IPCS International Programme on Chemical Safety

Environmental Health Criteria 93

Chlorophenols Other Than Pentachlorophenol

Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization

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World Health Organization
Geneva, 1989

The International Programme on Chemical Safety (IPCS) is a joint venture of the United Nations Environment Programme, the International Labour Organisation, and the World Health Organization. The main objective of the IPCS is to carry out and disseminate evaluations of the effects of chemicals on human health and the quality of the environment. Supporting activities include the development of epidemiological, experimental laboratory, and risk-assessment methods that could produce internationally comparable results, and the development of manpower in the field of toxicology. Other activities carried out by the IPCS include the development of know-how for coping with chemical accidents, coordination of laboratory testing and epidemiological studies, and promotion of research on the mechanisms of the biological action of chemicals.

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NOTE TO READERS OF THE CRITERIA DOCUMENTS

Every effort has been made to present information in the criteria documents as accurately as possible without unduly delaying their publication. In the interest of all users of the Environmental Health Criteria documents, readers are kindly requested to communicate any errors that may have occurred to the Manager of the International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda, which will appear in subsequent volumes.

* * *

A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Palais des Nations, 1211 Geneva 10, Switzerland (Telephone no. 7988400–7985850).

ENVIRONMENTAL HEALTH CRITERIA FOR CHLOROPHENOLS OTHER THAN PENTACHLOROPHENOL

A WHO Task Group on Environmental Health Criteria for Chlorophenols other than Pentachlorophenol met at the Monitoring and Assessment Research Centre, London, United Kingdom, on 21–25 March, 1988. Dr M. Hutton opened the meeting and welcomed the members on behalf of the host institute and on behalf of the United Kingdom Department of Health and Social Security, who sponsored the meeting. Dr G.C. Becking addressed the meeting on behalf of the three Cooperating Organizations of the IPCS (UNEP, ILO, and WHO). The Task Group reviewed and revised the draft criteria document and made an evaluation of the risks for human health and the environment from exposure to chlorophenols other than pentachlorophenol.

The drafts of this document were prepared by Mr R. NEWHOOK and Dr A. GILMAN, Health Protection Branch, Ottawa, Canada. Dr G. BECKING, IPCS Interregional Research Unit, was responsible for the overall scientific content of the document and Mrs M.O. HEAD, Oxford, England, for the editing.

The efforts of all who helped in the preparation and finalization of the document are gratefully acknowledged.

* * *

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1. SUMMARY

1.1 Identity, Physical and Chemical Properties, Analytical Methods

Chlorophenols (CPs) are organic chemicals formed from phenol (1-hydroxybenzene) by substitution in the phenol ring with one or more atoms of chlorine. Nineteen congeners are possible, ranging from monochlorophenols to the fully chlorinated pentachlorophenol (PCB). Chlorophenols, particularly trichlorophenols (T_3CP), tetrachlorophenols (T_4CP), and PCP, are also available as sodium or potassium salts.

Chlorophenols are solids at room temperature, except for 2-MCP, which is a liquid. The aqueous solubility of chlorophenols is low, but the sodium or potassium salts of chlorophenols are up to four orders of magnitude more soluble in water than the parent compounds. The acidity of chlorophenols increases as the number of chlorine substitutions increases. The *n*-octanol/water partition coefficients of chlorophenols increase with chlorination, indicating a propensity for the higher chlorophenols to bioaccumulate. Taste and odour thresholds are quite low.

Technical grade chlorophenol products are heterogeneous mixtures of chlorophenols, unreacted precursors, and a variety of dimeric microcontaminants. As a result of the semiquantitative nature of the reaction of chlorine with molten phenol, commercial formulations of chlorophenols contain substantial quantities of other chlorophenols. When the alkaline hydrolysis of chlorobenzenes is used to manufacture chlorophenols, the technical product can contain unreacted chlorobenzene.

A number of other compounds are present as microcontaminants in technical tri- and tetrachlorophenol preparations, as a result of the elevated reaction temperatures used. These include the polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), polychlorinated phenoxyphenols ("predioxins"), polychlorinated diphenyl ethers, polychlorinated benzenes, and polychlorinated biphenyls. Lower chlorophenol preparations do not contain detectable levels of dioxins, presumably because their manufacture does not occur at sufficiently high temperatures. Tri- and tetrachloro-dibenzo-*p*-dioxins predominate in T_3CP formulations, while the hexa, hepta, and octa congeners are the major PCDD contaminants in technical T_4CP and PCP. 2,3,7,8-Tetra-chlorodibenzo-*p*-dioxin (2,3,7,8-TCDD) occurs primarily as a contaminant of 2,4,5,-T_3CP, though it is present at low

μg/litre concentrations in T_4CP, PCP, and Na-PCP. Chlorophenol formulations contain a similar array of PCDFs. Phenoxyphenols may comprise as much as 1–5% of the formulation.

A large number of sampling and analytical methods have been developed for the determination of chlorophenols in different media. Sensitive methods, such as gas chromatography, high-performance liquid chromatography, and mass spectrometry are increasingly used.

1.2 Sources of Human and Environmental Exposure

1.2.1 Production figures

Recent data on production levels of chlorophenols other than PCP are not readily available. Around 1975, the combined global production of all chlorophenols approached 200 million kg; slightly more than half of this quantity consisted of non-PCP chlorophenols, primarily 2,4-dichlorophenol (2,4-DCP), 2,4,5-trichlorophenol (2,4,5-T_3CP), and 2,3,4,6-tetrachlorophenol (2,3,4,6-T_4CP). Consumption has since declined in some countries as a consequence of health-based concerns (particularly for 2,4,5-T_3CP), and the use of alternative wood preservatives. Some European countries and the USA are major producers and consumers of chlorophenols.

1.2.2 Manufacturing processes

The compounds 2-MCP, 4-MCP, 2,4-DCP, 2,3,4-T_3CP, 2,4,6-T_3CP, 2,3,4,6-T_4CP, and PCP have been made by direct stepwise chlorination of phenol or lower chlorinated phenols at a high temperature; a catalyst is necessary if the last two chlorophenols are being produced. Alternatively, some chlorophenols (2,5-DCP, 3,4-DCP, 2,4,5-T_3CP, 2,3,4,5-T_4CP and PCP) can be produced by the alkaline hydrolysis of the appropriate chlorobenzene.

Both methods yield contaminants that are themselves potential health hazards, including polychlorinated dibenzo-*p*-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs), and 2-phenoxyphenols.

1.2.3 Uses

Chlorophenols are toxic for a wide range of organisms, a property that accounts for many of their uses. Large quantities of higher chlorophenols are used in pressure treatment in the wood preservation industry;

in addition, substantial amounts of the sodium salts of T_4CP, PCP, and T_3CP are used to surface-treat fresh-cut logs and lumber against sapstain fungi and surface mould. Large quantities of lower chlorophenols serve as intermediates in the production of pesticides, such as T_4CP, PCP, 2,4-D, and 2,4,5-T. The use of 2,4,5-T has been discontinued in a number of countries. Lesser amounts of chlorophenols are used as wood preservatives in agricultural and domestic applications, and as additives to inhibit microbial growth in a wide array of products, such as adhesives, oils, textiles, and pharmaceutical products.

1.2.4 Waste disposal

As a result of process design, the quantities of chlorophenolic wastes generated are reportedly small. Available treatment methods for such waste should prove satisfactory, if they are carefully applied. Gravity separation is the primary treatment method most often used to recover oil and the associated chlorophenol for recycling and treatment. Organisms during secondary treatment degrade roughly 90% of most chlorophenol waste, provided that they are acclimated to the waste, and precautions are taken against shock loadings. Adsorption on activated carbon as a final clean-up step removes almost 100% of remaining waste chlorophenols in waste-streams. Incineration appears to be an effective means of disposal, if the temperatures are high enough and residence times long enough to ensure complete combustion and prevent the formation of PCDDs and PCDFs in the incinerator.

1.2.5 Release of chlorophenols into the environment

Patterns of losses to the environment appear similar in most industrialized countries. The majority of chlorophenol wastes are released in spills and leaching from treated lumber (PCP, NaPCP, NaT_4CP), and as contaminants or breakdown products of agricultural pesticides (2,4-DCP, 2,4,5-T_3CP). Substantial amounts of chlorophenol wastes (NaT_4CP, NaPCP) are released from sawmills, planer mills, and the incineration of wood wastes. Significant amounts of chlorophenols can be formed and subsequently released into the environment from the chlorine bleaching process in pulp and paper-mills, the chlorination of waste-water and drinking-water, and the incineration of municipal waste. A significant amount of wastes is discharged from manufacturing sites. Losses during storage and transport are negligible. No estimates are available of the quantities of chlorophenols released as a result of the

disinfection of waste-waters with chlorine, volatilization, or domestic uses of products containing these compounds.

1.2.6 Natural sources

While some chlorophenols and related organohalogens occur naturally, as metabolites of certain flora and fauna, these sources are thought to make a negligible contribution to overall environmental levels.

1.3 Environmental Transport, Distribution, and Transformation

Chlorophenols adsorb strongly on acidic soils, and those with a high organic content. Leaching is more significant in basic and mineral soils. Studies to date have not addressed the quantitative contribution of these processes to the transport of chlorophenols *in situ*.

Adsorption appears to play an important role in surface waters. Chlorophenols that are not degraded in the water body are incorporated into the sediments, most likely because they adsorb on sediment particulates. They may persist in sediments for years. However, it is not known how important this process is for lower chlorophenols, since they should be adsorbed to a lesser extent than the T_4CPs and PCP studied to date.

While a large part of the chlorophenols entering natural waters is probably degraded, they are nonetheless fairly persistent and, thus, may be transported considerable distances by water.

Although chlorophenols are principally water and soil contaminants, some atmospheric movement occurs, and low levels of PCP have been found in rain, snow, and outdoor air. No corresponding measurements have been made for other chlorophenols, but it is highly probable that they too are transported in this manner.

1.3.1 Degradation

Chlorophenol residues are removed from the environment by both biological and non-biological degradation. Laboratory studies have shown that ultraviolet radiation can break down chlorophenols in a matter of hours to days, and the shifts in the ratio of PCP to some of its breakdown products *in situ* suggest that this process is important in exposed habitats.

A large number of bacteria and fungi from different habitats are able to degrade chlorophenols in the laboratory, sometimes eliminating tens of mg/litre in a matter of hours or days. Degradation is generally slowest for the higher chlorinated phenols, and for those with a chlorine in the "meta" position. Previous exposure to a given chlorophenol or a related compound enables a microorganism to metabolize it immediately and/or at a faster rate, presumably by inducing the necessary enzymes. In general, anaerobic biodegradation of these compounds is much slower than aerobic metabolism. Considerable overlap appears to exist in the rates of biodegradation of the compounds in different habitats.

But chlorophenols should only persist in environments where the rates of these transformations are minor. The persistence of chlorophenols other than PCP has not been studied under controlled conditions, but spills and applications of PCP as a herbicide reportedly disappear in a matter of weeks or months.

1.3.2 Bioaccumulation

Bioaccumulation of chlorophenols appears to be moderate, and most bioconcentration factors (BCFs) fall roughly between 100 and 1000. The biocentration factor is usually a positive function of the chlorine number, and there are no obvious relationships between it and the type of organism (algae, plants, invertebrates, fish). Once exposure is discontinued, chlorophenols clear rapidly from biota, indicating that the bioaccumulation observed in field studies is the result of long-term exposure rather than persistence.

1.3.3 Effects of physical, chemical, and biological factors on degradation

Both the rate of evaporation and the extent of adsorption of PCP (and undoubtedly other chlorophenols) are inversely related to pH. In contrast, the rates of photolysis of 4-MCP and 2,4-DCP both increase with pH, and shortage of oxygen, inorganic nutrients, or organic matter may all influence the biodegradation rate of various lower chlorophenols. Higher temperatures increase the rates of evaporation, photolysis, and microbial degradation of chlorophenols, although the last process obviously has an upper limit.

1.4 Environmental Levels and Human Exposure

1.4.1 Chlorophenol levels in the environment

Data on levels of chlorophenols other than PCP in the environment are not available for air. Levels of PCP in outdoor air range from 1 to several ng/m^3. Work-place air concentrations of chlorophenols are much higher. Facilities in which chlorophenols are used, such as sawmills, often have air levels of several tens of μg/m^3, while in manufacturing facilities, concentrations may be in the mg/m^3 range.

Residues of all chlorophenol isomers have been found in fresh and marine waters. In relatively undeveloped areas, levels are often undetectable in receiving waters, and only occasionally exceed 1 μg/litre close to industrial sources of chlorophenols. In receiving waters from heavily industrialized regions, ambient levels are somewhat higher, but still median concentrations do not exceed 1 μg/litre, while the maximum concentrations in surface waters and ground waters can reach several μg/litre. As a result of spills, isolated levels as high as 61 000 μg/litre of chlorophenols (T_4CP + PCP) in ground water, and 18 090 μg/litre in surface waters have been reported.

Levels of some chlorophenols in effluents from chemical and wood preservation industries may reach several thousand μg/litre, though typical levels are in the low μg/litre range, and dilution apparently reduces these to the observed low ambient levels.

Chlorophenol concentrations in sediments are generally higher than those in the overlying water. Levels in sediments from waters not receiving large chlorophenol inputs generally contain less than 1 μg of the individual chlorophenols/kg dry sediment. The maximum levels of all chlorophenol isomers in fresh-water sediments in industrialized regions seldom exceed 50 μg/kg. However, in some instances, thousands of μg chlorophenols/kg have been detected in fresh-water sediments adjacent to point sources (spillage sites and effluent discharges).

In waters receiving chlorophenolic wastes, invertebrates generally contain from trace levels to 20 μg of chlorophenols from the surrounding environments/kg wet tissue, though levels approaching 200 μg/kg have been observed in some instances. Fish can contain similar whole-body levels of chlorophenols, usually concentrated in the liver and viscera. For example, liver tissues from sculpins inhabiting polluted waters contained up to 1600 μg/kg wet weight. In birds, muscle tissues exhibited only trace to moderate (50 μg/kg wet weight) levels of chlorophenols, however, higher concentrations have been found in single samples of liver, brain,

kidney, and eggs. For instance, a level of 1017 μg 2,4-DCP/kg (fresh weight) was found in the kidney of an eagle.

1.4.2 Chlorophenol levels in food, drinking-water, and treated wood

Quantities of T_4CP range from trace to several μg/kg in carrots, potatoes (also 2,4-DCP), turnips, cabbages, beets, and raw milk, though contamination from treated wood storage containers can elevate these levels considerably. Recent restrictions on the agricultural use of chlorophenols have reduced this contamination. T_4CP has been detected in poultry, but no reports of residues in other meat have been found.

Drinking-water supplies are characterized by relatively low concentrations of chlorophenols. While a variety of congeners have been detected, these are usually present in the range of 10^{-3} to 10^{-1} μg/litre.

Concentrations of PCP or T_4CP in treated wood are predictably high, and can reach several hundred mg/kg of wood dust or shavings.

1.5 Kinetics and Metabolism

The lower chlorophenols are readily absorbed across the skin of both laboratory animals and human beings. The results of studies on rats further suggest that absorption via the skin is greater for the sodium salts than for the parent molecules (2,3,5,6-T_4CP and its salt were used). Ingested chlorophenols are also readily taken up from the gastrointestinal tract. The absorption of inhaled lower chlorophenols by experimental animals has not been studied.

Experimental animals accumulate chlorophenols mostly in the liver and kidney, and to a lesser extent in the brain, muscle, and fat tissues. The higher levels in the liver and kidney may reflect their greater circulating blood volume, as well as the role these organs play in the detoxification and elimination of these compounds. Related compounds, such as trichlorophenyl acetate, 2,4-D, Nemacide, Silvex, 2,4,5-T, and lindane, yield similar tissue distributions of chlorophenol metabolites.

In the animals studied to date, most chlorophenols were rapidly conjugated to glucuronates or sulfates in the liver. This binding, and also dechlorination and methylation, serve to detoxify these compounds. At present, the only chlorinated phenol that is known to be metabolized to a more toxic substance is 2,3,5,6-T_4CP, which gives rise to tetrachloro-*p*-hydroquinone. The corresponding quinone has been shown to bind covalently to protein and DNA.

Chlorophenols are eliminated by test mammals primarily through the urine (roughly 80–90%), in both free and bound forms. Smaller amounts are eliminated in faecal matter. A single dose of chlorophenols is virtually eliminated within one to several days. Elimination rates appear to be even more rapid for some tissues.

1.6 Effects on Organisms in the Environment

The available information on the effects of chlorophenols in the environment centres primarily on aquatic organisms. Considerable overlap exists in the concentrations that are toxic for bacteria, phytoplankton, plants, invertebrates, and fish, most of the EC_{50} and LC_{50} values falling in the several mg/litre range. Toxicity generally increases with the degree of chlorination of the phenol ring. However, chlorophenols with chlorine in the 3 and 5 positions ("meta" chlorophenols) are often more toxic than expected solely on the basis of their chlorine number. Species-specific sensitivity can override these general patterns. Furthermore, particularly in the case of the higher chlorophenols, acute toxicity is a strong inverse function of pH, reflecting the degree of ionization of the chemical. In long-term studies, sublethal levels of 2,4-DCP reduced both growth and survival of fathead minnows. In one study, exposure to a concentration of only 0.5 μg 2,4,6-T_3CP/litre was fetotoxic in trout.

Fish kills have resulted from PCP spills, some of which have also involved T_4CP. In controlled field studies, exposure to large quantities (100–5000 μg/litre) of chlorophenols (4-MCP, 2,4-DCP, 2,4,6-T_3CP) generally impaired algal primary production and reproduction, altered algal species composition dramatically, and reduced zooplankton biomass and production. These studies shed little light on the hazard, if any, presented by the low-level contamination observed in most environments. The low concentrations of several chlorophenols typically found in moderately contaminated waters have been reported to impair the flavour of fish.

1.7 Effects on Experimental Animals and *In Vitro* Systems

In rats, lethal doses of lower chlorinated phenols resulted in tremors and convulsions (except for T_4CP and some T_3CPs), hypotonia, and, after death, a rapid onset of rigor mortis. Acute LD_{50}s for rats for all lower chlorophenols and routes of administration ranged from 130 to 4000 mg/kg body weight. The range of toxicity of the compounds

generally occurred in the following order: $T_4CPs > MCP > DCPs > T_3CPs$, when the toxicant was administered either orally or by subcutaneous injection. When injected intraperitoneally, the toxicities of MCP, DCPs, and T_3CPs were similar, while T_4CP was 2–3 times more toxic. In studies on dermal exposure, 2,3,5,6-T_4CP was the most toxic of the T_4CP isomers. These variations according to route of administration may reflect differences in the rate of absorption of the compounds. Acute effects are attributable to the parent chlorophenol itself rather than to the microcontaminants.

Some reports have indicated that lower chlorinated phenols cause mild irritation of the eye in rats. This effect increases with the number of chlorine atoms on the phenol ring. Skin sensitization has not been shown for the chlorophenols.

Short-term exposures of rats and mice to 2,4-DCP at hundreds of mg/kg have been consistently associated with increased spleen and liver weights and, in some instances, with haematological or immunological effects. The very few studies concerning exposure to various tri- and tetrachlorophenols have also identified exposure-related changes in the weight or histology of the liver and, in some instances, of the spleen or kidney. In one study, combined pre- and postnatal exposure to 2-MCP and 2,4-DCP resulted in haematological changes in exposed rats, but only 2,4-DCP elicited immune responses.

Several lower chlorophenols appear to be mildly fetotoxic, though the data are inconsistent in this regard. While female rats exposed to 2-MCP, 2,4-DCP, or 2,4,6-T_3CP in the drinking-water produced smaller litters with an increased frequency of stillborn offspring in one study, similar or higher exposures in other studies did not have any effects on these and other reproductive parameters. A dose of 30 mg/kg body weight per day of pure or technical 2,3,4,6-T_4CP delayed ossification of fetal skull bones, but was not embryolethal.

Birth defects did not arise as a result of daily exposure of rats to concentrations of up to 500 mg 2-MCP/litre, 300 mg 2,4-DCP/litre (both in the drinking-water), 1000 mg 2,4,6-T_3CP/kg body weight and 30 mg 2,3,4,6-T_4CP/kg body weight (both by gavage).

Limited information indicates that 2,4,6-T_3CP (in yeast and mammalian test systems) and 2,3,4,6-T_4CP (Chinese hamster cell cultures) elicited weak mutagenic responses, but were not clastogenic. Most of the other chlorophenols that have been tested have been found to be non-mutagenic in the few test systems used (primarily bacterial).

Exposure of rats and mice (both sexes) to 2,4-DCP for 2 years at doses as high as 440 and 1300 mg/kg body weight per day, respectively,

proved negative with respect to carcinogenicity. In a test with a similar design, 2,4,6-T_3CP at doses of up to 10 000 mg/kg body weight per day caused cancer in mice (hepatocellular carcinomas or adenomas) and male rats (lymphomas, leukaemia). The 2,4,6-T_3CP used was commercial grade and was not analysed for impurities, such as PCDDs and PCDFs.

Studies on rats on the carcinogenicity of 2-MCP or 2,4-DCP (500 µg/litre and 300 µg/litre, respectively, for 15–24 months) were inadequate. Some chlorophenols appeared to be promoters (MCPs, 2,4-DCP, and 2,4,5-T_3CP); others did not.

Exposure of female rats to 2,4-DCP in the drinking-water, at 0–300 mg/litre, altered the major immune function in offspring exposed prenatally and postnatally, but not in rats exposed only *in utero*. In contrast, in a similar study, a concentration of 2-MCP as high as 500 mg/litre did not have any adverse effects on the immune systems of rats.

The major effects observed with lethal exposures to chlorophenols indicated a general effect on the nervous system. Long-term studies implicated the liver and kidney as organs that accumulate high concentrations of chlorophenols and are often adversely affected by exposure to chlorophenols, perhaps reflecting their roles in the detoxification and elimination of xenobiotics. On the basis of the suppression of cell-mediated immunity in rats exposed to 2,4-DCP, it can be assumed that the thymus and spleen may be target organs.

The toxicology of chlorophenols is complicated by the presence of PCDD and PCDF microcontaminants in technical grade products. Assessment of toxicity studies with chlorophenols requires a knowledge of the types, levels, and effects of the microcontaminants that are present in the formulation studied, because some PCDDs and PCDFs are extremely toxic.

The major mode of action in the acute toxicity of chlorophenols involves the uncoupling of oxidative phosphorylation and the inhibition of the electron transport system. These effects are related to the number of chlorine atoms on the molecule and to a lesser extent by their positions on the molecule. PCP is 40 times more potent than 2,4-DCP as an uncoupler. The chlorophenate ion is evidently responsible for the uncoupling reaction, while the undissociated molecule causes convulsions.

Other enzyme systems are also inhibited by exposure to chlorophenols *in vitro*, though, in some instances, such inhibition is not observed with *in vivo* exposures.

1.8 Effects on Man

1.8.1 Non-occupational exposure

Low (usually 10 mg/kg) levels of the lower chlorinated phenols are found in the serum, urine, and adipose tissues of the general population. The major identifiable sources of these chlorophenols are food and drinking-water. Chlorophenol levels in the ambient atmosphere have not been measured.

In the only instance of acute exposure of the general population to chlorophenols, an explosion at a manufacturing plant contaminated an area, with a population of 37 000 persons, with sodium hydroxide, 2,4,5-T_3CP, and TCDD. However, the effects, if any, of the released 2,4,5-T_3CP were masked by those of TCDD. Clinical symptoms attributed to TCDD were recorded in the exposed individuals. No toxic effects have been attributed to the low concentrations of chlorophenols typical of most non-occupational exposures. However, undesirable organoleptic effects are produced by chlorophenols at very low concentrations.

1.8.2 Occupational exposure

Worker exposure is a major concern in industries in which chlorophenols are used extensively, as respiratory and dermal absorption of these compounds results in measurable levels in the blood and urine of exposed workers. In the manufacture of chlorophenols, clinical symptoms associated with exposure include eye, nose, and airway irritation, dermatitis, chloracne, and porphyria. Abnormal liver function tests, changes in brain wave activity, and slowed visual reaction time have been reported in association with high-level exposure.

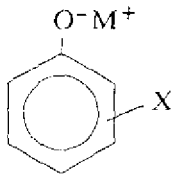
In sawmill workers, Na-T_4CP exposures have caused numerous cases of dermatitis and respiratory irritation. Eye, nose, and airway irritation from exposure to T_3CP have been reported by gas mask testers.

Conflicting results have come from epidemiological studies relating cancer incidence and mortality to chlorophenol exposure in the work place. Associations between soft-tissue sarcoma, malignant lymphoma, and nasal and nasopharyngeal cancer, have been shown in some epidemiological studies, but not in others. Exposure levels have not been accurately determined in these studies, and the conflicting results remain unresolved, at present.

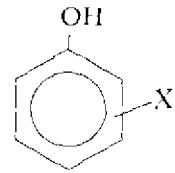
2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

2.1 Identity

Chlorophenols are organic chemicals formed from phenol (1-hydroxybenzene) by substitution in the phenol ring with one or more atoms of chlorine. Nineteen congeners are possible, ranging from monochlorophenols to the fully substituted pentachlorophenol.[a] However, this document does not deal with pentachlorophenol, which has been evaluated previously (WHO, 1987b). The chlorophenols (particularly trichlorophenols and tetrachlorophenols) are also used in the form of sodium or potassium salts. The CAS number, name, chemical (molecular) formula, commercial uses, and common synonyms and trade names for each chlorophenol congener, are presented in Table 1. The general chemical structure for the chlorophenol congeners is shown below.



X = 1-5 chlorine atoms
M^+ = Metal



X = 1-5 chlorine atoms

Technical grade chlorophenols are heterogeneous mixtures of chlorophenol congeners, unreacted precursors, and a variety of dimeric microcontaminants. For example, Cochrane et al. (1983) found that technical 2,4-DCP contained on average, 92.24% 2,4-DCP, 4.48% 2,6-DCP, 1.24% 2,4,6-T3CP, 1.09% 2-MCP, and 0.46% 4-MCP.

[a] The chlorophenol congeners are designated as follows: monochlorophenols (MCP); dichlorophenols (DCP); trichlorophenols (T3CP); tetrachlorophenols (T4CP); pentachlorophenol (PCP). Chlorine substitution is also indicated: 2,4-dichlorophenol (2,4-DCP); 2,4,6-trichlorophenol (2,4,6-T3CP), etc.

Table 1. Information on the identity of chlorophenol congeners[a]

CAS number[b]	Common name	Abbreviation	Molecular formula	Common synonyms[c]	Common trade names
95-57-8	2-monochlorophenol	2-MCP	C_6H_5ClO	*o*-chlorophenol; ortho-chlorophenol; 1-chloro-2-hydroxybenzene	
108-43-0	3-monochlorophenol	3-MCP	C_6H_5ClO	*m*-chlorophenol; meta-chlorophenol; 1-chloro-3-hydroxybenzene	
106-48-9	4-monochlorophenol	4-MCP	C_6H_5ClO	*p*-chlorophenol; para-chlorophenol; 1-chloro-4-hydroxybenzene	
576-24-9	2,3-dichlorophenol	2,3-DCP	$C_6H_4Cl_2O$		
120-83-2	2,4-dichlorophenol	2,4-DCP	$C_6H_4Cl_2O$	NCI-C55345	
583-78-8	2,5-dichlorophenol	2,5-DCP	$C_6H_4Cl_2O$		
87-65-0	2,6-dichlorophenol	2,6-DCP	$C_6H_4Cl_2O$		
95-77-2	3,4-dichlorophenol	3,4-DCP	$C_6H_4Cl_2O$		
591-35-5	3,5-dichlorophenol	3,5-DCP	$C_6H_4Cl_2O$		
15950-66-0	2,3,4-trichlorophenol	2,3,4-T_3CP	$C_6H_3Cl_3O$		
933-78-8	2,3,5-trichlorophenol	2,3,5-T_3CP	$C_6H_3Cl_3O$		
933-75-5	2,3,6-trichlorophenol	2,3,6-T_3CP	$C_6H_3Cl_3O$		
95-95-4	2,4,5-trichlorophenol	2,4,5-T_3CP	$C_6H_3Cl_3O$	NCI-C61187	Collunosol; Dowicide 2; Dowicide B; Nurelle; Preventol 1

Table 1 (contd).

CAS number[b]	Common name	Abbreviation	Molecular formula	Common synonyms[c]	Common trade names
88-06-2	2,4,6-trichlorophenol	2,4,6-T_3CP	$C_6H_3Cl_3O$	NCI-C02904	Dowicide 2S; Omal; Phenachlor
609-19-8	3,4,5-trichlorophenol	3,4,5-T_3CP	$C_6H_3Cl_3O$		
4901-51-3	2,3,4,5-tetrachlorophenol	2,3,4,5-T_4CP	$C_6H_2Cl_4O$		
58-90-2	2,3,4,6-tetrachlorophenol	2,3,4,6-T_4CP	$C_6H_2Cl_4O$		Dowicide 6
935-95-5	2,3,5,6-tetrachlorophenol	2,3,5,6-T_4CP	$C_6H_2Cl_4O$		

[a] From: Jones (1981).
[b] Chemical Abstracts Service Registry number.
[c] From: NIOSH (1983) and Verschueren (1983).

Note: Owing to the planar nature of the phenol ring, other congeners (e.g., 2,4,5,6-T_4CP) are possible, but these are identical in structure to the listed congeners.

Similarly, Levin et al. (1976) examined the composition of 3 commercial chlorophenol formulations used to control fungi in Swedish sawmills and found that Na-2,4,6-T_3CP contained approximately 5% T_4CP, Na-2,3,4,6-T_4CP included 5% T_3CP and 10% PCP, and technical NaPCP contained 5% T_4CP.

Kleinman et al. (1986) determined that commercial Na-T_4CP, used in the USA, contained 3.1% PCP, 20.7% 2,3,4,6-T_4CP, and less than 0.4% of other chlorophenol congeners. These results are typical, showing that roughly 2–12% T_4CP congeners occur in technical PCP formulations, together with trace quantities of several lower chlorophenols (Jones, 1981; Lanouette et al., 1984).

Contamination of technical chlorophenols varies according to the production process used. Because of the elevated reaction temperatures used to produce chlorophenols, a number of compounds are present as microcontaminants in technical chlorophenol preparations prepared by this procedure. These include the polychlorinated dibenzo-*p*-dioxins (PCDDs) polychlorinated dibenzofurans (PCDFs), polychlorinated diphenyl ethers, polychlorinated phenoxyphenols, polychlorinated benzenes, and polychlorinated biphenyls. Where the alkaline hydrolysis of chlorobenzenes is used to manufacture chlorophenols, the technical product also contains the unreacted chlorobenzene. Technical chlorophenol salts usually also contain an excess of sodium or potassium hydroxide.

While commercial MCP and DCP contain little or no detectable PCDDs and PCDFs, presumably because their manufacture does not involve high enough temperatures, other chlorophenols may contain up to many mg/kg of particular PCDDs, and PCDFs (Firestone et al., 1972; Woolson et al., 1972; Levin et al., 1976; Levin & Nilsson, 1977; Rappe et al., 1979; Cedar, 1984; Kleinman et al., 1986). Concentrations of PCDDs and PCDFs in some American and European chlorophenols are provided in Table 2. Tri- and tetrachloro-dibenzo-*p*-dioxins predominate in T_3CP formulations, while the hexa, hepta, and octa congeners are the major PCDD contaminants in technical T_4CP and PCP (Firestone et al., 1972; Rappe et al., 1978a). 2,3,7,8-Tetrachloro-dibenzo-*p*-dioxin (2,3,7,8-TCDD) occurs primarily as a contaminant of 2,4,5-T_3CP (Table 2), though it is present at low µg/kg concentrations in T_4CP, PCP, and NaPCP (Hagenmaier, 1986; Hagenmaier & Brunner, 1987). Predioxins (chlorinated phenoxyphenols) may comprise as much as 5% of technical CP preparations (Levin et al., 1976; Levin & Nilsson, 1977).

Most of the data in Table 2 concern chlorophenol formulations from the 1970s. As a result of modifications in production chemistry, it

is likely that the levels of microcontaminants in current formulations are somewhat lower. Indeed, all of the 1986 tetrachlorophenol products assayed by Agriculture Canada (1987) contained levels of H_6CDD that were several times lower than those in the earlier reports (Table 2).

2.2 Physical and Chemical Properties

Data on some physical and chemical properties of chlorophenols are summarized in Table 3. All of the CPs are solids at room temperature, except for 2-MCP, which is a liquid. They have strong odours that have been described as pungent or medicinal, particularly those of 2-monochlorophenol (2-MCP) and 2,4-dichlorophenol (2,4-DCP). Taste and odour thresholds are so low that Maximum Acceptable Concentrations of chlorophenols in drinking-water are based on organoleptic rather than toxicological criteria (US EPA, 1980c; WHO, 1984).

Although the solubility in water of all chlorophenols is poor, varying from 2.1×10^{-1} mol/litre for 2-MCP to 7.9×10^{-4} mol/litre for 2,3,4,6-T_4CP (US EPA ,1980c) they readily dissolve in a number of organic solvents. In contrast, the sodium or potassium salts of chloropenols (most commonly NaT_3CP, NaT_4CP, and NaPCP) are up to four orders of magnitude more soluble in water than the parent compounds. The acidity of chlorophenols increases as the number of chlorine substitutions increases. Thus, ionization of the higher chlorophenols begins at a lower pH than that of the lower chlorophenols (pH approximately 3.5 versus 7 for PCP and 2-MCP, respectively), with important implications for the interactions between pH and chlorophenol sorption (section 4.1.2.1), or toxicity (section 6.1.1). The *n*-octanol-water partition coefficient of chlorophenols also increases with chlorination, indicating a propensity on the part of the higher chlorophenols to bioaccumulate.

2.3 Conversion Factors

MCP 1 mg/m^3 = 0.190 ppm; 1 ppm = 5.258 mg/m^3
DCP 1 mg/m^3 = 0.150 ppm; 1 ppm = 6.667 mg/m^3
T_3CP 1 mg/m^3 = 0.124 ppm; 1 ppm = 8.076 mg/m^3
T_4CP 1 mg/m^3 = 0.105 ppm; 1 ppm = 9.488 mg/m^3

Table 2. Polychlorodibenzo-*p*-dioxins (PCDDs) and polychlorodibenzofurans (PCDFs) in some American and European mono-, di-, tri-, and tetrachlorophenols[a]

Formulation	PCDD	Concentration (mg/kg)	PCDF	Concentration (mg/kg)	Year sample received
2-MCP	ND		T_4CDF	present[b]	1967
2,4-DCP	ND		ND		1970
2,6-DCP	ND		ND		1970[d]
Na-2,4,5-T_3CP	ND		ND		1967
Na-2,4,5-T_3CP	2,7-D_2CDD 2,3,7,8-T_4CDD[c]	0.72 1.4	ND		1969
2,4,5-T_3CP	1,3,6,8-T_4CDD 2,3,7,8-T_4CDD[c]	0.30 6.2	ND		1969
2,4,5-T_3CP	P_5CDD	1.5	ND		1970
2,4,5-T_3CP	ND		T_3CDF	present[b]	1970
2,4,5-T_3CP	2,3,7,8-T_4CDD	0.07	ND		1970
2,4,6-T_3CP[f]	2,3,7-T_3CDD 1,3,6,8-T_4CDD	93 49	T_4CDF P_5CDF H_6CDF H_7CDF O_8CDF	1.5 17.5 36 4.8	1970[d]

Table 2 (contd).

Formulation	PCDD	Concentration (mg/kg)	PCDF	Concentration (mg/kg)	Year sample received
2,3,4,6-T_4CP	H_6CDD[c]	15	H_5CDF	present[b]	1970[d]
	H_6CDD[c]	14	H_7CDF	present[b]	
	H_6CDD[c]	5.1	O_8CDF		
	O_8CDD	0.17			
2,3,4,6-T_4CP	H_6CDD[c]	4.1	T_4CDF	< 0.5	1967
			P_5CDF	10	(PCDDs);
			H_6CDF	70	1967[d]
			H_7CDF	70	(PCDFs)
			O_8CDF	10	
2,3,4,6-T_4CP[f]	ND		T_4CDF	present[b]	1967[d]
			H_6CDF	present[b]	
2,3,4,6-T_4CP[e]	T_4CDD	0.7	T_4CDF	ca.10	1970[d]
	P_5CDD	5.2	P_5CDF	ca.10	
	H_6CDD	9.5	H_6CDF	ca.60–70	
	H_7CDD	5.6	H_7CDF	ca.60–70	
	O_8CDD	0.7	O_8CDF	ca.10	

Table 2 (contd).

2,3,4,6-T_4CP[e]	T_4CDD	0.4	T_4CDF	ca.10	1970[d]
	P_5CDD	3.5	P_5CDF	ca.10	
	H_6CDD	5.3	H_6CDF	ca.60-70	
	H_7CDD	2.1	H_7CDF	ca.60-70	
	O_8CDD	0.3	O_8CDF	ca.10	
TCP/PCP[g]	H_6CDD	1-4 ($n = 6$)	not reported		1986
	H_7CDD	40-102 ($n = 6$)	not reported		
	O_8CDD	27-55 ($n = 6$)	not reported		
Na-T_4CP/PCP[g]	H_6CDD	N.D.-4 ($n = 13$)	not reported		1986
	H_7CDD	10-119 ($n = 13$)	not reported		
	O_8CDD	5-330 ($n = 13$)	not reported		

[a] Reports of PCDDs from Firestone et al (1972), except where otherwise indicated; quantitative data on PCDF concentrations from Rappe et al. (1978a).
[b] Unquantified. See Firestone et al. (1972).
[c] Confirmed by combined gas chromatography-mass spectrometry.
[d] Not reported.
[e] Rappe et al. (1979).
[f] Rappe et al. (1978b).
[g] Agriculture Canada (1987).

ND: No congener detected; limit of detection from Firestone et al. (1972) is approximately 0.02 ppm for PCDDs, that from Rappe et al. (1978a) is roughly 0.01-0.04 mg/kg (Buser & Bosshardt, 1976).

Table 3. Physical and chemical properties of chlorophenols other than pentachlorophenol[a]

Compound	Relative molecular mass	Density	Boiling point (°C at 760 mm)	Melting point (°C at 760 mm)	Flash point (°C)	Vapour pressure (mm) (temperature)	log *n*-octanol/water partition coefficient
2-MCP	128.56	1.2634 (20/4)	174.9	9	63.9	1 (12.1 °C)	2.15[b]
3-MCP	128.56	1.268 (25/4)	214	33		1 (44.2 °C)	2.50[b]
4-MCP	128.56	1.2651 (30/4)	219.75	43.2–43.7	121.1	1 (49.8 °C)	2.39[b]
2,3-DCP	163		206	57–59			
2,4-DCP	163	1.38 (60/7)	210	45	62	1 (76.5 °C)	3.06[c]
2,5-DCP	163		211 (744 mm)	59			3.20[c]
2,6-DCP	163		219–220 (740 mm)	68–69		1 (59.5 °C)[d]	
3,4-DCP	163		253.5 (767 mm)	68			
3,5-DCP	163		253 (757 mm)	68			
2,3,4-T_3CP	197.45		sublimes	83.5			
2,3,5-T_3CP	197.45		248.5–249.5	62			
2,3,6-T_3CP	197.45		272	58			
2,4,5-T_3CP	197.45	1.68 (25/25)[e]	sublimes (275 mm)	68–70.5		1 (72 °C) 1 (53 °C) 1 (76.5 °C)	3.72[f] 3.62[c]
2,4,6-T_3CP	197.45	1.49 (75/4)[e]	246	69.5	113.9		
3,4,5-T_3CP	197.45		271–277 (746 mm)	101			

Table 3 (contd).

2,3,4,5-T_4CP	231.98	1.67[d]	sublimes	116 –117		
2,3,4,6-T_4CP	231.98	1.6 (60/4)[g]	150 (15 mm)	70	1 (100 °C)	4.10[c]
2,3,5,6-T_4CP	231.98		115			

[a] Principal source: Jones (1981).
[b] From: Fujita et al. (1964).
[c] From: Stockdale & Selwyn (1971).
[d] From: US EPA (1980a).
[e] From: Kozak et al. (1979).
[f] From: Leo et al. (1971).
[g] From: Verschueren (1983).

2.4 Analytical Methods

2.4.1 Sample collection and storage

Proper sampling and sample storage are essential prerequisites for residue determinations, particularly as picogram or nanogram quantities are often encountered in environmental samples. It is, therefore, important to minimize contamination, and to collect representative samples.

Chlorophenols in the air have been collected by drawing air through an absorbent liquid at a given rate for a given period, using absorbents such as potassium carbonate (Dahms & Metzner, 1979) or ethylene glycol (Wyllie et al., 1975). If a significant proportion of the chlorophenols present is likely to bind to container walls, as occurs with water samples, glass containers are preferable to plastic ones (Kozak et al., 1979).

To avoid erroneous determinations, samples should be processed immediately or appropriate steps taken to avoid losses through degradation. If samples are to be stored for an extended length of time after collection, major losses of chlorophenols may occur as a result of photodecomposition, oxidation, biodegradation, or evaporation (section 4). If it is necessary to store samples, changes in residue levels can be reduced by refrigeration or freezing. The American Public Health Association (Greenberg et al., 1985) recommends preserving waste-water samples containing phenolic compounds by acidification with phosphoric acid and treatment with copper sulfate, prior to refrigeration.

2.4.2 Sample preparation and analysis

The early procedures used to analyse for chlorophenols were reviewed by Bevenue & Beckman (1967). Most were colorimetric techniques, the most popular being the 4-aminoantipyrine method; none of the methods was either very specific or sensitive. They are no longer widely used, and are not discussed here. Instead, more sophisticated analytical techniques are being increasingly used, including thin-layer chromatography (TLC), gas chromatography (GC), high-performance liquid chromatography (HPLC), ion exchange chromatography, infrared (IR) and ultraviolet (UV) spectroscopy, mass spectrometry (MS), and mass fragmentography. Table 4 includes examples of the techniques available for the sampling and determination of chlorophenols other than pentachlorophenols. An indication of the sensitivity of each method is given, when available.

Table 4. Analytical methods for chlorophenols other than PCP[a]

Matrix	Chlorophenol	Sampling, extraction	Analytical method	Detection limit/ recovery	Reference
Air	T_4CP	Bubbler collection; absorption in potassium carbonate solution; hexane extraction	Derivatization with acetyl chloride; GC analysis, EC detector	0.05 $\mu g/m^3$	Dahms & Metzner (1979)
Air	3-MCP 4-MCP 2,4-DCP 2,4,5-T_3CP 2,4,6-T_3CP	Polyether-type polyurethane foam; Soxhlet extraction with diethyl ether/ hexane; evaporation; extraction with NaOH, buffered with phosphoric acid	HPLC analysis, EC detector	5 ng	US EPA (1980d)
Water	2-MCP 2,4-DCP 2,4,5-T_3CP 2,4,6-T_3CP	Adsorption on activated carbon; adsorbates extracted with chloroform then sodium hydroxide followed by ethyl ether	Florisil column with anhydrous sodium sulfate for clean-up; GC analysis		Eichelberger et al. (1970)

Table 4 (contd).

Matrix	Chlorophenol	Sampling, extraction	Analytical method	Detection limit/ recovery	Reference
Surface water	2-MCP 2,4-DCP	Adsorption on activated carbon; adsorbates extracted with chloroform then partitioned into acetone	Form pentafluoro-benzyl ether derivatives; GC analysis		Kawahara (1971)
Water	2-MCP 2,4-DCP 2,4,6-T_3CP	Methylene chloride extraction of acidified sample, followed by ion-pair extraction of basic sample with acetonitrile	HPLC analysis, UV_{254} detector	4.2-12.6 ng; 93-97%	Realini (1981)
Air	T_4CP	Collection in 0.1 N sodium hydroxide in impingers, acidification, extraction with toluene	GC analysis, EC detector	0.5 $\mu g/m^3$	Kleinman et al. (1986)
Air	T_3CP T_4CP	Collection in toluene in impingers, extraction into basic borax solution	Acetylation and extraction with hexane; GC analysis, EC detector	2-5 $\mu g/m^3$	Kauppinen & Lindroos (1985)

Table 4 (contd).

Water	4-MCP 2,4,6-T_3CP	Adsorb basic sample on anion exchange resin; extraction of hydrochloric acid and acetone-water eluates with methylene chloride	GC analysis, FI detector; confirmation by GC-MS	80–102%	Chriswell et al. (1975)
Water	T_3CP T_4CP	Adsorb on XAD-4 resin; extract with acetone, hydrochloric acid; concentrate, then dilute with water; partition with sodium sulfate, dry over dichloromethane	Derivatization with diazomethane; dissolve in hexane; HPLC clean-up on Partisil silica column; GC analysis with EC detector	T_3CP: 1 µg/litre, 74.8–77.7%; T_4CP: 0.5 µg/litre, 46.7–61.4%; PCP: 0.5 µg/litre, 72.5–85.1%	Woodrow et al.(1976)
Surface waste, or drinking-water	2,4-DCP 2,6-DCP 2,4,6-T_3CP 2,3,4,6-T_4CP	Addition of sodium phosphate buffer solution, for acid waste-water pH adjustment to 7 with sodium hydroxide	Extract & derivatize by adding hexane containing internal standard (2,6-dibromophenol) and acetic anhydride directly to sample; GC analysis, EC detector	1-2 ng/litre, 98–105%	Abrahamsson & Xie (1983)

Table 4 (contd).

Matrix	Chlorophenol	Sampling, extraction	Analytical method	Detection limit/ recovery	Reference
Urine (mouse)	2,4-DCP 2,4,5-T_3CP 2,4,6-T_3CP	Partitioned into ethanol or benzene, and water, both phases analysed; enzyme hydrolysis of water soluble CP conjugates	Purified by TLC; GC analysis thermal conductivity detector; confirmation by MS		Kurihara & Nakajima (1974)
Urine (human, rat)	T_3CP T_4CP	Benzene extraction from acidified, hydrolysed solution	Der. with diazom ethane; separation on acid alumina column; GC analysis, EC detector; GC-MS confirmation	1 µg/litre, 89.3–97.0%	Edgerton et al. (1979)
Urine (human)	T_4CP	Acidic hydrolysis; hexane/isopropanol extraction; evaporation and redistillation in methanol-water	LC analysis column: Spherisorb ODS; mobile phase: methanol + ammonium carbonate; UV_{254} detector	23 µg/litre, 54.6%	Pekari & Aitio (1982)

Table 4 (contd).

Urine (human)	2-MCP 4-MCP 2,4-DCP 2,6-DCP 2,4,5-T_3CP 2,4,6-T_3CP	Hydrolyse conjugates in acidified sample by boiling; make basic with sodium hydroxide extract with methylene chloride; neutralize, dry with sodium sulfate	Der. with sodium bicarbonate then acetic anhydride extraction methylene chloride; GC analysis, EC and FI detectors; confirmation by MS		Hargesheimer & Coutts (1983)
Blood (human)	3-MCP 4-MCP 2,4-DCP 2,4,5-T_3CP	Hydrolysis with hydrochloric acid extraction with hexane ethyl ether; extraction with sodium hydroxide, buffered with phosphoric acid	HPLC analysis, EC detector	5 ng, 80–100%	US EPA (1980d)

Table 4 (contd).

Matrix	Chlorophenol	Sampling, extraction	Analytical method	Detection limit/ recovery	Reference
Animal tissue (sheep cattle)	2,4-DCP 2,4,5-T_3CP	Optional alkaline digestion; acid hydrolysis; distillation with water; methylene chloride	Der. to trimethylsilyl ether; GC analysis	0.02 mg/kg (2,4-DCP); 0.01 mg/kg, >95% (2,4,5-T_3CP)	Clark et al. (1975)
Sediment and clams	T_4CP	Homogenization; toluene extraction from acidified sample 2,4,6-tribromophenol as internal standard	Derivatization pyrolytic ethylation with triethylsulfonium iodide; GC analysis, EC detector; Confirmation by MS	0.5–25 µg/kg, 76.7–98.8%	Butte et al. (1983)
Fish tissue	2-MCP 2,4-DCP 2,4,6-T_3CP	Gel permeation chromatography to remove lipids, free fatty acids; acid-base extraction	Derivatization with pentafluorobenzyl bromide; silica gel chromatography clean-up; GC analysis, EC detector	2-MCP-47% 2,4-DCP-78% 2,4,6-T_3CP-86% PCP-63%	Stalling et al. (1979)
Meat and poultry livers	2,4-DCP 2,3,4-T_3CP 2,4,5-T_3CP 2,4,6-T_3CP	Alkaline digestion; steam distillation of acidified sample; toluene extraction dry sodium sulfate, evaporate	Derivatization with methyl iodide; GC analysis; EC detector	10 µg/kg, 92–98%	Sackmauerova-Veningerova et al. (1981)

Table 4 (contd).

Muscle (hen)	2,4-DCP	Blended in hexane-sulfuric acid; extraction with NaOH, then hexane	GC analysis, EC detector		Sherman et al. (1972)
Liver (hen)	2,4-DCP	Ground; dried with sodium sulfate eluted with hexane; extraction of eluate with acetonitrile, then hexane; dried with sodium sulfate	Florisil column for clean-up; GC analysis, EC detector		Sherman et al. (1972)
Soil	2-MCP 2,4-DCP 2,4,6-T_3CP	Steam distillation of acidified sample; extraction with toluene dichloromethane eluted through anhydrous sodium sulfate extraction with hexane	GC analysis, EC detector	< 0.1 mg/kg 2-MCP-59%; 2,4-DCP-64%; 2,4,6-T_3CP-70%	Narang et al. (1983)

Table 4 (contd).

Matrix	Chlorophenol	Sampling, extraction	Analytical method	Detection limit/ recovery	Reference
Wood dust	2,3,4,6-T_4CP	Extraction with diethyl ether; evaporation; dissolve in acetone and TLC (silica gel)	Elution from TLC with *n*-hexane; derivatization with diazomethane; GC with Ni^{63} EC detector	200 mg/kg dust 70%	Levin & Nilsson (1977)
Wood dust	2,4,6-T_3CP 2,3,4,6-T_4CP	Pumped through membrane filter; Soxhlet extraction with diethyl ether; evaporate; dissolved in hexane	GC analysis, EC detector		Kauppinen & Lindroos (1985)

[a] GC = gas chromatography.
TLC = thin-layer chromatography.
HPLC = high-performance liquid chromatography.
MS = mass spectrometry.
EC = electron capture detection.
FID = flame ionization detection.

3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

3.1 Natural Occurrence

Some chlorophenols are present in the environment independent of man-made input. Dichlorophenols have been detected in a variety of organisms (Siuda, 1980). 2,4-Dichlorophenol occurs naturally in a *Penicillium* sp., while 2,6-DCP serves as a sex pheromone for several species of tick. A number of related organohalogens are also found in flora and fauna (Arsenault, 1976; Siuda, 1980). However, these sources cannot account for the significant amounts of chlorophenols, particularly the higher chlorinated phenols, found in the environment.

3.2 Man-made Sources

3.2.1 Production levels and processes

3.2.1.1 World production figures

Reliable data on production levels of chlorophenols other than PCP are not readily available. In 1975, the combined global production of all chlorophenols approached 200 million kilograms (Table 5). Slightly more than half consisted of chlorophenols other than PCP, with 2,4-DCP, 2,4,5-T_3CP, and 2,3,4,6-T_4CP predominating. Where commercial use data are available, recent figures indicate that consumption has declined (IARC, 1986). Chlorophenols are used in countries other than those shown in Table 5, but the quantities used are not known. Information on PCP production is presented in WHO (1987b).

3.2.1.2 Manufacturing processes

While most chlorophenols can be produced by several different procedures, only a few methods are actually used in commercial manufacture (Doedens, 1963; Freiter, 1979). Most chlorophenols are made by the direct stepwise chlorination of phenol or lower chlorinated phenols at an elevated temperature. The compounds 2-MCP, 4-MCP, 2,4-DCP, 2,6-DCP, 2,4,6-T_3CP, 2,3,4,6-T_4CP, and PCP are manufactured by this means. The manufacture of T_4CP or PCP requires the use of a catalyst, such as iodine, aluminium chloride ($AlCl_3$), ferric chloride ($FeCl_3$), or antimony chloride ($SbCl_3$). The process is not

Table 5. Production/consumption of chlorophenols other than PCP

Country	Compound	Year	Production/ consumption (kg/year)	Reference
Global	total chlorophenols	1975	1.8×10^8 (P)[a]	Levin & Nilsson (1977)
	non-PCP chlorophenols[b]	1978	0.98×10^8 (P)	Ahlborg & Thunberg (1980)
Canada	total chlorophenols	1976	3.4×10^6 (C)	Jones (1981)
	non-PCP chlorophenols		1.5×10^6 (C)[b]	
	total chlorophenols	1981	$> 5.266 \times 10^6$ (C)	Jones (1984)
		1981	4.000×10^6 (P)	
	non-PCP chlorophenols	1981	$> 3.730 \times 10^6$ (C)[b]	
	tetrachlorophenol and Na-T_4CP	1981	7.86×10^5 (C) 12.44×10^5 (P)	Jones (1984)
	Na-T_3CP	1981	3.0×10^3 (C) 1.0×10^3 (P)	Jones (1984)
	2,4-dichlorophenol	1981	3.700×10^6 (C) 1.850×10^6 (P)	Jones (1984)
	total chlorophenols	1984	3.89×10^6 (S)	Environment Canada (1986)
	non-PCP chlorophenols	1984	4.91×10^5 (S)[b]	
	tetrachlorophenol and Na-T_4CP	1984	4.9×10^5 (S)	Environment Canada (1986)
	2,4,5-trichlorophenol and Na-2,4,5-T_3CP	1984	$< 1.0 \times 10^3$ (S)	Environment Canada (1986)
Europe	monochlorophenols		4.5×10^6 (P)	Krijgsheld & van der Gen (1986)
	2,4-dichlorophenol		9.1×10^6 (P)	
United Kingdom	total chlorophenols	1972	$> 1.14 \times 10^6$ (C)[d]	Ahlborg & Thunberg (1980)

Table 5 (contd.)

USA	total chlorophenols	1976	$>2.421 \times 10^7$ (S,P)[c,d]	Buikema et al. (1979)
	non-PCP chlorophenols	1976	$>1.995 \times 10^6$ (S,P)[b]	Buikema et al. (1979)
	2,4-Dichlorophenol	1976	1.995×10^6 (S)	Buikema et al. (1979)

[a] P = production, C = consumption, S = sales volume.
[b] By difference, from data presented in reference.
[c] Sales approximate consumption, since most use is domestic (Jones, 1981).
[d] A conservative estimate, derived by adding figures for major chlorophenols.

quantitative, with the result that batches of one chlorophenol will usually contain substantial amounts of other CPs (section 2.1).

Alternatively, some chlorophenols are produced by the alkaline hydrolysis of hexachlorobenzene (HCB) or other chlorobenzenes in methanol, ethylene glycol, and other solvents. The compounds 2,5-DCP, 3,4-DCP, 2,4,5-T_3CP, 2,3,4,5-T_4CP, 2,3,5,6-T_4CP, and PCP can be synthesized by this type of reaction (Doedens, 1963; Freiter, 1979).

Both methods may yield contaminants that are themselves potential health hazards, specifically PCDDs, PCDFs, and 2-phenoxyphenols (section 2.1), especially if optimum reaction conditions are not maintained (particularly temperature and pressure) in the production of higher chlorophenols. In addition, chlorophenols derived from the hydrolysis of chlorobenzenes may include substantial amounts of the initial isomer in the final product.

3.2.2 Uses

The uses of commercial chlorophenols are summarized in Table 6. These compounds are biocides, a property that accounts for many of their uses. Chlorophenols, particularly tetra-, and to a lesser extent, trichlorophenols, have been used as bactericides, algicides, molluscicides, acaricides, fungicides, and mould inhibitors, and for less specific uses, such as general antiseptics and disinfectants. Chlorophenols are also used as intermediates in the production of certain herbicides, dyes, and drugs.

At present, use patterns are more restricted than is indicated in Table 6. For example, revisions to Canadian standards for chlorophenol in 1980 resulted in a sharp reduction in use in domestic interiors, agriculture, the leather industry, and as slimicides in the pulp and paper

Table 6. Principal uses and reactions of selected chlorophenols other than PCP [a]

Compound	Principal uses	Other uses
2-chlorophenol	Intermediate for further chlorination to 2,4-dichlorophenol, 2,4,6-trichlorophenol, and pentachlorophenol	Polymer intermediate for fire-retardant varnishes; cotton fabric treatment to provide rot resistance; ingredient in coal processing
4-chlorophenol[b]	Intermediate for higher chlorophenols; intermediate dyes, fungicides, and drugs	
2,4-dichlorophenol	Intermediate for production of 2,4-D and other herbicides; ingredient of antiseptics; starting material for higher chlorophenols	Intermediate for production of Sesone, Nitrofen, Nemacide, Genite-EM-923; raw material for polyester films; mothproofing; miticide
2,4,5-trichlorophenol	Intermediate in manufacture of 2,4,5-T and related herbicides; fungicide, bactericide, algicide	Germicides and ingredients of germicidal soaps
2,4,6-trichloropenol	Precursor for higher CPs; germicide, particularly for preservation of wood, leather, glue, and textiles; intermediate in preparation of insecticides and soap germicides	
2,3,4,6-tetrachlorophenol, and its sodium salt	Fungicide and bactericide for wood preservation; sodium salt is sapstain inhibitor; pesticide	Preservative for latex and leather; preservative in glue for plywood

[a] From: US EPA (1979).
[b] From: US EPA (1980c).

industries. Both the quantities and patterns of use are even more restricted in some countries. For example, in Sweden and Finland, chlorophenols are no longer used, or use is severely restricted in the wood preservation or pulp and paper industries (Ahlborg & Thunberg, 1980; Lindroos et al., 1987).

Most chlorophenols are applied in the form of a chlorophenol-oil mixture, but some are dissolved in a "clean" carrier that can be recovered, such as methylene chloride (Jones, 1981). In contrast, the sodium salts of higher chlorophenols (particularly T_3CP, T_4CP, and PCP) are readily soluble in water.

3.2.2.1 Wood treatment

Large quantities of higher chlorophenols are used in wood preservation (Table 6). In Canada in 1981, most chlorophenol-treated wood was preserved by pressure treatment with pentachlorophenol (Table 7). This compound has been evaluated previously (WHO, 1987b), and will not be covered here.

Substantial amounts of the sodium salts of T_4CP (ca. 13% of total 1981 chlorophenol consumption: Table 7), and lesser amounts of NaT_3CP and NaPCP have been used to protect fresh-cut logs and lumber. These compounds, which are readily soluble in water, are used to surface-treat lumber by dipping or spraying to protect against sapstain fungi or mould. Some plywood mills also use T_4CP to reduce decay and mould, and insect attack. The preservative is usually added to the glue.

3.2.2.2 Agriculture

At one time, chlorophenol-treatment was widely used in agriculture, to prevent wood decay in buildings, food containers, and horticultural timbers. Recently, such chlorophenol applications have been considerably restricted in some countries (section 3.2.2), and as a result, the quantities of non-PCP chlorophenols used in agriculture are minor (Jones, 1981).

3.2.2.3 Domestic

T_4CP is an active ingredient in formulations of PCP used as wood preservatives for homes, and as an additive to paints and stains (Table 6). Sales in Canada for these purposes contribute only a small fraction

Table 7. Canadian use patterns for chlorophenols and their sodium salts in 1981[a]

Use	Product	Consumption[b] (kg x 10^3/year)	% of Total
Wood preservation (pressure treatment)	PCP	1536	25.2
Wood protection (surface treatment)	Na-PCP	32	0.5
	Na-T_4CP	786	12.9
	Na-T_3CP[c]	1	0.02
Intermediates for phenoxy herbicides	2,4-DCP[d]	3700	60.7
Additives in products listed in footnote e	NaPCP	38	0.6
	NaT_3CP[c]	2	0.03
Total		6095	

[a] From: Jones (1984).
[b] Includes chlorophenols present in exports (13.6% of total consumption), principally treated wood products.
[c] Chlorophenols are no longer registered for use in Canada.
[d] 2,4-D is no longer produced domestically, though considerable quantities continue to be imported.
[e] Adhesives, construction materials, fabrics, fibreboard products, finished paper, leather, paper machine felts, photographic solutions, pulp and paper process solutions, rayon emulsions, rubber, rubber gaskets.

to the total PCP market (Jones, 1981) (Table 7) as a result of recent government restrictions on their use (section 3.2.2). T_3CP is used as a general-purpose home antiseptic and as the active ingredient in some throat lozenges. At one time, 4-MCP was found in disinfectants for home, farm, dental, hospital, and veterinary uses, but has been largely replaced by other chemicals (Exon, 1984).

3.2.2.4 Water treatment

Information is lacking on the use of non-PCP chlorophenols in water-treatment applications (Jones, 1981).

3.2.2.5 Additives

Sodium salts of T_3CP and T_4CP have been used to inhibit microbial growth in a diverse array of products (Tables 6 & 7). These applications

make up only a small fraction of the total consumption of chlorophenols (Jones, 1981).

3.2.2.6 Intermediates in industrial syntheses

Production of chlorophenols is stepwise and not quantitative, hence lower chlorophenols are generally recycled within a reactor system, or recycled from other manufacturing processes in the production of the higher chlorinated phenols. The lower chlorophenols also serve as intermediates in the production of other pesticides (Table 6). Large amounts of 2,4-DCP are consumed in the manufacture of the phenoxy herbicide 2,4-D (Table 7), and also as a precursor for the production of the pesticides Sesone, Nitrofen, Nemacide, and Genite-EM-923. 2,4,5-T_3CP is used in the manufacture Ronnel®, 2,4,5-T, and related herbicides, while 4-MCP is used in the production of the germicide 4-chlorophenol-*o*-cresol. Small amounts of lower chlorinated phenols have been used in the manufacture of some dyes and drugs.

3.2.3 Other sources

Chlorophenols are also generated by human activity via several indirect routes. They are formed as by-products of chlorine bleaching in paper-mills, and subsequently released into the environment (Ahlborg & Thunberg, 1980; Xie et al., 1986) (section 5.1.2.1). The chlorination of municipal and industrial wastes, and municipal drinking-water can give rise to mono-, di-, and trichlorophenols in the µg/litre range (NRCC, 1978). At these levels, the taste and odour of water may be affected locally, though the chlorophenol concentrations are well below those that produce any observable toxic effect in test organisms (section 6.1). The incomplete incineration of chlorophenol wastes can release substantial quantities of these compounds into the environment (section 3.4). The lower chlorinated phenols are also formed as a result of the bioconversion of lower chlorinated benzenes and related compounds (Ballschmiter & Scholz, 1980). The contributions of these sources to environmental release or human exposures to chlorophenols are generally not well-defined, and are not considered in subsequent sections.

3.3 Waste Disposal

Waste-waters containing chlorophenols arise from three sources, i.e., the manufacture of chlorophenols, the manufacture of compounds in which chlorophenols are used as intermediates, and wood-treatment facilities. Both manufacturers and regulatory agencies have emphasized appropriate process design, in order to minimize the volume of waste generated, particularly in the treatment of lumber (Richardson, 1978).

Information on the handling of chlorophenol-containing wastes in Canada is limited. In the past, some industries disposed of 2,3,4,6-T_4CP and PCP-contaminated wastes as raw effluent into deep wells, or into lagoons, prior to discharge into the North Saskatchewan River (Jones, 1981). However, most Canadian wood-treatment plants report that they do not have any discharge and are able to dispose of their minimal wastes by incineration, or containment and evaporation in lagoons. Data to confirm the adequacy of such treatments are generally not collected (Richardson, 1978), but they are probably adequate, if applied correctly.

While waste-water treatment plants have been used in only a few large wood-preserving plants and by some chemical manufacturers (US EPA, 1979), their use is increasing in response to environmental concerns. Such methods and their efficiency have been described (US EPA, 1979).

Usually primary treatment is applied only in instances where the chlorophenol in question is dissolved in a carrier oil, when gravity separation tanks are used to recover the oil and associated chlorophenol for subsequent recycling or waste treatment. A few plants also use hay or sand filtration to remove some oil droplets and wood particles (Richardson, 1978). Flocculation is not widely used, because flocculents have proved ineffective or inconsistent in removing chlorophenols (US EPA, 1979).

Chlorophenols are effectively removed by secondary treatment under favourable conditions. Roughly 90% of total phenols were removed from waters containing wastes from the manufacture of phenoxy herbicides in aerated lagoons (US EPA, 1971) or by trickling filter/activated sludge treatments (Mills, 1959). Several laboratory and treatment-plant studies have shown that PCP can be degraded by activated sludge (Dust & Thompson, 1973; Kirsch & Etzel, 1973; Etzel & Kirsch, 1974; Moos et al., 1983; Guthrie et al., 1984; Hickman & Novak, 1984), a fluidized bed reactor (Hakulinen & Salkinoja-Salonen, 1982), and a biofilm reactor (Salkinoja-Salonen et al., 1984). However, of 14 municipal treatment plants surveyed by the US EPA, 8 did not remove

any of the PCP load, while the remainder were considered to remove PCP (6–87%) primarily by adsorption on solids (Hickman & Novak, 1984). Furthermore, degradation by microorganisms is sharply reduced, when chlorophenol concentrations are excessive (Broecker & Zahn, 1977; Reiner et al., 1978; El-Gohary & Nasr, 1984; Salkinoja-Salonen et al., 1984). If secondary treatment facilities are to remove chlorophenols reliably, they must include acclimated organisms, and chlorophenol concentrations must be dilute and fairly stable (Hickman & Novak, 1984). These considerations suggest that such wastes are best handled by a facility designed specifically to treat them, rather than being treated at general-purpose sewage-treatment plants.

Chemical oxidation, using such chemicals as chlorine or potassium permanganate, may also be effective in treating chlorophenol-contaminated wastes. While chlorination of municipal wastes can actually produce mono-, di-, and tri- chlorophenols, they are subsequently oxidized together with higher chlorophenols to compounds that are less toxic and/or more biodegradable (US EPA, 1979; Sithole & Williams, 1986).

Adsorption of chlorophenols on activated carbon is sometimes used as a final clean-up step for waste-waters, though this is feasible only when waste treatment is handled in the same plant from start to finish. Removal of 2,4-DCP (Aly & Faust, 1964) and PCP (Richardson, 1978) approaches 100% using this method.

Incineration has also been used to dispose of chlorophenol wastes, but the available information deals mainly with PCP. A controlled air incinerator destroyed more than 99.99% of PCP in treated wood at combustion temperatures of between 916 and 1032 °C, and yielded no measurable T_4CDD or T_4CDF in the off-gas (Stretz & Vavruska, 1984). However, incinerator temperatures must be high enough and residence times long enough to ensure complete combustion. Rappe et al. (1978b) demonstrated that burning technical T_4CP at low temperatures increased the content of PCDDs. Similarly, low-temperature destruction in hog-fuel or "wigwam" burners fed chlorophenol-contaminated sawdust and wood shavings can lead to the formation of PCDDs and PCDFs (Crosby et al., 1981).

3.4 Losses of Chlorophenols into the Environment

In the absence of information from other countries, releases of chlorophenols into the Canadian environment for 1981 (Jones, 1984) are presented in Table 8 by way of an example. Of the 5.27×10^6 kg of

Table 8. Chlorophenol releases into the Canadian environment in 1981[a]

Source		Quantity (kg x 10^3/year)	
1. Releases in wastes from production sites			
	emissions	3	
	effluents	70	
	solids	-	
	sub-total	>73	
2. Releases in other wastes			
(a) Industrial			
(i) Wood preservation sites			
	liquid	2	
	solids	-	
	incineration (hog-fuel)	-	
	landfill	1	(PCP, T_4CP)
	sub-total	>3	
(ii) Saw-mill/planer mill			
	liquid	21	
	solids	-	
(iii) Incineration (hog-fuel)		272	
Pulp mills/landfill		-	
	sub-total	>293	(NaPCP, NaT_4CP)
(b) Agricultural			
solids (livestock litter)		-	
landfill		-	
(c) Domestic			
solids		-	
incineration (mun.)		-	
landfill		-	
3. Releases during storage and transport (solids and liquids)			
(a) Industrial		3.5	
(b) Agricultural		3.4	
(c) Domestic		0.1	
	sub-total	7.0	
4. Releases *in situ* from treated products (solids and liquids)			
(a) Industrial		618	
(b) Agricultural		370	(2,4-DCP)
(c) Domestic		1	
	sub-total	989	
Grand total		> 1365	

[a] From: Jones (1984).

chlorophenols consumed in Canada in 1984, 1.37×10^6 kg (26%) were eventually released into the environment. A large proportion (less than 28%) of these releases would have been as PCP and NaPCP, but the data compiled in the table do not distinguish these from T_4CP and Na-T_4CP.

In 1981, a significant amount (ca. 5%) of the total releases of chlorophenols in Canada occurred from production sites. Following this estimate, production of all chlorophenols ceased in Canada. However, this route could be a significant source of chlorophenol contamination in countries where they are still manufactured. Releases from plants will include a variety of chlorophenols from the manufacture of chlorophenols and chlorophenol-derived products. A small proportion of these materials reaches the environment after incineration (Table 8), but the bulk of the chlorophenols released from production sites in Canada is diluted and released as untreated effluent.

Losses into the environment during the storage and transport of chlorophenols are small (Table 8), comprising less than 1% of the total production.

The majority (>70%) of the chlorophenols released into the Canadian environment arose from treated products (Table 8). About two-thirds of these came from industrial sources, which were not identified by Jones (1984). Petrochemical drilling fluids contain large amounts of chlorophenols (from 700 to 1400 mg NaPCP/kg), to prevent fermentation of polysaccharides, starch, and polymers (Jones, 1981). Once used, the drilling waste is stored on site, in sumps that are often subject to flooding and washing out. In-service treatment with wood preservatives, principally PCP and its salts, also results in some spillage. Large spills have been responsible for fish kills in waters contaminated in this fashion (Jones, 1981). In addition, unknown, but presumably large, quantities of PCP and T_4CP are leached from treated lumber in storage or in service. The remaining third of the environmental releases, which Jones (1984) identifies as primarily 2,4-DCP, is from agricultural sources. Commercial preparations of pesticides, particularly 2,4-D, 2,4,5-T, and Lindane, contain chlorophenols as contaminants. Furthermore, chlorophenols are among the early degradation products of these widely-used chemicals. Chlorophenols from these sources contaminate soils treated with the pesticides, and runoff from these soils finds its way into adjacent water bodies and ground water.

Much of the remaining input of chlorophenols into the environment occurs in the form of industrial wastes. These comprise roughly 22% of the total chlorophenol releases, primarily as NaT_4CP and NaPCP. Most of these are released in liquid wastes from pulp-mills (where they are

by-products of chlorine bleaching), untreated wastes from sawmills, planer mills, and other facilities where they are used in wood preservation, and during incineration of contaminated sawdust and wood shavings. Losses of other chlorophenols from such commercial uses are negligible (Table 8).

The quantities of chlorophenols lost to the atmosphere by volatilization are not known. Nanogram-per-litre quantities of chlorophenols have been detected in rainfall and snow (Paasivirta et al.,1985), suggesting that significant quantities volatilize or are adsorbed on airborne particulates.

The contributions to the environmental load of chlorophenols from: municipal and industrial chlorination processes, the metabolism of other chlorinated compounds to chlorophenols, and the domestic use of such products as cosmetics, drugs, home-care products, stains, wood preservatives, and pesticides are not known.

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

4.1 Transport and Distribution

4.1.1 Atmospheric movement

While chlorophenols are considered to be primarily water and soil contaminants, atmospheric movement also occurs. Measurable quantities of chlorophenols have been detected in air, rainfall, and snow, sometimes far from obvious point sources (Paasivirta et al., 1985) (section 5.1.1). Furthermore, considerable quantities of chlorophenols are released as part of incinerator emissions. The relative contributions of volatilization and adsorption on particulates to these atmospheric levels are not known.

4.1.1.1 Volatilization

No estimates of the rate of volatilization of chlorophenols in the environment have been published. It appears that losses through this process are minimal in natural waters. If the half-times for volatilization of 2-MCP and 4-MCP from 0.38 cm of still water measured by Chiou et al. (1980) are extrapolated to 1 m depth, the estimated half-times are 395 h and 3421 h, respectively (Krijgsheld & van der Gen, 1986).

Diffusion, a process related to volatilization, does not contribute significantly to the long-range transport of substances in either the soil or aquatic habitats, though it is essential in the local replacement of materials lost through volatilization or breakdown.

4.1.2 Soil movement

4.1.2.1 Adsorption

Environmental transport of chlorophenols, particularly in soils, can be affected by adsorption on particulates. Such deposition is quite variable. Acidic soils bind chlorophenols strongly, while adsorption is minimal under alkaline conditions. Chlorophenols also adsorb on organic matter, with the result that adsorption is strong in organic soils, but low in mineral soils.

Thus, Aly & Faust (1964) found that large amounts of three types of clay were necessary to adsorb small quantities of 2,4-DCP in aqueous

suspensions, even under extremely acidic conditions (pH 3.6 - 4.8). Seip et al. (1986) compared the migration rates of tritiated water and of dilute solutions (12.5–25 μg/litre) of 2,4-DCP, 2,4,6-T_3CP, 2,3,4,6-T_4CP, and PCP through packed soil columns. All of the chlorophenols migrated more slowly than water. Adsorption was moderate in a weakly acid inorganic soil and a basic soil with a higher organic content, while no chlorophenols were detected in the eluate from a soil with both a low pH and a high content of organic matter. In studies by Choi & Aomine (1972, 1974), strongly acidic soils adsorbed PCP, while weakly acidic or neutral soils did not adsorb it at all. Moreover, soils with a high organic content adsorbed PCP strongly, regardless of their pH, while hydrogen peroxide digestion of organic matter reduced apparent adsorption (Choi & Aomine, 1974). Miller & Faust (1973) confirmed that sorption of a number of phenolic compounds on organo-clay was pH-dependent.

It is difficult to assess the impact of adsorption on chlorophenol transport in the environment from the results of the preceding studies. Chlorophenol dynamics observed by Seip et al. (1986) suggest that chlorophenols bound to soils are continually turned over, and that binding sites may be saturated under the appropriate conditions, leading to increased mobility and a decreased residence time of chlorophenols in the soil body.

4.1.2.2 Leaching

In instances when adsorption is minimal, leaching will be an important means of chlorophenol transport in the soil. Most chlorophenols should be carried into ground- and surface-waters from soils that are neutral or alkaline or have a low organic content, or through which material can percolate rapidly. No information has been found on the leaching of the lower chlorophenols, but Kuwatsuka (1972) noted that much of the PCP applied to flooded rice paddies was carried through the soil in solution, and it has been reported by Jones (1981) that Na-PCP leaches readily from soils.

4.1.3 Transport in aquatic environments

While a large fraction of the chlorophenols entering waters is probably degraded *in situ* (section 4.2), they are nonetheless moderately soluble and fairly persistent, and so can be transported considerable distances by water. For example, Fox & Joshi (1984) detected elevated levels of T_4CP and PCP in the surface waters of the Bay of Quinte, Lake

Ontario, as far away as 82 km from the wood-preserving plant where they originated.

Chlorophenols that are not degraded are concentrated in the sediments, perhaps through adsorption on sediment particulates. Schellenberg et al. (1984) determined that sorption of chlorophenols on natural sediments and aquifer materials was a combined function of the pH, the organic carbon content of the potential sorbent, and the partition coefficients (known also as soil adsorption coefficients). Adsorption was quite strong on non-mineral sediments. Xie et al. (1986) observed that the disappearance of chlorophenolic compounds discharged from a sulfate pulp-mill was related to the partition coefficients of the compounds, and that sediment concentrations were quite high near to their source (section 5.1.2.1), suggesting that adsorption strongly influenced the transport of chlorophenolic compounds. It was reported by Eder & Weber (1980) that the concentration factor (relative to water) of chlorophenols in the sediments (38- to 680-fold) and suspended solids (6.3- to 240-fold) of the Weser estuary was inversely related to the degree of ionization of the chlorophenol. In contrast, Kuiper & Hantsveit (1984) reported that both the water and the sediment on the bottom of marine enclosures contained similar levels of 4-MCP and 2,4-DCP; this discrepancy is not obviously attributable to differences in system pH, or the nature of the particulates.

4.2 Degradation and Bioaccumulation

4.2.1 Degradation

As yet, there are few studies addressing the persistence of chlorophenols in the environment.

4.2.1.1 Abiotic degradation

(a) Photodecomposition

Many, if not all, chlorophenol isomers are degraded to some extent by exposure to ultraviolet radiation (UVR). The breakdown most often involves an oxidation reaction that dechlorinates the molecule (Boule et al., 1982), though a variety of reactions have been described.

2,4-DCP in aqueous solution was decomposed in a matter of minutes by irradiation from a UV lamp (Aly & Faust, 1964; Crosby & Tutass, 1966; Nakagawa & Crosby, 1974). The major pathway involved

the degradation of 2,4-dichlorophenol to 4-chlorocatechol, which in turn produced 1,2,4-benzenetriol, and finally a mixture of polyquinoid humic acids (Crosby & Tutass, 1966). A similar sequential degradation was reported for 2,4,5-T_3CP (Crosby & Wong, 1973). Freitag et al. (1982) reported that 65.8% of ^{14}C-2,4,6-T_3CP on silica gel was degraded after 17 h of UVR exposure. No organic by-products were detected, most radioactivity being recovered as carbon dioxide.

The breakdown of chlorophenols is markedly affected by the number and position of chlorine substituents on the molecule. Under UVR, 2,4-DCP degrades to diameric products (Crosby & Tutass, 1966), while 2,5-DCP degrades to 4-resorcinol (Crosby & Wong, 1973). Omura & Matsuura (1971) found that alkaline solutions of monochlorophenols degraded as follows: 2-MCP (82.5% lost in 5 h at 40 °C) to a complex mixture with much resinous material, 3-MCP (70%) to resorcinol, and 4-MCP (55%) to hydroquinone, phenol, and three diphenyls. Aqueous solutions of the three monochlorophenol isomers yielded similarly varied products in studies by Boule et al. (1982). In later work, Boule et al. (1984) determined that among the dichlorophenol congeners, substitution at the ortho and meta positions made the chemical more reactive than para substitution.

Only one study has been reported on whether photolysis significantly reduces concentrations of chlorophenols other than PCP *in situ*. Hwang et al. (1986) concluded that photolysis was the principal degradative pathway (half-life of 3 h or less) for 2,4-DCP, 2,4,5-T_3CP, and PCP, but not 4-MCP, in estuarine surface waters (though they noted that mineralization by other mechanisms was substantially photoinhibited under the experimental conditions). Fox & Joshi (1984) observed an increase in the ratio of T_4CP/PCP in surface waters with increasing distance from a wood-preserving plant discharge, suggesting that substantial photolysis of PCP occurred, but noted that the concentrations were remarkably stable, once the chlorophenols were incorporated into the sediments.

(b) Chemical degradation

There is one report that indicates that chlorophenols may be degraded in the environment by chemical processes. Baker & Mayfield (1980) observed losses of 2-MCP, 4-MCP, and 2,4-DCP from sterile washed silica sand, sterile aerobic soils, non-sterile anaerobic soils, and sterile anaerobic soils. Microbial contamination, photolysis, and volatilization were eliminated as causes. The authors suggested that the

chlorophenols were auto-oxidized, or broken down at catalytic sites, but did not eliminate polymerization as a means of loss. A number of other research workers, using a wide range of chlorophenols, have not detected such abiotic losses (Alexander & Aleem, 1961; Aly & Faust, 1964; Tabak et al., 1964; Boyd & Shelton, 1984).

4.2.1.2 Degradation by microorganisms

Although chlorophenols are quite toxic for microorganisms in general, they are nonetheless readily metabolized by a large number that occur in soils, natural waters, sediments, and sewage sludges. This decomposition is often quite rapid, i.e., completed in a matter of hours or days. For instance, of 206 isolates from a petroleum waste lagoon, 46% were able to degrade chlorophenols as a sole source of carbon after acclimation to the particular chlorophenol (Tabak et al., 1964). Up to 95% of the added 3-MCP and 4-MCP (initially 150 and 300 mg/litre respectively) was consumed in 3–6 days, while the same amount of 2,4-DCP (200 mg/litre) and 2,4,6-T_3CP (initially 300 mg/litre) disappeared in 7–10 days. No breakdown of 2,6-DCP was observed. Similarly, in batch cultures enriched with 50 mg chlorophenol/litre and inoculated with soil, 2-MCP, 4-MCP, 2,4-DCP, and 2,4,6-T_3CP were readily biodegraded and were often removed completely in less than 10 days, while 2,6-DCP was only metabolized in some studies; 3-MCP, 2,5-DCP, 2,3-DCP, 3,4-DCP, 3,5-DCP, 2,4,5-T_3CP, 2,3,4,6-T_4CP and PCP were refractory (Alexander & Aleem, 1961). Using an acclimated, activated sludge derived from soil, Ingols et al. (1966) observed complete ring degradation of the following compounds at 100 mg/litre: 2-MCP in 3 days, 3-MCP in 2 days, 4-MCP in 3 days, 2,4-DCP in 5 days, and 2,4,6-T_3CP in 3 days. As much as 52% of 2,5-DCP disappeared in 4 days. No decomposition of sodium pentachlorophenate occurred. More recently, aerobic microorganisms in clay loam soils were able to degrade most of the 2-MCP, 4-MCP, 2,4-DCP, 2,6-DCP, or 2,4,6-T_3CP present (100 mg/kg) within a few days without a lag phase (Baker & Mayfield, 1980). More than 70% of added 3-MCP, 3,4-DCP, 2,4,5-T_3CP, and PCP disappeared within 80–100 days, while 3,4,5-T_3CP and 2,3,4,5-T_4CP levels were little changed after 160 days.

The results of many other studies have confirmed that most chlorophenols can be metabolized by certain microorganisms in water (Aly & Faust, 1964; Lee & Ryan, 1979; Baker et al., 1980; Blades-Fillmore et al., 1982; Hwang et al., 1986), sediment (Lee & Ryan, 1979; Baker et

al., 1980), soil (Walker, 1954; Loos et al., 1967; Spokes & Walker, 1974; Baker et al., 1980; Pal et al., 1980), and activated sludge (Baird et al., 1974; Pitter, 1976; Pal et al., 1980; Boyd & Shelton, 1984).

While bacteria are most frequently studied as the agents responsible for chlorophenol biotransformation, they are not alone in this capability. Fungi on wood shavings, used as litter for broiler chickens, converted 2,3,4,6-T_4CP to 2,3,4,6-tetrachloroanisole, leading to a musty taint in the chicken flesh (Curtis et al., 1972; Gee & Peel, 1974). The genera *Aspergillus* and *Penicillium* readily degrade chlorophenols. Walker (1973) determined that a yeast isolated from soil and grown on phenol could metabolize 2-MCP, 3-MCP, 4-MCP, and 2,4-DCP, but not 2,6-DCP.

The relative rate of degradation of chlorophenols generally decreases as the number of chlorine atoms on the phenolic ring increases (Alexander & Aleem, 1961; Tabak et al., 1964; Ingols et al., 1966; Baker & Mayfield, 1980). However, it is possible to obtain the reverse result with organisms able to use PCP as the sole carbon source: the KC3 bacterium studied by Chu & Kirsch (1973) grew on 2,3,4,6-T_4CP and 2,4,6-T_3CP, but metabolized the dichlorophenols poorly; the monochlorophenols were not metabolized at all. Rates of biodegradation are further affected by the relative position of the chlorine atoms on the phenolic ring. Compounds with a chlorine in the meta position are generally more stable than those without (Alexander & Aleem, 1961; Chu & Kirsch, 1973; Etzel & Kirsch, 1974; Baker & Mayfield, 1980). The chlorophenolic products of PCP degradation in soils *in vitro* support this hypothesis (Ide et al., 1972).

Microorganisms that have been previously exposed to a compound are usually able to metabolize it immediately when re-exposed, and at a faster rate than unexposed organisms (Walker, 1954; Alexander & Aleem, 1961; Tyler & Finn, 1974; Pal et al., 1980; Blades-Fillmore et al., 1982), presumably because exposure induces the enzymes necessary to metabolize the chlorophenol. Microorganisms not previously acclimated often exhibit a lag time of as much as several days before they begin to degrade the compound (Bollag et al., 1968; Spokes & Walker, 1974; Lee & Ryan, 1979; de Kreuk & Hantsveit, 1981). Similarly, prior exposure to a structurally related compound can facilitate the metabolism of chlorophenols, indicating that the enzymes induced by the original compound are somewhat nonspecific. As noted earlier, PCP-adapted microorganisms utilize T_3CPs and T_4CPs readily (Chu & Kirsch, 1973), while bacteria raised on phenol, lower chlorophenols, or phenoxyacetic acids are able to metabolize various other lower

chlorophenols (Tabak et al., 1964; Loos et al., 1967; Walker, 1973; Spokes & Walker, 1974; Boyd & Shelton, 1984).

Research workers have found little or no anaerobic biodegradation of chlorophenols (Gee & Peel, 1974; Lee & Ryan, 1979; Baker & Mayfield, 1980; Horowitz et al., 1982; Pignatello et al., 1986). The persistence of PCP and T_4CP in sediment cores, several decades old, which were presumably anaerobic, supports these findings (Fox & Joshi, 1984). However, under the right conditions, anaerobic metabolism can be substantial: acclimated anaerobic sludge from a municipal sewage plant degraded 25 mg monochlorophenols/litre in a few days (Boyd & Shelton, 1984).

Only a few studies can be used to compare chlorophenol biodegradation between habitats under conditions that may be readily extrapolated to a natural situation. The *in vitro* aerobic breakdown of 2-MCP, 4-MCP, and 2,4-DCP (100 mg/kg) has been studied in clay loam soil (Baker & Mayfield, 1980; Baker et al., 1980), freshwater sediments (Baker et al., 1980), and streams (Baker et al., 1980) at temperatures ranging from 0 to 23 °C. In soil incubated at 23 °C, at least 70% of added 2-MCP disappeared in 0.5–1.0 days, 4-MCP in 1–2 days, and 2,4-DCP in 7–20 days (Baker & Mayfield, 1980). In contrast, decomposition in sediments was slower: at 20 °C, 2-MCP disappeared in 10–15 days, 4-MCP, in 30 days, and 73% of 2,4-DCP, in 15 –30 days (Baker et al., 1980). Virtually no biological degradation of monochlorophenols occurred in the stream water at 20 °C, but 2,4-DCP levels were reduced by 74% in 10 days at 20 °C. These differences may be related to the favourable conditions for microorganisms that exist in soils and sediments, in which levels of organic matter and particulate surface area are high. Addition of sterile sediments or several inert substances enhanced the degradation of 50 µg 2,4,6-T_3CP/litre in river water (Blades-Fillmore et al., 1982).

In other reports, chlorophenol degradation in water has proceeded more rapidly (eliminated in 1–3 weeks) (de Kreuk & Hantsveit, 1981; Blades-Fillmore et al., 1982; Hwang et al., 1986). It is possible that chlorophenols are generally degraded faster in soils and aerobic sediments than in water but, wherever a suitable combination of microflora and physical and chemical factors occurs, these general differences can be overridden.

In summary, a number of microorganisms from a variety of habitats can readily degrade chlorophenols, especially if previous exposure to these compounds has induced the enzymes necessary for their metabolism. This process is slowest with exposure to the higher

chlorophenols, particularly those that are meta-substituted. The results of incubation studies in the laboratory suggest that biodegradation is most rapid in aerobic soils and sediments, and is reduced in anaerobic or nutrient-poor habitats.

4.2.2 Bioaccumulation

A number of field and laboratory studies have yielded information on the bioaccumulation of the chlorophenols. Most of these have involved aquatic organisms. Although organisms ranging from bacteria to fish generally contain higher levels of chlorophenol residues than the environment at large, the concentrations are not large compared with those of some other chemicals. Most bioconcentration factors (BCFs) fall between 1×10^2 and 1×10^3 (Table 9), and substantial biomagnification is not evident. Ernst & Weber (1978) and Ernst (1979) suggested that *Lanice conchilega* displayed exceptionally high BCFs because of an unusual halogen metabolism (detectable levels of bromophenols were noted, unlike the other invertebrates studied).

The results of most of the studies in which a range of chlorophenols has been surveyed have indicated that bioconcentration is a positive function of chlorine number (Kobayashi et al., 1979; Hattula et al., 1981b). The higher BCF with increasing chlorine substitution most likely results from the high partition coefficient or the lower dissociation constant. Other experimental conditions, such as length of exposure and exposure concentration, may also contribute to the substantial range of BCF values shown in Table 9.

Clearance rates of chlorophenols from biota are rapid, indicating that the bioaccumulation observed in field studies is the result of long-term exposure rather than persistence. Landner et al. (1977) reported that 2,4,6-T3CP was eliminated from rainbow trout livers, three weeks after dosing was discontinued. Similarly, 84-92% of 2,4,5-T3CP was lost from fathead minnows in the first day after exposure (Call et al., 1980), and the half-life for 2-MCP in bluegills was less than 1 day (Barrows et al., 1980).

4.3 Effects of Other Physical, Chemical, or Biological Factors

4.3.1 pH

One of the major factors affecting the transport, breakdown, and toxicity (section 6) of chlorophenols is pH. Because chlorophenols are

Table 9. Bioconcentration estimates for various chlorophenols from field and laboratory data

Organism	Compound	Length of exposure (days)	Bioconcentration factor[a]	Remarks	Reference
Plants					
Oedogonium	2,4,6-T_3CP	36	1720	Aquatic microcosm, 0.5 µg/litre, long-term exposure	Virtanen & Hattula (1982)
Echinodorus	2,4,6-T_3CP	36	1000	Aquatic microcosm, 0.5 µg/litre, long-term exposure	Virtanen & Hattula (1982)
Elodea	2,4,6-T_3CP	36	4460	Aquatic microcosm, 0.5 µg/litre, long-term exposure	Virtanen & Hattula (1982)
Chlorella fusca var. *vacuolate*	2,4,6-T_3CP	1	51	50 µg/litre screening test, as ^{14}C	Freitag et al. (1982)
	2,4,6-T_3CP	1	580	49 µg/litre screening test, as ^{14}C	Korte et al. (1978)
Invertebrates					
Lymnae (adult)	2,4,6-T_3CP	36	3020	Aquatic microcosm, 0.5 µg/litre long-term exposure	Virtanen & Hattula (1982)
Lanice conchilega	2,4,5-T_3CP	indefinite	24 088[b]	Field data	Ernst & Weber (1978)
	2,4,6-T_3CP	indefinite	20 269[b]	Field data	
	2,3,4,5-T_4CP	indefinite	17 625[b]	Field data	
	2,3,4,6 + 2,3,5,6-T_4CP	indefinite	11 163[b]	Field data	

Table 9 (contd).

Organism	Compound	Length of exposure (days)	Bioconcentration factor[a]	Remarks	Reference
Invertebrates (contd).					
Mytilus edulis	2,3,4,6-T_4CP	indefinite	45–60	Field data, receiving waters for dump leachate	Folke et al. (1984)
Fish					
Roach (*Rutilus*)	2,3,4,6-T_4CP	indefinite	200	Field data, pulp-mill inputs	Paasivirta et al. (1985)
Pike (*Esox lucius*)	2,3,4,6-T_4CP	indefinite	150	Field data, pulp-mill inputs	Paasivirta et al. (1985)
Trout (*Salmo trutta*)	2,4-DCP	1	10	1.7 mg/litre (LC_{50})	Hattula et al. (1981b)
	2,3,5-T_3CP	1	12	0.8 mg/litre (LC_{50})	
	2,3,4,6-T_4CP	1	450	0.5 mg/litre (LC_{50})	
Poecilia young	2,4,6-T_3CP	36	1 020	Aquatic microcosm, 0.5 µg/litre long-term exposure	Virtanen & Hattula (1982)
female	2,4,6-T_3CP	36	12 180		
male	2,4,6-T_3CP	36	7 000		
Fathead minnow (*Pimephales promelas*)	2,4,5-T_3CP	28	1900	Aquatic microcosm, 4.8 mg/litre, single addition, 49.3 µg/litre as ^{14}C	Call et al. (1980)
	2,4,5-T_3CP	28	1800		

Table 9 (contd).

Sunfish	2,3,5,6-T_4CP	indefinite		Muscle/field data, Mississippi lake/spill in December, n = 2	Pierce & Victor (1978)
		6 January[d]	79	Muscle/spill in December, n = 2	
		27 April[d]	21		
	2,3,5,6-T_4CP	indefinite		Liver/spill in December, n = 1	Pierce & Victor (1978)
		6 January[d]	962	Liver/spill in December, n = 2	
		27 April[d]	72		
Bluegill (*Lepomis macrochirus*)	2-MCP	28	214	Continuous-flow aquarium, 2-MCP at 9.18 µg/litre, as ^{14}C	Barrows et al. (1980)
Bass	2,3,5,6-T_4CP	indefinite		Muscle/field data, Mississippi lake	Pierce & Victor (1978)
		6 January[d]	218	Spill in December, n = 2	
		27 April[d]	4962	Muscle, n = 2	
Catfish	2,3,5,6-T_4CP	indefinite		Muscle, n = 1	
		6 January[d]	222	Muscle, n = 2	
		27 April[d]	53		
	2,3,5,6-T_4CP	indefinite		Liver, n = 1	
		6 January[d]	8608	Liver, n = 2	
		27 April[d]	1005		
Goldfish	2-MCP	25h	6.4	Static lab. assay, 16 mg/litre[c]	Kobayashi et al. (1979)
	4-MCP	25h	10.1	Static lab. assay, 9 mg/litre[c]	
	2,4-DCP	25h	34	Static lab. assay, 7.8 mg/litre[c]	
	2,4,5-T_3CP	25h	62	Static lab. assay, 1.7 mg/litre[c]	
	2,4,6-T_3CP	25h	20	Static lab. assay, 10.0 mg/litre[c]	
	2,3,4,6-T_4CP	25h	93	Static lab. assay, 0.75 mg/litre[c]	

Table 9 (contd).

Organism	Compound	Length of exposure (days)	Bioconcentration factor[a]	Remarks	Reference
Fish (contd.)					
Golden orfes (*Leuciscus idus melanotus*)	2,4,6-T_3CP	3	310	50 µg/litre, screening test	Freitag et al. (1982)
Golden orfes (*Leuciscus idus melanotus*)	2,4,6-T_3CP	3	250	30 µg/litre, screening test	Korte et al. (1978)

a Ratio of concentration in organism or tissue:water.
b Based on bioconcentration relative to PCP.
c Concentrations near LC_{50} values, but still sublethal.
d Sampling date.

weak acids in aqueous solution, they exist primarily in the molecular form under acidic conditions, while the anion predominates at neutral or basic pH. Since the molecular and ionic forms of chlorophenols react differently, pH affects a variety of processes that in turn influence chlorophenol dynamics. Ionization is further affected by the degree of chlorine saturation of the chlorophenol; in general, higher chlorophenols are increasingly acid. Throughout the pH range characterizing physiological and environmental situations, monochlorophenols are present mainly in their molecular form while, above pH 3.5, PCP is primarily dissociated. No information on the interaction of pH and evaporation of lower chlorophenols was available. In their studies on PCP volatilization, Kloppfer et al. (1982) determined that the half-life for PCP disappearance, through volatilization from their apparatus, was 167 h at pH 3.3 and 3120 h at pH 6. No evaporation was detected at pH8.

Similarly, pH influences particulate sorption phenomena through changes in the molecular form of the chlorophenol. As was discussed in section 4.2, adsorption on soils, sediments, and suspended solids is inversely related to pH.

The rate of the photolysis of chlorophenols is also altered by pH. Aly & Faust (1964) determined that the breakdown of 2,4-DCP in aqueous solution was extremely rapid under alkaline conditions and relatively slow under acidic conditions: approximate half-lives for photolysis at pH values of 4, 7, and 9 were 34, 15, and 2 min, respectively. Similarly, Omura & Matsuura (1971) reported that the rate of photolysis of 4-MCP increased as the pH increased. In addition, pH exerts an influence on the biodegradation of chlorophenols. An activated sludge culture grew well on 2-MCP and 3-MCP at neutral, but not at alkaline pH (Ingols et al., 1966). Tyler & Finn (1974) determined that a *Pseudomonas* species grew best on 2,4-DCP at a pH range of 7.1–7.8.

4.3.2 Lack of oxygen

In general, higher chlorinated phenols are persistent in anaerobic environments, because of the low microbial degradation of chlorophenols under such conditions. (section 4.2.1.2).

4.3.3 Inorganic nutrients

Inorganic nutrients may restrict the rate of chlorophenol biodegradation where a shortage of nutrients limits microbial activity. Striking seasonal variations noted in the rate of 4-MCP degradation in

natural sea water incubated in the laboratory (de Kreuk & Hantsveit, 1981) were not related to microbial biomass, but paralleled the levels of phosphate and nitrate in the samples. *In vitro* addition of nutrients to the sea water stimulated biodegradation. Similar results were reported by Kuiper & Hantsveit (1984).

4.3.4 Organic matter

Like inorganic nutrients, levels of organic matter can influence the microbial breakdown of chlorophenols through the control of microbial biomass and activity. For example, while chlorophenol decomposition was apparent in most soils studied (section 4.2.1.2), it was virtually absent from those containing little or no organic matter (Kuwatsuka, 1972). Similarly, low heterotrophic activity, determined by the low concentrations of organic substances in water (typically mg/kg) relative to those found in soils or sediments (g/kg), may account for differences observed in chlorophenol biodegradation between these environmental compartments (section 4.2.1.2). Organic matter bound to the surface of the soil or sediment particulates may also absorb chlorophenols and thereby affect their transport (sections 4.1.2.1, 4.1.3).

4.3.5 Temperature

Volatilization is a direct function of temperature. In their studies of PCP evaporation, Kloppfer et al. (1982) determined that the half-life for volatilization of PCP was 653 h at 23 °C, 328 h at 30 °C, and 211 h at 40 °C. Photolysis can also be temperature-dependent. Omura & Matsuura (1971) found that higher solution temperatures increased the photodecomposition of 4-MCP. The microbial breakdown of lower chlorophenols as a function of temperature was investigated in water, soil, and sediment by Baker et al. (1980). As expected, biodegradation was higher at 20 °C or 4 °C than at 0 °C. However, high temperatures also limit the microbial decomposition of chlorophenols; Tyler & Finn (1974) found that growth of *Pseudomonas* on 2,4-DCP fell off sharply above 25 °C.

Under some conditions, exposure of chlorophenols to elevated temperatures, such as those used in heating and burning, can lead to the formation of chlorinated dibenzo-*p*-dioxins (PCDDs) and dibenzofurans (PCDFs) (Rappe et al., 1978b). Many PCDDs and PCDFs are extremely persistent in the environment and are toxic for living systems (WHO, in press).

4.4 Persistence

As a consequence of chlorophenol decomposition through photolysis, biodegradation, and perhaps chemical catalysis, virtually all chlorophenol compounds will be eliminated from most environments. Some, notably PCP and the lower chlorophenols with a chlorine in the meta position, will persist for a longer time than others, but even these should eventually be broken down, wherever suitable light exposure or microorganisms occur.

No information is available on the persistence of chlorophenols in air. Photodecomposition may be an important removal mechanism, particularly for the higher chlorophenols (Callahan et al., 1979).

The long-term persistence of chlorophenol isomers is only expected where there is a lack of degradative activity and/or outward transport, allowing them to accumulate, as is illustrated by the range of residence times for chlorophenols in aquatic environments. Substantial quantities of chlorophenols were eliminated from *in situ* marine pelagic enclosures (4-MCP and 2,4-DCP) (Kuiper & Hansveit, 1984) and from fresh waters *in vitro*: 2-MCP and 4-MCP (Ettinger & Ruchhoft 1950; 2,4-DCP (Aly & Faust, 1964); 2,4,6-T_3CP and PCP (Schauerte et al., 1982; Sugiara et al., 1984) in roughly 1–3 weeks. In contrast, it has been shown that T_4CP and PCP in sediments, where photolysis and apparently biodegradation are minimal, may persist for years (Pierce & Victor, 1978; DeLaune et al.,1983; Fox & Joshi, 1984).

A similar range of persistences has been reported for soils. Most of 2-MCP and 4-MCP was removed by microorganisms in soil after 10 and 20 days, respectively (Walker, 1954). Virtually all of 2,3,4,5-, 2,3,4,6-, and 2,3,5,6-T_4CP (100 mg/kg dry soil) disappeared from paddy soils after 4 weeks of incubation *in vitro* (Ide et al., 1972). Concentrations of trichlorophenols and tetrachlorophenols derived from PCP degradation *in vitro* were in turn, substantially reduced after many days (Kuwatsuka & Igarashi, 1975). The disappearance of at least 90% of added PCP from soils *in vitro* took from 21 to 205 days, proceeding most rapidly in soils with a moderate to high organic content and acclimated microorganisms (Kozak et al., 1979).

Most studies of chlorophenol metabolism have only monitored the disappearance of the parent compound, but a few others have indicated that subsequent metabolism may completely mineralize CPs. Thus, labelled 4-MCP, 2,4-DCP, and 2,4,5-T_3CP were converted to $^{14}CO_2$ in the *in vitro* incubation of estuarine waters and sediments (Lee & Ryan, 1979; Hwang et al., 1986). About one half of the radioactivity added to

aerobic artificial streams as ^{14}C-PCP was recovered as carbon dioxide after 21 days (Pignatello et al., 1983). Pure cultures and activated sludges may also mineralize chlorophenols to carbon dioxide (Teidje & Alexander, 1969; Duxbury et al., 1970; Chu & Kirsch, 1973; Moos et al., 1983). Methane may be produced under anaerobic conditions (Boyd & Shelton, 1984), but more often little or no mineralization occurs in anaerobic sediments and sludges (Lee & Ryan, 1979; Horowitz et al., 1982; Pignatello et al., 1983).

In most instances, aerobic metabolism involves dechlorination and hydroxylation, which are usually followed by cleavage of the phenol ring at the ortho position and subsequent complete degradation. The products of ring cleavage at the meta position are more resistant to degradation and tend to accumulate in the medium. Reductive dechlorination is an initial step towards complete mineralization under anaerobic conditions (Krijgsheld & van der Gen, 1986).

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 Environmental Levels

A substantial amount of research has been carried out on the concentration of pentachlorophenol in the environment; however, relatively few studies have been concerned with the determination of the levels of other chlorophenols. Nonetheless, enough information is available to make a preliminary survey of the residues of these chlorophenols in the environment.

5.1.1 Air

No information is available on the ambient levels of chlorophenols, other than PCP, in the atmosphere. The data on PCP are limited but may provide a useful indication of the potential for atmospheric distribution of the other chlorophenols. Measurable quantities of PCP are present in ambient air, and are surprisingly ubiquitous: Cautreels et al. (1977) detected 0.93 and 0.25 ng PCP/m^3 in the mountains high above La Paz, Bolivia, a presumably uncontaminated environment. Concentrations at 4 sites in Antwerp, Belgium, ranged from 5.7 to 7.8 ng PCP/m^3. It is not known whether the compound was present as a vapour, or adsorbed on airborne particulates. Presumably as a result of such transport, chlorophenols have been detected in rainwater, alpine lakes, and snow (Bevenue et al., 1972; Paasivirta et al., 1985).

5.1.2 Water

Residues of all chlorophenol isomers have been detected in aquatic systems. Generally, residues are present at measurable concentrations in discharges from such sources as manufacturing plants, wood-treatment facilities, municipal waste discharges, and in the receiving waters adjacent to these sources. Concentrations in other receiving waters are more sporadic and quite low. While the levels are low, chlorophenols have been detected in some of the least polluted waters in the world.

Most reports of chlorophenol levels in water are from sites in the vicinity of wood-treatment facilities. For instance, Fox & Joshi (1984) measured concentrations of PCP and tetrachlorophenols in water, sediments, and selected biota from the Bay of Quinte, in an investigation

of contamination by a wood-treatment plant. Levels of both T_4CP (2,3,4,5 plus 2,3,5,6) and PCP generally declined with increasing distance from the source. Adjacent subsurface water levels of T_4CP ranged from 0.005 to 0.086 μg/litre over the summer of 1978, while at the furthest site, 100 km distant, the range was 0.005–0.030 μg/litre. Surface film samples contained T_4CP concentrations from 2.3–200 times higher than those below the surface. Bacon (1978) assayed chlorophenols in the effluent from a Kraft pulp-mill at St. John, New Brunswick, and found 2,4-DCP and 2,4,6-T_3CP in the samples before and after chlorination and caustic extraction. No chlorophenols were detected in the receiving waters, perhaps as a result of tidal flushing. Similarly, in a Great Lakes survey conducted by the Ontario Ministry of the Environment (Jones, 1981), chlorophenol congeners were detected in receiving waters: samples from the St. Mary's River near a pulp and paper-mill did not contain any detectable levels of chlorophenols, while 1 of 10 samples taken from near another mill on Thunder Bay, contained 4 μg DCP/litre, and 2 contained 3 and 23 μg T_3CP/litre, respectively.

An Environment Canada survey (1979) of British Columbia coastal waters for chlorophenol contaminants in surface waters, effluents, sediments (section 5.1.2.2), and biota (section 5.1.6) did not reveal any DCP or T_3CP residues in water samples, but low levels of T_4CP (and PCP) were present at almost all sites: tetrachlorophenol concentrations ranged from trace levels to 1.0 μg/litre in fresh waters and 5.2 μg/litre in sea water. Effluent concentrations of T_4CP were high at 2 out of 4 discharges sampled (530 and 8270 μg/litre), even exceeding PCP levels. Garrett (1980) reported sources and levels of chlorophenols in sediments (section 5.1.2.2), fish (section 5.1.6), and a variety of discharges from industry, waste disposal systems, and runoff from landfills in the lower Fraser River and estuary. The most frequently detected chlorophenols were 2,4,6-T_3CP, 2,3,4,6-T_4CP, and PCP. Levels in most discharges were less than 7 μg/litre. Discharges from municipal sewage-treatment plants in the same study also contained several chlorophenols, most frequently 2,4,6-T_3CP (trace–1.2 μg/litre), 2,3,4,6-T_4CP (trace–28.3 μg/litre) and PCP.

As in the Canadian studies, levels in receiving waters in the USA are typically low. Morgade and co-workers (1980) did not find any detectable levels of chlorophenols, other than PCP, in drinking-waters in Dade County, Florida. *In vitro* chlorination of secondary sewage effluent and power plant cooling waters, using chlorine levels and treatment times similar to those used in practice, yielded only μg/litre quantities of 2-MCP, 3-MCP, and 4-MCP (Jolley et al., 1975).

Pierce & Victor (1978) measured the levels of PCP and some of its degradation products (2,3,5,6-T_4CP and PCP-OCH_3) in a Mississippi lake contaminated by an overflow from a wood pole-treatment plant. Prior to the spill, levels of 2,3,5,6-T_4CP in the water were low, ranging from 0.07 to 0.21 μg/litre. Concentrations were higher after the spill (0.25–2 μg/litre), and remained relatively stable for at least 4 months. Sediment (section 5.1.2.2) and fish tissue (section 5.1.6) samples were also collected.

Dutch research workers have monitored chlorophenol levels in the water and sediments of the major rivers in industrial areas in the Netherlands since 1976 (Wegman & Hofstee, 1979; Wegman & van den Broek, 1983). In both reports, maximum levels of all chlorophenols, other than PCP, seldom exceeded 1 μg/litre. Medians for the most frequent congeners for 6 rivers in 1976 and 1977 ranged as follows: 2,6-DCP, trace–0.15 μg/litre; 2,4,5-T_3CP, trace–0.15 μg/litre; 2,4,6-T_3CP, trace–0.19 μg/litre; 2,3,4,6-T_4CP, trace–0.11 μg/litre (Wegman & Hofstee, 1979). Likewise, Piet & de Grunt (1975) reported that levels of monochlorophenols ranged from not detectable to 20 μg/litre, dichlorophenols from not detectable to 1.5 μg/litre, and trichlorophenols from not detectable to 0.1 μg/litre in Netherland rivers and coastal waters. These ranges include the levels reported by Zoeteman (1975) for Rhine river water and drinking-water. Zoeteman et al. (1981) compiled information on concentrations of a variety of chemicals in Dutch ground waters. The highest concentrations of chlorophenols reported were as follows: 2,3,6-T_3CP, 1 μg/litre; 2,4,5-T_3CP, 2 μg/litre; 2,3,4,6-T_4CP, 3 μg/litre; 2,3,5,6-T_4CP, 5 μg/litre; PCP, 1 μg/litre.

In the Glatt river in Switzerland, concentrations of 2,3,4,6-T_4CP over the year averaged about 0.04–0.05 μg/litre at each of several stations along a 35-km stretch of the river (Ahel et al., 1984).

Paasivirta et al. (1985), assayed water, snow, ash, benthic invertebrates, fish, and birds from relatively unpolluted Finnish lakes for chlorophenol residues. (Levels in the biota are reported in section 5.1.6). The compounds 2,6-DCP, 2,4-DCP, 2,4,6-T_3CP, 2,4,5-T_3CP, 2,3,4,6-T_4CP, and PCP were widespread, and present at μg/litre concentrations in pulp-bleaching liquors and ng/litre levels in lake waters (Table 10). Chlorination of some waters elevated the concentration of the total chlorophenols measured almost 6-fold, from 0.043 μg/litre to 0.243 μg/litre. Elevated levels have been associated with specific discharges in Europe. Leachate from a Danish chemical dump site used during 1953–71 contained, among other compounds, PCP and T_4CP, the

Table 10. Concentration (μg/litre) of chlorophenols in Finnish pulp mill waste liquors and fresh waters[a]

Chlorophenol	Type of sample				
	Waste liquors[b]	Fresh waters[b]	Janakka water		Jyvaskyla
			raw	tap	tap
2,6-DCP	ND - 12[c]	ND - 0.073	0.010	0.062	0.272
2,4-DCP	ND - 11	ND - 0.014	0.014	0.053	0.093
2,4,6-T_3CP	15 - 28	ND - 0.011	ND	0.030	0.014
2,4,5-T_3CP	ND - 66	ND - 0.019	0.019	0.059	0.035
2,3,4,6-T_4CP	ND - 10	ND - 0.090	ND	0.016	0.009
PCP	ND - 01	0.064 - 0.011		0.023	0.005

[a] From Paasivirta et al. (1985).
[b] Range reported.
[c] ND = Not detectable.

latter ranging in concentration from 0.030 to 80 μg/litre (Folke et al., 1984). Folke (1984) analysed effluent from a Danish sewage-treatment plant, which received a portion of its wastes from the manufacture of phenoxy herbicides, for a number of chlorophenols. The effluent contained 0.1 μg 2-MCP/litre, 0.03 μg 4-MCP/litre, 0.5 μg 2,4-DCP/litre, 0.6 μg 2,6-DCP/litre, 8 μg 2,4,6-T_3CP/litre, and 0.03 μg 2,3,4,6-T_4CP/litre.

A similar variety of congeners was detected in effluent from a sewage-treatment plant that was processing paper-mill wastes. Lindstrom & Nordin (1976) found 115 μg 2,4,6-T_3CP/litre in spent bleach liquors from kraft mill pulp chlorinated *in vitro*, and noted that dichlorophenols were also present.

As in Canada, high concentrations of chlorophenols in European fresh waters are associated with wood-treatment facilities. Waters on the sites of 2 Finnish sawmills, in which a sodium chlorophenate preservative (mostly Na-2,3,4,6- T_4CP, with substantial quantities of the 2,4,6-T_3CP and PCP salts) was used to protect against sapstain fungi, contained total chlorophenol concentrations ranging from 1.6 to 20 000 μg/litre. The highest concentration occurred in a blind drain adjacent to the dip site (Valo et al., 1984). Off-site levels in ground water and lake water were much lower, with a maximum of 1.17 μg chlorophenols/litre. Concentrations of chlorophenols in the effluent from a Swedish sawmill on two separate dates were, respectively: 8.3 and 24 μg 2,4-DCP/litre; 40 and 22 μg 2,4,6-T_3CP/litre; 7.5 and 5.8 μg 2,3,4,6-T_4CP/litre (Xie et al., 1986).

Chlorophenols are also widespread in European marine waters, generally at lower concentrations than in fresh waters. Weber & Ernst (1978) noted that coastal waters off the Federal Republic of Germany yielded only trace quantities (1 ng/litre) of 2,4-/2,5-DCP, 2,6-DCP, 2,4,5-T_3CP, 2,4,6- T_3CP, 2,3,4,5-T_4CP, and 2,3,4,6/2,3,5,6-T_4CP. Danish marine waters receiving chemical dump leachate including T_4CP (at 0.030–80 μg/litre) showed corresponding levels in water of 0.006–0.008 μg/litre (Folke et al., 1984). Chlorophenol levels in coastal waters off Sweden fell off rapidly with increasing distance from a sulfate pulp-mill, from maximum concentrations on one date of 0.123 μg 2,4-DCP/ litre, 0.040 μg 2,6-DCP/litre, 0.370 μg 2,4,6-T_3CP/ litre, and 0.084 μg 2,3,4,6-T_4CP/litre to undetectable levels (Xie et al., 1986). For example, the half-distances for 2,4,6-T_3CP and 2,3,4,6-T_4CP disappearance were 1 and 0.8 km, respectively (see also sections 4.1.3, 5.1.2.2).

5.1.2.1 Sediments

Chlorophenol concentrations in sediments are for the most part much greater than those in the overlying water. This may reflect adsorption of the chlorophenols on suspended particulates in the water column, with subsequent sedimentation. For instance, Eder & Weber (1980) reported higher levels of chlorophenols (di- to penta-) in both sediments and suspended solids compared with those in water.

Fox & Joshi (1984) analysed sediment cores for T_4CP and PCP in their study of chlorophenol contamination from a wood-preservation facility on the Bay of Quinte, Lake Ontario. For the upper sediments (1/2-cm sections of the top 5 cm of the core) levels ranged from 1 to 48 μg/kg dry weight. In a similar study, Environment Canada (1979) analysed sediments in British Columbia waters associated with wood-preservation plants. T_4CP was present at all 11 sites, and ranged from a trace to 1600 mg/kg dry sediment. T_3CP was found at 4 of the 11 sites, with as much as 170 μg/kg of dry sediment measured. Although the kraft pulp-mill effluent studied by Bacon (1978) contained 2,4-DCP and 2,4,6-T_3CP, only PCP was detected in sediment samples downstream.

As a result of a PCP spill from a pole-treatment plant, sediments in a Mississippi lake were contaminated with PCP and its degradation products, including 2,3,5,6-T_4CP (Pierce & Victor, 1978). Four months after the spill, the levels of 2,3,5,6-T_4CP in surface sediment ranged from

3.8 to 71 μg/kg dry sediment whereas, 1 month after the spill, levels of between 12 and 97 μg/kg dry sediment had been detected.

Interpretation of these results is confounded by their variability, the residence time (several weeks) of PCP in the water column, and a 1974 spill at the same site. T_4CP was present in the sediments of a nearby, reportedly uncontaminated, pond at 1 μg/kg.

High concentrations of DCP and T_3CP were present in sediments adjacent to hazardous waste dumps near the Niagara River, at maximum levels of approximately 2000 and 500 μg/kg, respectively (Elder et al., 1981).

In studies in progress on chlorophenols that are present in surface and coastal waters and sediments in The Netherlands, the compounds 2,5-DCP, 2,3,5-T_3CP, 2,4,5- T_3CP, 2,3,4,5-T_4CP, 2,3,4,6-T_4CP, and PCP are observed most frequently (Wegman & van den Broek, 1983). In the industrial regions that have been the focus of this research, moderate levels of contamination prevail (several μg/kg of dry sediment for most isomers) (Table 11).

Table 11. Levels of chlorophenols (μg/kg) in sediments from Dutch surface waters and the Weser estuary

Compound	Lake Ketelmeer[a]		Other Netherland[a] surface waters (Range)	Weser Estuary[b] (Mean)
	Median	Maximum		
3-MCP	-	43		
2,3-DCP	1.9	2.2		
2,4-DCP	4.4	10	ND - 3.6	1.170
2,5-DCP	6.3	11	ND - 3.8	
2,6-DCP	1.8	31	ND - 2.5	
3,4-DCP	9.8	49	ND - 4.1	
3,5-DCP	6.6	12	ND - 9.3	
2,3,4-T_3CP	0.7	0.8	ND - 0.6	
2,3,5-T_3CP	2.4	11	ND - 1.5	
2,4,5-T_3CP	6.4	15	ND - 6.3	1.170
2,4,6-T_3CP	1.9	3.7	ND - 0.9	0.300
3,4,5-T_3CP	1.2	19	ND - 1.7	0.310
2,3,4,5-T_4CP	0.9	8.9	ND - 0.9	
2,3,4,6-T_4CP	1.7	4.9	ND - 1.7	1.546
2,3,5,6-T_4CP	1.4	2.8	ND - 0.4	

[a] From:Wegman & van den Broek (1983) (dry sediment).
[b] From: Eder & Weber (1980) (wet sediment).

Paasivirta et al. (1980) analysed sediments and biota (section 5.1.6) from three Finnish lakes for several chlorophenols and related compounds. In one lake, contaminated only from sawmills upstream, concentrations of T_3CP and T_4CP were 4.68 and 33.4 μg/kg of sediment; respectively (Table 12, section 5.1.6.1), while in another lake downstream from a pulp-mill, the corresponding values were 27.7 and 50.1 μg/kg. The third lake, further downstream from pulp and paper inputs, contained intermediate levels of both compounds.

Levels in estuarine and marine sediments overlap considerably with those from fresh waters. Butte et al. (1985) determined chlorophenol concentrations in sediments and clams (section 5.1.6) from a German bight that had received untreated PCP waste from a pulp and paper-mill for 13 or 14 years, until 2 years before the study. Sediments from one site near the former discharge contained from 28.3 to 30.9 μg 2,3,4,5-T_4CP/kg of dry sediment, while those from another site contained 92.8 μg 2,3,4,5-T_4CP/kg and 7.9–11.6 μg 2,3,4,6- plus 2,3,5,6-T_4CP/kg. Sediments taken some distance from the discharge contained only 1.2 μg 2,3,4,5-T_4CP/kg or less. Eder & Weber (1980) reported levels of chlorophenols (di- to penta-) that corresponded with the lower end of the range for The Netherlands surface waters; mean concentrations of chlorophenols other than pentachlorophenol ranged from 0.300–1.546 μg/litre. Similar levels were found in Baltic Sea sediments from a site 2 km distant from a sulfate pulp-mill; these contained 0.9 μg/kg dry sediment of 2,4-DCP, 0.4 μg 2,4,6-T_3CP/kg, and 3.1 μg 2,3,4,6-T_4CP/kg (Xie, 1983). In a subsequent study, higher levels of the same congeners were found at this location (Xie et al., 1986). While surface sediments from sites roughly 5–10 km from the discharge contained levels of chlorophenol that were near or below the limits of detection, sediments 2 km or less from the mill contained as much as 16 μg 2,4-DCP/kg dry sediment, 19 μg 2,4,6-T_3CP/kg, and 89 μg 2,3,4,6-T_4CP/kg.

5.1.3 Soil

Information on ambient levels of chlorophenol residues in soils is limited, perhaps reflecting limited use of these compounds on soils. The processes of degradation and movement also combine to reduce soil residues (section 4).

The sole report on levels of chlorophenols in Canadian soils is undoubtedly atypical of the environment at large. Garrett (1980) reported that soil samples from the former site of a pesticide plant in

Richmond, British Columbia contained 2 mg T_4CP/kg dry soil, 0.18 mg T_3CP/kg, as well as low levels of PCP.

Valo et al. (1984) assayed chlorophenols in the soil and water (section 5.1.2) around two Finnish sawmills where lumber was treated against sap-staining fungi. Soils at both facilities were heavily contaminated with chlorophenols; up to 70 mg/kg were found near the dipping site, and up to 6 mg/kg occurred in a storage area for the preserved wood. Soil outside the storage area contained only 0.1 mg/kg. The most common chlorophenols in the preservative formulation also predominated in the near-surface soils, but lower chlorinated phenols (particularly dichlorophenols) became increasingly important further down the soil horizon, presumably as a result of decomposition of the preservative. In general, chlorophenol concentrations declined in the progressively deeper layers.

Kitunen et al. (1987) determined the concentrations of chlorophenols and their contaminants in soil near the preserving facilities at 4 different sawmills. Concentrations of chlorophenols in soil ranged from 500 to 3500 mg/kg, polychlorinated phenoxyphenols, from 1–5 mg/kg, and polychlorinated dibenzofurans, from 0.2–5 mg/kg. No clear decrease in the soil concentrations of these compounds was seen during the first year after the mill stopped using technical chlorophenol.

5.1.4 Food, feed, and drinking-water

5.1.4.1 Food

Little information is available on residues in food of chlorophenols, other than PCP. Low-level contamination undoubtedly occurs as a result of contact with treated wood storage and transport containers, and from herbicide applications. However, both of these uses are prohibited in a number of countries (section 3.2.2); hence, the following cases may overestimate the extent of contamination.

Both T_4CP and PCP were identified in agricultural products by the Alberta Department of Agriculture (Jones, 1981). Trace levels of T_4CP (mainly 1 μg/kg, maximum 45 μg/kg) occurred in grab samples of carrots, potatoes, turnips, and beets. T_4CP concentrations as high as 472 μg/kg occurred as a result of contamination from treated wood.

No residues were detected in 45 samples of Southern Ontario milk analysed for 2,4,5-T_3CP, 2,4,6-T_3CP, 2,3,4,6-T_4CP, and PCP (Frank et al., 1979).

In the USA, Bristol et al. (1982) determined 2,4-DCP concentrations in 3 varieties of potatoes sprayed with 2,4-D as a growth regulator at an application rate of 140 g/ha. Levels of chlorophenol, which could arise as a contaminant or degradation product of the herbicides, varied slightly in 3 varieties of potatoes, but ranged between 3 and 8.8 μg/kg. Potatoes not sprayed with 2,4-D did not contain any detectable 2,4-DCP.

Stijve (1981) determined chlorophenol residues in edible products derived from the bones and hides industry, where PCP was used as a preservative and disinfectant. Fleshing grease intended as an ingredient in cow feed, contained 50–480 μg 2,4,5-T_3CP/kg, 2060–13 400 μg 2,3,4,6-T_4CP/kg, and 210–1090 μg PCP/kg. A survey of 50 samples of edible gelatins (worldwide distribution), which are produced from the collagen in hides and bones, all contained PCP; 30% also contained 2,3,4,6-T_4CP and trace amounts of trichlorophenols. In some countries, where chlorophenols are used for the disinfection of hides, chlorophenol levels in some gelatins range from 1000 to 5000 μg/kg.

Chlorophenols have been found at very low levels in the tissues of commercial livestock and poultry. Farrington & Munday (1976) found 2,3,4,6-T_4CP (at 2–3 μg/kg) in chicken flesh from 3 out of 4 shops in the United Kingdom.

5.1.4.2 Livestock feed

No data are available on levels of the lower chlorophenols in animal feed. Jones (1981) cited a case in which a boxcar that had been used to ship PCP was later filled with feed oats, contaminating the oats with roughly 2000 mg PCP/kg. Presumably, the feed was simultaneously contaminated with T_4CP at roughly 10% of the PCP levels, given the usual formulation for technical Na-PCP. Livestock illness and mortality were associated with this incident.

5.1.4.3 Drinking-water

Data on chlorophenol residues in drinking-water are quite limited, but suggest that levels vary considerably between locations. Sithole & Williams (1986) reported that low levels of a number of lower chlorophenols occurred infrequently in potable waters at 40 Canadian treatment plants. Chlorination increased the concentrations of 2-MCP (maximum observed: 65 ng/litre), 4-MCP (127 ng/litre), 2,4-DCP (72 ng/litre), 2,6-DCP (33 ng/litre), and 2,4,6-T_3CP (719 ng/litre), but decreased those of 2,3,4,5-T_4CP (reduced below the limit of detection)

and PCP (34 ng/litre). Lower chlorophenols were not detected in drinking-water supplies from Dade County, Florida (Morgade et al., 1980). Dietz & Traud (1978) found low concentrations of a variety of CP congeners in drinking-water from the Ruhr area of the Federal Republic of Germany, including: 3–6 ng 2,4-DCP/litre; 20 ng 2,6-DCP/litre; 1 ng 2,4,6-T_3CP/litre; 1 ng 2,3,5-T_3CP/litre; 3 ng 2,4,5-T_3CP/litre; 1 ng 2,3,4,5-T_4CP/litre; and 3 ng 2,3,4,6-T_4CP/litre. For comparison, levels in the effluent from a sewage plant were concurrently 2 orders of magnitude higher.

In contrast, Paasivirta et al. (1985) found a number of chlorophenols in Finnish tap waters at levels roughly one order of magnitude higher than those in the German study (Table 10). As these data indicate, chlorophenol concentrations in drinking-water are generally quite low; indeed, the low threshold concentrations producing undesirable organoleptic (taste and odour) properties would make higher levels in drinking-water unacceptable (WHO, 1984 and Table 21).

5.1.5 Treated wood

The treatment of wood continues to be an important use for chlorophenols (section 3.2.2). with considerable potential for environmental contamination, as well as general and occupational human exposure. In 1978–79, levels of chlorophenols, principally PCP, were measured in samples of wood shavings that were used as livestock litter in Southern Ontario (Jones, 1981). No trichlorophenols were detected, but T_4CP, PCP, and related chlorinated anisoles were quantified. T_4CP levels were as high as 70 mg/kg. Daniels & Swan (1979) determined that 15 lumber samples from a British Columbia sawmill protected with a commercial formulation of T_4CP and PCP salts ("sodium penta") contained on average 44 μg chlorophenols/cm^2 (range, 29–86 μg/cm^2), most of which was T_4CP.

In the United Kingdom, Parr et al. (1974) found that wood shavings from imported wood used as litter for hens were contaminated with the sodium salts of T_4CP and PCP. When lumber is planed, most of the chlorophenates are removed in the shavings. As a result, levels of 2,3,4,6-T_4CP and PCP in fresh litter are quite high. According to Parr et al.(1974), T_4CP concentrations averaged 54 mg/kg and ranged from 4 to 310 mg/kg. When the litter is used, chlorophenol levels fall off as they are converted to their corresponding chloroanisoles (Gee & Peel, 1974): spent litter contained on average 0.7 mg T_4CP/kg. Similarly, Curtis et

al.(1972) measured as much as 100 mg 2,3,4,6-T_4CP/kg in fresh shavings and sawdust from the United Kingdom.

Levin & Nilsson (1977) assayed for T_4CP, PCP, and related compounds in wood dust from a Swedish sawmill. The wood had been treated with 2% Na-2,3,4,6-T_4CP; T_4CP levels in the dust ranged from 100 to 800 mg/kg.

5.1.6 Terrestrial and aquatic organisms

5.1.6.1 Invertebrates

Invertebrates contain levels of chlorophenols that are higher than those found in the environment at large, reflecting moderate bioconcentration by these organisms (section 4.2.2). Environment Canada (1979) found tetrachlorophenol in invertebrates from the receiving waters for wood-treatment plant effluents in British Columbia. In fresh waters, crayfish (*Pacifasticus sp.*) pincer muscle contained traces of T_4CP. The same tissue from a marine crab (*Cancer magister*) contained T_4CP levels ranging from a trace to 20 μg/kg wet weight. One clam (*Macoma*) sampled contained 12 μg T_4CP/kg, presumably in muscle tissue. T_3CP was not detected in any of the organisms. Similar chlorophenol burdens were reported by Bacon (1978), who assayed for 2,4-DCP, 2,4,6-T_3CP, and PCP in lipids from a clam (*Mya arenia*) and sandshrimp (*Crangon septemspinosa*) from waters receiving pulp-mill effluent. Trace quantities of 2,4-DCP were present in both organisms, while 2,4,6-T_3CP levels ranged from undetectable to 7.2 μg/kg wet weight for the clam and 9.2 μg/kg wet weight for the sandshrimp.

During the course of their survey of chlorophenol residues in the Weser Estuary and German Bight, Ernst & Weber (1978) determined that a polychaete (*Lanice conchilega*) contained on average 11.8 μg 2,4-DCP and 2,5-DCP/kg, 19.3 μg 2,4,5-T_3CP/kg, 26 μg 2,4,6-T_3CP/kg, 7 μg 2,3,4,5-T_4CP/kg, 66.9 μg 2,3,4,6-T_4CP and 2,3,5,6-T_4CP/kg, and 117.5 μg PCP/kg (all values wet weight).

Paasivirta et al. (1980) have surveyed levels of chlorophenols in a variety of biota in 3 lakes with different chlorophenol inputs (section 5.1.2.1 and Table 12). Plankton generally contained little or no trichlorophenol, but relatively high concentrations of tetrachlorophenol. Mussels (*Anodonta piscinalis*) and sponges (*Spongilla lacustris*) contained moderate levels of both T_3CP and T_4CP. Chlorophenol burdens in organisms from the different lakes generally ranked in the same order as the perceived chlorophenol inputs into the 3 lakes.

Table 12. Chlorophenol levels in various environmental compartments in three Finnish Lakes (μg/kg wet weight, except for sediment, dry weight)[a,b,c]

Population species	Lake	N	Trichlorophenol			Tetrachlorophenol		
			x	s	cv	x	s	cv
Pike	K[d]	8	0.79	1.6	2.03	20.2	40.0	1.98
	P[d]	6	17.3	18.1	1.05	11.1	14.9	1.34
	V[d]	10	13.6	19.1	1.40	19.0	12.4	0.65
Roach	K	9	ND	ND		2.19	1.82	0.83
	P	10	4.67	5.29	1.13	6.41	3.42	0.53
	V	10	55.9	53.4	0.96	11.5	8.26	0.72
Mussel	K	10	ND	ND		2.83	4.44	1.57
	P	9	1.44	2.21	1.53	7.44	3.47	0.47
Sponge	K	5	0.36	0.80	2.22	6.30	6.36	1.01
	P	5	6.86	9.14	1.33	1.45	2.43	1.68
	V	5	4.96	3.73	0.75	2.56	1.12	0.44
Plankton (100 μm)	K	4	ND	ND		ND	ND	
	P	4	ND	ND		9.28	10.0	1.08
	V	4	2.45	4.90	2.00	9.90	1.73	0.17
Plankton (25 μm)	K	4	ND	ND		7.95	15.6	1.96
	P	4	ND	ND		14.3	10.5	0.73
	V	3	ND	ND		23.1	4.08	0.18
Sediment (0–2 cm)	K	5	4.68	10.4	2.22	33.4	38.6	1.16
	P	5	10.7	15.1	1.42	37.5	29.3	0.78
	V	5	27.7	17.2	0.62	50.1	17.3	0.35

[a] From: Paasivirta et al. (1980).
[b] N = number of samples analysed;
x = mean;
s = standard deviation;
cv = coefficient of variation.
[c] Wet weight of plankton was calculated from dry weight by multiplying by 13.69.
[d] Lake areas: K = Konnevesi; P = Paijanne; V = Vatia.

In more recent work (Paasivirta et al., 1985), mussels, chironomids, sponges, and fly larvae from Lake Vatia, 5 km downstream from a pulp-mill, were analysed for several chlorophenols. Low levels (usually not detected to 20 μg/kg fresh weight) of chlorophenols were found in all invertebrates except sponges, which inexplicably contained 195 μg 2,4-DCP/kg fresh weight and 22 μg 2,4,6-T_3CP/kg.

Butte et al. (1985) analysed clams from a German bight that had received untreated PCP-contaminated discharge from a paper-mill for a number of years (section 5.1.2.1). Clams near the discharge contained 0.7–55.6 μg 2,3,4,5-T_4CP/kg dry tissue, while those further away contained, at the most, 2.6 μg 2,3,4,5-T_4CP/kg and 0.2 μg 2,3,4,6- plus 2,3,5,6-T_4CP/kg. Similar low concentrations of 2,3,4,6-T_4CP and PCP were found in blue mussels (*Mytilus edulis*) from Danish coastal waters (Folke & Birklund, 1986). Tissue levels of T_4CP averaged from 0.2 to 2.9 μg/kg fresh weight (1–23 μg/kg dry weight) for mussels from various locations in 1985, with no obvious relation to a nearby chemical dump from which chlorophenols were leaching.

5.1.6.2 Fish

In general, levels of chlorophenols in fish are similar to, or slightly higher than, those in invertebrates. Bacon (1978) studied chlorophenol levels in different tissues from several fish species from the St. John River estuary, New Brunswick, which receives pulp-mill effluents. Residues of 2,4-DCP and, 2,4,6-T_3CP were detected, usually at several tens of μg/kg wet weight and several μg/kg wet weight respectively, in all tissues including muscle, viscera, skin, and liver (calculated from per-lipid-weight data in original publication). In some instances, levels in liver were much higher than this; concentrations as high as 242.9 μg 2,4-DCP/kg and 128 μg T_3CP/kg (wet weight) were measured. In surface and coastal waters in British Columbia, Environment Canada (1979) detected T_4CP in marine and freshwater sculpins. Across all sites, skeletal muscle burdens averaged 30 μg/kg wet weight, and ranged from a trace to 100 μg/kg. Levels were roughly an order of magnitude higher in liver. Similarly, Garrett (1980) reported that marine sculpins (*Leptocottus armatus*) from the lower Fraser River were the principal fish with detectable amounts of T_4CP, averaging 24.9 μg/kg wet weight, and ranging from a trace to 62 μg/kg. Significant levels of T_4CP were also found in squawfish, which averaged 10.5 μg/kg wet weight and contained as much as 18 μg/kg. Chlorophenol levels were higher in fish that were caught in the industrialized areas of the river. Spottail shiners (*Notropis hudsonius*) from Lakes Erie and Ontario contained 2,4,5-T_3CP and 2,4,6-T_3CP at maximum concentrations of 22 and 33 μg/kg (wet weight, whole fish), respectively (Canada-Ontario Review Board, 1981).

Similar tissue concentrations have been detected in fish from European waters. In Finnish lakes spanning a gradient of chlorophenol inputs (Paasivirta et al., 1980), skeletal muscle of roach contained on

average 0–55.9 μg T_3CP/kg wet weight, and 2.19–11.5 μg T_4CP/kg (Table 12). Chlorophenol concentrations in roach muscle were related to the chlorophenol inputs into the lake. In contrast, levels in pike skeletal muscle (average ranges 0.79–17.3 μg T_3CP/kg, and 11.1–20.2 μg T_4CP/kg) bore no relation to chlorophenol inputs. In subsequent studies (Paasivirta et al., 1981, 1983, 1985), average CP levels in muscle of pike, burbot, ide, and roach taken from waters receiving pulp-mill discharges also fell within the same range, except in the case of heavily polluted waters.

In Lake Tiiranselka, which receives a large volume of pulp-mill effluent, average concentrations of 2,4,6-T_3CP and 2,3,4,6-T_4CP in pike muscle were 37.02 and 125.02 μg/kg wet weight, respectively. Two species of Baltic salmon analysed for chlorophenols contained similar levels of contamination to those found in fish from moderately polluted lakes (Paasivirta et al., 1985). Muscle tissue of salmon from 2 rivers and a hatchery contained an average of 3 μg 2,4,6-T_3CP/kg fresh weight, 1.8 μg 2,4,5-T_3CP/kg, and 12.5 μg 2,3,4,6-T_4CP/kg. Fish collected in the vicinity of a pulp-mill effluent in Sweden contained 2,4,6-trichlorophenol and related compounds that were present in the discharge (Landner et al., 1977). Perch (*Perca fluviatilis*) contained levels of 2700 μg/kg in liver fat (62.1 μg/kg fresh weight), while Northern Pike (*Esox lucius*) contained 400–500 μg/kg (27.5–40.4 μg/kg fresh weight).

Extremely high chlorophenol levels have occurred as a result of accidental spills. Following contamination of a Mississippi lake by PCP in December 1976 (section 5.1.2.1), levels of the degradation product 2,3,5,6-T_4CP in sunfish liver and muscle increased by 1–2 orders of magnitude (Pierce & Victor, 1978) (Table 13). Four to 5 months after the spill, liver levels in sunfish were approaching pre-spill levels, while levels in muscle tissue apparently cleared more slowly. Bass and catfish showed particularly high levels of T_4CP after the spill, but unfortunately no baseline data were provided.

5.1.6.3 Other non-human vertebrates

Data on chlorophenol concentrations in vertebrates other than fish or human beings are quite limited. Purple martin fledglings analysed for chlorophenol residues contained 2 μg T_4CP/kg (Jones, 1981). The tissue analysed was not specified. Levels of CP residues in eggs, embryos, and chick tissues of ring-billed gulls on the Ottawa and St Lawrence Rivers have been reported (NRCC, 1982). The compounds 2,4-DCP, 2,4,5-T_3CP, 2,4,6-T_3CP, and PCP were present in most tissues, the

highest concentrations occurring in liver and brain (Table 14). Paasivirta et al. (1985) measured chlorophenol residues in the muscle tissue of 45 juvenile starlings from southern Finland. Detectable levels of residues were not common: 2 birds contained 1 μg 2,3,4,6-T_4CP/kg fresh muscle and 2 others contained 1 and 2 μg 2,4,6-T_3CP/kg, respectively.

Table 13. Levels of 2,3,5,6-T_4CP in tissues of fish from a Mississippi lake (USA) contaminated by PCP from a wood-pole treatment facility[a]

Date	Fish	Concentration (μg/kg wet weight)	
		Muscle	Liver
October 11/76[b]	Sunfish 1	< 1	30
	Sunfish 2	< 1	50
January 6/77	Sunfish 1	95	950
	Sunfish 2	60	NA[c]
	Bass 2	300	1600
	Bass 3	130	8200
	Catfish 1	219	8500
April 27/77	Sunfish 1	27	25
	Sunfish 2	22	150
	Catfish 1	82	1400
	Catfish 2	41	940

[a] From: Pierce & Victor (1978).
[b] Spill in December, 1976.
[c] NA = not analysed.

Table 14. Range of concentrations (μg/kg) of several chlorophenols in ring-billed gull eggs, embryos, and chick tissues[a]

	Compound		
	2,4-DCP	2,4,5-T_3CP	2,4,6-T_3CP
Fresh eggs	0–176	0–26	12–87
Embryos		7	25
Chick liver	14–210	0	43–157
Chick brain	177–476	ND[b]	144–234

[a] From: NRCC (1982).
[b] ND = not detectable.

The same authors analysed osprey eggs, and the pectoral muscle, brain, liver, eggs, and kidney of white-tailed eagles. 2,3,4,6-T_4CP levels in osprey eggs ranged from 0 to 17 μg/kg fresh weight; MCPs, DCPs, and T_3CPs were not detected. Similarly, only 2,3,4,6-T_4CP occurred (15-22 μg/kg fresh weight)in fresh eagle eggs. Fresh eagle muscle tissue (2 samples) contained moderate levels of 2,4,6-T_3CP (26 and 50 μg/kg respectively) and 2,3,4,6-T_4CP (0 and 26 μg/kg). Single samples of eagle brain, liver, and kidney revealed that all of these tissues contained chlorophenol residues, some at high levels; kidney, for example, contained 1017 μg 2,4-DCP/kg.

5.2 General Population Exposure

The general population is exposed to chlorinated phenols through diverse sources and routes, which have been summarized by the NRCC (1982). Chlorophenols can be ingested as contaminants in food including produce sprayed with phenolic pesticides, flesh of livestock given feed contaminated with these pesticides, and general food items, usually at mg/kg levels (section 5.1.4).

In addition, sub-μg/litre quantities of chlorophenol congeners have been detected in drinking-water (section 5.1.4). These 2 routes of exposure are generally considered to be the major sources of exposure of the general population to chlorophenols (US EPA, 1980c). In addition, minor quantities may be taken up through the dermal and respiratory routes. Sources include industrial discharges (solid, liquid, atmospheric) of chlorophenolic wastes, exposure to treated wood, exposure to general consumer products including adhesives, textiles, wood-treatment products, mouth-washes and disinfectants, and break down products of hexachlorobenzene and phenoxy acid herbicides.

Because of this diversity of sources of chlorophenols, there are no comprehensive estimates of the chlorophenol levels to which the general population is exposed. On the basis of preliminary estimates from the literature of total chlorinated phenol residues in food, water, air, and miscellaneous sources, the Canadian Department of National Health and Welfare (NHW, 1988) estimated typical non-occupational exposure to all chlorophenols to be:

6.0 μg/person per day in food
2.8 μg/person per day in water
1.9 μg/person per day in air
2.0 μg/person per day from other sources
12.7 μg/person per day in total (= 0.18 μg/kg body weight per day for 70-kg adult).

Similarly, the NRCC (1982) estimated that the total chlorophenol exposure per day in the general population in Canada was 10–30 μg/person (0.17–0.50 μg/kg body weight per day for a 60-kg adult). This estimate was based on the following assumptions: 6 μg/ person per day from food; 4 μg/person per day from water; and 20 μg/person per day from air. The last figure is extremely high, based on monitoring data, and was derived by assuming that indoor rooms were treated with a chlorophenol preservative. This figure should be considered tentative in view of the meagre data base available on environmental levels.

On the basis of approximate levels of several trichlorophenols in drinking-water and fish flesh, SENES (1985) estimated the daily general population intake of each of 2,4,5-T_3CP, 2,4,6-T_3CP, and (2,3,5- + 2,3,6-) T_3CP to be 0.44 μg/person per day. If it is assumed that the uptake of each of the remaining 2 isomers is also 0.44 μg/person per day, the total T_3CP intake would then be 2.20 μg/person per day.

These low estimated levels of exposure are confirmed by the few studies in which the residue levels of lower chlorinated phenols have been determined in the general population. Although contamination generally appears to be widespread, the concentrations of chlorophenols in the tissues and fluids of people, not occupationally exposed, are extremely low.

Kutz et al. (1978) determined the levels of pesticide-related phenolic residues in human urine samples from all over the USA with a limit of detection of 5–30 μg/litre. In over 1.7% of 400 samples collected from the general population, 2,4,5-T_3CP was present at a mean concentration of less than 5 μg/litre, and a maximum of 32.4 μg/litre.

In comparing different methods of detection of hexachlorobenzene and 2,4,5-T_3CP in human serum and urine, Yost et al. (1984) found 2,4,5-T_3CP levels in the 2 fluids, in the USA, to be 0.25–6.7 μg/litre and 0.25–1.9 μg/litre, respectively. Samples were pooled from the general population, but neither the sample size nor the site of origin was specified.

As part of the development of an analytical method for chlorophenols, Edgerton et al. (1980) determined chlorophenol concentrations in urine samples from the general population. The origin of the samples was not specified, but was presumably the southeastern USA. Chlorophenol concentrations ranged widely as follows:

2,6-DCP, 1–112 μg/litre; 2,4-/2,5-DCP, 2–161 μg/litre (mean, 34.1); 3,5-DCP, 15–44 μg/litre; 2,4,5-T_3CP, 1–9 μg/litre; 2,4,6-T_3CP, 1–6 μg/litre; 2,3,4,6-T_4CP, 2–15 μg/litre.

Similar levels of T_4CP were found in urine samples from 25 members of the general population in Barcelona, Spain (Gomez-Catalan et al., 1987). The mean urine concentration was 6.2 μg/litre (standard error of mean = 1.6). No trichlorophenols were detected.

In Dade County, Florida, where large quantities of lindane (gamma-HCH) and Bromophos (*O*-(4-bromo-2,5-dichlorophenyl)*O*,*O* dimethyl-phosphorothioate) are used in agriculture, Morgade et al. (1980) measured the serum concentrations of 2,4-DCP, 2,3,5-, 2,4,5-, 2,4,6-T_3CP, 2,3,4,5-, 2,3,4,6-T_4CP, and PCP in 58 female residents. In addition, 10 samples of human adipose tissue from autopsies were analysed for the same series of compounds. No detectable levels of any of the non-fully substituted chlorophenols were found in the serum or adipose tissue of the study group, but traces of PCP were found in the drinking-water and in both biological compartments.

Williams et al. (1984) analysed adipose tissue from autopsies of male and female residents of Ottawa (n = 84) and Kingston (n = 91), Ontario, for organochlorine residues. Levels of 2,3,4,5-T_4CP were typically 6 or 7 μg/kg tissue, and did not differ significantly between locations or sexes. Tissues from Kingston contained roughly 3 times more of other T_4CPs (2,3,4,6 plus 2,3,5,6; male 24 μg/kg; female 20 μg/kg) than those from Ottawa (male 6 μg/kg; female 8 μg/kg), but this difference was not statistically significant.

These data support the hypothesis that the general population is exposed to very low levels of the lower-chlorinated phenols. However, estimates of this burden are highly speculative at present, as data are lacking for most congeners. Quantitative analyses for these compounds in meat, poultry, produce, and drinking-water are scarce. Atmospheric measurements have not been documented at all, and the extent of dermal absorption by the general population, assumed to be low, is not known.

5.3 Occupational Exposure

The potential for both acute and long-term exposure to chlorophenols may be heavy for workers from industries using these compounds. The routes of exposure for Canadian workers have been summarized by NRCC (1982); the same routes undoubtedly apply in most other countries. Large numbers of workers are exposed to chlorophenols, other than PCP, in the lumber industry, particularly in instances where lumber is surface-treated with Na-T_4CP, during the dipping, sorting, handling, planing, trimming, or the grading of lumber.

In-service treatment of wood by painters, wood preservation workers, or telephone linemen could result in similar dermal and inhalation exposure. Employees in the chemical industry, who are involved in the manufacture of chlorophenols or their derivatives, may also be exposed to high levels. The same is true of employees in manufacturing industries that use chlorophenols as preservatives, such as the photographic, paint, textile, rubber, construction, electrical, pharmaceutical, and disinfectant industries. Finally, employees working with products containing chlorophenols may be exposed, such as commercial applicators and farmers using phenoxy herbicides, or those exposed to treated wood in the fields of construction (carpentry), or railways. For such occupational exposures, inhalation and dermal absorption are the major routes of uptake.

Unfortunately, there is little quantitative information on occupational exposure to low chlorine-substituted chlorophenols. As might be expected of such moderately volatile compounds, high atmospheric concentrations are found in work areas where they are in use. In addition, the body fluids of persons working in such areas contain elevated levels of chlorophenols. In general, concentrations of chlorophenols in air at chemical manufacturing plants can reach mg/m^3 levels while much lower concentrations occur in facilities in the lumber industry that use chlorophenols.

Ott et al. (1980) examined worker exposure to T_3CP and 2,4,5-T at a manufacturing plant in the USA. The time-weighted average concentrations of T_3CP in the air at work locations adjacent to the reactor, salt wheel, acid wheel, and dryer, were 2.1, 2.1, 9.7, and 1.6 mg/m^3 respectively.

In a factory manufacturing PCP in Japan, crude exhaust air vented from a"drying room" contained 3.54 mg T_4CP/m^3 and 14.04 mg PCP/m^3 (Akisada, 1964). Urine-T_4CP concentrations of personnel in the factory ranged from 0.07 to 0.37 mg/litre, compared with 0.01–0.03 mg/litre for unexposed persons.

An industrial hygiene survey of worker exposure to chlorophenols and hexachlorobenzene at a PCP-production facility revealed that workers in different tasks were exposed to average concentrations of 2,3,4,6- plus 2,3,5,6-T_4CP of 0.016–0.320 mg/m^3 in conjunction with several-times-higher exposures to PCP. The highest average exposures were experienced by handymen and block-casting workers (Marlow, 1986).

Recent data from Kauppinen & Lindroos (1985) showed much lower average atmospheric chlorophenol levels in 10 Finnish sawmills,

ranging from 24 to 75 μg/m^3. The values given are the sum of the three chlorophenols present, as the Na-2,3,4,6-T_4CP formulation used also contained 10–20% 2,4,6-T_3CP and 5% PCP. The highest mean concentrations in the general work place occurred at the site where the solution was prepared and at the machine stacking the lumber. Much higher levels were also detected inside the drying kilns, where chlorophenol concentrations averaged 5800 μg/m^3. Levels of 2,4,6-T_3CP were measured separately; particularly high concentrations were noted at the machine stacking site (58 μg/m^3) and the outdoor dipping site (44 μg/m^3), while it could not be detected at the preparation site. Average urine levels of T_4CP and PCP (measured together) ranged from 0.10 to 3.3 μmol/litre (approximately 25–825 μg/litre). The highest mean concentration occurred among the loaders at the trough dipping area (mean air levels 55 μg/m^3, dermal uptake substantial), while the other urine values parallelled the atmospheric readings in terms of relative concentration.

Kauppinen (1986) reported that air concentrations of chlorophenols (T_4CP and PCP combined) for a variety of tasks in Finnish plywood plants usually ranged from <1 to 6 μg/m^3. The levels in air plus wood dust, where plywood was sawed, ranged from 3 to 6 μg/m^3 and were usually higher than those in air at work sites where wood dust was minimal.

A detailed study of the chlorophenol exposure of sawmill workers in a pulp, paper, and sawmill complex in British Columbia was conducted by Embree et al. (1984). They divided the workers into 3 groups: a control group of 351 workers in areas with no identifiable air contaminants; a group of 31 workers in close proximity to recently treated lumber, who did not have manual contact with it (airborne exposure); and a group of 40 who handled recently treated lumber (dermal plus airborne exposure). Air levels of chlorophenols were determined using personal monitors. Tetrachlorophenol levels in the plant air were elevated, and similar for the airborne group (3.3 ± 2.1 μg/m^3; mean ± standard deviation), and the dermal-plus-airborne group (3.0 ± 2.7 μg/m^3). Serum levels were related to perceived exposure in a dose-dependent manner; tetrachlorophenol concentrations for the dermal-plus- airborne group (204 ± 92 μg/litre) were approximately twice those in the airborne group (112 ± 136 μg/litre), and 8 times those in the controls (26 ± 7 μg/litre). Urine levels for the 2 exposed groups were also dose-dependent (airborne 93 ± 43 μg/litre; dermal-plus-airborne 125 ± 20 μg/litre). Urine levels in the control group were not reported.

Similar urine concentrations were reported for American woodworkers exposed to Permatox® (3% PCP, 21% 2,3,4,6- T_4CP) (Kalman & Hortsman, 1983). Of 47 workers, 28 showed urine levels of more than 100 µg 2,3,4,6-T_4CP/litre, 13, levels between 20 and 100 µg/litre, and 6, levels of less than 20 µg/litre. Air levels were reportedly below 25 µg/m^3. Because atmospheric concentrations were this low, the authors suggested that the individuals with the highest urine levels were taking up most of the dose through non-respiratory routes, most likely dermal. Over a 2-week holiday period, T_4CP levels in the three groups declined by averages of 84%, 67%, and 34%, respectively, a slower rate of elimination than that found in experimental animals (section 6.4).

Kleinman et al. (1986) and Fenske et al. (1987) also evaluated the extent and impact of occupational exposure to Permatox® in 100 workers from a lumber-mill in Washington State. Plant air concentrations of T_4CP ranged from 0.8 to 12.2 µg/m^3, while no PCP was detected (limit of detection 0.5 µg/m^3). It was estimated that dermal exposure accounted for 95% of the dose taken up by exposed workers. Average chlorophenol concentrations in the urine were higher for exposed workers than for controls (range of averages: T_4CP-exposed = 31.2–497.5 µg/litre, control = 6.3–28.7 µg/litre; PCP-exposed = 57.4–102.8 µg/litre, control = 28.9–38.8 µg/litre).

In a recent report, 230 sawmill workers in Finland were examined for urinary levels of chlorophenols (Lindroos et al., 1987). In occupations where dermal exposure was greatest, workers (n = 112) had a median urinary chlorophenol level of approximately 1.8 mg/litre (range, 0.02–49 mg/litre, assuming all chlorophenols were T_4CP) whereas employees (n = 34) exposed mainly via the respiratory route had a median urinary level of 0.2 mg chlorophenols/litre (range, 0.02–3.1 mg/litre). These results support the hypothesis of Kalman & Hortsman (1983) regarding the importance of the dermal route of exposure for chlorophenols.

The chlorophenol levels in urine among workers handling imported lumber treated with 2,3,4,6-T_4CP ranged from 0.13 to 2.2 µmol/litre (30.2–510.4 µg/litre, assuming all chlorophenols were T_4CP) with a mean value of 0.86 µmol/ litre (199.5 µg/litre) (Rappe et al., 1982).

These exposure data are static, and, as such, give no information on the actual amount of chlorophenols taken up by a worker. In the course of designating permissible levels of chlorophenol exposure for regulatory purposes, the US EPA (1978) modelled the chlorophenol exposure experienced by a worker performing various tasks (Table 15).

Table 15. Estimates of occupational exposure to 2,4,5-T_3CP[a]

Site	Dermal exposure (μg/kg body weight per day)	Inhalation exposure (μg/kg body weight per day)
Cooling tower	3.7[b]	23[c]
Water Systems	14[d]	90.3[e]
Pulp and paper mill	2[f]	55[g]
Tannery	49[h]	87[i]
Hospital	70[j]	9[k]

[a] From: US EPA (1978).
[b] Exposure to 100 ml containing 22 mg Na-2,4,5-T_3CP/litre; 10% absorption for 60-kg female maintenance worker.
[c] 100% relative humidity, 20 °C; therefore, 1 m^3 air contains 0.0173 litre H_2O with 22 mg Na-2,4,5-T_3CP/litre H_2O; breathing rate, 1.8 m^3/litre for 2 h; 60-kg female worker.
[d] Exposure to 100 ml containing 87 mg Na-2,4,5-T_3CP/litre; 10% absorption; 60-kg female worker.
[e] As footnote *c*, but product concentration 87 mg Na-2,4,5-T_3CP/litre H_2O.
[f] Exposure to 80 ml (8 x 10 ml; one hand) containing 15 mg Na-2,4,5-T_3CP/litre; 10% absorption; 60-kg female worker.
[g] As footnote *c*, but product concentration 15 mg Na-2,4,5-T_3CP/litre H_2O, 7-h exposure.
[h] Exposure to 1.4 litre containing 21 μg Na-2,4,5-T_3CP/litre; 10% absorption; 60-kg female worker.
[i] As footnote *c*, but product concentration 21 μg Na-2,4,5-T_3CP/litre H_2O, 8-h exposure.
[j] Exposure to 1 cup (0.24 litre; 16 cups per gallon) containing 686 mg Na-2,4,5-T_3CP per gallon; 10% absorption; 60-kg female worker.
[k] Hospital volume, 1800 m^3; recommended air ventilation rate, 60 m^3/h per person; 60 persons; 8-h day; total circulated air, 28 800 m^3; 100 gallons disinfectant used; 100 cups remain giving a total of 4.3 g Na-2,4,5-T_3CP; volatilization at 25 °C; breathing rate, 1.8 m^3/h; 8-h day; 60-kg worker.

The exposure levels indicate that, as expected, occupational exposure to chlorophenols is much higher than non-occupational; these rates of uptake are 2 or more orders of magnitude higher than estimates of exposure of the general population to all chlorophenols summarized in section 5.2.

However, the estimates of chlorophenol burdens given in Table 15 are for 2,4,5-T_3CP (the use of which has been discontinued in many countries), and are based on speculative scenarios that exaggerate worker exposure to this compound. Despite the longstanding concern for the potential health hazards associated with occupational exposure to chlorophenols, meaningful estimates of worker exposure to the chlorophenols that are currently extensively used do not appear to have

been made to date. Exposures have been estimated qualitatively or, at best, semi-quantitatively. Although occupational uptake of chlorophenols is thought to be principally through inhalation and dermal absorption, there are no data on the rates of such uptake. To obtain such information, air monitoring should be continuous throughout the shift, using personal monitors, and urine levels of chlorophenols should be measured for consecutive 24-h periods.

6. KINETICS AND METABOLISM

6.1 Absorption

Hoben et al. (1976a) exposed male Sprague-Dawley rats to an aerosol of sodium-PCP (repeated exposures to about 5.9 mg PCP/kg body weight) and found very rapid absorption into the blood. Unfortunately, no information is available on the absorption of the lower chlorinated phenols via the mammalian lung during inhalation exposure.

In general, chlorophenols are readily absorbed through the skin. Using the skin of the hairless mouse, Huq et al. (1986) found that aqueous solutions of 2-MCP, 2,4-DCP, and 2,4,6- T_3CP readily penetrated the skin, provided that the compound was not ionized (i.e., pH pKa). *In vitro* studies on epidermal membranes from human skin taken at autopsy showed penetration by 2-MCP, 4-MCP, 2,4-DCP, and 2,4,6-T_3CP (Roberts et al., 1977, 1978). The lipophilic character of the solutes and their hydrogen-bonding capacity are the 2 main features determining this penetration. Shen et al. (1983) investigated the dermal absorption of T_4CP in Sprague-Dawley rats and found the Na-2,3,5,6-T_4CP was more toxic than 2,3,5,6-T_4CP itself. Toxic amounts of 2,3,4,6-T_4CP in organic solvents can be absorbed through the skin (Gosselin et al., 1976), and the use of 2,4,5-T_3CP in hospitals has been suggested as a potential problem because of its absorption through the skin (US EPA, 1978). Similarly, on the basis of data concerning urine levels of chlorophenols, absorption through the skin has been reported to be a major route of exposure among workers occupationally exposed to chlorophenols or to their salts (section 5.3).

The greater part of orally-administered tri- and tetra-chlorophenols is recovered in the urine and faeces of test animals (section 6.4), indicating that lower chlorophenols are readily absorbed through the gastrointestinal tract. More than 90% of the oral dose was excreted in the urine of volunteers after ingestion of PCP, which indicates similarly effective absorption via the gastrointestinal tract in human beings (Braun et al., 1979).

6.2 Distribution

6.2.1 Tissue distribution following chlorophenol exposure

No information is available on the distribution of monochlorophenols in animal systems.

With respect to dichlorophenols, single intravenous injections of 2,4-DCP (10 mg/kg body weight) in Sprague-Dawley rats weighing 250–300 g resulted in a maximum concentration (17.7 mg/kg of tissue) in the kidney, 10 min after injection (Somani & Khalique, 1982). Levels in liver, brain, and fat peaked at 15 min at 10.5 mg/kg, 3.2 mg/kg, and 4.1 mg/kg tissue, respectively. A level of 1.64 mg/litre was recorded in plasma, 10 min after injection.

Following intraperitoneal administration of 25 mg 2,4,6-T_3CP/kg body weight to male Wistar rats (Pekari et al., 1986), concentrations in all tissues assayed were maximal, 30 min after injection: kidney levels peaked at 329 ± 117 nmol/g, while maximum concentrations were progressively lower in blood, liver, fat, muscle, and brain.

Hattula et al. (1981a) reported that Wistar rats fed 2,3,4,6-T_4CP in olive oil at 100 mg/kg intragastrically for 55 days showed the following tissue concentrations of 2,3,4,6-T_4CP: kidney, 5.1 mg/kg; spleen, 3.2 mg/kg; liver, 2.2 mg/kg; brain, 1.2 mg/kg; and muscle, 0.46 mg/kg tissue.

6.2.2 Tissue distribution following exposure to chemicals metabolized to chlorophenols

The distribution of chlorophenols as metabolites following the administration of other organochlorine compounds has been investigated in several studies. Like the original chlorophenols, these metabolites accumulate most often in the kidney and liver. Clark et al. (1975) investigated the tissue distribution of 2,4-DCP in sheep and cattle fed 2,4-D. Cattle were given a diet containing 2,4-D at 0, 300, 1000, or 2000 mg/kg (9, 30, or 60 mg/kg body weight per day). Muscle, fat, liver, and kidney were analysed for 2,4-DCP. Sheep were given a diet containing 2,4-D at 2000 mg/kg for 28 days. At 2000 mg 2,4-D /kg in the diet, 2,4-DCP concentrations in kidney and liver from sheep were 0.26 mg/kg tissue and 0.16 mg/kg tissue, respectively; in cattle, levels were 1.06 mg/kg and 0.31 mg/kg tissue, respectively.

In laying hens fed VC-13 Nemacide® [*O*-(2,4-dichloro- phenyl)-*O,O*-diethyl phosphorothioate] at a dose of 800 mg/kg for 55 days, Sherman et al. (1972) reported similar levels of 2,4-DCP in both liver tissue and egg yolk (average values ranged from 0.122 to 0.613 mg/kg). 2,4-DCP was not detected in the muscle and fat of these birds.

Levels of 2,4,5,-T_3CP in the tissues of sheep and cattle fed trichlorophenoxy acid herbicides for 28 days were determined by Clark et al. (1975). In sheep fed Silvex (2-(2,4,5- trichlorophenoxy)-propionic

acid) at 2000 mg/kg, residues of 2,4,5-T_3CP were 0.22 mg/kg in liver and 0.17 mg/kg in kidney.

Cattle fed this compound at 9, 30, or 60 mg/kg body weight had 2,4,5-T_3CP tissue concentrations ranging from 0.06 to 0.48 mg/kg in the liver and from 0.05 to 0.10 mg/kg in kidney. No residues were detected in samples of muscle and fat from sheep or cattle fed Silvex. Sheep exposed to 2,4,5-T in the diet at 2000 mg/kg for 28 days exhibited 2,4,5-T_3CP levels of 6.1 mg/kg, 0.90 mg/kg, 0.13 mg/kg, and 0.05 mg/kg tissue, in the liver, kidney, muscle, and fat, respectively.

Sheep dosed orally with Erbon® (2-(2,4,5-trichloro-phenoxy)-ethyl 2,2-dichloropropionate) metabolized it to 2,4,5-T_3CP and 2-(2,4,5-trichlorophenoxy) ethanol in less than 7 h (Wright et al., 1970). Most of these compounds were eliminated in the urine (section 6.4), but mg/kg quantities of 2,4,5-T_3CP and the other metabolite were found in the kidney, liver, omental fat, muscle, and brain of sheep given 100 mg Erbon®/kg body weight daily for 10 days (5.54, 3.14, 2.06, 1.00, and 0.21 mg/kg, respectively).

Male Wistar rats dosed with 8 mg lindane (gamma-hexachloro-cyclohexane) /kg body weight by gavage for 19 days showed 2,4,6-T_3CP and 2,3,4,6-T_4CP in heart tissue, 2,3,4,6- T_4CP and/or 2,3,5,6-T_4CP in the liver, and 2,4,6-T_3CP and 2,3,4,6-T_4CP in the kidney (Engst et al., 1976), but no quantitative data were given.

6.3 Metabolic Transformation

The major metabolic transformation for the lower chlorinated chlorophenols appears to be conjugation with sulfate or glucuronate, prior to clearance in the urine. Perhaps, because of similarities between the structure and lipophilicity of T_4CP and PCP, a small proportion of these congeners undergo the same dechlorination and/or oxidation reactions that PCP does prior to conjugation (Renner & Mücke, 1986).

As much as 84.7% of administered 2-MCP was reportedly excreted as sulfate and glucuronate conjugates in dogs (Karpow, 1893). In the rabbit, oral administration of monochlorobenzene resulted in sulfate and glucuronide conjugates of 2-MCP in the urine (Lindsay-Smith et al., 1972). It has been suggested that in mice *o*-methylation might be a relevant mechanism for 2-MCP detoxification (Angel & Rogers, 1972). Similarly, conjugates were detected in the kidney, liver, fat, brain, and plasma of rats after the iv injection of 2.5–3 mg 2,4-DCP (10 mg/kg body weight) (Somani & Khalique, 1982). Of the total conjugates determined,

glucuronide conjugates were the major metabolite in kidney (79.6%), liver (62.7%), brain (77.9%), and plasma (79.5%). No glucuronide conjugates were found in fat. Free 2,4-DCP did not accumulate in rat tissues and was rapidly metabolized to its conjugates. In another study using ^{14}C-2,4-DCP on isolated perfused rat liver, Somani et al. (1984) demonstrated that the liver is capable of the formation of glucuronide conjugates, and that 2 dichloromethoxyphenols are metabolites of 2,4-DCP when glucuronide formation is blocked by galactosamine (section 8.8).

Bahig et al. (1981) have suggested that, in rats, 2,4,6-T$_3$CP is isomerized to 2,4,5- and 2,3,6-T$_3$CP before being excreted as glucuronide conjugates. However, in a similar study on rats given 25 mg 2,4,6-T$_3$CP/kg body weight (ip), 83 ± 11% was present in the blood as glucuronides rather than being converted to another isomer (Pekari et al., 1986).

Concerning T$_4$CP, Ahlborg & Larsson (1978) showed that, of the 3 isomers, only 2,3,5,6-T$_4$CP was metabolized to a significant extent in the rat. Thirty-five percent of the given dose (10 mg/kg body weight by ip injection) was metabolized to tetrachloro-*p*-hydroquinone, which, when also given ip, is more toxic than the parent compound (section 8.9). Trichloro-*p*-hydroquinone was a minor metabolite of the other isomers. Recently, it has been shown that the microsomal metabolism of PCP yields tetrachloro-1,2-and tetrachloro-1, 4-hydroquinone (van Ommen et al. 1986). Covalent binding to protein and DNA occurs via the corresponding tetrachloroquinones (van Ommen et al., 1988). To what extent this kind of metabolic activation plays a role in the toxicity of lower chlorinated phenols is not known, at present.

The metabolism of compounds that are structurally related to chlorophenols also yields conjugates of chlorophenols. Kurihara & Nakajima (1974) studied the metabolism in mice of injected ^{14}C-hexachlorocyclohexane (^{14}C-HCH). The major metabolites were conjugates of 2,4,6-T$_3$CP with sulfate or glucuronide, as well as conjugates of 2,4-DCP. The proportion of 2,4,6-T$_3$CP sulfate to glucuronide conjugates varied from 80%:20% to 40%:60%, depending on whether gamma-HCH or beta-HCH was used. Trace amounts of free 2,4,6-T$_3$CP and 2,4,5-T$_3$CP were also found in the urine. Koransky et al. (1975) also found that injection of ^{14}C-HCH into rats resulted in glucuronide and sulfate urinary metabolites of 2,4,6- and 2,4,5-T$_3$CP; small amounts of the free phenols were also detected. The ratio of sulfate to glucuronide conjugates was not determined. Engst et al. (1976) found that lindane (gamma-HCH) administration in rats produced free 2,4,6-T$_3$CP, 2,3,4,6-

and/or 2,3,5,6-T_4CP and PCP in the urine, as well as glucuronide-bound 2,3,4-T_3CP, 2,3,4,5-, 2,3,4,6- and/or 2,3,5,6-T_4CP.

In terms of glucuronide formation of PCP, the rat is probably a better model for human beings than the monkey, which does not metabolize this compound (Braun et al., 1978, 1979). Whether the rat model can be used to predict human responses to the lower chlorinated phenols is not known at present, since no human data exist. However, hydrolysis of human urine samples indicated that most of the T_4CP in human urine is conjugated (Dahms & Metzner, 1979; Butte, 1984; Currie & McDonald, 1986).

6.4 Elimination and Excretion

In experimental mammals, chlorophenols are eliminated primarily in the urine. For example, Freitag et al. (1982) administered ^{14}C-2,4,6-T_3CP to rats orally for 3 days to examine retention, dispersion, and excretion rates. Within 7 days, 82.3% of the label was excreted in the urine and 22.2% in the faeces. At sacrifice on the 8th day, residues in the liver, lung, and adipose tissues were below the level of detection (i.e., less than 0.01% of the label), whereas the carcass retained 7.8% of the label. Bahig et al. (1981) found that 92.5% of a daily oral dose (25 µg by gavage) of ^{14}C-2,4,6-T_3CP was excreted by rats in the urine, while 6.4% was found in the faeces. Thus, the ingested 2,4,6-T_3CP was largely eliminated within 24 h. Similarly, Ahlborg & Thunberg (1980) reported that 2,4,5-T_3CP given to rats was excreted rapidly (within 24 h) with very little retention by the animal, and Pekari et al. (1986) estimated the half-times for the elimination of 2,4,6-T_3CP from the blood, liver, muscle, fat, brain, and kidney of rats at between 1.4 and 1.8 h, after dosing ip with 25 mg/kg body weight.

Excretion by rats of the different T_4CP isomers injected intraperitoneally was examined by Ahlborg & Larsson (1978). While 2,3,5,6-T_4CP was eliminated in the urine within 24 h and 2,3,4,6-T_4CP within 48 h, only 60% of the injected 2,3,4,5-T_4CP was collected in 72 h.

In a study on the elimination of 2,4,-DCP from various tissues in the rat following intravenous administration of 10 mg/kg body weight (Somani & Khalique, 1982), the compound was eliminated most rapidly from brain tissue followed by plasma, fat, liver, and kidney. Half-lives for 2,4-DCP were 6 min in the brain, 10 min in fat and plasma, 15.1 min in the liver, and 30.1 min in the kidney.

Much of the information on the excretion of chlorophenols has come from studies of the uptake and clearance of chlorophenols that

have been formed metabolically from other compounds. As in the studies described previously, these chlorophenols are generally eliminated rapidly in the urine. Thus, Lindsay-Smith et al. (1972) identified free and conjugated forms of all monochlorophenol isomers in the urine of rabbits dosed with ^{14}C-monochlorobenzene. Similarly, 2,4-DCP was eliminated in the urine of rats injected with Nemacide® (67% of dose excreted as 2,4-DCP within 3 days) (Shafik et al., 1973). Shafik et al. (1973) also found that rats cleared 53% of a dose of Ronnel® (*O,O*-dimethyl-*O*(2,4,5-trichloro-phenyl)phosphorothioate) as 2,4,5-T$_3$CP within 2 days. A sheep given 50 mg/kg body weight of Erbon® [2-(2,4,5-trichloro-phenoxy)-ethyl 2,2-dichloropropionate] as an oral drench metabolized it to 2,4,5-T$_3$CP and 2-(2,4,5-trichloro-phenoxy) ethanol in less than 7 h (Wright et al., 1970). Within 96 h, 68.42% of the dose was eliminated in the urine and 1.74% in the faeces, approximately half of these amounts as 2,4,5-T$_3$CP.

Karapally et al. (1973) identified chlorinated phenols derived from lindane in rabbit urine. Of the 14 chlorophenols identified, comprising at least 19.9% of the total dose, the most abundant were (in decreasing order) 2,4,5-T$_3$CP, 2,3,5-T$_3$CP, 2,4,6-T$_3$CP, 2,3,4,6-T$_4$CP, 2,3-DCP, 2,4-DCP, and 2,3,4-T$_3$CP. The results of a similar study on the rat (Engst et al., 1976) showed that 2,4,6-T$_3$CP, 2,3,4,6-T$_4$CP and/or 2,3,5,6-T$_4$CP, and 2,3,4,5-T$_4$CP derived from lindane were eliminated via the urine. Chadwick & Freal (1972) observed that, following one week of dosing with lindane, rats excreted 3,4-DCP, 2,4,5-T$_3$CP, 2,3,5-T$_3$CP, 2,4,6-T$_3$CP, 2,3,4,5-T$_4$CP, and 2,3,4,6-T$_4$CP for at least 1 month.

The clearance from tissues of chlorophenols derived from other compounds may be slower than their elimination via the urine. Sherman et al. (1972) found that from 60 to 83% of the 2,4-DCP metabolized from Nemacide® disappeared from the liver of chickens within 21 days of the cessation of dosing. 2,4-DCP found in the yolk of eggs from these hens dropped to non-detectable levels in 10 days for the high-dose (800 mg/kg diet) group, while at the lower dosages (50, 100, 200 mg/kg diet), a shorter time was required for complete clearance (see also section 6.2). In sheep fed 2,4,5-T$_3$CP at 2000 mg/kg diet (Clark et al., 1975), liver and kidney 2,4,5-T$_3$CP levels remained relatively constant one week after exposure ceased, while muscle concentrations dropped roughly 3-fold.

7. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

There are few studies on the effects of chlorophenols, other than PCP, on organisms in the environment. This lack of information may stem, in part, from the fact that many wastes contain other potentially toxic components in addition to chlorophenols. Moreover, most laboratory studies on the toxicity of chlorophenols for environmental organisms have involved much higher exposure levels than those that are usually found in the environment.

The information that is available on the effects of chlorophenols deals primarily with aquatic habitats, perhaps because many point discharges of chlorophenols are released into water bodies.

7.1 Laboratory Studies

7.1.1 Acute toxicity

Recent laboratory studies on the acute toxicity of chlorophenols for aquatic biota are summarized in Table 16. The data are derived primarily from studies published since 1980; information from research prior to this date is presented by Jones (1981). In general, the patterns evident in the review by Jones (1981) are also seen in the more recent data (Table 16).

Considerable overlap exists in the chlorophenol levels that produce toxic effects in bacteria, phytoplankton, macrophytes, invertebrates, and fish (Table 16). For instance, LeBlanc (1984) (Table 16) reported that LC_{50} values compiled for 4-MCP toxicity in algae (*Selenastrum capricornutum*, *Skeletonema costatum*), invertebrates (*Daphnia magna*), and fish (*Lepomis macrochirus, Cyprinidon variegatus*) ranged from 3.27–5.35 mg/litre. Most of the EC_{50}/LC_{50} values for other organisms compiled in Table 16 also fall within the several mg/litre range. However, there are isolated reports of certain bacterial, fungal, and protozoan processes that are insensitive to chlorophenol exposure (Table 16).

In general, chlorophenol toxicity for aquatic organisms increases with the degree of chlorination of the phenol ring (Table 16), presumably as a result of increasing lipophilicity (Table 3).

Table 16. Acute toxicity of chlorophenols for aquatic biota

Test organism	Test conditions	Chlorophenol	Concentration (mg/litre)	Criterion	Reference
Phytoplankton					
Scenedesmus spicatus	SB, FW	3,5-DCP	5.32 (EC_{50}) 5.87 (EC_{50}) 6.10 (EC_{50})	Growth rate, Weibull model Growth rate, Probit model Growth rate, Logit model	Christensen & Nyholm (1984)
Selenastrum capricornutum	SB, FW	4-MCP	5.01 (EC_{50})	Growth	LeBlanc (1984)
Skeletonema costatum	SB, FW	4-MCP	3.27 (EC_{50})	Growth	LeBlanc (1984)
Bacteria					
Bacillus sp.	SB, FW	2-MCP	700		
		3-MCP	450		
		4-MCP	400		
		2,3-DCP	130		
		2,4-DCP	75		
		2,5-DCP	85		
		2,6-DCP	550		
		3,4-DCP	52	IC_{50}[c], reduction in activity after 30 min incubation with toxicant	Liu et al. (1982)
		3,5-DCP	25		
		2,3,4-T3CP	13		
		2,3,5-T_3CP	10		
		2,3,6-T_3CP	190		

Table 16 (contd).

Test organism	Test conditions	Chlorophenol	Concentration (mg/litre)	Criterion	Reference
Bacteria (contd).					
Bacillus sp. (contd).		2,4,5-T_3CP	12		
		2,4,6-T_3CP	240		
		3,4,5-T_3CP	5		
		2,3,4,5-T_4CP	4		
		2,3,5,6-T_4CP	54		
Photobacterium phosphoreum (Microtox®)	SW	2-MCP	33.8		Ribo & Kaiser (1983)
		3-MCP	14.1		
		4-MCP	8.30		
		2,3-DCP	4.92		
		2,4-DCP	5.52		
		2,5-DCP	9.38	EC_{50} for inhibition	
		2,6-DCP	13.2	of light emission with	
		3,4-DCP	1.63	30-min toxicant exposure	
		3,5-DCP	2.77		
		2,3,4-T_3CP	1.25		
		2,3,5-T_3CP	1.11		
		2,3,6-T_3CP	12.7		
		2,4,5-T_3CP	1.27		
		2,4,6-T_3CP	7.68		
		3,4,5-T_3CP	0.359		
		2,3,4,5-T_4CP	0.176		
		2,3,4,6-T_4CP	1.27		
		2,3,5,6-T_4CP	2.22		

Table 16 (contd).

Activated sludge	SB, FW	3,5-DCP	30.2	IC_{50} for O_2 consumption, 3 h	Dutka & Kwan (1984)
Photobacterium phosphoreum (Microtox®)	SW 2,4-DCP 3.36	2-MCP	22.1	EC_{50} for inhibition of light emission with toxicant exposure	Indorato et al. (1984)
Activated sludge	SB, FW	3,5-DCP	7	EC_{50} for O_2 consumption	King (1984)
Nitrifying activated sludge			5	EC_{50} for nitrate and nitrite production	
Photobacterium phosphoreum (Microtox®)	SW		3.2	EC_{50} for light emission	
Sewage microorganisms			8	EC_{50} for growth inhibition, 6 h	
Sewage microorganisms			6	EC_{50} for growth inhibition, 16 h	
Sewage effluent			15	EC_{50} for BOD, 5 days, supplemented	
Photobacterium phosphoreum (Microtox®)	SW	3,5-DCP	2.9	EC_{50} for light emission after 15 min	Dutka & Kwan (1984)

Table 16 (contd).

Test organism	Test conditions	Chlorophenol	Concentration (mg/litre)	Criterion	Reference
Bacteria (contd).					
Pseudomonas fluorescens	SB, FW	3,5-DCP	3.2	EC_{50} for growth inhibition, 18 h	Dutka & Kwan (1984)
Activated sludge	FB, FW	2-MCP	104.4		Beltrame et al. (1984)
		3-MCP	67.5		
		4-MCP	71.0		
		2,3-DCP	55.1		
		2,4-DCP	47.6		
		2,5-DCP	50.2		
		2,6-DCP	65.2	IC_{50} for phenol biodegradation	
		3,4-DCP	42.7		
		3,5-DCP	58.3		
		2,3,4-T_3CP	27.4		
		2,3,5-T_3CP	22.3		
		2,3,6-T_3CP	39.3		
		2,4,5-T_3CP	23.6		
		2,4,6-T_3CP	42.0		
		3,4,5-T_3CP	19.6		
		2,3,4,5-T_4CP	20.4		
		2,3,4,6-T_4CP	40.5		
		2,3,5,6-T_4CP	44.3		

Table 16 (contd).

Bacteria (contd).					
Nitrobacter	SB, FW	2-MCP	50	25 and 27% inhibition of nitrite uptake	Wang & Reed (1984)
		3-MCP	50	0 and 15 % inhibition of nitrite intake	
		4-MCP	50	0 and 5 % inhibition of nitrite intake	
		2,3-DCP	30	96 and 73 % inhibition of nitrite intake	
		2,4-DCP	30	21 and 77 % inhibition of nitrite intake	
		2,4,6-T_3CP	10	88 and 100% inhibition of nitrite intake	
Nitrosomonas europa	SB, FW	2-MCP	100	24 % loss in ATP	Parker & Pribyl (1984)
		2,4,6-T_3CP	150	17.6 % loss in ATP	
Escherichia coli	SB, FW	2-MCP	100	6.5 % loss in ATP	
		2,4,6-T_3CP	150	12.9 % loss in ATP	
Pseudomonas fluorescens	SB, FW	2,3,4,5-T_4CP	10	0 % reduction in CFUs, 1-h exposure	Trevors et al. (1982)
			25	86.6 and 87.2 % reduction in CFUs, 1-h exposure	
			35	99.4 and 99.9 % reduction in CFUs, 1-h exposure	
			23.2	LC_{50} of CFUs, 1-h exposure	

Table 16 (contd).

Test organism	Test conditions	Chlorophenol	Concentration (mg/litre)	Criterion	Reference
Protozoa					
Tetrahymena		2-MCP	67.97		
		4-MCP	36.68	IC_{50} for growth	Schultz &
		2,4-DCP	15.00	at 60 h	Riggin (1985)
		2,5-DCP	12.15		
		2,4,6-T_3CP	3.99		
		2,3,5,6-T_4CP	1.40		
Fungi					
16 fungal strains, (14 genera)	SB	3-MCP	257.1	Average minimum concentration for complete inhibition of growth	Ruckdeschel & Renner (1986)
		4-MCP	184.9		
		2,3-DCP	60.8		
		2,4-DCP	54.1		
		2,5-DCP	54.8		
		2,6-DCP	180.8		
		3,4-DCP	30.1		
		3,6-DCP	13.2		
	SB	2,3,4-T_3CP	11.6		
		2,3,5-T_3CP	9.9		
		2,3,6-T_3CP	140.4		
		2,4,5-T_3CP	19.2		
		2,4,6-T_3CP	93.4		
		3,4,5-T_3CP	4.1		
		2,3,4,5-T_4CP	4.6		
		2,3,4,6-T_4CP	72.8		
		2,3,5,6-T_4CP	119.7		

Table 16 (contd).

Fungi (contd).					
Pichia (fermentative yeast)	SB	Na-4-MCP	145	IC_{50} for culture growth	Kwasniewska & Kaiser (1983)
		Na-2,4-DCP	42.5		
		Na-2,4,5-T_3CP	4.3		
Rhodoturula rubra (oxidative yeast)	SB	Na-4-MCP	62.5	IC_{50} for culture growth	
		Na-2,4-DCP	16.5		
		Na-2,4,5-T_3CP	2.0		
Invertebrates					
Daphnia magna (water flea)	SB, FW	2-MCP	22	24-h LC_{50}	LeBlanc (1980)
			2.6	48-h LC_{50}	
		4-MCP	8.8	24-h LC_{50}	
			4.1	48-h LC_{50}	
		2,4-DCP	> 10	24-h LC_{50}	
			2.6	48-h LC_{50}	
		2,4,5-T_3CP	3.8	24-h LC_{50}	
			2.7	48-h LC_{50}	
		2,4,6-T_3CP	15	24-h LC_{50}	
			6.0	48-h LC_{50}	
		2,3,4,6-T_4CP	> 1.0	24-h LC_{50}	
			0.29	48-h LC_{50}	
		2,3,5,6-T_4CP	2.5	24-h LC_{50}	
			0.57	48-h LC_{50}	

Table 16 (contd).

Test organism	Test conditions	Chlorophenol	Concentration (mg/litre)	Criterion	Reference
Daphnia magna (water flea)		2-MCP	17.95	IC_{50} for immobilization after 24 h	Devillers & Chambon (1986)
		3-MCP	15.78		
		4-MCP	8.07		
		2,3-DCP	5.19		
		2,4-DCP	2.68		
		2,6-DCP	9.38		
		3,4-DCP	2.77		
		3,5-DCP	2.09		
		2,3,4-T_3CP	2.24		
		2,3,5-T_3CP	2.28		
		2,3,6-T_3CP	7.38		
		2,4,5-T_3CP	2.08		
		2,4,6-T_3CP	5.47		
		3,4,5-T_3CP	0.88		
		2,3,4,5-T_4CP	1.76		
		2,3,5,6-T_4CP	2.27		
Astacus fluviatilis	SB, FW	2,3,6-T_3CP	5.4 at pH 6.5	8-day LC_{50}	Kaila & Saarikoski (1977)
			19.0 at pH 7.5	8-day LC_{50}	
Mysidiopsis bahia	SB, SW	4-MCP	29.7 at pH 6	96-h LC_{50}	LeBlanc (1984)

Table 16 (contd).

Invertebrates (contd)					
Palaemonetes pugio (grass shrimp)	SS, SW	2,4-DCP	2.55(I)[a]; 2.16 (M)[b]	96-h LC_{50}	Rao et al. (1981)
		2,4,6-T_3CP	3.95(I); 1.21 (M)	96-h LC_{50}	
		2,4,5-T_3CP	1.12(I); 0.64 (M)	96-h LC_{50}	
		2,3,4,5-T_4CP	0.86(I); 0.37 (M)	96-h LC_{50}	
		2,3,4,6-T_4CP	3.70(I); 0.81 (M)	96-h LC_{50}	
		2,3,5,6-T_4CP	4.10(I); 1.17 (M)	96-h LC_{50}	
Palaemonetes pugio (grass shrimp)	SS, SW	2,3,4,5-T_4CP	0.30	EC_{50} for intermolt limb regeneration	Rao et al. (1981)
		2,3,4,6-T_4CP	0.78	EC_{50} for intermolt limb regeneration	
Fish					
Pimephales promelas (fathead minnow)	SB/FB, FW	2-MCP	11.0–13.0	96-h LC_{50} *flowthrough*	Phipps et al. (1981)
			6.3	192-h LC_{50} *flowthrough*	
			9.7	48-h LC_{50} *static*	
		2,4-DCP	8.2–8.3	96-h LC_{50} flowthrough	
			6.5	192-h LC_{50} flowthrough	
			8.4	48-h LC_{50} Static	
		2,4,6-T_3CP	8.6–9.7	96-h LC_{50} flowthrough	
			5.8–6.4	192-h LC_{50} flowthrough	
			7.7	48-h LC_{50} static	
Cyprinidon variegatus (sheepshead minnow)	SB, SW	4-MCP	5.7	24-h LC_{50}	Heitmuller et al. (1981)
			5.4	48-h LC_{50}	
			5.4	72-h LC_{50}	
			5.4	96-h LC_{50}	
			3.2	NOEC[c]	

Table 16 (contd).

Test organism	Test conditions	Chlorophenol	Concentration (mg/litre)	Criterion	Reference
Fish (contd).					
Cyprinidon variegatus (contd).		2,4,5-T_3CP	2.4	24-h LC_{50}	
			1.7	48-h LC_{50}	
			1.7	72-h LC_{50}	
			1.7	96-h LC_{50}	
			1.0	NOEC[c]	
		2,3,5,6-T_4CP	2.0	24-h LC_{50}	
			2.0	48-h LC_{50}	
			2.0	72-h LC_{50}	
			1.9	96-h LC_{50}	
			1.0	NOEC[c]	
Salmo trutta (trout)	SB, FW	2,4-DCP	1.7	24-h LC_{50}	Hattula et al. (1981b)
		2,6-DCP	4.0		
		2,3,5-T_3CP	0.8		
		2,4,5-T_3CP	0.9		
		2,3,4,6-T_4CP	1.1		
Poecilia reticulatus (guppy)	SS, FW	4-MCP	49.0 at pH 5	96-h-LC_{50}	Saarikoski & Viluksela (1981)
			61.0 at pH 6	96-h LC_{50}	
			66.0 at pH 7	96-h LC_{50}	
		2,4,5-T_3CP	50.0 at pH 5	96-h LC_{50}	
			6.3 at pH 7	96-h LC_{50}	
			15.3 at pH 8	96-h LC_{50}	
		2,4,6-T_3CP	3.1 at pH 5	96-h LC_{50}	
			4.5 at pH 6	96-h LC_{50}	
			11.6 at pH 7	96-h LC_{50}	
			39.8 at pH 8	96-h LC_{50}	

Table 16. (contd).

Poecilia reticulatus (guppy)	SB, FW	2-MCP	13.5 at pH 7.8	24-h LC_{50}	Könemann & Musch (1981)
			7.1 at pH 6.1	24-h LC_{50}	
		3-MCP	7.9 at pH 7..8	24-h LC_{50}	
			6.4 at pH 6.1	24-h LC_{50}	
		2,4-DCP	5.9 at pH 7.8	24-h LC_{50}	
			3.3 at pH 6.1	24-h LC_{50}	
		3,5-DCP	4.7 at pH 7.8	24-h LC_{50}	
			2.6 at pH 6.1	24-h LC_{50}	
		2,3,5-T_3CP	4.7 at pH 7..8	24-h LC_{50}	
			0.88 at pH 6.1	24-h LC_{50}	
		2,3,6-T_3CP	13.3 at pH 7.8	24-h LC_{50}	
			0.94 at pH 6.1	24-h LC_{50}	
		3,4,5-T_3CP	2.4 at pH 7.8	24-h LC_{50}	
		2,3,4,5-T_4CP	1.1 at pH 6.1	24-h LC_{50}	
		2,3,5,6-T_4CP	2.3 at pH 7.8	24-h LC_{50}	
			0.44 at pH 6.1	24-h LC_{50}	
			3.9 at pH 7.8	24-h LC_{50}	
			0.36 at pH 6.1	24-h LC_{50}	
Carassius auratus (goldfish)	SB, FW	2-MCP	16	25-h LC_{50}	Kobayashi et al. (1979)
		4-MCP	9.0		
		2,4-DCP	7.8		
		2,4,5-T_3CP	1.7		
		2,4,6-T_3CP	10.0		
		2,3,4,6-T_4CP	0.75		

Table 16 (contd).

Test organism	Test conditions	Chlorophenol	Concentration (mg/litre)	Criterion	Reference
Fish (contd).					
Lebistes reticulatus (guppy)	SB, FW	2-MCP	13.4	24-h LC_{50}	Benoit-Guyod et al. (1984)
		3-MCP	27.0		
		4-MCP	9.0		
		2,3-DCP	18.0		
		2,4-DCP	6.8		
		2,5-DCP	11.0		
		2,6-DCP	8.9		
Lebistes reticulatus (guppy)		3,4-DCP	7.4		
		3,5-DCP	6.1		
		2,3,6-T_3CP	53.0		
		2,4,5-T_3CP	2.7		
		2,4,6-T_3CP	2.3		
		2,3,4,5-T_4CP	1.70		
		2,3,5,6-T_4CP	3.60		
Lepomis macrochirus (bluegill)	SB, FW	2-MCP	7.2	24-h LC_{50}	Buccafusco et al. (1981)
			6.6	96-h LC_{50}	
		4-MCP	4.0	24-h LC_{50}	
			3.8	96-h LC_{50}	
		2,4-DCP	4.7	24-h LC_{50}	
			2.0	96-h LC_{50}	
		2,4,5-T_3CP	0.61	24-h LC_{50}	
			0.45	96-h LC_{50}	
		2,4,6-T_3CP	0.72	24-h LC_{50}	
			0.32	96-h LC_{50}	

Table 16 (contd).

		2,3,4,6-T_4CP	0.19	24-h LC_{50}	
			0.14	96-h LC_{50}	
		2,3,5,6-T_4CP	0.40	24-h LC_{50}	
			0.17	96-h LC_{50}	
Plants					
Lemna minor (duckweed)	SB, FW	4-MCP	282.8	50 % chlorosis of fronds	Blackman et al. (1955)
		2,4-DCP	58.7		
		2,4,6-T_3CP	5.9		
		2,4,5-T_3CP	1.7		
		2,3,4,6-T_4CP	0.6		

[a] SB = Static bioassay.
SS = Semistatic bioassay.
SW = Marine.
FB = Continuous flow bioassay.
FW = Fresh water.
M = Molting.
I = Intermolt.

[b] NOEC = No-observed-effect concentration.

[c] IG_{50} = Concentration resulting in 50% inhibition.

The position of the chlorines on the phenol ring also influences chlorophenol toxicity. Chlorophenols with chlorines in the 2 and 6 positions are often relatively non-toxic (Kobayashi et al., 1979; Hattula et al., 1981b; Liu et al., 1982; Ribo & Kaiser, 1983; Devillers & Chambon, 1986; Ruckdeschel & Renner, 1986), perhaps, because the chlorines shield the hydroxyl group. These patterns parallel the biodegradability of the compounds, as ortho-substituted chlorophenols are less stable than their meta-substituted isomers (section 4.2.1.2). However, the effects of chlorine position on toxicity are not evident in all of the studies included in Table 16, suggesting that the toxicity of any particular chlorophenol is highly species-specific.

In addition, pH affects the toxicity of chlorophenols (Table 16). At low pH, a given chlorophenol is relatively toxic, because it is mainly in the form of molecules that can readily cross biological membranes. As the pH is increased, chlorophenol toxicity is reduced because the ionic form becomes abundant. Under the range of conditions in most natural habitats, this effect becomes more important as the number of chlorines in the chlorophenol increases, because the pKa is related to chlorine number. Thus, monochlorophenol toxicity is relatively unchanged by environmental pH, whereas that of pentachlorophenol, which is present in the molecular form only under very acid conditions, is greatly affected.

Studies on the toxicity of chlorophenols for terrestrial organisms in the environment are much more limited. Blackman et al. (1955) determined that the EC_{50}s of several chlorophenols for the inhibition of radial growth of the mould *Trichoderma viride* were as follows: 4-MCP, 47.6 mg/litre agar; 2,4-DCP, 8.6 mg/litre; 2,4,6-T_3CP, 5.7 mg/litre; and 2,3,4,6-T_4CP, 0.8 mg/litre. A similar pattern of increasing toxicity with increasing chlorination of chlorophenols was also observed by Sund & Nomura (1963) in their investigation of the inhibition of seed germination by a number of chlorophenols. In addition, they noted that chlorination at the 3 or 5 position enhanced chlorophenol toxicity for germinating seeds. In a survey on the contact toxicity of chemicals for the earthworm *Eisenia foetida* (Roberts & Dorough, 1984), 2,4-DCP and 2,4,5-T_3CP were classified as extremely toxic, on the basis that their 48-h LC_{50} values fell within the range of 1–10 $\mu g/cm^2$ of filter paper.

7.1.2 Long-term toxicity

There are very few studies on the long-term effects of chlorophenols on environmental organisms. Holcombe et al. (1982) exposed

the embryo, larval, and early juvenile stages of fathead minnows to a range of sublethal concentrations of 2,4-DCP and other phenolic compounds, in 32-day flow-through tests using Lake Superior water. Survival of larvae and juvenile minnows was significantly reduced after exposure for 28 days to 2,4-DCP at 460 μg/litre. The growth of larval and juvenile stages was reduced by 1240 μg 2,4-DCP/litre. Hatching success was unaffected by the maximum concentration used (1240 μg/litre).

Survival, reproduction, and growth were all reduced in *Daphnia magna* exposed to 2,4-DCP concentrations of 1.48 mg/litre in long-term (21-day) static renewal tests (Gersich & Milazzo, 1988).

In a study more relevant to field conditions, Virtanen & Hattula (1982) used a flow-through aquarium microcosm with levels of 2,4,6-T_3CP of 0.5 μg/litre, in order to track its incorporation into sediment, algae, invertebrates, and fish. Male and female *Poecilia reticulatus* fish were included in the microcosm, and aspects of their reproduction and histopathology were monitored. Over a 10-month period following their 56-day exposure in the aquarium and subsequent transfer to uncontaminated water, only 90 offspring were born to exposed fish and 22 of these died. Control fish produced 180 offspring, only 8 of which died. In addition, several offspring from exposed parents had abnormally curved spines. Thus, under the test conditions, 2,4,6-T_3CP appeared to be very fetotoxic, and perhaps teratogenic. No histological changes were noted in the livers or kidneys of *P. reticulatus* as a result of these exposures.

7.1.3 Organoleptic effects

Exposure to low levels of chlorophenols can also impair the flavour of fish (see section 7.2.4). According to Boetius (1954), as little as 0.1 Ul 2-MCP/litre (v/v) tainted the flesh of eels and oysters after exposure for 11 and 4 days, respectively. Shumway & Palensky (1973) estimated the threshold concentrations of several chlorophenols for the impairment of the flavour of rainbow trout to be: 2-MCP, 60 μg/litre; 3-MCP, 25 μg/litre; 4-MCP, 45 μg/litre; 2,3-DCP, 84 μg/litre; 2,4-DCP, 1 μg/litre; 2,5-DCP, 23 μg/litre; 2,6-DCP, 35 μg/litre; and 2,4,6-T_3CP, 52 μg/litre.

7.2 Toxicity Studies under Natural Environmental Conditions

7.2.1 Bacteria

During the course of studies in Dutch coastal waters, Kuiper & Hantsveit (1984) examined the effects of the addition of 4-MCP and 2,4-DCP on plankton communities enclosed in 1500-litre plastic bags. In the first of 3 studies, total bacterial densities (by direct count) were prevented from increasing by 0.1 and 1 mg 2,4-DCP/litre but, in a second study, 2,4-DCP at 1 mg/litre did not have any effect on total bacterial densities, and, in the final study, 1 mg 2,4-DCP/ litre was necessary to inhibit bacterial population growth. No effects of 4-MCP were detected, even at 1 mg/litre. As treatments were not replicated and bacterial densities were quite variable, it is not clear whether the effects observed were in fact responses to chlorophenol exposure.

In contrast, when 5 mg 2,4,6-T_3CP/litre was added to enclosures in a West German pond, the numbers of aerobic heterotrophic bacteria (by plate count) in the water increased more than 10 times compared with the controls, within 4 days (Schauerte et al., 1982). This response coincided with the disappearance of *Daphnia* from the CP-treated tubes, suggesting that the increase was the result of a release from grazing by the *Daphnia*.

There has been some concern that chlorophenols in industrial wastes may impair the efficiency of secondary waste treatment through their toxic effects on bacteria. Using a bench-scale activated sludge plant, Broecker & Zahn (1977) determined that the degradation of waste water declined after exposure to 25 μg 3,5-DCP/litre. Similarly, in a laboratory scale model of a trickling filter (El-Gohary & Nasr, 1984), exposure of acclimated microbes to 50 mg 2,4-DCP/litre reduced Biological Oxygen Demand (BOD), and Chemical Oxygen Demand (COD). However, chlorophenols in industrial wastes are unlikely to pose a serious hazard for organisms important for secondary treatment. Levels of chlorophenol entering treatment facilities are far below those used in the studies just described (Folke, 1984), and recovery from shock loadings of chlorophenols is rapid (El-Gohary & Nasr, 1984).

7.2.2 Phytoplankton

Kuiper & Hantsveit (1984) monitored the response of enclosed marine plankton to chlorophenol additions, and determined that exposure to chlorophenols affected algal biomass, composition, and

activity. In the first of 3 studies, 1 mg 4-MCP or 2,4-DCP/litre prevented the increase in algal biomass (as chlorophyll) that occurred in control enclosures. Large flagellates made up a greater proportion of the algal community in 1 mg/litre-treated enclosures compared with controls, perhaps because grazing was reduced (section 7.3). Primary productivity generally parallelled the dynamics of algal biomass, as it was reduced by exposure to 1 mg 4-MCP/litre; however, the addition of 1 mg 2,4-DCP/litre did not affect photosynthetic radiolabelled dissolved inorganic carbon (DIC) uptake. Results were generally similar during the 2 subsequent manipulations, though the magnitude and timing of the effects varied.

In their studies on ponds, Schauerte et al. (1982) observed major shifts in the species composition of the phytoplankton following the addition of 5 mg 2,4,6-T3CP/litre. The large population of the blue-green alga *Chroococcus limneticus* was sharply reduced, and the diatom *Nitzschia acicularis* was eliminated, while the flagellated algae *Euglena* and *Trachelomonas* appeared in large numbers following exposure to 2,4,6-T3CP. The dynamics of other phytoplankton, which were less abundant, were not discussed.

Chlorophenols were among the toxicants used by Erickson & Hawkins (1980), who measured the response of estuarine phytoplankton communities to 15 compounds produced during the chlorination of sea water. Natural phytoplankton assemblages, pumped from the estuary to flow-through aquaria in the laboratory, were insensitive to chlorophenol concentrations of 0.5–2 mg/litre. Photosynthetic radiolabelled DIC uptake was not depressed by exposure to 2 mg 2,4,6-T3CP or 4-MCP/litre.

7.2.3 Zooplankton

Marine zooplankton were strongly affected by chlorophenol additions during field studies in 1500-litre plastic enclosures (Kuiper & Hantsveit, 1984). While the zooplankton communities in the control enclosures and those treated with 0.1 mg 4-MCP/litre or 0.1 mg 2,4-DCP/litre displayed similar dynamics, total biomass and production in enclosures treated with 1 mg 4-MCP/litre and 1 mg 2,4-DCP/litre were reduced relative to controls throughout the first three-quarters of the study. All life-history stages of several copepod species were similarly affected. Results in subsequent studies were generally similar, though the magnitude of the impact varied.

More severe effects for *Daphnia* exposed to 5 mg 2,4,6-T_3CP/litre were reported by Schauerte et al. (1982) during studies on a pond. From initial levels of more than 20 individuals per 100 ml before the toxicant was added, *Daphnia* was eliminated from T_3CP-treated enclosures in 3 days. The abundance of *Daphnia* in control enclosures was high and stable during the 24 days of the study.

7.2.4 Fish

There are no controlled field studies on the effects of chlorophenols on fish, but fish kills have occurred as a result of chlorophenol spills. Mackenzie et al. (1975) compiled information on such incidents in British Columbia salmon waters during 1960–73. In one instance, an over- flow from a lumber-treatment tank released both T_4CP and PCP into the Mamquam Channel in 1973, killing an estimated 500 adult and juvenile coho salmon.

Chlorophenols may also impair the flavour of fish, even when present in the minute quantities detected in moderately-contaminated natural waters (section 7.1.3). Chatterjee (1974) reported that kraft and groundwood pulp discharges into Lakes Superior and Huron, which included phenolic compounds, were apparently responsible for the tainting of flesh from fish captured nearby.

7.2.5 Effects on physical and chemical variables

The only instance in which chlorophenols affected physical or chemical factors in the environment apparently involved a secondary effect. In studies in which 5 mg 2,4,6-T_3CP/ litre was added to enclosures in a pond, oxygen levels declined from initial levels of 3–4 mg/litre to less than 1 mg/litre, within 6 days of treatment, as the balance between heterotrophic and autotrophic metabolism shifted (Schauerte et al., 1982). Apart from this secondary effect, physical and chemical variables appear insensitive to CP additions. Schauerte et al. (1982) did not find any significant differences in temperature, pH, hardness, sulfide, carbonate, or chloride levels between control and 2,4,6-T_3CP-treated enclosures. Similarly, levels of phosphate, ammonia, nitrate, nitrite, silicate, and pH were unaffected by additions of as much as 1 mg 4-MCP or 2,4-DCP/litre (Kuiper & Hantsveit, 1984).

7.3 Treatment Levels

Unfortunately, the effects of chlorophenols at the low (mg/litre) levels that characterize the aquatic environment at large (section 5.1.2) were not examined in most of these studies. As a result, they shed little light on the possible hazards presented by the widespread low-level contamination observed in most environments. The microcosm study by Virtanen & Hattula (1982) was an exception in this regard. However, the mg/litre concentrations used by most research workers are relevant to major accidental spills of chlorophenols in the environment.

8. EFFECTS ON EXPERIMENTAL ANIMALS AND *IN VITRO* SYSTEMS

8.1 Acute Studies

In general, the toxicity of chlorophenols increases with an increase in the chlorination of the phenol molecule. A convulsant effect is associated with the less-chlorinated phenols and oxidative phosphorylation uncoupling is more prominent with the highly substituted compounds (Ahlborg & Thunberg, 1980; Jones, 1981; Exon, 1984).

Farquharson et al. (1958) studied the effects of a series of chlorophenols on male albino rats (Table 17). Symptoms associated with the lethal intraperitoneal injection of the monochlorophenols, 2,6-DCP and 2,4,6-T_3CP, as well as phenol, included an initial increase in physical activity (rapid running, nose rubbing) followed by tremors, convulsions, and loss of righting reflex. With 2,3,6-T_3CP, rats suffered convulsions only when handled, and otherwise lay prostrate with hypotonia. Hypotonia, starting at the hind limbs, was observed within 2–3 min of injection with 2,4-DCP, 2,3,6-, 3,4,5- and 2,4,5-T_3CP, T_4CP, and PCP. Body temperature was slightly reduced by phenol, MCPs and DCPs, while T_3CP caused a slight elevation and T_4CP and PCP a marked rise in temperature (4–4.5 °C). Respiratory rate increased initially then declined as coma developed, especially with T_4CP and PCP. The extremities were cyanosed and asphyxial spasms occurred about 30 seconds before death. With T_4CP and PCP, respiration stopped usually one-half to 2 min before cessation of the heart, whereas with the other chlorophenols, respiration ceased concomitantly with the heart or just before.

Animal studies indicate that most mono-, di-, and tri- chlorophenols are moderately toxic when administered orally, with LD_{50} values ranging between 230 and 4000 mg/kg body weight (Table 18). In general, the less-chlorinated phenols have an acute oral toxicity very close to that of phenol. T_4CP is considerably more acutely toxic, with LD_{50} values of between 100 and 400 mg/kg body weight (Ahlborg & Thunberg, 1980; Hattula et al., 1981a). Thus, the data indicate that the general order of decreasing acute toxicity is: T_4CP, MCP, DCP, T_3CP.

The subcutaneous and intraperitoneal routes of exposure have also been investigated (Table 18). As with oral administration, subcutaneous injections revealed a general order of decreasing acute toxicity of: T_4CP, MCP, DCP, T_3CP.

Table 17. Effect of lethal chlorophenol doses given intraperitoneally to rats[a]

Compound	Convulsant activity	Hypotonia onset (min)	Max. change in temp. (°C)	Respiration	Rigor mortis onset (min)
Ether					50
Monochlorophenols					
2(*o*)	+	-[b]	-2.0	-[d]	>5.2 <50
3(*m*)	+	-[b]	-2.5	-[d]	>5.2 <50
4(*p*)	+	-[b]	-2.5	-[d]	>5.2 <50
Dichlorophenols					
2,4-	(occasional twitches)	2–3[c]	-0.5	-[d]	>5.2 <50
2,6-	+	-[b]	-0.7	-[d]	>5.2 <50
Trichlorophenols					
3,4,5-	-	2-3	+0.5	-[d]	<5
2,4,5-	-	2-3	+0.5	-[d]	<5
2,4,6-	+	-[b]	+0.5	-[d]	<5
2,3,6-	(sometimes convulsions when handled)	2–3	+0.5	-[d]	<5
Tetrachlorophenol					
2,3,4,6-	-	2–3	+4.0	-[e]	<6
Pentachlorophenol					
2,3,4,5,6-	-	2–3	+4.5	-[e]	<5

[a] From Farquharson et al. (1958).
[b] Apparent after convulsions have lessened.
[c] Muscle twitches evoked by auditory and mechanical stimuli.
[d] Initial increase, then decrease as coma developed; asphyxial spasms 30 seconds before death; ceases just before or simultaneously with cardiac arrest.
[e] Ceases 1/2 to 2 min before stopping of heart.

Table 18. Acute toxicity (LD_{50}s) of phenols and chlorophenols for rats and mice[a]

	RAT				MOUSE		
	Oral	Sub-cutaneous	Dermal	IP	Oral	Sub-cutaneous	IP
Phenol	530–650[b]	669	250	300	344	360	-
Monochlorophenol							
-2(*o*)	670	950	-	230	347, 345[c]	-	-
-3(*m*)	570	1390	-	355	521, 530[c]	-	-
-4(*p*)	261	1030	-	281	1373, 1422[c]	-	-
Dichlorophenol							
-2,3	-	-	-	-	2585, 2376[c]	-	-
-2,4	580, 4000[d]	1730	-	430	1276, 1352[c] 1600[h]	-	-
-2,5	-	-	-	-	1600, 946[c]	-	-
-2,6	2940	1730	-	390	2198,2120[c]	-	-
-3,4	-	-	-	-	1685, 2046[c]	-	-
-3,5	-	-	-	-	2643, 2389[c]	-	-
Trichlorophenol							
-2,3,6	-	-	-	308	-	-	-
-2,4,5	820[e]	2260	-	355	-	-	-
-2,4,6	820[e]	-	-	276	-	-	-
-3,4,5	-	-	-	372	-	-	-

Table 18 (contd).

Tetrachlorophenol							
-2,3,4,5	-	-	>2000[h]	-	400[g]	-	97[g]
-2,3,4,6	140, 360[f]	210[g]	-	130	131[g]	120[j]	82[g]
-2,3,5,6	-	-	>2000[h]	-	109[g]	-	48[g]
-Commercial mix	-	-	485–565[h]	-		-	-
Tetrachlorophenate-Na							
-2,3,4,5	-	-	>2000[h]	-	-	-	-
-2,3,5,6	-	-	294–469[h]	-	-	-	-

[a] Principle database NIOSH (1983). LD_{50} values given as mg/kg body weight.
[b] Babich & Davis (1981).
[c] Borzelleca et al. (1985a). Data for males presented first, then females.
[d] Kobayashi et al. (1972).
[e] More recent values in US EPA (1979) are 4 times higher (2460–2960 mg/kg).
[f] Hattula et al. (1981a).
[g] Ahlborg & Larsson (1978).
[h] Shen et al. (1983) commercial mixture was primarily 2,3,4,6-T_3CP.
[i] Kozak et al. (1979).

However, in ip injection studies, the toxicities of the mono-, di-, and trichlorophenols were comparable while T_4CP was 2–3 times more toxic.

The only study available on the acute dermal toxicity of the less chlorinated phenols was carried out by Shen et al. (1983). In this investigation, Sprague-Dawley rats of both sexes were given 2,3,4,5-, 2,3,5,6-T_4CP, their sodium salts, or a commercial T_4CP preparation containing over 90% of 2,3,4,6-T_4CP and 5–10% of PCP. A very low dermal toxicity was reported for 2,3,4,5-T_4CP, its phenate salt, and 2,3,5,6-T_4CP, while the sodium salt of 2,3,5,6-T_4CP had the highest toxicity of all, followed by the commercial T_4CP (Table 18). The relatively high toxicity of the commercial T_4CP could result from its content of PCP. The rapid death of the rats (usually 6 h) argues against any role being played by the microcontaminants, because the PCDDs and PCDFs are usually associated with delayed acute toxicity.

The effects on animals of these less-chlorinated phenols administered via inhalation have not been investigated. However, it can be inferred from the one report on the inhalation of sodium-PCP (Hoben et al., 1976b) that the toxicity via inhalation would be greater than that associated with the oral, intraperitoneal, subcutaneous, or dermal routes.

In their study on the toxicity of 3 different T_4CP isomers in mice, Ahlborg & Larsson (1978) noted that the LD_{50} values for all 3 isomers were lower with ip injection than with oral (gavage) administration. This effect of the mode of administration on toxicity is apparent in the data on the other chlorophenols (Table 18) and may be related to differences in the rates of absorption, metabolism, and excretion of these compounds. The low toxicity values obtained with subcutaneous injections may be due to a low rate of absorption. The vehicle used for administration can also have a significant influence on absorption.

8.2 Skin and Eye Irritation; Sensitization

Very little information is available on skin and eye irritation or sensitization in experimental animals exposed to chlorophenols. Only very slight irritation was noted in rabbits following the application of dry 2,4,5-T_3CP to their skin (McCollister et al., 1961). The authors suggested that mild erythema might be caused by high concentrations of the material in solution. In a study on the dermal toxicity of the T_4CP isomers, Shen et al. (1983) found that dermatosis occurred in rats painted with 2,3,4,5-T_4CP or its phenate salt but not with the other 2 isomers or their salts.

8.3 Short-term Exposure

All the available information on short-term exposure has been obtained by means of oral studies, except for one report concerning dermal application. Information is lacking on the effects of inhalation and other routes of exposure in experimental animals.

Exon & Koller (1985) investigated the possible immunological effects of 3 chlorophenols on rats exposed both prenatally and postnatally. Weanling female rats (3 weeks of age) were given 2-MCP (98% pure) (0, 5, 50, or 500 mg/litre), 2,4-DCP (99% pure), or 2,4,6-T_3CP (98% pure); (both at 0, 3, 30, or 300 mg/litre) in the drinking-water, for 90 days from weaning through breeding and pregnancy. A randomly chosen group of offspring was given the same dose regime as the dams for an additional 12–15 weeks after weaning. Both groups were observed for another 10 weeks. 2-MCP did not have any adverse effects on humoral immunity, cell-mediated immunity, or macrophage function in the exposed progeny at any of the exposure levels. Exposure of progeny to the highest concentration of 2,4-DCP significantly enhanced (P less than 0.05) humoral immune responsiveness and decreased cell-mediated immunity in rats with both prenatal and postnatal treatments, but not in rats exposed only *in utero*. 2,4,6-T_3CP did not have any effects on the immune responses tested. Spleen and liver weights were increased in the progeny receiving water containing 2,4-DCP or 2,4,6-T_3CP at 300 mg/litre, but not 2-MCP. The authors suggested that this increase in organ weight was due to hyperplasia, as no histological anomalies were observed.

Exon & Koller (1985) also monitored haematological parameters and organ weights in exposed rat progeny. Combined pre- and postnatal (24 months) exposure to 500 mg 2-MCP/litre or 300 mg 2,4-DCP/litre significantly elevated red blood cell counts, haemoglobin concentrations, and packed cell volumes of offspring. Each of the 3 compounds was also fetotoxic (section 8.5).

In studies by Kobayashi et al. (1972), 2,4-DCP in the diet at the maximum dose of 230 mg/kg body weight per day, over a 6-month period, caused swelling of the hepatocytes in male mice but did not substantially affect liver, kidney, spleen, or adrenal histology. Furthermore, no significant exposure-related changes were observed in organ weight, body weight, food consumption, serum concentrations of liver enzymes, or numbers of red and white blood cells.

In a 90-day study, Borzelleca et al. (1985b) exposed mice of both sexes to 2,4-DCP in their drinking-water at mean daily doses of 40, 114,

or 383 mg/kg body weight for males, and 50, 143, or 491 mg/kg body weight for females. These dosages were calculated from daily water consumption data and the concentrations added to the drinking-water. At the end of the study period, there were no significant treatment-related differences in organ weights, electrolyte levels, haematological factors, or the activities of hepatic mixed-function oxidases (MFO) or serum enzymes.

In short-term studies that were preliminary to a carcinogenicity bioassay (section 8.6), rats and mice of both sexes were fed diets containing 2500–40 000 mg 2,4-DCP/kg for 13 weeks (NTP, 1988). All animals survived to the end of the study, except the mice receiving the highest dose, all of which died. Male mice and rats of both sexes receiving the 20 000 mg/kg diet showed reduced final mean body weights. Dose-related effects were apparent in the form of bone-marrow atrophy in rats and liver damage (necrosis, multi-nucleated hepatocytes) in mice.

A study on the short-term exposure of rats and rabbits to 2,4,5-T_3CP was carried out by McCollister et al. (1961). Rabbits, given 20 oral doses of 500 mg/kg body weight over a 28-day period, showed only "very slight kidney and liver changes". In rats receiving 18 doses of 1000 mg/kg body weight over a 24-day period, there was a slight increase in kidney weight, while growth, mortality, haematological parameters, and the histology of the lung, heart, liver, kidney, spleen, adrenal, pancreas, and testis were unaffected.

In the same report, male and female rats given a diet containing 0, 0.1, 0.3, or 1.0 g 2,4,5-T_3CP/kg for 98 days did not exhibit behavioural changes, increased mortality, changes in food consumption, growth, or histology (McCollister et al., 1961). At the 10 g/kg level, an increase in the frequency of day-time urination was noted in both males and females, as well as significant growth retardation in females. Kidney and liver degeneration, which was judged reversible, was also found at this exposure level.

During the course of a study on reproduction (section 8.5.1), Blackburn et al. (1986) dosed rats for 5 days per week (males, 11 weeks; females, 2 weeks and through gestation) by gavage with 0, 100, 500 or 1000 mg 2,4,6-T_3CP/kg body weight in corn oil. A number of rats from the 1000 mg/kg group died as a result of treatment (males, 8 out of 25; females, 3 out of 40). Males and females in this group exhibited significant but transitory weight loss compared with controls. Male kidney, liver, lung, adrenal, spleen, heart, testis, prostate, seminal vesicle, and epididymis weights were unaffected by all levels of 2,4,6-T_3CP

exposure. Females dosed at 1000 mg/kg body weight lost hair, were lethargic, and breathed irregularly.

In a range-finding study, rats and mice of both sexes were exposed to 2,4,6-T_3CP for 7 weeks to determine the maximum tolerated dose (NCI, 1979). The compound was given in the feed up to a maximum level of 46 000 mg/kg for rats and 31 500 mg/kg for mice. Weight gain was reduced in both male and female rats at all exposure levels, but only at the 2 highest dose levels (21 500 and 31 500 mg/kg) in mice. At the highest dose, a moderate to marked increase in splenic haematopoeisis was found in the rats and midzonal vacuolation of hepatocytes was seen in 2 males. All tissues in the mice were normal at the end of 7 weeks.

Hattula et al. (1981a) dosed rats by gavage daily with 0, 10, 50, or 100 mg 2,3,4,6-T_4CP/kg body weight in olive oil for 55 days. Histological changes were found only in the liver, even though the kidneys and spleen contained higher concentrations of 2,3,4,6-T_4CP. This finding suggests that 2,3,4,6-T_4CP has a specific effect on the liver of rats.

8.4 Long-Term Exposure

Investigations of the effects of long-term exposure to chlorophenols have been designed primarily to test their carcinogenic properties and are described in section 8.7.

8.5 Reproduction, Embryotoxicity, and Teratogenicity

Exon & Koller (1981, 1983) and Exon et al. (1984) examined the effects of 2-MCP (98% pure; 0, 5, 50, or 500 mg/litre), 2,4-DCP (99% pure; 0, 3, 30, or 300 mg/litre), and 2,4,6- T_3CP (98% pure; 0, 3, 30, or 300 mg/litre) on reproductive parameters in mice exposed via drinking-water (section 8.3). Females were exposed from 3 weeks of age until breeding at 90 days, and through-out gestation to parturition. Reanalysis of their original data (Exon & Koller, 1985) led the authors to conclude that there was a weakly significant (P less than 0.1) effect of 2-MCP at 500 mg/litre and 2,4-DCP and 2,4,6-T_3CP at 300 mg/litre, expressed as reduced litter size. The percentage of stillborn offspring compared with controls tended to increase in all exposed groups. However, the differences were not significant at P less than 0.05.

In mice, sperm motility and penetration of ova were not affected by acute (0.1 to 1 mmol/litre) and long-term exposure (90 days at 50–500 mg/kg body weight per day) to 2,4-DCP (Seyler et al., 1984). *In*

vitro penetration was depressed by 2,5-, 3,4-, or 3,5-DCP at 1 mmol/litre, and it appeared that this concentration of 3,4- or 3,5-DCP also disrupted the sperm acrosome.

The effects of oral dosing with 2,4,6-T_3CP on rat reproduction were investigated by Blackburn et al. (1986). Male rats were given 0, 100, 500, or 1000 mg 2,4,6-T_3CP/kg body weight in corn oil, by gavage, 5 days per week, for 11 weeks.

These exposures to T_3CP did not significantly affect male sexual behaviour (mount and ejaculation latencies, number of mounts and intromissions), plasma-testosterone levels, or sperm counts, motility, or morphology. Males from the control and 1000 mg/kg groups were then mated with unexposed females, which were sacrificed on day 18 of gestation. The exposure regime of the males did not significantly affect litter size, sex ratio, mean pup weight by sex, number of dead fetuses, or the numbers of resorptions or implantation sites. As part of the same study, female rats were dosed in the same manner as the males for 5 days per week over 2 weeks and then mated, after which dosing continued until day 21 of gestation. No treatment-related effects were evident in the breeding success, mean litter size, or offspring survival of these females. Litter weights were initially significantly reduced in the 500 and 1000 mg/kg body weight groups, but this difference had disappeared at 4 days postpartum. This effect was suggested to have been a secondary manifestation of female toxicity (section 8.2), or of initial differences in litter size between treatments.

In a teratogenicity study of 2,4,5-trichlorophenoxyacetic acid (Neubert & Dillman, 1972), 2,4,5-T_3CP was also tested, but only at doses of 0.9 or 9 mg/kg body weight per day. A slight increase in embryo mortality was observed at the higher dose, but its significance is unclear. No teratogenic effects were observed.

Schwetz et al. (1974) studied the embryotoxic and fetotoxic effects on rats of purified (99.6%) 2,3,4,6-T_4CP and commercial grade 2,3,4,6-T_4CP (73% T_4CP + 27% PCP plus 100 ppm total of each of dioxins and dibenzofurans). Doses of 10 and 30 mg/kg were given by gavage to pregnant rats from day 6 to day 15 of gestation, after which they were sacrificed on day 21. A delay in ossification of the skull bones was found. Neither of the compounds was embryolethal (evidenced by no increase in resorptions or abortions) even at the high dose of 30 mg/kg per day. No differences were observed in the toxicity of the 2 grades of T_4CP.

Chlorinated phenols do not appear to be teratogenic for experimental animals. Of the compounds tested, levels as high as 500 mg

2-MCP/litre in drinking-water (Exon & Koller, 1981), 300 mg 2,4-DCP/litre in drinking-water (Exon et al., 1984), 1000 mg 2,4,6-T_3CP/kg body weight (Blackburn et al., 1986), and 30 mg 2,3,4,6-T_4CP/kg body weight (Schwetz et al. 1974) did not produce any teratogenic effects in rats.

8.6 Mutagenicity and Related End-Points

Rasanen et al. (1977) found that all dichlorophenol isomers, 4 out of 6 trichlorophenols, and 2,3,4,6-T_4CP were negative in *Salmonella typhimurium* mutagenicity bioassays. Similarly, Haworth et al. (1983) reported that 2,3-, 2,4-, 2,5-, 2,6-, 3,4-, 3,5-DCPs and 2,4,5- and 2,4,6-T_3CP were negative in *S. typhimurium* TA 98, 100, 1535 and 1537 strains. Nestmann et al. (1980) reported similar findings for 2,6-DCP and 2,4,5-T_3CP. It was reported by Kinae et al. (1981) that 2,4,6-T_3CP was negative in *S. typhimurium* TA 98, 100, and 1537 strains, with and without exogenous metabolic activation, but positive in a *B. subtilis* recombination assay. At a concentration of 400 mg/litre, purified 2,4,6-T_3CP caused a weak but significant increase in the frequency of forward mutations, but did not affect intergenic or intragenic recombinations in the yeast *Saccharomyces cervisiae* MP-1 strain (Fahrig et al. 1978).

In mutagenicity studies conducted to supplement a carcinogenicity bioassay (NTP, 1988), 2,4-DCP did not produce any revertant colonies in *S. typhimurium* strains TA 98, 100, or 1537 and yielded equivocal results with TA 1535 only in the presence of hamster S9 activation. In the mouse L5178Y assay (without metabolic activation), trifluorothymidine resistance was increased by 2,4-DCP exposure. In the same study, *in vitro* exposure of Chinese hamster ovary cells to 2,4-DCP increased the frequency of sister chromatid exchanges, but did not cause chromosomal aberrations.

Hattula & Knuutinen (1985) showed that purified 2,4,6- T_3CP and 2,3,4,6-T_4CP were weakly mutagenic in V-79 Chinese hamster cells *in vitro*, in the absence of metabolic activation by hepatocyte co-cultures. They were both non-mutagenic in the presence of metabolic activation by hepatocyte co-cultures. 2,6-DCP and PCP were negative regardless of the presence of metabolic activators, and 2,4,6-T_3CP did not induce chromosomal aberrations or sister chromatid exchanges in cultures of Chinese hamster ovary cells (Galloway et al., 1987).

Only very few data are available from *in vivo* studies, and these are limited to the mouse spot test (Fahrig et al., 1978). Pregnant mice were injected intraperitoneally with 50 or 100 mg purified 2,4,6-T_3CP/kg body weight on day 10 of gestation. Examination of offspring revealed an increased frequency of coat spots (0.6% in the 50 mg/kg group versus 0.1% in controls), indicative of a weak mutagenic response.

8.7 Carcinogenicity

Both 2,4,6-T_3CP and 2,4-DCP have been tested for carcinogenicity in a 2-year bioassay. The other lower chlorophenols have not been adequately tested for their carcinogenic properties.

A 2-year carcinogenicity study on 2,4-DCP was recently completed under the US National Toxicology Program (NTP, 1988). Test animals fed diets containing 2,4-DCP (more than 99% pure) received the following average calculated doses (mg/kg body weight):

	F344/N rats		B6C3F1 mice	
	Male	Female	Male	Female
Low dose	210	120	800	430
High dose	440	250	1300	820

Mean body weights were reduced, usually by several percent, in all of the high-dose groups, as well as the low-dose groups of female mice. Mean food consumption was reduced in all treated groups, by several percent in rats, and in a dose-related manner in mice (up to 22%). No significant differences in the survival of any treated group occurred. There were dose-related increases in the incidence of multinucleated hepatocytes in male mice. No compound-related increases in the incidence of neoplastic lesions were observed; in fact, these were reduced for mononuclear cell leukaemia in male rats (both doses) and malignant lymphomas in female mice (high dose only).

Innes et al. (1969) tested 120 pesticides and industrial chemicals for tumorigenicity in male and female mice. The individual compounds were administered at a maximum tolerated dose, by stomach tube, from 7 days of age to 4 weeks old, and then in the diet at approximately the same dosage. The 100 mg/kg daily dose of Omal or Dowicide 2S (2,4,6-T_3CP) increased tumour incidence in the treated animals at the end of 72 weeks. The authors recommended additional statistical

evaluation and/or studies before a meaningful interpretation could be made.

A long-term oral exposure study was carried out on rats and mice to test the carcinogenicity of 2,4,6-T_3CP (NCI, 1979). Male and female F344 rats were given dose levels of 2,4,6-T_3CP of 5000 and 10 000 mg/kg in the feed for 106 weeks. Male B6C3F1 mice were dosed at the same levels as the rats for 105 weeks. Female mice were initially given dietary levels of 10 000 and 20 000 mg/kg for 38 weeks, which were then reduced to 2500 and 5000 mg/kg, respectively, for the remaining 67 weeks of the study, because they showed a marked reduction in weight gain. At the end of the study, the treated male rats showed a significantly higher incidence of malignant lymphomas and leukaemias. Leukocytosis and monocytosis of the peripheral blood and hyperplasia of the bone marrow were found in those that did not show lymphomas and leukaemias. No lymphomas and/or leukaemias were detected in female rats, but leukocytosis and monocytosis of peripheral blood and bone-marrow hyperplasia were evident. Both male and female mice displayed a dose-related statistically significant incidence of both hepatocellular carcinomas and adenomas. It was concluded that 2,4,6-T_3CP was carcinogenic for male Fisher rats and both sexes of B6C3F1 mice under the assay conditions used.

Boutwell & Bosch (1959) studied the tumour-promoting action of 2- and 3-MCP, 2,4-DCP, 2,4,5-T_3CP, and 2,4,6- T_3CP in mice following the dermal application of 9,10- dimethyl-1,2-benzanthracene (DMBA) (25 µl of 0.3% DMBA in benzene) as an initiator. One week after a single exposure to DMBA, twice weekly applications of 25 µl of a 20% solution of the test compound in benzene were made for 12–24 weeks. The control group received the pre-treatment dose of DMBA only. The authors reported that the monochlorophenols, 2,4- DCP, and 2,4,5-T_3CP all had a tumour-promoting action similar to that of phenol, while 2,4,6-T_3CP did not have any effect on tumour promotion.

Exon & Koller (1981,1985) carried out 15 to 24-month studies on the effects of pre- and postnatal exposure of rats to 2-MCP and 2,4-DCP. No evidence of tumour initiation was revealed with exposure to 2-MCP (98% pure) at 500 mg/litre drinking-water, or to 2,4-DCP (99% pure) at 300 mg/litre drinking-water (Exon & Koller, 1985). However, 2-MCP acted as a promoter of the carcinogenic activity of ethylnitrosourea (ENU), reducing tumour latency and increasing tumour incidence in male rats exposed both pre- and postnatally, compared with controls receiving only ENU.

There is sufficient evidence of the carcinogenicity for animals of 2,3,7,8-TCDD (IARC, 1987) and a mixture of two H_6CDD isomers (NCI, 1979), which may be present as microimpurities in some technical chlorophenols.

8.8 Factors Modifying Toxicity Metabolism

Any factor that can interfere with sulfate and/or glucuronide conjugation would modify the toxicity of a chlorophenol by inhibiting chlorophenol detoxification. Somani et al. (1984) demonstrated with an isolated liver-perfusion system that the glucuronide conjugation of ^{14}C-2,4-DCP can be blocked by galactosamine in the rat. In high enough concentrations, galactosamine or similar compounds would prolong the residence time in the body and thus the toxicity of the chlorophenol molecule.

In some instances, metabolism of chlorophenol yields molecules that are more, rather than less, toxic than the parent molecule. For example, when injected into rats intraperitoneally, tetrachloro-*p*-hydroquinone, a metabolite of 2,3,5,6-T_4CP, is much more toxic than the parent compound (Ahlborg & Larsson, 1978).

The toxicology of chlorophenols is further complicated by microcontaminants in technical grade products, particularly in the higher chlorinated compounds. Some of these impurities are themselves extremely toxic. Conversely, microcontaminants are known to induce enzymes that can affect the rate of chlorophenol metabolism and excretion (Ahlborg & Thunberg, 1978). For these reasons, assessment of toxicity studies with chlorophenols requires a knowledge of the types, levels, and toxicology of the contaminants present. This is particularly true when extrapolating animal studies (which often involve the use of purified compounds) to human beings, who are generally exposed to technical formulations. The residue concentrations and toxicology of the dibenzodioxin and dibenzofuran microcontaminants have been reviewed by WHO (in press).

8.9 Mechanisms of Toxicity, Mode of Action

The major mode of action of chlorophenols appears to be the uncoupling of oxidative phosphorylation. The strength of the uncoupling effect is related to the degree of chlorination: PCP is the strongest inhibitor of oxidative phosphorylation, MCP the weakest (Farquharson

et al., 1958; Mitsuda et al., 1963; Weinbach & Garbus, 1965; Carlson, 1978). To a lesser extent, inhibition of oxidative phosphorylation is affected by the positions of the chlorine atoms on the molecule. There appears to be a relationship between chlorination and the toxicity of PCP and T_4CP (Table 18), although there is no clear-cut relationship between the degree of chlorination and toxicity in MCP, DCP, and the T_3CP series. PCP and to a lesser extent other chlorophenols, depending on their degree of chlorination, have been shown to bind strongly to mitochondrial protein (Weinbach & Garbus, 1965). At low levels, PCP uncouples oxidative phosphorylation, at intermediate levels, it inhibits the formation of high-energy intermediates in the phosphorylation system and, at high concentrations, it inhibits the electron transport system (Mitsuda et al., 1963). PCP has been shown to bind directly to mitochondrial ATPase (Stockdale & Selwyn, 1971). Inhibition of ATPase would prevent the breakdown of ATP to ADP and energy release to the mitochondria. In response to the reduced availability of energy, a compensatory increase in catabolism would be expected. Increased catabolism would result in higher rates of oxygen consumption and, under short-term exposure conditions, depletion of metabolic stores. With oxidative phosphorylation uncoupled, the energy provided by catabolism would be released as heat. This process would underlie, respectively, the elevated respiratory rate and body temperature, and the long-term weight loss observed in intoxicated organisms (Weinbach, 1957; Farquharson et al., 1958; Mitsuda et al., 1963; Wood et al., 1983). Similarly, Exon & Koller (1985) suggested that the immune effects of 2,4-DCP might result from the uncoupling of oxidative phosphorylation, thus impairing cellular energy production in immunocompetent cells, or perhaps, from a direct toxic effect on subpopulations of cells involved in immune responses. The uncoupling of phosphorylation appears to be due to the chloro- phenate ion, while the convulsant action is caused by the undissociated molecule (Farquharson et al., 1958).

Chlorophenol toxicity may also result from a more general inhibition of enzyme activity by these compounds. Arrhenius et al. (1977) demonstrated that, in rat liver microsomal preparations, purified chlorophenols selectively inhibited cytochrome P-450 activity at the terminal oxygenation step of the MFO enzyme system by interfering with the coupling of flavin to this enzyme. 2,4-DCP, 2,4,6-T_3CP, and 2,3,4,6-T_4CP concentrations of 0.3 mmol–3 mmol/litre showed a weaker inhibition of C-oxygenation than PCP. Kaneki & Tanaka (1984) reported that the inhibition of porcine lipase activity and, to a lesser extent, wheat germ lipase activity increased with the number of chlorine atoms on the

phenol ring. The inhibiting action of PCP was greater than that of 2,3,4,6-T_4CP, which in turn was stronger than 2,3,6- T_3CP, while DCP and MCP did not have any effect. Carlson (1978) found that certain T_3CP isomers inhibited glucuronyl transferase activity and EPN detoxification *in vitro*, but not *in vivo*. The reason for these effects could be the absence from the *in vitro* preparations of binding proteins or alternate metabolic enzyme systems (Somani et al., 1984).

The mechanisms of carcinogenicity or co-carcinogenicity of chlorophenols (section 8.7) remain unresolved at present. Exon & Koller (1985) suggested that chlorophenols may play a role in carcinogenicity by altering the toxicity of carcinogens (by inhibiting detoxifying enzymes, damaging DNA, or altering DNA repair) or by reducing immunosurveillance. It has been shown by Vizethun & Goerz (1979) that 2,4,5-T_3CP and PCP can induce different species of cytochrome P-450 in nuclei and microsomes. The importance of this finding in relation to carcinogenesis is as yet unclear, but nuclear monoxygenases could play a critical role in cell alterations, because of their proximity to DNA and their ability to induce binding of electrophilic compounds.

9. EFFECTS ON MAN

As a result of the diverse range of applications of chlorophenols (section 3.2.2), there is considerable potential for human exposure to these compounds and their associated contaminants. Knowledge concerning the toxic effects of chlorophenols on people is based primarily on studies on persons employed in the chemical-manufacturing industry, where mainly DCP and T_3CP are involved, and the wood-preservation/protection industries, where T_3CP, T_4CP, and PCP are the major forms used (see reviews by Behrbohm, 1959, Kozak et al., 1979, and Ahlborg & Thunberg, 1980). Reports of chlorophenol toxicity in the general population are few in number, though chlorophenol contamination of human tissues and fluids seems widespread (sections 5.2, 5.3).

9.1 Acute Toxicity

Accidental and suicidal poisonings with commercial chlorinated phenols have been reported (WHO, 1987b), and a number of the most heavy acute exposures have resulted in death. With the support of animal studies, the signs and symptoms of acute exposure to chlorinated phenols include: convulsions (especially with less-chlorinated phenols), ataxia, mental and physical fatigue, headache, dizziness, disorientation, tachycardia, body temperature change (decreased with monochlorophenols, increased with, particularly, tetrachlorophenols and pentachlorophenol), and increased sweating. Cyanosis and asphyxia spasms shortly precede death. Death is apparently due to cardiac arrest and is followed, at least in animals, by rapid rigor mortis, especially with T_3CP and T_4CP poisoning.

In general, the acute toxicity of chlorophenols in animals increases with the number of chlorine atoms in the molecule (section 7.1.1). In man, the only published estimate of a minimum lethal oral dose (LD_{Lo}) for any chlorophenol is for PCP (29 mg/kg body weight, approximately 2 g for an average person) (WHO, 1987b). The human LD_{Lo} for unchlorinated phenol is estimated to be 140 mg/kg body weight.

Acute exposure of human beings to lower chlorophenols has also occurred as a result of industrial accidents during the production of 2,4,5-T_3CP and has been most consistently associated with chloracne (a persistent form of acne with keratotic follicles associated with exposure to chlorinated compounds) and symptoms of liver toxicity.

For example, in April 1968, an explosion in a reactor producing 2,4,5-T_3CP at a manufacturing plant in England released a considerable

amount of 2,4,5-T3CP and TCDD, exposing 14 people inside the plant (May, 1973). Abnormalities in liver function tests (elevated thymol turbidity, zinc turbidity), serum-transaminases, and urine analyses were detected immediately after the incident; 10 days later, the same tests gave normal values. Plant activity resumed but, by December, 79 cases of chloracne were reported, some of whom also suffered from conjunctivitis. The entire building was then thoroughly cleaned, the interior walls resurfaced, and contaminated equipment was buried. In a follow-up study conducted 10 years after the accident, the frequencies of chromosomal aberrations and sister chromatid exchange rates in lymphocyte cultures from exposed subjects were normal (Blank et al., 1983).

To date, acute exposure of the general population to lower chlorinated chlorophenols has been documented only from the ICMESA plant accident in Seveso, Italy. An over-heated chemical reactor discharged a cloud containing sodium hydroxide, Na-T3CP, and TCDD into the atmosphere, contaminating an area south of the factory containing 37 000 people (Hay, 1976; Del Corno et al., 1982). Within 2 weeks of the accident, toxic effects were being treated in some 500 people (Hay, 1976). The most prevalent signs of exposure were skin burns and chloracne, which was evident in 193 of the inhabitants. The highest soil concentrations of 2,3,7,8-TCDD were associated with the most severe cases of chloracne (Caramaschi et al., 1982). An international steering group formed by the Italian government stated in their final 1984 document that, with the exception of chloracne, no clear health effects remained in the 193 persons in Seveso who were registered as having chloracne, 20 of whom still showed symptoms in 1984. Exposed children had indications of increased enzyme activities (increased D-glucaric acid in the urine) up to 3 years after exposure (WHO, in press).

9.2 Long-term Exposure

9.2.1 Effects on skin and mucous membranes

Workers may display a variety of overt symptoms of chlorophenol exposure. Persons often complain of irritations of the skin, mucous membranes and respiratory tract as a result of direct airborne contact. In addition, chronic skin ailments, particularly chloracne, but also other skin lesions, ulcerations, and porphyria cutanea tarda have been

reported, mainly from plants manufacturing chlorophenols for phenoxy-acetic acid herbicides. Clinical indications of liver damage and haematological and neurological effects have also been reported, particularly in association with high exposures.

For instance, among workers in a 2,4-DCP and 2,4,5-T_3CP manufacturing plant in the USA, 29 cases of chloracne and 11 cases of porphyria were detected (Bleiberg et al., 1964). In addition to the two chlorophenols, PCDDs and PCDFs, acetic acid, phenol, mono-chloroacetic acid, and sodium hydroxide may have contributed to the symptoms of the workers. Poland et al. (1971) examined employees from the same plant 6 years after the report of Bleiberg et al. (1964). Of the 73 male workers examined, 48 (66%) had some degree of acne, and chloracne was found in 13 workers (18%). The severity of the chloracne was not correlated with job location within the plant or duration of employment, suggesting that there is a large variation in the susceptibility of individuals to exposure to chlorophenols or their contaminants.

Workers exposed to 2,4,5-T_3CP in a production plant in the USSR also developed dermatitis, as reported by Kozak et al. (1979). Similarly, an incident of acute dermatitis in Russian agricultural workers exposed to copper trichlorophenate was reported (Kozak et al., 1979).

Ott et al. (1980) examined the effects of exposure to commercial 2,4,5-T_3CP and 2,4,5-T at a plant in the USA. In unacclimated personnel, levels of less than 4 mg T_3CP/m^3 and/or 0.1 mg 2,4,5-T/m^3 caused nasal irritation, sneezing, and a bitter taste in the mouth. TCDD concentrations in both preparations were less than 1 mg/kg, in 1966, and 0.1 mg/kg, after 1972. Medical records of 204 exposed employees over the period 1950–76, did not reveal any cases of chloracne or porphyria. The mortality rate of employees was lower than expected (6 versus 13.3 expected) in workers exposed for less than 1 year and close to expected in those exposed for 1 year or more (5 versus 7 expected).

In clinical studies on workers at a 2,4,5-T-manufacturing plant (presumably exposed to 2,4,5-T_3CP and its microcontaminants), exposure was strongly associated with the development of chloracne, plus increased prevalences of actinic elastosis and hirsutism (Suskind & Hertzberg, 1984).

Jirasek et al. (1974) and Pazelerova et al. (1974) reported the cases of about 80 people with both acute (industrial accident) and long-term (up to 6 years) exposure to Na-T_3CP, tetrachlorobenzene, the sodium salt of trichlorophenoxyacetate, and their contaminants. Symptoms developed as long as 18 months after exposure. Chloracne appeared in 96% of 55 people examined.

In lumber-mill workers, lesions and ulcerations were found in skin areas in direct contact with a Na-T_4CP solution, usually through soaked clothing (Stingily, 1940). On the basis of roughly 300–400 cases, it was concluded that Na-T_4CP caused the dermatitis while the subsequent chronic lesions and ulcerations were caused by fungal infections.

Kleinman et al. (1986) and Fenske et al. (1987) evaluated the extent and impact of occupational exposure to Permatox 100 (20.7% 2,3,4,6-T_4CP, 3.1% PCP, plus substantial quantities of PCDDs and PCDFs) in workers from a lumber mill in Washington state. The results of their monitoring of air and urine are presented in section 5.3. In health effects questionnaires, exposed workers complained significantly more frequently than controls of headaches, eye and upper respiratory irritations, and unusual sweating, though there was no significant correlation between urinary levels and the frequency of these symptoms. The effects of exposure to a commercial Na-T_4CP solution (containing hexa-, hepta-, and octachlorodibenzo-*p*-dioxins, dibenzofurans, and probably PCP and T_3CP) were investigated by Sterling et al. (1982) in workers at 2 sawmills in British Columbia, Canada. The study included 1014 men with from 1 to over 20 years of known exposure, compared with 103 loggers and outdoor municipal workers, who served as controls. In self-administered questionnaires, exposed workers reported significantly increased incidences of various dermatological, upper respiratory, and general respiratory symptoms, as well as eye irritation. These disorders were significantly more frequent in the high-exposure group (247 workers) than in the workers considered to be in the low/moderate-exposure group (767 workers), who, in turn, had a higher incidence than the controls.

A detailed study of chlorophenol exposure in a sawmill in the same geographical area was carried out by Embree et al. (1984) (section 5.3). They divided the workers into a control group from areas with no identifiable air contaminants, a group of workers who worked in close proximity to recently treated lumber but who did not have manual contact (airborne), and a group who were responsible for the manual handling of recently treated lumber (dermal plus airborne). Serum and urine levels of chlorophenols were related to exposure in a dose-dependent manner (section 5.3). From health histories, the only symptoms that occurred significantly more frequently in exposed workers were a productive cough and a reduced rate of forced exhalation in the "airborne" group. These symptoms could not be attributed to chlorophenol exposure, as the "dermal-plus-airborne" group were exposed to similar atmospheric chlorophenol levels and had higher levels

of overall exposure, yet recorded a significantly lower incidence of productive coughing.

Alexandersson & Hedenstierna (1982) examined the effects of long-term exposure to T_3CP vapours in workers at a gas-mask factory. Trichlorophenol vapour, because of its characteristic smell, was used at the factory for checking leaks in gas masks. Complaints of eye, nose, and airway irritation were voiced by 7 individuals who had been employed in testing masks for from 2 to 10 or more years. Pulmonary function tests revealed that exposed workers displayed reduced forced expiratory flow and increased closing volume in the lungs compared with controls.

9.2.2 Systemic effects

Effects on liver and kidney function and haematological parameters have also been investigated in workers exposed to chlorophenols. The findings have been generally negative. In studies on Canadian sawmill workers (Enarson et al., 1986), serum levels of creatinine, bilirubin, glutamic oxaloacetic transaminase, and alkaline phosphatase, and patient histories of jaundice, liver, kidney, and heart disease did not differ from those of the controls. Blood-leukocyte counts and haematocrit decreased, and urine-erythrocyte levels increased following chlorophenate exposure. These effects were significant only for the haematocrit and haematuria, and only for workers handling treated lumber.

Sterling et al. (1982) reported that chlorophenol-exposed sawmill workers filling out self-administered questionnaires reported significantly increased incidences of gastrointestinal, musculoskeltal, acute systemic, liver, kidney, and neurological symptoms.

In the study on industrial workers exposed to di- and trichlorophenols, Bleiberg et al. (1964) reported elevated coproporphyrin excretion in the maintenance men that could have been due to more intense, though sporadic, exposure. Hepatotoxic effects were not found in the study group.

Initially, more than one-third of Czechoslovakian 2,4,5-T_3CP- and 2,4,5-T-manufacturing workers described by Jirasek et al. (1974) and Pazelerova et al. (1974) showed indications of mild liver damage, which, in some instances, was confirmed by needle biopsy. The workers had increased serum levels of cholesterol (56%), total lipids (67%), and lipid-phosphorus (42%). A small but significant decrease in serum-albumin, and an increase in serum-globulin were also found.

9.2.3 *Psychological and neurological effects*

A range of psychological and neurological symptoms have also been associated with exposure to chlorophenols, often in association with other chemicals. Workers from a plant in the USSR who were occupationally exposed to 4-MCP complained of "... sleep disorders (usually sleepiness and sometimes insomnia), irritability, frequent mood changes, and rapid fatigability" (Gurova, 1964).

Similarly, Kleu & Goltz (1971) reported that 10 persons suffering from chloracne as a result of 15 years' exposure to a T_3CP formulation complained of "...decreased sexual activity, easy fatigability, alcohol intolerance, and loss of interest ... reduced vital psychic and intellectual capacities combined with neurasthenia and mental depression". The actual occupations of these individuals were not stated.

Gilioli et al. (1983) conducted electroencephalographic analyses of workers exposed to T_3CP and TCDD at the Seveso plant in Italy, site of an accident in 1976. These workers had both long-term, and possibly acute high-level exposure to TCDD and T_3CP. Exposed workers generally exhibited an increased incidence of abnormal EEG tracings, which were particularly associated with increased proportions of theta waves, and had a slower visual reaction time than a non-exposed group.

The 2,4,5-T_3CP-and 2,4,5-T-manufacturing employees reported by Jirasek et al. (1974) and Pazelerova et al. (1974) showed neurological abnormalities, including myographic changes in 23% of those tested. Neurasthenic symptoms were present in 60% of the workers, compared with 30–40% of the general population. Some of the workers complained of fatigue, loss of appetite, weight loss, and abdominal pain.

9.2.4 *Reproductive effects*

The effects of chlorophenols on reproduction have been investigated in 3 studies. Corddry (1981) provided data on pregnancy outcomes in women married to workers from a sawmill in British Columbia using Na-T_4CP and Na-PCP. Analysis of data from 43 women, with a total of 100 pregnancies, did not reveal any significant differences in the pregnancy outcomes of women living with exposed men compared with those living with unexposed men. A slight trend towards more adverse pregnancy outcomes in the exposed group disappeared when corrected for alcohol consumption. Male fertility was not studied.

Suskind & Hertzberg (1984) reported pregnancy outcomes in the families of male workers manufacturing 2,4,5-T (and with probable

exposure to 2,4,5-T_3CP and 2,3,7,8-T_4CDD) compared with those of other males from the same plant. There were no significant differences between the families of exposed and non-exposed workers, but the rates for stillbirth and death during the first 4 weeks were higher in the families of exposed workers.

The pregnancy outcomes were surveyed in wives of workers from a chlorophenol-manufacturing plant in Michigan, USA, potentially exposed to PCP, 2,4,5-T_3CP, and their microcontaminants for the group as a whole (Townsend et al., 1982). There was no significant association between exposure to dioxins (these were the focus of the study) and adverse pregnancy outcomes. When the conceptions were divided into subgroups according to risk factors associated with the mother, a subgroup of 9 TCDD-exposed conceptions was identified of which 3 were spontaneous abortions.

9.2.5 Carcinogenicity

A large number of epidemiological studies have been published concerning human cancer outcomes following occupational exposure to chlorophenols, phenoxy herbicides (made from and contaminated with chlorophenols), and chlorinated dibenzo-*p*-dioxins and dibenzofurans (microcontaminants found in some chlorophenols and phenoxy herbicides). Most of these studies have been described and reviewed in several publications by the International Agency for Research on Cancer (IARC, 1979, 1986, 1987), and readers are referred to the IARC monographs for details of individual studies. Only the conclusions of these studies are given in this publication with the emphasis on studies that specifically concern exposure of populations to chlorophenols. Studies that address the effects of exposure to phenoxy herbicides in general and MCPA, and do not involve substantial concomitant exposure to chlorophenols are not discussed. These include: cohort studies on phenoxy herbicide sprayers (Axelson et al., 1980; Hogsted & Westerlund, 1980); studies on Vietnam war veterans (Royal Commission on the Use and Effects of Chemical Agents on Australian Personnel in Vietnam, 1985; Lathrop et al., 1987); and workers involved in the manufacture of MCPA (Coggon et al., 1986). Case-control studies covering phenoxy herbicide exposure, but with no mention of exposure to chlorophenols (Balarajan & Acheson, 1984; Greenwald et al., 1984; Kogan & Clapp, 1985; Hoar et al., 1986; Kang et al., 1986; Vineis et al., 1987) and data from occupational mortality statistics in which exposure data are inferred only from job titles are also not included (Milham, 1982, 1985; Callagher & Threlfall, 1984).

9.2.5.1 Case-control studies reviewed by IARC

Soft tissue sarcoma (STS) was studied in individuals exposed to chlorophenols and other chlorophenol-based chemicals in Sweden (Hardell & Sandstrom, 1979; Eriksson et al., 1981), New Zealand (Smith et al., 1984), and the USA (Woods et al., 1987). Relative risks (RR) of STS for exposure to chlorophenols alone were elevated in both of the Swedish studies (RR = 6.6; 96% CI, 2.1–20.9; and RR = 3.3; 95% CI, 1.3–8.1) and for one potentially exposed subgroup in the New Zealand study (RR = 7.2; 90% CI, 1–ND). They were not elevated in the US study, unless the subgroup of cases with Scandinavian names (RR = 7.2; 95% CI, 2.1–24.7) and the subgroup of lumber graders (RR = 2.6, 95% CI, 1.1–6.4) were considered separately. Chlorophenol exposures (2,4,6-T_3CP, PCP, and others) were poorly described and not quantified. Case-control studies of malignant lymphomas (Hodgkins disease and non-Hodgkins lymphoma) have also been carried out in Sweden (Hardell et al., 1981), New Zealand (Pearce et al., 1986), and the USA (Woods et al., 1987). In Sweden, low-grade exposure (up to one week continuous or 1 month intermittent) and high-grade exposure (greater than the low-grade exposure criteria) to unspecified types of chlorophenols resulted in relative risk values of 2.2 (95% CI, 1.1–4.6) and 7.6 (95% CI, 3.2–17.7), respectively. In the New Zealand study of 83 cases of non-Hodgkins lymphoma, exposures were not classified into high or low, and were not quantified; however, some cases were not likely to have been exposed to 2,4,6-T_3CP and PCP.

The relative risk for non-Hodgkins lymphoma in pelt department workers with potential exposure to 2,4,6- T_3CP was 1.9 (90% CI, 0.9 - 4.0); however, other meat workers without exposure to chlorophenols had a relative risk of the same order. In the US study, the relative risks for non-Hodgkins lymphoma were not elevated for groups exposed to low, medium, or high levels of chlorophenols.

A statistically significant increase in nasal and nasopharyngeal cancer was found among workers exposed to chlorophenols (mainly tri-, tetra-, and pentachlorophenol) in a Swedish case-control study (Hardell et al., 1982). In an inter-Nordic study, 2 cases of sinonasal cancer out of 167 were identified as having been exposed to chlorophenols (not further specified) compared with 0/167 colorectal cancer controls (Hernberg et al., 1983). In a Danish study, no association was found between sinonasal cancer and potential exposure to chlorophenols, as inferred from employment records (Olsen & Moller-Jensen, 1984).

The results of 2 Swedish studies did not show statistically significant associations between primary liver cancer or colon cancer, and exposure to chlorophenols (mainly tri-, tetra-, and pentachlorophenol) (Hardell, 1981; Hardell et al., 1984).

No significant associations were found between multiple myeloma and potential exposure to chlorophenols (probably mainly pentachlorophenol) in a case-control study carried out in New Zealand (Pearce et al., 1986).

9.2.5.2 Cohort studies reviewed by IARC

Three follow-up studies have been undertaken on small groups of workers exposed to 2,3,7,8-TCDD during accidents in the manufacture of 2,4,5-T_3CP (Cook et al., 1980; Zack & Suskind, 1980; Thiess et al., 1982). When combined, these cohort studies show 19 cancer deaths observed versus 14.7 expected (RR = 1.29; 95% CI, 0.78–2.02). Two studies (Ott et al., 1980; Zack & Gaffey, 1983) covered workers employed in the manufacture of 2,4,5-T from 2,4,5-T_3CP. The observed cancer deaths versus expected cancer deaths for these cohorts were 1 versus 3.6 and 35 versus 30.9, respectively.

A total of 3 deaths from soft-tissue sarcoma (STS) were identified in US cohorts studied by Honchar & Halperin (1981). This was equivalent to 2.9% of the deaths in the 4 cohorts, where approximately only 0.07% would be expected. Later, one additional STS case was observed in one of these cohorts (Cook, 1981), and an additional 3 cases of STS were reported in workers in 2,4,5-T-manufacturing plants (Johnson et al., 1981; Moses & Selikoff, 1981). Fingerhut et al. (1984) reviewed the histological specimens for the 7 cases reported as having STS. In the review, 5 of the 7 cases were diagnosed as having STS. A review of the employment records for the 7 patients showed that all of them had worked in 2,4,5-T-manufacturing plants; 4 of the patients had specific assignments to 2,4,5-T_3CP or 2,4,5-T departments.

A cohort study on workers in 2 Danish chemical plants (Lynge, 1985), in which 2,4-D and 2,4-DP were produced together with MCPA and MCPP, showed the overall cancer incidence to be close to that of the Danish population (208 observed cases and 216.5 expected). In men, 5 cases of STS were observed, where 1.84 were expected. The number of malignant lymphoma cases in men was 7, with 5.37 expected cases. In the subgroup of men assigned to the phenoxy herbicide-manufacturing department, 11 lung cancer cases were observed in men, when 5.33 cases were expected.

9.2.5.3 More recent studies

A Swedish study on soft-tissue sarcoma and exposure to phenoxy acid herbicides and chlorophenols was recently repeated using 55 new cases diagnosed in 1978–83 (Hardell & Eriksson, 1988). In addition to comparing the cases with controls from the general population, a control group of patients with cancers other than malignant lymphoma and nasopharyngeal cancer was selected. An elevated relative risk for exposure to phenoxy herbicides was found, but no statistically significant differences were observed between cases and controls with regard exposure to chlorophenols. The relative risk for chlorophenols was based on only 4 exposed cases.

In a case-control study nested within a cohort of Finnish woodworkers, no association was found between respiratory cancer and exposure to chlorophenols (mainly tetra- and trichlorophenols), but this result was based on only 3 exposed cases (Kauppinen et al., 1986).

In a more recent cohort study on 2192 employees at a plant involved in the production of higher chlorophenols and phenoxy acids (Cook et al., 1987; Ott et al., 1987), mortality during the period 1940–82 among workers with potential occupational exposure to chlorophenols was similar to that of US white males for all causes and for all cancers; there were 81 observed cancer deaths versus 79.3 expected deaths. No statistically significant excesses of mortality were observed for the cancers of a prior interest (nasal and nasopharyngeal, stomach, liver, connective and soft tissue, lymphomas). Excesses in mortality that did not reach the 5% level of probability were reported for stomach cancer (6/3.8) and non-Hodgkins lymphoma (5/2.6).

A cohort of 878 persons, employed in the manufacture of 2,4-D at the same plant between 1945 and 1983, was followed up for mortality until 1983. Some of these employees may also have been exposed to other chlorophenols at the plant site. There were 20 cancer deaths against 16.9 expected. There were 5 deaths from lymphatic and haematopoietic cancer against 2.5 expected. Two cases had lymphosarcoma and reticulosarcoma, and there was one case of Hodgkins disease. Both workers who died from non-Hodgkins lymphoma had had potential exposure to PCDDs. Death certificates were reviewed with special attention directed to soft-tissue sarcoma, but no cases were identified (Bond et al., 1988).

10. EVALUATION OF HUMAN HEALTH RISKS AND EFFECTS ON THE ENVIRONMENT

10.1 Evaluation of Human Health Risks

10.1.1 Exposure levels

10.1.1.1 Non-occupational exposure

Exposure to chlorophenols other than pentachlorophenol may occur via ingestion, inhalation, or dermal absorption (section 5.2). The general population is thought to be exposed mainly through the ingestion of food and drinking-water. These compounds have not been quantified in the ambient atmosphere, but atmospheric levels are likely to be of the same order of magnitude (ng/m^3) as those of PCP. Even with 100% absorption, uptake via this route would be much less than 1 μg/day. Similarly, even though low levels of the lower chlorinated phenols occur widespread throughout the environment, direct dermal contact with these compounds will not be an important route of exposure for the general population. Non-occupational exposure (inhalation, dermal) to chlorophenol-treated lumber has not been investigated, but may be significant, if chlorophenols are used for extensive treatment of the interior of houses. Significant exposures may also occur if consumers use chlorophenol-based products without appropriate care and protection.

An estimate of non-occupational exposure through the ingestion of drinking-water and food can be made using representative published concentrations of the major commercial chlorophenols other than pentachlorophenol. The daily exposure of a 60-kg person in Canada to 2,4-DCP, 2,4,5-T_3CP, and 2,3,4,6-T_4CP is estimated in Table 19, on the basis of assumptions detailed in the table. These calculated exposures may be overestimates in that residue determinations are generally taken from contaminated areas, and because kinetic or metabolic studies usually involve high chlorophenol concentrations. On the other hand, estimates have not been made for all foodstuffs; for example, no data were found for fruits, dairy products, or nuts. Exposure to other chlorophenols, in particular 2,4,6-T_3CP, cannot be estimated, because there are insufficient data on the concentrations present in water and food. Nevertheless, the values calculated should suffice as a first approximation of exposure.

Table 19. Estimated daily per capita exposure to 2,4-DCP, 2,4,5-T_3CP, and 2,3,4,6-T_4CP from food and drinking-water in Canada

Source	Daily consumption in Canada (kg)[a]	2,4-DCP		2,4,5-T_3CP		2,3,4,6-T_4CP	
		Concentration (μg/kg fresh weight)	Exposure (μg/kg body weight per day)[b]	Concentration (μg/kg fresh weight)	Exposure (μg/kg body weight per day)	Concentration (μg/kg fresh weight)	Exposure (μg/kg body weight per day)
Tap water	1.4 (litres)[d]	0.093[c]	0.002	0.035[c]	0.0008	0.009[c]	0.0002
Vegetables and potatoes	0.36	6[e]	0.036	0.041[f]	0.0002	1.917[g]	0.011
Meat and poultry	0.26	5[h]	0.022	0.034[f]	0.0002	3[i]	0.013
Fish and seafood	0.019	13.75[j]	0.004	0.76[k]	0.0002	10 .3[k]	0.003
Total exposure			0.064		0.0014		0.027

Table 19 (contd).

Tolerable daily intake (μg/kg body weight per day)	200.0[l]	100.0[m]	10.0[n]

[a] Per capita per day in 1984 (Statistics Canada, 1986).
[b] Based on a 60-kg person.
[c] Jyvaskyla, Finland (Paasivirta et al., 1985).
[d] Water consumption for 60 kg man per day (NHW, 1983).
[e] Average for potatoes treated with 2,4-D (Bristol et al., 1982).
[f] Assuming that the ratio of 2,4-DCP: 2,4,5-T_3CP is the same as for 1984 Canadian imports.
[g] Average from Alberta Government assay (Jones, 1981), assuming all T_4CP is 2,3,4,6-T_4CP.
[h] Muscle concentration from chickens fed 50 mg Nemacide/kg, 7 days post-treatment (Sherman et al., 1972).
[i] Upper concentration detected in chicken flesh from British shops (Farrington & Munday, 1976).
[j] Mean muscle concentration calculated as μg/kg wet weight Bacon, (1978).
[k] Mean muscle concentration (Paasivirta et al., 1985)
[l] NOEL taken from Kobayashi et al. (1972) using a 500-fold safety factor.
[m] NOEL taken from McCollister et al. (1961) using a 1000-fold safety factor.
[n] NOEL taken from Schwetz et al. (1974) using a 1000-fold safety factor.

The daily ingestion of these chlorophenols by a 60-kg person is estimated to be 3.84 μg of 2,4-DCP; 0.084 μg of 2,4,5-T_3CP, and 1.62 μg of 2,3,4,6-T_4CP (on the basis of data in Table 19 and calculated for a 60-kg person). These values are presented on a per-unit-weight basis in Table 19. In Canada, the amount of PCP used is approximately equal to the amounts of all other chlorophenols combined, suggesting that PCP exposure is roughly equal to that of the other chlorophenols. Thus, the total estimated exposure of Canadians to all chlorophenols including PCP is about 10 μg/person per day. This value agrees with the 10–30 μg/person per day estimated by NRCC (1982) and the 12.7 μg/person per day estimated by NHW (1988) (section 5.2) for the general population in Canada. The total estimated exposure levels in other countries may differ from this value, depending on product use patterns, food and water consumption, and levels of environmental contamination.

Although the above estimate of exposure is based on limited information on residue levels and uptake rates, it is supported by the low levels of chlorophenols found in human tissues and fluids; in the few studies available, μg/kg quantities have been detected in human tissues and fluids (section 5.2).

10.1.1.2 Occupational exposure

The potential exposure to chlorophenols may be significant for certain workers employed in the lumber industry, pesticide manufacture and use, use of treated wood for construction, railroad ties, or telephone poles, and a variety of other industries in which chlorophenols are used as biocides. In the work place, exposure would be mainly through dermal absorption and inhalation; ingestion of the compounds is more likely to occur if eating, drinking, and smoking are allowed in the work area, or if proper cleansing procedures are not practised. The air in work areas where chlorophenols are used contains elevated concentrations of chlorophenols. Concentrations of 14 mg/m^3 have been reported in such work areas, but typical concentrations were 1–3 orders of magnitude below this in work places studied recently in North America and Scandinavia (section 5.3). Persons working in high exposure areas have elevated levels of chlorophenols in their body fluids, particularly if their job combines dermal and inhalation exposure to chlorophenols. Urine levels of up to 49 mg T_4CP/litre have been reported (section 5.3).

Few data are available with which to model uptake and excretion of chlorophenols other than PCP. However, preliminary estimates of some occupational exposures can be derived from recent reports of concentrations in the urine of workers in the sawmill industry, where handling of treated wood and the proximity of workers to the open-treatment apparatus can result in relatively high uptake of chlorophenols.

Urinary concentrations of employees at Finnish, American, and Canadian sawmills have been compiled in Table 20, and have been used to estimate worker exposure in this industry. These estimates are based on two principal assumptions. First, it was assumed that urinary concentrations of T_4CP reach a sustained level following long-term exposure, since Braun et al. (1979) calculated that PCP in the urine of exposed persons reached a fairly constant level within one week. Second, it was assumed that all T_4CP is cleared in the urine, because it is known that human beings clear 86% of administered PCP in urine (Braun et al., 1979) and that rats clear more than 95% of single doses of 2,3,4,6-T_4CP and 2,3,5,6-T_4CP (the major tetrachlorophenols in commercial preparations) via the urine (Ahlborg & Larsson, 1978).

On the basis of these assumptions, the urinary concentrations in Table 20, and a urine production of 1.4 litres daily, a 60-kg sawmill worker is estimated to take up from 2 to 42 μg/kg per day on average (Table 20). Estimates of the exposure of workers with the highest urine concentrations from each study, who presumably had extensive dermal uptake of chlorophenates, ranged from 53 to 1142 μg/kg per day. A more comprehensive knowledge of chlorophenol levels and fluxes and their dynamics would be necessary for a better estimate.

As expected, the estimated occupational exposure is much higher (often 2 or more orders of magnitude) than that calculated for members of the general population. This difference is confirmed by levels of chlorophenols measured in the biological tissues and fluids of workers, and the ambient atmosphere (sections 5.2, 5.3), as well as the association of intoxications and adverse symptoms with occupational exposure to chlorophenols (section 9).

Since the foregoing calculations are based on only 5 studies, all involving sawmills, these estimates are not directly applicable to other occupations and/or geographical regions.

Table 20. Estimates of occupational exposure to tetrachlorophenols (based on urinary concentrations from recent studies on exposed workers)

Situation	Urinary concentrations (μg/litre)		Estimated intake (μg/kg body weight per day)[a]		Reference
	Median/mean	Maximum	Average[b]	Maximum	
Finnish sawmill; workers exposed to KY-5 (NaT_4CP) formulation; 1980-81	Dermal exposure primarily 1809.4[c] (median)	48 924.6	Dermal exposure 42	1142	Lindroos et al. (1987)
	Respiratory exposure primarily 208.8[c] (median)	3085.3	Respiratory exposure 5	72	
Finnish sawmill; workers exposed to NaT_4CP	2841.5[d,e] (mean)	39 436.6[d,e]	66 (1985)	920	Kauppinen & Lindroos (1985)
Canadian (British Columbia) planer mill; workers exposed to NaT_4CP; 1985	423[f] (mean)	1479[f]	10 (1986)	35	Currie & McDonald (1986)
Washington state (USA) sawmill; workers exposed primarily to NaT_4CP; 1981-82	160.4[g] (mean)	2255	4	53	Kleinman et al. (1986)

Table 20 (contd).

Canadian (British Columbia) sawmill; workers; exposed to Na-T_4CP; 1978-79	Dermal + airborne exposure 1250[e] (mean)	Dermal + airborne exposure 29	Embree et al. (1984)
	Airborne only 930[e]	Airborne only 22	

[a] For a 60-kg worker.
[b] Based on mean concentration, except for estimate from Lindroos et al. (1987), which is based on the median.
[c] Assumes all chlorophenols are T_4CP, which predominates in these formulations.
[d] Not clear if sample hydrolysed.
[e] Assumes free concentrations are 10% of total concentrations.
[f] From samples collected on final morning of a 5-day work week.
[g] Grand mean for exposed workers, all dates.

Note: No correction for density has been made in any table entries.

10.1.2 Toxic effects

Acute lethal doses of lower chlorophenols in experimental mammals (section 8.1) are associated with restlessness, hyperpyrexia, rapid respiratory rates, ataxia, and eventually dyspnoea, coma, and death. MCPs, DCPs, and 2,4,6-T_3CP are convulsive agents, while the other trichlorophenols and tetrachlorophenols are not. All of the chlorophenols are irritating or corrosive to the skin, eyes, and mucuous membranes (section 8.2).

Short-term exposure of experimental animals to 2,4-DCP, 2,4,5-T_3CP, 2,4,6-T_3CP, or 2,3,4,6-T_4CP produces moderate adverse effects on the liver, kidney, and spleen, while 2,4-DCP is also haematotoxic and immunotoxic (section 8.2). 2-MCP, 2,4-DCP, 2,4,5-T_3CP, 2,4,6-T_3CP, and 2,3,4,6-T_4CP produce fetotoxic or embryotoxic effects, but none of the chlorophenols tested to date has produced teratogenic effects. Isomers of DCP other than 2,4-DCP may reduce male fertility (section 8.5).

2,4,6-T_3CP and 2,3,4,6-T_4CP appear to have some mutagenic capability; however, chlorophenols do not appear to be potent mutagens capable of exerting significant genotoxic effects (section 8.6). There is sufficient evidence that 2,4,6-T_3CP (commercial grade) is an animal carcinogen. However, the trichlorophenol used in this study was not analysed for PCDD and PCDF microcontaminants. 2,4-DCP (more than 99% pure) was found not to be carcinogenic in mice and rats. The other lower chlorophenols have not been adequately tested for their carcinogenic properties. Some chlorophenols appear to be tumour promoters; others do not (section 8.6).

The microcontaminants in the commercial grades of the more highly chlorinated phenols can lead to toxic effects even more severe than those produced by the chlorophenol itself (sections 6.3, 8.9). Their possible significance in terms of the carcinogenicity of 2,4,6-T_3CP should not be overlooked.

Toxic effects in man from acute exposure to high concentrations of the lower chlorinated phenols include acute and chronic skin irritation, chloracne, respiratory disorders, recurring headaches, dizziness, nausea, vomiting, loss of coordination, tremor, weakness, and lethargy (section 9.1).

The question of carcinogenicity in man from exposure to chlorophenols is a matter of controversy. IARC concluded that there is limited evidence of carcinogenicity from occupational exposure to

chlorophenols. Following a review of studies published since the IARC evaluation, the Task Group still finds this conclusion appropriate.

10.1.3 Risk Evaluation

The information available to date indicates that the general population is exposed to low levels of chlorinated phenols. As derived in section 10.1, the estimated exposure to the major chlorophenols other than PCP of a person who does not work with these compounds is 0.0833 μg/kg per day. This burden is made up of 0.058 μg 2,4-DCP/kg per day, 0.0013 μg 2,4,5-T_3CP/kg per day, and 0.024 μg 2,3,4,6-T_4CP/kg per day. People who manufacture or apply chlorophenols predictably experience much higher levels of exposure. As an example, the total estimated average exposures to T_4CP for sawmill workers ranged from 2 to 42 μg/kg per day (section 10.1.1.2).

For comparison with these estimated exposures, Tolerable Daily Intake (TDI) levels have been calculated (from no-observed-effect levels determined in short- term studies) of 100 mg/kg body weight for 2,4-DCP (mice, in feed) (Kobayashi et al., 1972), 100 mg/kg body weight for 2,4,5-T_3CP (rats, oral) (McCollister et al., 1961), and 10 mg/kg body weight for 2,3,4,6-T_4CP (rats, oral) (Schwetz et al., 1974). Using an uncertainty factor of 1000 for 2,4,5- T_3CP and 2,3,4,6-T_4CP, because of the lack of long-term animal data, and an uncertainty factor of 500 for 2,4-DCP, because of the availability of long-term data (WHO, 1986), the TDI values for 2,4-DCP, 2,4,5-T_3CP, and 2,3,4,6-T_4CP were estimated to be 200, 100, and 10 μg/kg per day, respectively. The long-term carcinogenicity study available for 2,4-DCP (section 8.7) does not provide data that would alter this estimate. The embryotoxicity data available for 2,4,5- T_3CP (section 8.5) were found to be of too limited significance to be taken into consideration.

Non-occupational exposure levels are usually well below these values, indicating that the anticipated health hazards for the general population from exposure to chlorophenols other than PCP are minimal. The estimated occupational intakes are considerably higher, especially when there is skin contact with chlorophenols (Table 20). Exposure levels in sawmills may, in some cases, exceed the TDI values.

If tetra- or trichlorophenol preparations are used in wood protection, workers can also be exposed to 2,4,6-T_3CP. There is sufficient evidence that 2,4,6-T_3CP is carcinogenic for mice and rats. Because of the arbitrary nature of assumptions inherent in developing estimates of exposure, and extrapolating from effects on animals to effects on human

beings, risk assessments are never precise. Nevertheless, it is prudent to ensure that human exposure to 2,4,6-T3CP is kept to a minimum.

Acute exposure to high concentrations of chlorophenol formulations can be a significant hazard for the health of workers involved in the production or use of chlorophenols. While no deaths have been reported with exposure to chlorophenols other than PCP, fatalities due to high exposure to the latter are well documented. Exposures to non-PCP chlorophenols result in adverse signs and symptoms similar to those caused by PCP. Exposure to commercial formulations of chlorinated phenols has been associated with an increased relative risk of soft-tissue sarcomas, lymphomas, and nasal and nasopharyngeal cancers in some studies; such associations have not been found in other similar studies.

On the basis of toxicological effects and current exposure levels, there does not appear to be any strong reason for eliminating all use of chlorophenols. Furthermore, the need to reduce the levels of exposure to chlorophenols appears minimal as long as the necessary precautions to prevent high-level dermal and respiratory uptake are observed. Exposure of the general population is much lower, and in the absence of release from an industrial accident, the overall risk from sustained non-occupational exposure is probably negligible. Chlorophenols produce undesirable organoleptic effects at very low concentrations. Contamination of the environment and of drinking-water with chlorophenols above the threshold for organoleptic effects is therefore unacceptable. Comprehensive monitoring of chlorophenol levels, sources, and fluxes is essential to characterize both occupational and non-occupational exposure to these compounds, and to alert the responsible agency to potentially hazardous exposures where they exist.

Microcontaminants, in particular PCDDs and PCDFs, found in commercial formulations of tri-, tetra-, and pentachlorophenol, are probably the causal agents for chloracne in human beings. PCDD and PCDF levels in commercial preparations should be kept as low as technically feasible. Care should also be taken to minimize their formation during the incineration of wastes containing chlorophenols.

10.2 Evaluation of Effects on the Environment

10.2.1 Levels of exposure

Data on levels of chlorophenol residues other than PCP in the environment are limited primarily to aquatic habitats, and indicate that chlorophenol contamination is widespread in these systems. This

contamination may result from either the use or the formation of chlorophenols, e.g., in the chlorine-bleaching process in pulp and paper-mills (sections 3.2, 3.3, 3.4). Where data are not available on levels of other chlorophenols in the environment and for evaluation purposes, examples of monitoring data on PCP are used. On the basis of relative rates of degradation and use patterns, it is likely that, in general, environmental levels of other chlorophenols would be lower than those found for PCP.

Ambient levels of PCP in air are less than 1 ng/m^3 in uncontaminated areas, while concentrations of several ng/m^3 have been detected in residential areas. Other chlorophenols may well be present at comparable levels, but confirmatory data are lacking.

Residues of all chlorophenol congeners have been found in fresh and marine waters (section 5.1.2). In Canada, concentrations are often undetectable at the ng/litre level in receiving waters, and only occasionally exceed 1 µg/litre; these higher levels are only observed in close proximity to industrial sources of chlorophenols, particularly pulp and paper-mills. Ambient levels are higher in waters in the industrialized areas of Europe, but median concentrations still do not exceed 1 µg/litre, and maximum concentrations in surface waters and groundwaters only reach several µg/litre in heavily industrialized regions. Levels of particular chlorophenols in industrial effluents can reach several thousand µg/litre (section 5.1.2), but dilution apparently reduces these to the low ambient levels observed.

Chlorophenol concentrations in sediments are usually higher than those in the overlying water (section 5.1.2), as a result of adsorption and low rates of anaerobic degradation. Water bodies not receiving large chlorophenol inputs generally contain less than 1 µg of chlorophenol congeners per kg dry sediment. Typical levels of all chlorophenol congeners in fresh-water sediments of industrialized regions are less than 50 µg/kg of dry sediment. In some instances, hundreds or thousands of µg/kg have been detected from sites adjacent to spills or discharges.

Soils may contain significant quantities of chlorophenols, particularly at timber preservation facilities, or where phenoxy herbicides have been applied. Levels as high as 70 mg chlorophenols/kg were detected in soils from Finnish sawmills (section 5.1.3), but ambient levels in soil were found to be much lower (< 0.1 mg/kg).

10.2.2 Transport

While chlorophenols are considered to be mainly water and soil contaminants, some atmospheric movement also occurs. PCP has been

detected in rain, snow, and in the air (section 5.1.1), and presumably other chlorophenols are also transported in this manner. Adsorption controls chlorophenol transport in acidic or organic soils, but is much less important in basic or mineral soils (section 4.1.2.1). In surface waters, the fraction that is not degraded is incorporated into the sediments, most likely through adsorption on sedimenting particulates (section 4.1.3). While much of the chlorophenols entering natural waters are probably degraded by photolysis or microorganisms, they are moderately soluble and fairly persistent, and so can be transported considerable distances by water (section 4.1.3).

10.2.3 Degradation

Both abiotic and biotic degradation eliminate chlorophenols from the environment. Numerous *in vitro* studies have shown that ultraviolet radiation can rapidly break down chlorophenols. Evidence suggests that photolysis is important in natural surface waters (section 4.2.1.1), and presumably in other exposed habitats. A large number of micro-organisms from different habitats are able to degrade chlorophenols in laboratory cultures. In some instances, quantities as high as tens of mg/litre are eliminated in a matter of hours or days (section 4.2.1.2), though it is necessary to acclimate them first. Degradation is generally slowest for the higher chlorinated congeners or those with a chlorine atom in the meta position. In general, anaerobic biodegradation of these compounds, if it occurs at all, is much slower than aerobic metabolism. Some evidence suggests that biodegradation is faster in soil than in sediments, and slower in stream waters.

10.2.4 Bioaccumulation

Bioaccumulation of chlorophenols appears moderate, and most bioconcentration factors (BCFs) fall between 100 and 1000. Bio-concentration is usually a positive function of chlorine number. There are no obvious patterns in BCF in relation to the type of organism (for algae, plants, invertebrates, and fish). Once exposure is discontinued, chlorophenols clear rapidly from biota, indicating that the bioaccumulation observed in field studies is the result of long-term exposure rather than persistence.

10.2.5 Persistence

Chlorophenols should only persist in the environment where the rates of the various degradative processes are minor. Indeed, residues in sediments, where photolysis and apparently microbial degradation are minimal, have been estimated to be decades old (section 4.4). Herbicidal applications and spills of PCP in soils reportedly disappear in a matter of weeks or months.

10.2.6 Toxic effects on environmental organisms

Considerable overlap exists in the chlorophenol concentrations that are toxic for bacteria, phytoplankton, plants, invertebrates, and fish. Most of the LC_{50} and EC_{50} values for these organisms, which to date have been primarily aquatic, fall within the several mg/litre range (Table 16). Toxicity generally increases with the degree of chlorination of the phenol ring, though chlorophenols with chlorines in the 2 and 6 positions are often less toxic than expected on the basis of the number of chlorines. Particularly in the case of the higher chlorophenols, acute toxicity is a strong inverse function of pH, as the phenol form of the compound is more toxic than the ionized form. Exposure to chlorophenols affects a wide variety of processes in environmental organisms (section 7) (Table 16).

In controlled field studies on aquatic ecosystems, exposure to high concentrations (100–5000 mg/litre) of lower chlorophenols generally impairs algal production and reproduction, alters the algal species composition dramatically, and reduces zooplankton biomass and production. The low levels of chlorophenols present in moderately contaminated waters have been reported to impair the flavour of fish. There is very little information on the toxic effects exerted by concentrations similar to ambient levels.

10.2.7 Risk evaluation

The information available to assess the environmental hazards presented by chlorophenols other than PCP is deficient in at least 2 respects: (*a*) knowledge of the quantities of chlorophenols entering the environment, and of their subsequent dynamics, is insufficient for all chlorophenols other than PCP; and (*b*) not enough toxicology studies

using concentrations characteristic of the environment have been conducted. As a result, it is not yet possible to predict quantitatively the environmental impact of the widespread low-level contamination that has recently become apparent (section 5).

However, it is possible to get a first approximation of the hazard presented by a given chlorophenol, by comparing the levels that produce toxic effects on test organisms *in vitro* with the residue concentrations that have been measured in the environment. The information for such a comparison is presented in Table 21, using data for aquatic organisms and environments. It is necessary to restrict the data in this manner because the vast majority of studies on the environmental toxicity of chlorophenols have been on aquatic test systems.

Furthermore, this focus is appropriate because many producers and users of chlorophenols still discharge them as wastes into water bodies (section 3.2.3).

The environmental data in Table 21 include measured levels for each chlorophenol in water, sediment, and effluent, since these are the environmental sources most readily comparable with the results of toxicity studies. The latter data are taken from the laboratory toxicity studies outlined in section 5.1.2 and include the concentrations that cause toxic effects, the no-observed-effect levels, and those showing organoleptic effects in fish and drinking-water. In order to ensure that the comparison of environmental concentrations and toxic levels provides a margin of safety, the environmental data used for evaluation are the maximum values reported in highly-contaminated industrialized waters, while the levels producing toxic effects are the minimum levels reported to cause effects from a large number of studies compiled by Buikema et al. (1979), and Jones (1981, 1984). Table 21 is designed so that comparisons can be made across the rows; because of the diversity of test conditions, organisms, and response variables, the data on the toxicity of the individual compounds are not directly comparable.

In virtually all instances, the maximum ambient levels in water and sediments are orders of magnitude below the lowest concentrations that are toxic for aquatic organisms: effects typically occur in the mg/litre range, while environmental levels are generally in the µg/litre range. On this basis, it appears that the ambient chlorophenol levels measured in aquatic environments are unlikely to have adverse effects on the ecosystems receiving them, except in the case of accidental spills, high-concentration, point-source discharges, or in the immediate vicinity of manufacturers' undiluted waste streams. However, the elevated concentrations found in some industrialized regions, or in habitats

adjacent to discharges, can compromise the flavour and/or smell of drinking-water and fish.

It is advisable to control chlorophenol discharges into the environment at levels that would not increase the present environmental concentrations, in view of the taste and odour effects of chlorophenols and the lack of data on the long-term effects on ecosystems from the present low levels of chlorophenols detected. Furthermore, the levels of such microcontaminants as PCDDs and PCDFs in technical formulations of T_3CP and T_4CP should be reduced as much as possible, in order to decrease the levels of such toxic chemicals released into the environment.

Table 21. Maximum reported water, sediment, and effluent levels, contrasted with minimum levels producing toxic and organoleptic effects and no-observed-effect levels

Compound	Maximum reported environmental levels			Lowest reported levels causing toxic effects		No-observed-effect level (NOEL)		Organoleptic threshold in water (µg/litre)	
	Water (µg/litre)	Sediment[n] (µg/kg)	Effluents (µg/litre)	Level (µg/litre)	Effect (µg/litre)	Level	Parameter	Drinking-water[a]	Fish flesh[a]
2-MCP	2.3[m]		4[p]	2600	*Daphnia magna* 48-h LC50[b]	1000	*Daphnia magna* survival[b]		60
3-MCP	6.0[m]	43	6[p]	1800	Unidentified fish 24-h TLm[d]	10000	*Chlorella pyrenoidosa* growth[c]	0.1	25
4-MCP	3.9[m]		150[q]	4100	*Daphnia magna* 48-h LC50[b]	500	Estuarine phytoplankton growth[e]	0.1	45
2,3-DCP	0.72[m]	2.2						0.04	84

Table 21 (contd).

2,4-DCP	0.59[m]	10	330[q]	100	Crayfish elevation of blood-glucose[f]	0.3–8.0	1.0
2,5-DCP	0.29[m]	11				0.5	23
2,6-DCP	0.45[m]	31	220[q]	4000	*Salmo trutta* 24-h LC50[g]	0.2–2.0	35
3,4-DCP	0.23[m]	49		5000	Fish death 3 h[h]	0.3	
3,5-DCP	0.52[m]	12		1500	Shrimp 96-h lethal threshold[i]		
2,3,4-T_3CP	0.04[n]	0.8	3.6[q]	2000	Shrimp 96-h lethal threshold[i]		
2,3,5-T_3CP	0.28[n]	11		800	Salmo trutta[g] 24-h LC_{50}		

Table 21 (contd).

Compound	Maximum reported environmental levels			Lowest reported levels causing toxic effects		No-observed-effect level (NOEL)		Organoleptic threshold in water (μg/litre)	
	Water (μg/litre)	Sediment[n] (μg/kg)	Effluents (μg/litre)	Level (μg/litre)	Effect (μg/litre)	Level	Parameter	Drinking-water[a]	Fish flesh[a]
2,3,6-T_3CP	0.36[n]			2700	Shrimp 96-h lethal threshold[l]			0.5	
2,4,5-T_3CP	0.66[m]	15	2400[q]	640	*Palaemonetes puglo* 96-h LC50[j]	100	Rainbow trout	1.0	52
2,4,6-T_3CP	2.5[m]	3.7	3120[q]	0.5	Guppy fecundity offspring survival[k]	< 410	*Daphnia magna* survival	2.0	
2,4,6-T_3CP	2.5[m]	3.7	3120[q]	> 100–< 1000	Fathead minnow 96-h TLm[l]				

Table 21 (contd).

2,3,4,5-T_4CP 0.02 [n]	8.9	12 [q]	<300	Grass shrimp EC_{50}-limb regeneration [j]			
2,3,4,6-T_4CP 3 [r]	4.9	2100 [q]	290	*Daphnia magna* 48-h LC50 [b]	10	*Daphnia magna* survival [b]	1.0
2,3,5,6-T_4CP 5 [r]	2.8	35	570	*Daphnia magna* 48-h LC50 [b]	10	*Daphnia magna* survival [b]	

[a] Organoleptic threshold is for drinking-water (US EPA, 1980c) and ambient water that leads to the tainting of fish flesh (Shumway & Palensky, 1973).
[b] LeBlanc (1980).
[c] Huang & Gloyna (1968).
[d] Ingols et al. (1966).
[e] Erickson & Hawkins (1980).
[f] Telford (1974).
[g] Hattula et al. (1981b).
[h] Jones (1981).
[i] McLeese et al. (1979).
[j] Rao et al. (1981).
[k] Virtanen & Hattula (1982).
[l] Barnhart & Campbell (1972).
[m] Wegman & Hofstee (1979).
[n] Wegman & van den Broek (1983).
[p] Jolley et al. (1975).
[q] Garrett (1980).
[r] Zoeteman et al. (1981).

11. RECOMMENDATIONS

11.1 Production

(*a*) The concentrations of microcontaminants in chlorophenols and products derived from them should be determined and specified.

(*b*) Levels of PCDDs and PCDFs in chlorophenols and related products should be kept as low as is technically possible.

(*c*) Since data on the quantities of chlorophenols produced and consumed are not available for most countries, international agencies should seek the assistance of industry to compile such data in different countries.

11.2 Disposal

(*a*) Disposal of chlorophenols and chlorophenol-contaminated waste should be carried out in a manner that minimizes their release into the environment. Contaminated waste waters should undergo primary and secondary treatment. Chlorophenols should only be incinerated at high temperatures and under strictly controlled conditions.

(*b*) Contamination of surface and ground waters with chlorophenols arising as a result of industrial chlorination processes or waste treatments using chlorine should be avoided as far as is technically feasible.

11.3 Occupational Exposure

(*a*) Work-place exposure to chlorophenols should be minimized, and absorption of these compounds through the dermal and inhalation routes prevented, by:

- enclosure and automation of industrial processes that use chlorophenols;
- adequate ventilation of the work area;
- provision of appropriate protective clothing for employees working with chlorophenols;

–provision of proper washing and laundry facilities;

–instruction of workers in the safe use and handling of chlorophenols, the importance of personal hygiene (washing before eating or smoking, showering before leaving work, and daily laundering of clothing), and the application of proper emergency procedures;

–provision of eating and rest areas in the work place that are isolated from potential chlorophenol contamination.

(*b*) The effectiveness of measures to reduce occupational exposure should be surveyed by monitoring both the work-place air and the urine of the workers.

11.4 General Population Exposure

(*a*) The availability and use of consumer products containing chlorophenols should be reduced wherever practicable.

(*b*) Products containing chlorophenols should be clearly labelled by the manufacturer to alert the consumer to their toxicity and to instruct consumers in the safe use and handling of these products.

(*c*) The use of tri- and tetrachlorophenols for wood preservation should be avoided where such wood is to be used:

–for shipping or storing food;

–for the retention of soil on which food may be grown;

–for animal housing or bedding on farms.

11.5 Recommendations for Future Research

11.5.1 Environmental Aspects

Given the continued release of chlorophenols into the environment, research is needed to study:

(*a*) the transport and distribution of chlorophenols in the environment;

(*b*) the effects of long-term exposure to chlorophenols on both aquatic and terrestrial organisms at concentrations typical of the environment;

(*c*) the suitability of controlled landfill sites for the disposal of chlorophenols and related wastes;

(*d*) means of reducing the contribution of industrial and municipal chlorination to the overall environmental releases of chlorophenols.

11.5.2 Toxicology

The toxicology database for chlorophenols other than PCP has major deficiencies, particularly for tetrachlorophenols. A more accurate estimate of the risk posed by these chemicals necessitates research into:

(*a*) uptake, distribution, metabolism, and excretion of chlorophenols, especially in man;

(*b*) further study of the effects of chlorophenols on reproduction;

(*c*) the *in vivo* genotoxic potential of chlorophenols;

(*d*) long-term carcinogenicity studies with pure and technical grade 2,4,5-T_3CP, 2,4,6-T_3CP, and 2,3,4,6-T_4CP;

(*e*) the cancer-promoting potential of chlorophenols;

(*f*) the mechanism of toxicity of chlorophenols at the molecular level;

(*g*) the extent to which the toxic effects exerted by technical grade chlorophenols are attributable to microcontaminants;

(*h*) the contribution made by the biotransformation of other chlorinated compounds (e.g., hexachlorobenzene) to the human body burden of chlorophenols.

11.5.3 Epidemiology

(*a*) Epidemiological investigations of previously-studied cohorts should be followed-up and updated.

(*b*) Studies on new groups of workers exposed specifically to chlorophenols, i.e., sawmill employees working with these compounds, should be conducted. End-points studied should not only be cancers, but should also include pulmonary, reproductive, and other effects.

(*c*) The higher chlorinated PCDDs and PCDFs, which occur as contaminants in several chlorophenols, have long half-lives in human beings and can therefore be used as indicators of exposure to the higher chlorophenols. Since the present contradictory results from epidemiological studies may, in part, be because of inaccurate information on exposure to CPs, the potential use of PCDD and PCDF concentrations in human tissues and fluids as markers of previous exposure to these chlorophenols should be investigated.

12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

A guideline value of 10 μg/litre was recommended by WHO (WHO, 1984) for 2,4,6-trichlorophenol in drinking-water, based on animal carcinogenicity data using a conservative mathematical model. In the supporting documentation for this guideline value (WHO, 1985), it was noted that the taste threshold level for 2,4,6-T_3CP was 1.0 μg/litre and that, on the basis of aesthetic qualities, the level would be 0.1 μg/ litre. Guideline values for other individual CPs were not set, but the odour threshold concentration of 0.1 μg/litre was considered appropriate for chlorophenols other than pentachlorophenol.

The carcinogenicity of 2,4,5- and 2,4,6-T_3CP has been evaluated by the International Agency for Research on Cancer (IARC, 1979, 1986). It was concluded that: there was sufficient evidence for carcinogenicity in animals for 2,4,6-T_3CP and inadequate data for the assessment of the carcinogenicity of 2,4,5-T_3CP in animals. IARC (1986) also concluded that there was limited evidence for the carcinogenicity of occupational exposures to all chlorophenols for human beings. Although not stated directly in the IARC monographs, occupational exposures were primarily to T_3CP and T_4CP formulations.

Regulatory standards for chlorophenols established by national bodies in different countries and the EEC are summarized in the Legal File of the International Register of Potentially Toxic Chemicals (IRPTC, 1986).

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