if aquatic organisms are exposed. Indeed, the n-octanol solubility suggests that lipid solubility might be relatively high, and fat tissue was the most important reservoir for the substance in a study involving Domestic Chickens (Zheng *et al*., 2011a). In addition, several studies suggest that factors other than lipid solubility (e.g. hepatic binding enzymes, blood perfusion and sequestration by proteins) could play important roles in determining tissue deposition (e.g. Zeng *et al*. (2014a), de la Torre *et al*. (2012), Guerra *et al*. (2011), Zhang *et al*. (2011a) and Li *et al*. (2013a&b) and Chen *et al*. (2013b)). The log K_{OA} >5 also suggests that it has a high biomagnification potential in terrestrial wildlife.

- The key dietary bioaccumulation study of Tomy *et al*. (2008) with juvenile Rainbow Trout *O. mykiss* is reliable with restrictions. In the absence of the original raw data, a definitive conclusion about the BMF from this study cannot be drawn. The theoretical BMF could have been around 0.12 for the syn- isomer. A BMF of 0.1 or above correlates with a lipid-normalised BCF of 2 000 L/kg based on both theoretical arguments and empirical observations (MacKay *et al*., 2013 and Inoue *et al.*, 2012).

- With one exception (musk xylene), substances already agreed to meet the vB criterion or identified as POPs based on BCF values generally have relatively long depuration half-lives of 20 days or more in at least one fish species (see Appendix 6 and 7). A depuration half-life above around 8-10 days is also suggestive of a lipid-normalised and growth-corrected BCF above 5 000 L/kg according to the analysis in EA (2012). The depuration half-life for Dechlorane Plus was around 30-40 days for the anti- isomer and 50-70 days for the syn-isomer in the dietary study of Tomy *et al*. (2008) with juvenile Rainbow Trout *O. mykiss*.[35] Zeng *et al*. (2014a) found that residues remained in all tissues in a study using Common Carp *C. carpio* after 45 days of depuration. The long depuration half-life for Dechlorane Plus in fish is therefore highly indicative of a very bioaccumulative substance. Dechlorane Plus also has an elimination half-life from liver in the region of 180 days or more in Brown Rats *Rattus norvegicus* (Li *et al*., 2013b). These findings are assigned a high weight in the bioaccumulation assessment.

- Dechlorane Plus is bioavailable in laboratory studies. For example, juvenile *O. mykiss* can absorb at least 16 % of the dose from a single feed (Xiao *et al*., 2013). All available dietary laboratory studies suggest that it takes a long time to reach steady-state. Monitoring studies show that the two isomers of Dechlorane Plus are widely dispersed in aquatic and terrestrial food webs, including in areas relatively remote from human activity such as the Arctic and Antarctic. This involves invertebrates and fish as well as predatory birds and mammals such as Double-crested Cormorant *Phalacrocorax auritus*, Bald Eagle *Haliaeetus leucocephalus*, Peregrine Falcon *Falco peregrinus*, Eurasian Otter *Lutra*, Wolf *Canis lupus*, Polar Bear *Ursus maritimus* and cetaceans (e.g. *Delphinus delphis*). The highest levels are observed in polluted environments in China and near the U.S. manufacturing facility.

[35] Arnot & Quinn (2015) estimated a growth-corrected depuration half-life of about 100 days for a ca. 15 g fish with 5 % lipid content using the results of the Zitko (1980) study with Atlantic Salmon *S. salar*. However, this study is not valid for a variety of reasons: in particular co-exposure to other related substances might have affected the uptake or metabolism of Dechlorane Plus, as well as the health of the fish.

- Wang *et al*. (2015) reported field BSAFs above 1 for three fish species, with values up to 3.2 and 9.0 for the anti- and syn- isomers, respectively and Jia *et al*. (2011) reported BSAFs above 2 for molluscs. A BSAF above 2 suggests that the substance can accumulate to a greater extent than by simple partitioning alone.

- There is some field evidence of biomagnification between trophic levels:

  i) Wu *et al*. (2010) calculated a TMF above 1 for both Dechlorane Plus isomers (11.3 for the syn- isomer and 6.5 for the anti- isomer) in a freshwater food web from South China. The TMF depends on the assignment of one species (a water snake) to the highest trophic position. Inclusion of a top predatory fish (Northern Snakehead) results in a lack of biomagnification (and even biodilution for the anti- isomer). Levels in three benthic-feeding carp species were consistently higher than potential invertebrate prey, suggesting that biomagnification may occur for some feeding relationships although this might also be influenced by sediment ingestion.

  ii) Tomy *et al*. (2007) reported a lipid weight TMF value above 1 for the anti- isomer in Lake Winnipeg (TMF = 2.5, r^2 = 0.12, p = 0.04), but not for the syn- isomer, or either isomer in Lake Ontario. In Lake Winnipeg, trophic level-adjusted BMFs (based on the ratio of lipid-corrected concentrations) for four feeding relationships were all below 1 for both syn- and anti- isomers, with the exception of the Walleye/Whitefish predator-prey relationship (BMF of 11, for the anti- isomer only). In Lake Ontario, trophic level-adjusted BMFs calculated for four feeding relationships were below 1 for both isomers, with the exception of the Lake Trout/Smelt predator-prey relationship (12 for the syn- isomer and 11 for the anti- isomer).

  iii) Wang *et al*. (2015) reported a statistically significant TMF of 1.9 (95 % CI: 1.1–3.4) for anti-Dechlorane Plus in an aquatic food chain in China. Concentrations in fish were much higher than in the study of Tomy *et al*. (2007), although sample sizes were small.

  iv) Sun *et al.* (2015) reported a TMF for total Dechlorane Plus of 2.31 in a Chinese aquatic food web, although the regression was not statistically significant (p = 0.07). Estimated BMFs for various predator-prey combinations were in the range 1.27 to 11.8. These calculations assume that a predator consumes one prey species only, and this is unlikely to be the case in reality.

  v) Several studies have attempted to investigate biomagnification potential in food chains involving birds, and some suggest BMFs above 1 for some feeding relationships or a positive trend with apparent trophic position (e.g. Yu *et al*., 2013; Barón *et al*., 2014a; Sun *et al*., 2012; Peng *et al.*, 2015). As well as the usual interpretational issues surrounding field studies, uncertainties about the relevance of lipid normalisation and trophic positioning of the sampled species mean that firm conclusions about trophic transfer in birds cannot be drawn from the available data. These studies therefore only provide equivocal evidence that contamination levels increase with trophic position in birds.

  Field studies are difficult to interpret because there are many confounding factors, including variable exposure across concentration gradients in the sampled environment, small sample size and a limited choice of tissues that might not actually be representative of whole body concentrations. TMF values obtained for polluted environments close to point sources are also subject to uncertainty because organisms higher in the food chain may be receiving the substance directly via water or sediment in addition to exposure via food. Because of the confounding factors, all of these studies are assigned a low weighting in the bioaccumulation assessment.

  Dechlorane Plus has been detected in human cord serum, which indicates transfer across the placenta and exposure of human foetuses. The presence of the substance in human breast milk also means that exposure can continue prior to weaning. These data have generally been obtained in areas where high exposure to the chemical occurs (e.g.

e-waste recycling sites in Asia). It cannot be stated with certainty whether the presence of a substance in human tissues alone is indicative of a B or vB substance, so this information is assigned a moderate weighting for the bioaccumulation assessment.

- The REACH PBT Guidance (ECHA, 2017a) suggests a value of 0.001 mmol/kg ww [0.02 mmol/kg lipid (normalised to a lipid content of 5 %)] as a level of accumulation that is unlikely to lead to high body burdens. This is divided by a factor of 10 to account for species differences and organ versus body differences. In the case of Dechlorane Plus (with a molecular weight of 653.73 g/mol), this "critical concentration" is equivalent to 0.65 mg/kg ww [13 mg/kg lw] (without the additional factor of 10), or 0.065 mg/kg ww [1.3 mg/kg lw] (with the additional factor of 10) (see Appendix 7).

  The following maximum concentrations have been reported for environmental biota samples:

  ca. 1 mg/kg ww [~95 mg/kg lw] in fish muscle (Wang *et al.*, 2015);
  ca. 1 mg/kg ww [~7 mg/kg lw] in terrestrial bird eggs (Zheng *et al.*, 2014b);
  ca. 0.5 mg/kg ww [~3.8 mg/kg lw] in terrestrial bird liver and muscle (Sun *et al.*, 2012; Chen *et al.*, 2013b);
  ca. 3 mg/kg lw in human blood (Zhang *et al.*, 2013);
  1 mg/kg ww for vegetables and 0.9 mg/kg ww for grains (with a maximum for one vegetable type of 2.72 mg/kg ww) (Wang *et al.*, 2013a).

  In addition, a concentration of ca. 1 000 mg/kg [ca. 1 g/kg] lw in liver in Brown Rats *Rattus norvegicus* was achieved under laboratory conditions when dosed at 100 mg/kg/d via oral gavage for 90 days (Li *et al.*, 2013b). Similar findings were made in Common Quail *Coturnix coturnix* (Li *et al.*, 2013a), with the highest concentrations (ca. 1 750 mg/kg lw) detected in livers of the 10 mg/kg/d dose group after 90 days. None of the available laboratory fish studies using aqueous exposure are valid and they are confounded by variable exposure concentrations and potential ingestion of particulates and the substance adsorbed to food. Nevertheless, (non-steady state) concentrations up to 8.78 mg/kg ww were observed in Bluegill Sunfish *Lepomis macrochirus* (Boudreau and Rausina, 1973).

  Some of these concentrations exceed the critical concentration without the factor of 10, and all exceed the critical concentration with the factor of 10. The accumulation in rat liver exceeds the highest critical concentration by a factor of around 75. On this basis, Dechlorane Plus can clearly achieve concentrations in biota that are of concern in a bioaccumulation context. This finding is assigned a high weighting in the bioaccumulation assessment.

Negative evidence

- Some field studies do not indicate biomagnification (e.g. Klosterhaus *et al.*, 2012; Barón *et al.*, 2013; Peng *et al.*, 2014), or suggest BSAFs below 1 (Zhang *et al.*, 2011c; Shen *et al.*, 2011a; Wang *et al.*, 2012; He *et al.*, 2014). One non-standard laboratory study also gave BSAF values below 1 for *Lumbriculus variegatus* (Li *et al.*, 2014a). However, the use of field evidence is given a low weighting in this analysis, and there are complications in the interpretation of BSAF data for highly hydrophobic substances. It may also be noted that for two studies where the BSAF was below 1, the BSAF values for Dechlorane Plus were similar to those for BDE-183 (a heptabromodiphenyl ether) in the same samples.

Significant limitations in the available regulatory data set create uncertainty in the bioaccumulation assessment. A high level of bioaccumulation can be expected based on simple screening data related to physico-chemical properties and molecular parameters. There are no definitive data from fully valid studies showing that Dechlorane Plus has a fish BCF above 5 000 L/kg, a fish BMF > 1 or BSAF > 1 in the laboratory. Evidence from field studies is

conflicting; whilst some suggest TMF/BMF/BSAFs above 1, none of the studies is considered to be particularly reliable. Nevertheless, the substance is widely dispersed in both aquatic and terrestrial food chains, including top predators. In terms of the aim of protecting organisms from unpredictable adverse effects, a long depuration half-life is a key factor since substance concentrations may take a long time to decline once emissions cease. Dechlorane Plus has a long depuration half-life in fish consistent with other substances that have a fish BCF above 5 000 L/kg (supported by a long depuration half-life in mammalian liver). Levels achieved in laboratory exposures and detected in a variety of wildlife species indicate that Dechlorane Plus can achieve a relatively high body burden in some cases, consistent with levels that may be associated with toxic effects due to baseline narcosis (see Appendix 3, 4 and 6). These are the principle reasons why the substance is concluded to meet the very bioaccumulative (vB) criteria[36] in Annex XIII of REACH.

6.2.1.3 Toxicity

6.2.1.3.1 Fulfilment of the T criterion based on human health classification

The substance does not appear to cause relevant adverse effects in mammals via oral or dietary exposure at concentrations above 1 000 mg/kg bw/d, although there are some data gaps (e.g. there are no long-term studies exceeding 90 days, which might be important given the apparently slow uptake of the substance). The dosing vehicles might also limit exposure (e.g. due to the presence of undissolved micro-crystals), such that the high “doses” might not truly reflect the degree of exposure of the organisms.

Nevertheless, based on the available data, Dechlorane Plus does not meet the classification criteria for mutagenicity, toxicity to reproduction or specific target organ toxicity. The data are considered to be conclusive but not sufficient for classification for these endpoints. Carcinogenicity data are lacking (and are not required at the registration tonnage). There is some evidence for potential liver impairment in mice (Wu *et al*., 2012), but the significance of these findings is unclear.

Based on this information, the T criterion is not fulfilled at present.

6.2.1.3.2 Fulfilment of the T criterion based on ecotoxicity data

The very limited available data do not indicate that Dechlorane Plus fulfils the T criterion for the environment. All the available aquatic toxicity studies were conducted at concentrations significantly above the solubility limit of the substance in pure water (2 ng/L), and studies using dietary and gavage exposure also used relatively high concentrations that may not be environmentally relevant. The study of Liang *et al*. (2014) suggests that the substance might induce potentially toxic effects in fish liver, but is inconclusive. However, similar findings were also observed in a study with mice via oral exposure (see Wu *et al*. (2012) in Section 4.2.1 of

[36] A substance fulfils the vB criterion when the BCF in aquatic species is higher than 5 000 L/kg; or other information on the bioaccumulation potential [is available] … such as:

- Results from a bioaccumulation study in terrestrial species;
- Data from scientific analysis of human body fluids or tissues, such as blood, milk, or fat;
- Detection of elevated levels in biota, in particular in endangered species or in vulnerable populations, compared to levels in their surrounding environment;
- Results from a chronic toxicity study on animals;
- Assessment of the toxicokinetic behaviour of the substance;
- Information on the ability of the substance to biomagnify in the food chain, where possible expressed by biomagnification factors or trophic magnification factors.

Appendix 1). Recent non-standard studies with adult and embryo/larval Zebrafish suggest that Dechlorane Plus has biological activity and can induce effects such as oxidative stress, thyroid hormone-related gene up-regulation and neurobehavioural changes (Hang *et al*., 2013 [ABST]; Noyes *et al*., 2015; Kang *et al*., 2016; Chen *et al*., 2017). However, the reliability of the findings is uncertain, their links to population-relevant adverse apical effects is unknown, and benchmarking with other substances would be beneficial (where this has been done, the level of response seems lower for Dechlorane Plus than (chlorinated) phosphate esters). In general, the NOEC from these studies appears to be above 0.01 mg/L (for aqueous exposures), i.e. above the T criterion (and also significantly above the solubility limit in pure water).

It is highly unlikely that effects would be observed in short- or long-term toxicity tests involving aqueous exposure, as there would be difficulties in maintaining test concentrations given the very low water solubility and high hydrophobicity[37]. A more appropriate test might be a long-term fish toxicity study with relevant life stages using dietary exposure, although a standard test guideline does not exist.

Several studies show that maternal uptake and transfer to eggs can occur in birds (e.g. Guerra *et al*., 2011; Munoz-Arnanz *et al*., 2011; Gauthier *et al.*, 2007; Barón *et al*., 2014a; and Zheng *et al*., 2014b) and fish (e.g. Wu *et al*., 2013; Sühring *et al*., 2015). The studies of Zhang *et al*. (2011a) and Zeng *et al*. (2014a) also show that the substance can cross the blood-brain barrier, is present in gonads and can be passed from females to eggs in fish. Li *et al*. (2014b) found that the substance can cross the blood-brain barrier in frogs. Similarly, detection of these substances in human cord serum indicates transfer across the placenta and exposure of foetuses, and presence in human breast milk also means that exposure can continue prior to weaning (e.g. Ben *et al*. (2014) and Zhou *et al*. (2014)). Sensitive life stages and tissues are therefore exposed to the substance following prolonged exposure, and there is a possibility that they might experience subtle but important adverse effects that are not detectable in the studies currently available (e.g. because of their short duration).

No sediment toxicity studies are available.

Suitable long-term soil organism toxicity data are also unavailable, although two studies investigating molecular and biomarker end points have detected signs of oxidative stress and other damage (including on DNA) in the earthworm *Eisenia fetida* following exposures up to 14 days (Zhang *et al*., 2014) and 28 days (Yang *et al*., 2014), with a 28-d NOEC below 0.1 mg/kg dw. Although these findings cannot be related directly to adverse population-relevant apical effects, they imply that effects (e.g. on behaviour and reproduction) cannot be excluded in earthworms over the longer term.

Results from long-term or reproductive avian toxicity studies may also be used assess the T criterion. No mortalities occurred in male Common Quail (*Coturnix coturnix*) exposed up to 1 000 mg/kg bw/d for 90 days (Li *et al.*, 2013a). No effects were observed in Domestic Chicken (*Gallus gallus domesticus*) embryonic hepatocytes *in vitro* or embryos following egg injection (although there was a possible dose-dependent decrease in pipping success, the results were within the historical control range so cannot be considered significant). The available data do not suggest significant toxicity in birds, but a standard test guideline study is not available so the findings cannot be considered conclusive.

Dechlorane Plus is structurally related to known pesticides such as heptachlor (CAS no. 76-44-8) and chlordane (CAS no. 57-74-9) (see Section 1.4). However, the structures and physico-chemical properties of the analogues and Dechlorane Plus are not similar enough to conclude that Dechlorane Plus would have similar toxic properties.

[37] Indications of effects on growth of Sea Lettuce (*Ulva pertusa*) have been reported in a 14-d bioconcentration study by Zhao *et al*. (2014). However, the results of this study are not considered to be sufficiently robust to conclude that the T criterion is met.

In summary, the available information is insufficient to make a full assessment of the T criterion based on ecotoxicity data.

6.2.1.4 Additional considerations

As summarised in Appendix 2, several studies have detected 1,3- or 1,5-Dechlorane Plus monoadduct (DPMA) in environmental samples such as sediment and fish (e.g. Sverko *et al*., 2010b; Guerra *et al*., 2011; Tomy *et al*., 2013; Sühring *et al*., 2014; Wang *et al*., 2015; Wolschke *et al*., 2015; Rjabova *et al*., 2016). In some cases, the concentrations of DPMA isomers are greater than the total Dechlorane Plus concentration in the same samples. In addition, it is possible that failure to use a non-destructive clean-up procedure for sample preparation could lead to under-reporting of this substance (Rjabova *et al*., 2016).

Whilst there is uncertainty in the QSAR predictions, 1,3-/1,5-DPMA screens as being potentially PBT and/or vPvB. No information is available on mammalian toxicity, but if it reacts like aldrin or heptachlor via epoxidation in the environment, it could be neurotoxic and/or cause hepatotoxicity.

Given its structure, Dechlorane Plus is the only likely source of DPMA in the environment. There is no information on reaction rates or amounts that can be formed under relevant environmental conditions. Some other possible transformation products (e.g. hexachloronorbornadiene) also screen as potentially PBT and/or vPvB.

A definitive conclusion would require experimental data to confirm that these degradants are formed in relevant amounts in standard transformation studies, and also to confirm their properties. However, DPMA in particular flags an additional relevant concern as it is has been detected in biota (including in the Antarctic).

6.2.2 Summary and overall conclusions on the PBT and vPvB properties

Persistence

Based on the weight of evidence of the data available, it is concluded that Dechlorane Plus meets the criteria for vP in Annex XIII of REACH. This is based on:

- modelling of degradation potential and microbial metabolic pathways which suggests that biodegradation is likely to be very slow; and
- a low probability that it will degrade any faster than structural analogues that are considered to be very persistent under the Stockholm Convention.

This conclusion is also supported by the very low water solubility (suggesting limited bioavailability to micro-organisms once bound to solid matrices), monitoring data indicating that the substance can persist in sediments (a major sink) for many years, lack of evidence of biotransformation in fish (supporting the premise that the molecule is metabolically recalcitrant) and widespread occurrence in remote regions.

Bioaccumulation

Using a weight of evidence assessment of the data available, Dechlorane Plus meets the vB criteria in Annex XIII of REACH. This is based on:

- the long-depuration half-life determined in fish feeding studies which is indicative of a

BCF above 5 000 L/kg, by comparison with other substances (supported by a long depuration half-life in mammalian liver);

- numerous studies that show that the substance is widely dispersed in freshwater, marine and terrestrial food chains, including top predators; and

- evidence that the substance can exceed levels in biota that are of concern based on critical body burden considerations related to baseline narcosis.

This conclusion is supported by the detection of the substance in human blood, placenta and breast milk.

Toxicity

Based on the available ecotoxicity and mammalian data, Dechlorane Plus does not currently meet the T criterion. Long-term toxicity studies using relevant life stages of fish (via diet), sediment or soil organisms, and/or birds could be performed to clarify whether adverse effects can occur via these exposure routes. However, as the substance meets both the vP and vB criteria, these are not scientifically necessary for environmental risk management purposes.

Other concerns

The substances 1,3- and 1,5-Dechlorane Plus monoadduct (DPMA) have been detected in the environment, sometimes at higher concentrations than Dechlorane Plus in the same samples. DPMA might be under-reported because destructive sample preparation methods may degrade it. Dechlorane Plus is the only likely source of these two substances, although there is no information on reaction rates or amounts that can be formed under relevant environmental conditions. Based on predictive models, DPMA screens as being potentially PBT and vPvB on the basis of QSAR (although some of the predictions are uncertain). No information is available on its mammalian toxicity, but due to structural similarities to aldrin or heptachlor it might be epoxidised in the environment to form a substance that could be neurotoxic and/or cause hepatotoxicity. Experimental data would be needed to confirm these properties. However, as a degradation product of Dechlorane Plus, any concerns about DPMA would be alleviated by the identification of Dechlorane Plus as a substance of very high concern.

In conclusion, despite the lack of definitive data, Dechlorane Plus is proposed to be identified as a vPvB substance according to Art. 57(e) of REACH by comparing all relevant and available information listed in Annex XIII of REACH with the criteria set out in the same Annex, in a weight-of-evidence determination.

Part II

7. Registration and C&L notification status

7.1 Registration status

Table 14: Registration status

From the ECHA dissemination site[38]	
Registrations	2 Full registration(s) (Art. 10)

7.2 CLP notification status

Table 15: CLP notifications

	CLP Notifications[39]
Number of aggregated notifications	2
Total number of notifiers	170

8. Total tonnage of the substance

Table 16: EU and global tonnage status

Total tonnage band for the REACH registered substance (excluding the volume registered under Art 17 or Art 18)[40]	100-1 000 tonnes/year
Tonnage information from public sources other than registration dossiers, global volume[41]	5 000 tonnes/year

[38] https://echa.europa.eu/registration-dossier/-/registered-dossier/11906/1 (accessed 04/07/2017)

[39] C&L Inventory database, http://echa.europa.eu/web/guest/information-on-chemicals/cl-inventory-database (accessed 13/07/2017)

[40] https://echa.europa.eu/registration-dossier/-/registered-dossier/11906/1 (accessed 04/07/2017)

[41] Ren *et al.*, 2009.

9. Information on uses of the substance

Dechlorane Plus is an additive chlorinated flame retardant, introduced in the 1960s as a substitute for Dechlorane (Mirex) (CECBP, 2008). Its market is therefore presumably mature.

According to the website of one of the few known global producers (Oxychem Corp, USA)[42], Dechlorane Plus is used as a non-plasticizing flame retardant in a wide variety of polymeric systems, with applications in moulded or extruded electrical/electronic applications and 'wire and cable', including nuclear power plant control cable. A submission to the U.S. EPA in 2004[43] mentioned uses of the polymers in coatings for commercial electrical wires and cables, in connectors used in computers, and in plastic roofing material used for commercial buildings. Claimed benefits include maintaining electrical and physical properties, excellent UV stability, an increase in heat distortion temperature, and no blooming. It is claimed to be a more efficient flame retardant than brominated additives in some polymers. It also produces less smoke in polyolefin compositions than decabromodiphenyl ether.

Dechlorane Plus is not manufactured in the EU by Registrants to date[44]. It is noted that at the time of writing, only manufacturers and importers of quantities in excess of 100 tonnes per year are obliged to have registered. Non-confidential uses are listed below (taken from the ECHA public dissemination site, unless otherwise stated). A broad range of uses and applications are indicated, but it is not clear how many are currently relevant. Descriptor codes defined by the Registrant (taken from the ECHA public dissemination site) are presented in Table 19.

Use in an industrial setting (use of substance as such):

- Formulation (types of formulated products identified as adhesives, sealants; explosives; metal surface treatment products; polymer preparations and compounds).
- Formulation [mixing] of preparations and/or re-packaging (excluding alloys).
- Manufacture of plastics products, including compounding and conversion.
- Manufacture of other non-metallic mineral products, e.g. plasters, cement.
- Manufacture of computer, electronic and optical products, electrical equipment.
- General manufacturing, e.g. machinery, equipment, vehicles, other transport equipment.
- Manufacture of food products.
- Manufacture of fine chemicals.

The SPIN database confirms the use of Dechlorane Plus in adhesives and binding agents in the air transport sector over the past eight years, but does not present the volumes in use in this sector[45].

Dechlorane Plus is listed in the SPIN database. The annual use of Dechlorane Plus in Sweden from 1999 to 2006 was reported by Kaj *et al* (2010) and is listed below in Table 13. No use was reported for Finland, Norway and Denmark during this time. It was reported that in 2008 there was one preparation registered as raw material for production of plastic material, but there was no sale (KEMI, 2010 cited in Kaj *et al*., 2010). There do not appear to be any more recent notifications.

[42] http://www.oxy.com/OurBusinesses/Chemicals/Products/Documents/dechloraneplus/ dechlorane_plus.pdf. Another major producer mentioned in the scientific literature is Anpon Electrochemical Co., Ltd in Jiangsu, China.

[43] http://www.epa.gov/hpv/pubs/summaries/dechlorp/c15635.pdf

[44] Non-confidential extracts of registration dossier for Dechlorane Plus, published (disseminated) by ECHA via its Registered Substances information web pages, http://apps.echa.europa.eu/registered/data/dossiers/DISS-dffb4072-e357-47ae-e044-00144f67d031/DISS-dffb4072-e357-47ae-e044-00144f67d031_DISS-dffb4072-e357-47ae-e044-00144f67d031.html, accessed August 2017.

[45] http://spin2000.net/ accessed August 2017.

Table 17: Use of Dechlorane Plus and total number of preparations containing Dechlorane Plus in Sweden

Year	Amount (tonnes)	Number of preparations
2006	5	3
2005	11	3
2004	7	3
2003	4	3
1999	2	7

Source: (SPIN, 2010 cited in Kaj *et al*., 2010)

Use by professional users (use of substance as such):

- Formulation [mixing] of preparations and/or re-packaging (excluding alloys).
- Manufacture of rubber products.
- Manufacture of plastics products, including compounding and conversion.
- Manufacture of computer, electronic and optical products, electrical equipment.
- General manufacturing, e.g. machinery, equipment, vehicles, other transport equipment.
- Manufacture of fine chemicals.

Use by consumers (use of formulated products only):

- Adhesives, sealants.
- Explosives.
- Metal surface treatment products, including galvanic and electroplating products.
- Polymer preparations and compounds.

Service life release from wide dispersive exposure:

- Vehicles.
- Machinery, mechanical appliances, electrical/electronic articles.
- Electrical batteries and accumulators.
- Stone, plaster, cement, glass and ceramic articles.
- Fabrics, textiles and apparel.
- Leather articles.

Service life release in industrial setting:

- Rubber articles.

Product literature (OxyChem, 2007) available from the lead Registrants' website provides some useful additional information regarding performance and recommended loading rate of Dechlorane Plus in different polymer systems. This manual refers to the use of Dechlorane Plus in the following polymer systems: ABS; Chloroprene; DAP; EEA; EPDM; Epoxy; Neoprene; Nylon (6, 6/6, 12); PBT; Phenolics; Polyester; Polyethylene; EPR; EVA; Hypalon®; Hytrel®; Kraton; Natural Rubber TPU; High Impact Polystyrene; Polypropylene; Polyurethanes; SBR Block Copolymer; Silicon Rubber; TPE. It is unknown which of these are relevant in EU.

Table 18: Uses according to the REACH registration(s)

	Use(s)	Registered use?	Use in the scope of Authorisation?
Uses as intermediate	None registered	No	No
Formulation or repacking	• Polymer preparations and compounds • Semiconductors	Yes	Yes
Uses at industrial sites	• Adhesives, sealants • Polymer preparations and compounds • Semiconductors Sector of end use: • Formulation [mixing] or preparations and/or re-packaging (excluding alloys) • Manufacture of plastic products, including compounding and conversion • Manufacture of computer, electronic and optical products, electrical equipment	Yes	Yes
Uses by professional workers	Article category related to subsequent service life • Vehicles • Machinery, mechanical appliances, electrical/electronic articles • Electrical batteries and accumulators • Fabrics, textiles and apparel • Plastic articles	Yes	Yes
Consumer uses	• Adhesives, sealants. • Explosives. • Metal surface treatment products, including galvanic and electroplating products. • Polymer preparations and compounds.	Yes	Yes
Article service life	• Vehicles. • Machinery, mechanical appliances, electrical/electronic articles. • Electrical batteries and accumulators. • Stone, plaster, cement, glass and ceramic articles. • Fabrics, textiles and apparel. • Leather articles. • Rubber articles	Yes	Potentially

Quantities

Table 19: Non-confidential descriptor codes used in registration

Life cycle stage	Descriptor codes
Formulation	Process category PROC 23: Open processing and transfer operations with minerals/metals at elevated temperature Environmental release category ERC 2: Formulation of preparations Substance supplied to that use in form of As such
Formulation	Process category PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 6: Calendering operations PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 13: Treatment of articles by dipping and pouring PROC 14: Production of preparations or articles by tabletting, compression, extrusion, pelletisation PROC 27a: Production of metal powders (hot processes) PROC 27b: Production of metal powders (wet processes) Chemical product category PC 1: Adhesives, sealants PC 11: Explosives PC 14: Metal surface treatment products, including galvanic and electroplating products PC 32: Polymer preparations and compounds Environmental release category ERC 2: Formulation of preparations ERC 3: Formulation in materials Substance supplied to that use in form of As such
Use at industrial sites to manufacture products	Process category PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 6: Calendering operations PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 14: Production of preparations or articles by tabletting, compression, extrusion, pelletisation Environmental release category ERC 4: Industrial use of processing aids in processes and products, not becoming part of articles ERC 5: Industrial use resulting in inclusion into or onto a matrix ERC 6a: Industrial use resulting in manufacture of another substance (use of intermediates) ERC 6d: Industrial use of process regulators for polymerisation processes in production of resins, rubbers, polymers

Life cycle stage	Descriptor codes
	Substance supplied to that use in form of As such Sector of end use SU 10: Formulation [mixing] of preparations and/or re-packaging (excluding alloys) SU 12: Manufacture of plastics products, including compounding and conversion SU 13: Manufacture of other non-metallic mineral products, e.g. plasters, cement SU 16: Manufacture of computer, electronic and optical products, electrical equipment SU 17: General manufacturing, e.g. machinery, equipment, vehicles, other transport equipment SU 4: Manufacture of food products SU 9: Manufacture of fine chemicals Subsequent service life relevant for that use? No
Use by professional workers	Process category PROC 1: Use in closed process, no likelihood of exposure PROC 2: Use in closed, continuous process with occasional controlled exposure PROC 3: Use in closed batch process (synthesis or formulation) PROC 4: Use in batch and other process (synthesis) where opportunity for exposure arises PROC 5: Mixing or blending in batch processes for formulation of preparations and articles (multistage and/or significant contact) PROC 6: Calendering operations PROC 8a: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at non-dedicated facilities PROC 8b: Transfer of substance or preparation (charging/discharging) from/to vessels/large containers at dedicated facilities PROC 9: Transfer of substance or preparation into small containers (dedicated filling line, including weighing) PROC 14: Production of preparations or articles by tabletting, compression, extrusion, pelletisation Environmental release category ERC 8a: Wide dispersive indoor use of processing aids in open systems ERC 8c: Wide dispersive indoor use resulting in inclusion into or onto a matrix ERC 8f: Wide dispersive outdoor use resulting in inclusion into or onto a matrix Substance supplied to that use in form of As such Sector of end use SU 10: Formulation [mixing] of preparations and/or re-packaging (excluding alloys) SU 11: Manufacture of rubber products SU 12: Manufacture of plastics products, including compounding and conversion SU 16: Manufacture of computer, electronic and optical products, electrical equipment SU 17: General manufacturing, e.g. machinery, equipment, vehicles, other transport equipment SU 9: Manufacture of fine chemicals Subsequent service life relevant for that use? No
Consumer Use	Chemical product category PC 1: Adhesives, sealants PC 11: Explosives PC 14: Metal surface treatment products, including galvanic and electroplating products PC 32: Polymer preparations and compounds Environmental release category ERC 8a: Wide dispersive indoor use of processing aids in open systems Substance supplied to that use in form of In a mixture Subsequent service life relevant for that use? No
Service life (consumers)	Environmental release category ERC 10a: Wide dispersive outdoor use of long-life articles and materials with low release ERC 11a: Wide dispersive indoor use of long-life articles and materials with low release Article category related to subsequent service life AC 1: Vehicles AC 2: Machinery, mechanical appliances, electrical/electronic articles AC 3: Electrical batteries and accumulators AC 4: Stone, plaster, cement, glass and ceramic articles AC 5: Fabrics, textiles and apparel AC 6: Leather articles
Service life	Process category PROC 21: Low energy manipulation of substances bound in

Life cycle stage	Descriptor codes
(worker at industrial site)	materials and/or articles PROC 24: High (mechanical) energy work-up of substances bound in materials and/or articles PROC 25: Other hot work operations with metals Environmental release category ERC 12b: Industrial processing of articles with abrasive techniques (high release) ERC 12a: Industrial processing of articles with abrasive techniques (low release) Article category related to subsequent service life AC 10: Rubber articles

10. Information on structure of the supply chain

The lead Registrant has indicated that their supply chain is relatively short, with direct supply by them to formulators and industrial users. However, there is no information from the joint Registrant (or other suppliers yet to register). The structure of the supply chain for imported treated articles (if any) is unknown.

11. Additional information

11.1 Substances with similar hazard and use profiles on the Candidate List

There are three flame retardants on the Candidate List with PBT/vPvB properties, i.e. short-chain chlorinated paraffins (SCCPs) (CAS no. 85535-84-8), decabromodiphenyl ether (decaBDE) (CAS no. 1163-19-5) and hexabromocyclododecane (HBCDD) (CAS no. 3194-55-6). Dechlorane Plus is a potential substitute for decaBDE (according to U.S. EPA, 2014), for which an Annex XVII restriction has recently been adopted (with some derogations) and a proposal to list decaBDE as a POP under the Stockholm Convention is also under consideration.

Other substances with flame retardant uses and similar hazardous properties are or have been included on Annex XVII of REACH (for example polybromodiphenyl ethers and polybromobiphenyls), but are not on the Candidate List.

11.2 Alternatives

The lead Registrant has confirmed that they do not make any alternatives to Dechlorane Plus themselves. Further information on alternatives to Dechlorane Plus was gathered through direct contact with two of the lead Registrant's EU customers (downstream users of Dechlorane Plus). Some alternatives have been considered but to date no suitable alternatives have been identified that meet the mechanical and flame retardant properties of Dechlorane Plus.

11.3 Existing EU legislation

There are currently no legislative controls on Dechlorane Plus.

11.4 Previous assessments by other authorities

No other EU Member States have assessed Dechlorane Plus in detail.

Dechlorane Plus is being assessed by Environment and Climate Change Canada (ECCC) as part

of the 'Certain Organic Flame Retardants Grouping' under the Substance Groupings Initiative of Canada's Chemicals Management Plan. The ECCC has published a draft screening assessment with the conclusion that Dechlorane Plus meets the criteria for further risk management measures '*because it is entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity*' (Canada, 2016a). The public consultation for these reports is currently ongoing and ECCC expect to publish their final conclusions in late 2017 or early 2018.

If the proposed conclusion is confirmed in the final screening assessment, the ECCC will consider options for risk management including the implementation of regulatory and non-regulatory controls on its import, manufacture and use and will also consider additional measures to address potential transboundary sources.

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List of appendices

Appendix 1 Detailed summaries of data cited in the main report

Appendix 2 Transformation products

Appendix 3 Measured concentrations of Dechlorane Plus in biota associated with the aquatic environment

Appendix 4 Measured concentrations of Dechlorane Plus in biota associated with the terrestrial environment

Appendix 5 Other European monitoring studies

Appendix 6 Comparison of laboratory bioconcentration data between substances

Appendix 7 Benchmarking of bioaccumulation using Polychlorobiphenyls (PCBs)

Appendix 8 Predicted aquatic toxicity of selected Dechlorane Plus analogues using EPISuite v4.11

Appendix 9 Further references that appear relevant but are not included in the assessment