



Canadian Environmental Protection Act

Priority Substances List Assessment Report

Chlorinated Paraffins



Government
of Canada

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Environment
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**PRIORITY SUBSTANCES LIST
ASSESSMENT REPORT**

CHLORINATED PARAFFINS

Government of Canada
Environment Canada
Health and Welfare Canada

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TABLE OF CONTENTS

Synopsis	v
1.0 Introduction	1
2.0 Summary of Information Critical to Assessment of "Toxic"	5
2.1 Identity, Properties, Production, and Use.....	5
2.2 Entry into the Environment.....	6
2.3 Exposure-related Information.....	7
2.3.1 <i>Fate</i>	7
2.3.2 <i>Concentrations</i>	8
2.4 Effects-related Information.....	8
2.4.1 <i>Experimental Animals and In Vitro</i>	8
2.4.2 <i>Humans</i>	14
2.4.3 <i>Ecotoxicology</i>	14
3.0 Assessment of "Toxic" Under CEPA	17
3.1 CEPA 11(a) Environment.....	17
3.2 CEPA 11(b) Environment on Which Human Life Depends.....	18
3.3 CEPA 11(c) Human Life or Health.....	18
3.3.1 <i>Population Exposure</i>	18
3.3.2 <i>Effects</i>	19
3.4 Conclusion.....	23
4.0 Recommendations for Research and Evaluation	25
5.0 References	26

Synopsis

The term "chlorinated paraffin waxes" is generally restricted to chlorinated paraffins having long carbon chains (i.e., $\geq C_{18}$). However, the scope of this assessment was broadened to include the short chain (i.e., $\leq C_{13}$) and medium chain (i.e., C_{14-17}) chlorinated paraffins which are also of concern because of their potential effects on the environment and human health.

Chlorinated paraffins (CPs) are produced in, and imported into, Canada for use as plasticizers and flame retardants as well as extreme-pressure additives in lubricating oils. They are persistent compounds and have the potential to bioaccumulate in aquatic organisms. No data were identified on the concentrations of these substances in any medium in the Canadian environment. However, data from other countries (including the United States) where these compounds are produced and used confirm their presence in the environment, particularly near production facilities.

Short chain chlorinated paraffins cause adverse effects in fish and aquatic invertebrates at concentrations below 1 $\mu\text{g/L}$ in laboratory studies. However, owing to the lack of information on concentrations of short chain chlorinated paraffins in the Canadian environment, it is not possible to estimate exposure of Canadian biota or to compare this exposure with levels estimated to cause adverse effects.

Short chain chlorinated paraffins have caused cancer in experimental animals, although relevant data for humans are not available. Therefore, short chain chlorinated paraffins are considered to be "non-threshold toxicants", i.e., substances for which there is believed to be some chance of adverse effects at any level of exposure. For such substances, where data permit, estimated exposure is compared to quantitative estimates of cancer potency in order to characterize risk and provide guidance for further action, such as analysis of options to reduce exposure, under the *Canadian Environmental Protection Act* (CEPA). However, owing to the lack of information on concentrations of short chain chlorinated paraffins in environmental media to which humans are exposed, it is not possible to quantitatively estimate the total average daily intake of these compounds by the general population in Canada, or to subsequently compare these values to quantitative estimates of cancer potency.

There is also a lack of information on concentrations of **medium and long chain chlorinated paraffins** in environmental media to which humans and other biota are exposed. Therefore, it is not possible to estimate exposure of Canadian biota or to compare this exposure with levels estimated to cause adverse effects. Similarly, it is not possible to quantitatively estimate the total average daily intake of these compounds by the general population in Canada. The Tolerable Daily Intakes (i.e., the intake to which it is believed that a person can be exposed over a lifetime without deleterious effect) are derived on the basis of data from bioassays in animal species for these two groups of chlorinated paraffins and therefore cannot be compared with the estimated total daily intake in the general environment in Canada.

None of the chlorinated paraffins volatilizes readily to the atmosphere. Due to their predicted short tropospheric residence time (a few days), these compounds are not expected to contribute significantly to depletion of stratospheric ozone or global warming.

Based on these considerations, the Minister of the Environment and the Minister of National Health and Welfare have concluded that short chain chlorinated paraffins are considered to be "toxic" as defined under Paragraph 11(c) of the *Canadian Environmental Protection Act*. Available data are considered inadequate to evaluate whether medium and long chain chlorinated paraffins are considered to be "toxic" as defined under Paragraphs 11(a) or (c) of the *Canadian Environmental Protection Act*.

1.0 Introduction

The *Canadian Environmental Protection Act* (CEPA) requires the Minister of the Environment and the Minister of National Health and Welfare to prepare and publish a Priority Substances List that identifies substances, including chemicals, groups of chemicals, effluents, and wastes that may be harmful to the environment or constitute a danger to human health. The Act also requires both Ministers to assess those substances to determine whether they are "toxic" as defined under Section 11 of the Act which states:

"...a substance is toxic if it is entering or may enter the environment in a quantity or concentration, or under conditions:

- (a) having or that may have an immediate or long-term harmful effect on the environment;
- (b) constituting or that may constitute a danger to the environment on which human life depends; or
- (c) constituting or that may constitute a danger in Canada to human life or health."

Substances that are assessed as "toxic" as defined under Section 11 may be placed on Schedule I of the Act. Consideration can then be given to developing regulations, guidelines, or codes of practice to control any aspect of these substances' life cycle, from the research and development stage through manufacture, use, storage, transport, and ultimate disposal.

The substance "chlorinated paraffin waxes" was included in Group 3 of the Priority Substances List. This term is generally restricted to chlorinated paraffins having long carbon chains. However, the scope of the assessment was broadened to include the short chain and medium chain chlorinated paraffins since they are also of concern due to their potential effects on the environment and human health. In this report, chlorinated paraffins having carbon chain lengths of 13 or less ($\leq C_{13}$) are termed "short", those having 14 to 17 carbon atoms (C_{14-17}) are considered to be "medium", and those having 18 or more ($\geq C_{18}$) are considered to be "long". To the extent possible, in each section of this report, these compounds are addressed in this order.

The assessment of whether chlorinated paraffins are "toxic", as defined under CEPA, was based on the determination of whether they **enter** or are likely to enter the Canadian environment in a concentration or quantities or under conditions that could lead to **exposure** of humans or other biota at levels that could cause adverse **effects**.

To identify data relevant to the assessment of effects on human health, literature searches of the following computerized databases were conducted: Medline (1966 to 1989), Hazardous Substances Data Bank (HSDB), Registry of Toxic Effects of Chemical Substances (RTECS), Integrated Risk Information System (IRIS), Chemical Carcinogenesis Research Information System (CCRIS) (all to January, 1992), Toxline

(1965 to 1992), Toxlit (1981 to 1992), and EMBASE (1985 to 1992). Data included in an unpublished background document prepared under contract (Mitchell, 1991) were also considered in the preparation of this report.

To identify data relevant to the estimation of exposure of the general population to chlorinated paraffins, literature searches were conducted in the following computerized databases: Environment Canada Departmental Library Catalogue (ELIAS) (1992), AQUAREF (1970 to 1992), Canadian Research Index (MICROLOG) (1979 to 1992), and Co-operative Documents Project (CODOC) (1992). Dr. G. Jenkins of the Ontario Ministry of the Environment, Mr. D. Spink of the Alberta Ministry of Environment, and Mr. H. St.-Martin of the Quebec Ministry of the Environment were also consulted in an attempt to identify relevant information on concentrations of chlorinated paraffins in environmental media to which humans are exposed, i.e., drinking water.

With respect to the approach adopted for identifying the data relevant to assessment of effects on the environment, literature searches of the following computerized databases were conducted: Chemical Abstracts (1967 to 1992), BIOS IS Previews (1969 to 1992), National Technical Information Service (NTIS) (1980 to 1992), and Pollution and Toxicology Database (POLTOX) (1982 to 1992). Other sources of information were identified through FATERATE (1989) and the Chemical Evaluation Search and Retrieval System (CESARS) (1988).

Information on both the environmental and health aspects was also sought from the following agencies:

- Umweltbundesamt, Berlin, Federal Republic of Germany;
- Norwegian State Pollution Control Authority, Oslo, Norway;
- Office fédéral de l'environnement, des forêts et du paysage, Berne, Switzerland;
- National Chemicals Inspectorate, Solna, Sweden;
- National Environmental Protection Board, Solna, Sweden;
- National Board of Waters and Environment, Helsinki, Finland;
- British Industrial Biological Research Association, Surrey, England;
- World Health Organization, Geneva, Switzerland;
- Environmental Protection Agency, Copenhagen, Denmark;
- Environmental Agency, Japan; and
- International Agency for Research on Cancer, Lyon, France.

Every effort was also made to obtain all the detailed reports of an extensive series of studies conducted by the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium which are briefly described in Serrone *et al.* (1987). Assistance in this regard was requested from Dr. D.M. Serrone of Ricerca Inc., Painesville, Ohio, Mr. R.J. Fensterheim of the Chlorinated Paraffins Industry Association, Dr. M.T. Richardson of Imperial Chemical Industries (ICI), U.K., and Mr. R. Zampini of ICI Canada, who were unable to provide the requested reports. However, full reports of the studies in this series, which were considered critical to this assessment, were obtained from the United States Environmental Protection Agency (U.S. EPA).

Data relevant to the assessment of whether chlorinated paraffins are "toxic" to human health obtained after completion of the peer review of human health-related sections of the report in August 1992 were not considered for inclusion. Similarly, data relevant to assessment of whether chlorinated paraffins are "toxic" to the environment obtained after completion of peer review of those sections of the report in June 1992 were not considered.

The results of recent investigations and all original studies relevant to the assessment of whether chlorinated paraffins are "toxic" as defined under Section 11 of CEPA have been critically evaluated by the following Health and Welfare Canada staff (exposure of the general population and effects on human health), Environment Canada staff (entry, environmental exposure and effects), and Fisheries and Oceans staff (environmental exposure and effects):

<u>Environment Canada</u>	<u>Health and Welfare Canada</u>	<u>Fisheries and Oceans</u>
L. Brownlee	P.K.L. Chan	V. Zitko
K.M. Lloyd	M.E. Meek	
	D. Riedel	

Following circulation and external peer review of the health-related sections by staff of British Industrial Biological Research Association (BIBRA) Toxicology International, U.K. and Dr. D.M. Serrone of Ricerca Inc., Painesville, Ohio (Supporting Document only), they were reviewed and approved by the Guidelines and Standards Rulings Committee of the Bureau of Chemical Hazards of Health and Welfare Canada. As part of the review and approval process established by Environment Canada, the environmental sections of the Assessment Report and Supporting Document were reviewed by Drs. J.A. Cotruvo, P. Miller, M. Zeeman, and W.S. Rabert of the U.S. EPA and Dr. D.C.G. Muir of Fisheries and Oceans. In addition, Mr. R. Zampini of ICI Canada and Dr. M.T. Richardson of ICI U.K. provided comments on Subsections 2.2 and 2.3 and Dr. N. Bunce of the University of Guelph provided comments on Subsection 2.3. The final Assessment Report was reviewed and approved by the Environment Canada/Health and Welfare Canada CEPA Management Committee.

In this report, a Synopsis is presented which will appear in the Canada Gazette. An extended summary of technical information that is critical to the assessment is presented in Section 2.0. This information is presented in greater detail in a Supporting

Document which is available upon request. The assessment of whether chlorinated paraffin waxes are "toxic" under CEPA is presented in Section 3.0.

Copies of this Assessment Report and the unpublished Supporting Document are available upon request from:

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Environment Canada
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351 St. Joseph Boulevard
Hull, Quebec
K1A 0H3

Environmental Health Centre
Health and Welfare Canada
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2.0 Summary of Information Critical to Assessment of "Toxic"

2.1 Identity, Properties, Production, and Use

Chlorinated paraffins (CPs) are chlorinated derivatives of n-alkanes, having carbon chain lengths ranging from 10 to 38, and a chlorine content ranging from about 30 to 70% (by weight). Commercial products, of which there are over 2000, (Serrone *et al.*, 1987) are complex mixtures of homologues and isomers. The products vary in the distribution, possibly type, and range of chain lengths, and in the degree of chlorination.

The melting point of CPs increases with increasing carbon chain length and with increasing chlorine content. Consequently, at room temperature, CPs range from colourless to yellowish liquids at about 40% chlorine, to white solids (softening point at about 90°C) at 70% chlorine. Chlorinated paraffins have very low vapour pressures (e.g., 1.3×10^{-4} Pa for C₁₄₋₁₇, 52% Cl at 20°C) and solubilities in water, the latter ranging from 95 to 470 µg/L for some of the short chain mixtures (C₁₀₋₁₃) to as low as 3.6 to 6.6 µg/L for some of the long chain mixtures (C₂₀₋₃₀) (Campbell and McConnell, 1980). Log octanol:water partition coefficients (i.e., log K_{ow}) values (as measured by high performance thin layer chromatography) are very high, ranging from about 5 to 12 (Renberg *et al.*, 1980).

Chlorinated paraffins are obtained by direct chlorination of n-alkanes of high purity in the liquid phase, in the presence of hydrogen chloride. They are manufactured commercially by letting gaseous chlorine flow or bubble into straight chain C₉₋₃₀ petroleum fractions, such as normal paraffins, at least 98% linear, and wax fractions averaging as many as 24 carbon atoms. The process is catalyzed by ultraviolet light (Mukherjee, 1990; ICI, 1992a).

The high molecular weight, large number of isomers and congeners, low volatility, non-polar character, and loss of hydrochloric acid or chlorine at elevated temperatures make it very difficult to measure low concentrations of chlorinated paraffins. The current method of choice is gas chromatography with negative ions chemical ionization mass spectrometry. This method is described in Muller and Schmid (1984), Schmid and Muller (1985), and Jansson *et al.* (1991).

Imperial Chemical Industries Canada is the only producer of CPs in Canada, operating a plant with a production capacity of 5-kt/year in Cornwall, Ontario. This plant, however, has been operating well below capacity for several years, producing approximately 2.9 kt in 1990 (Camford Information Services, 1991). Specific information was not found on the amounts of each chain length (i.e., short, medium, and long) produced. Chlorinated paraffins produced in Canada are sold under the trade name Cereclor.

Estimated total imports from the United States, United Kingdom, and Germany were 2.3 kt for 1990 (Camford Information Services, 1991), although it is expected that total imports for 1992 will be between 1.0 and 1.5 kt (ICI, 1992a). Total exports from Canada are considerably lower at about 200 t/yr (Camford Information Services, 1991).

Again, specific information was not found on the amount of each chain length imported and exported.

In Canada, CPs are used mainly in plastics as a plasticizer and flame retardant (65% of use). The other major market (20%) for CPs is as an extreme-pressure additive in metal-working fluids to lower the heat and allow faster metal working. Smaller applications for chlorinated paraffins include flame-retardant additives in heavy-duty rubber (8%), paints (3%), and adhesives and sealants (2%) (ICI, 1992b). Total Canadian demand is about 3.5 to 4 kt/yr (ICI, 1992a). The short chain CPs ($\leq C_{13}$) are used primarily as lubricants, flame retardants, and sealants; the medium chain CPs (C_{14-17}) as plasticizers; and the long chain CPs ($\geq C_{18}$) are used in paints and as lubricants and flame retardants.

2.2 Entry into the Environment

Chlorinated paraffins are not known to occur naturally. There are no recorded releases of CPs into the Canadian environment and estimates of releases have not been identified. Although releases of CPs could occur during their manufacture, use, transport, and disposal, the major sources of release into the environment are likely manufacturing and lubricant applications. These two sources are discussed in this subsection, based on data prepared by the Chlorinated Paraffins Industry Association for the U.S. EPA (CPIA, 1992).

Waterborne releases from manufacturing can occur from spills, facility wash-down, and stormwater runoff. As CPs are insoluble in water, and releases from these sources are routinely collected and treated in the facilities' wastewater treatment system, the CPIA considers these releases to be negligible (CPIA, 1992).

The formulation and use of metal-working fluids, composed of short-chain, 50 to 60% CPs, are potential sources of release of CPs into aquatic environments. The release from process metal-working fluids results from disposal of used drums, carry-off from work pieces, and disposal of spent baths. Release to the environment from drum recycling is considered negligible, although relevant data have not been identified. No data were identified for Canada, but the U.S. EPA estimates that fluid releases in the United States due to carry-off from work pieces may range from 2.5 kg/site per year for a small user (100-L capacity) to 2500 kg/site per year for a large user (95 000-L capacity). Similarly, for small and large users, CPIA (1992) estimates that releases to water in the United States from disposal of spent chlorinated paraffin baths vary from 12 to 1500 kg/site per year, respectively, with 90% of the shops discharging near the lower end of the range.

These estimates are considerably lower than those from Sweden, where it is estimated that about 50% of the used oils may be directly discharged (KEMI, 1991). Minimal release is expected because of paint formulating or when CPs are used as flame retardants (a major use in Canada). According to Swedish estimates, less than 0.001% of CPs is released during use as a flame retardant (KEMI, 1991).

2.3 Exposure-related Information

2.3.1 Fate

Few data are available on the environmental fate of CPs because of the complex nature of the mixtures and difficulties in measuring low levels. Based on general patterns of behaviour of hydrophobic organics in the environment, it is likely that CPs are fairly immobile, remain adsorbed onto soil or sediment particles, and are slowly degraded. In the natural environment, CPs are generally stable, but degradation is possible by micro-organisms (Madeley and Birtley, 1980). The ability of aerobic micro-organisms to oxidize a range of CPs depends on the previous acclimatization of the microbes, the chain length, and the degree of chlorination of the CPs. Short and medium chain CPs (i.e., C₁₀₋₂₀) are degraded most rapidly. The longer the carbon chain and the higher the chlorine content, the less chlorine that is released (Omori *et al.*, 1987).

Few data have been identified on the mobility and transport of CP residues from sites of manufacturing, use, or disposal. However, some of the calculated Henry's Law constants for CPs are similar to those for chlorinated aliphatic pesticides, such as toxaphene, chlordane, and aldrin (Sunito *et al.*, 1988), which are known to be transported in the atmosphere. Airborne dispersion of CPs has been found in the United Kingdom and Sweden where monitoring data indicate widespread levels of low contamination in water, sediments, aquatic and terrestrial biota, and even commercial foods (Campbell and McConnell, 1980; Jansson *et al.*, 1993).

Chlorinated paraffins are generally considered to be persistent. Hydrolysis, oxidation, and photolysis with visible or near ultraviolet radiation are insignificant routes of transformation at ambient temperatures. No experimental data are available on the fate of any CPs that volatilize to the atmosphere. However, it may be assumed that any volatilized CPs would be subject to attack by hydroxyl radicals in the troposphere. Using the method of Atkinson (1986) for estimating the rate constant for reaction of chlorinated paraffins with hydroxyl radicals, the likely tropospheric half-life is a few days under summer conditions.

While data indicate a potential for bioaccumulation, few bioconcentration factors (BCFs) or biomagnification factors (BAFs) have been experimentally determined. The uptake and accumulation of CPs in fish from water and food appear to be inversely proportional to molecular weight, i.e., CPs with short chain length and a low chlorine content are taken up most rapidly. Similarly, depuration is slowest for highly chlorinated forms. Measurement of BCFs and BAFs is difficult due to the low water solubility of these substances, and subsequent slow uptake rates requiring long exposure periods to achieve steady-state equilibrium. In several of the reviewed tests, it was unclear whether steady-state had been achieved. Reported bioconcentration factors vary dramatically between different CPs and between species, ranging from 0.007 to 139 000 (Sundstrom and Renberg, 1985). The highest bioconcentration factor, which was observed for mussels (Renberg *et al.*, 1986), was reported at a much lower concentration of chlorinated paraffins in water than that in most other studies. Observations for dioxins

and furans have been similar, with Cook *et al.* (1991) reporting much higher BCFs when aquatic species were exposed to concentrations of pg/L rather than ng/L.

Based on log K_{ow} s of >6 , accumulation of CPs via the food chain (i.e., biomagnification) could be significant (Thomann, 1989). In studies on uptake of various short chain (C_{10-13}) chlorinated paraffins from food using rainbow trout (*Oncorhynchus mykiss*) and bleaks (*Alburnus alburnus*), BAFs ranged from 2 to 41 on a wet weight (w.w.) basis (Lombardo *et al.*, 1975; Bengtsson and Ofstad, 1982), indicating that biomagnification could occur in the environment.

2.3.2 Concentrations

No information was identified on levels of CPs in any environmental medium in Canada. In a study conducted in Atlantic Canada to monitor organic and inorganic contaminants in edible shellfish, CPs were not detected (detection limit = 0.4 $\mu\text{g/g}$ w.w.) in any of the 30 assayed samples from various locations (Environment Canada, 1989). Environmental fate modelling (e.g., Fugacity model; Mackay *et al.*, 1985) was considered unsuitable for predicting levels in the Canadian environment, as CPs are mixtures of paraffins of varying chain lengths and chlorination, each with very high log K_{ow} values, making model predictions unreliable. In addition, there is little information on transformation and release rates for specific CPs.

Data on environmental levels of CPs in other countries are also sparse. Murray *et al.* (1988) found that short, medium, and long chain CPs were generally present at quantifiable concentrations in sediment, suspended solids, and biota in a creek downstream from the discharge of a chlorinated paraffin manufacturing plant in Ohio. Campbell and McConnell (1980) reported detectable concentrations of C_{10-20} and C_{20-30} CPs in marine and fresh waters, and sediment, as well as in birds, seals, fish, and mussels, both close to and far from manufacturing sites in the United Kingdom. Jansson *et al.* (1993) reported residues of CPs in all samples of various species from several terrestrial, freshwater, and marine ecosystems in Sweden. These monitoring studies demonstrate the potential for presence and transport in the environment.

Only one study was identified in which levels of chlorinated paraffins were determined in a limited range of foodstuffs and human tissues (Campbell and McConnell, 1980). Data available in the published account of this early study were insufficient, however, to permit evaluation of the validity of these results.

2.4 Effects-related Information

2.4.1 Experimental Animals and In Vitro

The acute toxicity of all chlorinated paraffins is considered to be low with oral LD_{50} s for rats and mice being greater than 4 g/kg b.w. (Dover Chemical Corp., 1975; Birtley *et al.*, 1980; Bucher *et al.*, 1987). Signs of toxicity in rats, which were most evident following oral administration of the shorter chain CPs (doses greater than

4 g/kg b.w.) included piloerection, muscular incoordination, and urinary and fecal incontinence (Birtley *et al.*, 1980).

Short Chain Chlorinated Paraffins ($\leq C_{13}$) - In a well documented study by the National Toxicology Program, enlarged livers (mice), decreased body weights (rats), and diarrhea (both species) were reported in F344/N rats and B6C3F₁ mice following administration of a short chain CP (C₁₂, 60% C1) by gavage in corn oil for 16 days (NTP, 1986a; Bucher *et al.*, 1987). The lowest-observed-effect-levels (LOEL) based on the compound-related hepatomegaly were 469 mg/(kg b.w.·day) and 938 mg/(kg b.w.·day) for rats and mice, respectively. In 14-day studies in F344 rats conducted by the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, the no-observed-effect-level (NOEL) for a short chain CP (C₁₀₋₁₃, 58% C1) administered by gavage in corn oil was considered to be 30 mg/(kg b.w.· day), based on enlarged livers and hepatocellular hypertrophy at dose levels of 100 mg/(kg b.w.· day) or above (IRDC, 1981a; Serrone *et al.*, 1987).

A NOEL was not established in a 13-week study in which a short chain CP (C₁₂, 60% C1) was administered by gavage in corn oil to B6C3F₁ mice and F344/N rats [LOELs were 313 and 125 mg/(kg b.w.· day) for mice and rats, respectively, based on dose-related increases in relative liver weights] (NTP, 1986a; Bucher *et al.*, 1987). For short chain CPs (C₁₀₋₁₃, 58% C1), a NOEL of 10 mg/(kg b.w.· day) in F344 rats was reported following administration for 90 days by gavage in corn oil or in the diet, on the basis that no treatment-related microscopic changes were found in any tissues at this dose (Serrone *et al.*, 1987). In this study, there were increases in liver and kidney weights, increases in the incidence of hepatocellular hypertrophy, increases in thyroid-parathyroid weights, and hypertrophy and hyperplasia of the thyroid. There were high incidences of trace-to-mild chronic nephritis in the kidneys of male rats and increased pigmentation of the renal tubules in female rats.

In a study conducted by the National Toxicology Program on a short chain CP (C₁₂, 58% C1) in which F344/N rats and B6C3F₁ mice were administered the compound by gavage in corn oil for two years (NTP, 1986a; Bucher *et al.*, 1987), mean body weights of high-dose male rats [625 mg/(kg b.w. · day)] were 8 to 12% lower than that in controls after week 20. The body weights of exposed female mice were about 10% lower than those of the controls during the second year. Survival of both low-dose [312 mg/(kg b.w · day)] and high-dose [625 mg/(kg b.w. · day)] male rats and low-dose female rats was significantly less than controls after week 90. Survival of high-dose [250 mg/(kg b.w.·day)] female mice was significantly less than that of controls after week 100. The incidence of hepatocellular neoplasms (primarily neoplastic nodules) and adenomas or adenocarcinomas (combined) of the liver were significantly increased at both dose levels in both species and sexes. The incidence of adenomas or hyperplasia of the renal tubular cells increased significantly in exposed male rats. The incidence of follicular cell adenomas or carcinomas (combined) of the thyroid gland was increased in exposed female rats and female mice. In addition, alveolar/bronchiolar adenomas or carcinomas (combined) were induced in male mice, and mononuclear cell leukemia was significantly increased in exposed male rats and in low-dose female rats.

Non-neoplastic lesions induced by the short chain CP in exposed rats included necrosis, hypertrophy, and angiectasis of the liver; erosion, inflammation, and ulceration of the glandular stomach and forestomach; and the formation of multiple cysts in the kidneys of males. The incidence of nephropathy was also increased in exposed female rats and mice but was decreased in male mice as compared with controls [LOAEL = 312 mg/(kg b.w. · day) for rats and 125 mg/(kg b.w. · day) for mice]. It was concluded by the NTP that "under the conditions of these 2-year gavage studies, there was clear evidence of carcinogenicity of chlorinated paraffins (C₁₂, 60% C1) for F344/N rats and B6C3F₁ mice. However, the maximum tolerated dose may have been exceeded in male and female rats" (NTP, 1986a).

Available data are limited on the genotoxicity of the short chain CPs. Although not mutagenic in bacterial assays *in vitro* with or without metabolic activation (Birtley *et al.*, 1980; NTP, 1986a), short chain CPs have been clastogenic in *in vitro* bioassays in the absence of metabolic activation (Myhr *et al.*, 1990) and have also induced cell transformation in the majority of available *in vitro* assays of this endpoint (ICI, 1982a). In two identified *in vivo* studies, the complete reports of which were not available for this assessment, short chain CPs did not induce dominant lethal mutations in rats or increase the frequency of chromosomal aberrations in bone marrow cells in rats (Serrone *et al.*, 1987).

In a series of developmental studies conducted for the Chlorinated Paraffins Manufacturers Toxicology Testing Consortium, the number and location of viable and nonviable fetuses, early and late resorptions, the number of total implantations and corpora lutea, and the incidence of fetal malformations were examined following administration of a short chain CP (C₁₀₋₁₃, 58% C1) by gavage in corn oil to pregnant Charles River rats on days 6 to 19 of gestation and pregnant Dutch Belted rabbits on days 6 to 27 of gestation. An increase in the incidence of adactyly and/or shortened digits in the offspring of rats exposed to a maternally toxic dose [2000 mg/(kg b.w. · day) by gavage in corn oil] (IRDC, 1982) and embryo- or fetotoxic effects at doses less than those that were toxic to the mothers were observed in rabbits exposed to 30 and 100 mg/kg b.w. (IRDC, 1983a).

Available data are extremely limited on the potential neurotoxicity of the short chain chlorinated paraffins. Following oral administration of a single dose (1 mg/kg b.w.) of a short chain CP (polychlorohexadecane) to 10-day-old male and female mice, there was no effect on muscarinic receptors, though it was suggested on the basis of an observed decrease in the V_{max} for sodium-dependent choline uptake, that there was a presynaptic effect on the cholinergic system (Eriksson and Nordberg, 1986). There was a dose-related trend to decreased motor capacity in adult NMRI male mice administered a single dose of 30 to 300 mg/kg b.w. of a short chain CP (C₁₀₋₁₃, 49% C1) intraperitoneally, which was statistically significant at the highest dose (Eriksson and Kihlstrom, 1985).

Data were not found on the immunotoxicity of the short chain chlorinated paraffins.

Medium Chain Chlorinated Paraffins (C₁₄₋₁₇) - In 14-day studies conducted by the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium as summarized by Serrone *et al.* (1987) in which F344 rats were administered a medium chain CP (C₁₄₋₁₇, 52% C1) in the diet, the no-observed-effect-level (NOEL) was considered to be 500 ppm [30 mg/(kg b.w. · day)], based on increases in liver weight and diffuse hepatocellular hypertrophy.

For a medium chain CP (C₁₄₋₁₇, 52% C1), a NOEL of 10 mg/(kg b.w. · day) (more appropriately a NOAEL since an increase in liver weight was observed at this dose) in F344 rats was reported following administration by gavage in corn oil or in the diet for 90 days, on the basis that no treatment-related microscopic changes were found in any tissues at this dose (Serrone *et al.*, 1987). There were increases in liver and kidney weights, increases in the incidence of hepatocellular hypertrophy, increases in thyroid-parathyroid weights, and hypertrophy and hyperplasia of the thyroid. There were also high incidences of trace-to-mild chronic nephritis in the kidneys of male rats and increased pigmentation of the renal tubules in female rats.

In another 90-day study in which a medium chain CP (C₁₄₋₁₇, 52% C1) was administered in the diet, Birtley *et al.* (1980) reported dose-related proliferation of the smooth endoplasmic reticulum in the hepatic cells of rats at 500 ppm and above {NOEL = 250 ppm [12.5 mg/(kg b.w. · day)], LOEL = 500 ppm [25 mg/(kg b.w. · day)]}. In beagle dogs exposed to the same compound in the diet, exposure-related effects were confined principally to male dogs receiving 100 mg/(kg b.w. · day) (significant increases in serum alkaline phosphatase activity and liver-weight-to-body-weight ratios). Electron microscopy also revealed an increase in the smooth endoplasmic reticulum of hepatocytes in all exposed animals [(NOEL = 10 mg/(kg b.w. · day), LOEL = 30 mg/(kg b.w. · day)].

Available limited data on the genotoxicity of medium chain CPs indicate that these compounds are not mutagenic in bacterial assays *in vitro* with or without metabolic activation (Birtley *et al.*, 1980). They have been negative in *in vitro* assays of cell transformation (Birtley *et al.*, 1980) and in the only identified *in vivo* study (the complete report of which was not available for this assessment). Oral administration of a medium chain CP did not increase the frequency of chromosomal aberrations in bone marrow cells in rats (Serrone *et al.*, 1987).

Only one reproductive study has been identified in which rats were exposed to a medium chain CP (C₁₄₋₁₇, 52% C1) (IRDC, 1985; Serrone *et al.*, 1987). In this investigation, although there were no dose-related differences in appearance, fertility, body weight gain, food consumption, or reproductive performance in the parental generation, there were adverse effects on body weight and condition, and possibly haematological parameters in the pups at all doses (100 to 6250 ppm) [LOEL = 100 ppm or 5.7 mg/(kg b.w. · day) for the males and 7.2 mg/(kg b.w. · day) for the females]. Observations in pups included bruised areas, decreased activity, laboured breathing, pale discolouration, and/or blood around the orifices. Pup survival was also decreased at doses \geq 1000 ppm in the diet. Observations at necropsy in pups that died during the study

included pale liver, kidneys, and lungs, and blood in the cranial cavity, brain, stomach, and intestines. The authors suggested that these effects were more likely attributable to lactational rather than *in utero* exposure and added that, based on preliminary results from a cross-fostering study, mortality in pups exposed via milk was greater than that in pups exposed only *in utero* (Serrone *et al.*, 1987).

In a series of developmental studies conducted for the Chlorinated Paraffins Manufacturers Toxicology Testing Consortium, the number and location of viable and nonviable fetuses, early and late resorptions, the number of total implantations and corpora lutea, and the incidence of fetal malformations were examined following administration of a medium chain CP (C₁₄₋₁₇, 52% C1) by gavage in corn oil to pregnant Charles River rats on days 6 to 19 of gestation and pregnant Dutch Belted rabbits on days 6 to 27 of gestation. Teratogenic effects were not observed and embryo- or fetotoxic effects were observed only at doses greater than those that were toxic to the mothers [lowest NOAEL in mothers was 30 mg/(kg b.w. · day) in rabbits and in offspring, 100 mg/(kg b.w. · day) in rabbits] (IRDC, 1983b; 1984).

Data were not identified on the neurotoxicity or immunotoxicity of the medium chain chlorinated paraffins.

Long Chain Chlorinated Paraffins (\geq C₁₈) - Following administration of a long chain CP (C₂₃, 40% C1) by gavage in corn oil for 16 days, no compound-related clinical signs or gross pathological effects were observed in F344 rats or B6C3F₁ mice. The no-observed-effect-levels (NOELs) were considered to be the highest doses [3750 mg/(kg b.w. · day) for the rats and 7500 mg/(kg b.w. · day) for the mice (NTP, 1986b; Bucher *et al.*, 1987)]. In 14-day studies in F344 rats conducted by the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, the no-observed-effect-levels (NOELs) were considered to be 3000 mg/(kg b.w. · day) for a long chain CP (C₂₀₋₃₀, 43% C1) administered by gavage in corn oil and 15 000 ppm [1715 mg/(kg b.w. · day)] for another long chain CP (C₂₂₋₂₆, 70% C1) administered in the diet, respectively, based on a lack of observed compound-related effects on clinical signs or organ weights or in the tissues examined microscopically (IRDC, 1981b; 1981c; Serrone *et al.*, 1987).

Based on the results of a well documented, 13-week study, a NOEL for a long chain CP (C₂₃, 43% C1) administered to mice by gavage was reported to be 7500 mg/(kg b.w. · day), based on no effects noted at any dose (Bucher *et al.*, 1987; NTP, 1986b). In rats, the same CP caused a dose-related granulomatous inflammation of the liver in all exposed females [LOEL = 235 mg/(kg b.w. · day)]. Serrone *et al.* (1987) reported similar hepatic lesions in female rats following administration by gavage of another long chain CP (C₂₀₋₃₀, 43% C1). In addition, mild nephrosis was observed in the kidneys of male rats as was mineralization in the kidneys of female rats administered 3750 mg/(kg b.w. · day). [The authors considered the NOEL to be 3750 mg/(kg b.w. · day) for males, though this is more appropriately a NOAEL, based on observed effects in the kidneys.] A NOEL could not be established for the females [LOEL = 100 mg/(kg b.w. · day)]. In similar studies in which a long chain

CP (C₂₂₋₂₆, 70% C1) was administered in the diet, hepatocellular hypertrophy and cytoplasmic fat vacuolation in the liver and increases in serum hepatic enzymes of both sexes were observed at 3750 mg/(kg b.w. · day) [NOEL was 900 mg/(kg b.w. · day)].

In the study conducted by the National Toxicology Program (NTP, 1986b; Bucher *et al.*, 1987), the carcinogenic response following exposure to the long chain CP (C₂₃, 43% C1), administered to rats and mice under identical conditions to those of the short chain CP, was not as clear as that for the short chain CP; however, there were some increases in tumor incidence in both species. Doses administered were 0, 1875, or 3750 mg/(kg b.w. · day) to male rats; 0, 100, 300, or 900 mg/(kg b.w. · day) to female rats; and 0, 2500, or 5000 mg/(kg b.w. · day) to male and female mice. There were no significant differences in survival and clinical signs of toxicity between exposed and control groups in both sexes and species. Mean body weights of rats were similar in exposed and control animals but both male and female mice in the low-dose group gained less weight than those in the control or high-dose groups. There was a statistically significant increase in the incidence of malignant lymphomas in male mice, a marginal (not statistically significant) increase of hepatocellular carcinomas in female mice, and adenomas or carcinomas (in both males and females). There was a positive trend for increased incidence of pheochromocytomas of the adrenal medulla with increased dose in female rats.

The primary non-neoplastic lesion related to administration of this CP included a diffuse lymphohistiocytic inflammation in the liver and in the pancreatic and mesenteric lymph nodes of male and female rats. Splenic congestion was a secondary effect. These lesions occurred earlier in female rats and at lower doses than in male rats [LOAEL = 100 mg/(kg b.w. · day)]. No significant non-neoplastic lesions were attributed to exposure in mice; however, for female mice, 60 to 70% of the early deaths in each group were attributed to utero-ovarian infection and this may have decreased the sensitivity of the study to detect a carcinogenic effect. Under the conditions of these two-year gavage studies, the NTP concluded that there was no evidence of carcinogenicity for male F344/N rats, equivocal evidence of carcinogenicity for female F344/N rats and female B6C3F₁ mice, and clear evidence of carcinogenicity for male B6C3F₁ mice. Members of the NTP Peer Review Panel commented that, although the high viscosity of the vehicle may have prevented administration of maximum tolerated doses (as indicated by the lack of observed effects on survival or body weight gain), the linear increase in liver weight and increases in serum enzyme levels in concurrent six-month and one-year studies in rats indicated achievement of a biologically effective dose.

Available limited data on the genotoxicity of long chain CPs indicate that these compounds are not mutagenic in bacterial assays *in vitro* with or without metabolic activation (Birtley *et al.*, 1980; NTP, 1986b). They have been negative in an *in vitro* assay of cell transformation (ICI, 1982b) and, in the only identified *in vivo* study, the complete report of which was not available for this assessment, oral administration of the long chain CPs did not increase the frequency of chromosomal aberrations in bone marrow cells in rats (Serrone *et al.*, 1987).

In a series of developmental studies conducted for the Chlorinated Paraffins Manufacturers Toxicology Testing Consortium, the number and location of viable and nonviable fetuses, early and late resorptions, the number of total implantations and corpora lutea, and the incidence of fetal malformations were examined following administration of one long chain CP (C₂₀₋₃₀, 43% C1) by gavage in corn oil and another (C₂₂₋₂₆, 70% C1) in 1% carboxymethyl cellulose to pregnant Charles River rats on days 6 to 19 of gestation and pregnant Dutch Belted rabbits on days 6 to 27 of gestation. Teratogenic effects were not observed and embryo- or fetotoxic effects were observed only at doses greater than those that were toxic to the mothers [lowest LOEL in mothers = 100 mg/(kg b.w. · day) in rabbits exposed to the C₂₂₋₂₆, 70% C1 CP; lowest NOEL in offspring = 1000 mg/(kg b.w. · day) in rabbits exposed to the C₂₂₋₂₆, 70% C1 CP] (IRDC, 1983c; 1981d; 1983d; 1982).

Data have not been identified on the neurotoxicity and immunotoxicity of the long chain chlorinated paraffins.

2.4.2 Humans

Epidemiological studies of populations exposed to CPs are not available and data on effects in humans are restricted to poorly documented clinical studies of the potential to induce irritation or sensitization of the skin following dermal application (Dover Chemical Corp., 1975; Howard *et al.*, 1975; English *et al.*, 1986).

2.4.3 Ecotoxicology

No data were identified on the toxicity of any of the chlorinated paraffins to microorganisms, amphibians, reptiles, plants, and terrestrial invertebrates. No field data were found for any terrestrial species and laboratory studies on the acute or chronic effects of chlorinated paraffins are sparse. The relevant studies are described here, with the exception of mammalian data; the effects on laboratory mammals are described in Subsection 2.4.1.

In 1983, the Chlorinated Paraffins Producers Testing Consortium (a consortium of international manufacturers) determined the aquatic toxicity of C₁₀₋₁₃, 58% C1; C₁₄₋₁₉, 52% C1; C₂₀₋₃₀, 42% C1; and C₂₀₋₃₀, 70% C1, to the common mussel (*Mytilus edulis*) and rainbow trout (*Oncorhynchus mykiss*). Further testing was conducted on the most toxic of the four substances, the short chain CP (C₁₀₋₁₃), in several species. The results of several of these studies are discussed here. The chlorinated paraffins were dissolved in acetone before dilution with water in most studies because of their low water solubility. Values for toxicity are based on measured, rather than nominal, concentrations.

Short Chain Chlorinated Paraffins ($\leq C_{13}$) - The species most acutely sensitive to the short chain CP (C₁₀₋₁₃, 58% C1) were daphnids (*Daphnia magna*) and mysid shrimp (*Mysidopsis bahia*) with 96-hour LC₅₀ values of 18 µg/L and 14 µg/L, respectively, in flow-through tests (Thompson and Madeley, 1983a; 1983b). The value for daphnids is based on data presented in the 21-day, chronic study (as opposed to an acute study), where 70% mortality was seen at 25.5 µg/L after three days. In addition, in another

chronic, 14-day, static-renewal study using daphnids, 50% mortality was seen after five days at 10 µg/L.

The sensitivities of the two species of algae tested varied, with the marine diatom *Skeletonema costatum* being more sensitive, having a 96-hour EC₅₀ of 42.3 µg/L for growth. For the freshwater green alga *Selenastrum capricornutum*, the lowest reported EC₅₀ was 1310 µg/L after 10 days (Thompson and Madeley, 1983c; 1983d). Interpretation of the results in algae is complicated by the loss (50 to 80%) of residues from the water during the course of the studies due to sorption to algal cells. In addition, effects noted on the diatom were transient over a 10-day test period, and may have been caused by a decrease in nutrient levels.

Significant chronic adverse effects were noted in the range of 2.4 to 20 µg/L for the freshwater species, daphnids and rainbow trout, and the marine species, common mussels and mysid shrimp. In the 21-day chronic flow-through study on *Daphnia magna*, the percentage of dead offspring per female was significantly increased at 8.9 µg/L, the highest concentration at which adults survived. Although the number of offspring per female appeared to be reduced even at the lowest concentration (i.e., 2.7 µg/L), interpretation of results is complicated due to variability in control results (Thompson and Madeley, 1983a). The toxicity to rainbow trout was demonstrated in a bioconcentration study by Madeley and Maddock (1983a), in which trout were exposed to concentrations of 3.1 and 14.3 µg/L for 168 days. The fish were removed to fresh water for a depuration period of 105 days. Starting at day 63 of depuration, fish which previously had been exposed, began to exhibit behavioural symptoms associated with exposure to high concentrations. By day 69, all fish exposed to the higher concentration had died, as well as 50% of those from the group exposed to the lower concentration. Results from this study indicate that aquatic organisms may require a long exposure period for the toxicity of chlorinated paraffins to be demonstrated, and that based on results of other studies using short exposure periods, toxicity may be underestimated. In an 84-day flow-through test, reduction of mussel growth, as measured by shell length and weight of soft tissues, occurred at 9.3 µg/L, with no significant response at 2.3 µg/L (Thompson and Shillabeer, 1983). In a 28-day chronic flow-through study, mysids were exposed to measured concentrations of between 0.6 and 7.3 µg/L. Although no dose-response curve was established and mortalities in controls exceeded the commonly accepted value of 20%, mortality in mysids exceeded that of controls at all concentrations tested, significantly so at 1.2 and 2.4 µg/L (Thompson and Madeley, 1983b).

Based on the studies previously described, a no-observed-effect-level (NOEL) has not been determined for aquatic organisms, since the lowest level tested (i.e., 0.6 µg/L) did cause effects.

For the terrestrial environment, no acute studies were identified for any species. In a one-generation reproductive study in which mallard ducks (*Anas platyrhynchos*) were fed 28, 166, and 1000 mg/kg-diet of a short chain CP (C₁₀₋₁₃), at the highest dose level

there was a slight decrease in eggshell thickness and 14-day embryo viability (Serrone *et al.*, 1987). The NOEL for this study was, therefore, 166 mg/kg-diet.

Medium Chain Chlorinated Paraffins (C₁₄₋₁₇) - The toxicity over 60 days to common mussels and rainbow trout in a flow-through system was determined for a 52% chlorinated medium chain (C₁₄₋₁₇) chlorinated paraffin. The measured concentrations to which mussels were exposed were 220 and 3800 µg/L, and 1050 and 4800 µg/L for rainbow trout. In both studies, at the higher concentration, some of the chlorinated paraffins were lost from the dispersion due to their low solubility. This loss was not reduced significantly by dissolution in 1000 ppm of acetone. Although there was no mortality at either concentration for either species, reduced filtration activity of the mussels was consistently observed at the higher concentration (Madeley and Thompson, 1983a; Madeley and Maddock, 1983b).

Based on the limited studies available, the acute toxicity of medium chain CPs to birds is low. In a study of the medium chain CP, Cereclor S52, (C₁₄₋₁₇, 52% C1), the acute oral LD₅₀s were >24 606 mg/kg for ring-necked pheasants (*Phasianus colchicus*) and >10 280 mg/kg for mallard ducks. The acute dietary LC₅₀ for the latter species was >24 063 mg/kg-diet (Madeley and Birtley, 1980).

Long Chain Chlorinated Paraffins (≥C₁₈) - As with the medium chain length paraffins, the toxicity over 60 days of two long chain CPs (43% and 70% C1) to common mussels and rainbow trout in a flow-through system was determined. The measured concentrations to which mussels were exposed were 120 and 2200 µg/L for the 43% chlorinated CP, and 460 and 1330 µg/L for the 70% chlorinated CP. In the studies on rainbow trout, the measured concentrations tested were 970 and 4000 µg/L for the 43% chlorinated CP, and 840, 1900, and 3800 µg/L for the 70% chlorinated CP. For all studies, at the higher concentration, some of the chlorinated paraffins were lost from dispersion. Although there was no mortality at any concentration for either species, reduced filtration activity of the mussels was consistently observed at the higher concentration of both substances (Madeley and Thompson, 1983b; 1983c; Madeley and Maddock, 1983c; 1983d).

No relevant data were identified for any terrestrial species.

3.0 Assessment of "Toxic" Under CEPA

3.1 CEPA 11(a) Environment

Chlorinated paraffins are used in relatively large quantities in Canada, with demand being about 3.5 to 4 kt/yr. They are considered persistent as hydrolysis, oxidation, and photolysis are insignificant routes of transformation at ambient temperatures. Bioconcentration factors as high as 139 000 have been measured, and potential for biomagnification exists. Airborne dispersion of chlorinated paraffins has been reported in the United Kingdom and Sweden where monitoring data indicate widespread levels of low contamination in water, sediments, aquatic and terrestrial biota, and even commercial foods (Campbell and McConnell, 1980; Jansson *et al.*, 1993). Data on levels in any medium in the Canadian environment were not identified. Although data do exist for other countries, the relevance of these data could not be assessed due to the lack of information on comparability between Canadian production and that of other countries. As noted in Subsection 2.3.2, the use of modelling to predict environmental concentrations was considered unsuitable.

Short Chain Chlorinated Paraffins ($\leq C_{13}$) - Statistically significant effects were observed in aquatic invertebrate and fish species following chronic exposure to a range of concentrations from about 2.4 to 20 $\mu\text{g/L}$ of a short chain CP (58% C1). Even at the lowest concentration tested, i.e., 0.6 $\mu\text{g/L}$, mortality of mysid shrimp exceeded that in controls. Results also indicate that toxicity may have been underestimated in available studies. Rainbow trout exposed to 14.3 $\mu\text{g/L}$ for 168 days, and then removed to uncontaminated water, began on day 63 of depuration, to exhibit signs similar to those seen following exposure to acutely toxic concentrations. By day 69, all had died, suggesting delayed toxicity, as has been seen for other hydrophobic substances such as tetrachlorodibenzodioxin (TCDD).

Studies are lacking on the effects on terrestrial organisms. For short chain length paraffins, the NOEL for a one-generation reproductive study on mallard ducks was 166 mg/kg-diet.

Medium Chain Chlorinated Paraffins (C_{14-17}) - The toxicity of the medium chain chlorinated paraffins is lower than that of the short chain based on 60-day studies with mussels and rainbow trout. When exposed to a 52% chlorinated medium chain (C_{14-19}) CP, at concentrations of 3800 $\mu\text{g/L}$ (mussels) or 4800 $\mu\text{g/L}$ (rainbow trout), there was no mortality of either species, although reduced filtration activity of the mussels was consistently observed at the higher concentration (Madeley and Thompson, 1983a; Madeley and Maddock, 1983b).

Based on the limited studies available, the acute toxicity of medium chain chlorinated paraffins to birds is low. In a study of Cereclor S52, (C_{14-17} , 52% C1), the acute oral LD_{50} s were >24 606 mg/kg for ring-necked pheasants and >10 280 mg/kg for

mallard ducks. The acute dietary LC₅₀ for mallard ducks was >24 063 mg/kg-diet (Madeley and Birtley, 1980).

Long Chain Chlorinated Paraffins ($\geq C_{10}$) - The toxicities of the long chain chlorinated paraffins are lower than those of the short chain CPs based on 60-day studies using mussels and rainbow trout. When mussels were exposed to concentrations of 2200 $\mu\text{g/L}$ (C_{20-30} , 43% C1) or 1330 $\mu\text{g/L}$ (C_{20-30} , 70% C1), there was no mortality, although reduced filtration activity was consistently observed. Similarly, no mortality was observed in rainbow trout at concentrations of 4000 $\mu\text{g/L}$ (C_{20-30} , 43% C1) or 3800 $\mu\text{g/L}$ (C_{20-30} , 70% C1) (Madeley and Thompson, 1983b; 1983c; Madeley and Maddock, 1983c; 1983d).

No relevant data were identified on the terrestrial toxicity of long chain chlorinated paraffins.

Conclusion - Data were not identified on the concentrations of short, medium, or long chain chlorinated paraffins in the Canadian environment. As such, there are no data with which to compare levels reported as causing adverse effects in biota.

Therefore, it is not possible to assess whether these compounds are "toxic" as defined under Paragraph 11(a) of the *Canadian Environmental Protection Act*.

3.2 CEPA 11(b) Environment on Which Human Life Depends

None of the chlorinated paraffins is volatile. As such, only minor amounts of these compounds are expected to volatilize into the troposphere. Once in the troposphere, their estimated half-lives are short (few days in the summer) since they are subject to attack by hydroxyl radicals. Therefore, chlorinated paraffins are not expected to contribute significantly to depletion of stratospheric ozone or global warming.

On the basis of the available data, chlorinated paraffins are not considered to be "toxic" as defined under Paragraph 11(b) of the *Canadian Environmental Protection Act*.

3.3 CEPA 11(c) Human Life or Health

3.3.1 Population Exposure

Owing to their high octanol:water partition coefficients, it is likely that food is the principal source of exposure of the general population to chlorinated paraffins. However, because of the lack of adequate information on concentrations in environmental media to which humans are exposed and the lack of suitability of available models to estimate such levels (see Subsection 2.3.2), it is not possible to quantitatively estimate the total daily intake of chlorinated paraffins by the general population in Canada.

3.3.2 Effects

Available data on the toxicity of the chlorinated paraffins are limited. Epidemiological studies of exposed populations are not available and data on effects in humans are restricted to poorly documented clinical studies of the potential to induce irritation or sensitization of the skin following dermal application. Investigations of sub-chronic toxicity in experimental animals are available for the short, medium, and long chain CPs, although information on chronic toxicity or carcinogenicity in studies in experimental animals is available for only the short and long chain CPs. In general, results indicate that the target organs are the liver, kidneys, and the thyroid and parathyroid glands and that toxicity is inversely related to chain length and possibly increases with greater degrees of chlorination.

Information on developmental toxicity in experimental animals is available for the short, medium, and long chain CPs. Teratogenic effects have not been observed at dose levels below those that were toxic to the mothers. With the exception of one study using a short chain CP, embryo- and fetotoxic effects have not been observed at doses less than those that were toxic to the mothers. Identified studies of the reproductive toxicity of chlorinated paraffins are restricted to one for a medium chain CP only. The results indicated that suckling pups were more sensitive than those exposed *in utero*. Available data are inadequate to assess the neurotoxicity or immunotoxicity of the CPs.

Short Chain Chlorinated Paraffins ($\leq C_{13}$) - Based on available data, carcinogenicity is potentially the most sensitive endpoint for the assessment of "toxic" for the short chain chlorinated paraffins under CEPA. The first step in evaluating whether short chain CPs are "toxic" as defined under Paragraph 11(c) of CEPA is, therefore, an assessment of the weight of evidence for genotoxic carcinogenicity, an effect for which it is believed there is no threshold.

Though the available information is inadequate to assess the carcinogenicity of short chain CPs in humans, in a well documented carcinogenesis bioassay, there was clear evidence of carcinogenicity of chlorinated paraffins (C_{12} , 60% C_{11}) in B6C3F₁ mice and F344/N rats. It was further specified, however, that the maximum tolerated dose may have been exceeded in male and female rats (NTP, 1986a; Bucher *et al.*, 1987). It should be noted, however, that increases in tumor incidence were observed in rats in the absence of histopathological damage in at least one organ, i.e., the thyroid. Moreover, most of the mortality in exposed male rats occurred after 80 weeks, whereas overall survival in exposed female rats was reasonable compared with that in vehicle controls. The fact that the maximum tolerated dose may have been exceeded has, therefore, probably not significantly jeopardized the validity of the findings. Available data, though limited, also indicate that the short chain CPs are clastogenic and induce cell transformation in *in vitro* assays.

Based on these considerations, the short chain CPs have been classified in Group II ("Probably Carcinogenic to Humans") of the classification scheme developed by the

Bureau of Chemical Hazards for the assessment of "toxic" as defined under Paragraph 11(c) of CEPA (EHD, 1992).

The results of two studies (one for which the published account is only an abstract), indicate that short chain CPs may not be genotoxic but may act as peroxisome proliferators in the induction of liver adenomas in rats based on their lack of effect on unscheduled DNA synthesis but their positive response on cell proliferation following exposure of rats to single doses of a short chain CP up to 2000 mg/kg b.w. (Elcombe *et al.*, 1989; Ashby *et al.*, 1990). However, the pattern of tumor development in the NTP bioassay for short chain chlorinated paraffins is not entirely the same as that of identified epigenetic carcinogens. In addition, short chain chlorinated paraffins have been clastogenic and induced cell transformation in *in vitro* studies, though they have not been clastogenic or mutagenic in a limited number of *in vivo* assays. Therefore, available data are insufficient to conclude that short chain chlorinated paraffins induce any of the observed tumors in an epigenetic manner.

For substances classified in Group II, where data permit, estimated exposure is compared to quantitative estimates of cancer potency in order to characterize risk and provide guidance for further action, such as analysis of options to reduce exposure, under CEPA. However, because of the lack of adequate information on concentrations of short chain chlorinated paraffins in environmental media to which humans are exposed and the lack of suitability of available models to predict levels in the environment, it is not possible to quantitatively estimate the total average daily intake of these compounds by the general population in Canada, or to compare these estimates to quantitative estimates of cancer potency.

Substances classified in Groups I and II on the basis of the weight of evidence of carcinogenicity are considered non-threshold toxicants - substances for which there is some probability of harm for the critical effect at any level of exposure.

Short chain CPs are, therefore, considered to be "toxic" as defined under Paragraph 11(c) of the *Canadian Environmental Protection Act*.

This approach is consistent with the objective that exposure to non-threshold toxicants should be reduced wherever possible and obviates the need to establish an arbitrary "de minimis" level of risk for determination of "toxic" under the Act.

Medium Chain Chlorinated Paraffins (C₁₄₋₁₇) - Information has not been found on chronic toxicity or carcinogenicity of the medium chain chlorinated paraffins in studies in experimental animals. The weight of available limited data indicates that the medium chain CPs are not genotoxic.

Based on these considerations, medium chain CPs have been classified in Group VI ("Unclassifiable with respect to Carcinogenicity in Humans") of the classification scheme for carcinogenicity developed for the assessment of "toxic" under

Paragraph 11(c) of CEPA (EHD, 1992). For compounds classified in Group VI, a Tolerable Daily Intake (TDI) is derived on the basis of division of a no- or lowest-observed-(adverse)-effect-level [NO(A)EL or LO(A)EL] in animal species by an uncertainty factor.

The lowest effect level in the longer term studies of the effects of medium chain CPs was reported in a reproductive bioassay in which rats were exposed to one of three doses of a C₁₄₋₁₇ (52% C1) CP in the diet for 28 days before mating, during mating, and for females, continuously up to postnatal day 21. Pups were also exposed from weaning to 70 days of age (IRDC, 1985). The lowest reported effect level in this study was in exposed pups - at 100 ppm in the diet [5.7 mg/(kg b.w. · day) in males and 7.2 mg/(kg b.w. · day) in females], there was a decrease in body weight gain by day 21 of lactation, an effect which continued after weaning but became less pronounced in males. (Histopathological effects were not observed at this concentration.) These effects appeared to be attributable to lactational rather than to *in utero* exposure.

The lowest reported effect levels in sub-chronic studies are similar to those observed in the reproductive study previously mentioned. In three sub-chronic studies, in which the medium chain CPs were administered in the diet to rats and dogs (Birtley *et al.*, 1980; Serrone *et al.*, 1987), the NO(A)ELs have ranged from 10 to 13 mg/(kg b.w. · day); effects observed at the next highest doses included increases in organ weights (liver and kidney), in serum hepatic enzymes, and in the smooth endoplasmic reticulum of the hepatocytes.

On the basis of these results, a tolerable daily intake (TDI) is conservatively (owing to the shortage of available data) derived as follows:

$$\begin{aligned} \text{TDI} &= \frac{5.7 \text{ mg}(\text{kg b.w.} \cdot \text{day})}{1000} \\ &= 0.006 \text{ mg}/(\text{kg b.w.} \cdot \text{day}) [6 \mu\text{g}/(\text{kg b.w.} \cdot \text{day})] \end{aligned}$$

where:

$$\begin{aligned} 5.7 \text{ mg}/(\text{kg b.w.} \cdot \text{day}) &= \text{the lowest effect level reported to date (reproductive study)} \\ 1000 &= \text{uncertainty factor [x 10 for intraspecies variation; x 10 for interspecies variation; x 10 for lack of data on carcinogenicity and less than chronic study; no uncertainty factor incorporated for LOEL rather than a NO(A)EL owing to the minor nature of the effects observed at this concentration]} \end{aligned}$$

In developmental studies on rats and rabbits, the medium chain CPs have not induced adverse effects at concentrations below those upon which the TDI derived for medium chain CPs is based (IRDC, 1984; 1983b).

Since it is not possible to quantitatively estimate exposure of the general population in Canada to medium chain chlorinated paraffins, the calculated TDI cannot be compared with the estimated total daily intake of these compounds in the general environment in Canada.

Available data are, therefore, considered inadequate to evaluate whether current concentrations of medium chain chlorinated paraffins present in the environment constitute a danger in Canada to human life or health; as a result, it is not possible to assess whether these compounds are "toxic" as defined under Paragraph 11(c) of the Canadian Environmental Protection Act.

Long Chain Chlorinated Paraffins ($\geq C_{18}$) - Based on available data, carcinogenicity is potentially the most sensitive endpoint for the assessment of "toxic" for the long chain chlorinated paraffins under CEPA. Therefore, the first step in evaluating whether long chain CPs are "toxic" as defined under Paragraph 11(c) of CEPA is an assessment of the weight of evidence for genotoxic carcinogenicity, an effect for which it is believed there is no threshold.

Though the available information is inadequate to assess the carcinogenicity of long chain CPs in humans, in a well documented carcinogenesis bioassay in rats and mice, there was no evidence of carcinogenicity for male F344/N rats, there was equivocal evidence of carcinogenicity for female F344/N rats and female B6C3F₁ mice, and there was clear evidence of carcinogenicity for male B6C3F₁ mice (NTP, 1986b). (For female mice, 60 to 70% of the early deaths in each group were attributed to utero-ovarian infection and it was noted that this may have decreased the sensitivity of the study to detect a carcinogenic effect.) The weight of available limited data indicates that the long chain CPs are not genotoxic.

Based on these considerations, the long chain CPs have been classified in Group III ("Possibly Carcinogenic to Humans") of the classification scheme for carcinogenicity developed for the assessment of "toxic" under Paragraph 11(c) of CEPA (EHD, 1992). For compounds classified in Group III, a Tolerable Daily Intake (TDI) is derived on the basis of division of a no- or lowest-observed-(adverse)-effect- level [NO(A)EL or LO(A)EL] in animal species by an uncertainty factor, that takes into account where appropriate, the limited evidence of carcinogenicity.

The lowest dose at which non-neoplastic effects have been observed in the longest term bioassay conducted to date following exposure to the long chain chlorinated paraffins is 100 mg/(kg b.w. · day) (NTP, 1986b; Bucher *et al.*, 1987). At this dose, there was a diffuse lymphohistiocytic inflammation in the liver and in the pancreatic and mesenteric lymph nodes in female rats. Splenic congestion was a secondary effect. In sub-chronic studies, the lowest reported effect level was 100 mg/(kg b.w. · day), which induced increases in liver weight and multifocal granulomatous hepatitis (characterized by inflammatory changes) and necrosis in female rats (Serrone *et al.*, 1987).

On the basis of these data, the TDI for the long chain CPs is derived as follows:

$$\begin{aligned} \text{TDI} &= \frac{[100 \text{ mg}/(\text{kg b.w.} \cdot \text{day})] \times 5/7}{1000} \\ &= 0.071 \text{ mg}/(\text{kg b.w.} \cdot \text{day}) [71 \text{ } \mu\text{g}/(\text{kg b.w.} \cdot \text{day})] \end{aligned}$$

where:

100 mg/(kg b.w. · day) = the lowest effect level reported to date (well documented, two-year carcinogenicity bioassay)

5/7 = conversion of 5 days/week administration to daily exposure

1000 = uncertainty factor (x 10 for intraspecies variation; x 10 for interspecies variation; x 10 for use of a LOAEL rather than a NOAEL; additional factor for limited evidence of carcinogenicity not incorporated since there was no increase in tumor incidence in female rats in the target organ for the non-neoplastic effect on which the LOAEL is based)

In developmental studies in rats and rabbits, the long chain CPs have not induced adverse effects at concentrations below those upon which the TDI derived for long chain CPs is based (IRDC, 1981d; 1982b; 1983c; 1983d).

Since it is not possible to quantitatively estimate exposure of the general population in Canada to long chain chlorinated paraffins, the calculated TDI cannot be compared with the estimated total daily intake of these compounds in the general environment in Canada.

Available data are, therefore, considered inadequate to evaluate whether current concentrations of long chain chlorinated paraffins present in the environment constitute a danger in Canada to human life or health; as a result, it is not possible to assess whether these compounds are "toxic" as defined under Paragraph 11(c) of the *Canadian Environmental Protection Act*.

3.4 Conclusion

Due to their carcinogenicity, short chain chlorinated paraffins are considered to be "toxic" as defined under Paragraph 11(c) of the *Canadian Environmental Protection Act*. Data are considered inadequate to determine whether they are "toxic" as defined under Paragraph 11(a).

Available data are considered inadequate to determine whether medium or long chain chlorinated paraffins are "toxic" as defined under Paragraphs 11(a) and 11(c) of the *Canadian Environmental Protection Act*.

On the basis of available data, short, medium, and long chain chlorinated paraffins are not considered to be "toxic" as defined under Paragraph 11(b) of the *Canadian Environmental Protection Act*.

4.0 Recommendations for Research and Evaluation

Due to the relative persistence of the chlorinated paraffins, their potential for bioaccumulation, observed toxicity of short chain compounds to environmental organisms in experimental studies at concentrations similar to those measured in other countries, and potential carcinogenicity to humans (particularly for the short chain compounds), the first three recommendations are considered to be of high priority. The last two recommendations are considered to be of medium priority.

1. To complete the assessment of whether short, medium, or long chain chlorinated paraffins are "toxic" as defined under Paragraph 11(a) of CEPA, data are required on levels in the aquatic environment (particularly in biota and sediments) around the manufacturing site.
2. The releases of chlorinated paraffins to the environment from industrial sources (particularly metal-working) are not well characterized, but such characterization is needed to guide more widespread monitoring of CPs in the environment. This additional monitoring should be undertaken if estimates of releases show it to be warranted.
3. To enable the assessment of whether the medium or long chain CPs are "toxic" under Paragraph 11(c) of CEPA, development of suitable analytical methods and monitoring of these compounds in environmental media to which humans are exposed (particularly in food and mothers' milk) is required. Such information is also required in order to compare quantitative estimates of cancer potency to estimated total daily intake of the short chain chlorinated paraffins to characterize risk and provide guidance in establishing priorities for further action under CEPA.
4. A carcinogenicity bioassay for the medium chain CPs and additional data on the neurotoxicity and immunotoxicity for all of the CPs are desirable.
5. Additional research is also recommended on the mechanisms by which the short chain CPs induce tumors.

5.0 References

- Ashby, J., P.A. Lefevre, and C.R. Elcombe, "Cell Replication and Unscheduled DNA Synthesis (UDS) Activity of Low Molecular Weight Chlorinated Paraffins in the Rat Liver *In Vivo*", *Mutagenesis*, 5:515-518 (1990).
- Atkinson, R., "Kinetics and Mechanisms of the Gas-phase Reactions of the Hydroxyl Radical with Organic Compounds under Atmospheric Conditions", *Chem. Rev.*, 86:69-201(1986).
- Bengtsson, B.E. and E.B. Ofstad, "Long-term Studies on Uptake and Elimination of Some Chlorinated Paraffins in the Bleak, *Alburnus alburnus*", *Ambio*, 11(1): 38-40 (1982).
- Birtley, R.D.N., D.M. Conning, J.W. Daniel, D.M. Ferguson, E. Longstaff, and A.A.B. Swan, "The Toxicological Effects of Chlorinated Paraffins in Mammals", *Toxicol. and Appl. Pharmacol.*, 54:514-525 (1980).
- Bucher, J.R., R.H. Alison, C.A. Montgomery, J. Huff, J.K. Haseman, D. Farnell, R. Thompson, and J.D. Prejean, "Comparative Toxicity and Carcinogenicity of Two Chlorinated Paraffins in F344/N Rats and B6C3F₁ Mice", *Fund. Appl. Toxicol.*, 9:454-468 (1987).
- Camford Information Services, "Chlorinated Paraffins", CPI Product Profile, Camford Information Services, Don Mills, Ont. (1991).
- Campbell, I. and G. McConnell, "Chlorinated Paraffins and the Environment. 1. Environmental Occurrence", *Environ. Sci. and Technol.*, 14:1209-1214 (1980).
- Cook, P.M., M.K. Walker, D.W. Kuehl, and R.E. Peterson, "Bioaccumulation and Toxicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxins and Related Compounds in Aquatic Ecosystems", *In: Biological Basis for Risk Assessment of Dioxins and Related Compounds*, Banbury Report, Vol.35, M.A. Gallo, R.J. Scheuplein, and C.A. VanderJeijden (eds.), Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pp. 143-167 (1991).
- CPIA, Letter to G. Macek, U.S. Environmental Protection Agency from R.J. Fensterheim, Chlorinated Paraffins Industry Association (January 13, 1992).
- Dover Chemical Corp., "Oral Toxicity of Chlorez 700", Technical Information Report 530, 2 pp. (1975).
- EHD (Environmental Health Directorate), "Approach to the Assessment of 'Toxic' Under Paragraph 11(c) of CEPA", Bureau of Chemical Hazards, Health and Welfare Canada (1992). (Unpubl.)

- Elcombe, C.R., S.C. Watson, A.R. Soames, and J.R. Foster, "Hepatic Effects of Chlorinated Paraffins," *Proc. 5th Int. Cong. of Toxicol.*, Brighton, Abstract 327 (1989).
- English, J.S.C., I. Floulds, I.R. White, and R.J.G. Rycroft, "Allergic Contact Dermatitis from an Epoxy Compound in a Cutting Oil, *Br. J. Dermatol.*, 115 (Suppl. 30):33 (abstract) (1986).
- Environment Canada, "Analysis of Shellfish for Organic and Inorganic Contaminants", Prepared by Zenon Environmental Inc. for Environment Canada, Conservation and Protection Branch, Dartmouth, N.S. (1989).
- Eriksson, P. and J.E. Kihlstrom, "Disturbance of Motor Performance and Thermoregulation in Mice Given Two Commercial Chlorinated Paraffins", *Bull. Environ. Contam. Toxicol.*, 34:205-209 (1985).
- Eriksson, P. and A. Nordberg, "The Effects of DDT, DDOH-palmitic Acid, and a Chlorinated Paraffin on Muscarinic Receptors and the Sodium-dependent Choline Uptake in the Central Nervous System of Immature Mice", *Toxicol. and Appl. Pharmacol.*, 85:121-127(1986).
- Howard, P.H., J. Santodonato, and J. Saxena, "Investigation of Selected Potential Environmental Contaminants: Chlorinated Paraffins", EPA-560/2-75-007 (NTIS Rep. PB-248 634 and NTIS Rep. 243075), 109 pp. (1975).
- ICI (Imperial Chemical Industries Limited), "Cell Transformation Test for Potential Carcinogenicity of Chlorinated Paraffin (58% Chlorination of Short Chain Length n-paraffins)", Imperial Chemical Industries Limited, Nr Macclesfield Cheshire, England, May 14, 1982 (1982a).
- ICI (Imperial Chemical Industries Limited), "Cell Transformation Test for Potential Carcinogenicity of Chlorinated Paraffin (70% Chlorination of Long Chain Length n-paraffins)", Imperial Chemical Industries Limited, Nr Macclesfield Cheshire, England, July 2, 1982 (1982b).
- ICI (Imperial Chemical Industries), Letter to K. Lloyd, Environment Canada from R.A. Zampini, ICI Canada Inc., June 29, 1992 (1992a).
- ICI (Imperial Chemical Industries), Letter to K. Lloyd, Environment Canada, from R.A. Zampini, ICI Canada Inc., May 8, 1992 (1992b).
- IRDC (International Research and Development Corporation), "14-day Oral Toxicity Study in Rats With Chlorinated Paraffin: 58% Chlorination of Short Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-006 (1981a).

- IRDC (International Research and Development Corporation), "14-day Oral Toxicity Study in Rats With Chlorinated Paraffin: 43% Chlorination of Long Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-005 (1981b).
- IRDC (International Research and Development Corporation), "14-day Dietary Range-finding Study in Rats With Chlorinated Paraffin: 70% Chlorination of Long Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-004 (1981c).
- IRDC (International Research and Development Corporation), "Teratology Study in Rabbits With Chlorinated Paraffin: 43% Chlorination of Long Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-030 (1981d).
- IRDC (International Research and Development Corporation), "Teratology Study in Rabbits With Chlorinated Paraffin: 70% Chlorination of Long Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-039 (1982).
- IRDC (International Research and Development Corporation), "Teratology Study in Rabbits With Chlorinated Paraffin: 58% Chlorination of Short Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-031 (1983a).
- IRDC (International Research and Development Corporation), "Teratology Study in Rabbits With Chlorinated Paraffin: 52% Chlorination of Intermediate Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-032 (1983b).
- IRDC (International Research and Development Corporation), "Teratology Study in Rats With Chlorinated Paraffin: 43% Chlorination of Long Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-015 (1983c).
- IRDC (International Research and Development Corporation), "Teratology Study in Rats With Chlorinated Paraffin: 70% Chlorination of Long Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-045 (1983d).
- IRDC (International Research and Development Corporation), "Teratology Study in Rats With Chlorinated Paraffin: 52% Chlorination of Intermediate Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-017 (1984).

- IRDC (International Research and Development Corporation), "Reproduction Range-finding Study in Rats With Chlorinated Paraffin: 52% Chlorination of Intermediate Chain Length n-paraffin", Studies conducted for the Working Party of the Chlorinated Paraffin Manufacturers Toxicology Testing Consortium, Report Number 438-049 (1985).
- Jansson, B., R. Andersson, L. Asplund, A. Bergman, K. Litzén, K. Nylund, L. Reutergardh, U. Sellstrom, U.-B Uvemo, C. Wahlberg, and U. Wideqvist, "Multi-residue Method for the Gas-chromatographic Analysis of Some Polychlorinated and Polybrominated Pollutants in Biological Samples", *Fresenius J. Anal. Chem.*, 340:439-445 (1991).
- Jansson, B., R. Andersson, L. Asplund, K. Litzén, K. Nylund, U. Sellstrom, U.-B Uvemo, C. Wahlberg, and U. Wideqvist, "Chlorinated and Brominated Persistent Organic Compounds in Biological Samples from the Environment", *Environ. Toxicol. Chem.*(1993).(In press)
- KEMI (Swedish National Chemicals Inspectorate), *In: Risk Reduction of Chemicals*, Chapter 9, "Chlorinated Paraffins", pp. 167-187, A Government Commission Report, KEMI Report 1/91, 231 pp.(1991). (English translation of original Swedish report.)
- Lombardo, P., J.L. Dennison, and W.W. Johnson, "Bioaccumulation of Chlorinated Paraffin Residues in Fish Fed Chlorowax 500C", *J. Assoc. of Anal. Chem.*, 58(4):707-710 (1975).
- Mackay, D., S. Paterson, B. Cheung, and W.B. Neely, "Evaluating the Environmental Behaviour of Chemicals With a Level III Fugacity Model", *Chemosphere*, 14:335-374 (1985).
- Madeley, J.R. and R.D.N. Birtley, "Chlorinated Paraffins and the Environment. 2. Aquatic and Avian Toxicology", *Environ. Sci. and Technol.*, 14(10): 1215-1221 (1980).
- Madeley, J.R. and B.G. Maddock, "The Bioconcentration of a Chlorinated Paraffin in the Tissues and Organs of Rainbow Trout (*Salmo gairdneri*), Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2310, October, 1983 (1983a).
- Madeley, J.R. and B.G. Maddock, "Toxicity of a Chlorinated Paraffin to Rainbow Trout Over 60 Days", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2202, May, 1983 (1983b).
- Madeley, J.R. and B.G. Maddock, "Toxicity of a Chlorinated Paraffin to Rainbow Trout Over 60 Days", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BI/B/2201, May, 1983 (1983c).

Madeley, J.R. and B.G. Maddock, "Toxicity of a Chlorinated Paraffin to Rainbow Trout Over 60 Days", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2200, May, 1983 (1983d).

Madeley, J.R. and R.S. Thompson, "Toxicity of Chlorinated Paraffin to Mussels (*Mytilus edulis*) Over 60 Days", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2289, May, 1983 (1983a).

Madeley, J.R. and R.S. Thompson, "Toxicity of Chlorinated Paraffin to Mussels (*Mytilus edulis*) Over 60 Days", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2288, May, 1983 (1983b).

Madeley, J.R. and R.S. Thompson, "Toxicity of Chlorinated Paraffin to Mussels (*Mytilus edulis*) Over 60 Days", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2290, May, 1983 (1983c).

Mitchell, M., "Review of Chlorinated Paraffins", Contract No. KE144-0-6539, Environment Canada (1991).

Mukherjee, A.B., "The Use of Chlorinated Paraffins and their Possible Effects in the Environment", National Board of Waters and the Environment, Helsinki, Finland, Series A 66, 53 pp.(1990).

Muller, M. and P. Schmid, "GC/MS Analysis of Chlorinated Paraffins With Negative Ion Chemical Ionization", *J. High Res. Chrom. Corn.*, 7:33-37 (1984).

Murray, T., M. Frankenberry, D.H. Steele, and R.G. Heath, "Chlorinated Paraffins: A Report on the Findings from Two Field Studies, Sugar Creek, Ohio, Tinkers Creek, Ohio", Vol. 1, Technical Report, U.S. Environmental Protection Agency, EPA/560/5-87/012, 150 pp. (1988).

Myhr, B., D. McGregor, L. Bowers, C. Riach, A.G. Brown, I. Edwards, D. McBride, R. Martin, and W.J. Caspary, "L5178Y Mouse Lymphoma Cell Mutation Assay Results With 41 Compounds", *Environ. Mol. Mutagen.*, 16 (Suppl 18):138-167 (1990).

NTP (The National Toxicology Program), "NTP Technical Report on the Toxicology and Carcinogenesis Studies of Chlorinated Paraffins (C12, 60% chlorine) (CAS No. 63449-39-8) in F344/N Rats and B6C3F₁ Mice (Gavage Studies)", NTP TR 308, NIH Publication No. 86-2564, Research Triangle Park, NC (1986a).

NTP (The National Toxicology Program), "NTP Technical Report on the Toxicology and Carcinogenesis Studies of Chlorinated Paraffins (C23, 43% chlorine) (CAS No. 63449-39-8) in F344IN Rats and B6C3F₁ Mice (Gavage Studies)", NTP TR 305, NIH Publication No. 86-2561, Research Triangle Park, NC (1986b).

- Omori, T., T. Kimura, and T. Kodama, "Bacterial Cometabolic Degradation of Chlorinated Paraffins", *Appl. Microbiol. Biotechnol.*, 25: 553-557 (1987).
- Renberg, L., G. Sundstrom, and K. Sundh-Nygaard, "Partition Coefficients of Organic Chemicals derived from Reversed Phase Thin Layer Chromatography. Evaluation of Methods and Application on Phosphate Esters, Polychlorinated Paraffins and Some PCB-substitutes", *Chemosphere* 9:683-691(1980).
- Renberg, L., M. Tarkpea, and G. Sundstrom, "The Use of the Bivalve *Mytilus edulis* as a Test Organism for Bioconcentration Studies. II. The Bioconcentration of Two ¹⁴C-labelled Chlorinated Paraffins", *Ecotoxicol. and Environ. Safety*, 11(3): 361-372 (1986).
- Schmid, P.P. and M.D. Muller, "Trace Level Detection of Chlorinated Paraffins in Biological and Environmental Samples, Using Gas Chromatography/Mass Spectrometry With Negative-ion Chemical Ionization", *J. Assoc. Off Anal. Chem.*, 68(3): 427-430(1985).
- Serrone, D.M., R.D.N. Birtley, W. Weigand, and R. Millischer, "Toxicology of Chlorinated Paraffins", *Food Chem. Toxicol.*, 25(7):553-562 (1987).
- Sundstrom, G. and L. Renberg, "Bioaccumulation of Chlorinated Paraffins - A Review, In: *Proceedings from the Fourth European Symposium on Organic Micropollutants in the Aquatic Environment*, Vienna, Austria, pp. 230-244 (Oct. 22-24, 1985).
- Sunito, L.R., W.Y. Shiu, D. Mackay, J.N. Seiber, and D. Glotfelty, "Critical Review of Henry's Law Constants for Pesticides", *Rev. Environ. Contam. Toxicol.*, 103:1-59 (1988).
- Thomann, R.V., "Bioaccumulation Model of Organic Chemical Distribution in Aquatic Food Chains", *Environ. Sci. Technol.*, 23:699-707 (1989).
- Thompson, R.S. and J.R. Madeley, "The Acute and Chronic Toxicity of a Chlorinated Paraffin to *Daphnia magna*", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2358, September, 1983 (1983a).
- Thompson, R.W. and J.R. Madeley, "The Acute and Chronic Toxicity of a Chlorinated Paraffin to the Mysid Shrimp (*Mysidopsis bahia*)", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2373, September, 1983 (1983b).
- Thompson, R.S. and J.R. Madeley, "Toxicity of a Chlorinated Paraffin to the Green Algae *Selenastrum capricornutum*", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2321, June, 1983 (1983c).

Thompson, R.S. and J.R. Madeley, "Toxicity of a Chlorinated Paraffin to the Marine Algae *Skeletonema costatum*", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2328, July, 1983 (1983d).

Thompson, R.S. and N. Shillabeer, "Effect of a Chlorinated Paraffin on the Growth of Mussels (*Mytilus edulis*)", Imperial Chemical Industries PLC, Devon, England, Brixham Report No. BL/B/2331, August, 1983 (1983).