Update on the Human Health Assessment of Long-Chain Chlorinated Alkanes

Health Canada

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SYNOPSIS

Chlorinated paraffins (CPs) were included in 1989 on the Priority Substances List under the 1988 *Canadian Environmental Protection Act* (CEPA 1988) for assessment of potential risks to the environment and human health.

The use of the term paraffins to identify these substances was recently changed to alkanes to harmonize with more current nomenclature that is recognized by other jurisdictions and international bodies.

CPs are chlorinated alkanes that have carbon chain lengths ranging from 10 to 38 with varying degree of chlorination. They are subdivided into three groups: short-chain chlorinated paraffins with 10-13 carbon atoms (SCCPs), medium-chain chlorinated paraffins with 14-17 carbon atoms (MCCPs) and long-chain chlorinated paraffins with 18 to 38 carbon atoms (LCCPs).

In 1993, Environment Canada and Health Canada published an assessment report that concluded SCCPs constitute or may constitute a danger to human health or life according to the criteria described in the CEPA 1988. However, available data at that time were considered insufficient to conclude whether short-, medium- or long-chain chlorinated paraffins were harmful to the environment or whether medium- or long-chain chlorinated paraffins were considered a danger to human health.

After addressing the critical data gaps identified in the 1993 assessment report, a draft follow-up report was published in 2005, which was followed by a 60-day comment period. The final follow-up report was published in 2008 with the conclusion that all CPs are harmful to human health under paragraph 64(*c*) of CEPA 1999 and CPs containing up to 20 carbon atoms are harmful to environment under paragraph 64(*a*) of CEPA 1999.

In 2009, the Environment Agency of United Kingdom published an environmental risk assessment report on LCCPs and this new information informed an update to the exposure characterization for various human subpopulations for LCCPs.

There were no new critical health effects identified for LCCPs. Therefore, the tolerable daily intake (TDI) (i.e., the level of intake to which it is believed that a person may be exposed daily over a lifetime without deleterious effects) of 71 µg/kg-bw per day, derived for non-neoplastic effects in the follow-up assessment in 2008, was used for risk characterization.

Upper-bounding estimates of daily intakes of LCCPs by the general population of Canada are well below the established TDI, and therefore, it is concluded that long-chain chlorinated alkanes *that have the molecular formula* $C_nH_xCl_{(2n+2-x)}$ in which $18 \leq n \leq 38$ are not harmful to human health as defined in paragraph 64(*c*) of CEPA 1999.

INTRODUCTION

Chlorinated paraffins (CPs) are chlorinated alkanes that have carbon chain lengths ranging from 10 to 38. They are subdivided into three groups: short-chain chlorinated paraffins with 10-13 carbon atoms (SCCP), medium-chain chlorinated paraffins with 14-17 carbon atoms (MCCP) and long-chain chlorinated paraffins with 18 to 38 carbon atoms (LCCP).

CPs were included in 1989 on the Priority Substances List under the 1988 *Canadian Environmental Protection Act* (CEPA 1988) for assessment of potential risks to the environment and human health. In 1993, Environment Canada and Health Canada published an assessment report that concluded that SCCPs constitute or may constitute a danger to human health or life according to the criteria described in the CEPA. However, available data at that time were considered insufficient to conclude whether short-, medium- or long-chain chlorinated paraffins were harmful to the environment or whether medium- or long-chain chlorinated paraffins were considered a danger to human health.

Following the publication of the assessment report, research to address data gaps relevant to the assessment of impacts of CPs on the environment was undertaken. Furthermore, an industry survey on the manufacture, import and uses of CPs in Canada was conducted for the years 2000 and 2001 through a *Canada Gazette* Notice issued pursuant to section 71 of CEPA 1999. Finally, the scientific literature was reviewed to identify new exposure and toxicological data.

On June 11, 2005, the Ministers of the Environment and of Health published the summary of the scientific results of the follow-up assessment on CPs in the *Canada Gazette*, Part I for a 60-day public comment period. At the same time, a statement outlining the proposed risk management measure - a prohibition regulation - was also published. Comments were subsequently received from industry and industry associations. The draft follow-up assessment report was revised based on these comments and the final was published on August 30, 2008. The final follow-up assessment report concluded that CPs containing between 10 and 38 carbon atoms are harmful to human health under paragraph 64(*c*) of CEPA 1999 and CPs containing up to 20 carbon atoms are harmful to the environment under paragraph 64(*a*) of CEPA 1999.

In 2011, Health Canada made a decision to update the human health assessment of LCCPs based on new information relevant to exposure characterization for the general population in Canada.

This *Update on the Human Health Assessment of Long-Chain Chlorinated Alkanes*, which was built upon the final follow-up assessment report published in 2008, was prepared by staff in the Existing Substances Program at Health Canada and incorporates input from other programs within the department. The external peer review of exposure assessment was conducted by WECC Wania Environmental Chemists Corp., Toronto, Canada. The draft *Update on the Human Health Assessment of Long-Chain Chlorinated Alkanes* that was published in September 2011 was subject to a 60-day public comment

period. Although external comments were taken into consideration, the final content and outcome of this assessment report remain the responsibility of Health Canada.

SUMMARY OF INFORMATION CRITICAL TO THE ASSESSMENT UNDER CEPA 1999

In the 2008 follow-up assessment, upper-bounding intake estimates for long-chain chlorinated paraffins (LCCPs) were calculated using concentrations in a limited number of foodstuffs in the United Kingdom (Campbell and McConnell 1980). Furthermore, concentrations in foods were represented by the limits of detection for five of eight food groups in the calculation of daily intake. The confidence in exposure was low because of high uncertainty in estimating total daily intakes of LCCPs from drinking water, food and soil. For the general population, none of those intakes exceeded the TDI (71 µg/kg bw/day). However, for infants, non-formula fed, the total daily intake of LCCPs of 16 µg/kg bw/day was within the same order of magnitude. It was on this basis that LCCPs were concluded to be harmful to human health as defined in paragraph 64(*c*) of the *Canadian Environmental Protection Act, 1999* (CEPA 1999).

Since then, in 2009, the United Kingdom Environment Agency published an environmental risk assessment report on LCCPs (Environment Agency 2009). In the absence of monitoring data, environmental concentrations of three main types of LCCPs, $C_{18\text{-}20}$ liquid, $C_{>20}$ liquid and $C_{>20}$ solid, were predicted using European Union System for the Evaluation of Substances (EUSES) modelling based on physical chemical properties. Furthermore, EU release volume for the selective types of LCCPs was used as no UK release data was identified.

Health Canada has updated its assessment of LCCPs, informed by the United Kingdom Environment Agency report. As there is no Canadian release data for LCCPs, an EU release value of 140,000 kg/year is used in the prediction. This value is considered conservative as chlorinated paraffins are no longer produced in Canada. Use volume in Canada in 2001 was approximately 200,000 kg with no reportable releases identified to the National Pollutants Release Inventory (NPRI) as of 2009 (NPRI 2009). Exposure estimates from the environment and food for $C_{18\text{-}20}$ and $C_{>20}$ liquid LCCPs are estimated using a Farfield Human Exposure model (FHX 2008). Analytical methods currently available for LCCPs do not routinely differentiate the types of chlorinated paraffins either in terms of chlorine content or chain length distribution. The FHX model, developed by the Centre for Environmental Modelling and Chemistry of Trent University for Health Canada, brings together information on chemical partitioning, degradation, environmental fate and transport and food web bioaccumulation for assessing human age-class-specific exposure from chemicals released to the environment. The FHX model calculates steady-state concentrations in the multi-media compartments such as air, water and soil and various food groups, including fruits, vegetables, milk, dairy, fish, and meats based on the unit emission rate. The EPIsuite v.4.0 predicted physical chemical properties (MW, VP, water solubility, log Kow and half-lives in air, water, soil and sediment, in fish) (EPIsuite 2008) for $C_{18}H_{37}Cl_1$ (CAS 106232-85-3), $C_{18}H_{22}Cl_{16}$ and

$C_{18}H_{30}C_{l8}$ of the $C_{18\text{-}20}$ alkanes group and $C_{22}H_{45}Cl_1$ (CAS 85535-86-0) of the $C_{>20}$ alkane group were used in the FHX model (Appendix 1).

There were no new critical health effects identified for LCCPs. Therefore, the tolerable daily intake (TDI) (i.e., the level of intake to which it is believed that a person may be exposed daily over a lifetime without deleterious effects) of 71 µg/kg-bw per day, derived for non-neoplastic effects in the follow-up assessment in 2008 was used for risk characterization. This TDI value was based on the lowest dose of LCCP (Lowest-Observed-Adverse-Effect Level [LOAEL] = 100 mg/kg-bw per day) at which adverse effects (diffuse lymphohistiocytic inflammation in the liver and in the pancreatic and mesenteric lymph nodes in female rats) were observed, in a carcinogenicity bioassay in which an adequate range of endpoints had been examined (NTP, 1986; Bucher *et al*., 1987), divided by an uncertainty factor of 1000 (×10 for intraspecies variation; ×10 for interspecies variation; ×10 for use of a LOAEL rather than a NOAEL) and multiplied by 5/7 (for conversion of 5 days/week administration to daily exposure) (Health Canada, 2008).

Intake of $C_{18}H_{37}Cl_1$ with its upper bounding intake estimates ranging from 0.007 µg per kg-bw per day for 60+ age group to 0.024 µg per kg-bw per day for 0.5-4 years age group, is the highest among the three substances within $C_{18\text{-}20}$ alkanes group. These intake estimates are 10000 and 3000 times lower, respectively, than the tolerable daily intake of 71 µg per kg-bw per day (Appendix 2). The intake estimates for the other two representative substances in the $C_{18\text{-}20}$ substances, $C_{18}H_{22}Cl_{16}$ and $C_{18}H_{30}C_{l8}$, were found at an order of magnitude lower than $C_{18}H_{37}Cl_1$. This could possibly be due to the higher vapour pressure and water solubility of the latter substance. The estimated upper bound intakes of the $C_{>20}$ type is predicted to range from 0.013 µg per kg-bw per day for 60+ age group to 0.040 µg per kg-bw per day for 0.5-4 years age group, which are 5500 and 1800 times lower, respectively, than the tolerable daily intake.

As these estimates are well below than the derived TDI, it is concluded that LCCPs are not harmful to human health as defined in paragraph 64(*c*) of the *Canadian Environmental Protection Act, 1999*.

Uncertainties in Evaluation of Risk to Human Health

There is high degree of confidence in the database of toxicological studies upon which the TDI for LCCPs is based as the database is complete, including a well documented carcinogenicity bioassay in rat and mice.

The commercial products in the $C_{18\text{-}20}$ and $C_{>20\ \text{liquid}}$ groups contain a mixture of many components with different carbon chain length and various chlorine weight content which can range from a low of 20% to a high of 70%. The upper bounding exposure estimates of $C_{18\text{-}20}$ and $C_{>20}$ LCCPs are based on the predicted physical chemical properties of the specific $C_{18\text{-}20}$ and $C_{>20\ \text{liquid}}$ compounds with different chlorine content. There is considerable uncertainty over the physical chemical properties chosen for the environmental modelling and the bioconcentration factor used to estimate the uptake

from soil into root crops, from air into leaf crops and the subsequent transfer into the food chain. However, given the very conservative input values of the predicted physical chemical, confidence is high that estimated exposure to LCCPs from the environment and food for different age class of the general population are considerably lower than the TDI of 71 µg/kg bw/day.

CONCLUSION

Based on the information presented, it is concluded that LCCPs (i.e., chlorinated paraffins with 18 to 38 carbon atoms) are not entering the environment in a quantity or concentration or under conditions that may constitute a danger to human life or health as defined in the paragraph 64(*c*) of CEPA 1999.

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Appendix 1: Predicted physical/chemical properties of the C_{18-20} and $C_{>20}$ alkane group

Parameter	$C_{18}H_{37}Cl_1$ C_{18-20} alkanes group	$C_{18}H_{22}Cl_{16}$ C_{18-20} alkanes group	$C_{18}H_{30}C_{l8}$ C_{18-20} alkanes group	$C_{22}H_{45}Cl_1$ $C_{>20}$ alkane group
Molecular Weight	288.95	530.06	805.6	345.06
Vapour Pressure (Pa)	3.79E-01	3.32E-06	6.43E-11	9.7E-04
Solubility (g/m^3)	1.4E-04	3.87E-07	3.39E-10	1.4E-06
Log Kow	9.36	10.6	12.07	11.2
Half-life in air (day)	0.51	0.94	5.45	0.41
Half-life in water (days)	38	180	180	15
Half-life in soil (days)	75	360	360	30
Half-life in sediment (days)	337	1620	1620	135
Metabolic half-life in fish (days)[1]	143	811	6440	495
Metalic half-life in avian and mammals (days)	143	811	6440	495

[1] Calculated from first order rate constant value for 1 kg fish -BCFBAF (EPISuite 2008)

Appendix 2: Predicted upper-bounding daily intakes of $C_{18}H_{37}Cl_1$ for the general population in Canada

Route of exposure	Estimated intake (µg/kg-bw per day) of C_{18-20} LCCPs by various age groups						
	0–6 months[1, 2],		0.5–4 years[3]	5–11 years[4]	12–19 years[5]	20–59 years[6]	60+ years[7]
	formula fed	not formula fed					
Ambient air	$1.92x10^{-6}$		$4.12x10^{-6}$	$3.21x10^{-6}$	$1.83x10^{-6}$	$1.57x10^{-6}$	$1.36x10^{-6}$
Indoor air	$1.35x10^{-5}$		$2.88x10^{-5}$	$2.25x10^{-5}$	$1.28x10^{-5}$	$1.10x10^{-5}$	$9.54x10^{-6}$
Drinking water	$2.26x10^{-7}$	$8.49x10^{-8}$.	$9.58x10^{-8}$	$7.53x10^{-8}$	$4.29x10^{-8}$	$4.49x10^{-8}$	$4.72x10^{-8}$
Food and beverages[8]		0.018	0.024	0.017	0.010	0.009	0.007
Soil	NA		NA	NA	NA	NA	NA
Total intake	<0.01	0.018	0.024	0.017	0.010	0.009	0.007

Abbreviation: NA, not available.

1 Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day, to drink 0.8 L of water per day (formula fed) or 0.3 L/day (not formula fed) and to ingest 30 mg of soil per day (Health Canada 1998). Formula-fed infants are assumed to consume no other foods.

2 For exclusively formula-fed infants, intake from water is synonymous with intake from food. The concentration of LCCPs in water used to reconstitute formula was based on predicted water concentration. data.. Approximately 50% of infants are introduced to solid foods by 4 months of age and 90% by 6 months of age (NHW 1990).

3 Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day, to drink 0.7 L of water per day and to ingest 100 mg of soil per day (Health Canada 1998).

4 Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day, to drink 1.1 L of water per day and to ingest 65 mg of soil per day (Health Canada 1998).

5 Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day, to drink 1.2 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

6 Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day, to drink 1.5 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

7 Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day, to drink 1.6 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

8 The food group includes fruits, vegetables, dairy, fish and meats based on mechanistic mass bioaccumulation models that include biotransformation loss