United States
Environmental Protection Agency

Premanufacture Notification Number: P-12-0453-0433
Office of Chemical Safety and Pollution Prevention

TSCA NEW CHEMICALS REVIEW PROGRAM STANDARD REVIEW RISK ASSESSMENT ON

MEDIUM-CHAIN CHLORINATED PARAFFINS (PMN P-12-0453)

AND

LONG-CHAIN CHLORINATED PARAFFINS (PMN P-12-0433)

This assessment was conducted under EPA's TSCA Section 5 New Chemicals Review Program. EPA is assessing Medium-Chain Chlorinated Paraffin (MCCP) and Long-Chain Chlorinated Paraffin (LCCP) chemicals as part of its New Chemicals Review program. As with all Premanufacture Notice (PMN) submissions, EPA followed the approaches, methods and statutory provisions of TSCA section 5 for the chlorinated paraffin PMNs assessments.

CONCLUSIONS

Based on its assessment of the available surrogate hazard and exposure information on P-12-0453 and P-12-0433, EPA/OPPT concludes the following pertaining to the manufacturing, processing and use of these PMN substances:

1. Occupational Exposures: given the assumptions, data and scenarios evaluated in this assessment, there were low risks found for workers from either dermal or inhalation exposures.

2. General Population Exposures (from environmental releases): given the assumptions, data and scenarios evaluated in this assessment, there were low risks found to humans from environmental releases via exposure to either drinking water or fish ingestion.

3. Environmental Assessment:
   a. Using estimated environmental concentrations, the PMN substances **may present an unreasonable risk following acute and chronic exposures to aquatic organisms.**

   b. Using available measured concentrations of MCCP and LCCP congener groups in the environment as supporting information, the PMN substances:
      i. Are expected to partition to sediment and may partition to soil through land application of biosolids and,
      ii. May be released to the environment at levels at or above estimated concentrations of MCCP and LCCP congener groups that **may present an unreasonable risk following acute and chronic exposures to aquatic organisms.**

4. PBT Assessment: The PMN substances **may be very persistent and very bioaccumulative**.

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1 INTRODUCTION

1.1 PMNS RECEIVED

INEOS Chlor Americas, Inc. (hereinafter "INEOS") submitted two Premanufacture Notices (PMNs) identified by EPA/OPPT as either medium-chain chlorinated paraffins (MCCPs; P-12-0453) of varying chain lengths with the formula $C_xH_{(2x-y+2)}Cl_y$ and "x" equaling 14 to 17 and "y" equaling 6 to > 24 or long-chain chlorinated paraffins (LCCPs; P-12-0433) of varying chain lengths with the formula of $C_xH_{(2x-y+2)}Cl_y$ and "x" equaling 18 to 20 and "y" equaling 6 to > 24. Table 1 lists the basic information INEOS supplied on these two PMNs which are intended to be sold under the trade name "Cereclor®".

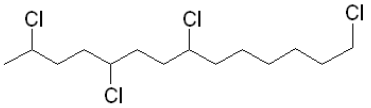
Table 1: Identification, Production Volume and Use of P-12-0453 and P-12-0433

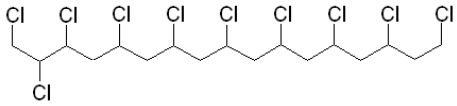
PMN	Chemical Name	1st Year Production Volume (kg)	% PMN in final Product	Uses	Log Kow	Water Solubility
P-12-0453	Alkanes, C_{14-17}, chloro (MCCPs; 40-60 wt% Cl)	CBI	5-20	74%: lubricant in MWFs; 17%: flame retardant/plasticizer in polymers; 7%: plasticizer in adhesives; and 2%: lubricant in sealants.	4.70 (E)	< 0.03 mg/L (E)
P-12-0433	Alkanes, C_{18-20}, chloro (LCCPs; 40-55 weight percent chlorination [wt% Cl])	CBI	15	100%: lubricant in metal working fluids (MWFs).	7.46 (E)	< 0.006 mg/L (E)
E = Estimated						

Though the specific PMNs in this application include MCCPs and LCCPs, this standard review presents data and information on short-chain chlorinated paraffins (SCCPs) and on very long-chain chlorinated paraffins (vLCCPs) analogs. The continuum of carbon chain length and degree/percent chlorination (wt% Cl) in all of the chlorinated paraffins (CPs) is important and the relationship among them needs to be kept in mind.

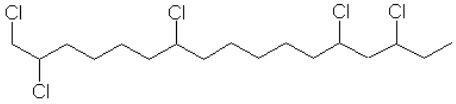
1.2 CHEMISTRY

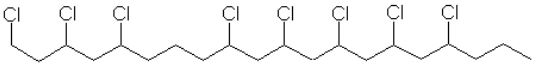
Shown below are the structures and chlorine content of P-12-0453 and P-12-0433 products are shown below.





P-12-0453: the average molecular formula ranges from C14H26Cl4 (low weight at ~40 wt% Cl) to C17H26Cl10 (high weight at ~60 wt% Cl). The parent hydrocarbon had the following measured composition: C14, 36 wt% (range 30-40 wt%); C15, 30 wt% (range 25-35 wt%); C16, 24 wt% (range 20-30 wt%); and C_{17}, 10 wt% (8-18 wt%).





P-12-0433: the average molecular formula ranges from $C_{17}H_{31}Cl_5$ (low weight ~40 wt% Cl) to $C_{20}H_{34}Cl_8$ (high weight ~50 wt% Cl). The parent hydrocarbon had the following measured composition: C_{17}, 17.06 wt% (max 20 wt%); C_{18}, 64.71 wt% (range 45-70 wt%); C_{19}, 13.67 wt% (range 15-27 wt%); and C_{20}, 2.13 wt% (range 4-12 wt%).

CPs have an unknown or variable composition (classified as UVCB[1] compounds for TSCA Inventory purposes) of polychlorinated n-alkanes. The carbon chain length usually varies between 10 and 30 carbon atoms and the degree of chlorination can vary between 30 and 75 wt%. EPA/OPPT subdivides CPs according to their carbon chain length into the following categories:

1. SCCPs ($C_{10\text{-}13}$)
2. MCCPs ($C_{14\text{-}17}$)
3. LCCPs ($C_{18\text{-}20}$)
4. Very long-chain CPs (vLCCP, $C_{>20}$)

SCCPs and MCCPs exist as liquids at standard temperature and pressure. CPs with a carbon chain length $\geq$ 18 are subdivided based on their physical state, which is a function of chain length and chlorine content. The LCCPs and vLCCPs up to 70 wt% Cl are typically liquids (40 – 55 wt% Cl) while above 70 wt% CL they are waxy solids.

CP products contain a variety of carbon chain lengths that have been chlorinated to different degrees (*i.e.*, variation in the number and position of the chlorine atoms on the carbon chain). The individual isomer content of commercial CPs is rarely identified because the number of

[1] UVCB are chemical substances whose composition is Unknown or Variable compositions, Complex reaction products and Biological materials.

possible individual congener group is extremely large. Consequently, the physicochemical properties of CPs vary by carbon chain length and chlorine content. Increased molecular weight correlates to higher melting and boiling points, lower vapor pressures and water solubilities, and greater LogK_{OW} (logarithm of octanol:water partition coefficient). EPA/OPPT used the physicochemical properties listed in Table 2 for informing its evaluation of P-12-0453 and P-12-0433.

Table 2: Summary of Physiochemical Information[a,b]

	wt% Cl	Melting Point	Boiling Point	Vapor Pressure	Water Solubility	Log K_{OW}
MCCPs	> 40	< 25°C (pour point)	> 200°C (dec)	< 0.036 Pa at 20 °C	27 µg/L at 20°C	> 5.5 (measured) 8.30 (estimated)[c,d]
LCCPs	> 40	< 25°C (pour point)	> 200°C (dec)	< 2.7×10^{-4} Pa at 20 °C	5 µg/L at 20°C	> 8

[a]Source: EURAR (ECB, 2008); EA (2009)
[b]Because most CP products are liquids and the CPs begin decomposing at 200 °C (via loss of HCl), melting point and boiling points are considered less important in characterizing hazard and risk.
[c]Value calculated using the KOWWIN Program (v1.68) available in EPA/OPPT's Estimation Programs Interface (EPI) Suite TM. This estimate was generated using a representative MCCP (*i.e.*, $C_{14}H_{24}Cl_6$, 52 wt% Cl) with the following SMILES notation: CCC(Cl)CC(Cl)CCCl)CC(Cl)CC(Cl)CC(Cl)C.
[d]The EURAR (ECB, 2008) cited Renberg's liquid chromatography to measure a LogK_{OW} between 5.5 and 8.2 and then chose to use a Log K_{OW} = 7 as a representative LogK_{OW} for MCCPs with 45-52 wt% Cl.

Analytical challenges exist with evaluating CPs due to the sheer number of congener groups[2] that may be present in CP products. The existence of multiple chain lengths in the UVCBs such as P-12-0453 and P-12-0433 requires the use of analytical methods that separate congener groups based on retention time in a column and mass spectrum of the respective peaks. Several lines of evidence support the use of a representative SCCP or MCCP product as a surrogate for congener groups present in MCCP or LCCP commercial products, respectively.

Hüttig (2006) and Hüttig and Oehme (2006) reported that most commercial MCCP products were > 60 wt% of the C_{14} chain-length congener groups and the C_{15} chain-length congener groups comprised the majority of the remaining ~ 40 wt%. The authors found < 15 wt% C_{16} chain-length congener groups present in most commercial MCCP samples and little to no C_{17} chain-length congener groups. Additional studies have reported that the C_{14} and C_{15} chain-length congener groups are the predominant MCCPs present in environmental media and in human breast milk (Bayen et al., 2006; Chen et al., 2011; Reth et al., 2006; Wang et al., 2013). Some variation is possible in commercial products where the C_{14} and C_{15} chain-length congener groups may not be the predominant congener groups in a specific MCCP product; however, even in these products, the C_{14} and C_{15} chain-length congener groups may serve as reasonable worse case surrogates for the $C_{16\text{-}17}$ chain-length congener groups, due to their greater bioavailability and mobility in environmental media (ECB, 2005).

[2] For this report, congener groups are used to recognize the existence of different chain lengths and degrees of chlorination that could be present in any given CP product.

These analyses, in conjunction with measured or estimated physicochemical and environmental fate properties, allow for the reasonable use of associating commercial products with CP levels found in environmental media and biota. For example, the experimental observation that MCCPs (C_{14-17}) are abundant in sediment has been explained using known water solubility and vapor pressure values in conjunction with predicted degradation pathways (de Boer, 2010). EPA/OPPT determined that the toxic endpoints of interest were measured for only one CP commercial product (*i.e.*, Cereclor S52®). Therefore, this approach of relating one commercial product with other commercial products is critical for attributing the hazard characterization to CPs of different sources. Thus available information (hazard and environmental monitoring data on one commercial product (Cereclor S52®) is used as representative CP for this assessment. Furthermore, experimental data on SCCPs show that these products are more toxic than the longer chain CPs (*e.g.*, MCCPs). Therefore, when endpoint specific data were lacking for the PMNs, EPA/OPPT used measured data from SCCPs as surrogates for potential hazard and risks for the PMNs.

1.3 USES

INEOS reported four uses in the PMN for P-12-0453, including:

1) 73.8% as a lubricant in metal working fluids (MWF) (no commercial or consumer uses). The notification substance is blended into the MWFs at 15%.
2) 16.8% as a flame retardant/plasticizer in poly(vinyl chloride) (PVC) resins (no commercial or consumer uses). The notification substance is blended into the PVC resins at 15%.
3) 7.4% as a plasticizer in adhesives (no commercial or consumer uses). The notification substance is blended into the adhesives at 5%.
4) 2% as a lubricant in sealants (no commercial or consumer uses). The notification substance is blended into the sealants at 20%.

INEOS reported one category of use in the PMN for P-12-0433. This PMN substance is intended for use solely (*i.e.*, 100% of the production volume) as a lubricant in MWF (no commercial or consumer uses). The PMN substance will be used at 15% in the final working formulation.

2 ENVIRONMENTAL FATE

EPA/OPPT reviewed available information on the environmental fate of MCCPs and LCCPs in different environmental compartments and the properties that control transport (summarized in Appendix A). In addition, EPA/OPPT reviewed assessments performed by Canada (EC, 2008a) and the EU (EA, 2009; ECB, 2005) to inform its assessment.

2.1 ENVIRONMNETAL PERSISTENCE

Abiotic studies have shown that MCCPs and LCCPs are stable to hydrolysis and to direct photolysis in water and air. In laboratory studies using hydrocarbon solvents, CPs were shown to poorly absorb ultraviolet (UV) light and no direct photodegradation was observed. The atmospheric half-life for MCCPs and LCCPs has been estimated at 1 - 2 days (EA, 2009; ECB, 2005), based on estimated values for the second order rate constant for reaction with atmospheric hydroxyl radicals for MCCPs (40-56 wt% Cl) and LCCPs (42-54 wt% Cl) (EA, 2009; ECB,

2005). The persistence of MCCPs increases with carbon chain length and higher chlorine content (EA, 2009; ECB, 2005).

Existing biotic degradation data suggest there are a number of microbial species that are capable of degrading shorter chain, lower chlorinated MCCP congeners. Longer and higher chlorinated chemicals also may be degraded, but at much slower rates (Allpress and Gowland, 1999; Muir, 2010; Omori et al., 1987). The results from laboratory studies of microbial metabolism, using both isolated species and mixed cultures of acclimated microbes, show that MCCPs and LCCPs may be degraded by direct metabolism or co-metabolism by some microbes and microbial consortia in soil, wastewater treatment systems, sediment and other environmental media. Overall, the existing studies suggest that with microbial degradation, dechlorination and carbon chain cleavage may be possible in some media (see Table A-1); however, the degree of degradation is generally low (Allpress and Gowland, 1999; Muir, 2010; Omori et al., 1987).

In general, MCCP and LCCP congeners with longer chain lengths and higher degrees of chlorination are expected to be highly persistent in some environmental compartments. In contrast, shorter and lesser-chlorinated congeners are likely to degrade rapidly, especially in aerobic environments. Because persistence increases with chain length, LCCPs are generally expected to be more persistent than MCCPs with comparable degrees of chlorination (EA, 2009; ECB, 2005).

Based on the review of available literature and studies submitted by various manufacturers, including confidential business information (CBI) not publicly available, EPA/OPPT's conclusions regarding environmental persistence of MCCPs and LCCPs are consistent with those provided by Canada and the EU.

The Canadian assessment on MCCPs and LCCPs states (EC, 2008a):

> *"Information on physical properties of MCCPs, and especially LCCPs, is limited. Values used in this assessment are based on extrapolations mainly from SCCPs or QSARs. The analysis of SCCPs and MCCPs in sediment cores and associated calculations provide strong evidence for the persistence of these substances in the environment. Even though there are no data for persistence of LCCPs in sediment, based on biodegradation data which indicate increasing stability with increasing carbon chain length, it is reasonable to conclude that LCCPs are persistent in sediment."*

The EU assessment on MCCPs states (ECB, 2005):[3]

> *"No standard ready or inherent biodegradation tests results are available for medium-chain chlorinated paraffins. From the available information, medium-chain chlorinated paraffins can be considered to be not biodegradable in such test systems and so a biodegradation rate MCCPs of 0 day-1 is used in the risk assessment.*

[3] Note, since the EU issued its assessment in 2005, standard inherent biodegradation studies were performed and are summarized in Appendix A.

There is evidence that some microorganisms may be capable of degrading MCCPs in the environment in acclimated or co-metabolic systems. The potential for biodegradation appears to increase with decreasing chlorine content. However, it is not possible from the available data to derive rate constants for biodegradation in soil, surface water and sediment systems. As a worst case approach, no biodegradation will be assumed in these media in the PEC calculations.

Hydrolysis is not expected to be a significant degradation process for medium-chain chlorinated paraffins in the environment. An atmospheric half-life of 1-2 days is estimated for reaction with hydroxyl radicals. A value for the rate constant for the reaction (k_{OH}) of 8 x 10^{-12} cm^3 $molecule^{-1}$ s^{-1} is used for the environmental modelling in the risk assessment."

The UK assessment on LCCPs[4] concluded the following (EA, 2009):

"Based on the laboratory studies and other data available, LCCPs are unlikely to be readily or inherently biodegradable. Although there is some evidence that they may biodegrade in the environment, it is thought likely that this process will be sufficiently slow that LCCPs meet the P or vP (very persistent) criteria."

EPA/OPPT generally concurs with these characterizations. In the absence of information on specific congener groups and data for MCCP or LCCP products, EPA/OPPT concludes that at least some congener groups present in both MCCP and LCCP products are persistent to very persistent; with estimated half-lives in air exceeding 2 days and estimated half-lives in water, sediment and soil exceeding 2 months (60 days) (ECB, 2005; EA, 2009).

2.2 BIOCONCENTRATION AND BIOACCUMULATION

Recent reviews of the potential for MCCPs and LCCPs to bioaccumulate have shown that, while data are limited, some congener groups are bioaccumulative or very bioaccumulative (EC, 2008a; ECB, 2005; Houde et al., 2008; Thompson and Vaughan, 2014). A summary of studies reviewed by EPA/OPPT is provided in Appendix A.

Based on EPA/OPPT's review of existing studies (Bengtsson et al., 1979; CPC, 1980, 1983a, 1983b; Fisk et al., 1999; Fisk et al., 1998; Houde et al., 2008; Madeley and Maddock, 1983a, 1983b; Madeley and Thompson, 1983; Renberg et al., 1986; Thompson et al., 2000), EPA/OPPT concludes that the bioconcentration potential of MCCP and LCCP congener groups varies with the chain lengths and degree of chlorination and species evaluated. Shorter and less chlorinated chemicals are readily taken up by organisms but also may be excreted or degraded after absorption (Arnot, 2013). Longer and more highly chlorinated chemicals are typically not absorbed across cellular membranes and are not accumulated in tissues. Some MCCP chemicals with intermediate chain length and chlorination may be absorbed and retained. The available evidence for MCCP and LCCP congener groups with intermediate chain lengths and chlorination suggests that some may have bioconcentration factors (BCFs) or bioaccumulation factors (BAFs)

[4] Note, the UK assessment evaluated the following CPs under the term LCCP: C_{18-20} liquid products, $C_{>20}$ liquid products, and $C_{>20}$ solid products.

greater than 1000 or 5000 (EC, 2008a; ECB, 2005, 2008). This suggests that some congener groups in MCCP and LCCP products may be bioaccumulative or very bioaccumulative.

The Canadian assessment on MCCPs and LCCPs states (EC, 2008a):

> *"On the basis of the available information, and in particular the field BAF estimates, it is concluded that MCCPs are bioaccumulative substances…"*
>
> *"On the basis of the available information, and in particular the BAF model and empirical BMF estimates, it is concluded that C18–20 liquid LCCPs are bioaccumulative substances…" [page 27] and "…While there is a lack of empirical bioaccumulation data for LCCPs, the modelling results provided by the Modified Gobas BAF Model - which suggest that of all the LCCPs congeners only liquid C18-20 LCCPs have significant bioaccumulation potential -- are considered credible."*

The UK assessment on LCCPs states (EA, 2009):

> *"The available data for LCCPs do show that uptake into fish from food occurs in the laboratory, and that this uptake can be significant in some cases. The degree of uptake appears to be highest for the C18–20 liquid chlorinated paraffins, but uptake of C>20 liquid chlorinated paraffins has also been demonstrated. The uptake of the highly chlorinated C>20 solid chlorinated paraffins from food appears to be minimal."*

EPA/OPPT generally concurs with these characterizations. In the absence of information on specific congener groups and data for MCCP or LCCP products, EPA/OPPT concludes that at least some congener groups present in both MCCP and LCCP products are bioaccumulative to very bioaccumulative based on multiple lines of evidence, including: Log K_{OW} values, modeled BCFs, laboratory-measured BCFs, field-measured BAFs, field-measured biomagnification factors (BMFs), laboratory-measured biota-sediment accumulation factors (BSAFs) and the presence of MCCPs and LCCPs in human and wildlife biota.

3 ECOLOGICAL HAZARD OVERVIEW

The available ecotoxicity data on MCCPs and LCCPs are summarized in Appendix B, along with the criteria EPA/OPPT used for identifying the highest quality studies. Ecotoxicity studies for MCCPs have been conducted in fish, aquatic invertebrates and plants, sediment and soil invertebrates, and terrestrial plants and invertebrates. Though no avian reproduction studies were available on MCCPs, a high quality study was available on an SCCP product ($C_{10\text{-}12}$, 58 wt% Cl) with similar physicochemical properties to MCCPs and was used for informing EPA/OPPT's hazard evaluation (ECB, 2000).

For LCCPs, ecotoxicity studies were only identified for aquatic invertebrates and vertebrates. No data were available on sediment-dwelling or terrestrial organisms. Overall, the available data on LCCPs were of low quality; therefore, the EPA/OPPT used data on MCCPs to inform its hazard evaluation of LCCPs. This decision was considered a reasonable worst-case scenario because P-12-0433 contains up to 20 wt% C_{17}, a component of MCCPs (*e.g.*, P-12-0453 contains between

8-18 wt% C_{17}). EPA/OPPT concludes that the studies summarized in Table 3 were the highest quality for assessing potential hazards in the aquatic, sediment and terrestrial compartments.

Table 3: Summary of Aquatic, Sediment and Terrestrial Ecotoxicity Data for MCCPs and LCCPs

Test Substance	Test Organism (Species)	Test Guideline; Study type	End-point	Value[a]	Reference
Aquatic Invertebrates					
Cereclor S-52 (52 wt% Cl, C_{14-17})	Water flea (*Daphnia magna*)	OECD 202, 1984; Acute immobilization test	EC_{50}	0.0059	CPA (1996)
Cereclor S-52 (52 wt% Cl, C_{14-17})	Water flea (*Daphnia magna*)	OECD 202- Part II, 1984; Reproduction test	NOEC LOEC MATC	0.01 0.018 0.013	Thompson, Williams et al. (1997)
Sediment-Dwelling Invertebrates					
Cereclor S-52 (52 wt% Cl, C_{14-17})	Amphipod (*Hyalella azteca*)	OECD 218- Draft, 2001; 28-day prolonged sediment toxicity study	NOEC LOEC MATC	130 270 187	Thompson et al. (2002)
Terrestrial Invertebrates					
Cereclor S-52 (52 wt% Cl, C_{14-17})	Earthworm (*Eisenia fetida*)	OECD Guideline-Draft, 2000; 28-day reproductive toxicity test	NOEC LOEC MATC	79 280 149	Thompson et al. (2001d)
Terrestrial Vertebrates					
Commercial CP (58 wt% Cl, C_{10-12})	Mallard duck (*Anas platyrhynchos*)	EPA 560/6-82-002; 22-week reproduction test	NOEC LOEC	168 1000	ECB (2000)

[a]Units are mg/L for aquatic invertebrates, mg/kg dry weight (dw) sediment for sediment-dwelling invertebrates; mg/kg dw soil for earthworm study; and mg/kg diet for the duck study.

Using the concentrations in the "value" column in Table 3 to represent hazard, EPA/OPPT derived concentrations of concern (COCs) by applying assessment factors of five or ten for acute or chronic exposures, respectively, which account for laboratory variability and represents species sensitivity distributions (following US EPA, 2012). The COCs derived for aquatic-, sediment- and terrestrial-dwelling organisms are explained below and summarized thereafter in Table 4.

The most reliable and acceptable toxicity studies to aquatic organisms indicate that for MCCPs and LCCPs, the toxicity to aquatic organisms are from the CPA (1996) study for acute toxicity and the Thompson et al. (1997) study for chronic toxicity.

- Acute COC: The 48-hour EC_{50} value 0.0059 mg/L is divided by an assessment factor of 5 to yield an acute concentration of concern (COC) of 0.00118 mg/L, or 0.001 mg/L, or 1 µg/L (1 ppb).
  Aquatic Acute COC = 1 ppb.
- Chronic COC: The chronic value 0.013 mg/L is divided by an assessment factor of 10 to yield 0.0013 mg/L or 1.3 µg/L or 1.3 ppb.
  Aquatic Chronic COC = 1 ppb.

The most reliable and acceptable value for the acute toxicity to aquatic sediment invertebrate organisms is based on the MCCP material from the Thompson et al. (2002) 28-d study. The 28-d sediment invertebrate GMATC value of 187 mg/kg dry wt sediment is used to assess hazard. Using methods in US EPA (2012):

- Acute COC: The chronic value 187 mg/kg dry wt. is multiplied by an acute to chronic ratio for invertebrates (10) to yield 1,870 mg/kg dry wt. This value is then divided by an assessment factor of 5 to yield 374 mg/kg dry wt.
  Aquatic Sediment Acute COC = 374 mg/kg dry wt sediment.
- Chronic COC: The 28-d sediment invertebrate GMATC of 187 mg/kg dry wt sediment is divided by an assessment factor of 10 to yield 18.7 mg/kg dry wt sediment.
  Aquatic Sediment Chronic COC = 18.7 mg/kg dry wt sediment.

The most reliable and acceptable value for acute toxicity to terrestrial invertebrates is based on the MCCP material from the Thompson et al. (2001a) study. The 28-d terrestrial invertebrate GMATC value of 149 mg/kg dry wt soil from this study will be used. Using methods in US EPA (2012):

- Acute COC: To calculate an acute concern concentration from the chronic value the value 149 mg/kg dry wt, is multiplied by an acute to chronic ratio for invertebrates (10) to yield 1,490 mg/kg dry wt. This value is then divided by an assessment factor of 5 to yield 298 mg/kg dry wt.
  Terrestrial Invertebrate Acute COC = 298 mg/kg dry wt.
- Chronic COC: The 28-d terrestrial invertebrate GMATC of 149 mg/kg dry wt is divided by an assessment factor of 10 to yield 14.9 mg/kg dry wt.
  Terrestrial Invertebrate Chronic COC = 14.9 mg/kg dry wt.

The most reliable and acceptable value for acute toxicity to terrestrial vertebrates is based on the MCCP material from the ECB (2001) study. The 22-week terrestrial vertebrate NOEC value of 168 mg/kg dry wt soil from this study will be used. Using methods in US EPA (2012):

- Acute COC: To calculate an acute concern concentration from the chronic value the value 168 mg/kg diet is multiplied by an acute to chronic ratio for invertebrates (10) to yield 1,680 mg/kg diet. This value is then divided by an assessment factor of 5 to yield 336 mg/kg diet.
  Terrestrial Vertebrate Acute COC = 336 mg/kg diet.
- Chronic COC: The 22-week terrestrial vertebrate NOEC of 168 mg/kg diet is divided by an assessment factor of 10 to yield 16.8 mg/kg diet.
  Terrestrial Vertebrate Chronic COC = 16.8 mg/kg diet.

Table 4: COCs for Environmental Toxicity of MCCPs and LCCPs

Compartment	Test organism	Endpoint	Value	Assessment factor	COC
Surface water	Water flea	EC_{50}	0.0059 mg/L	5	0.001 mg/L
		21-day MATC	0.013 mg/L	10	0.001 mg/L
Sediment	Amphipod	MATC	187 mg/kg dw	10	18.7 mg/kg dry wt. sediment
Terrestrial	Earthworm	28-day MATC	149 mg/kg dw	10	14.9 mg/kg dry wt. sediment
	Mallard duck	22-week NOEC	168 mg/kg diet	10	16.8 mg/kg diet

4 HUMAN HEALTH HAZARD OVERVIEW

A summary of EPA/OPPT's evaluations on MCCPs and LCCPs is provided in sections 4.1 and 4.2, respectively; individual study reviews are provided in Appendix C.

4.1 MCCP HEALTH DATA REVIEW

There is no information on inhalation absorption of MCCPs in humans or in animals. Based on their low vapor pressure and low water solubility, absorption following inhalation or dermal exposure is expected to be limited; previous evaluations concluded that absorption by the inhalation and dermal routes of exposure will not exceed 50 or one percent, respectively (ECB 2005; EA 2009). Some MCCPs demonstrated moderate absorption and metabolism following oral exposure in animals. In general, absorption and metabolism are related to their carbon chain length and degree of chlorination; the longer the carbon chain length and the higher the degree of chlorination, the less absorption and metabolism.

No information is available on the toxicity of MCCPs in humans; however, the toxicology of these compounds has been evaluated in experimental animals. Studies in rats and rabbits have shown that MCCPs only caused slight skin irritation and have low eye irritation potential. No evidence of skin sensitization was found when tested in guinea pigs. The liver, kidney and thyroid are the target organs of MCCPs in oral repeated dose studies in experimental animals (see Table C-1 in Appendix C). MCCPs induced increased liver weight, enzyme activity and histopathological changes at high dose levels. Some of these hepatic effects are likely related to an increase in metabolic demand as an adaptive response, as well as to peroxisome proliferation, which are considered of limited toxicological significance to humans. However, liver necrosis was observed in a 90-day study in rats at 360 mg/kg-bw/day; this effect is considered relevant to humans. The reported effects in the kidney may have been produced by the parent compound or from metabolites. Mechanistic data cannot totally rule out that some kidney effects are relevant to humans. From the data available, a LOAEL of 625 mg/kg-bw/day based on histopathological changes in the kidneys of female rats is identified in a 90-day toxicity study and a NOAEL of 23 mg/kg-bw/day based on increased kidney weight at 222 mg/kg-bw/day is identified from another 90-day study in rats (CXR, 2005). Repeated dose studies in rats reported some changes in histopathology and hormone levels of the thyroid. However, it may be concluded based on an evaluation of the mechanistic data that the thyroid effects observed in rats is of little relevance to chronic toxicity in humans.

There is no information on the carcinogenicity of MCCPs; however, carcinogenicity studies on a SCCP and a vLCCP are available. These studies, along with the genotoxicity data on MCCPs, were used to inform the carcinogenic potential of MCCPs. When administered by gavage, a SCCP (C_{12}, 60 wt% Cl) caused increased incidences of liver tumors in male and female rats, kidney tumors in male rats and thyroid tumors in female rats. However, based on mechanistic considerations, these tumors are considered to be of little or no relevance to humans (details in ECB, 2008 and in Appendix C). An increased incidence of malignant lymphoma in male mice was reported at the highest dose of 5,000 mg/kg-bw/day in carcinogenicity studies of a vLCCP (C_{23}, 43 wt% Cl) in male and female rats and mice. However, malignant lymphoma is one of the more variable tumors in mice and has a viral origin in many cases. No increased incidence of malignant lymphoma was observed in the carcinogenicity study on a SCCP. Further, MCCPs are non-genotoxic. Therefore, it may be concluded that MCCPs are unlikely to pose a carcinogenic hazard to humans.

A series of range-finding and definitive prenatal developmental and reproductive toxicity studies were conducted in rats and rabbits with MCCPs. These studies were conducted between 1981 and 1986. They appear to be valid toxicity studies, conducted according to the standard methodologies available at the time.

In several prenatal developmental toxicity studies with MCCPs conducted *via* gavage, no signs of maternal toxicity were seen at doses as high as 500 mg/kg-bw/day in rats and 100 mg/kg-bw/day in rabbits. Likewise, no signs of developmental toxicity were observed at doses as high as 5000 mg/kg-bw/day in rats and 100 mg/kg-bw/day in rabbits.

Two reproductive toxicity studies with MCCPs in rats have been conducted. A one-generation reproductive toxicity range-finding study showed that administration of approximately 100 and 400 mg/kg-bw/day MCCPs *via* the diet had no effect on fertility or other reproductive parameters; however, internal hemorrhaging and deaths in pups were observed beginning from 74 mg/kg-bw/day (1000 ppm) up to approximately 400 mg/kg-bw/day (6250 ppm). These effects in the pups were not seen in a more recent definitive one-generation reproductive toxicity study with exposure to MCCPs for 11-12 weeks to doses as high as 100 mg/kg-bw/day (1200 ppm). Internal hemorrhaging was not seen in the adult animals in either of these studies at doses as high as 400 mg/kg-bw/day (6250 ppm), or in another study in non-pregnant female rats repeatedly exposed to doses as high as 1000 mg/kg-bw/day. However, when dams were exposed to approximately 500 mg/kg-bw/day (6250 ppm) MCCPs during cohabitation, gestation and lactation, signs of hemorrhaging were observed in dams that died at the time of parturition. Taken together, the results of these studies suggest that newborns during lactation and pregnant females at the time of parturition are a potentially sensitive subpopulation with a possible LOAEL for internal hemorrhaging and deaths in pups at an oral dose of 74/mg/kg-bw/day.

Additional studies with MCCPs have been conducted in an effort to clarify the possible causes of the hemorrhaging in the pups. One (single-dose; 6250 ppm or 538 mg/kg-bw/day) study showed maternal death during parturition due to low levels of vitamin K and related hemorrhaging, suggesting that the act of parturition places dams at higher risk. It was concluded in data from this study and a cross-fostering study that the fetus relies on clotting factors *via* mother's milk

and severe deficiencies in vitamin K levels and related clotting factors in the pups results in hemorrhaging.

No guideline developmental neurotoxicity studies on MCCPs were located. It is not clear if any developmental neurotoxicity endpoints were measured in the available prenatal developmental/reproductive toxicity studies; none were explicitly stated. The only information available regarding behavior during development is from cage-side observations in pups through lactation day 21. In these cases, no dose-related differences were reported in F_1 post-weaning appearance or cage-side behaviors. While thyroid hormone induced effects were observed in adults, no data exist for developmental studies. Current studies do not evaluate developmental neurotoxicity following perinatal exposures.

In this assessment, the lowest NOAEL (90-day value of 23 mg/kg-bw/day from the rat study described above; CXR, 2005) was used to assess occupational and non-occupational *(i.e.,* general population) risk of MCCPs.

4.2 LCCP HEALTH DATA REVIEW

There is no information on inhalation absorption of v/LCCPs in humans or in animals. Based on their low vapor pressure and water solubility, absorption following inhalation or dermal exposure is expected to be limited. Some absorption and metabolism following oral exposure are possible for v/LCCPs with shorter carbon chain length and lower degree of chlorination.

No information is available on the toxicity of v/LCCPs in humans. Acute oral toxicity data in animals show that v/LCCPs are of very low acute toxicity. Studies in animals have shown that some v/LCCPs may have the potential to cause slight skin irritation and sensitization but no eye irritation potential. The liver is the main target organ of v/LCCPs in repeated dose studies in experimental animals. Inflammatory and necrotic changes of the liver were observed in rats exposed to a $C_{20\text{-}30}$ v/LCCP with 43 wt% Cl at dose levels of 100 mg/kg-bw and above. For another v/LCCP with $C_{20\text{-}26}$ 70 wt% Cl, effects in the liver occurred at a very high exposure level of 3,750 mg/kg-bw/day; the NOAEL was 900 mg/kg-bw/day.

An increased incidence of malignant lymphoma in male mice was reported at the highest dose of 5,000 mg/kg-bw/day when tested using a C_{23} vLCCP with 43 wt% Cl in carcinogenicity studies in male and female rats and mice. However, malignant lymphoma is one of the more variable tumors in mice and has a viral origin in many cases. Data on the analogous SCCPs have shown no increase in the incidence of malignant lymphoma in a carcinogenicity study of SCCPs. v/LCCPs are non-genotoxic and they are not expected to pose a carcinogenic hazard to humans.

Based on the LOAEL (100 mg/kg-bw) of the liver effects in female rats of repeated dose studies Health Canada calculated a tolerable daily intake (TDI) of 71 µg/kg-bw/day with LCCPs. Using upper bounding intake estimates ranging from 0.007 µg/kg-bw/day for 60+ age group to 0.024 µg/kg-bw/day for 0.5 years age group, Environment Canada determined that the exposure levels are 10,000 and 3,000 times lower, respectively, than the TDI.

The National Research Council (NRC, 2000) reviewed the toxicological risks of selected flame retardants, including a vLCCP containing C_{24} with 70 wt% Cl. Based on the NOAEL of 900

mg/kg-bw/day (liver toxicity), NRC derived an RfD of 0.3 mg/kg-bw/day. Using this RfD and the worst case average daily exposure to be 0.16 mg/kg-bw/day, NRC concluded: "*LCCP do not pose a noncancer risk when incorporated into residential furniture at the estimated application levels*." Further, it was concluded that: "*LCCP are not likely to be a human carcinogen and derivation of a cancer potency factor is unnecessary*."

In this assessment, the LOAEL of 100 mg/kg-bw/day from the 90-day and two-year studies described above) was used to assess potential occupational and non-occupational (*i.e.*, general population) risk of LCCPs.

5 EXPOSURE INFORMATION

EPA/OPPT used the information in this section and our standard PMN approaches to estimate potential worker exposures from activities associated with manufacturing, processing and use of P-12-0453 and P-12-0433. Environmental releases from these activities were also estimated for use in assessing risk to both human health (general population) and the environment (aquatic organisms). In addition, EPA/OPPT reviewed the available information on measured environmental concentrations of MCCPs and LCCPs, which are not normally available for PMNs.

5.1 ENVIRONMENTAL MONITORING

For this assessment, environmental monitoring data consisting of measured levels of MCCPs and LCCPs in surface water, sediment and soil were used to characterize potential environmental exposure to MCCPs and LCCPs. These data are not amenable to determining the ultimate release source (*i.e.*, manufacturing, processing, or use) into the environment; however, they provide some insight on the geographical and temporal distribution of MCCPs and LCCPs. Appendix D contains information and data used in this risk assessment.

Studies published between 1980 and 2013 that reported environmental concentrations of MCCPs and/or LCCPs were reviewed for this assessment. Monitoring studies from the early 1980s could not distinguish between the different chain lengths of CPs. The introduction of modern techniques, such as electron capture negative ion mass spectrometry (ECNI-MS) allowed for the detection of specific congeners, although difficulties with these methods have persisted (*e.g.*, detection of low chlorination congeners in samples). Tomy (2010) performed a round robin laboratory study of SCCPs that highlighted the inability of the ECNI-MS method to consistently measure a reference sample, with concentrations varying up to a factor of six. Subsequent work showed that significant errors (up to a factor of ten) could be introduced by the improper selection of the calibration standards (Coelhan et al., 2000). A more recent inter-laboratory study of SCCPs found good agreement amongst the laboratories that used ECNI-MS (Pellizzato et al., 2009), but similar inter-laboratory studies for MCCPs or LCCPs have not been completed (Tomy, 2010).

The majority of the monitoring data were collected in Europe and some more recent monitoring data were collected in China. Over time and across countries, industrial practices and effluent pre-treatment have varied. Some of the monitoring studies only published their final measured concentrations and did not include the details of the analytical techniques and sampling locations. Generally, EPA/OPPT used studies sponsored by the environmental agencies, but full

documentation is lacking for even these studies. The industrial sectors studied by other countries also are present in the US, suggesting that conditions in the US may be similar.

The level of detail provided in the studies varied. Some studies provided detailed information regarding sampling locations (*e.g.*, impacted sites), analytical methodology and final sample results including detection limits, quantitation limits and estimated values. In contrast, other studies provided only a summary of the results combined from a number of studies. These summaries also did not provide details of the data analysis to obtain sample results. In addition, certain studies reported concentrations within a given country but did not provide additional details about the exact sampling location. Given the disparate conditions (*i.e.*, number of sites sampled, temporal period over which samples collected, differing analytical methods, *etc*.) across the data sets, EPA/OPPT was unable to determine a central tendency or distribution for the data sets and a range was used instead. Studies using older analytical techniques that did not distinguish CP congeners were not used in this assessment. Other nations' assessments that used newer, more reliable, analytical techniques were considered.

EPA/OPPT used the following selection criteria to identify the studies included in this assessment:

- Specific mention of MCCP/LCCP chain length;
- Use of modern analytical techniques to distinguish categories of CPs; and
- At a minimum, general information on sampling location.

EPA/OPPT used the monitoring data summarized in Tables 5 and 6 for this assessment. When a limit of detection (LOD) value was reported for non-detectable results[5], EPA/OPPT used one-half of the LOD value.

Even though the existing monitoring data were limited in quality and quantity and it remains unclear how well the measured data describe the potential range of US MCCP and LCCP use scenarios, EPA/OPPT concluded that the data in Tables 5 and 6 represented the best available monitoring information for MCCPs and LCCPs, respectively. These data provide some evidence that MCCPs and LCCPs are released into the environment; however, these data reflect discrete locations and times and the extent to which they are representative of the overall distribution of MCCPs and LCCPs is unknown.

[5] Examples would be "not detected" (ND), negligible, or with a "less than" qualifier.

Table 5: Summary of Measured Concentrations of MCCPs in Environmental Media and Biota.

Media Category	n	Min	Unit	Max	Unit	References
Surface water (non-marine)	15	$<2.50 \times 10^{-10}$	mg/L	1.49×10^{-3}	mg/L	Coelhan (2010); EC (2008b); Houde et al. (2008); IPCS (1996); Muir et al. (2003); Petersen et al. (2006)[a]; USEPA (1988)
Sediment (non-marine)	78	2.00×10^{-3}	mg/kg[b]	6.51×10^{1}	mg/kg dw	Borgen et al. (2003); Chen et al. (2011); EC (2008a); Iozza et al. (2008); IPCS (1996); Nicholls et al. (2001); Petersen et al. (2006); Pribylova et al. (2006); Tomy et al. (1998); Tomy et al. (1999); USEPA (1988)
Sediment (marine)	54	5.00×10^{-3}	mg/kg dw	1.64×10^{1}	mg/kg dw	Hüttig et al. (2004); Hüttig and Oehme (2005, 2006); Kemmlein et al. (2002); Muir et al. (2000)
Sludge	9	5.00×10^{-5}	mg/kg[b]	9.70×10^{3}	mg/kg dw	Stevens et al. (2003); Pribylova et al. (2006)
Soil	12	2.1×10^{-6}	mg/kg dw	8.5×10^{-2}	mg/kg dw	Iozza (2010); Wang et al. (2013)
Biota (aquatic)	120	$<2.00 \times 10^{-7}$	mg/kg	2.63	mg/kg ww	Bennie et al. (2000); EC (1993, 2008a); Houde et al. (2008); IVL (2009); Kemmlein et al. (2002); Muir (2010); Muir et al. (2003); Muir et al. (2000); Reth et al. (2005,2006); Tomy et al., (1999a); USEPA (1988)
Biota (terrestrial)	8	5.00×10^{-3}	mg/kg ww	3.70×10^{-1}	mg/kg ww	Reth et al. (2006)

[a]Petersen et al. (2006) reported results for two water samples; EPA/OPPT assumed these were non-marine surface water samples.
[b]The weight type was not reported (*i.e.*, wet, dry, or lipid weight).
Notes:
1. All values provided in the table above represent total MCCPs and not individual MCCP isomers.
2. The "n" value represents the number of media-specific MCCP monitoring data values that were compiled from various articles in the raw data table (provided in Appendix D).
3. In some cases, the minimum values in the table are preceded by "<". This indicates that the value reported in article was reported as a non-detect. In such cases, one half of the lowest reported detection limit was compiled as the 'minimum' reported monitoring data.
4. dw – dry weight and ww – wet weight.

Table 6 below summarizes the available environmental monitoring data for LCCPs. Environmental data were available for marine sediment and aquatic invertebrates. Though no data were available for other media categories (*e.g.*, surface water, non-marine sediment, terrestrial invertebrates), limited high quality data (from Table 6) were available for MCCPs which could be used for informing concentrations of LCCPs in the environment. This decision is

based on the following information: 1) P-12-0433 commercial products contain up to 20% of C_{17}, an MCCP congener (see Section 1.2 Chemistry), 2) LCCP congener groups are expected to behave in a manner similar to MCCP congener groups with comparable wt% Cl when released to the environment and 3) MCCP and LCCP commercial products have similar uses (see Table 1) and hence may have similar releases at facilities that process and use these chemicals.

Table 6: Summary of Measured Concentrations of LCCPs in Environmental Media and Biota.

Media Category	n	Min	Units	Max	Units	References
Sediment (marine)	4	1.02×10^{-1}	mg/kg dw	4.31×10^{-1}	mg/kg dw	Kemmlein et al. (2002)
Biota (aquatic)	2	2.80×10^{-6}	mg/kg lw	6.90×10^{-6}	mg/kg lw	Kemmlein et al. (2002)

Notes:
1. All values provided in the table above represent total LCCP $C_{18\text{-}20}$ and not individual LCCP isomers.
2. The "n" value represents the number of media-specific LCCP $C_{18\text{-}20}$ monitoring data values that were compiled from various articles in the raw data table (provided in Appendix D).
3. dw – dry weight and lw – lipid weight.

5.2 MODELED ENVIRONMENTAL RELEASES

EPA/OPPT used screening-level models to generate environmental release estimates for P-12-0453 and P-12-0433, which were used to calculate exposure concentrations for estimating risks to humans and aquatic organisms. EPA/OPPT used the Chemical Screening Tool for Exposures and Environmental Releases (ChemSTEER ver.2) to estimate environmental releases from industrial processes; the results are provided in Appendix E. Inputs to the ChemSTEER ver. 2 release modeling were based on multiple sources, including information provided by INEOS, published OECD Emission Scenario Documents, EPA Generic Scenarios and EPA models for estimating environmental releases. Table 7 provides a general summary of the release assessment.

Table 7: Summary of Estimated Release to Water

PMN	Chemical Name	Manufacturing	Processing (PROC)	Use
P-12-0453	Alkanes, $C_{14\text{-}17}$, chloro (MCCPs; 40-60 wt% Cl)	No, import only	PROC1: Formulation of MWFs (73.8% of PV)	USE1: Use of MWF (73.8% of PV)
			PROC2: PVC compounding (16.8% of PV)	USE2: PVC converting (16.8% of PV)
			PROC3: Formulation of adhesives and sealants (9.4% of PV)[a]	USE3: Use of adhesives and sealants (9.4% of PV)
P-12-0433	Alkanes, $C_{18\text{-}20}$, chloro (LCCPs; 40-55 wt% Cl)	No, import only	PROC1: Formulation of MWFs (100% of PV)	USE1: Use of MWFs (100% of PV)

[a]Note, adhesives and sealants were assessed as a single process and use when evaluating potential environmental releases because of the comparable activities associated with each.

Exposure pathways of interest for human health include drinking water, fish ingestion and air stack emissions. For aquatic organisms, the exposure pathway of concern is from direct releases to water. EPA/OPPT assessed each of these pathways by using the ChemSTEER ver. 2 release estimates as inputs to the Exposure and Fate Assessment Screening Tool (E-FAST V2.0) for

estimating industrial releases and concentrations in the foregoing exposure pathways. EPA/OPPT assumed that potential releases to water occurred from indirect discharges to publicly owned treatment works (POTW). The E-FAST V2.0 modeling applied an assumption of 90% removal of MCCPs and LCCPs at the POTW. Water concentrations were estimated using E-FAST V2.0's probabilistic dilution model (PDM), which predicts downstream chemical concentrations from industrial discharges. These values were reported as the central tendency for a median flow site, a low flow site and the lowest seven-day average flow that occurs on average once every ten years (*i.e.*, 7Q10). These estimated water concentrations were compared to the COC of 1 µg/L for chronic aquatic invertebrates (see Table 4). Air stack emissions were estimated using generic scenarios, which assumed inhalation exposures occurring 100 meters downwind of a facility. EPA/OPPT used these estimated values for calculating human health and environmental risks of P-12-0453 and P-12-0433.

The results of the E-FAST V2.0 modeling are provided in Appendix F. Table 8 presents the values used in the risk assessment. As explained in the footnotes in Table 8, the values represent reasonable worst-case scenarios based on the processing and use scenarios presented in Table 7. However, these estimates require consideration of two important caveats: (1) limited environmental monitoring data are available and (2) MCCPs and LCCPs are expected to partition to particulates and sediment; however, E-FAST V2.0 models do not account for this partitioning.

Table 8: E-FAST Modeling Values Used for MCCPs [1]

Scenario	Water Release - Human[2]		Air Release - Human[2]	Water Release – Aquatic Organisms[3]
	Drinking Water (mg/kg-bw/day)	Fish Ingestion (mg/kg-bw/day)	Stack Air LADD (mg/kg-bw/day)	Range of Concentrations (µg/L)
P-12-0453				
PROC1: Formulation of MWFs	4.20×10^{-5}	5.15×10^{-4}	2.99×10^{-4}	6.5-47 (240)
PROC2: PVC compounding	7.30×10^{-5}	8.95×10^{-4}	3.68×10^{-4}	7-54 (278)
PROC3: Formulation of adhesives and sealants	1.30×10^{-4}	1.59×10^{-3}	6.50×10^{-4}	7-150 (258)
USE1: Use of MWF	3.35×10^{-4}	4.09×10^{-3}	8.95×10^{-4}	11-144 (1.30×10^{3})
USE2: PVC converting	7.15×10^{-5}	8.70×10^{-4}	2.18×10^{-4}	1-27 (148)
USE3: Use of adhesives and sealants	2.00×10^{-5}	2.45×10^{-4}	2.82×10^{-5}	2-20 (210)
P-12-0433				
PROC1: Formulation of MWFs	1.04×10^{-6}	4.47×10^{-5}	N/A	5-36 (184)
USE1: Use of MWFs	2.38×10^{-4}	1.02×10^{-3}	6.30×10^{-4}	7-92 (829)

[1] Taken from Appendix E. Values represent the highest concentrations/estimated doses (reported as the lifetime average daily dose, or LADD) for chronic (*i.e.*, repeated exposure scenarios) for human health.

[2] Estimated exposure values were corrected for absorption by the oral (50% absorption) and inhalation (50% absorption) routes of exposure (ECB 2005; EA 2009).

[3] For PMNs, environmental risk was evaluated by performing a PDM as described above and in the E-FAST Manual (2007). The ranges encompass concentrations from the central tendency for a median flow site (*e.g.*, 6.5 µg/L) up to the central tendency for a low flow site (*e.g.*, 47 µg/L) – this example was taken from the first row, last column, under P-12-0453. The central tendency was calculated using the harmonic mean flow. The value in parentheses represents the 7Q10 (*e.g.*, 240 µg/L) value normally used to determine potential chronic risk to aquatic organisms.

5.3 EXPOSURE ESTIMATES

5.3.1 OCCUPATIONAL EXPOSURE ESTIMATES

EPA/OPPT calculated screening-level workplace exposure estimates with ChemSTEER ver. 2. Table 9 provides a summary of the exposure estimates used in this risk assessment for evaluating worker exposures to P-12-0453 and P-12-0433. Detailed information is provided in Appendix E.

Table 9: Summary of Occupational Exposure Estimates Used.

Scenario[1]	Route of Exposure	
	Inhalation (mg/day)	Dermal (mg/day)
P-12-0453		
PROC1: Formulation of MWFs	N/A[2]	350 – 1,800
PROC2: PVC compounding	0.030 – 4.4	1,800
PROC3: Formulation of adhesives and sealants	N/A[2]	530 – 1,800
USE1: Use of MWF	2.0 – 7.1	350 – 3,900
USE2: PVC converting	12 – 22	N/A[2]
USE3: Use of adhesives and sealants	23	530
P-12-0433		
PROC1: Formulation of MWFs	N/A[2]	350 – 1,800
USE1: Use of MWFs	2.0 – 7.1	350 – 3,900

[1]The following represent the estimated number of sites, workers per scenario and exposure over the course of the stated number of days: P-12-0453 = PROC1: 59 sites, 472 workers and 84 days/year; PROC2: 8 sites, 192 workers and 126 days/year; PROC3: 3 sites, 66 workers and 200 days/year; USE1: 207 sites, 9936 workers and 247 days/year; USE2: 8 sites, 384 workers and 250 days/year; USE3: 58 sites, 2784 workers and 250 days/year; P-12-0433 = PROC1: 3 sites, 24 workers and 27 days/year; USE1: 4 sites, 192 workers and 247 days/year.
[2]Not applicable, the use category does not result in exposures that are relevant for this route.

5.3.2 CONSUMER EXPOSURE ESTIMATES

INEOS did not identify consumer uses in its PMN applications for P-12-0453 and P-12-0433; therefore, EPA/OPPT did not perform an assessment for these types of exposures.

6 RISK ASSESSMENT

6.1 ENVIRONMENTAL ASSESSMENT

PMN risk assessments typically use modeled exposure values because new chemical substances are not in the stream of US commerce; however, for MCCPs and LCCPs, measured environmental data are available for some locations in the US and abroad. Though these data are not specific to P-12-0453 and P-12-0433, the data contain MCCP and LCCP congener groups that may be present in the PMN substances. However, EPA/OPPT used modeled exposure values as an important source for its assessment of potential risks because the modeled exposure values were generated using exposure scenarios that are representative of the types of uses and releases that may occur with P-12-0453 and P-12-0433. In contrast, the measured environmental data are generally not amenable for identifying the types of uses or releases from which the measured congeners originated. Therefore, EPA/OPPT used these measured data as supporting information, along with modeled exposure values, to calculate potential environmental risks using the risk quotient (RQ) method.

The RQ method integrates the results of exposure and ecotoxicity data (USEPA, 1998).

An RQ is defined as:

$$RQ = \text{Environmental Concentration} \div \text{Effect Level}$$

where, the environmental concentration represents measured (see Tables 5 and 6) or estimated (see Table 8) values for each compartment (*i.e.*, water, sediment and soil) and the effect level represents the COC for aquatic, benthic, or terrestrial species (see Table 4).

An RQ greater than one serves as a benchmark for identifying whether aquatic concentrations of P-12-0453 and P-12-0433 may present a risk to aquatic- and sediment-dwelling organisms.

6.1.1 Risk Estimates Using Environmental Monitoring Concentrations

The RQs shown in Table 10 suggest that measured concentrations of MCCPs and LCCPs in water and sediment may present a risk of acute and chronic injury to aquatic organisms and may present a risk of chronic injury to sediment-dwelling organisms. However, several limitations must be noted about the monitoring studies and the level of uncertainty that they contribute to the basis of these findings. First, the reported concentrations represent minimum and maximum values that span, at a minimum, several orders of magnitude and translate to RQs of less than one (*i.e.*, low risk finding) or greater than one (*i.e.*, risk finding), respectively. Second, the temporal and geographical distributions of these data, along with the different types of uses and releases that may have served as the originating sources, make it impossible to describe the central tendency of these data. Finally, the frequency and magnitude of locations with relevant use and release scenarios to the PMN substances, which may result in environmental releases of MCCPs or LCCPs that exceed the relevant COCs, is unknown. In addition to these general limitations, there are specific limitations and uncertainties that preclude using these values as the sole source

from which to inform potential environmental concentrations and risks that may result from the specific uses and releases associated with P-12-0453 and P-12-0433.

Table 10: Risk Quotients Calculated for MCCPs from Environmental Monitoring Data for Surface Water, Sediment and the Terrestrial Environment.

	Environmental Concentration	Effect Level (*i.e.*, COC)	RQs
Acute Risk Aquatic Species	$< 2.50\times10^{-10}$ to 1.49×10^{-3} mg/L	0.001 mg/L	$< 2.50\times10^{-7}$ to **1.49**[1]
Chronic Risk Aquatic Species	$< 2.50\times10^{-10}$ to 1.49×10^{-3} mg/L	0.001 mg/L	$< 2.50\times10^{-7}$ to **1.49**
Chronic Risk Sediment-dwelling Species Non-marine Environment	0.002 to 65 mg/kg dw	18.7 mg/kg dw	1.07×10^{-4} to **3.5**
Chronic Risk Terrestrial Species	Insufficient Data	14.9 mg/kg dw[2]	Not calculated

[1]**Bolded values represent those that may present an unreasonable risk of injury.**

[2] The COCs for terrestrial invertebrates and vertebrates were 14.9 mg/kg dw and 16.8 mg/kg diet, respectively. Since these values were comparable, EPA/OPPT used the lowest value as a potential means for calculating RQs for this compartment, once relevant data are available.

For surface water, EPA/OPPT based the aquatic risk findings for MCCPs and LCCPs on the highest concentration reported by Petersen et al. (2006). These authors collected two surface water samples from an undisclosed location(s) in Norway and measured the concentration of MCCP congener groups (*i.e.*, $C_{14\text{-}17}$). The authors reported a concentration of 1.49×10^{-3} mg/L for MCCP congener groups in one sample; however, a numerical value was not provided for the second sample, rather the distribution of congener groups was displayed in a bar graph. Based on the ordinate scale, the concentration of MCCP congener groups in the second sample was greater than zero, but less than 5.0×10^{-4} mg/L. Of the monitoring studies reviewed by EPA/OPPT (see Appendix D), the Petersen et al. (2006) value of 1.49×10^{-3} is the only surface water concentration that resulted in an RQ greater than one. All other surface water concentrations are at least one order of magnitude below 1.49×10^{-3} mg/L (*i.e.*, RQs < 1).

For sediment concentrations, EPA/OPPT reviewed multiple studies, some of which reported values that exceeded the COC. Nicholls et al. (2001) reported the most relevant data for P-12-0453 and P-12-0433. These authors measured concentrations of MCCPs at locations in the United Kingdom where specific industries were known to employ MCCPs in the use categories identified for the PMN substances (*e.g.*, lubricant in MWFs, plasticizer in PVC resins, and lubricant in sealants). Eight locations were sampled at three distances downstream (*i.e.*, 100 meters, 300 meters, and 1-2 kilometers) from the respective sewage treatment works. At four of the locations, at least one of the sampled downstream values exceeded the COC (*i.e.*, RQs > 1, risk finding). Though it is not possible to parse out the contribution of specific uses to the measured values, these data support that releases occur at locations with relevant uses to the PMN substances, which contribute to the environmental load of MCCP congener groups and in some cases result in RQs greater than one.

For soil concentrations, EPA/OPPT was unable to calculate RQs for terrestrial organisms due to the absence of relevant measured data from biosolid-amended soils. Though Iozza (2010) and Wang et al. (2013) reported measured levels of MCCPs in soil, the samples were collected from

sites in remote alpine locations or industrialized areas, respectively. These data are relevant for assessing airborne deposition of MCCPs/LCCPs; however, the reported concentrations are of questionable relevance with informing concentrations of MCCPs/LCCPs that may occur in biosolid-amended agricultural soils.

Due to the foregoing limitations and resulting uncertainties with the measured environmental data, EPA/OPPT used these data in a limited capacity for estimating potential risks associated with the use categories identified for P-12-0453 and P-12-0433. Specifically, these data were used as supporting information to inform the relevant pathways for estimating potential releases from relevant use categories for the PMN substances. A summary of the estimated release values and associated RQs that EPA/OPPT used as a key basis for evaluating the potential risks of P-12-0453 and P-12-0433 is presented in the following section.

6.1.2 Risk Estimates Using Modeled Exposures

The RQs shown in Table 11 suggest that the intended processes and uses for P-12-0453 and P-12-0433 are expected to result in releases to surface water at concentrations that may present a risk of injury to aquatic organisms.

It is noteworthy that these estimated concentrations are within the range of measured surface water concentrations reported for MCCP congener groups (Table 5). Though there is uncertainty whether the form (*i.e.*, dissolved or particle bound) of MCCP impacts the aquatic toxicity, the estimated values suggest that either form may exist. The median stream flow estimates are all below the reported water solubility for P-12-0453 and slightly above or below the water solubility reported for P-12-0433 (Table 1). Since the available aquatic toxicity data support that dissolved MCCP congener groups cause toxicity, the median stream flow values suggest that the risk finding for this scenario is plausible. The low stream flow and 7Q10 flow scenarios estimate water concentrations that far exceed the estimated water solubility of P-12-0453 and P-12-0433. Under these scenarios, the MCCP or LCCP congener groups would likely be bound to particulates and would eventually settle out in sediment. Nicholls et al. (2001) provided support for this pathway and showed that sediment concentrations of MCCP congener groups generally increased with distance downstream from the source outfall. Based on the foregoing information, EPA/OPPT concludes that the median stream flow values were adequate for determining that environmental releases of P-12-0453 and P-12-0433 may present a risk of injury to aquatic organisms.

Table 11: Risk Assessment of Aquatic Organisms Using Modeled Exposures[1]

Scenario	Estimated Water Concentrations (µg/L)[2]			RQs
	Median Stream Flow Scenario	Low Stream Flow Scenario	7Q10 Flow Scenario	
P-12-0453				
PROC1: Formulation of MWFs	6.5	47	240	**6.5-240**
PROC2: PVC compounding	7	54	278	**7-278**
PROC3: Formulation of adhesives and sealants	7	150	258	**7-258**
USE1: Use of MWF	11	144	1300	**11-1300**
USE2: PVC converting	1	27	148	**1-148**
USE3: Use of adhesives and sealants	2	20	210	**2-210**
P-12-0433				
PROC1: Formulation of MWFs	5	36	184	**5-184**
USE1: Use of MWFs	7	92	829	**7-829**

[1]Taken from full model run of summary data presented in Appendix E.
[2]For PMNs, EPA/OPPT evaluated potential environmental risks by performing a PDM as described above and in the "Exposure and Fate Assessment Screening Tool (E-FAST) Version 2.0 Documentation Manual (2007)", available at: http://www.epa.gov/tsca-screening-tools/e-fast-exposure-and-fate-assessment-screening-tool-2014-documentation-manual

6.2 HUMAN HEALTH

EPA/OPPT assessed potential risks to workers and the general population by calculating margins of exposure (MOE). This approach is performed according to the following equation:

MOE = Point of Departure (POD) ÷ Estimated human exposure

For the PODs, EPA/OPPT identified effect levels from three oral repeated dose toxicity studies, which served as the basis for calculating human equivalent doses (HEDs) (CXR 2005; NTP 1986). In the first study, CXR (2005) reported a NOAEL of 23 mg/kg-bw/day based on increased kidney weight at 222 mg/kg-bw/day in male rats exposed through diet for 90 days to an MCCP congener group (C_{14-17}, 52 wt% Cl). In the second and third studies, NTP (1986) reported LOAELs of 100 mg/kg-bw/day based on granulomatous inflammation of the liver in female rats administered an LCCP congener (C_{23}, 43 wt% Cl) by gavage for 5 days/week for 12 months or two years.

Using the effect levels of 23 mg/kg-bw/day or 100 mg/kg-bw/day, EPA/OPPT performed route-to-route extrapolations to develop HEDs for inhalation and dermal exposures in workers and for inhalation and oral exposures in the general population. EPA/OPPT did not assess oral exposures for workers, due to the unlikely nature of exposures occurring by this route. The respective HEDs served as the PODs for calculating MOEs, along with the previously reported estimated human exposure values for workers (Table 9) and the general population (Table 8).

EPA/OPPT compared the MOEs to a benchmark value that consisted of a multiplicative composite of three possible uncertainty factors (UFs): intraspecies variability (UF_H; default value = 10), interspecies variability (UF_A; default value = 10), and LOAEL-to-NOAEL extrapolation uncertainty (UF_L; default value =10). The UF_H and UF_A may each be subdivided to account for

toxicokinetics (TK; default value = 3.16) and toxicodynamics (TD; default value = 3.16). When effect levels from experimental animal studies are converted to HEDs, EPA/OPPT's default approach is to reduce the TK subfactor of UF_A to 1 (*i.e.*, $UF_A = TK \times TD = 1 \times 3.16 \approx 3$).

EPA/OPPT interprets MOEs that were equal to or below a benchmark value (*e.g.*, MOE $\leq$ 1000 [$UF_H \times UF_A \times UF_L = 1000$]) as an indication that the scenario(s) may present a risk of injury to human health, whereas MOEs that were above the benchmark value as a low risk finding. In the following sections, more detailed descriptions are provided on: 1) converting effect levels to route- and exposure-specific HEDs; 2) determining the appropriate UFs for the benchmark value, and 3) evaluating risk estimates for workers and the general population.

6.2.1 Workers

EPA/OPPT performed route-to-route extrapolations to convert the oral NOAEL of 23 mg/kg-bw/day (*i.e.*, MCCP congener groups) and the oral LOAEL of 100 mg/kg-bw/day (*i.e.*, LCCP congener) to HED values for inhalation exposures to workers (*i.e.*, $HED_{INHAL\text{-}WORKER}$) using the following equation:

$$HED_{INHAL\text{-}WORKER} = NOAEL_{ORAL} \times (1 \div sRV_{RAT}) \times (ABS_{ORAL\text{-}RAT} \div ABS_{INHAL\text{-}HUMAN}) \times (sRV_{HUMAN} \div wRV)$$

where,

$NOAEL_{ORAL}$ = 23 or 100 mg/kg-bw/day
sRV_{RAT} = rat standard respiratory volume for 8-hours = 0.38 m^3/kg bw
$ABS_{ORAL\text{-}RAT}$ = percent absorption by the oral route in rats = 50%
$ABS_{INHAL\text{-}HUMAN}$ = percent absorption by inhalation in humans = 50%
sRV_{HUMAN} = human standard respiratory volume for 8-hours = 6.7 m^3
wRV = worker respiratory volume for 8-hours = 10 m^3

For the oral NOAEL of 23 mg/kg-bw/day and the oral LOAEL of 100 mg/kg-bw/day, the $HED_{INHAL\text{-}WORKER}$ values equal 41 mg/m^3 and 176 mg/m^3, respectively.

EPA/OPPT calculated the HED values for dermal exposures to workers (*i.e.*, $HED_{DERM\text{-}WORKER}$) based on the following equation:

$$HED_{DERM\text{-}WORKER} = NOAEL_{ORAL} \times (ABS_{ORAL\text{-}RAT} \div ABS_{DERMAL\text{-}HUMAN}) \times (BW_{RAT} \div BW_{HUMAN})^{1/4}$$

where,

$NOAEL_{ORAL}$ = 23 or 100 mg/kg-bw/day
$ABS_{ORAL\text{-}RAT}$ = percent absorption by the oral route in rats = 50%
$ABS_{DERM\text{-}HUMAN}$ = percent absorption by the dermal route in humans = 1%
BW_{RAT} = rat bodyweight = 0.250 kg
BW_{HUMAN} = human bodyweight = 71.8 kg

The resulting $HED_{DERM\text{-}WORKER}$ values equal 4600 mg/kg-bw/day for MCCP congener groups and 20,000 mg/kg-bw/day for the LCCP congener.

EPA/OPPT used the foregoing HED values to inform the appropriate application of UFs to derive benchmark values. For MCCP congener groups and the LCCP congener, a benchmark value of 30 or 300 was applied, respectively. These values consisted of the following individual UFs. A default UF_H of 10 was applied to each benchmark value, due to the absence of experimental data to inform the TK and TD subfactors of this UF. A reduced UF_A of 3 was applied to each benchmark value, which accounted for a TK subfactor of 1 after converting the effect levels to HEDs. The UF_A of 3 accounted for the remaining uncertainty associated with TD variability. A default UF_L of 10 was only used for the benchmark value compared to the MOE derived from an LCCP congener because the underlying study reported a LOAEL, not a NOAEL.

EPA/OPPT used the $HED_{INHAL\text{-}WORKER}$ and $HED_{DERM\text{-}WORKER}$ values for calculating the respective MOEs using the estimated exposure values presented in Table 9. As shown in Table 13, the MOEs for P-12-0453 and P-12-0433 all exceeded the respective benchmark values, which indicate a finding of low risk to workers for the processes and uses evaluated in this assessment.

Table 13: Occupational MOEs for P-12-0453 and P-12-0433

Exposure Route	Exposure Scenario	Margin of Exposure
P-12-0453		**Benchmark MOE = 30**
Inhalation	PROC1: Formulation of MWFs	NA
	PROC2: PVC compounding	186 - 27,333
	PROC3: Formulation of adhesives and sealants	NA
	USE1: Use of MWF	115 - 410
	USE2: PVC converting	37
	USE3: Use of adhesives and sealants	36
Dermal	PROC1: Formulation of MWFs	18,349 - 94,366
	PROC2: PVC compounding	18,349
	PROC3: Formulation of adhesives and sealants	18,349 - 62,317
	USE1: Use of MWF	8,469 - 94,366
	USE2: PVC converting	NA
	USE3: Use of adhesives and sealants	62,317
P-12-0433		**Benchmark MOE = 300**
Inhalation	PROC1: Formulation of MWFs	NA
	USE1: Use of MWFs	496 - 1,760
Dermal	PROC1: Formulation of MWFs	79,778 - 410,286
	USE1: Use of MWFs	36,821 - 410,286

6.2.2 General Population

EPA/OPPT converted the oral NOAEL of 23 mg/kg-bw/day (*i.e.*, MCCP congener groups) and the oral LOAEL of 100 mg/kg-bw/day (*i.e.*, LCCP congener) to HED values for oral exposures to the general population (*i.e.*, $HED_{ORAL\text{-}GENPOP}$) using the following equation:

$$HED_{ORAL\text{-}GENPOP} = NOAEL_{ORAL} \times (ABS_{ORAL\text{-}RAT} \div ABS_{ORAL\text{-}HUMAN}) \times (BW_{RAT} \div BW_{HUMAN})^{1/4} \times (5 \text{ days} \div 7 \text{ days})^{a}$$

where,

$NOAEL_{ORAL}$ = 23 or 100 mg/kg-bw/day
$ABS_{ORAL\text{-}RAT}$ = percent absorption by the oral route in rats = 50%
$ABS_{ORAL\text{-}HUMAN}$ = percent absorption by the oral route in humans = 50%
BW_{RAT} = rat bodyweight = 0.250 kg
BW_{HUMAN} = human bodyweight = 71.8 kg
[a]A duration-specific adjustment was only applied to the oral LOAEL of 100 mg/kg-bw/day because the animals were gavaged five days per week.

For assessing inhalation exposures to the general population, EPA/OPPT performed route-to-route extrapolations to convert the oral NOAEL of 23 mg/kg-bw/day (*i.e.*, MCCP congener groups) and the oral LOAEL of 100 mg/kg-bw/day (*i.e.*, LCCP congener) to HED values for inhalation exposures to the general population (*i.e.*, $HED_{INHAL\text{-}GENPOP}$) using the following equation:

$$HED_{INHAL\text{-}HUMAN} = NOAEL_{ORAL} \times (1 \div sRV_{RAT}) \times (ABS_{ORAL\text{-}RAT} \div ABS_{INHAL\text{-}HUMAN}) \times (5 \text{ days} \div 7 \text{ days})^{a}$$

where,

$NOAEL_{ORAL}$ = 23 or 100 mg/kg-bw/day
sRV_{RAT} = rat standard respiratory volume for 8-hours = 1.15 m^3/kg bw
$ABS_{ORAL\text{-}RAT}$ = percent absorption by the oral route in rats = 50%
$ABS_{INHAL\text{-}HUMAN}$ = percent absorption by inhalation in humans = 50%
[a]A duration-specific adjustment was only applied to the oral LOAEL of 100 mg/kg-bw/day because the animals were gavaged five days per week.

For the oral NOAEL of 23 mg/kg-bw/day and the oral LOAEL of 100 mg/kg-bw/day, the $HED_{INHAL\text{-}GENPOP}$ values equal 20 mg/m^3 and 62 mg/m^3, respectively.

The same benchmark values of 30 or 300 were used for evaluating the general population MOEs. These benchmark values consisted of the same individual UFs and rationale discussed previously for workers.

EPA/OPPT used the $HED_{ORAL\text{-}GENPOP}$ and $HED_{INHAL\text{-}GENPOP}$ values for calculating the respective MOEs using the estimated exposure values presented in Table 8. As shown in Table 14, the MOEs for P-12-0453 and P-12-0433 all exceeded the respective benchmark values, which indicate a finding of low risk to the general population for environmental exposures that may occur due to the processes and uses evaluated in this assessment.

Table 14: General Population MOEs for P-12-0453 and P-12-0433[1]

Scenario	Water Release		Air Release
	Drinking Water MOE	Fish Ingestion MOE	Stack Air MOE
P-12-0453 (Benchmark MOE = 30)			
PROC1: Formulation of MWFs	2.2×10^6	1.8×10^5	3.1×10^5
PROC2: PVC compounding	1.3×10^6	1.0×10^5	2.5×10^5
PROC3: Formulation of adhesives and sealants	7.1×10^5	5.8×10^4	1.4×10^5
USE1: Use of MWF	2.8×10^5	2.2×10^4	1.0×10^5
USE2: PVC converting	1.3×10^6	1.1×10^5	4.2×10^5
USE3: Use of adhesives and sealants	4.6×10^6	3.8×10^5	3.3×10^6
P-12-0433 (Benchmark MOE = 300)			
PROC1: Formulation of MWFs	2.8×10^8	6.4×10^6	N/A
USE1: Use of MWFs	1.2×10^6	2.8×10^5	9.8×10^4

[1]Taken from Appendix E. Values represent the highest concentrations/estimated doses (reported as the lifetime average daily dose, or LADD) for chronic (*i.e.*, repeated exposure scenarios) for human health.

7 CONCLUSIONS

Based on its assessment of the available surrogate hazard and exposure information on P-12-0453 and P-12-0433, EPA/OPPT concludes the following pertaining to the manufacturing, processing and use of these PMN substances:

1. Occupational Exposures: given the assumptions, data and scenarios evaluated in this assessment, there were low risks found for workers from either dermal or inhalation exposures.

2. General Population Exposures (from environmental releases): given the assumptions, data and scenarios evaluated in this assessment, there were low risks found to humans from environmental releases via exposure to either drinking water or fish ingestion.

3. Environmental Assessment:
   a. Using estimated environmental concentrations, the PMN substances **may present an unreasonable risk following acute and chronic exposures to aquatic organisms.**

   b. Using available measured concentrations of MCCP and LCCP congener groups in the environment as supporting information, the PMN substances:
      iii. Are expected to partition to sediment and may partition to soil through land application of biosolids and,
      iv. May be released to the environment at levels at or above estimated concentrations of MCCP and LCCP congener groups that **may present an unreasonable risk following acute and chronic exposures to aquatic organisms.**

4. PBT Assessment: The PMN substances **may be very persistent and very bioaccumulative**.

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9 APPENDICES

Appendix A ENVIRONMENTAL FATE AND BIOACCUMULATION STUDY SUMMARIES

A-1 ENVIRONMENTAL PERSISTENCE

A-1-1 Abiotic Degradation

Generally, CPs are stable to hydrolysis and to direct photolysis in air and water, though very limited data exist on hydrolysis and direct and indirect photolysis in soil, water, or air. In studies using aliphatic hydrocarbon solvents, CPs were shown to be poor absorbers of UV light and no direct photodegradation was observed (Friedman and Lombardo, 1975; Lombardo et al., 1975). Koh and Thiemann (2001) studied photolysis of aqueous solutions for CPs products with chain lengths ranging from C_{10} to C_{24} including an MCCP product, Hoechst CP52, with chain lengths from C_{12} to C_{18} and an average of 52 wt% Cl. A mercury vapor lamp with main radiation wavelengths of 254, 302, 313, 366,405/408, and 436 was used in batch experiments. Following a 5 hour radiation time, estimated atmospheric degradation rates showed photolysis half-lives of less than 20 hours based on measurement of free chloride and analysis of degradation products. The MCCP product had a $T_{1/2}$ of 12.8 hour in aqueous solution. The addition of peroxide or acetone increased the photolysis rate suggesting that indirect photolysis may be significant. The authors also reported that longer chain CPs were formed during this study and speculated that recombination of smaller alkyl radicals could occur under some conditions.

Thermal degradation data for MCCPs and LCCPs are limited, but studies of SCCPs and Polyvinyl chlorides suggest MCCPs are degraded rapidly at 250 - 350 °C (Bergman et al., 1984). Dehydrohalogenation may lead to the formation of a large number of aliphatic and aromatic compounds. Chlorine radical formation can lead to production of highly chlorinated aromatics including polychlorinated biphenyls. Higher Cl content results in production of greater numbers and amounts of chlorinated aromatics (Bergman et al., 1984).

A-1-1-1 Fate in Air

As noted above, CPs lack structural components that absorb light in the UV or visible spectrum, so direct photolysis is not expected to occur. The atmospheric half-life has been estimated at 1 - 2 days (EA, 2009; ECB, 2005), based on estimated values for the second order rate constant for reaction with atmospheric hydroxyl radicals for MCCPs with lower chlorine contents between 40 and 56 wt%. EPA/OPPT also estimated atmospheric half-lives for MCCPs (40 and 70 wt% Cl) calculated using EPI Suite™/AOPWIN™ (v. 1.92a) that range from about 1 to > 4 days (see Table_Apx A-1). MCCPs with the shorter chain lengths and higher chlorine contents were calculated to be more persistent.

MCCPs have low estimated vapor pressures (4.5×10^{-8} to 2.27×10^{-3} Pa at 20 - 25°C) and a Henry's law constant (HLC) (0.014 - 51.3 Pa × m^3/mol for $C_{14\text{-}17}$ congener groups) and are not expected to partition to air. They may be transported associated with particulate matter, and have been reported in indoor and outdoor air and house dust (Barber et al., 2005; Fridén et al., 2011; Hilger et al., 2013). Wide spread soil contamination and occurrence in artic samples suggest that MCCPs behave similarly to other chlorinated persistent organic pollutants (POPs) with high

production volumes and releases, and are subject to long range transport (Dick et al., 2010; Medeiros et al., 2011; Tomy et al., 2000).

Table_Apx A-1: Estimated Atmospheric Half Lives Using EPI Suite™/AOPWIN™ (v. 1.92a) for Varying MCCP Chain Length and Chlorination Percents Based on Wt.

Chain Length	40 wt% Cl	70 wt% Cl
C_{14}	1.0	4.4
C_{15}	0.8	3.0
C_{16}	0.8	3.0
C_{17}	0.8	2.9

A-1-2 Biodegradation

EPA/OPPT reviewed studies from the open literature and submitted to EPA/OPPT including those described in the Canada and EU assessments and referenced in Table_Apx A-2 (EC, 2008a; ECB, 2005) to determine biodegradation under a variety of environmental conditions. Some of these studies used modified test conditions to enhance or maximize biodegradation. EPA/OPPT concurs with the EU's conclusions that under these modified test conditions, C_{14} 41.3% by wt. Cl and a C_{14} 45.5% by wt. Cl substances are readily biodegradable. C_{15} 51% by wt. Cl were found to be inherently degradable and possibly readily degradable in modified OECD 301 and 301D tests. This suggests that CPs with these chain lengths and shorter, and this degree of chlorination and lower, are inherently degradable. More highly chlorinated and longer carbon chain CPs ($C_{14\text{-}17}$ 51.7% by wt. Cl, C_{14} 55% by wt. Cl, C_{14} 60.2% by wt. Cl, and $C_{14\text{-}17}$ 63.2% by wt. Cl) biodegraded over a range of 2-54% in 28 days to 4-57% at up to 60 days. The most highly chlorinated, (C14-17, 63.2 wt% Cl) biodegraded 5% in 28 days and 10% at 60 days in the enhanced biodegradation studies, suggesting that longer chain and higher chlorination can contribute to greater persistence under most environmental conditions. (Van Ginkel, 2014 a and b; Van Ginkel 2010 a-d; Van Ginkel and Louwerse 2010 a and b).

A-1-2-1 Fate in Wastewater Treatment

In its review of the available measured data on MCCPs in wastewater treatment from data in from other countries, EPA/OPPT determined that CPs are present in the majority of municipal waste water treatment plant (WWTP) influent (Coelhan, 2010; Nicholls et al., 2001; Stevens et al., 2003; Zeng et al., 2013). Low water solubility and relatively high partitioning coefficients suggest that most of the MCCPs and LCCPs entering WWTP systems will associate with solids. Some biodegradation of shorter chain, lower chlorinated MCCP congener groups may occur, while longer chain length, more chlorinated congener groups will be resistant to aerobic and anaerobic degradation. Shorter and lower chlorinated congener groups have higher vapor pressure and may be lost to the vapor phase during aeration. WWTP effluent also contains some particulate-associated MCCPs. Because of their low water solubility, little MCCP or LCCP will be in the dissolved phase, and the majority will be removed along with settled sludge. Once associated with the sludge, the CPs will generally be stable in sludge treatment and remain in the residual biosolids. Land application of biosolids will transfer the MCCPs and LCCPs to agricultural and other soils (Nicholls et al., 2001; Stevens et al., 2003). Because 50 - 60% of

biosolids in the US are land applied, the majority of MCCPs and LCCPs entering WWTPs may be released to the environment via application to soil, and may be transported from contaminated soil to other locations and media by soil erosion, runoff, and wind borne particulates, and volatilization.

A-1-2-2 Fate in Surface and Groundwater

Because they generally have low water solubility, high sorption coefficients, and tend to partition to solids, MCCPs and LCCPs released to surface water will partition to surficial sediment where they may be buried and removed from potential degradation processes. This explains what is found in the limited monitoring data that exist - MCCP concentrations in surface water are generally in the low pg/L range, while sediment concentrations are several orders of magnitude higher (EC, 2008a).

MCCPs may leach from soil and be transported to groundwater, but low solubility and high sorption will act to keep dissolved concentrations very low. Facilitated transport with colloids and particulates may occur so that MCCPs can be transported in groundwater, but in general, concentrations in this compartment are expected to be very low. MCCPs that are introduced to groundwater will tend to partition to the solid phase and not be mobile.

A-1-2-3 Fate in Soil

Existing monitoring data suggest that MCCPs are present in soil, probably as a result of atmospheric transport and deposition. Areas near sources, such as land receiving wastewater biosolids, manufacturing and processing facilities, and electronic waste processing and recycling facilities are shown to have higher levels (Wang et al., 2013). MCCPs are expected to be stable in soil, and once deposited, could remain/persist in the soil for years or decades. Burial and advective transport away from the site of deposition are the major dissipation processes. No data are available on soil photolysis, although aqueous photolysis data suggest that indirect photolysis may result in degradation to shorter and less chlorinated CP congener groups. No soil biodegradation data exists, but some strains of bacteria that can co-metabolize MCCPs have been identified (Allpress and Gowland, 1999). If degradation does occur, it is expected to be slow with $T_{1/2}$ of at least months to years.

Table_Apx A-2: Review of MCCP and LCCP Biodegradation Studies.

Biodegradation Studies on MCCPs (C_{14-17}) and LCCPs ($C_{>18}$)					
Study Authors	**Publication Date**	**MCCP/LCCP Chemicals Evaluated (*i.e.*, C-length, wt% Cl)**	**Method**	**Study Duration**	**Noteworthy Results and Implications**
MCCPs					
Van Ginkel	2010d	C_{14} 45 wt% Cl	Closed bottle	28 days	Approximately 64% degraded in 28 days Based on oxygen demand
Van Ginkel	2010b	C_{14-17} 45.6 wt% Cl	Closed bottle	28 days	Approximately 51% in 28 days and 63% in 42 days degradation Based on oxygen demand
Van Ginkel	2010c	C_{14-17} 51.7 wt% Cl	Closed bottle	28 days	Approximately 27% degradation in 28 days and 57% after 60 days

Biodegradation Studies on MCCPs (C_{14-17}) and LCCPs ($C_{>18}$)					
Study Authors	**Publication Date**	**MCCP/LCCP Chemicals Evaluated (*i.e.*, C-length, wt% Cl)**	**Method**	**Study Duration**	**Noteworthy Results and Implications**
					Based on oxygen demand
Van Ginkel	2010a	C_{14-17} 63.2 wt% Cl	Closed bottle	28 days	Approximately 5% degradation after 28 days and 10% after 60 days.
Van Ginkel and Louwerse	2010a	C_{14} 41.3-60.2 wt% Cl%	Closed bottle with river water and sludge inoculum	28 days	Approximately 66% (41.3 wt% Cl) to 11 (60.2 wt% Cl) degradation in 28 days respectively
Van Ginkel and Louwerse	2010b	C_{14} 41.3-50 wt% Cl	Batch reactor	21 and 105 days	41.3 wt% Cl: 79% degradation in 21 days and 94% at 105 days 50 wt% Cl: 14% degradation by 21 days 5 wt% Cl in 80 days based on quantitation of released chloride
Conclusions: Quantification of degradation was by oxygen uptake or chloride release. No information on the chemical distribution in the test material or degradates was provided. These studies used modified test conditions to enhance or maximize biodegradation. Under these modified test conditions, C_{14} 41.3 wt% Cl and a C_{14} 45.5 wt% Cl substances are readily biodegradable. More highly chlorinated and longer carbon chain CPs (C_{14-17} 51.7 wt% Cl, C_{14} 55 wt% Cl, C_{14} 60.2 wt% Cl, and C_{14-17} 63.2 wt% Cl) biodegraded over a range of 2 – 54% in 28 days to 4 – 57% at up to 60 days. The most highly chlorinated, (C_{14-17} 63.2 wt% Cl) biodegraded 5% in 28 days and 10% at 60 days in the enhanced biodegradation studies, suggesting that longer chain and higher chlorination can contribute to greater persistence under most environmental conditions.					
Van Ginkel	2014b	C_{15} 51 wt% Cl	Closed bottle (301D)	60 day	43% and 63% degradation at 28 and 60 days
Van Ginkel	2014a	C_{15} 51wt% Cl	Closed bottle (301)	60 day	37% and 57% degradation at 28 and 60 days
Conclusions: Unlike the 2010 series of studies, these most recent biodegradation studies did not have significant protocol modifications and the C_{15} 51 wt% Cl were found to be inherently degradable and possibly readily degradable in OECD 301 and 301D tests.					
Madeley and Birtley	1980	C_{14-17} mixed product, 40 wt% Cl	BOD test	25 days	Approximately 15.5% degradation as measured by theoretical BOD in non-acclimated samples and 22.5% degradation in acclimated samples.[1]
Madeley and Birtley	1980	C_{14-17} mixed product, 45 wt% Cl	BOD test	25 days	Approximately 10% degradation as measured by theoretical BOD in non-acclimated samples and 30% degradation with acclimated soil microbes added.[1]
Madeley and Birtley	1980	C_{14-17} mixed product, 52 wt% Cl	BOD test	25 days	Approximately 4% degradation as measured by theoretical BOD in non-acclimated samples and 6% degradation with acclimated soil microbes added.[1]

Biodegradation Studies on MCCPs (C_{14-17}) and LCCPs ($C_{>18}$)					
Study Authors	**Publication Date**	**MCCP/LCCP Chemicals Evaluated (*i.e.*, C-length, wt% Cl)**	**Method**	**Study Duration**	**Noteworthy Results and Implications**
Madeley and Birtley	1980	C_{14-17} mixed product, 58 wt% Cl	BOD test	25 days	No significant degradation
Conclusions: The data from Madeley and Birtley suggests the potential for biodegradation but has significant limitations. The BOD studies were done on mixed products. No attempt was made to determine which specific congeners were degraded or the reaction products. No identification of the congeners present was provided. The degradation was estimated from the BOD but other compounds may have contributed to the ThBOD in the bottles. BOD measurements are highly variable as evidenced by the decrease in the C_{20-30} 42% of > 50% between day 20 and 25. [1]The ThOD (theoretical oxygen demand) was estimated (ThOD (g O_2/g substance) = 16[2×c+0.5×(h-cl)]/mw; where c=number of carbon atoms, h=number of hydrogen atoms, cl=number of chlorine atoms and MW = molecular weight). This is questionable for a product containing mixture of congeners as was used in all studies.					
LCCPs					
Madeley and Birtley	1980	C_{20-30} mixed product, 42 wt% Cl	BOD test	25 days	Approximately 7.5% degradation as measured by theoretical BOD in non-acclimated samples and 23% degradation with acclimated soil microbes added.[1]
Madeley and Birtley	1980	C_{25} "chlorinated pentacosane"	^{14}C on central carbon	8 weeks (mean)	11% of ^{14}C- released as CO_2. Non-acclimated microbes.
Conclusions: The data from Madeley and Birtley suggests the potential for biodegradation but has significant limitations. The BOD studies were done on mixed products. No attempt was made to determine which specific congeners were degraded or the reaction products. No identification of the congeners present was provided. The degradation was estimated from the BOD but other compounds may have contributed to the ThBOD in the bottles. BOD measurements are highly variable as evidenced by the decrease in the C_{20-30} 42% of > 50% between day 20 and 25. [1]The ThOD (theoretical oxygen demand) was estimated (ThOD (g O_2/g substance) = 16[2×c+0.5×(h-cl)]/mw; where c=number of carbon atoms, h=number of hydrogen atoms, cl=number of chlorine atoms and MW = molecular weight). This is questionable for a product containing mixture of congeners as was used in all studies.					
Hildebrecht	1972	C_{20-30} mixed product, 42 wt% Cl	BOD test	5 days	25% degradation. Degradation was estimated by the authors as the% of the theoretical BOD based on the total carbon content of the test solution. Substances other than the chlorinated paraffin contributed to this total carbon content.
Hildebrecht	1972	> C_{20-30} mixed product, 70 wt% Cl	BOD test	5 days	2% degradation. Degradation was estimated by the authors as the% of the theoretical BOD based on the total carbon content of the test solution. Substances other than the chlorinated paraffin contributed to this total carbon content.
Hildebrecht	1972	> C_{20-30} mixed product, 70 wt% Cl	BOD test	5 days	65% degradation. Degradation was estimated by the authors as the% of the theoretical BOD based on the total carbon content of the test solution.

Biodegradation Studies on MCCPs (C_{14-17}) and LCCPs ($C_{>18}$)					
Study Authors	**Publication Date**	**MCCP/LCCP Chemicals Evaluated (*i.e.*, C-length, wt% Cl)**	**Method**	**Study Duration**	**Noteworthy Results and Implications**
					Substances other than the chlorinated paraffin contributed to this total carbon content.
Conclusions: As described by the (EA, 2009), Hildebrecht's results are questionable (Hildebrecht, 1972). This report is not available so it cannot be reviewed directly, but others have reported that it provided limited details. A surfactant, other carbon sources, and nutrients were added that may have contributed BOD. The extent of degradation was determined by the comparing the oxygen consumption in the test with the theoretical oxygen demand (ThOD) based on oxidation to CO_2 of the total organic carbon present in the solution from all sources. This estimation of ThOD does not take into account oxygen consumption by other compounds or the unknown composition. Of the CPs in the mixture, as the UK report concludes, "It is not possible to draw definite conclusions as to the degradability of the chlorinated paraffins in these tests" (EA, 2009).					
Hoechst AG	1976 and 1977	C_{18-20}, 35 wt% Cl	BOD test	5 days	0.7% degradation
Hoechst AG	1976 and 1977	C_{18-20}, 44 wt% Cl	BOD test	5 days	< 1.2% degradation
Hoechst AG	1976 and 1977	C_{18-20}, 49 wt% Cl	BOD test	5 days	< 2.3% degradation
Hoechst AG	1976 and 1977	C_{18-20}, 52 wt% Cl	BOD test	5 days	< 0.6% degradation
Conclusions: The Hoechst reports from early industry studies are not available so it is not possible to directly review the data (Hoechst, 1976, 1977). Others (EA, 2009) have reported the limitations of the studies. Limited details of the studies were apparently reported by Hoechst. These tests were done on mixtures of congeners with unknown composition. They reported that the majority of the CPs were removed by sorption on to the solids so no degradation may have occurred that would have been detected as BOD. The tests were run for 5 days using non-acclimated sludge microbes so degradation may have been possible but had not yet occurred.					
Omori *et al.*	1987	$C_{24.5}H_{44.5}Cl_{6.5}$, 40.5 wt% Cl	Chloride release	48 hours	9.9% degradation using bacterial strain HK-3; 13% H15-4; 2.2% HK-6; 3.5% HK-8; 33% using mixed bacterial culture (HK-3, HK-6, HK-8 and HK-10)
Omori *et al.*	1987	$C_{24.5}H_{41}Cl_{10,}$ 50 wt% Cl	Chloride release	48 hours	3% degradation using bacterial strain HK-3; 9% H15-4; 1.8% HK-6; 2.6% HK-8
Omori *et al.*	1987	$C_{24.5}H_{30}Cl_{21,}$ 70 wt% Cl	Chloride release	48 hours	2.6% degradation using bacterial strain HK-3; 12% H15-4; 1.4% HK-6; 1.7% HK-8; 15% using mixed bacterial culture (HK-3, HK-6, HK-8 and HK-10)
Conclusions: Omori et al. (1987) showed the potential for biodegradation using pure and mixed cultures in short (48 hour) incubations. No information on the starting mixtures were provided except average compositions. No data					

Biodegradation Studies on MCCPs (C_{14-17}) and LCCPs ($C_{>18}$)					
Study Authors	**Publication Date**	**MCCP/LCCP Chemicals Evaluated (*i.e.*, C-length, wt% Cl)**	**Method**	**Study Duration**	**Noteworthy Results and Implications**
on the products were reported. Loss of Cl suggests dechlorination can occur and that lower Cl content or shorter chain lengths may be produced.					
Allpress and Gowland	1999	C_{18-20}, 48 wt% Cl	Chloride release	71 days	11% degradation using *Rhodococcus* sp. bacteria
Allpress and Gowland	1999	$C_{>20}$, 42 wt% Cl	Chloride release	71 days	14% degradation using *Rhodococcus* sp. bacteria
Conclusions: Allpress and Gowland (1999) also showed that CPs have the potential to biodegrade using pure culture. They used mixed congener products and did not provide any information on the composition of the starting material or the degradation products. They found that the *Rhodococcus* sp. was able to use CPs as carbon source as well as an energy source.					

[1]The ThOD (theoretical oxygen demand) was estimated (ThOD (g O_2/g substance) = 16[2×c+0.5×(h-cl)]/mw; where c=number of carbon atoms, h=number of hydrogen atoms, cl=number of chlorine atoms and MW = molecular weight). This is questionable for a product containing mixture of congeners as was used in all studies.

A-2 BIOCONCENTRATION AND BIOACCUMULATION

EPA/OPPT's review of measured data on bioaccumulation of MCCPs are somewhat limited and conclusions vary with type of CP mixture and species evaluated (Bengtsson et al., 1979; CPC, 1980, 1983a, 1983b; Fisk et al., 1999; Fisk et al., 1998; Houde et al., 2008; Madeley and Maddock, 1983a, 1983b; Madeley and Thompson, 1983; Renberg et al., 1986; Thompson et al., 2000).

The limited measured data on MCCPs and LCCPs, informed by data on SCCPs, suggests that bioaccumulation is a function of chain length and degree of chlorination (see Table_Apx A-3). Some MCCP chemicals with intermediate chain length and chlorination may be absorbed and retained. The available evidence for MCCP congeners with intermediate chain lengths and chlorination suggests that some may have BCFs or BAFs greater than 1000 or 5000 (EC, 2008b; ECB, 2008). This suggests that some congeners in MCCP product mixtures may be bioaccumulative or very bioaccumulative. In conclusion, some MCCP congeners present in the mixtures are both very persistent and very bioaccumulative.

Additional evidence for bioaccumulation of MCCPs is provided by Houde et al. (2008). Field-derived log BAFs for MCCPs (C_{14-15}), ranging from 6.5 to 7.3, were reported for several Lake Ontario aquatic species from multiple trophic levels. Canada's assessment of MCCPs also indicates that modeled BAFs for a number of MCCPs (using the Modified Gobas BAF Model with assumption of no metabolism), were all above 5000, suggesting high to very high bioaccumulation (EC, 2008a). Evidence of bioaccumulation in sediment-dwelling organisms is also provided in a study by Fisk et al. (1998). Biota-sediment accumulation factors (BASFs) ranging from 0.6 to 4.4 were reported for oligochaetes, which indicate bioaccumulation of MCCPs from sediment to biota (USEPA, 2009).

The Houde et al. (2008) study also provides evidence of biomagnification of MCCPs. BMFs derived for food chains in Lake Ontario and Lake Michigan ranged from 1 to 15. More

specifically, large BMFs were observed for all MCCP chain lengths in Lake Ontario, and for C_{14} MCCPs in Lake Michigan, indicating biomagnification. BMFs (2.4 – 7.7) were also above 1 for smelt and lake trout in Lake Michigan.

In laboratory studies with rainbow trout and oligochaetes, lipid-normalized equilibrium BMFs estimated from a first-order bioaccumulation model for constant dietary exposure ranged from 0.4 - 5.0 (Fisk et al., 1996; Fisk et al., 2000; Fisk et al., 1998).

Most of the laboratory-based BCF studies (Bengtsson et al., 1979; CPC, 1980, 1983a, 1983b; Fisk et al., 1999; Fisk et al., 1998; Houde et al., 2008; Madeley and Maddock, 1983a, 1983b; Madeley and Thompson, 1983; Renberg et al., 1986; Thompson et al., 2000), were reported to have been conducted at MCCPs concentrations above the water solubility limit and hence likely underestimate the true BCF. Furthermore, acetone as a solvent in these tests, so they do not adhere to OECD guidelines. Nonetheless, some BCF values estimated from these studies indicate MCCPs are bioaccumulative (*e.g.*, bleak and rainbow trout (32-2856) and BCF of 6920 for common mussel).

Table_Apx A-3: Review of MCCP and LCCP Bioaccumulation Studies

Bioaccumulation studies on MCCPs (C_{14-17}) and LCCPs (> C_{18})					
MCCPs					
Study Authors	**Publication Date**	**MCCP/LCCP Chemicals Evaluated (*i.e.*, C-length,% Cl)**	**Method**	**Study Duration**	**Noteworthy Results and Implications**
Houde *et al.*	2008	C_{14-15} Only	BAF = ([predator]/[water (filtered)]); BMF) = [predator]/[prey]) where the concentrations in predator and prey are on a lipid basis	Three sampling periods: October 2000, June 2002, and July 2004.	Issues related to the temporal variability of water concentrations over the period of biota sampling (1999 – 2004) in this study have been raised (ECB, 2005; EC, 2008) contributing to uncertainties associated with the reported BAF values. Log BAF = Plankton: C14=6.2; C15=6.6; ∑=6.5 Alewife: C14=7.0; C15=6.8; ∑=6.9 Sculpin: C14=7.4; C15=7.2; ∑=7.3 Rainbow smelt: C14=7.4; C15=7.1; ∑=7.2 Lake trout: C14=6.8; C15=6.5; ∑=6.6 BMF (Lake Ontario) = 0.25 (lake trout – alewife); 0.14 (lake trout – smelt); 8.7 (sculpin –Diporeia) BMF (Lake Michigan) = 0.22 (lake trout – alewife); 0.94 (lake trout – sculpin); 0.88 (sculpin – Diporeia)
Thompson et al.; as summarized in ECB, 2005	2000	n-pentadecane-8-^{14}C, 51% Cl mixed with a non-radio-labelled C14-17, 51% Cl chlorinated paraffin	Freshwater; flow-through; acetone solvent used;	35 days	Steady-state may not have been achieved, so kinetic BCF data considered more reliable. BCF = 860 L/kg at 35 days when exposed at 0.9 ug/L BCF = 265 L/kg at 35 days when exposed at 4.9 ug/L kinetic BCF = 1,087 L/kg at 35 days when exposed at 0.9 ug/L kinetic BCF = 349 L/kg at 35 days when exposed at 4.9 ug/L

CPC (Madeley et al.); as summarized in ECB, 2005	1983	commercial product mixed with a n-pentadecane-8-^{14}C chlorinated to a similar degree	freshwater; flow-through; rainbow trout; acetone solvent used	60 days	Concentrations above water solubility; hence, water concentrations may be overestimated and BCF underestimated. Uncertainty as to whether steady-state was reached. BCF = 32-45 l/kg on a wet weight basis when exposed at 1.05 mg/l; BCF = 42-67 l/kg on a wet weight basis when exposed at the 4.5 mg/l
CPC (Madeley and Pearson); as summarized in ECB, 2005	1980	C14-17, 45% Cl	freshwater; flow-through; rainbow trout;	28 days	Measured water concentrations questionable; water concentrations may be overestimated and BCF underestimated. BCF = 50-60 l/kg based on nominal exposure concentrations BCF = 280-600 l/kg based on measured water concentrations
Madeley and Maddock; as summarized in ECB, 2005	1983	Total MCCPs	Bioconcentration factors. MCCPs concentrations were above the water solubility limit, using acetone as the co-solvent in the test solutions, and hence are not in compliance with OECD guideline requirements	No Information	BCF = 32 – 2856 for common mussel, bleak and rainbow trout. May not have reached steady-state.
Fisk et al.	1999	Average formula: C14H23.3Cl6.7, 55% Cl	freshwater; medaka eggs	20-days	Uncertainty as to whether steady-state was reached; hence BCFs probably represent lower limit of true value BCF = 32- 680 L/kg
Fisk et al.	1998	$^{14}C_{16}$ 35% Cl and $^{14}C_{16}$ 69% Cl	Lake sediments were spiked and worms added after 18 and 32	No Information	Kinetic BAF probably represents the upper limit of the true bioaccumulation factor $^{14}C_{16}$ 35% Cl 14-day BSAFss = 0.7 Kinetic BSAF = 4.4 $^{14}C_{16}$ 69% Cl

					14-day BSAFss = 0.2 Kinetic BSAF = 0.6
Bengtsson et al.	1979	C14-17, 50% Cl	seawater; semi-static; bleak; acetone solvent used	14 days	Measured water concentrations questionable; water concentrations may be overestimated and BCF underestimated. BCF ~ 40 L/kg
Madeley and Thompson; as summarized in ECB, 2005	1983	commercial C14-17, 52% Cl	seawater; flow-through; mussel acetone solvent used	60 days	BCFs = 2,182 L/kg (parent compound analysis) or 2,856 L/kg (^{14}C-measurements) when exposed to 0.22 mg/l BCF = 339 L/kg (parent compound analysis) or 429 l/kg (^{14}C measurements) when exposed to 3.8 mg/l.
Renberg et al.	1985	$C_{16}H_{30.7}Cl_{3.3}$ (34% Cl) and $C_{12}H_{16}Cl_{9.8}$ (68.5% Cl) mixture synthesized with ^{14}C radiolabel	Flow through exposure to mussel (*Mytilus edulis*) C_{16} - 0.13 and 5.0 µg/L	C_{16} - 28 day uptake C_{12} - 21 day uptake followed by 28 day depuration	Steady state BCF about 7000 for C16 and 140,000 for C12 based on 14C quantification. No chemical specific analysis for CPs. Metabolism and accumulation of degradation products may have accounted for high values.
LCCPs					
Bengtsson et al.; as summarized in ECB, 2005	1979	$C_{18–26}$	concentrations were above the water solubility limit and hence are not in compliance with OECD guideline requirements	No Information	Concentrations above water solubility; hence, water concentrations may be overestimated and BCF underestimated. Uncertainty as to whether steady-state was reached. BCF reported = 8 – 16 L/kg

Appendix B ECOTOXICITY STUDY SUMMARIES

B-1 MCCP ECOTOXICITY DATA

B-1-1 Acute Fish Toxicity

(1) A series of 96-hour acute fish toxicity studies were conducted by Mayer an Ellersieck (1986) with Paroil 1048 (50-52% Cl, $C_{15}H_{26}C_{l6}$) similarly to ASTM (1980). Bluegill sunfish (*Lepomis macrochirus*) and yellow perch (*Perca flavescens*) were exposed to the test substance in a flow-through test system and channel catfish (*Ictalurus punctatus*) and rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance in a static test system. Solvent use was not specified for this compound. The average pH level was between 7.4 and 7.5 for all tests. Test temperature was 12 ºC for bluegill sunfish, rainbow trout, and yellow perch and 20 ºC for channel catfish. Dilution water hardness was 44 mg $CaCO_3$/L in the rainbow trout and channel catfish test system and 314 mg $CaCO_3$/L for the bluegill sunfish and yellow perch test system. Reported effect levels are considered to be nominal with LC_{50} values of >10 mg/L for bluegill sunfish, channel catfish, and yellow perch and >0.011 mg/L for rainbow trout; all values are greatly above the limit of solubility.

EPA/OPPT Conclusion
Using a weight-of-evidence approach, these studies were considered acceptable to characterize the acute fish toxicity endpoint.
96-hr LC_{50} = NES

(2) A 96-hour acute fish toxicity study was published by Linden et al. (1979). Groups of 10 Bleak (*Alburnus alburnus*) were exposed to six nominal unspecified concentrations of Cereclor S52® (C_{14-17}, 52% Cl), Chloroparaffin huls 40G ($C_{15.5}$, 40% Cl), and Witaclor 50 (C_{14-17}, 50% Cl) under static test conditions. Salinity was 7 ppt, pH was 7.8, temperature was 10 ºC, and dissolve oxygen was considered by study authors to be satisfactory. EPA/OPPT requires reporting of dissolved oxygen concentrations to determine study adequacy. EPA/OPPT also does not consider the test species, the bleak, a standard test species. The 96-hour fish LC_{50} values were >10,000 mg/L, >5,000, and >5,000 for Cereclor S52®, Chloroparaffin huls 40G, and Witaclor 50.

EPA/OPPT Conclusion
Given effect levels observed in Mayer and Ellersieck (1986) and the reported water solubility of medium chain paraffins, these studies were considered acceptable using a weight-of-evidence approach to characterize the acute saltwater fish toxicity endpoint.
96-hr LC_{50} = NES

(3) Bengtsson et al. (1979) also studied the toxicity of a medium-chain chlorinated paraffin to Bleak (*Alburnus alburnus*) as part of a bioaccumulation study. The chlorinated paraffin tested was a C14-17, 50% wt. Cl substance. The tests were performed at 10 °C using a semi-static procedure in which the test solutions containing 125 µg/L of the substance were renewed every two to three days over the 14-day exposure period. The water used in the experiment was Baltic Sea water with a salinity of 7‰, and acetone was present in all aquaria, including controls at a concentration of 0.1 ml/l. The fish used in the experiment had an average weight of 4.5 g and

were not fed during the exposure period. Six groups of 15 fish were used for both the exposure and control solutions. No mortality or effect on behavior was seen in fish exposed to the medium-chain chlorinated paraffin during the test.

EPA/OPPT Conclusion
This data review was part of a BAF study and as such will be used as a weight of evidence to support other data for this category of organisms.

B-1-2 Acute Aquatic Invertebrate Toxicity

(1) A 48-hour acute *Daphnia magna* toxicity study was conducted by Thompson et al. (1996) according to OECD TG 202 (1984) with GLP compliance using a static test system. The test substance was identified as Cereclor S52®, a C_{14-17} chlorinated paraffin with 52% chlorination that contained 0.3% epoxy soya bean oil stabilizer as well as a small amount of radiolabelled n-pentadecane-8-^{14}C (51% chlorinated). Four replicates of 5 *Daphnia magna* Straus (<24 hours old) were exposed to nominal concentrations of 0 (dilution water control), 0 (solvent control), 0.0032, 0.0056, 0.01, 0.018, 0.032, 0.056, and 0.1 mg/L test substance in acetone (0.1 mL/L). Test solutions were prepared by adding the appropriate stock solution to dilution water while continuously and vigorously stirring with a magnetic follower. Appearance of test solutions was not provided. Corresponding mean measured concentrations determined by radiochemical methods were 0.0025, 0.0041, 0.0094, 0.015, 0.024, 0.047, and 0.095 mg/L. Daphnid loading was 25 daphnids/L. Over the course of the study dissolved oxygen concentrations remained between 9 and 9.2 mg/L, pH remained within 8 and 8.1, and temperatures were 20 ±1 ºC. Dilution water had a total water hardness of 248 mg $CaCO_3$/L. At 48 hours, 0%, 45%, 90%, 75%, 85%, 100%, and 100% immobilization was observed at the mean measured concentrations of 0.0025, 0.0041, 0.0094, 0.015, 0.024, 0.047, and 0.095 mg/L, respectively. Red coloration on parts of the exoskeleton was observed in animals exposed to each of the test substance treatments, which the laboratory notes as being of an uncertain significance.

EPA/OPPT Conclusion
The study is acceptable.
48-hr EC_{50} = 0.0059 mg/L

(2) A 48-hour acute *Daphnia magna* toxicity study was conducted the University of Bremen, Department of Physical and Environmental Chemistry with CP 52 (C_{12-18}, 52% chlorination) according to DIN 38412 by Koh and Thiemann (2001). Study methods were not fully characterized. Additional communications with the study author Wolfram Thiemann clarified that a static test system was used with nominal test concentrations. Based on communications with the study author, local (Bremen, Germany) tap water was used without adjustments. Presumed pH was between 5 and 6 and water hardness was between 35.7 and 53.5 mg $CaCO_3$/L. Ambient laboratory air temperature was around 21 ºC. The solvent acetone was used to maintain test substance in solution. Floating effects at the surface of the water were observed in individual cases due to undissolved oil slicks, but communications with the study author noted that there was no significant loss of daphnids due to mechanical trapping since most daphnid swam away from these occasional slicks observed at the higher test concentrations.

EPA/OPPT Conclusion
This study is considered acceptable.
48-hr EC_{50} = 0.052 mg/L

(3) A 48-hour acute *Daphnia magna* toxicity study was conducted by Thompson et al. (1994) according to OECD TG 202 (1984) with GLP compliance using a static test system. The test substance was identified as Cereclor S52®, a C_{14-17} chlorinated paraffin with 52% chlorination that was mixed with an equal weight of radiolabeled n-pentadecane-8-^{14}C (51% chlorinated). Four replicates of 5 *Daphnia magna* (<24 hours old) were exposed to 0% (dilution water control), 6.3%, 12.5%, 25%, 50%, and 100% of stock solution containing test substance. The test substance was prepared in solution by (1) combining 0.75 g test substance and 25 mL acetone to a borosilicate glass conical flask, (2) evaporation of the acetone using a stream of nitrogen, (3) addition of 1.5 L dilution water, (4) stirring for three days, and (5) filtration of the aqueous phase. Radiochemical methods were used to determine the concentration of test substance in solution. Nominal concentrations of 0 (dilution water control), 0.14, 0.28, 0.55, 1.1, and 2.2 mg/L were within 86-100% of measured concentrations. Concerns regarding test solution preparation methods and analytical technique were identified by the submitter that included increasing the level of more soluble impurities (i.e., short chain chlorinated paraffins), questionable analytical monitoring results due to the presence of radio-labeled impurities, and abnormally low recovery of the chlorinated paraffin into hexane. Over the course of the study dissolved oxygen concentrations remained between 8 and 9 mg/L, pH remained within 8 and 8.1, and temperatures were 20 ±1 ºC. Dilution water had a total water hardness of 237 mg $CaCO_3$/L. Observed immobilization was limited to the highest test concentration (100% solution) with 55% immobilization.

EPA/OPPT Conclusion

The study is unacceptable since EPA/OPPT agrees that methods used to prepare the test solution and analyze the test concentrations were questionable.

4) The following study summary (Frank, 1993; Frank and Steinhäuser, 1994) provided in the 2005 European Chemical Bureau Risk Assessment of MCCP was considered supportive of the aquatic invertebrate hazard determination. The chlorinated paraffin used in these studies was a commercial C_{14-17} product with a 52% by weight chlorine content. *Daphnia magna* were exposed to nominal concentrations of either 100 mg/L or 10,000 mg/L. The 100 mg/L solution was sonicated for 1 hour and then left to stand in the dark for 48 hours before use. The 10,000 mg/L solution also stood for 48 hours in the dark before use, but this time without sonication. After this period, both solutions were filtered firstly with glass filters and then with membrane filters to remove undissolved test substance. The concentrations of medium-chain chlorinated paraffin in the water soluble fractions were then determined by AOX (adsorbable organic halogen) analysis (detection limit of 10 µg/L Cl was equivalent to around 20 µg/L of the chlorinated paraffin). This analysis showed that the concentration of chlorinated paraffin present in the water soluble fraction was around 0.404-0.500 mg/L for the 10,000 mg/L nominal solution and 0.071-0.142 mg/L L for the 100 mg/L stock solution. The acute (48-hour) toxicity tests were carried out using dilutions of the two prepared water soluble fractions. The method used was DIN 38 412, Teil 11, which is equivalent to OECD 202.

In the tests using the water soluble fraction from the 100 mg/L nominal solutions no toxicity was seen at concentrations up to the undiluted stock solution (i.e. no effects up to around 0.071-0.142 mg/L). In experiments using the water soluble fraction from the 10,000 mg/L stock solution, an EC_0 of 0.140 mg/L (also reported as 0.100-0.110 mg/L in the paper) and an EC_{25} of 0.423 mg/L (also reported as 0.420-0.470 mg/L in the paper) was determined (maximum mortality seen was 25%) (Frank, 1993). The latter results for the 10,000 mg/L stock solution were reported by Frank and Steinhäuser (1994) as EC_0 = 0.140 mg/L and EC_{25} = 0.339 mg/L, and it was noted that some

of the Daphnia were floating on the surface of the test solution. In the later study (Frank and Steinhäuser, 1994), the results of further acute toxicity studies were reported using the same test method. An EC_{50} of 0.037 mg/L and an EC_0 of 0.009 mg/L were determined using the water soluble fraction from the 100 mg/L stock solution and no toxic effects were seen in tests with the water soluble fraction from the 10,000 mg/L stock solution (approximately $EC_0 \geq 0.525$ mg/L). The authors noted that the effects seen in the acute tests showed poor reproducibility, probably because effects were seen only around the water solubility limit of the substance. However, the authors thought that the possibility of undissolved droplets affecting the results could be ruled out, as floating Daphnia were only sporadically observed in the test.

EPA/OPPT Conclusion

Tthe results of these studies should be treated with caution, as the effects were mainly seen in the saturated solutions only.

48-hour EC_{50} = 0.037 mg/L; 100 mg/L stock (Frank and Steinhäuser, 1994)

5) The following study summary (Thompson and Gore, 1999) provided in the 2005 European Chemical Bureau Risk Assessment of MCCP was considered supportive of the aquatic invertebrate hazard determination. The acute toxicity of C14-17, 52% wt. Cl substance was tested using the freshwater crustacean *Gammarus pulex* and the freshwater daphnid, *Daphnia magna*. The medium-chain chlorinated paraffin used was dissolved in acetone and then added to beakers in two separate studies containing either *Gammarus* or *D. magna* to give nominal concentrations of 0.1, 0.32, and 1.0 mg/L. A control and solvent control (containing 0.1 mL/L acetone) were also run. The tests were carried out for 96 hours at 15 ºC, with the solutions being renewed after 48 hours. The water used in the study had a hardness of 220 mg/L as $CaCO_3$ and had a pH of 8.0-9.2. No mortalities of the *Gammarus* were seen in any of the test substance solutions or control. One animal died in the solvent control. Therefore, no significant toxic effects were seen with the medium-chain chlorinated paraffin over the concentration range tested. This contrasted markedly to the situation when *Daphnia magna* were exposed using the same test system at 20 ºC over 48 hours, where complete immobilization was seen at the lowest test concentration (0.1 mg/L).

EPA/OPPT Conclusion

The high immobilization rate observed in *Daphnia magna* in this study appears consistent with the other studies and *Gammarus pulex* appear to be a less sensitive to medium chained chlorinated paraffins then *Daphnia magna*. EPA/OPPT reserves judgment on the acceptability of this study until further details become available.

96-hr EC_{50} (*Gammarus pulex*) > 1 mg/L

48-hr EC_{50} (*Daphnia magna*) < 0.1 mg/L

6) The following study summary (Tarkpea et al., 1981; as quoted in WHO, 1996) provided in the 2005 European Chemical Bureau Risk Assessment of MCCP was considered supportive of the aquatic invertebrate hazard determination. The results of tests with the brackish water harpacticoid *Nitocra spinipes* have been reported (Tarkpea et al., 1981). No other details of the test were reported but the test method was probably the same as reported by Tarkpea et al. (1986), where a static method was employed using water of salinity 7‰ at a temperature of 20-22 ºC without aeration, probably using acetone as cosolvent.

EPA/OPPT Conclusion

The results are considered supportive to address aquatic invertebrate acute toxicity.
96-hour LC_{50} = 9 mg/L (C14-17, 45% wt Cl)
96-hour LC_{50} >10,000 mg/L (C14-17, 52% wt. Cl)

B-1-3 Algae Toxicity

(1) A 72-hour algae toxicity study was conducted by the University of Bremen, Department of Physical and Environmental Chemistry with CP 52 (C_{12-18}, 52% chlorination) according to DIN 38412 by Koh and Thiemann (2001). Study methods were not fully characterized. Additional communications with the study author Wolfram Thiemann clarified that a static test system was used with nominal test concentrations. *Scenedesmus subspicatus* were exposed to the test substance and cell density was determined using a particle counter. Based on communications with the study author, local (Bremen, Germany) tap water was used without adjustments. Presumed pH was between 5 and 6 and water hardness was between 35.7 and 53.5 mg $CaCO_3$/L. Ambient laboratory air temperature was around 21 ºC. The solvent acetone was used to maintain test substance in solution. Effects were calculated based on growth rate. No effects were observed up to 0.1 mg/L.

EPA/OPPT Conclusion
Due to deficiencies/missing details in the study methods, the study alone was not acceptable to characterize aquatic toxicity to plants.
72-hr NOEC = 0.1 mg/L (Highest Test Concentration)

(2) A 96-hour algae toxicity study was conducted according to OECD TG 201 (2006). The test substance was a commercial product of a C_{14-17} chlorinated paraffin with 52% chlorination that contained 0.3% epoxy soya bean oil stabilizer as well as a small amount of radiolabeled n-pentadecane-8-^{14}C (51% chlorinated). *Selenastrum capricornutum* were exposed to nominal concentrations of 0 (dilution water control), 0 (solvent control), 0.1, 0.18, 0.32, 0.56, 1, 1.8, and 3.2 mg/L test substance in the solvent acetone. Six replicates were tested for each control and three replicates were tested for each treatment. A mean measured concentration of 0.49, 0.77, and 1.2 mg/L was determined using radiochemical analysis for the nominal concentrations of 1, 1.8, and 3.2 mg/L, respectively, but effects were reported based on nominal test concentrations. At the start of the test, the pH was 7.4-7.5, but had reached 10.0-10.3 by the end of the test. The shift in pH was thought to be a function of the high control growth rates observed in the test according to the study summary. The section-by-section coefficient of variation for the solvent control remained below 35% indicating acceptable control growth rates throughout the duration of the study.

EPA/OPPT Conclusion
The maximum inhibition in the growth rate and biomass seen was 3% and 18%, respectively, but a dose response relationship was not seen. The nominal NOEC was 0.1 mg/L and the nominal LOEC based on 18% biomass inhibition was 0.18 mg/L. A GMATC of 0.134 mg/L was calculated. The study was considered acceptable.
72-hour EC_{50} = >3.2 mg/L (nominal); 1.2 mg/L (mean measured).
96-hour EC_{50} = >3.2 mg/L (nominal); 1.2 mg/L (mean measured).
72-hr $NOEC_b$ = 0.1 mg/L
72-hr $LOEC_b$ = 0.18 mg/L
72-hr GMATC = 0.134 mg/L

B-1-4 Chronic Fish Toxicity

(1) A 60-day fish toxicity study was conducted by Brixham Laboratories in 1983 with radio-labeled chlorinated (52%) n-pentadecane (Trade Name: Cereclor S52®) under flow through testing conditions. A full non-CBI study report was submitted under TSCA in 1983 as DCN 40-8332184 (OTS Fiche 0507258). Two replicates of 3 immature rainbow trout (*Salmo gairdneri*) per concentration were exposed to nominal concentrations of 0 (dilution water control), 0 (acetone control, 500 ppm), 1, or 5.6 mg/L in 500 ppm acetone. Corresponding mean measured concentrations were 0, 0, 1.05, and 4.5 mg/L. Test concentrations were determined by radio activity measurements. Flow rate of the test system was 0.25 mL/minute for exposure concentrations. No mortality or adverse sub-lethal behavioral effects were observed for the duration of the 60-day exposure period. Effects observed were limited to the highest test concentration and involved sluggish movements. The measured NOEC was identified as 4.5 mg/L. In addition to the hazard assessment, the submitter provided an assessment of bioconcentration which indicated that analytically determined exposure concentrations of 1.05 and 4.5 mg/L resulted in fish tissue concentrations of 34 and 190 µg/g wet weight, respectively.

EPA/OPPT Conclusion

This study appears to have been previously reviewed by EPA in 1985. The previous conclusion that "a fish full life cycle toxicity test or modification thereof is needed to address the effects of CPs present in fish eggs during embryonic development" (U.S. EPA Memorandum, 1991) is still relevant for MCCPs. Thus, this study is considered unacceptable to characterize chronic population-level effects in fish.

60-day NOEC = 4.5 mg/L

(2) A 28-day fish toxicity study was conducted by Brixham Laboratories in 1978 with a $C_{14\text{-}17}$ chlorinated paraffin having 45% chlorination under unspecified testing conditions. The study report was submitted under TSCA in 1992 as DCN 88920006972 (OTS Fiche 0545375). Rainbow trout (*Salmo gairdneri*) per concentration were exposed to nominal concentrations of 0 (dilution water control), 0.1, or 1 mg/L in acetone. The age and size of the rainbow trout used in the study were not specified in the study. The specific environmental conditions of the test, such as pH, temperature and water quality were not specified in the report. Concentrations of the chlorinated paraffin in the test water were measured using TLC analytical procedures resulting in mean measured concentrations of 0.01 and 0.18 mg/L. Mortality and behavior (response to food, general behavior, swimming behavior and pigmentation) were assessed during the 28-day study. Survival was 96.6 and 100% for the mean measured exposures of 0.01 and 0.18. No behavioral effects were seen over the course of the study.

EPA/OPPT Conclusion

The study was considered unacceptable to characterize the chronic fish toxicity endpoint since insufficient study details were provided including the age and/or the life-stages of the exposed organisms.

(3) A 20-day Japanese medaka (*Oryzias latipes*) embryo toxicity study was conducted with the formulation $C_{14}H_{24.9}Cl_{5.1}$, 48%Cl (composition: 10.5% 1, 2, 13, 14-tetrachlorotetradecane (42.3% Cl); 74.3% x, 1, 2, 13, 14-pentachlorotetradecane (47.7% Cl); 14.2% x, y, 1, 2, 13, 13-hexachlorotetradecane (52.6% Cl); 1.0% x, y, z, 1, 2, 13, 14-heptachlorotetradecane (56.4% Cl)) by Fisk et al. (1999) under static testing conditions. Five sets of 10 vials containing 1 egg each were exposed to nominal concentrations of 0.001, 0.010, 0.100, 1, or 10 mg/L test substance

starting after fertilization and terminating approximately 3 days post-hatch. No adverse effects were reported in exposed embryos.

EPA/OPPT Conclusion

The study was considered unacceptable primarily due to insufficient exposure duration and insufficient number of eggs per exposure concentration.

(4) A 20-day Japanese medaka (*Oryzias latipes*) embryo toxicity study was conducted with the formulation ^{14}C-$C_{14}H_{23.3}Cl_{6.7,}$ 55% Cl (composition: 0.2% $C_{14}H_{26}Cl_4$ (42.3% Cl), 4.4% $C_{14}H_{25}Cl_5$ (47.7% Cl), 34% $C_{14}H_{24}Cl_6$ (52.6% Cl), 45% $C_{14}H_{23}Cl_7$ (56.4% Cl), 14% $C_{14}H_{22}Cl_8$ (59.9% Cl), and 1.9% $C_{14}H_{21}Cl_9$ (62.8% Cl)) by Fisk et al. (1999) under static testing conditions. Five sets of 10 vials containing 1 egg each were exposed to measured concentrations of 0.0014, 0.012, 0.120, 0.420, or 1.6 mg/L test substance starting after fertilization and terminating approximately 3 days post-hatch. No adverse effects were reported in exposed embryos. Concentrations of the test substance were found in larvae and eggs in a dose-dependent manner (with exception of the highest concentration) suggesting that the substance can diffuse through the egg. Corresponding measured concentrations in eggs were 0.04, 8.4, 63, 110, and 72 mg/kg and corresponding measured concentrations in larvae were 0.24, 8.2, 45, 84, and 51 mg/L.

EPA/OPPT Conclusion

The study was considered unacceptable primarily due to insufficient exposure duration and insufficient number of eggs per exposure concentration.

(5) The following summary provided in the 2005 European Chemical Bureau Risk Assessment of MCCP was considered supportive, but did not characterize all fish life-cycle stages. Cooley et al. (2001) studied the toxicity of $C_{14}H_{24.9}C_{l5.1}$, 48%Cl (as described in Fisk et al., 1999) to juvenile rainbow trout (*Oncorhynchus mykiss*) through dietary exposure. Treatment groups of 10 fish were exposed to 0.78 and 2.9 mg/kg for 21 days and 0.082 mg/kg for 85 days. Three control groups were also run. Histological examination and analysis of the chlorinated paraffin concentration was performed in five fish per treatment after 21 days in the two higher test concentrations and in three fish per treatment after 85 days in the lowest test concentration. Three fish were also sacrificed from each low exposure group and the remaining control group (but were not analyzed) after 21 days of exposure. Quantitative histomorphological measurements were also carried out on livers and thyroid of the exposed fish in the middle exposure group after 21 days, and also the low exposure group after 85 days. The parameters investigated included hepatocyte nuclear diameter, hepatocyte volume index, nucleus:cytoplasm area ratio and thyroid epithelium cell height. Livers displaying mild hepatocyte necrosis and moderate to severe depletion of glycogen/lipids were reported for the 0.78 mg/kg exposure. At 2.9 mg/L abnormal behavior was observed from day 3 onwards. Quantitative effects following 21 days of exposure were limited to a significantly ($p=0.05$) reduced mean hepatocyte volume in 2.9 mg/L exposure group.

EPA/OPPT Conclusion

This study is considered unacceptable to characterize chronic mortality in fish because it did not characterize life stages but instead characterized physiological effects.

(6) Cooley et al. (2001) studied the toxicity of another medium chain chlorinated paraffin with a slightly different chemical composition and at slightly different concentration levels. The chemical formula was ^{14}C-$C_{14}H_{23.3}Cl_{6.7,}$ 55% Cl (as described in Fisk et al., 1999) and was juvenile rainbow trout (*Oncorhynchus mykiss*) were exposed through the diet. Treatment groups of 10 fish were exposed to 29 and 78 mg/kg for 21 days and 5.7 mg/kg for 85 days. Three control groups were also run. Histological examination and analysis of the chlorinated paraffin concentration was performed in five fish per treatment after 21 days in the two higher test concentrations and in three fish per treatment after 85 days in the lowest test concentration. Three fish were also sacrificed from each low exposure group and the remaining control group (but were not analyzed) after 21 days of exposure. Quantitative histomorphological measurements were also carried out on livers and thyroid of the exposed fish in the middle exposure group after 21 days, and also the low exposure group after 85 days. The parameters investigated included hepatocyte nuclear diameter, hepatocyte volume index, nucleus:cytoplasm area ratio and thyroid epithelium cell height. At 29 mg/kg abnormal behavior was observed from day 2 onwards and livers exhibited mild to moderate hepatocyte necrosis and moderate to severe depletion of glycogen lipids. Abnormal behavior from day 3 onward was also observed at 78 mg/kg.

EPA/OPPT Conclusion

This study is considered unacceptable to characterize chronic mortality in fish because it did not characterize life stages but instead characterized physiological effects.

B-1-5 Chronic Aquatic Invertebrate Toxicity

(1) A 21-day chronic *Daphnia magna* reproduction toxicity study was conducted by Thompson et al. (1997b) according to OECD 202, Part II (1984) using a static-renewal test system with renewal 3 times/week. The test substance was identified as Cereclor S52® , a $C_{14\text{-}17}$ chlorinated paraffin with 52% chlorination that contained 0.3% epoxy soya bean oil stabilizer as well as a small amount of radiolabeled n-pentadecane-8-^{14}C (51% chlorinated). Ten replicates of 1 *Daphnia magna* Straus (<24 hours old) were tested per exposure concentration, which did not comply with OECD 202, Part II requirements that at least 40 daphnid be tested per concentration. Nominal concentrations were 0 (dilution water control), 0 (solvent control), 0.0056, 0.01, 0.018, 0.032, 0.056, and 0.1 mg/L test substance in acetone (0.025 mL/L). Results from the acute daphnid study by the same author do not appear to have been considered when selecting concentrations for this study. Test solutions were prepared by adding the appropriate stock solution to dilution water while continuously and vigorously stirring with a magnetic follower. The submitter does not indicate whether renewal of the static-renewal test systems was carried out at regular intervals (e.g, Monday-Wednesday-Friday). Corresponding mean measured concentrations determined by radiochemical methods were 0.0037, 0.005, 0.01, 0.018, 0.032, and 0.065 mg/L and were 78-94% of nominal concentrations at the start of the renewal period and 7.3-61% of nominal concentrations at the end of the renewal period indicating a notable loss of test substance. Also, analysis of test concentrations appears to be at irregular intervals. In the dilution water control, 20% mortality was observed. Overall, dilution water control and solvent control results were significantly different for reproductive parameters. The test was carried out at temperatures of 19.5-20.3 °C, at pH levels of 7.41-8.13, and at dissolved oxygen concentrations of 6.2-9.2 mg/L. A significant decrease in the number of live offspring was reported at the mean measured concentration of 0.018 mg/L and delayed release of first offspring was observed at higher concentrations. Percentage dead offspring reported was 0%, 0%, 5.9%,

20.4%, and 18.5% for the 0.0037, 0.005, 0.01, 0.018, 0.032, and 0.065 mg/L mean measured exposures.

EPA/OPPT Conclusion

The inability to maintain test concentrations, unspecified renewal periods, and a smaller population size may have affected subsequent reproductive results. Given the uncertainties of the test, reported effect levels may not represent a worst case scenario but do exhibit a clear dose response relationship with a clearly defined statistically significant effect level. Thus, using a weight of evidence approach, the study is considered acceptable for this endpoint.

21-day LC_{50} value of 0.025 mg/L (parent mortality)
21-d NOEC = 0.01 mg/L
21-d LOEC = 0.018 mg/L
21-d GMATC = 0.013 mg/L

(2) A 60-day mussel toxicity study was conducted by Brixham Laboratories in 1983 with radio-labeled chlorinated (52%) n-pentadecane (Trade Name: Cereclor S52®) under flow through testing conditions. A full non-CBI study report was submitted under TSCA in 1983 as DCN 40-8332184 (OTS Fiche 0507258). Blue mussels (*Mytilus edulis*) were exposed to nominal concentrations of 0 (dilution sea water control), 0 (acetone control, 500 ppm), 0.56, or 5.6 mg/L in 500 ppm acetone. Two replicates of 50 mussels were tested for the dilution water and solvent controls and a single replicate of 50 mussels was exposed for each treatment concentration. Corresponding mean measured concentrations were 0, 0, 0.22, and 3.8 mg/L. Test solutions were cloudy at the higher test concentration. Test concentrations were determined by radio activity measurements. Flow rate of the test system was 0.25 mL/minute for exposure concentrations. Over the course of the study, water temperature ranged from 14.6 – 15.6 °C, pH ranged from 8.0 – 8.3, and the dissolved oxygen concentrations ranged from 6.1 – 8.25 mg/L. Dilution water salinity was 34-35.5 ppb, which is high by OCSPP standards.

EPA/OPPT Conclusion

One mussel exposed to 0.56 mg/L died, and two mussels exposed to the controls died; this was not considered to be a test substance related effect. Decreases in filter feeding were observed at 5.6 mg/L. In addition, the submitter provided an assessment of bioconcentration, but this assessment does not appear to include a depuration phase. Overall, the 60 day NOEC and LOEC were 0.22 and 3.8 mg/L based on reduced filtration. The study was acceptable to characterize mussel toxicity, but mussels are not considered a standard species to fulfill the chronic aquatic invertebrate toxicity endpoint.

60-d NOEC = 0.22 mg/L
60-d LOEC = 3.8 mg/L (reduced filtration)

(3) The following study summary (Frank, 1993; Frank and Steinhäuser, 1994) provided in the 2005 European Chemical Bureau Risk Assessment of MCCP was considered supportive of the aquatic invertebrate hazard determination. A 21-day chronic *Daphnia magna* reproduction toxicity study was conducted using a static-renewal test system (renewal 3 times/week). The test substance was identified as $C_{14\text{-}17}$ chlorinated paraffin with 52% chlorination, which was tested as a water soluble fraction of two stock solutions (dilutions used 1:2 to 1:32). Nominal test concentrations prepared from the 100 mg/L stock solution were 3.125, 6.25, 12.5, 25, and 50

mg/L. Nominal test concentrations prepared from the 10,000 mg/L stock solution were 312.5, 625, 1250, 2500, and 5000 mg/L. Analytical monitoring of test concentrations was conducted, but only the final effect levels were presented as measured concentrations. Methods for test solution preparation were not provided in the summary. The tests were carried out at 20 °C and at pH 7.79-8.44.

In the experiments using the 100 mg/L stock solution the mortality seen in the exposed populations was 0% at 3.125 mg/L, 0% at 6.25 mg/L, 20% at 12.5 mg/L, 90% at 25 mg/L, and 100% at 50 mg/L. In the experiments using the 10,000 mg/L stock solution the mortality seen in the exposed populations was 0% at 312.5 mg/L, 30% at 625 mg/L, 70% at 1250 mg/L, and 100% at lower dilutions (>1250 mg/L). In the experiments using the 100 mg/L stock solution the average number of young/adult was 82 at 3.125 mg/L, 89 at 6.25 mg/L, 80 at 12.5 mg/L, 15 at 25 mg/L and 0 at 50 mg/L (all parents died). Similarly in the experiments using the 10,000 mg/L stock solution the average number of young/adult was 74 at 312.5 mg/L, 64 at 625 mg/L, 43 at 1250 mg/L, and 0 at 2,500 and 5,000 mg/L (all parents died). Based on these effects, survivability/mortality appears to be the more sensitive endpoint. Based on the known measured concentrations in the stock solutions and the dilution rates used the NOEC for mortality was around 0.0044-0.0089 mg/L for the 100 mg/L nominal stock solution experiments and 0.0126-0.0156 mg/L for the 10000 mg/L nominal stock solution experiments. The corresponding LOECs were 0.0089- 0.0178 mg/L (100 mg/L nominal stock) and 0.0253-0.0313 µg/L (10 g/L nominal stock). The GMATC of 0.006 mg/L was calculated using the geometric mean from the most conservative NOEC (0.0044 mg/L) and LOEC (0.0089 mg/).

EPA/OPPT Conclusion
EPA/OPPT reserves judgment on the acceptability of this study until further details become available.
21-d NOEC = 0.0044 mg/L
21-d LOEC = 0.0089 mg/L
21-d GMATC = 0.006 mg/L

3) The following study summary (TNO, 1993) provided in the 2005 European Chemical Bureau Risk Assessment of MCCP was considered supportive of the aquatic invertebrate hazard determination. A 21-day chronic *Daphnia magna* reproduction toxicity study was conducted using a static-renewal test system (renewal 3 times/week). The test substance was identified as $C_{14\text{-}17}$ chlorinated paraffin with 52% chlorination. The test solutions were prepared by stirring 20 g of the test substance in 2 litres of heated water (60 °C) with stirring and then filtration through a 0.8 µm and 0.2 µm filter. This resulting stock solution was referred to as a water soluble fraction, but given that each concentration was not independently prepared, the test solutions is considered by EPA/OPPT to be merely a mixed and filtered solution that was subsequently diluted. Following dilution of the stock solution, exposure concentrations were analytically determined using the extractable organic halogen method, but not provided in the study summary. The test was carried out at 20 ± 1 ºC and solutions were gently aerated from day 9 onwards. The pH of the test water varied between 7.7 and 8.3, the dissolved oxygen concentration was > 7 mg/L, and the hardness was 214 mg CaCO3/L. Test solutions were clear.

EPA/OPPT Conclusion
Although analytical results obtained were considered to be too erratic to allow precise determination of concentrations (according to the study summary in ECB, 2005), the NOEC was reported based on survivability and/or reproductive effects. A LOEC in mg/L was not reported in the

summary, nor could EPA/OPPT extrapolate one. EPA/OPPT reserves judgment on the acceptability of this study until further details become available.
21-d NOEC = 0.004-0.008 mg/L

B-1-6 Chronic Aquatic Sediment Invertebrate Toxicity

1) Thompson et al. (2001c) conducted a 28-day prolonged sediment invertebrate toxicity study with spiked sediment was conducted according to OECD 218 draft guideline (February 2000 version) using a static test system. The substance used in the test was commercial C_{14-17}, 52% wt. Cl substance containing no stabilizers (the substance was reported to have a C_{14-17} content of 99.06% with 0.67% of C10-13 chain length substances) that was mixed with a small amount of a radio labeled n-pentadecane-8-^{14}C, 51% wt. Cl substance (radiochemical purity >96.6%). The sediment used in the test was an artificial sediment that did not fully adhere to the final OECD TG recommendations, but the composition of 10% sphagnum moss peat, 70% quartz sand, 20% kaolinite clay, and <0.1% calcium carbonate are not considered to be significantly different. The sediment had a mean organic carbon content of 4.9% and a pH of 6.0. The sediment was spiked with the test substance by firstly mixing a solution of the test substance in acetone with the dry sand component of the sediment and allowing the acetone to evaporate overnight under an air stream. Measured concentrations were determined using radiochemical analysis. Over the course of the study, temperature was maintained at 20 ºC, pH levels were 6.2-7.6, and dissolved oxygen in overlying water was maintained at 7.3-8.6 mg/L. Three replicates of 15 midge (*Chironomus riparius*) larvae (<48 hours post hatch) were exposed to mean measured concentrations of 0 (sediment control), 0 (solvent sediment control), 36, 110, 370, 1200, 3800, or 13000 mg/kg dry wt. sediment. Time to first emergence, mean emergence time, mean number emerged per replicate, and sex ratio was assessed for each exposure group. Statistically significant effects (p = 0.05) were limited to a decrease in mean number emerged per replicated in the 13,000 mg/kg dry wt. sediment exposed midges.

EPA/OPPT Conclusion
The overall NOEC of 3,800 mg/kg dry wt. sediment corresponded to 1,460 mg/kg on a wet weight basis. The study is acceptable.
28-d NOEC = 3,800 mg/kg dry wt sediment
28-d LOEC = 13,000 mg/kg dry wt sediment
28-d GMATC = 7,029 mg/kg dry wt sediment

2) Thompson et al. (2001d) conducted a 28-day prolonged sediment invertebrate toxicity study with spiked sediment according to methods described in Phipps et al. (1993) using a static test system. The substance used in the test was commercial C_{14-17}, 52% wt. Cl substance containing no stabilizers (the substance was reported to have a C_{14-17} content of 99.06% with 0.67% of C10-13 chain length substances) that was mixed with a small amount of a radio labelled n-pentadecane-8-14C, 51% wt. Cl substance (radiochemical purity >96.6%). The sediment used in the test was an artificial sediment consisting of 10% sphagnum moss peat, 70% quartz sand, 20% kaolinite clay, and <0.1% calcium carbonate. The sediment had a mean organic carbon content of 4.9% and a pH of 6.0. The test sediments were made up by adding the test substance to the sand phase as a solution in acetone, evaporating the acetone overnight and mixing the spiked sand with the rest of the sediment for 16 hours. Six replicates of 10 oligochaete (*Lumbriculus variegatus*) adults were exposed to mean measured concentrations of 0 (sediment control), 0 (solvent sediment control), 39, 130, 410, 1300, 4000, or 13000 mg/kg dry wt. sediment.

Throughout the duration of the study, water temperature was maintained at 20 ± 1 Cº, and pH remained between 6.3 and 7.9. Mortality and reproductive success were determined by total number of worms at study termination since differentiation of adult and young worms is difficult. Mean number of worms per replicate and mean total dry weight of worms per replicate was significantly different from controls ($p = 0.01$) at mean measured concentrations of 410 mg/kg dry weight sediment and greater. Statistical methods used were not reported, and a p-value of 0.01 was used.

EPA/OPPT Conclusion

Given that a clear decline in the mean number of worms per replicate and mean total dry weight of worms per replicate was observed at the lowest test concentration (39 mg/kg dry weight sediment) a conservative LOEC of 39 mg/kg dry weight sediment will be used based on noticeable differences. EPA/OPPT reserves judgment on the acceptability of this study until further details become available regarding the analytical measurements of the chlorinated paraffin mixture.

28-d NOEC = 130 mg/kg dry wt sediment
28-d LOEC = 410 mg/kg dry wt sediment
GMATC = 230.9 mg/kg dry wt sediment

3) Thompson et al. (2002) conducted a 28-day prolonged sediment toxicity study with amphipod *Hyalella azteca* in spiked sediment using a static-renewal test system with weekly renewals. The substance used in the test was a mixture of a commercial medium-chain chlorinated paraffin product (C14-17, 52.5% wt. Cl) mixed with a small amount of a radiolabeled chlorinated n-pentadecane-8-14C (51% wt. Cl). The sediment used in the test was an artificial sediment consisting of 10% sphagnum moss peat, 70% quartz sand, 20% kaolinite clay, and <0.1% calcium carbonate. The sediment had a mean organic carbon content of 4.9% and a pH of 6.0. The test sediments were made up by adding the test substance to the sand phase as a solution in acetone, evaporating the acetone overnight and mixing the spiked sand with the rest of the sediment and water. Six replicates per concentration of ten juvenile *Hyalella azteca* (~7-day-old) were exposed to 0 (sediment control), 0 (acetone sediment control), 38, 75, 150, 300, or 600 mg/kg dry weight sediment. The concentration of the test substance was measured in the sediment phase by radiochemical analysis with concentrations at the start of the exposure period of 85-97% of the nominal values and concentrations at the end of the 29-day exposure period of 78-90% of nominal. Results of the test were expressed as the arithmetic mean concentration. Over the course of the study, dissolved oxygen ranged from 7.7 to 8.4 mg/L, pH ranged from 7.0 to 7.6, water hardness ranged from 41 to 42 mg $CaCO_3$/L, and temperature ranged from 22.4-23.2ºC. The endpoints investigated in the study included survival, growth (dry weight) and sexual development of females (proportion of gravid females).

EPA/OPPT Conclusion

Controls responded adequately. For the survival endpoint, a statistically significant ($p=0.05$) reduction in survival was seen at 470 mg/kg dry weight. A statistically significant reduction in mean weight was seen in females only at exposures of 470 g/kg dry weight sediment and a statistically significant ($p=0.05$) reduction in mean weight was seen at 270 mg/kg dry weight. For the sexual development endpoint, there was a statistically significant ($p=0.05$) reduction in the proportion of gravid females in the 470 mg/kg dry weight treatment. This study was acceptable.

28-d NOEC = 130 mg/kg dry wt sediment
28-d LOEC = 270 mg/kg dry wt sediment
28-d GMATC = 187 mg/kg dry wt sediment

B-1-7 Avian Toxicity

(1) An acute avian toxicity study conducted according to OPPTS guidelines was published by Madeley & Birtley (1980). Following a range-finding study, groups of 5 male and 5 female ring-necked pheasants (*Phasianus colchicus*) were exposed by gavage to 0 (control) or 24,606 mg/kg Cereclor S52® (C_{14-17}, 52% Cl) and then observed for 14 days. Based on reported tissue concentrations, the test substance is believed to have been absorbed by the ring-necked pheasant. Doses up to 24,606 mg/kg failed to produce any abnormal clinical signs or mortality.

EPA/OPPT Conclusion
Acute LD50 > 24,606 ppm

(2) An acute avian toxicity study conducted according to OCSPP guidelines was published by Madeley & Birtley (1980). Following a range-finding study, groups of 5 male and 5 female mallard ducks (*Anas platyrynchos*) were exposed by gavage to 0 (control) or 10,280 mg/kg Cereclor S52® (C14-17, 52% Cl) and then observed for 14 days. Based on reported tissue concentrations, the test substance is believed to have been absorbed by the mallard ducks. Doses up to 10,280 mg/kg failed to produce any abnormal clinical signs or mortality.

EPA/OPPT Conclusion
Acute LD_{50} > 10,280 ppm

(3) A sub-acute dietary avian toxicity study conducted according to OPPTS guidelines was published by Madeley & Birtley (1980). Following a range-finding study, groups of 5 male and 5 female ring-necked pheasants (*Phasianus colchicus*) were exposed to diets containing 0 (control), 1,000, or 24,063 ppm Cereclor S52® (C14-17, 52% Cl) for 5 days. Three groups were exposed to the negative control and two groups were exposed to each of the treatment concentrations. Based on reported tissue concentrations, the test substance is believed to have been absorbed by the ring-necked pheasant. Good health was noted in all control and treatment groups. No abnormal effects were noted at necropsy.

EPA/OPPT Conclusion
5-day LD_{50} > 24,063 ppm

(3) A sub-acute dietary avian toxicity study conducted according to OPPTS guidelines was published by Madeley & Birtley (1980). Following a range-finding study, groups of 5 male and 5 female mallard ducks (*Anas platyrynchos*) were exposed to diets containing 0 (control), 1,000, or 24,063 ppm Cereclor S52® (C14-17, 52% Cl) for 5 days. Three groups were exposed to the negative control and two groups were exposed to each of the treatment concentrations. Inferior food intake was noted for ducks, but weight gain was comparable to controls. Based on reported tissue concentrations, the test substance is believed to have been absorbed by the mallard ducks. Good health was noted in all control and treatment groups. No abnormal effects were noted at necropsy.

EPA/OPPT Conclusion
5-day LD_{50} > 24,063 ppm

B-1-8 Terrestrial Invertebrate Toxicity

1) A 28-day earthworm reproductive toxicity test was conducted by Thompson et al., 2001a according to OECD guideline (2000 draft version). The substance tested was commercial C14-17, 52% wt. Cl substance containing no stabilizers (the substance was reported to have a C14-17 content of 99.06% with 0.67% of C10-13 chain length substances) and a small amount of 14C-labelled n-pentadecane, 51% wt. Cl substance. Four replicates per concentration of 10 adult earthworm (*Eisenia fetida*) were exposed to nominal concentrations of 0 (soil control), 0 (solvent soil control), 100, 320, 1000, 3200, or 10,000 mg/kg dry wt. soil. Corresponding mean measured concentrations of 0 (soil control), 0 (solvent soil control), 79, ~280, 900, ~2,800, or 9,300 mg/kg dry wt. was determined using radiochemical analysis; concentrations identified as approximate (~) were approximated using the mean% of nominal (87%) determined in other treatments. Measured tissue concentrations in adults on day 28 were 169, 802, and 732 mg/kg wet weight for the 79, 900, and 9,300 mg/kg dry weight exposure groups. Measured tissue concentrations in juveniles on day 56 were 140 and 1,011 mg/kg wet weight for the 79 and 900 mg/kg dry weight exposure groups. The soil used in the test was an artificial soil consisting of 10% sphagnum moss peat, 70% quartz sand, 20% kaolinite clay, and 0.25% calcium carbonate. The soil had an organic carbon content of 4.7% and a pH of 6.66-7.09. Nominal test temperatures remained at 20 ± 1 ºC. The soils were prepared up by firstly adding the test substance in solution with acetone to a small portion of soil, evaporating out the acetone overnight under a stream of compressed air, and then mixing with the remainder of the soil. Before use, distilled water was added to the dry soil to provide a soil wet:dry ratio of 1.35. Following the 28-day parental exposure period, adult earthworms were removed, and vessels were incubated for an additional 28 days to allow hatching of any egg cocoons produced by parent. Effects assessed were parental survival, growth as determined by change in weight of parents, and reproduction as determined by number of live offspring. A statistically significant (p = 0.05) reduction in parental survival (85%) was observed at 9,300 mg/kg dry wt. soil. A statistically significant (recalculated with Dunnett's Procedure, P = 0.05) reduction in parental weight was reported at 2800 mg/kg dry wt. soil. A statistically significant (recalculated with Dunnett's Procedure, P = 0.05) reduction in number of live offspring was reported at 280 mg/kg dry wt. soil. In addition, the submitter assesses corresponding tissue concentrations in earthworms and determines that at nominal concentrations of 100 mg/kg dry wt. soil the concentration in parental earthworm tissue after 28 days is 850 mg/kg dry wt.and in juvenile worms after 56 days was 703 mg/kg dry wt.

EPA/OPPT Conclusion
The study was acceptable.
28-d NOEC = 79 mg/kg dry wt soil
28-d LOEC = 280 mg/kg dry wt soil
28-d ChV = 149 mg/kg dry wt soil

2) The following study summary (Thompson et al., 2001a) provided in the 2005 European Chemical Bureau Risk Assessment of MCCP was used to characterize terrestrial invertebrate hazard in a screening level risk assessment. A 28-day earthworm reproductive toxicity test was conducted according to OECD guidelines. The substance tested was commercial C_{14-17}, 52% wt. Cl substance containing no stabilizers (the substance was reported to have a C_{14-17} content of 99.06% with 0.67% of C10-13 chain length substances). The test substance contained a small amount of 14C-labelled n-pentadecane, 51% wt. Cl substance so that radiochemical analysis could be used to analytically determine test concentrations in soil. The soil used in the test was an artificial soil consisting of 10% sphagnum moss peat, 70% quartz sand, 20% kaolinite clay, and 0.25% calcium carbonate. The soil had an organic carbon content of 4.7% and a pH of 6.66-

7.09. The soils were prepared up by firstly adding the test substance in solution with acetone to a small portion of soil, evaporating out the acetone overnight under a stream of compressed air, and then mixing with the remainder of the soil. Before use, distilled water was added to the dry soil to provide a soil wet:dry ratio of 1.35. Four replicates per concentration of 10 adult earthworm (*Eisenia fetida*) were exposed to mean measured concentrations of 0 (soil control), 0 (solvent soil control), 79, ~280, 900, ~2800, or 9300 mg/kg dry wt. for 28 days; concentrations identified as approximate (~) were approximated using the mean% of nominal (87%) determined in other treatments. Measured tissue concentrations in adults on day 28 were 169, 802, and 732 mg/kg wet weight for the 79, 900, and 9300 mg/kg dry weight exposure groups. Measured tissue concentrations in juveniles on day 56 were 140 and 1011 mg/kg wet weight for the 79 and 900 mg/kg dry weight exposure groups. Following the 28-day parental exposure period, adult earthworm were removed, and vessels were incubated for an additional 28 days to allow hatching of any egg cocoons produced by parent. Effects assessed were parental survival, growth as determined by change in weight of parents, and reproduction as determined by number of live offspring. Statistical methods used to calculate significance were not provided. A statistically significant ($p = 0.05$) reduction in parental survival (85%) was observed at 9300 mg/kg dry wt. soil. A statistically significant ($p = 0.01$) reduction in parental weight was reported at 2800 mg/kg dry wt. soil and a noticeable reduction in parental weight was reported at 280 mg/kg dry wt. soil. A statistically significant ($p = 0.01$) number of live offspring was reported at 1000 mg/kg dry wt. soil and a noticeable reduction in number of live offspring was reported at 320 mg/kg dry wt. soil. A clear decline in parental weight and number of live offspring was observed at 280 mg/kg dry wt. soil.

EPA/OPPT Conclusion
This study is acceptable.
28-d NOEC = 79 mg/kg dry wt soil
28-d LOEC = 280 mg/kg dry wt soil
28-d GMATC = 149 mg/kg dry wt soil

B-1-9 Terrestrial Plant Toxicity

1) Thompson et al., 2001ab conducted a 28-day seed germintation and vegetative vigor study. The toxicity of a $C_{14\text{-}17}$, 52% wt. Cl substance (99.06% purity) to wheat (*Triticum aestivum*; monocotyledon), oilseed rape (*Brassica napus*; ditcotyledon), and mung bean (*Phaseolus aureus*; dicotyledonous legume) has been studied using OECD guideline 208 (July, 2000 Revision). The test substance contained a small amount of 14C-labelled n-pentadecane, 51% wt. Cl substance so that radiochemical analysis could be used to analytically determine test concentrations in soil. The soils were prepared up by firstly adding the test substance in solution with acetone to dry silver sand, evaporating the acetone overnight, and mixing the spiked sand with the soil. Four replicate pots per exposure concentration each containing 9 seeds were exposed for 28 days to nominal exposure concentrations of 0 (soil control), 0 (solvent soil control), 50, 158, 500, 1,580, or 5,000 mg/kg dry wt.. According to the E.U. Risk Assessment, use of nominal test concentrations to determine effect levels is based on test substance stability determined at the 50, 500, and 5,000 mg/kg dry wt. concentrations (corresponding mean measured concentrations: 49, 520, and 5,800 mg/kg dry wt.). Effects assessed were seed germination, emergence (% emerged plants on Day 14), vegetative growth (mean shoot dry weight per plant), and visual appearance of seedling. No statistically significant differences ($p = 0.05$) were observed in wheat, oilseed rape. A statistically significant reduction in growth was seen at 1,580 and 5,000 mg/kg dry wt. for mungbean when compared to soil control results.

EPA/OPPT Conclusion
Since soil control and solvent control means were equal (two tailed T-Test) indicating no solvent interference, comparison of treatments was made to the soil control. Thus, the NOEC and LOEC for terrestrial plants was 500 and 1,580 mg/kg dry wt. soil and the GMATC (geometric mean of the NOEC and LOEC) was 888.8 mg/kg dry wt. soil. The study was acceptable to characterize both monocot (wheat) and dicot (mung bean) seed germination and vegetative vigor; reproductive effects remain uncharacterized.
28-d NOEC = 500 mg/kg dry wt soil
28-d LOEC = 1,580 mg/kg dry wt soil
28-d GMATC = 888.8 mg/kg dry wt soil

B-1-10 Conclusions

Sufficient data were available to characterize the acute fish, the acute aquatic invertebrate, the chronic aquatic invertebrate, the chronic aquatic sediment invertebrate, avian, and terrestrial plant toxicity endpoints for MCCPs. Data for other toxicity endpoints (i.e., chronic fish, aquatic plant, etc.) were inconclusive due to lack of study details, uncertainties in analytical methods, or test material preparation methods; thus, these data are included in order to characterize risk in a qualitative manner, but are used as supportive for the categories under which they are provided. Supporting data were included in order to provide a weight-of-evidence approach used to characterize some endpoints.

Most of the data provided in this review indicated several difficulties were encountered when testing in an aquatic environment. These included: (1) getting the material into solution, (2) measuring the material in solution, and (3) characterizing the effects for each study listed. Often there were many details of a given study omitted, prohibiting a full and robust review of the data. The (estimated) physical-chemical properties of MCCPs (water solubility values of approximately 30 µg/L and Log K_{ow} values between 4-8) suggest these materials may not partition to the aquatic media or elicit toxicity to aquatic organisms within the water column.

The most reliable and acceptable studies indicate that for MCCPs, the toxicity to aquatic organisms for acute endpoints are from the Thompson et al. 1996 study for aquatic invertebrates. Where the 48-hour EC_{50} value = 0.0059 mg/L. Using the methods described in the Sustainable Futures/P2 Manual (US EPA, 2012), the acute and chronic concentrations of concern (CoC) are derived as follows:

- Acute CoC: The 48-hour EC_{50} value = 0.0059 mg/L is divided by an assessment factor of 5 to yield an acute concentration of concern (CoC) of 0.00118 mg/L, or 0.001 mg/L, or 1 µg/L (1 ppb). **Aquatic Acute Concern Concentration= 1 ppb**
- Chronic CoC: The aquatic invertebrate chronic value of 0.013 mg/L from the 1997 Thompson et al. study based on a MCCP material is divided by an assessment factor of 10 to yield 0.0013 mg/L or 1.3 µg/L or 1.3 ppb. **Aquatic Chronic Concern Concentration = 1 ppb**

The most reliable and acceptable value for the toxicity to aquatic sediment invertebrate organisms acute endpoint is based on the MCCP material from the Thompson et al. 2002 28-d study. The 28-d sediment invertebrate GMATC value of 187 mg/kg dry wt sediment is used to assess hazard. Again, using methods in US EPA (2012):

- Acute CoC: Calculating an acute concern concentration from the chronic value of 187 mg/kg dry wt. The 187 value is multiplied by an acute to chronic ratio for invertebrates (10) to yield 1,870 mg/kg dry wt. This value is then divided by an assessment factor of 5 to yield 374 mg/kg dry wt. **Aquatic Sediment Acute Concern Concentration = 374 mg/kg dry wt sediment.**
- Chronic CoC: The 28-d sediment invertebrate GMATC of 187 mg/kg dry wt sediment is divided by an assessment factor of 10 to yield 18.7 mg/kg dry wt sediment. **Aquatic Sediment Chronic Concern Concentration = 19 mg/kg dry wt sediment.**

The most reliable and acceptable value for the toxicity to terrestrial invertebrates acute endpoint is based on the MCCP material from the Thompson et al. 2001a study. The 28-d terrestrial invertebrate GMATC value of 149 mg/kg dry wt sediment from this study will be used. Again, using methods in US EPA (2012):

- Acute CoC: Calculating an acute concern concentration from the chronic value of149 mg/kg dry wt, this value is multiplied by an acute to chronic ratio for invertebrates (10) to yield 1,490 mg/kg dry wt. This value is then divided by an assessment factor of 5 to yield 298 mg/kg dry wt. **Terrestrial Invertebrate Acute Concern Concentration = 298 mg/kg dry wt sediment.**
- Chronic CoC: The 28-d terrestrial invertebrate GMATC of 149 mg/kg dry wt is divided by an assessment factor of 10 to yield 14.9 mg/kg dry wt sediment. **Terrestrial Invertebrate Chronic Concern Concentration = 15 mg/kg dry wt sediment.**

The most reliable and acceptable value for the toxicity to terrestrial plants is based on the MCCP material from the Thompson et al. 2001ab study. For LCCPs, the analog approach using the values from this study may be used. However, there is no OPPT guidance regarding assessing concern concentrations for terrestrial plants.

B-2 LCCP ECOTOXICITY DATA

Where data are absent for long chain chlorinated paraffins for ecotoxicity endpoints, data from sources using medium chain chlorinated paraffins will be used to inform the hazard for these endpoints.

B-2-1 Acute Fish Toxicity

(1) Johnson and Finely 1980

A series of 96-hour acute fish toxicity studies were conducted by the United States Geological Survey's Columbia National Fisheries Research Laboratory, over the years 1965 – 1978, with several long-chain chlorinated paraffins (Chlorowax LV, $C_{>17}$, 39% Cl; Chlorowax 40, $C_{>20}$, 40 - 42% Cl; Chlorowax 50, $C_{>20}$, 48 - 54% Cl; Chlorowax 70, $C_{>20}$, 70% Cl) published by Johnson and Finely (1980). Bluegill sunfish (*Lepomis macrochirus*) and rainbow trout (*Oncorhynchus mykiss*) were exposed to the test substance (100% commercial formulation) in a static test system. Stock solutions were prepared immediately before each test with acetone used as a carrier solvent. The average pH level was between 7.2 and 7.5 for all tests and the test temperature was 20 ± 1°C for Bluegill sunfish and 10 ± 1 ºC for Rainbow trout. Dilution water hardness ranged from 40 to 50 mg/L as $CaCO_3$. Reported effect levels are considered to be nominal with LC_{50} values of >300 mg/L for bluegill sunfish and rainbow trout for all LCCPs tested; all values are above the limit of solubility.

EPA/OPPT Conclusions
Using a weight-of-evidence approach, these studies were considered acceptable to characterize the acute fish toxicity endpoint.
96-hr LC_{50} = NES (> 300 mg/L)

(2) Bengtsson et al. 1979
A 96-hour acute fish toxicity study as part of a bioaccumulation study was published by Bengtsson et al. (1979). Bleak (*Alburnus alburnus*) were exposed to a long-chain chlorinated paraffin, Witaclor 549 (C_{18-26}, 49% Cl). The test was performed at 10 °C under semi-static testing conditions. A nominal concentration of 0.125 mg/L was prepared by first dissolving Witaclor in acetone and then added to the dilution water. The treatment vessels and acetone control vessels consisted of six groups of 15 fish (average 4.5 g per fish). The acetone in all treatments did not exceed 0.1 ml/L. The test solutions were renewed every two to three days over the 14-day exposure period. Specific details of the test conditions were not provided other than the tests were performed at 10°C in seawater with a salinity of 7 ppt. Even though the test duration was 14-days, no mortality occurred within 96-hours or 14-days, thus the 96-hour LC_{50} was > 0.125 mg/L.

EPA/OPPT Conclusions
This study was considered supplemental to characterize the acute saltwater fish toxicity endpoint using a weight-of-evidence approach.
96-hr LC_{50} = NES (> 0.125 mg/L)

B-2-2 Acute Aquatic Invertebrate Toxicity

(1) Frank (1993) and Frank and Steinhäuser (1994)
The following study summary (Frank, 1993; Frank and Steinhauser, 1994), provided in the ECB (2005) MCCP risk assessment, was considered supportive of the aquatic invertebrate hazard determination. The chlorinated paraffin used in these studies was a commercial C_{14-17} product with a 52 wt% Cl. Daphnia magna were exposed to nominal concentrations of either 100 mg/L or 10,000 mg/L. The 100 mg/L solution was sonicated for 1 hour and then left to stand in the dark for 48 hours before use. The 10,000 mg/L solution also stood for 48 hours in the dark before use, but this time without sonication. After this period, both solutions were filtered firstly with glass filters and then with membrane filters to remove undissolved test substance. The concentrations of medium-chain chlorinated paraffin in the water soluble fractions were then determined by AOX (adsorbable organic halogen) analysis (detection limit of 10 µg/L Cl was equivalent to around 20 µg/L of the chlorinated paraffin). This analysis showed that the concentration of chlorinated paraffin present in the water soluble fraction was around 0.404 - 0.500 mg/L for the 10,000 mg/L nominal solution and 0.071 - 0.142 mg/L for the 100 mg/L stock solution. The acute (48-hour) toxicity tests were carried out using dilutions of the two prepared water soluble fractions. The method used was DIN 38 412, Teil 11, which is equivalent to OECD 202.

In the tests using the water soluble fraction from the 100 mg/L nominal solutions no toxicity was seen at concentrations up to the undiluted stock solution (i.e., no effects up to around 0.071-0.142 mg/L). In experiments using the water soluble fraction from the 10,000 mg/L stock solution, an EC_0 of 0.140 mg/L (also reported as 0.100 - 0.110 mg/L in the paper) and an EC25 of 0.423 mg/L (also reported as 0.420-0.470 mg/L in the paper) was determined (maximum mortality seen was 25%) (Frank, 1993). The latter results for the 10,000 mg/L stock solution were reported by Frank and Steinhauser (1994) as EC_0 = 0.140 mg/L and EC_{25} = 0.339 mg/L,

and it was noted that some of the Daphnia were floating on the surface of the test solution. In the later study (Frank and Steinhauser, 1994), the results of further acute toxicity studies were reported using the same test method. An EC_{50} of 0.037 mg/L and an EC_0 of 0.009 mg/L were determined using the water soluble fraction from the 100 mg/L stock solution and no toxic effects were seen in tests with the water soluble fraction from the 10,000 mg/L stock solution (approximately $EC_0 \geq 0.525$ mg/L). The authors noted that the effects seen in the acute tests showed poor reproducibility, probably because effects were seen only around the water solubility limit of the substance. However, the authors thought that the possibility of undissolved droplets affecting the results could be ruled out, as floating Daphnia were only sporadically observed in the test.

EPA/OPPT Conclusions
This study could not be adequately assessed due to inconsistencies in the hazard data for the different dilutions of the test material. In addition, the authors noted that the effects seen showed poor reproducibility, most likely due to effects observed only around the solubility limit in the test system used. The results of this test should therefore be treated with caution, as the effects were mainly seen in the saturated solutions only.

(2) Tarkpea et al. 1981
The Tarkpea et al. (1981); as quoted in IPCS (1996) summary, provided in the ECB (2005) MCCP risk assessment, was considered supportive of the aquatic invertebrates hazard determination.

The results of tests with the brackish water harpacticoid Nitocra spinipes have been reported (Tarkpea et al., 1981). No other details of the test were reported but the test method was probably the same as reported by Tarkpea et al. (1981), where a static method was employed using water of salinity 7‰ at a temperature of 20 - 22°C without aeration, probably using acetone as co-solvent.

EPA/OPPT Conclusions
This study could not be adequately assessed due to the lack of details provided regarding specific conditions of the test and the preparation of the test solutions. The lack of detail prohibits a review and adequacy of the study. However, the harpaticoid, *Nitocra spinipes*, is not a standard test species and the test concentrations greatly exceed the limit of solubility. The 96-hour LC_{50} values for both chlorinated paraffins were identified, but the reliability of the results cannot be determined. Overall, EPA/OPPT reserves judgment on the acceptability of this study. Therefore, data from sources using medium chain chlorinated paraffins will be used to inform the hazard for these endpoints.

B-2-3 Aquatic Plant Toxicity

(1) Koh and Thiemann 2001
A 72-hour algae toxicity study using *Scenedesmus subspicatus,* was conducted at the University of Bremen, Department of Physical and Environmental Chemistry with CP 30 (C_{17-24}, 35% chlorination), CP 40 (C_{17-20}, 44% chlorination) and Hordaflex LC50 (C_{17-20}, 52% chlorination) according to DIN 38412 by Koh and Thiemann (2001). Additional communications with the study author Wolfram Thiemann clarified that nominal test concentrations and local tap water

(Bremen, Germany) was used without adjustments however, the study methods were not fully characterized. The stock solutions were prepared to a concentration 6 mg/mL of test substance in acetone. The individual stock solutions were diluted with distilled water to prepare individual standard solutions of 0.250 mg/L for CP 30 and CP 40 and 0.125 mg/L for Hordaflex LC 50. pH was between 5 and 6 and water hardness was between 35.7 and 53.5 mg $CaCO_3$/L. Ambient laboratory air temperature was ~ 21 ºC. The solvent acetone was used to maintain test substance in solution. Effects were calculated based on growth rate; no effects were observed up to 0.250 and 0.125 mg/L.

EPA/OPPT Conclusions
All three of the chlorinated paraffins tested contain C_{17} and C_{18} constituents which are considered to have LCCP-like properties. More information concerning composition would be needed to accept these results for long-chain chlorinated paraffins. Overall, EPA/OPPT reserves judgment on the acceptability of this study.
72-hr EC_{50} (growth rate) = NES (> 0.250 mg/L; CP 30 and CP 40)
72-hr EC_{50} (growth rate) = NES (> 0.125 mg/L; Hordaflex LC 50)
72-hr NOEC ≥ 0.250 mg/L (CP 30 and CP 40)
72-hr NOEC ≥ 0.125 mg/L (Hordaflex LC 50)

B-2-4 Chronic Fish Toxicity

No data are available.

B-2-5 Chronic Aquatic Invertebrate Toxicity

(1) Frank 1993 and Frank Steinhäuser 1994
The following data review of Frank (1993) and Frank and Steinhäuser (1994) were directly excerpted from the U.K. Environmental Risk Assessment of long-chain chlorinated paraffins:

> The test substance was identified as C_{18-20} chlorinated paraffin with 52% chlorination. Frank (1993) carried out a series of acute and longer-term studies with *Daphnia magna* using a commercial C_{18-20}, 52% wt. Cl product. The tests were carried out using dilutions of the water-soluble fraction of the chlorinated paraffin. Stock solutions of the chlorinated paraffin were made up in water to give nominal concentrations of either 100 mg/L or 10 g/L. The 100 mg/L solution was sonicated for one hour and then left to stand in the dark for 48 hours before use. The 10 g/L solution also stood for 48 hours in the dark before use, but this time without sonication. After this period, both solutions were filtered firstly with glass filters and then with membrane filters to remove undissolved test material (microscopic and spectroscopic investigation of the filtered solutions gave no indication of the presence of droplets) to give the respective water-soluble fractions. The concentration of the chlorinated paraffin in the water-soluble fractions was determined by AOX (adsorbable organic halogen) analysis. The detection limit of the method used was around 10 µg Cl/L, which is equivalent to around 20 µg/L of the chlorinated paraffin. This analysis showed that the concentration of chlorinated paraffin present in the water-soluble fraction was around 462–519 µg/L for the 10 g/L nominal solution but was not detectable in the 100 mg/L solution (i.e. <20 µg/L). Experiments were carried out to show that in the test vessels, although the concentration of chlorinated paraffin present fell over time, it remained within 80 per cent of the initial concentration over 2–3 days. This time period was used in the long term tests as the renewal period for the solution (semi-static method).

Long-term (21-day) reproduction studies were also performed using dilutions of the water-soluble fractions of the two stock solutions. The dilutions used were 1:2, 1:4, 1:8 and 1:16 for the 100 mg/L loading and 1:4, 1:8, 1:16, 1:32 and 1:64 for the 10 g/L loading. In these experiments, the test medium was changed three times per week and 10 animals were used per concentration. The tests were carried out at 20°C and a pH of 7.79–8.44. Two endpoints were determined in the study: effects on parent mortality and effects on reproduction (number of offspring per adult). Parent mortality in the controls was 0 per cent in the test carried out with the 10 g/L nominal stock solution and 10 per cent in the test carried out with the 100 mg/L nominal stock solution.

Elevated mortality was seen in the exposed populations. For the 10 g/L stock solution the LOEC was determined as the 1:8 dilution (approximately 58–65 μg/L) and the NOEC was determined as the 1:16 dilution (approximately 29–32 μg/L). For the 100 mg/L nominal stock solution the LOEC was determined as the 1:4 dilution and the NOEC was determined as the 1:8 dilution. These dilutions are based on the detection limit for the analysis of the 100 mg/L stock solution, and equate to LOEC and NOEC [values] of <5 and <2.5 μg/L respectively). From the dose response curves it appears that 100% parent mortality occurred at a concentrations of around <10 μg/L in the 100 mg/L nominal stock solution experiments and around 125 μg/L in the 10 g/L nominal stock solution experiments.

For the reproduction endpoint, the average number of young per adult in controls was 72.3 in the 100 mg/L nominal stock solution series of experiments and 73.5 in the 10 g/L nominal stock solution experiments. A significant reduction in the number of young per adult was seen in some of the exposed organisms. For the 100 mg/L nominal stock solution, this effect on reproduction was significantly different from the control groups at the lowest concentration tested (a 1:16 dilution which is equivalent to a chlorinated paraffin concentration of <1.2 μg/L, based on the detection limit of the analytical method used). Thus the NOEC/LOEC for this series of experiments was <1.2 μg/L. Similarly, for the 10 g/L nominal stock solution effects were again seen at the lowest concentration tested (a 1:64 dilution, which is equivalent to a chlorinated paraffin concentration of 7.3–8.1 μg/L). This value is treated as the LOEC for this series of experiments. The report also indicates that the NOEC is very close to this value, since using a different statistical method (Dunnett's Test rather than Williams' Test), the effects seen at this concentration were not statistically significantly different from controls.

EPA/OPPT Conclusions

The interpretation of the results is complicated by the difficulties interpreting the effects from the different loading and dilution concentrations used. The actual exposure concentration in the 100 mg/L nominal stock solution is unknown and the measured concentration in the 10 g/L nominal stock solution (500 μg/L) is above the reported (estimated) water solubility of LCCPs. It was also noted in the U.K. environmental risk assessment, that the data for the 10 g/L loading were reanalyzed by Thompson (2001). The reanalysis suggests that the statistical significance of parent mortality is questionable and that the 1:8 dilution (20% mortality) considered as the LOEC is a marginal effect at best. The NOEC for parent mortality could be considered to be the 1:8 dilution (0.058 – 0.065 mg/L). In addition, there was a serious error found by Thompson (2001) in the statistical method. They determined that the

statistical software misinterpreted increasing dilutions as increasing concentrations based on how the data were entered. Re-analysis of the data showed that effects were statistically significant compared with the controls only at the 1:8 dilution, leading to a NOEC at the 1:16 dilution (0.029 – 0.032 mg/L). This problem with the statistical analysis may also explain why the NOEC and LOEC from the 100 mg/L stock were observed below the lowest concentration tested; thus, the NOEC/LOEC of < 0.0012 mg/L is questionable. The data from these studies should be approached with caution due to deficiencies and uncertainties with the statistical analysis. The NOEC and LOEC values that follow are questionable.

21-day NOEC = 0.029 – 0.032 mg/L (10 g/L solution; parent mortality)
21-day LOEC = 0.058 – 0.065 mg/L (10 g/L solution; parent mortality)
21-day NOEC < 0.0025 mg/L (below detection limit; 100 mg/L solution; parent mortality)
21-day LOEC ≤ 0.0050 mg/L (below detection limit; 100 mg/L solution; parent mortality)
21-day NOEC < 0.0073 mg/L (10 mg/L solution; reproduction)
21-day LOEC ≤ 0.0073 mg/L (10 mg/L solution; reproduction)
21-day NOEC < 0.0012 mg/L (100 mg/L solution; reproduction)
21-day LOEC ≤ 0.0012 mg/L (100 mg/L solution; reproduction)

(2) TNO 1993
The test was carried out according to the OECD [211] methodology using a semi-static test procedure (test solution renewal was carried out every 48–72 hours). The test substance was identified as $C_{18\text{-}20}$ chlorinated paraffin with 52% chlorination (Chloroparaffin Hoechst 56 Flüssig, Chloroparaffin Hoechst 52 Flüssig, and Hordaflex LC50. The dilution water used was a synthetic medium (DSWL) prepared by the addition of various salts to ground water. The hardness of the medium was 214 mg/L as $CaCO_3$. The test was carried out using saturated solutions of the chlorinated paraffin using a column technique. The column was prepared by firstly dissolving/suspending 0.1 g of the test substance in 25 mL of acetone. This solution was then added to 10 g of the packing material for the column (chromosorb 60/80 mesh) and the acetone removed by rotation evaporation. The coated packing material was stored at room temperature in the dark until needed. The columns were stainless steel (25 cm long with an internal diameter of 4.3 mm) filled with 1 g of the coated packing material. The column was conditioned by pumping dilution water through at a flow rate of 6.2 mL every three minutes; the first 500 mL was collected and discarded. Around 18 litres of dilution water was then collected in a bottle and continually re-circulated through the column at a flow rate of 3.4 mL per minute throughout the test. The required amount of the saturated solution needed for the start of the test, and at each renewal period, was then taken from the bottle.

Four replicates (10 daphnids in 400 mL of test solution) were carried out for each treatment. The tests were performed in 600 mL beakers and these were conditioned to the test solutions for two days prior to the start of the test. The solutions were renewed every Monday, Wednesday and Friday during the test.

The concentration of test substance was determined at each renewal time in both the “fresh” solution and the “spent” solution. The analytical method used was based on extractable organic

halogen (EOX; similar in principle to AOX) analysis. The mean EOX measured in the test solution over the course of the test was around 1 μg/L (the range found in the "fresh" solutions was 1.0–1.5 μg/L and the range in the "spent" solutions was 0.5–1.5 μg/L. The EOX concentrations in the control solutions were generally <0.5 μg/L in the "fresh" solution but the range found in the spent solutions was <0.5–1.0 μg/L for the blank control and 0.5 2.0 μg/L for the column control.

The temperature, DO, and pH during the test were 19.2 - 20.3 ºC, ≥7.1 mg/L and 7.6 - 8.5, respectively. The parent survival in both of the control groups was 97.5%. In the $C_{18–20}$, 52% wt. Cl treatment group the parent survival was 92.5%. This survival was not significantly different (at the p=0.05 level) from the control group. Therefore, it was concluded that no treatment related effects on parent morality were seen in the study. The reproduction rate (expressed as the cumulative number of young per living female) in the study was 113.6 in the blank control and 127.3 in the column control. The response of the two controls was not significantly different (at the p=0.05 level). The reproduction rate in the C18–20, 52% wt. Cl treatment group was 100.8. This was 88.7 per cent of the blank control response and 79.1 per cent of the column control response. These responses were analyzed statistically in TNO (1993) using the two-tailed Dunnett-test. No statistically significant differences were found between the $C_{18–20}$, 52% wt. Cl treatment group and the blank control, or the column control.

EPA/OPPT Conclusions

Thompson (2007) conducted a further analysis of the results, due to the author's perception of discrepancies in the UK's (2009) Environmental Risk Assessment. The discrepancy was based on a seemingly contradictory statement from pg. 7 of the TNO report where the reproduction rate of the Hodaflex LC50 and Hoechst 52 Flüssig was stated as being significantly different from the controls (Pg.7 of the report) but not significantly different from the controls (Pg. 16 of the report). The data were re-analyzed by Thompson (2007) and no differences in the reproduction rate were observed between the C_{18-20}, 52 wt% chlorination treatment groups Hodaflex LC50 and Hoechst 52 Flüssig, the column control, blank control or the pooled control group (combined blank control and column control). An additional statistical analysis was conducted by OPPT and no differences were determined for reproduction rate in the treatment groups versus controls using SAS (v. 9.3). Regardless of the discrepancy in the TNO report, statistically significant differences were reported by Thompson (2007) for adult mortality, reproduction rate, and mortality in general for *Daphnia* exposed to Hoechst 52 Flüssig compared to both controls. However, it is still unclear as to the levels of saturation of each solution the organisms were exposed to based on the extraction technique and nominal loading rates. Therefore, EPA/OPPT will reserve judgment on the acceptability of this study based on a weight of evidence approach.

21-day NOEC = 0.002 mg/L (reproduction Hoechst 56 Flüssig)

B-2-6 Chronic Aquatic Sediment Invertebrate Toxicity

No data are available. Data from secondary sources using medium-chain chlorinated paraffins for chronic aquatic sediment invertebrate toxicity can be used to fill data gaps for the long-chain chlorinated paraffin; and these data were described above in the MCCP section.

B-2-7 Avian Toxicity

No data are available. Data from secondary sources using medium-chain chlorinated paraffins for avian toxicity can be used to fill data gaps for the long-chain chlorinated paraffins; and these data were described above in the MCCP section.

B-2-8 Terrestrial Invertebrate Toxicity

No data are available. Data from secondary sources using medium-chain chlorinated paraffins for terrestrial invertebrate toxicity can be used to fill data gaps for the long-chain chlorinated paraffins; and these data were described above in the MCCP section.

B-2-9 Terrestrial Plant Toxicity

No data are available. Data from secondary sources using medium-chain chlorinated paraffins for terrestrial plant toxicity can be used to fill data gaps for the long-chain chlorinated paraffins; and these data were described above in the MCCP section.

B-2-10 Conclusions

Sufficient data were available to characterize the acute fish, the acute aquatic invertebrate, the chronic aquatic invertebrate, the chronic aquatic sediment invertebrate, avian, and terrestrial plant toxicity endpoints for MCCPs and LCCPs by read across in some instances. Data for other toxicity endpoints (i.e., chronic fish, aquatic plant, etc.) were inconclusive due to lack of study details, uncertainties in analytical methods, or test material preparation methods; thus, these data are included in order to characterize risk in a qualitative manner, but are used as supportive for the categories under which they are provided. Supporting data were included in order to provide a weight-of-evidence approach used to characterize some endpoints.

Most of the data provided in this review indicated several difficulties were encountered when testing in an aquatic environment. These included: (1) getting the material into solution, (2) measuring the material in solution, and (3) characterizing the effects for each study listed. Often there were many details of a given study omitted, prohibiting a full and robust review of the data. The (estimated) physical-chemical properties of LCCPs and MCCPs (water solubility values between 2 and 30 μg/L and Log K_{ow} values between 4-8) suggest these materials may not partition to the aquatic media or elicit toxicity to aquatic organisms within the water column.

Specifically for the chronic and acute aquatic invertebrate, aquatic sediment, avian, and terrestrial plant endpoints for LCCPs, other analog data provided was acceptable using compounds with chlorination percentage of 52 wt% and carbon chain lengths of C_{14-17} which is defined as a MCCP material. These data are used in this assessment to fill data gaps for the C_{18-20} LCCPs as this would be a conservative approach to charactering hazard in the absence of data. Concern concentrations based on these data are again a very conservative approach in the

absence of data for the LCCP materials themselves and therefore may not inherently characterize toxicity to LCCPs directly.

The most reliable and acceptable studies indicate that for MCCPs, the toxicity to aquatic organisms for acute endpoints are from the Thompson et al. 1996 study for aquatic invertebrates. Where the 48-hour EC_{50} value = 0.0059 mg/L. Using the methods described in the Sustainable Futures/P2 Manual (US EPA, 2012), the acute and chronic concentrations of concern (CoC) are derived as follows:

- Acute CoC: The 48-hour EC_{50} value = 0.0059 mg/L is divided by an assessment factor of 5 to yield an acute concentration of concern (CoC) of 0.00118 mg/L, or 0.001 mg/L, or 1 µg/L (1 ppb). **Aquatic Acute Concern Concentration= 1 ppb**
- Chronic CoC: The aquatic invertebrate chronic value of 0.013 mg/L from the 1997 Thompson et al. study based on a MCCP material is divided by an assessment factor of 10 to yield 0.0013 mg/L or 1.3 µg/L or 1.3 ppb. **Aquatic Chronic Concern Concentration = 1 ppb**

For LCCPs, the acute concern concentration may be derived from the Johnson and Finely (1980) studies. For the chronic concern concentration, the results from the Thompson et al. 1997 study based on a MCCP material will be used as a conservative qualitative assessment due to the lack of overly reliable data for this endpoint for LCCPs.

- Acute CoC: **Aquatic Acute Concern Concentration= NES**
- Chronic CoC: The aquatic invertebrate chronic value of 0.013 mg/L from the 1997 Thompson et al. study based on a MCCP material is divided by an assessment factor of 10 to yield 0.0013 mg/L or 1.3 µg/L or 1.3 ppb. **Aquatic Chronic Concern Concentration = 1 ppb (MCCP and LCCP)**

The most reliable and acceptable value for the toxicity to aquatic sediment invertebrate organisms acute endpoint is based on the MCCP material from the Thompson et al. 2002 28-d study. For both MCCPs and LCCPs, the 28-d sediment invertebrate GMATC value of 187 mg/kg dry wt sediment is used to assess hazard. The 28-d sediment invertebrate GMATC value of 187 mg/kg dry wt sediment is used to assess hazard. Again, using methods in US EPA (2012):

- Acute CoC: Calculating an acute concern concentration from the chronic value of 187 mg/kg dry wt. The 187 value is multiplied by an acute to chronic ratio for invertebrates (10) to yield 1,870 mg/kg dry wt. This value is then divided by an assessment factor of 5 to yield 374 mg/kg dry wt. **Aquatic Sediment Acute Concern Concentration = 374 mg/kg dry wt sediment. (MCCP and LCCP)**
- Chronic CoC: The 28-d sediment invertebrate GMATC of 187 mg/kg dry wt sediment is divided by an assessment factor of 10 to yield 18.7 mg/kg dry wt sediment. **Aquatic Sediment Chronic Concern Concentration = 19 mg/kg dry wt sediment. (MCCP and LCCP)**

The most reliable and acceptable value for the toxicity to terrestrial invertebrates acute endpoint is based on the MCCP material from the Thompson et al. 2001a study. For LCCPs, the 28-d terrestrial invertebrate GMATC value of 149 mg/kg dry wt sediment will be used as an analog approach to assess hazard. The 28-d terrestrial invertebrate GMATC value of 149 mg/kg dry wt sediment from this study will be used. Again, using methods in US EPA (2012):

- Acute CoC: Calculating an acute concern concentration from the chronic value of149 mg/kg dry wt, this value is multiplied by an acute to chronic ratio for invertebrates (10) to yield 1,490 mg/kg dry wt. This value is then divided by an assessment factor of 5 to yield 298 mg/kg dry wt. **Terrestrial Invertebrate Acute Concern Concentration = 298 mg/kg dry wt sediment. (MCCP and LCCP)**
- Chronic CoC: The 28-d terrestrial invertebrate GMATC of 149 mg/kg dry wt is divided by an assessment factor of 10 to yield 14.9 mg/kg dry wt sediment. **Terrestrial Invertebrate Chronic Concern Concentration = 15 mg/kg dry wt sediment. (MCCP and LCCP)**

The most reliable and acceptable value for the toxicity to terrestrial plants is based on the MCCP material from the Thompson et al. 2001ab study. For LCCPs, the analog approach using the values from this study may be used. However, there is no OPPT guidance regarding assessing concern concentrations for terrestrial plants.

Appendix C HUMAN HEALTH HAZARD STUDY SUMMARIES

C-1 MCCP HEALTH DATA REVIEW

There is no information on inhalation absorption of MCCPs in humans or in animals. Based on their low vapor pressure and low water solubility, absorption following inhalation or dermal exposure is expected to be limited. Some MCCPs demonstrated moderate absorption and metabolism following oral exposure in animals. In general, absorption and metabolism are related to their carbon chain length and degree of chlorination; the longer the carbon chain length and the higher the degree of chlorination, the less absorption and metabolism.

No information is available on the toxicity of MCCPs in humans; however, the toxicology of these compounds has been evaluated in experimental animals. Studies in rats and rabbits have shown that MCCPs only caused slight skin irritation and have low eye irritation potential. No evidence of skin sensitization was found when tested in guinea pigs. The liver, kidney and thyroid are the target organs of MCCPs in oral repeated dose studies in experimental animals. MCCPs induced increased liver weight, enzyme activity, and histopathological changes at high dose levels. Some of these hepatic effects are likely related to an increase in metabolic demand as an adaptive response, as well as to peroxisome proliferation, which are considered of limited toxicological significant to humans. However, liver necrosis was observed in a 90-day study in rats at 360 mg/kg-bw/day; this effect is considered relevant to humans. The reported effects in the kidney may have been produced by the parent compound or from metabolites. Mechanistic data cannot totally rule out that some kidney effects are relevant to humans. From the data available, a LOAEL of 625 mg/kg-bw/day based on histopathological changes in the kidneys of female rats is identified in a 90-day toxicity study, and a NOAEL of 23 mg/kg-bw/day based on increased kidney weight at 222 mg/kg-bw/day is identified from another 90-day study in rats. Repeated dose studies in rats reported some changes in histopathology and hormone levels of the thyroid. However, it may be concluded based on an evaluation of the mechanistic data that the thyroid effects observed in rats is of little relevance to chronic toxicity in humans.

There is no information on the carcinogenicity of MCCPs; however, carcinogenicity studies on a short-chain chlorinated paraffin (SCCP) and a long-chain chlorinated paraffin (LCCP) are available. These studies, along with the genotoxicity data on MCCPs, may be used to inform the carcinogenic potential of MCCPs. When administered by gavage, a SCCP (C_{12}, 60 wt% Cl) caused increased incidences of liver tumors in male and female rats, kidney tumors in male rats, and thyroid tumors in female rats. However, based on mechanistic considerations, these tumors are considered to be of little or no relevance to humans. An increased incidence of malignant lymphoma in male mice was reported at the highest dose of 5,000 mg/kg-bw/day in carcinogenicity studies of a LCCP (C_{23}, 43 wt% Cl) in male and female rats and mice. However, malignant lymphoma is one of the more variable tumors in mice and has a viral origin in many cases. No increased incidence of malignant lymphoma was observed in the carcinogenicity study on an SCCP. Further, MCCPs are non-genotoxic. Therefore, it may be concluded that MCCPs are unlikely to pose a carcinogenic hazard to humans.

When evaluating the risks of workers from exposure to MCCPs based on the available repeated-dose toxicology studies, the EU's draft Risk Assessment Report (RAR) on MCCPs concluded that except metal working fluids (MWF) use, "*There is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied already*" (EURAR, 2008).

Using the NOAEL (23 mg/kg-bw/day) of kidney toxicity identified in the 90-day oral study in rats (CXR, 2005), a MOS of 70,000 was estimated for dermal exposure of consumers resulting from wearing leather clothes treated with MCCP. For inhalation exposure of consumers using metal fluids containing MCCP, a MOS of 2,875 was obtained. Therefore, it was also concluded that: "*There is present no need for further information and/or testing or for risk reduction measures beyond those which are being applied already*" (EURAR, 2008).

C-1-1 Metabolism

There is no information on inhalation absorption of MCCPs in humans or in animals. Based on their low vapor pressure and low water solubility, absorption following inhalation or dermal exposure is expected to be limited. An *in vitro* study using human skin showed that after 24 hours, approximately 0.7% of a C_{15} chlorinated paraffin was absorbed (Scott, 1984; *cited in:* EURAR, 2008). Oral studies (IRDC, 1984, CXR, 2005; *cited in:* EURAR, 2008) showed that approximately 50% of a single dose of [8-^{14}C]-labeled C_{15} chlorinated paraffin (52 wt% Cl) was absorbed from the GI tract in rats. Excretion *via* feces was the major route of elimination of radiolabeled material. Elimination of radioactivity from body tissues occurred with an elimination half-life of approximately 2-5 days (liver and kidney) or approximately 2 weeks (adipose tissue).

C-1-2 Acute Toxicity

There is no information on the effects of a single exposure to MCCPs in humans. No deaths and only limited, non-specific clinical signs of toxicity resulting from exposure of rats to very high doses were observed in an acute oral toxicity study of MCCPs ($C_{14\text{-}17}$, 51-60 wt% Cl); the LD_{50} was reported to be > 4,000 mg/kg bw (Birtley *et al*., 1980; *cited in*: IPCS, 1996). Though no acute toxicity data are available for MCCP by the inhalation or dermal route of exposure, the low acute toxicity data for SCCPs by these routes suggest that MCCPs are likely to have low acute inhalation and dermal toxicity.

C-1-3 Irritation and Sensitization

No signs of skin irritation were seen with MCCPs (C_{14-17}, 45 wt% Cl), and only slight erythema on the shaved skin was reported in one rabbit at 24 hours exposed to MCCPs (C_{14-17}, 40 wt% Cl) (Chater, 1978; *cited in:* EURAR, 2008). A mild skin irritancy response was reported in one of nine unpublished skin irritation studies of MCCPs (C_{14-17}, 51-60% Cl) in rats (Birtley *et al*., 1980; *cited in:* EURAR, 2008). The material caused slight, transient eye irritation in rabbits (Birtley *et al*., 1980; Kuhnert *et al*., 1986; *cited in:* EURAR, 2008).

No skin sensitization reactions were produced in guinea pig maximization tests conducted on MCCPs (C_{14-17}, 40-45 wt% Cl) (Murmann, 1988; Chater, 1978; *cited in:* EURAR, 2008).

C-1-4 Repeated-dose Toxicity

There are a number of repeated dose toxicity studies (up to 90-days duration) of MCCPs (C_{14-17} 40 wt% Cl or 52 wt% Cl) in rats by oral exposure (CXR, 2005; Poon *et al*., 1995; IRDC, 1984; Birtley *et al*., 1980; and Wyatt *et al*., 1997; *cited in:* EURAR, 2008). Though the quality and reliability of these studies differs, the liver, kidney, and thyroid were consistently established as the target organs. A summary of the results from these studies is provided in Table 1.

MCCPs caused an increase in liver weight in male rats at exposure levels of $\geq$ 100 mg/kg-bw/day) and in female rats at exposure levels of $\geq$ 32 mg/kg-bw/day. Liver enzyme induction was reported in male and female rats starting from 222 and 100 mg/kg-bw/day, respectively. Liver hypertrophy of trace to minimal severity was reported in male rats at dose levels of $\geq$ 100 mg/kg-bw/day and higher. Collectively, these changes are likely to be related to an increase in metabolic demand as an adaptive response and to peroxisome proliferation, both of which are considered of no or limited toxicological significance to humans. Though Poon *et al*. (1995) reported various histopathological effects in the liver of male and female rats at dose levels $\geq$ 36 mg/kg-bw/day, there are a number of deficiencies with this study, including the scoring and classification of histopathological findings and limited reporting of data, which preclude its utility in hazard evaluation. This conclusion is consistent with previous evaluations of this study (EURAR, 2008). Further, despite the consistency of findings reported in the review article by Birtley *et al*. (1980) with other 90-day studies, these findings should be viewed cautiously because the original full study report is not available. Based on the available data, the studies by IRDC (1984) and CXR (2005) provide the most reliable data for identifying effect levels of MCCPs on the liver. For the purposes of this assessment, a NOAEL of 100 mg/kg-bw/day was chosen based on increases in absolute liver weight (*i.e.*, 22-26%), liver hypertrophy of trace severity, and enzyme induction (*i.e.*, 30% increase).

Kidney effects have been reported in a number of studies, with effect levels typically being observed at the limit doses. MCCPs (C_{14-17} 52 wt% Cl) caused significant increases (9-13%) in kidney weight at 222 mg/kg-bw/day (CXR, 2005; *cited in:* EURAR, 2008), as well as "chronic nephritis" and tubular pigmentation in the kidney of female rats at 625 mg/kg-bw/day (IRDC, 1984, *cited in:* EURAR, 2008). One study reported a dose-related increase in congestion starting at 32 mg/kg-bw/day; however, no information was provided on the incidence or severity of this effect (Birtley *et al*., 1980; *cited in:* EURAR, 2008). An additional study reported minimal to mild hyaline-droplet like cytoplasmic inclusions, starting at $\geq$ 0.4 mg/kg-bw/day in male rats. This effect is considered of limited relevance to humans. The authors also reported minimal dose-related increases with inner medullary tubular dilation at an incidence of 1/10, 4/10, and 8/10 female rats at 4, 42, and 420 mg/kg-bw/day, respectively (Poon *et al*., 1995; *cited in:*

EURAR, 2008). Though this effect is considered relevant to humans, the study suffers from a number of limitations, which preclude utilizing it for hazard evaluation. However, based on the incidence reported by the authors, the NOAEL of 42 mg/kg-bw/day for kidney effects is consistent with the NOAEL of 23 mg/kg-bw/day reported in the CXR (2005) study. Therefore, a NOAEL of 23 mg/kg-bw/day was chosen for the kidney, based on increases in organ weight at the next highest dose level.

MCCPs (C_{14-17} 52 wt% Cl) have been reported to cause minimal to mild adaptive histopathological changes in the thyroid (*i.e.*, follicular cell hypertrophy and hyperplasia) in two studies in rats starting at 50 ppm (4 mg/kg-bw/day) and above (Poon *et al*., 1995; IRDC, 1985). Decreased T_4 levels and increased TSH levels in the plasma were also seen at similar dose levels. As noted previously, these results have been drawn into question based on the scoring and classification for histopathology, the limited reporting of data, and the inconsistent findings from other more robust studies (EURAR, 2008). Therefore, these studies will not be considered further for hazard identification. IRDC (1985) reported mild to moderate hypertrophy and hyperplasia in male rats at dose levels of $\geq$ 10 mg/kg-bw/day and higher, whereas changes in absolute organ weights of male and female rats were not observed except at the limit dose of 625 mg/kg-bw/day (IRDC, 1985; *cited in:* EURAR, 2008). The remaining studies that evaluated thyroid hormone levels identified a decrease in plasma free T_3 in male rats, but not total T_3 or free/total T_4, and an increase in TSH in female rats at dose levels of 24.6 or 242 mg/kg-bw/day, respectively (CXR, 2005; *cited in:* EURAR, 2008), or fluctuations in thyroid hormones in male or female rats at doses of $\geq$ 312 mg/kg-bw/day or higher (Wyatt *et al*., 1997; *cited in:* EURAR, 2008). There is evidence that the thyroid effects observed are attributable to stimulation of this organ arising from a negative feedback effect arising from plasma T_4 depletion following increased excretion of this hormone. This depletion of plasma T_4 results from the induction of hepatic UDPG-transferase, increased glucuronidation, and ultimately excretion of T_4 following exposure to MCCPs. The pituitary responds to the decreased levels of T_4 by releasing more TSH, which in turn leads to increased production of T_4 by the thyroid. The continuous stimulation of the thyroid in response to the increased excretion of plasma T_4 is predicted to ultimately give rise to hypertrophy and hyperplasia in this organ. Humans, unlike rodents, possess T_4-globulin binding protein and are therefore less susceptible to plasma T_4 depletion and hence any resultant thyroid stimulation. The thyroid effects observed in rats are not considered to be of relevance to chronic human health at relevant levels of exposure, although these changes may be relevant for assessing potential adverse outcomes during reproduction and development, as discussed under section.

C-1-5 Genotoxicity

MCCPs (C_{14-17} 40-52 wt% Cl) are not mutagenic to bacteria. Three *in vivo* bone marrow studies also show that MCCPs are not clastogenic (*cited in:* EURAR, 2008). Therefore, it may be concluded that MCCPs possess a low potential to cause genotoxic effects.

C-1-6 Carcinogenicity

There is no information on the carcinogenicity of MCCPs. When administered by gavage, a SCCP (C_{12}, 60 wt% Cl) caused increased incidences liver tumors in male and female rats, kidney tumors in male rats, and thyroid tumors in female rats (NTP, 1986). However, on mechanistic considerations, these tumors are considered to be of little or no relevance to humans. This conclusion is consistent with previous carcinogenicity evaluations (EURAR, 2008). An increased incidence of malignant lymphoma in male mice was reported at the highest dose of

5,000 mg/kg-bw/day in carcinogenicity studies of a LCCP (C_{23}, 43 wt% Cl) in male and female rats and mice. However, malignant lymphoma is one of the more variable tumors in mice and has a viral origin in many cases. No increased incidence of malignant lymphoma was observed in the carcinogenicity study on a SCCP (C_{12}, 60 wt% Cl). Based on structure-activity relationships and the absence of positive genotoxicity data on MCCPs, the available carcinogenicity studies on a SCCP and a LCCP suggest that MCCPs are not expected to pose a carcinogenic hazard to humans.

Table_Apx C-1: Summary of Results from 90-day Studies in Rats Administered MCCPs

Strain (sample size)	*Test substance and dose levels*	*Target organ*	*Effect levels*
F-344 (10 rats/sex/group)[1]	C_{14-17}, 52 wt% Cl Dietary intake for ♂: 0, 2.38, 9.34, 23.0, or 222 mg/kg-bw/day. Dietary intake for ♀: 0, 2.51, 9.70, 24.6, or 242 mg/kg-bw/day.	Liver	♂ at 222 and ♀ at 242 mg/kg-bw/day, 13-31% ↑ in organ weight ♂ at 222 mg/kg-bw/day, minimal centrilobular hypertrophy in 9/10 animals ♂ at 222 mg/kg-bw/day, 82% ↑ in microsomal T_4-UDPGA-glucuronyl transferase activity ♀ at 100, 300, and 300 mg/kg-bw/day, 30, 30, and 252% ↑ in microsomal T_4-UDPGA-glucuronyl transferase activity, respectively
		Kidney	♂ at 222 and ♀ at 242 mg/kg-bw/day, 9-13% ↓ in organ weight ♂ at > 222 and ♀ at 242 mg/kg-bw/day, no treatment-related histopathology
		Thyroid	♂ at 222 mg/kg-bw/day, 17% ↑ in plasma TSH ♂ at 23.0 and 222 mg/kg-bw/day, 26% or 22% ↓ in plasma free T_3, respectively, but no effects on total T_3 or on free/total T_4 at any dose ♀ at > 242 mg/kg-bw/day, no effects on free/total T_3 or T_4 ♀at 24.6 and 242 mg/kg-bw/day, 20 and 39% ↑ in plasma TSH ♂at > 222 and ♀ at 242 mg/kg-bw/day, no treatment-related histopathology
Sprague-Dawley (10 rats/sex/group)[2]	C_{14-17}, 52 wt% Cl Dietary intake for ♂: 0, 0.4, 4, 36, or 360 mg/kg-bw/day. Dietary intake for ♀: 0, 0.4, 4, 42, or 420 mg/kg-bw/day.	Liver	♂ at 360 and ♀ at 420 mg/kg-bw/day, 28 and 48% ↑ in absolute and relative weights, respectively ♂ and ♀ at ≤ 4 mg/kg-bw/day, no treatment-related histopathology ♂at 36 and ♀ at 42 mg/kg-bw/day, minimal increase in anisokaryosis and vesiculation of the nuclei ♂ at 360 and ♀ at 420 mg/kg-bw/day, mild increase in anisokaryosis and vesiculation of the nuclei (7-10 animals) ♂ at 360 mg/kg-bw/day, ↑ in perivenous homogeneity ♀ at 42 and 420 mg/kg-bw/day, ↑ in perivenous homogeneity ♂ at 360 and ♀ at 420 mg/kg-bw/day, ↑ in single cell necrosis (incidence not reported)
		Kidney	♂ at 360 and ♀ at 420 mg/kg-bw/day, 11% ↑ in absolute and relative weights ♂ at ≥ 0.4 mg/kg-bw/day, minimal to mild hyaline-droplet like cytoplasmic inclusions, with significant accumulation at

Table_Apx C-1: Summary of Results from 90-day Studies in Rats Administered MCCPs

Strain (sample size)	*Test substance and dose levels*	*Target organ*	*Effect levels*
			the limit dose ♀ at ≥ 4 mg/kg-bw/day, minimal dose-related inner medullary tubular dilation seen in 0/10, 0/10, 1/10, 4/10, and 8/10 animals
		Thyroid	♂ at 36 and 360 mg/kg-bw/day, minimal to mild morphological changes affecting the architecture (*i.e.*, reduced follicle sizes and collapsed angularity) and the epithelium (*i.e.*, increased height, cytoplasmic vacuolation, and nuclear vesiculation) ♀ at ≥ 4 mg/kg-bw/day, minimal to mild morphological changes affecting the architecture (*i.e.*, reduced follicle sizes and collapsed angularity) and the epithelium (*i.e.*, increased height, cytoplasmic vacuolation, and nuclear vesiculation)
F-344 (15 rats/sex/group)[3]	C_{14-17}, 52 wt% Cl Dietary intake for ♂ and ♀: 0, 10, 100, or 625 mg/kg-bw/day.	Liver	♂ and ♀ at 100 and 625 mg/kg-bw/day, 22-26% and 64-92% ↑ in absolute weight values, respectively ♂ at 100 and 625 mg/kg-bw/day, hypertrophy of trace severity seen in 1/15 and 13/15 animals, respectively ♀ at 625 mg/kg-bw/day, hypertrophy of trace severity seen in 13/15 animals
		Kidney	♂ and ♀ at 625 mg/kg-bw/day, 18% ↑ in absolute weight values ♂ at ≥ 10 mg/kg-bw/day, trace to mild nephritis seen in 1/15, 3/15, 4/15, and 10/15 animals ♀ at 625 mg/kg-bw/day, tubular pigmentation (9/14 animals)
		Thyroid	♂ at 625 mg/kg-bw/day, 50% ↑ in absolute weight values ♂ at ≥ 10 mg/kg-bw/day, mild to moderate hypertrophy observed in controls with a dose-dependent trend towards ↑ severity in treated animals ♂ at ≥ 10 mg/kg-bw/day, trace to mild hyperplasia with a dose-dependent trend towards ↑ severity
		Adrenal	♂ and ♀ at 625 mg/kg-bw/day, 25% ↑ in absolute weight values
Wistar-derived (24 rats/sex/group)[4]	C_{14-17}, 52 wt% Cl, containing epoxidized vegetable oil as a stabilizer Dietary intake for ♂: 0, 33, 167, or 333 mg/kg-bw/day.	Liver	♂ at 167 and 333 mg/kg-bw/day, 15 and 22% ↑ in relative weight values, respectively ♀ at 32, 160, and 320 mg/kg-bw/day, 11, 21, and 48% ↑ in relative weight values, respectively ♂ at 333 and ♀ at 320 mg/kg-bw/day, no histopathological abnormalities ♂ at ≥ 33 and ♀ at ≥ 32 mg/kg-bw/day, dose-related ↑ in proliferation of smooth endoplasmic reticulum (electron microscopy)

Table_Apx C-1: Summary of Results from 90-day Studies in Rats Administered MCCPs

Strain (sample size)	*Test substance and dose levels*	*Target organ*	*Effect levels*
	Dietary intake for ♀: 0, 32, 160, or 320 mg/kg-bw/day.	Kidney	♂ and ♀ at limit dose, 15% ↑ in relative weight ♂ and ♀, dose-related ↑ in congestion (incidence and severity not reported) ♂ and ♀ at > limit dose, no histopathological abnormalities
F-344 (10 rats/sex/group)[5]	C_{14-17}, 40 wt% Cl Oral gavage for ♂ and ♀: 0, 312, or 625 mg/kg-bw/day	Liver	♂ and ♀ at 312 and 625 mg/kg-bw/day, 37 and 72% ↑ in relative weight, respectively, (absolute weight and bodyweight not presented) ♂ and ♀, dose-related ↑ in centrilobular hypertrophy (incidence and severity not reported) ♂ and ♀ at 312 and 625 mg/kg-bw/day, dose-related ↑ in β-oxidation from day 29 onwards (~2.7- and 3.3-fold ↑, respectively, at study termination) ♂ and ♀ at 312 and 625 mg/kg-bw/day, dose-related ↑ in UDPG-transferase activity from day 15 onwards (up to 100% ↑, respectively)
		Thyroid	♂ and ♀ at 312 and 625 mg/kg-bw/day, ↓ in levels of free and plasma T_3, which reached statistical significance on days 15 and 57 ♂ at 312 and 625 mg/kg-bw/day, ↑ TSH up to 2-fold on day 8 only ♀ at 312 and 625 mg/kg-bw/day, T_3 significantly ↑ by day 91 ♀ at 312 and 625 mg/kg-bw/day, total plasma T_4 significantly ↓ by up to 25% on day 57 ♂ and ♀ at 312 and 625 mg/kg-bw/day, ↑ follicular cell hypertrophy throughout the study, and accompanied by follicular cell hyperplasia on days 55 and 91 (incidence and severity not reported) ♂ and ♀ at 312 and 625 mg/kg-bw/day, significantly ↑ replicative DNA synthesis on day 29, but not on day 91

[1] CXR (2005), *cited in:* EURAR (2008).
[2] Poon *et al*. (1995), *cited in:* EURAR (2008).
[3] IRDC (1984), *cited in:* EURAR (2008).
[4] Birtley *et al*. (1980), *cited in:* EURAR (2008); note, this study was only summarized in the review by Birtley *et al*. (1980). The underlying original study report was not available.
[5] Wyatt *et al*. (1997), *cited in:* EURAR (2008).

C-1-7 Developmental Reproductive Toxicity Review

A series of range-finding and definitive prenatal developmental and reproductive toxicity studies were conducted in rats and rabbits with medium-chain chlorinated paraffins (MCCPs). These studies were conducted between 1981 and 1986. They appear to be valid toxicity studies, conducted according to the standard methodologies available at the time. More recently, additional studies with MCCPs have been conducted in an attempt to determine the cause of hemorrhaging in the pups observed in a one-generation reproductive toxicity range-finding study.

In several prenatal developmental toxicity studies with MCCPs conducted *via* gavage, no signs of maternal toxicity were seen at doses as high as 500 mg/kg-bw/day in rats and 100 mg/kg-bw/day in rabbits. Likewise, no signs of developmental toxicity were observed at doses as high as 5000 mg/kg-bw/day in rats and 100 mg/kg-bw/day in rabbits.

Two reproductive toxicity studies with MCCPs in rats have been conducted. A one-generation reproductive toxicity range-finding study showed that administration of approximately 100 and 400 mg/kg-bw/day MCCPs *via* the diet had no effect on fertility or other reproductive parameters; however, internal hemorrhaging and deaths in pups were observed beginning from 74 mg/kg-bw/day (1000 ppm) up to approximately 400 mg/kg-bw/day (6250 ppm). These effects in the pups were not seen in a more recent definitive one-generation reproductive toxicity study with exposure to MCCPs for 11-12 weeks to doses as high as 100 mg/kg-bw/day (1200 ppm). Internal hemorrhaging was not seen in the adult animals in either of these studies at doses as high as 400 mg/kg-bw/day (6250 ppm), or in another study in non-pregnant female rats repeatedly exposed to doses as high as 1000 mg/kg-bw/day. However, when dams were exposed to approximately 500 mg/kg-bw/day (6250 ppm) MCCPs during cohabitation, gestation, and lactation, signs of hemorrhaging were observed in dams that died at the time of parturition. Taken together, the results of these studies suggest that newborns during lactation and pregnant females at the time of parturition are a potentially sensitive subpopulation.

The UK Risk Assessment (February, 2008) did not use the LOAEL of 74 mg/kg-bw/day (1000 ppm) from the one-generation reproductive toxicity range-finder study as a point of departure because the pup deaths at that dose were not statistically significant. The study itself used a limited number of animals and was intended for dose range-finding purposes only and, more importantly, the pup deaths were not repeated in a more recently conducted definitive study. With respect to developmental/reproductive toxicity, the UK Risk Assessment identified two subpopulations at risk: offspring during lactation and pregnant dams at parturition. The NOAELs from the definitive one-generation reproductive toxicity study (a maternal NOAEL ~ 47 mg/kg-bw/day (600 ppm) for effects on the offspring mediated *via* lactation; and a maternal NOAEL ~ 100 mg/kg-bw/day (1200 ppm) for effects on the dam during the time of parturition) were used to calculate risk. Assuming a conservative value of 50% oral absorption, the margin of safety (MOS) for effects on the offspring mediated *via* lactation and effects on the dam during the time of parturition were calculated for workers, consumers, and other scenarios. In all but one scenario (oil-based metal working fluids), the margins of safety were above 100 and in many cases, several fold above. In addition, margins of exposure were calculated for infants exposed *via* breast milk and *via* cow's milk, and in both instances, large MOEs (*i.e.*, > 100) were calculated.

Additional studies with MCCPs have been conducted in an effort to clarify the possible causes of the hemorrhaging in the pups. One (single-dose; 6250 ppm or 538 mg/kg-bw/day) study showed

maternal death during parturition due to low levels of vitamin K and related hemorrhaging, suggesting that the act of parturition places dams at higher risk. It was concluded in data from this study and a cross-fostering study that the fetus relies on clotting factors *via* mother's milk and severe deficiencies in vitamin K levels and related clotting factors in the pups results in hemorrhaging.

No definitive developmental neurotoxicity studies on MCCPs were located. It is not clear if any developmental neurotoxicity endpoints were actually measured in the available prenatal developmental/reproductive toxicity studies; none were explicitly stated. The only information available regarding behavior during development is from cage-side observations in pups through LD 21. In these cases, no dose-related differences were reported in F_1 post-weaning appearance or cage-side behaviors.

In the prenatal developmental toxicity study in rats, the **LOAEL for maternal toxicity was 2000 mg/kg-bw/day based on clinical signs. The NOAEL for maternal toxicity was 500 mg/kg/day. The NOAEL for developmental toxicity was 5000 mg/kg-bw/day, the highest dose tested.**

In the prenatal developmental toxicity study in rabbits, no adverse, treatment-related effects were reported in the dams or the offspring. **The NOAEL for both maternal and developmental toxicity was 100 mg/kg-bw/day, the highest dose tested.**

In the reproduction range-finding study in rats, the **LOAEL for maternal toxicity was 6250 ppm (463 mg/kg-bw/day) based on reductions in body weight gains. The NOAEL for maternal toxicity was 1000 ppm (74 mg/kg-bw/day). The LOAEL for developmental toxicity was 1000 ppm (62/74 mg/kg/day) based on pup mortality associated with internal hemorrhages. The NOAEL for developmental toxicity was 100 ppm (6/8 mg/kg-bw/day). No effects on any reproductive parameters were reported. The NOAEL for reproductive toxicity was 6250 ppm (384/463 mg/kg-bw/day).**

In the one-generation reproduction toxicity study in rats**,** the **LOAEL for maternal toxicity was 1200 ppm (~100 mg/kg-bw/day) based on increases in liver weight; the NOAEL for maternal toxicity was 600 ppm (~ 47 mg/kg-bw/day). The NOAEL for developmental and reproductive toxicity was 1200 ppm (~ 84/99 mg/kg-bw/day), the highest dose tested.**

Basis for Conclusions

In a range-finding prenatal developmental toxicity study in pregnant Charles River COBS CD rats administered MCCPs ($C_{14\text{-}17}$, 52 wt% Cl) *via* gavage at dose levels of 0, 1000, 1500, and 2500 mg/kg-bw/day on gestation days (GD) 6-20, no effects were observed in the dams at doses up to 2500 mg/kg-bw/day (IRDC, 1983, 1984; *cited in:* EURAR, 2008). As a result, doses greater than 2500 mg/kg-bw/day were selected for the definitive study.

In the definitive study, four groups of 25 pregnant Charles River COBS CD rats were administered MCCPs ($C_{14\text{-}17}$, 52 wt% Cl) *via* gavage at doses of 0, 500, 2000, and 5000 mg/kg-bw/day on GD 6-19 (IRDC, 1984; *cited in:* EURAR, 2008). Unmated males and females were individually housed and acclimated for 21-days in an environmentally controlled room. At the end of the acclimation period, all animals were weighed and subjected to a detailed physical examination. One female and one male rat were placed together for mating. Confirmation of mating was based on evidence of a copulatory plug or by vaginal smear for sperm. The day

mating was confirmed was designated as day 0 of gestation. Test article was administered to pregnant females orally by gavage as a single daily dose on GD 6-19. During treatment, pregnant females were observed daily for mortality and clinical signs of toxicity. Any females not surviving to scheduled sacrifice were necropsied. Body weights were recorded on GD 0, 6, 9, 12, 16, and 20. All females were sacrificed on GD 20 and the uterus and ovaries excised for examination. The number and location of viable and nonviable fetuses, early and late resorptions, and the number of total implantations and corpora lutea were recorded. The uterus was weighed. The abdominal and thoracic cavities underwent gross examination. Maternal tissues were preserved for future histopathological analysis. Fetuses were weighed, sexed, tagged, and examined for external malformations and variations, including the palate and the eyes. The fetuses underwent visceral and skeletal examinations for malformations and developmental variations.

The only effects reported in dams consisted of an increased incidence in wet matted and yellow stained haircoat in the anogenital area at 5000 mg/kg-bw/day, and soft stool at $\geq$ 2000 mg/kg-bw/day. No treatment-related adverse effects were reported in offspring at doses up to 5000 mg/kg-bw/day. The LOAEL for maternal toxicity was 2000 mg/kg-bw/day based on clinical signs; the NOAEL for maternal toxicity was 500 mg/kg-bw/day. The NOAEL for developmental toxicity was 5000 mg/kg-bw/day, the highest dose tested.

In a range-finding prenatal developmental toxicity study in pregnant Dutch Belted rabbits administered MCCPs (C_{14-17}, 52 wt% Cl) *via* gavage at dose levels of 0, 100, 300, 1000, 2000, and 3000 mg/kg/day on GD 6-27, an increase in the number of abortions was observed at $\geq$ 1000 mg/kg/day (IRDC, 1982a; *cited in:* EURAR, 2008). Body weight reductions in the dams were reported at 100 and 300 mg/kg/day. As a result, another range-finding prenatal developmental toxicity study in rabbits was initiated. This second range-finding study showed decreases in maternal weight gain at 80 and 160 mg/kg-bw/day (IRDC, 1982b; *cited in:* EURAR, 2008).

Based on the results of these range-finding studies, dose levels of 10, 30, and 100 mg/kg-bw/day were selected for the definitive prenatal oral gavage developmental toxicity study (IRDC, 1983; *cited in:* EURAR, 2008). In the definitive study, four groups of 16 pregnant Dutch Belted rabbits were administered 0, 10, 30, and 100 mg/kg-bw/day MCCPs (C_{14-17}, 52 wt% Cl) *via* gavage on GD 6-27. Unmated males and females were individually housed and acclimated for 50-days in an environmentally controlled room. As a result of a positive finding for parasites in stool samples collected during acclimation, all rabbits received sodium sulfamethazine in their drinking water for 16 days during the acclimation period. This treatment was terminated 4 weeks prior to study initiation and only rabbits testing negative for parasites were placed on study. At the end of the acclimation period, all animals were weighed and subjected to a detailed examination. Females were impregnated *via* artificial insemination. Three weeks prior to artificial insemination, females were given chorionic gonadotropin *via* an injection in a marginal ear vein in order to induce superovulation. Semen was collected from males of proven fertility and evaluated for motility. The day of artificial insemination was designated as day 0 of gestation. During treatment, pregnant females were observed for mortality and clinical signs of toxicity. Body weights were recorded on GD 0, 6, 12, 18, 24, and 28. Any females not surviving to scheduled sacrifice were necropsied. On GD 28, all surviving females were sacrificed and the uterus and ovaries excised for examination. The location and number of viable and nonviable fetuses, early and late resorptions, and the number of total implantations and corpora lutea were recorded. The uterus was weighed. The thoracic and abdominal cavities underwent gross examination. Pooled samples of abdominal adipose tissue from 3 dams were frozen for future analysis. Each fetus was sexed, weighed, and examined for external malformations and

variations, including the palate and the eyes, as well as visceral and skeletal examinations for malformations and developmental variations, including examination of the brain and the heart.

No adverse, treatment-related effects were reported in the dams or the offspring at doses up to 100 mg/kg-bw/day. The NOAEL for both maternal and developmental toxicity was 100 mg/kg-bw/day, the highest dose tested.

In a one-generation reproductive toxicity range-finding study, four groups of 5 male and 10 female Charles River COBS SC rats were administered MCCP (C_{14-17}, 52 wt% Cl) *via* the diet at 0, 100, 1000, and 6250 ppm (~ 0, 6, 62, and 384 mg/kg-bw/day, respectively, in males; and 0, 8, 74, or 463 mg/kg-bw/day, respectively, in females) (IRDC, 1985; *cited in:* EURAR, 2008). F_0 animals were exposed to test substance from 28 days prior to mating until sacrifice; F_1 animals were treated from weaning until sacrifice, with additional potential exposures occurring *in utero* and during lactation. All F_0 males were sacrificed after the mating period. Following the premating period, each male was cohabited with two females for 10 days. Females were examined for evidence of copulation by means of vaginal smears and/or the appearance of a vaginal plug. The day evidence of copulation was determined was designated as day 0 of gestation. Direct dosing began at 83 days of age for the F_0 parents and at 21 days of age for the F_1 weanlings. The F_0 and F_1 animals were observed for clinical signs of toxicity, changes in general appearance and behavior, and mortality. In the F_0 adults, body weights and food consumption were measured weekly; in addition, body weights were measured in F_0 females on GD 0, 7, 14, and 20; and on lactation days (LD) 0, 7, 14, and 21. Estrous cyclicity was determined in F_0 females prior to mating, during mating, and prior to dosing. All F_0 females were allowed to deliver. The day the entire litter was found and delivery was judged to be complete was designated as LD 0. Gestation duration was calculated. Following delivery, all pups were examined for external malformations and the numbers of live births and stillbirths (litter size) was recorded for each dam. Pups were weighed, sexed, and examined externally on LD 0, 7, 14, and 21. Litter size was determined on LD 0, 4, 10, and 21. The number of male and female pups was recorded on LD 4. Litters were examined daily for survival. F_0 females were examined for behaviors in nesting and nursing. On LD 21, all dams were sacrificed and a gross necropsy performed, including examination of the uterine contents for implantation sites; and ten F_1 weanlings/sex/dose were sacrificed and necropsied. Five F_1 males and ten F_1 females/dose group were retained after LD 21 and sacrificed at 70 days (10 weeks) of age and necropsied. Due to high mortality in high-dose F_1 pups, the surviving F_1 pups in the high-dose group and an equal number of control pups were sacrificed on LD 6 and 7 and necropsied. Blood was collected *via* heart puncture and complete blood counts performed. Bone marrow smears were collected from the femur, and the abdominal contents of the pups with milk in the stomach were collected and frozen for future analyses.

Effects in the adults consisted of isolated reductions food consumption and body weight in the dams at 6250 ppm. Effects in the offspring consisted of significant reductions in pup survival at the high dose (none of the F_1 pups in the high-dose group survived until lactation day 21); and slight (11%, not statistically significant) decreases in pup survival, and labored breathing, subcutaneous hematoma, pale discoloration, blood around the orifices, pale liver, kidney, and spleen, and blood in the cranial cavity and brain beginning at the mid-dose. No dose-response, treatment-related adverse effects were reported in the offspring in the low dose group. Reductions in body weight in F_1 male and female pups occurred during LD 7, 14, and 21, but these reductions were not statistically significantly different from controls, and were seen only in the low- and mid-dose groups but not the high-dose group. There were no dose-related differences in F_1 post-weaning appearance, behavior, food consumption, or clinical or

anatomical pathology in the low- and mid-dose groups. Based on the results of this study, it was recommended that dosage levels in a two-generation reproduction toxicity study not exceed 1000 ppm. The LOAEL for maternal toxicity was 6250 ppm (~463 mg/kg-bw/day) based on reductions in body weight gains. The NOAEL for maternal toxicity was 1000 ppm (~74 mg/kg-bw/day). The LOAEL for developmental toxicity was 1000 ppm (~62/74 mg/kg-bw/day) based on pup mortality due to hemorrhaging. The NOAEL for developmental toxicity was 100 ppm (~6/8 mg/kg-bw/day). No effects on any of the reproductive parameters were reported. The NOAEL for reproductive toxicity was 6250 ppm (~384/463 mg/kg-bw/day).

In an effort to determine the cause of hemorrhaging in the pups at the high dose from the reproductive toxicity range-finding study, a screening level cross-fostering developmental toxicity study was conducted in Charles River COBS Wistar rats fed diets containing either 0 or 6250 ppm (~ 3125 mg/kg-bw/day) MCCPs (C_{14-17}, 52 wt% Cl) for 4 weeks prior to mating and throughout pregnancy in a series of groups (Hart *et al*., 1985; *cited in:* EURAR, 2008). Offspring from two of these groups (pups from control females reared from treated females, and pups reared from their treated mothers) showed high-pup mortality associated with internal hemorrhages. Hematological assays in the pups from these two groups showed decreases in factor X, resulting in a disruption of a vitamin K-dependent clotting system (lower plasma vitamin K levels). It was concluded that the pup mortalities were due to internal hemorrhages caused by a decrease in the vitamin K-dependent hemostatic mechanism (not examined in this study), induced during lactational exposures *via* the milk from mothers receiving MCCPs.

Additional studies have been conducted to investigate two hypotheses in an effort to clarify the possible causes of the hemorrhaging in the pups.

The first hypothesis proposes that MCCPs induce a catabolism of vitamin K in lactating rats leading to decreased plasma concentrations and ultimately low levels of vitamin K in the milk pups receive (vitamin K controls the formation of several clotting factors in the liver). In order to test this hypothesis, a preliminary study (CXR Biosciences Ltd., 2003; *cited in:* EURAR, 2008) was conducted in which three groups of 6 female adult Sprague-Dawley were administered MCCPs (C_{14-17}, 52 wt% Cl) *via* gavage at doses of 0, 500, or 1000 mg/kg-bw/day for 21 days while being fed a normal diet or a vitamin K-deficient diet. Following exposures to MCCPs, significant decreases in plasma concentrations of a clotting factor were seen in rats fed a normal diet; however, these decreases did not affect prothrombin clotting times. Reductions of a clotting factor in both treated and control groups were also seen in animals fed a vitamin-K deficient diet. Plasma vitamin K levels were not affected by treatment in the normal diets, but they were lower in high-dose animals fed vitamin K-deficient diets. The results from this study suggested that MCCPs did not adversely affect the blood clotting system in adult female rats treated for 3 weeks up to a dose of 1000 mg/kg-bw/day; and the hemorrhaging effects in pups are unlikely to be mediated by reduced vitamin K levels in breast milk.

The second hypothesis proposes that MCCPs transferred to the pups through breast milk causes disruption of the pup clotting system. In order to test this hypothesis, a study (CXR Biosciences Ltd., 2004; *cited in:* EURAR, 2008) was conducted in two groups of 16 male and 32 female Sprague-Dawley rats administered 0 or 6250 ppm (~ 0 and 513 and 538 mg/kg-bw/day in males and females, respectively) MCCPs (C_{14-17}, 52 wt% Cl) for 4 weeks prior to mating, during cohabitation, gestation, and lactation until study termination (at about 2 weeks after the first litters were born, due to high rate of pup mortality). Milk, blood, and liver samples from lactating dams, and blood and liver samples from lactating pups were assessed for plasma vitamin K levels. Five dams died or were killed at the time of parturition (16% mortality). These

deaths were considered to be treatment-related as there was no indication of obstruction or hindrance to delivery. The clinical necropsy of these dams showed effects suggestive of hemorrhaging in 3 out of the 5 dams and one male who died. Slight reductions in food consumption and body weight gains were observed during gestation and lactation. There were no effects on mating performance or duration of gestation. Concentrations of plasma vitamin K levels in adult females having gone through lactation and pregnancy was markedly decreased by treatment with MCCPs, which in turn produced a decrease in activity of the plasma clotting factors in treated dams. Prothrombin clotting times were not affected in the dams, suggesting that the functional reserve in these adult animals was sufficient. Pup plasma volumes were reportedly insufficient to measure vitamin K directly, but clotting factor activities were possible to analyze. No effects on litter size at birth or on pup mortality from birth to LD 4 were reported; however, after pup mortality increased significantly after LD 4. The majority of these pups showed internal hemorrhages at necropsy. It was concluded that data from this study and the cross-fostering study performed by Hart *et al*. (1985) suggest that the fetus receives sufficient vitamin K *via* the placenta, but after birth becomes severely deficient in vitamin K and related clotting factors and relies on these factors *via* mother's milk. In addition, the pups also receive considerable levels of MCCPs *via* lactation (through mother's milk) which may also contribute to further reducing the vitamin K levels. These severe deficiencies in vitamin K levels and related clotting factors in the pups results in hemorrhaging. It was also concluded that the act of parturition places dams at higher risk.

More recently, a definitive one-generation reproductive toxicity study was conducted to refine the NOAEL for effects in the offspring and to further explore the mechanisms of hemorrhaging (CXR, 2006; *cited in:* EURAR, 2008). This study was reportedly conducted in compliance with OECD TG 421 and Good Laboratory Practice standards. Four groups of 12-17 male and female Sprague-Dawley rats were administered 0, 300, 600, and 1200 ppm (~ 0 and 21, 44, and 84 mg/kg-bw/day in males; and 0, 23, 47, and 99 mg/kg-bw/day in females) MCCPs (C_{14-17}, 52 wt% Cl) for 4 weeks prior to mating, during cohabitation, gestation, and lactation until study termination (for a total treatment of 11-12 weeks). Males were terminated on LD 4 (9 weeks of treatment) and females were allowed to litter and rear their offspring until PND 21. Females were sacrificed on LD 21. Adult males were assessed for signs of clinical toxicity, body weight, food consumption, and macropathology. Adult females were assessed for signs of clinical toxicity, body weight, food consumption, gestation length, parturition, liver weights, and macropathology. Mating performance and fertility were also evaluated. Offspring evaluations included clinical signs of toxicity, litter size, survival, sex ratio, body weight, and pathological examinations at necropsy. Milk, blood, and liver samples were obtained from selected offspring at specific time points between birth of litters and PND 21. In addition, blood, liver, and milk samples from a satellite group of five females and their litters from the control and high-dose group (1200 ppm) were collected for future analysis. Analysis of these samples was still pending at the time of the UK assessment.

No adverse effects were reported in the adult animals for clinical condition, body weight, body weight gain, food consumption, estrous cycling, mating performance, pre-coital interval, fertility, number of implantations, gestation lengths, or parturition. The only effect reported was for higher absolute and relative liver weights in high-dose females (1200 ppm; 99 mg/kg-bw/day). Likewise, no adverse effects were in the offspring at any dose level for litter size, sex ratio, offspring survival, body weights, body weight gains, macropathology and liver weights. No adverse effects were reported on pre- and post-natal survival and growth up to sacrifice (weaning). Though no histopathology was performed, the body cavity and cranial cavity were opened and examined for any signs of hemorrhaging. None was reported. Based on the results of

this study, the LOAEL for maternal toxicity was 1200 ppm (~100 mg/kg-bw/day) based on increases in liver weight; the NOAEL for maternal toxicity was 600 ppm (~ 47 mg/kg-bw/day). The NOAEL for developmental and reproductive toxicity was 1200 ppm (~ 84/99 mg/kg-bw/day), the highest dose tested.

C-2 LCCP HEALTH DATA REVIEW

There is no information on inhalation absorption of LCCPs in humans or in animals. Based on their low vapor pressure and water solubility, absorption following inhalation or dermal exposure is expected to be limited. Some absorption and metabolism following oral exposure are possible for LCCPs with shorter carbon chain length and lower degree of chlorination.

No information is available on the toxicity of LCCPs in humans. Acute oral toxicity data in animals show that LCCPs are of very low acute toxicity. Studies in animals have shown that some LCCPs may have the potential to cause slight skin irritation and sensitization but no eye irritation potential. The liver is the main target organ of LCCPs in repeated dose studies in experimental animals. Inflammatory and necrotic changes of the liver were observed in rats exposed to a $C_{20\text{-}30}$ LCCP with 43 wt% Cl at dose levels of 100 mg/kg-bw and above. For another LCCP with $C_{20\text{-}26}$ 70 wt% Cl, effects in the liver occurred at a very high exposure level of 3,750 mg/kg-bw/day; the NOAEL was 900 mg/kg-bw/day.

An increased incidence of malignant lymphoma in male mice was reported at the highest dose of 5,000 mg/kg-bw/day when tested using a C_{23} LCCP with 43 wt% Cl in carcinogenicity studies in male and female rats and mice. However, malignant lymphoma is one of the more variable tumors in mice and has a viral origin in many cases. Data on the analogous short-chain chlorinated paraffins (SCCPs) have shown no increase in the incidence of malignant lymphoma in a carcinogenicity study of SCCPs. LCCPs are non-genotoxic and they are not expected to pose a carcinogenic hazard to humans.

No testing is needed for the PMN substances. Based on the LOAEL (100 mg/kg-bw) of the liver effects in female rats of repeated dose studies, Health Canada calculated a tolerable daily intake (TDI) of 71 µg/kg-bw/day. Using upper bounding intake estimates ranging from 0.007 µg/kg-bw/day for 60+ age group to 0.024 µg/kg-bw/day for 0.5 years age group, Environment Canada determined that the exposure levels are 10,000 and 3,000 times lower, respectively, than the TDI. Based on these evaluations, Health Canada concluded: "*LCCP are not harmful to human health as defined in the Canadian environmental Protection Act.*"

The National Research Council (NRC, 2000) reviewed the toxicological risks of selected flame retardant, including a LCCP containing C_{24} with 70 wt% Cl. Based on the NOAEL of 900 mg/kg-bw/day (liver toxicity), the NRC derived an RfD of 0.3 mg/kg-bw/day. Using this RfD and the worst case average daily exposure to be 0.16 mg/kg/day, NRC concluded: "*LCCP do not pose a noncancer risk when incorporated into residential furniture at the estimated application levels*." Further, it was concluded that: "*LCCP are not likely to be a human carcinogen and derivation of a cancer potency factor is unnecessary.*"

C-2-1 Metabolism

There is no information on inhalation absorption of LCCPs in humans or in animals. Based on their low vapor pressure and low water solubility, absorption following inhalation or dermal exposure is expected to be limited.

Oral (gavage) studies (IRDC, 1981; *cited in:* UK, 2009) showed that approximately 82-95% of a single dose of [8-^{14}C]-labeled C_{22-26} chlorinated paraffin (43% Cl) was recovered in the feces in rats during the seven-day collection period. Only 0.1-0.8% of the radiolabel was excreted in the urine. For C_{22-26} chlorinated paraffin (70 wt% Cl), it was found that 61-88% of the administrated radioactivity was recovered in the feces in rats during the seven-day collection period. Less than 0.1-1% was excreted in the urine.

C-2-2 Acute Toxicity

Acute toxicity studies have been conducted in rats, mice or dogs on five LCCPs: C_{20-30}, 41-50 wt% Cl; C_{22-26}, 42 wt% Cl, C_{23}, 43 wt% Cl; C_{20-30}, 61-70 wt% Cl; C_{24}, 70% Cl. The maximum dose levels used in these studies ranged from 4-50 g/kg-bw. No deaths were reported in any of the studies (IUCLID, 2003; *cited in:* UK, 2009).

C-2-3 Irritation and Sensitization

Skin irritation testing has been conducted on four LCCPs: C_{19}, 44 wt% Cl; C_{22-26}, 42 wt% Cl; C_{20-30}, 41-50 wt% Cl; C_{20-30}, 70 wt% Cl. No evidence of irritation was seen in three of the four LCCPs. For the C_{22-26}, 42 wt% Cl product, erythema was observed in two of six animals tested; the severity threshold was below the classification of the EU system (IUCLID, 2003; *cited in:* UK, 2009).

Evidence of slight eye irritation was seen in a test of a C_{22-26}, 42 wt% Cl product. However, the criteria for classification as an eye irritant were not met (IUCLID, 2003; *cited in:* UK, 2009).

In a maximization test and a Buehler test using guinea pig, a C_{22-26}, 42 wt% Cl product was negative (IUCLID, 2003; Bailey and Sheldon, 1998; *cited in:* UK, 2009). A C_{18-27}, 40 wt% Cl product was reported to elicit a positive response in the guinea pig maximization test (IUCLID, 2000; *cited in:* UK, 2009). However, no information is available on the quality of this study.

C-2-4 Repeated-dose Toxicity

LCCPs with C_{20-30}, 43 wt% Cl were dissolved in corn oil and given by gavage at 100, 900 or 3,750 mg/kg-bw/day to groups of 15 male and female Fisher 344 rats in a 14- and a 90-day studies (IRDC1981, 1984; cited in: Serront *et al*., 1987). There was a treatment-related effect on the liver of female rats at all dose levels, but no liver effects were seen in the males. Female liver weights were increased and a multifocal granulomatous hepatitis characterized by inflammatory changes and necrosis. Nephrosis was observed in the kidney of male rats and mineralization in the kidneys of female rats at 3,750 mg/kg-bw/day. Similar liver effects were observed in the high-dose (3,750 mg/kg-bw/day) rats of both sexes in a 90-day study on LCCPs with C_{22-26}, 70 wt% Cl (IRDC1981; cited in: Serront *et al*., 1987) and in a 90-day study as well as a 2-year bioassay on a LCCP with an average of C_{23}, 43 wt% Cl at 100 mg/kg-bw/day (NTP, 1986). Based on the liver toxicity, a LOAEL of 100 mg/kg-bw/day is established for the LCCPs with 43 wt% Cl and a NOAEL of 900 mg/kg-bw/day is identified for the LCCPs with 70 wt% Cl.

C-2-5 Genotoxicity

Both LCCPs of C_{22-26}, 43 wt% Cl and $C_{23,}$ 43 wt% Cl were negative in several *Salmonella* strains of the Ames test with or without metabolic activation (IUCLID, 2003; NTP, 1986; *cited in:* UK, 2009). LCCPs with C_{20-30} with 43 wt% Cl or C_{22-26} with 70 wt% Cl did not induce significant increases of chromosomal or chromatid aberrations in bone marrow cells of rats (IRDC1983; *cited in*: Serrone *et al*., 1987).

C-2-6 Carcinogenicity

The carcinogenicity of an LCCP ($C_{23,}$ 43 wt% Cl) was studied by administering the chemical in corn oil by gavage to groups of 50 F344/N rats and 50 B6C3F1 mice of each sex, 5 days per week for 103 weeks. Male rats received doses of 0, 1,875 or 3,750 mg/kg-bw/day; female rats received 0, 2,500 or 5,000 mg/kg-bw/day. An increased incidence of malignant lymphomas was reported for male mice given the LCCP; the incidences for the controls, low- and high dosed groups are 6/50, 12/50, and 16/50, respectively. However, mice are prone to the development of lymphomas with a range of tumor incidence of 2-73, and viruses may be the causative agent of lymphomas in laboratory strains of mice. It has been concluded that LCCPs of C_{20-30} with 43 wt% Cl did not produce clear evidence of carcinogenicity when tested in rats and mice (Serrone *et al*., 1987).

C-2-7 Developmental Reproductive Toxicity Review

In a prenatal developmental toxicity study in rats, no treatment-related effects were reported. **The NOAEL for both maternal and developmental toxicity was 5000 mg/kg-bw/day, the highest dose tested.**

In a prenatal developmental toxicity study in rabbits, the **LOAEL for maternal toxicity was 500 mg/kg-bw/day (the lowest dose tested) based on increased incidence of clinical signs. The NOAEL for developmental toxicity was $\geq$ 2000 mg/kg-bw/day, the highest dose tested.**

In a prenatal developmental toxicity study in rabbits, the **NOAEL for both maternal and developmental toxicity was 1000 mg/kg-bw/day, the highest dose tested.**

Basis for Conclusions

In a range-finding study (Study # 438-033, October 27, 1981; Chlorinated Paraffin Consortium), in pregnant Charles River COBS rats administered LCCP (22-26 carbons, 43 wt% Cl) *via* gavage at dose levels of 0, 3000, and 5000 mg/kg-bw/day on GD 6-19, the only effects reported occurred in dams and consisted of a slight increased incidence in anogenital matting during the latter portion of the treatment period at 5000 mg/kg-bw/day. No adverse treatment-related effects were reported in offspring at doses up to 5000 mg/kg-bw/day.

Based on the findings of the range-finding study, four groups of 25 pregnant Charles River COBS CD rats were administered LCCP (22-30 carbons, 70 wt% Cl) *via* gavage at doses of 0, 500, 2000, and 5000 mg/kg-bw/day on GD 6-19 (Study # 438-045, April 11, 1984; Chlorinated Paraffin Consortium). Unmated males and females were individually housed and acclimated for 15-days in an environmentally controlled room. At the end of the acclimation period, all animals were weighed and subjected to a detailed physical examination. One female and one male rat were placed together for mating. Confirmation of mating was based on evidence of a copulatory

plug. The day mating was confirmed was designated as day 0 of gestation. Test article was administered to pregnant females orally by gavage as a single daily dose on GD 6-19. During treatment, pregnant females were observed daily for mortality and clinical signs of toxicity. Any females not surviving to scheduled sacrifice were necropsied. Body weights were recorded on GD 0, 6, 9, 12, 16, and 20. All females were sacrificed on GD 20 and the uterus and ovaries excised for examination. The number and location of viable and nonviable fetuses, early and late resorptions, and the number of total implantations and corpora lutea were recorded. The uterus was weighed. The abdominal and thoracic cavities underwent gross examination. Maternal tissues were preserved for future histopathological analysis. Fetuses were weighed, sexed, tagged and examined for external malformations and variations, including the palate and the eyes. The fetuses underwent visceral and skeletal examinations for malformations and developmental variations.

No adverse treatment-related effects were reported in the dams or offspring at doses up to 5000 mg/kg-bw/day. The NOAEL for both maternal and developmental toxicity was 5000 mg/kg-bw/day, the highest dose tested.

In a range-finding study (Study # 438-018, October 27, 1981; Chlorinated Paraffin Consortium) in pregnant Dutch Belted rabbits administered LCCP (22-26 carbons, 43 wt% Cl) *via* gavage at doses of 0, 500, 1000, 2000, 3000, and 5000 mg/kg-bw/day on GD 6-27, a slight decrease in the amount of feces and a slight increase in matting and/or staining of the haircoat was reported in the dams at $\geq$ 3000 mg/kg-bw/day. No other effects were reported. Observations of offspring did not appear to be included.

Based on the results of the range-finding study, four groups of 16 Dutch Belted pregnant rabbits were administered LCCP (22-26 carbons, 43 wt% Cl) *via* gavage at doses of 0, 500, 2000, and 5000 mg/kg-bw/day on GD 6-27 (Study # 438-030, August 26, 1982; Chlorinated Paraffin Consortium). Unmated males and females were individually housed and acclimated for 9-weeks in an environmentally controlled room. As a result of a positive finding for parasites in stool samples collected during acclimation, all rabbits received sodium sulfamethazine in their drinking water for 19 days during the acclimation period. This treatment was terminated 5 weeks prior to study initiation and only rabbits testing negative for parasites were placed on study. At the end of the acclimation period, all animals were weighed and subjected to a detailed examination. Females were impregnated *via* artificial insemination. Immediately after insemination, ovulation was induced via an injection of chorionic gonadotropin in a marginal ear vein. Semen was collected from males of proven fertility and evaluated for motility. The day of artificial insemination was designated as day 0 of gestation. During treatment, pregnant females were observed for mortality and clinical signs of toxicity. Body weights were recorded on GD 0, 6, 12, 18, 24, and 28. Any females not surviving to scheduled sacrifice were necropsied. On GD 28, all surviving females were sacrificed and the uterus and ovaries excised for examination. The location and number of viable and nonviable fetuses, early and late resorptions, and the number of total implantations and corpora lutea were recorded. The uterus was weighed. The thoracic and abdominal cavities underwent gross examination. Pooled samples of abdominal adipose tissue from 3 dams were frozen for future analysis. Each fetus was sexed, weighed, and examined for external malformations and variations, including the palate and the eyes, as well as visceral and skeletal examinations for malformations and developmental variations, including examination of the brain and the heart.

A dose-related trend in an increased incidence in soft stool and/or anogenital matting or staining was observed in the dams beginning at the low-dose group. Three dams aborted and were

sacrificed during treatment; one in the mid-dose group, and two in the high-dose group. Increases in postimplantation loss and corresponding decreases in viable fetuses, and increases in late resorptions were reported at the high-dose group, however, these effects were not reported as being statistically significant. No signs of treatment-related developmental toxicity were reported in the offspring at $\leq$ 5000 mg/kg-bw/day, although the sample size in the high-dose group was limited, precluding any definitive conclusions. Therefore, the LOAEL for maternal toxicity was 500 mg/kg-bw/day (the lowest dose tested), based on increased incidence of clinical signs. The NOAEL for developmental toxicity was $\geq$ 2000 mg/kg-bw/day.

In a range-finding study (Study # 438-038, November 1, 1982; Chlorinated Paraffin Consortium) in pregnant Dutch Belted rabbits administered LCCP (22-30 carbons, 70 wt% Cl) *via* gavage at doses of 0, 2000, 3750, and 5000 mg/kg-bw/day on GD 6-27, increases in abortions, reductions in maternal body weight, and increases in post-implantation losses were reported at $\geq$ 2000 mg/kg-bw/day. Therefore, a second range-finding study was conducted at dose levels of 0, 50, 200, and 1000 mg/kg-bw/day (Study # 438-040, November 4, 1982; Chlorinated Paraffin Consortium). A slight decrease in viable fetuses and a slight increase in postimplantation loss were reported at 1000 mg/kg-bw/day. No other effects were reported.

Based on the results of the range-finding studies, four groups of 16 Dutch Belted pregnant rabbits were administered LCCP (22-30 carbons, 70 wt% Cl) *via* gavage at doses of 0, 100, 300, and 1000 mg/kg-bw/day on GD 6-27 (Study # 438-039, July 18, 1983; Chlorinated Paraffin Consortium). Unmated males and females were individually housed and acclimated for 40-days in an environmentally controlled room. At the end of the acclimation period, all animals were weighed and subjected to a detailed examination. Females were impregnated via artificial insemination. Immediately after insemination, ovulation was induced *via* an injection of chorionic gonadotropin in a marginal ear vein. Semen was collected from males of proven fertility and evaluated for motility. The day of artificial insemination was designated as day 0 of gestation. During treatment, pregnant females were observed for mortality and clinical signs of toxicity. Body weights were recorded on GD 0, 6, 12, 18, 24, and 28. Any females not surviving to scheduled sacrifice were necropsied. On GD 28, all surviving females were sacrificed and the uterus and ovaries excised for examination. The location and number of viable and nonviable fetuses, early and late resorptions, and the number of total implantations and corpora lutea were recorded. The uterus was weighed. The thoracic and abdominal cavities underwent gross examination. Pooled samples of abdominal adipose tissue from 3 dams were frozen for future analysis. Each fetus was sexed, weighed, and examined for external malformations and variations, including the palate and the eyes, as well as visceral and skeletal examinations for malformations and developmental variations, including examination of the brain and the heart.

No treatment-related adverse effects were observed in the dams or the offspring at any dose level. The increases in postimplantation losses noted in the two previous range-finding studies reported above were not reproduced in the definitive study. Therefore, the NOAEL for both maternal and developmental toxicity was 1000 mg/kg-bw/day, the highest dose tested.

Appendix D ENVIRONMENTAL MONITORING

D-1 MCCP MONITORING DATA

D-1-1 Surface Water

It is known that over time, based on their molecular weight and physicochemical properties, MCCPs in surface water will partition to suspended particulates, sediment, sludge, or soil. Reported MCCP concentrations in surface water range from $< 2.50 \times 10^{-10}$ to 1.49×10^{-3} mg/L (Table_Apx D-1-1). Very little information is available on the specific sampling locations for many of the surface water measurements reported in Table_Apx D-1-1. Limited documentation is available on two of the studies (Petersen et al., 2006 and Muir, 2003). Two sources provide a review of the literature with very little details (IPCS, 1996 and EC, 2008b). Two studies do provide detailed information on the sampling approach, including location (Houde et al., 2008 and USEPA, 1988). The Petersen et al. (2006) study, which had the highest published concentration, reported results for water samples collected from different Norwegian locations. EPA/OPPT assumes that these samples were collected in non-marine waters. Three studies found were not used in this assessment (BUA, 1992; Hoechst, 1987; and Willis, 1994). However, all of the studies used in the assessment use modern analytical techniques, reference the specific CPs of interest, and provide, at a minimum, general information on the sampling location. Given the paucity of surface water data available, EPA/OPPT used measurements from the selected studies and used the minimum and maximum values in this assessment.

Measurements of dissolved (filtered) concentrations were generally non-detectable (ND) with few exceptions. Concentrations measured in surface water were largely from studies that measured total water concentrations which included MCCPs sorbed to particulates. More recent monitoring studies (Table_Apx D-1-1) have focused on measuring MCCPs in suspended solids, sediment pore water, and sediment.

Early analytical methods using thin layer chromatography (TLC) were used to measure CPs in surface water. However, this method has poor sensitivity and reproducibility, and provide false negative results. Current methods of quantification using gas or liquid chromatography coupled with a range of detectors (*i.e.*, mass spectrometry; MS) are more reliable. Nearly all of the water concentrations were measurements taken at a single point in time (*i.e.*, the samples were not time series samples). Absent more extensive monitoring data, EPA/OPPT assumed that the available data could be extrapolated to longer time periods for determination of a chronic exposure concentration.

MCCP concentrations in surface water, reported in Table_Apx D-1-1, rely on test methods that filtered or pre-filtered samples before they were analyzed, which can underestimate environmental concentrations. Where appropriate, reported values were converted to a common unit, as presented in the table. For the purposes of this assessment, in the studies considered acceptable, EPA/OPPT used the lowest and highest reported concentrations ($< 2.50 \times 10^{-10}$ to 1.49×10^{-3} mg/L; Table_Apx D-1-1) to evaluate risks of potential concern to aquatic organisms.

Table_Apx D-1-1: Surface Water Concentrations of MCCPs, Sorted by Country

Media	Country	Location City, State or Province	Comments	Converted Concentration	Common Units	Analytical Method	References
Surface Water	Canada	Lake Ontario	Maximum	2.60×10^{-9}	mg/L	NR	EC (2008b)
			<	2.50×10^{-10}	mg/L	GC-HRMS-MAB	Houde et al. (2008)
			<	1.00×10^{-8}	mg/L	GC-ECNI-MS	Muir et al. (2003)
			Maximum	4.70×10^{-8}	mg/L	GC-HRMS-MAB	Houde et al. (2008)
			Mean	9.00×10^{-10}	mg/L	GC-HRMS-MAB	Houde et al. (2008)
	Germany	River Lech at Langsweid	---	1.90×10^{-4}	mg/L	NR	IPCS (1996)
		River Lech at Rain	---	1.70×10^{-4}	mg/L	NR	IPCS (1996)
		River Lech at Gersthofen	---	9.00×10^{-5}	mg/L	NR	IPCS (1996)
		River Lech at Augsburg	<	2.50×10^{-5}	mg/L	NR	IPCS (1996)
		River Danube at Marxheim	---	7.00×10^{-5}	mg/L	NR	IPCS (1996)
			<	3.00×10^{-5}	mg/L	NR	IPCS (1996)
	Norway	NR	---	1.49×10^{-3}	mg/L	GC-ECNI-MS	Petersen et al. (2006)
	United Kingdom	Multiple locations	<	1×10^{-4}	mg/L	GC-ECNI-MS	Nicholls et al. (2001)
	United States	Sugar Creek, Ohio	<	7.50×10^{-5}	mg/L	GC-ECNI-MS	USEPA (1988)
	Central European Country	NR	<	5.00×10^{-5}	mg/L	GC-ECNI-MS	Coelhan (2010)

NR: Not recorded. Location description was not provided in the study.
--: Single sample value reported above the detection limit; therefore, no data qualifier required.
GC-HRMS-MAB: Gas chromatography-high resolution mass spectrometry with metastable atom bombardment ionization
GC-ECNI-MS: Gas chromatography in combination with electron capture negative ion mass spectrometry
Notes:
1. All values provided in the table above represent total MCCP and not individual MCCP isomers
2. In some cases, the minimum values in the table are preceded by "<". This indicates that the value reported in article was reported as a non-detect. In such cases, one half of the lowest reported detection limit was compiled as the 'minimum' reported monitoring data
3. All concentrations measured from impoundment lagoons and drainage ditches from the USEPA (1988) study have not been included as they are not considered as surface water concentrations
4. All concentrations measured from suspended solid matter fraction from influents from the Coelhan (2010) study have not been included as they are not considered as surface water concentrations

D-1-2 Sediment

MCCP sediment concentrations from marine and non-marine environments ranged from 5.00×10^{-3} to 1.64×10^{1} mg/kg dw and from 2.0×10^{-3} to 6.51×10^{1} mg/kg dw, respectively.

For the purposes of this assessment, in the studies considered acceptable, EPA/OPPT used the lowest and highest reported marine and non-marine sediment concentrations (5.00×10^{-3} to 1.64×10^{1} mg/kg dw and 2.00×10^{-3} to 6.51×10^{1} mg/kg dw, respectively) to evaluate risks of potential concern to sediment organisms (Table_Apx D-1-2). Where appropriate, reported values were converted to a common unit, as presented in the table.

Table_Apx D-1-2: Sediment Concentrations of MCCPs, Sorted by Country

Media	Country	Location	Comments	Converted Concentration	Common Units	References
		City, State or Province				
Sediment (Marine)	Australia	NR	---	1.11	mg/kg dw	Kemmlein et al. (2002)
			---	1.17	mg/kg dw	Kemmlein et al. (2002)
			---	3.11	mg/kg dw	Kemmlein et al. (2002)
			---	1.64×10^{1}	mg/kg dw	Kemmlein et al. (2002)
	Canada	Hamilton Harbour (Windemere basin)	---	2.90×10^{-1}	mg/kg*	Muir et al. (2000)
	Germany	German Bight, North Sea	---	5.00×10^{-3}	mg/kg dw	Hüttig et al. (2004)
			---	9.00×10^{-3}	mg/kg dw	Hüttig et al. (2004)
			---	9.00×10^{-3}	mg/kg dw	Hüttig et al. (2004)
			---	1.30×10^{-2}	mg/kg dw	Hüttig et al. (2004)
			---	2.80×10^{-2}	mg/kg dw	Hüttig et al. (2004)
			---	1.46×10^{-1}	mg/kg dw	Hüttig et al. (2004)
		Baltic Sea	---	9.30×10^{-2}	mg/kg dw	Hüttig et al. (2004)
			---	1.15×10^{-1}	mg/kg dw	Hüttig et al. (2004)
			---	1.22×10^{-1}	mg/kg dw	Hüttig et al. (2004)
			---	2.11×10^{-1}	mg/kg dw	Hüttig et al. (2004)
			---	4.99×10^{-1}	mg/kg dw	Hüttig et al. (2004)
		North and Baltic Sea	---	2.20×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)

Media	Country	Location	Comments	Converted Concentration	Common Units	References
		City, State or Province				
			---	2.30×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	3.30×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	3.40×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	3.70×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	3.90×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	4.30×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	4.30×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	4.80×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	5.40×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	5.80×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	6.10×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	7.20×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	7.60×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	7.70×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	8.10×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	8.50×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	8.70×10^{-2}	mg/kg dw	Hüttig and Oehme (2006)
			---	1.49×10^{-1}	mg/kg dw	Hüttig and Oehme (2006)

Media	Country	Location	Comments	Converted Concentration	Common Units	References
		City, State or Province				
			---	1.49×10^{-1}	mg/kg dw	Hüttig and Oehme (2006)
			---	1.49×10^{-1}	mg/kg dw	Hüttig and Oehme (2006)
			---	2.75×10^{-1}	mg/kg dw	Hüttig and Oehme (2006)
			---	9.10×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
			---	4.80×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
			---	1.98×10^{-1}	mg/kg dw	Hüttig and Oehme (2005)
			---	1.31×10^{-1}	mg/kg dw	Hüttig and Oehme (2005)
			---	1.32×10^{-1}	mg/kg dw	Hüttig and Oehme (2005)
			---	3.03×10^{-1}	mg/kg dw	Hüttig and Oehme (2005)
			---	1.53×10^{-1}	mg/kg dw	Hüttig and Oehme (2005)
			---	1.14×10^{-1}	mg/kg dw	Hüttig and Oehme (2005)
			---	4.00×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
			---	2.70×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
			---	1.80×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
			---	1.90×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
			---	3.00×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
			---	3.20×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
			---	1.80×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)

Media	Country	Location	Comments	Converted Concentration	Common Units	References
		City, State or Province				
			---	2.40×10^{-2}	mg/kg dw	Hüttig and Oehme (2005)
Sediment (Non-marine)	Canada	Lake Erie	---	6.80×10^{-2}	mg/kg dw	Tomy and Stern (1999)
		Lake St Francis	Minimum	7.50×10^{-1}	mg/kg dw	EC (2008b)
			Maximum	1.2	mg/kg dw	EC (2008b)
	Czech Republic	NR	Minimum	2.00×10^{-3}	mg/kg*	Pribylova et al. (2006)
		Labe	Sum	1.80×10^{-2}	mg/kg dw	Pribylova et al. (2006)
			Sum	7.30×10^{-2}	mg/kg dw	Pribylova et al. (2006)
		Libis-Labe	Sum	1.6	mg/kg dw	Pribylova et al. (2006)
		Bilina	Sum	3.10×10^{-2}	mg/kg dw	Pribylova et al. (2006)
		Mala Becva	Sum	1.13×10^{-1}	mg/kg dw	Pribylova et al. (2006)
		Becva	Sum	1.20×10^{-1}	mg/kg dw	Pribylova et al. (2006)
		Morava	Sum	1.93×10^{-1}	mg/kg dw	Pribylova et al. (2006)
		Ohre	Sum	3.08×10^{-1}	mg/kg dw	Pribylova et al. (2006)
			Sum	6.00×10^{-1}	mg/kg dw	Pribylova et al. (2006)
			Sum	5.58	mg/kg dw	Pribylova et al. (2006)
		Morava	Sum	4.16×10^{-1}	mg/kg dw	Pribylova et al. (2006)
		Dyje	Sum	7.57×10^{-1}	mg/kg dw	Pribylova et al. (2006)
		Drevnice	Sum	8.93×10^{-1}	mg/kg dw	Pribylova et al. (2006)
	Germany	Bodensee (middle)	<	5.00×10^{-3}	mg/kg dw	IPCS (1996)

Media	Country	Location	Comments	Converted Concentration	Common Units	References
		City, State or Province				
			---	7.00×10^{-2}	mg/kg dw	IPCS (1996)
		River Lech	<	5.00×10^{-3}	mg/kg dw	IPCS (1996)
			---	3.25×10^{-1}	mg/kg dw	IPCS (1996)
			Maximum	7.00×10^{-1}	mg/kg*	Tomy et al. (1998)
		River Rhine	---	6.00×10^{-2}	mg/kg dw	IPCS (1996)
			---	8.50×10^{-2}	mg/kg dw	IPCS (1996)
			---	1.40×10^{-1}	mg/kg dw	IPCS (1996)
			Minimum	1.45×10^{-1}	mg/kg dw	IPCS (1996)
			Maximum	2.05×10^{-1}	mg/kg dw	IPCS (1996)
		River Elbe at Hamburg	Minimum	1.30×10^{-1}	mg/kg dw	IPCS (1996)
			Maximum	2.30×10^{-1}	mg/kg dw	IPCS (1996)
		River Main	Minimum	1.60×10^{-1}	mg/kg dw	IPCS (1996)
			Maximum	2.60×10^{-1}	mg/kg dw	IPCS (1996)
		Outer Alster, Hamburg	---	3.70×10^{-1}	mg/kg dw	IPCS (1996)
	Norway	NR	minimum	5.00×10^{-2}	mg/kg dw	Petersen et al. (2006)
			maximum	3.24	mg/kg dw	Petersen et al. (2006)
			---	2.7	mg/kg ww	Borgen et al. (2003)
			---	1.14×10^{1}	mg/kg ww	Borgen et al. (2003)
	South China	Pearl River Delta	Minimum	8.80×10^{-1}	mg/kg dw	Chen et al. (2011)
			Minimum	1.1	mg/kg dw	Chen et al. (2011)
			Minimum	1.4	mg/kg dw	Chen et al. (2011)
			Maximum	1.4	mg/kg dw	Chen et al. (2011)
			Maximum	3.8	mg/kg dw	Chen et al. (2011)
			Mean	3.9	mg/kg dw	Chen et al. (2011)
			Mean	2.10×10^{1}	mg/kg dw	Chen et al. (2011)
			Maximum	3.80×10^{1}	mg/kg dw	Chen et al. (2011)

Media	Country	Location	Comments	Converted Concentration	Common Units	References
		City, State or Province				
	Switzerland	Lake Thun	Minimum	5.00×10^{-3}	mg/kg dw	Iozza et al. (2008)
			Maximum	2.60×10^{-2}	mg/kg dw	Iozza et al. (2008)
		Lake Zurich	Maximum	5.00×10^{-3}	mg/kg*	Tomy et al. (1998)
	United Kingdom	NR	<	1.00×10^{-1}	mg/kg dw	Nicholls et al. (2001)
		South West Region: Grand Union Canal	---	3.00×10^{-1}	mg/kg dw	Nicholls et al. (2001)
			---	2.7	mg/kg dw	Nicholls et al. (2001)
			---	2.8	mg/kg dw	Nicholls et al. (2001)
		South West Region; Bristol Avon River	---	5.00×10^{-1}	mg/kg dw	Nicholls et al. (2001)
			---	6.00×10^{-1}	mg/kg dw	Nicholls et al. (2001)
			---	8.00×10^{-1}	mg/kg dw	Nicholls et al. (2001)
		North East Region: Hull River	---	1.0	mg/kg dw	Nicholls et al. (2001)
			---	1.35×10^{1}	mg/kg dw	Nicholls et al. (2001)
			---	1.1	mg/kg dw	Nicholls et al. (2001)
		South West Region: Colne River	---	1.4	mg/kg dw	Nicholls et al. (2001)
			---	2.0	mg/kg dw	Nicholls et al. (2001)
		West Midlands Region: Trent River	---	3.8	mg/kg dw	Nicholls et al. (2001)
			---	6.02×10^{1}	mg/kg dw	Nicholls et al. (2001)
			---	6.51×10^{1}	mg/kg dw	Nicholls et al. (2001)
		North West Region: Hornsmill brook	---	5.6	mg/kg dw	Nicholls et al. (2001)

Media	Country	Location	Comments	Converted Concentration	Common Units	References
		City, State or Province				
			---	1.25×10^{1}	mg/kg dw	Nicholls et al. (2001)
			---	1.83×10^{1}	mg/kg dw	Nicholls et al. (2001)
		North East Region: Hull River	---	1.0	mg/kg dw	Nicholls et al. (2001)
			---	1.1	mg/kg dw	Nicholls et al. (2001)
			---	1.35×10^{1}	mg/kg dw	Nicholls et al. (2001)
		East Midlands Region: Idle River	---	1.62×10^{1}	mg/kg dw	Nicholls et al. (2001)
			---	4.39×10^{1}	mg/kg dw	Nicholls et al. (2001)
		Northumberland Region: Skerne River	---	1.80×10^{1}	mg/kg dw	Nicholls et al. (2001)
			---	2.56×10^{1}	mg/kg dw	Nicholls et al. (2001)
			---	5.84×10^{1}	mg/kg dw	Nicholls et al. (2001)
		East Anglia Region: Lark River	---	3.22×10^{1}	mg/kg dw	Nicholls et al. (2001)
			---	4.50×10^{1}	mg/kg dw	Nicholls et al. (2001)
			---	6.04×10^{1}	mg/kg dw	Nicholls et al. (2001)
	United States	Detroit River	---	6.80×10^{-2}	mg/kg dw	Tomy et al. (1999)
		Sugar Creek, Ohio	Reported as trace with range of 1.5-5; used the average	3.25×10^{-3}	mg/kg dw	USEPA (1988)
			Reported as trace with range of 1.5-5; used the average	3.25×10^{-3}	mg/kg dw	USEPA (1988)

Media	Country	Location	Comments	Converted Concentration	Common Units	References
		City, State or Province				
			---	6.80×10^{-3}	mg/kg dw	USEPA (1988)
			---	8.20×10^{-3}	mg/kg dw	USEPA (1988)
			---	7.60×10^{-1}	mg/kg dw	USEPA (1988)
			---	2.10×10^{1}	mg/kg dw	USEPA (1988)
			---	3.40×10^{1}	mg/kg dw	USEPA (1988)
			---	5.00×10^{1}	mg/kg dw	USEPA (1988)

Note:
NR: Not recorded. Location description was not provided in the study.
--: Single sample value reported above the detection limit; therefore, no data qualifier required.
1. All values provided in the table above represent total MCCP and not individual MCCP isomers
2. In some cases, the minimum values in the table are preceded by "<". This indicates that the value reported in article was reported as a non-detect. In such cases, one half of the lowest reported detection limit was compiled as the 'minimum' reported monitoring data
3. dw – dry weight and ww – wet weight

D-1-3 Biosolids and Soil

CPs are detected more frequently and at higher concentrations in treated sewage sludge (*i.e.*, biosolids) than in soil. MCCP concentrations ranged from 5.00×10^{-5} to 9.70×10^{3} mg/kg dw in sludge and from 1.5×10^{-2} to 8.5×10^{-2} mg/kg dw in soil. It is unclear if the difference in MCCP concentrations in sludge and soil is related to the smaller sample sizes for these media compared to the typically larger data sets available for water and sediment. To determine the most reliable studies for its consideration, EPA/OPPT used the following criteria: designation of specific MCCP chain length and the appropriate analytical methodology. Based these criteria, EPA/OPPT determined that the data reported by Stevens et al. (2003) were the most reliable for its use in this assessment: data are summarized below.

Stevens et al. (2003) measured MCCP concentrations in sludge samples obtained from 14 WWTPs in the UK. MCCP concentrations ranged from 3.00×10^{1} to 9.70×10^{3} mg/kg dw. The authors concluded that these very high concentrations were likely the result of releases from numerous and ongoing diffuse sources. EPA/OPPT did not use information from other published studies reporting measured CPs in sludge and soil because they did not distinguish the CPs measured (Nicholls et al., 2001). These studies reported total CP concentrations at much lower levels ranging from 3.00×10^{-5} to 2.3 mg/kg dw.

Although risk to terrestrial species was not calculated, EPA/OPPT notes that the lowest and highest reported biosolid and soil concentrations (5.00×10^{-5} to 9.70×10^{3} mg/kg dw and 1.5×10^{-2} to 8.5×10^{-2} mg/kg dw, respectively) represents a very large range (up to eight orders of magnitude (Table_Apx D-1-3).

Table_Apx D-1-3: Biosolid and Soil Concentrations of MCCPs

Location	Media	Concentration		Units	References
		Minimum	Maximum		
Switzerland	Soil	1.5×10^{-2}	8.5×10^{-2}	mg/kg dw	Iozza (2010)
China	Soil	2.1×10^{-6}	1.53×10^{-3}	mg/kg dw	Wang et al. (2013)
Czech Republic	Sewage Sludge	7.36×10^{-1}	2.30	mg/kg dw	Pribylova et al. (2006)
United Kingdom	Sewage Sludge	3.00×10^{1}	9.70×10^{3}	mg/kg dw	Stevens et al. (2003)
United States	Sewage Sludge	5.00×10^{-5}	5.00×10^{-5}	mg/kg dw	Pribylova et al. (2006)

D-1-4 Biota

EPA/OPPT reviewed available published literature and summarized MCCP concentrations in tissues of aquatic and terrestrial biota (Table_Apx D-1-4). Measured tissue concentrations for aquatic biota ranged from ND to 2.63 mg/kg ww (*i.e.*, beluga whales, seals, rainbow trout, carp, mackerel, arctic char, mussels, crustaceans, and plankton) and ranged from 5.00×10^{-3} to 3.70×10^{-1} mg/kg ww in terrestrial biota. The concentrations measured in the terrestrial studies did not designate the specific CP congeners measured.

As a result of EPA/OPPT's evaluation, MCCPs were found in organisms across many different trophic levels indicating widespread environmental contamination (Table_Apx D-1-4). The data were insufficient for EPA/OPPT to draw conclusions about trends based on region, species, time, or other factors.

While EPA/OPPT determined the concentrations of MCCPs in aquatic and terrestrial biota range from ND to 2.63 mg/kg ww from 5.00×10^{-3} to 3.70×10^{-1} mg/kg ww, respectively, in this assessment, EPA/OPPT did not use tissue concentrations to determine risks of potential concern for biota Table_Apx D-1-4. Rather, it used the risk quotient (RQ) method as described in Section 6.

Table_Apx D-1-4: Biota Concentrations of MCCPs

Location	Media Description	Minimum	Units	Min Reference	Maximum	Units	Max Reference
Aquatic Biota							
Australia	Invertebrates	2.32×10^{-5}	mg/kg lw	Kemmlein et al. (2002)	3.05×10^{-5}	mg/kg lw	Kemmlein et al. (2002)
Canada	Mammals	5.45×10^{-7}	mg/kg ww	Bennie et al. (2000)	8.00×10^{-5}	mg/kg ww	Bennie et al. (2000)
	Fish	2.57×10^{-7}	mg/kg ww	Bennie et al. (2000)	2.63	mg/kg ww	Muir et al. (2000)
	Invertebrates	ND[1]	mg/kg ww	EC (1993)	ND[1]	mg/kg ww	EC (1993)
	Total	ND[1]	mg/kg ww	EC (1993)	2.63	mg/kg ww	Muir et al. (2000)
Europe	Fish	7.00×10^{-3}	mg/kg ww	Reth et al. (2006)	4.70×10^{-2}	mg/kg ww	Reth et al. (2006)
North Sea/Baltic Sea Region[2]	Fish	ND[3]	mg/kg ww	IVL (2009)	2.6×10^{-1}	mg/kg ww	Reth et al. (2005)
United States	Fish	2.90×10^{-3}	mg/kg ww	Tomy and Stern (1999)	9.04×10^{-1}	mg/kg ww	Tomy and Stern (1999)
	Invertebrates	3.50×10^{-3}	mg/kg ww	USEPA (1988)	1.70×10^{-1}	mg/kg ww	USEPA (1988)
	Total	2.90×10^{-3}	mg/kg ww	Tomy and Stern (1999)	9.04×10^{-1}	mg/kg ww	Tomy and Stern (1999)
United States / Canada - Great Lakes	Fish	1.80×10^{-3}	mg/kg ww	Muir et al. (2003)	1.10×10^{-1}	mg/kg ww	Muir et al. (2003)
	Invertebrates	2.40×10^{-3}	mg/kg ww	EC (2008a)	1.60×10^{-2}	mg/kg ww	Muir et al. (2003)
	Total	1.80×10^{-3}	mg/kg ww	Muir et al. (2003)	1.10×10^{-1}	mg/kg ww.	Muir et al. (2003)
Terrestrial Biota							
Europe	Birds	5.00×10^{-3}	mg/kg ww	Reth et al. (2006)	3.70×10^{-1}	mg/kg ww	Reth et al. (2006)

Notes:
Summary values represent total MCCP and not individual MCCP isomers.
[1] MCCPs were not detected in Invertebrates from Canada. Detection limit = 4.0×10^{-7} mg/kg; ½ DL = 2.0×10^{-7} (EC, 1993).
[2] North Sea/Baltic Sea Region includes the following countries: Estonia, Latvia, Lithuania, Norway, Poland, and Sweden.
[3] The minimum MCCP concentration value for fish from the North Sea/Baltic Sea Region was non-detect. The detection limit = 2.5×10^{-4} mg/kg; ½ DL = 1.25×10^{-4} (IVL 2009)

D-2 LCCP MONITORING DATA

Kemmlein et al. (2002) optimized and tested the carbon skeleton reaction gas chromatography analytical method to analyze environmental samples for CPs. The optimized method was used for marine sediments, mussels and crabs taken from an area influenced by a CP manufacturer in Yarraville, Australia. LCCP (C_{18-20}) concentrations in marine sediment ranged from 1.02×10^{-1} to 4.31×10^{-1} mg/kg dw (Table_Apx D-2-1), those in mussels ranged from 4×10^{-1} to 1.9 mg/kg lw, and those in crab ranged from 3×10^{-2} to 4.4 mg/kg lw. The results presented in this paper show that bioaccumulation is evident. The mussel samples contained approximately two times and crab tissue around six times the concentration of CPs found in the most contaminated sediment sample. No other adequate studies were found to characterize LCCP concentrations in surface water, fresh water sediment or soil.

Table_Apx D-2-1: Marine Sediment Concentrations of LCCPs

Media	Country	Location	Comments	Concentration	Units	References
		City, State or Province				
Sediment (Marine)	Australia	NR	Sum	1.02×10^{-1}	mg/kg dw	Kemmlein et al. (2002)
			Sum	1.28×10^{-1}	mg/kg dw	Kemmlein et al. (2002)
			Sum	3.04×10^{-1}	mg/kg dw	Kemmlein et al. (2002)
			Sum	4.31×10^{-1}	mg/kg dw	Kemmlein et al. (2002)

Notes:
1. Values provided in the table above represent total LCCP (C_{18-20}) and not individual isomers.
2. dw – dry weight

Table_Apx D-2-2: Biota Concentrations of LCCPs

Media	Country	Location	Minimum	Maximum	Units	References
		City, State or Province				
Aquatic Biota	Australia	NR	2.89×10^{-6}	6.90×10^{-6}	mg/kg lw	Kemmlein et al. (2002)

Notes:
1. Minimum and Maximum concentrations provided in the table above represent total LCCP (C_{18-20}) and not individual isomers.
2. lw – lipid weight

Appendix E ENGINEERING (ChemSTEER) REPORTS ON P-12-0-0433 and P-12-0453

(Used for both identifying potential releases to the environment and for estimated occupational exposures. SEE APPENDIX G FOR REFERENCE TO FULL REPORTS UNDER SEPARATE COVER)

P-12-0433

Scenario	# Sites	# Workers
PROC: Formulation of Metalworking Fluids	3	24

Exposure		mg/day	day/yr
Inhalation -	negligible (VP < 0.001 torr)		
Dermal - Liquid	High End	1.8E+3	27
Dermal - Liquid	High End	3.5E+2	27
Release		**kg/site/day**	**day/yr**
Water or Incineration or Landfill	High End	8.6E+0	27
Water or Incineration or Landfill	Conservative	5.7E+0	27
Air	Suggested Estimate	5.7E-1	27
Incineration or Landfill	Suggested Estimate	5.7E+0	27

Scenario	# Sites	# Workers
USE: Use of Metalworking Fluids	4	192

Exposure		mg/day	day/yr
Inhalation - Mist	High End of Range / Typical	7.1E+0 / 2.0E+0	247
Dermal - Liquid	High End	3.5E+2	247
Dermal - Mist	/	/ 3.9E+3	247
Release		**kg/site/day**	**day/yr**
Water	Output 2	2.5E+0	247
Water or Incineration or Landfill	High End	1.2E+0	139
Water or Incineration or Landfill	Output 2	8.2E+0	247
Water or Incineration or Landfill	Output 2	1.0E+1	247
Air	Output 2	1.1E+0	247

Scenario	# Sites	# Workers
PROC2: PVC Compounding (16.8% of PV)	8	192

Exposure		mg/day	day/yr
Inhalation - Particulate	High End of Range / Low End of Range	4.4E+0 / 3.0E-2	126
Dermal - Liquid	High End	1.8E+3	126
Release		**kg/site/day**	**day/yr**
Water	Output 2	4.3E-3	126
Water or Incineration	Output 1	8.5E+0	126
Water or Incineration or Landfill	Output 1	1.3E+1	126
Water or Incineration or Landfill	Suggested Value	4.3E-2	126
Air	Output 2	4.3E-3	126

Scenario	# Sites	# Workers
USE2: PVC Converting (16.8% of PV)	8	384

Exposure		mg/day	day/yr
Inhalation - Particulate	OSHA PEL / EU Data from Submitter	2.2E+1 / 1.2E+1	250
Dermal -	PMN will be encapsulated in plastic pellets during handling of plastic raw material. While some surface contact may occur, dermal exposure to solids in this form are non-quantifiable (2004 ESD; Cast Solids, CEB Method for Screening-Level Assessments of Dermal Exposure).		
Release		**kg/site/day**	**day/yr**
Water	Suggested Estimate	1.6E-1	250
Water or Incineration or Landfill	Suggested Estimate	2.1E-2	250
Water or Incineration or Landfill	Output 2	2.1E+0	250
Water or Incineration or Landfill	Conservative	4.3E+0	250
Water or Landfill	Suggested Estimate	5.3E+0	250
Air	Suggested Estimate	1.6E-1	250
Air	Output 2	2.4E-2	250
Landfill	Output 2	2.4E+0	250

Scenario	# Sites	# Workers
PROC1: Formulation of Metalworking Fluids (73.8% of PV)	59	472

Exposure		mg/day	day/yr
Inhalation -	negligible (VP < 0.001 torr)		
Dermal - Liquid	High End	1.8E+3	84
Dermal - Liquid	High End	3.5E+2	84
Release		**kg/site/day**	**day/yr**
Water or Incineration or Landfill	High End	1.1E+1	84
Water or Incineration or Landfill	Conservative	7.6E+0	84
Air	Suggested Estimate	1.9E-1	84
Incineration or Landfill	Suggested Estimate	7.6E+0	84

Scenario	# Sites	# Workers
USE1: Use of Metalworking Fluids (73.8% of PV)	207	9936

Exposure		mg/day	day/yr
Inhalation - Mist	High End of Range / Typical	7.1E+0 / 2.0E+0	247
Dermal - Liquid	High End	3.5E+2	247
Dermal - Mist	/	/ 3.9E+3	247
Release		**kg/site/day**	**day/yr**
Water	Output 2	3.9E+0	247
Water or Incineration or Landfill	High End	1.2E+0	218
Water or Incineration or Landfill	Output 2	1.3E+1	247
Water or Incineration or Landfill	Output 2	1.6E+1	247
Air	Output 2	1.8E+0	247

Scenario	# Sites	# Workers
PROC3: Formulation of Adhesives and Sealants (9.4% of PV)	3	66

Exposure		mg/day	day/yr
Inhalation -	negligible (VP < 0.001 torr)		
Dermal - Liquid	High End	1.8E+3	200
Dermal - Liquid	High End	5.3E+2	200
Release		**kg/site/day**	**day/yr**
Water or Incineration or Landfill	High End	1.2E+1	200
Water or Incineration or Landfill	Output 2	8.0E+0	200
Water or Incineration or Landfill	Output 2	2.0E+2	4

Scenario		# Sites	# Workers
USE3: Use of Adhesives and Sealants (9.4% of PV)		58	2784
Exposure		**mg/day**	**day/yr**
Inhalation - Mist	What-If	2.3E+1	250
Dermal - Liquid	High End	5.3E+2	250
Release		**kg/site/day**	**day/yr**
Water or Incineration or Landfill	High End	1.9E+0	66
Water or Incineration or Landfill	Conservative	3.3E-1	250
Air	Output 2	1.2E+0	250
Landfill	Output 2	1.1E+1	250

Appendix F EXPOSURE SCENARIO ESTIMATES

(E-FAST Model Run. SEE APPENDIX G FOR REFERENCE TO FULL REPORTS UNDER SEPARATE COVER)

INEOS: P12-0433 Exposure 1

Exposure Scenario[1]			Water				Landfill	Stack Air		Fugitive Air	
Drinking Water			Fish Ingestion								
ADR		LADD	ADR	LADD	7Q10[4] COC = 1	PDM Days Exceeded	LADD	ADR	LADD	ADR	LADD
Release activity(ies)[2]; exposure calculation(s)[3]	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	µg/l	# Days	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day
Proc: Max ADR, PDM, LADD	**8.99E-03**	**2.08E-05**	**6.49E-02**	**8.93E-05**	**184.28**	**27**	**1.12E-04**	---	---	**1.43E-02**	**3.39E-05**
USE: Max ADR, PDM1	**3.90E-02**	---	**0.17**	---	**829.55**	**139**	---	---	---	**2.76E-02**	---
USE: PDM2	---	---	---	---	**784.09**	**247**	---	---	---	---	---
USE: Max LADD	---	**4.75E-04**	---	**2.04E-03**	---	---	**9.71E-04**	---	**1.26E-03**	---	**5.99E-04**

[1]Exposure scenario titles consist of release activity followed by exposure calculation abbreviation.
[2]Release activities are from engineering report's Manufacturing (Mfg), Processing (Proc) and Use release activity labels. Multiple release activities are combined in one exposure scenario if their releases occur at same location.
[3]Exposure calculations are Acute Dose Rate (ADR), Lifetime Average Daily Dose (LADD), and Probabilistic Dilution Model (PDM). There may be one, two, or all three exposure calculations per exposure scenario. COC is the aquatic concentration of concern.
[4]This column displays concentration values for the 7Q10 streamflow, which is defined as the average streamflow of the 7 consecutive days of lowest flow within a 10 year period.

INEOS: P12-0453 Exposure 1

Exposure Scenario[1]			Water				Landfill	Stack Air		Fugitive Air	
Drinking Water			Fish Ingestion								
ADR		LADD	ADR	LADD	7Q10[4] COC = 1	PDM Days Exceeded	LADD	ADR	LADD	ADR	LADD
Release activity(ies)[2]; exposure calculation(s)[3]	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	µg/l	# Days	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day	mg/kg/day
PROC1: Max ADR, PDM, LADD	**1.17E-02**	**8.43E-05**	**0.24**	**1.03E-03**	**239.69**	**84**	**4.58E-04**	**3.31E-02**	**5.97E-04**	**4.78E-03**	**3.52E-05**
USE1: Max ADR, PDM1	**6.08E-02**	---	**0.74**	---	**1291.67**	**218**	---	**3.68E-02**	---	**4.60E-02**	---
USE1: PDM2	---	---	---	---	**1246.21**	**247**	---	---	---	---	---
USE1: Max LADD	---	**7.55E-04**	---	**9.24E-03**	---	---	**1.55E-03**	---	**2.01E-03**	---	**9.78E-04**
PROC2: Max ADR, PDM, LADD	**1.35E-02**	**1.46E-04**	**0.28**	**1.79E-03**	**277.67**	**126**	**3.42E-04**	**2.76E-02**	**7.35E-04**	**1.08E-04**	**1.19E-06**
USE2: Max ADR, PDM, LADD	**7.24E-03**	**1.43E-04**	**0.14**	**1.74E-03**	**148.14**	**248**	**7.35E-04**	**7.94E-03**	**4.35E-04**	**4.61E-03**	**1.01E-04**
PROC3: Max ADR, Max acute eco	**0.14**	---	**2.85**	---	**2835.05**	---	---	**0.27**	---	---	---
PROC3: PDM	---	---	---	---	**257.73**	**200**	---	---	---	---	---
PROC3: Max LADD	---	**2.59E-04**	---	**3.17E-03**	---	---	**1.00E-03**	---	**1.30E-03**	---	---
USE3: Max ADR, PDM1	**9.61E-03**	---	**0.10**	---	**210.38**	**64**	---	**2.76E-03**	---	**2.94E-02**	---
USE3: PDM2	---	---	---	----	**31.13**	**186**	---	---	---	---	---
USE3: Max LADD	---	**4.00E-05**	---	**4.89E-04**	---	---	**6.16E-04**	---	**5.64E-05**	---	**6.60E-04**

[1]Exposure scenario titles consist of release activity followed by exposure calculation abbreviation.
[2]Release activities are from engineering report's Manufacturing (Mfg), Processing (Proc) and Use release activity labels. Multiple release activities are combined in one exposure scenario if their releases occur at same location.
[3]Exposure calculations are Acute Dose Rate (ADR), Lifetime Average Daily Dose (LADD), and Probabilistic Dilution Model (PDM). There may be one, two, or all three exposure calculations per exposure scenario. COC is the aquatic concentration of concern.
[4]This column displays concentration values for the 7Q10 streamflow, which is defined as the average streamflow of the 7 consecutive days of lowest flow within a 10 year period.

Appendix G SUPPLEMENTAL INFORMATION

SUPPLEMENTAL DATA FOR APPENDIX E (ChemSteer Engineering Reports):

p120433.ceb – 23 page pdf file
p120453.ceb - 60 page pdf file

SUPPLEMENTAL DATA FOR APPENDIX F (E-FAST Exposure Reports):

P-12-0433.exp1_Draft Final_REVISED_022013 – 9-page pdf file
P-12-0453.exp1_Draft Final_102512 – 21-page pdf file