International Programme on Chemical Safety

Environmental Health Criteria 71

Pentachlorophenol

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

WORLD HEALTH ORGANIZATION GENEVA 1987

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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 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.

ISBN 92 4 154271 3

ISSN 0250-863X
PRINTED IN FINLAND
87/7273 - VAMMALA — 5500

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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. 988400 - 985850).

ENVIRONMENTAL HEALTH CRITERIA FOR PENTACHLOROPHENOL

A WHO Task Group on Environmental Health Criteria for Pentachlorophenol met at the Fraunhofer Institute for Toxicology and Aerosol Research, Hanover, Federal Republic of Germany from 20 to 24 October, 1986. Dr W. Stöber opened the meeting and welcomed the members on behalf of the host Institute, and Dr U. Schlottmann spoke on behalf of the Federal Government, who sponsored the meeting. Dr K.W. Jager addressed the meeting on behalf of the three co-operating organizations of the IPCS (UNEP/ILO/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 pentachlorophenol.

The drafts of this document were prepared by DR G. ROSNER of the Fraunhofer Institute for Toxicology and Aerosol Research, Hanover, Federal Republic of Germany, and DR A. GILMAN of the Health Protection Branch, Ottawa, Canada.

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

* * *

Partial financial support for the publication of this criteria document was kindly provided by the United States Department of Health and Human Services, through a contract from the National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, USA - a WHO Collaborating Centre for Environmental Health Effects. The United Kingdom Department of Health and Social Security generously supported the costs of printing.

1. SUMMARY

1.1 Identity, Physical and Chemical Properties, Analytical Methods

Pure pentachlorophenol (PCP) consists of light tan to white, needlelike crystals and is relatively volatile. It is soluble in most organic solvents, but practically insoluble in water at the slightly acidic pH generated by its dissociation (pKa 4.7). However, its salts, such as sodium pentachlorophenate (Na-PCP), are readily soluble in water. At the approximately neutral pH of most natural waters, PCP is more than 99% ionized.

Apart from other chlorophenols, unpurified technical PCP contains several microcontaminants, particularly polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), of which H_6CDD is the most relevant congener toxicologically. 2,3,7,8-T_4CDD has only once been confirmed in commercial PCP samples (0.25 - 1.1 µg/kg). Depending on the thermolytic conditions, thermal decomposition of PCP or Na-PCP may yield significant amounts of PCDDs and PCDFs. The use and the uncontrolled incineration of technical grade PCP is one of the most important sources of PCDDs and PCDFs in the environment.

Most of the analytical methods used today involve acidification of the sample to convert PCP to its non-ionized form, extraction into an organic solvent, possible cleaning by back-extraction into a basic solution, and determination by gas chromatography with electron-capture detector (GC-EC) or other chromatographic methods as ester or ether derivatives (e.g., acetyl-PCP). Depending on sampling procedures and matrices, detection limits as low as 0.05 µg/m³ in air or 0.01 µg/litre in water can be achieved.

1.2 Sources of Human and Environmental Exposure

PCP is mainly produced by the stepwise chlorination of phenols in the presence of catalysts. Until 1984, Na-PCP was partly synthesized by means of the alkaline hydrolysis of hexachlorobenzene, but it is now produced by dissolving PCP flakes in sodium hydroxide solution.

World production of PCP is estimated to be of the order of 30 000 tonnes per year. Because of their broad pesticidal efficiency spectrum and low cost, PCP and its salts have been used as algicides, bactericides, fungicides, herbicides, insecticides, and molluscicides with a variety of applications in the industrial, agricultural, and domestic fields. However, in recent years, most developed countries have restricted the

use of PCP, especially for agricultural and domestic applications.

PCP is mainly used as a wood preservative, particularly on a commercial scale. The domestic use of PCP is of minor importance in the overall PCP market, but has been of particular concern because of possible health hazards associated with the indoor application of wood preservatives containing PCP.

1.3 Environmental Transport, Distribution, and Transformation

The relatively high volatility of PCP and the water solubility of its ionized form have led to widespread contamination of the environment with this compound. Depending on the solvent, temperature, pH, and type of wood, up to 80% of PCP may evaporate from treated wood within 12 months.

The adsorption and leaching behaviour of PCP varies from soil to soil. Adsorption of PCP decreases with rising pH and so PCP is most mobile in mineral soils, and least mobile in acidic clay and sandy soils.

Solid or water-dissolved PCP can be photolysed by sunlight within a few days, yielding aromatic (lower chlorinated phenols, etc.) and nonaromatic fragments, as well as hydrogen chloride (HCl) and carbon dioxide (CO_2). Traces of PCDDs, mainly OCDD are formed photochemically on irradiation of Na-PCP in aqueous solution.

PCP degrading microorganisms have been isolated from waters and soils. High organic matter and moisture content, median temperatures, and high pH enhance microbial breakdown in soil (half-life = 7 - 14 days). Low oxygen conditions are generally unfavourable for the biodegradation of PCP, allowing it to persist in soil (half-life = 10 - 70 days under flooded conditions), water (half-life = 80 - 192 days in anaerobic water), and sediments (10% decomposition within 5 weeks to almost no degradation). Several studies have proved that PCP can be degraded by activated sludge. However, in full-scale treatment plants the treatment efficiency is often reduced.

Numerous metabolites have been identified resulting from the methylation, acetylation, dechlorination, or hydroxylation of PCP. Of the possible metabolites, at least tetrachlorocatechol seems to be relatively persistent. However, there is a lack of data concerning the fate of the intermediate products of both the abiotic and biotic degradation of PCP.

1.4 Environmental Levels and Human Exposure

The ubiquitous occurrence of PCP is indicated by its detection, even in ambient air of mountain rural areas (0.25 -

0.93 ng/m³). In urban areas, PCP levels of 5.7 - 7.8 ng/m³ have been detected.

While elevated PCP concentrations can be found in groundwater (3 - 23 µg/litre) and surface water (0.07 - 31.9 µg/litre) within wood-treatment areas, the PCP level of surface waters is usually in the range of 0.1 - 1.0 µg/litre, with maximum values of up to 11 µg/litre. PCP concentrations in the mg/litre range can be encountered near industrial discharges.

Sediments of water bodies generally contain much higher levels of PCP than the overlying waters. Soil samples from PCP or pesticide plants contain around 100 µg PCP/kg (dry weight); heavily contaminated soil (up to 45.6 mg PCP/kg) can be found in the vicinity of wood-treatment areas.

Residues of PCP in the aquatic invertebrate and vertebrate fauna are in the low µg/kg range (wet weight). Very high levels (up to 6400 µg/kg) are found in fish from waters that are contaminated with wood preservatives, while sediment-dwelling organisms, such as clams, show PCP levels of up to 133 000 µg/kg. Fish kills result in PCP residues in fish of between 10 and 30 mg/kg.

After agricultural PCP application, birds can be highly contaminated (47 mg/kg wet weight in liver). Exposure of farm animals to PCP-treated wood shavings used as litter causes a musty taint of the flesh as a result of contamination with pentachloroanisole, a metabolite of PCP biodecomposition. PCP levels ranging from not detectable to 8571 µg/kg have been found in the muscle tissue of wild birds.

The general population is exposed to PCP through the ingestion of drinking-water (0.01 - 0.1 µg/litre) and food (up to 40 µg/kg in composite food samples). Apart from the daily dietary intake (0.1 - 6 µg/person per day) resulting from direct food contamination with PCP, continuous exposure to hexachlorobenzene and related compounds in food, which are biotransformed to PCP, may be another important source.

In addition, because of its widespread use, the general population can be exposed to PCP in treated items such as textiles, leather, and paper products, and above all, through inhalation of indoor air contaminated with PCP. Generally, PCP concentrations of up to about 30 µg/m³ can be expected, for up to the first month, after indoor treatment of large surfaces; considerably higher levels (up to 160 µg/m³) cannot be excluded under unfavourable conditions. In the long term, values of between 1 and 10 µg/m³ are typical PCP concentrations after extensive treatments, though higher levels, up to 25 µg/m³, have been found in rooms treated one to several years earlier. For comparison, PCP indoor air levels in untreated houses are generally below 0.1 µg/m³.

According to the usage pattern, the main sources of occupational exposure to PCP are the treatment of lumber in sawmills and treatment plants, and exposure to treated wood during carpentry and other wood-working activities. Most of the reported air concentrations at the work-place are below the TWA MAC value of 500 $\mu g/m^3$ that has been established by several countries. Occupational exposure to PCP mainly occurs via inhalation and dermal exposure.

Since the PCP concentrations in the sources (air, food) do not directly indicate the actual PCP intake by the different routes, extrapolation from urine residue data has been used to estimate human total body exposure. Mean or median urine-PCP levels range around 10 µg/litre for the general population without known exposure, around 40 µg/litre for non-occupationally exposed persons, and around 1000 µg/litre for occupationally exposed people.

The ranges of urine levels observed in exposed and unexposed persons overlap considerably. This overlap probably occurs because occupational exposure does not necessarily involve high loading, while non-occupationally exposed people may, in some instances, be exposed to PCP at levels encountered at the work-place.

1.5 Effects on Organisms in the Environment

As a result of its biocidal properties, PCP negatively affects non-target organisms in soil and water at relatively low concentrations. Algae appear to be the most sensitive aquatic organisms; as little as 1 µg/litre can cause significant inhibition of the most sensitive algal species. Less sensitive species show EC_{50} values of around 1 mg/litre.

Most aquatic invertebrates (annelids, molluscs, crustacea) and vertebrates (fish) are affected by PCP concentrations below 1 mg/litre in acute toxicity tests. Generally, reproductive and juvenile stages are the most sensitive, with LC_{50} values as low as 0.01 mg/litre for fish larvae. Low levels of dissolved oxygen, low pH, and high temperature increase the toxic effects of PCP. Concentrations causing sublethal effects on fish are in the low µg/litre range. As PCP contamination in many surface waters is in this range, population and community effects cannot be ruled out. This is also indicated by the substantial alterations in the community structure of model ecosystems that are induced by PCP.

PCP is accumulated by aquatic organisms. Fresh-water fish show bioconcentration factors of up to 1000 compared to < 100 in marine fish. The portion of PCP taken up, either through the surrounding water or along the food chain, is probably species specific.

PCP taken up by terrestrial plants remains in the roots and is partly metabolized.

1.6 Kinetics and Metabolism

PCP is readily absorbed through the intact skin and respiratory and gastrointestinal tracts, and distributed in the tissues. Highest levels are observed in liver and kidney, and lower levels are found in body fat, brain, and muscle tissue. There is only a slight tendency to bioaccumulate, and so relatively low PCP concentrations are found in tissues. In rodent species, detoxication occurs through the oxidative conversion of PCP to tetrachlorohydroquinone, to a small extent also to trichlorohydroquinone, as well as through conjugation with glucuronic acid. In rhesus monkeys, no specific metabolites have been detected. In man, metabolism of PCP to tetrachlorohydroquinone seems to occur only to a small extent.

Rats, mice, and monkeys excrete PCP and their metabolites, either free or conjugated with glucuronic acid, mainly in urine (rodents, 62 - 83%; monkeys, 45 - 75%) and to a lesser extent with the faeces (rodents, 4 - 34%; monkeys, 4 - 17%). The pharmacokinetic profile following single doses depends on the species and possibly on the sex of the test animals. Rats and mice eliminate PCP rapidly, with a half-life of 6 - 27 h. The kinetics in rats follow a biphasic elimination scheme with a comparatively slow second elimination phase (half-life, 33 - 374 h), perhaps because extensive enterohepatic circulation retains PCP in the liver. Retention may also be the result of plasma-protein binding of PCP, which seems to become stronger at lower PCP concentrations.

In rats, 90% of an applied single oral dose is excreted by day 3 with small amounts still remaining in the liver (0.3%) and kidney (0.05%) after 9 days. On the other hand, monkeys show a much slower elimination rate (half-life, 41 - 92 h), apparently because they do not metabolize PCP; even 15 days after oral application of a single dose (10 mg/kg bodyweight), about 11% of the total dose remained in the body, particularly in the intestines and liver.

The elimination kinetics of PCP in human beings are a controversial subject. A study on 4 male volunteers ingesting a single oral dose of water-soluble Na-PCP at 0.1 mg/kg body weight showed a rapid elimination of PCP both in urine (half-life, 33 h) and plasma (30 h). Within 168 h, 74% of the dose was excreted in urine as free PCP and 12% as its glucuronide, while about 4% was eliminated in the faeces. In contrast to this study, the application of oral doses of between 0.016 and 0.31 mg PCP/kg body weight in 40% ethanol revealed a substantially slower PCP excretion rate, with elimination half-

lives of 16 days (plasma) and 18 - 20 days (urine). These low elimination rates have been ascribed to the high protein binding tendency of PCP.

Some animal data indicate that there may be long-term accumulation and storage of small amounts of PCP in human beings. The fact that urine- or blood-PCP levels do not completely disappear in some occupationally exposed people, even after a long absence of exposure, seems to confirm this, though the biotransformation of hexachlorobenzene and related compounds provides an alternative explanation of this phenomenon. However, there is a lack of data concerning the long-term fate of low PCP levels in animals as well as in man. Furthermore, no data are available on the accumulation and effects of microcontaminants taken up by people together with PCP.

1.7 Effects on Experimental Animals and In Vitro Test Systems

In the main, mammalian studies have been relatively consistent in their demonstration of the effects of exposure to PCP. In rats, lethal doses induce an increased respiratory rate, a marked rise in temperature, tremors, and a loss of righting reflex. Asphyxial spasms and cessation of breathing occur soon before cardiac arrest, which is in turn followed by a rapid, intense rigor mortis.

PCP is highly toxic, regardless of the route, length, and frequency of exposure. Oral LD_{50} values for a variety of species range between 27 and 205 mg/kg body weight according to the different solvent vehicles and grades of PCP. There is limited evidence that the most dangerous route of exposure to PCP is through the air.

PCP is also an irritant for exposed epithelial tissue, especially the mucosal tissues of the eyes, nose, and throat. Other localized acute effects include swelling, skin damage, and hair loss, as well as flushed skin areas where PCP affects surface blood vessels. Exposure to technical formulations of PCP may produce chloracne. Comparative studies indicate that this is a response to microcontaminants, principally PCDDs, present in the commercial product. The parent molecule appears responsible for immediate acute effects, including irritation and the uncoupling of oxidative phosphorylation with a resultant elevated temperature.

Short- and long-term studies indicate that purified PCP has a fairly limited range of effects in test organisms, primarily rats. Exposure to fairly high concentrations of PCP may reduce growth rates and serum-thyroid hormone levels, and increase liver weights and/or the activity of some liver enzymes. In contrast, technical formulations of PCP usually

at much lower concentrations can decrease growth rates, increase the weights of liver, lungs, kidneys, and adrenals, increase the activity of a number of liver enzymes, interfere with porphyrin metabolism, alter haematological and biochemical parameters and interfere with renal function. Apparently microcontaminants are the principal active moities in the nonacute toxicity of commercial PCP.

PCP is fetotoxic, delaying the development of rat embryos and reducing litter size, neonatal body weight, neonatal survival, and the growth of weanlings. The no-observed-adverse-effect-level (NOAEL) for technical PCP is a maternal dose of 5 mg/kg body weight per day during organogenesis. The NOAEL for purified PCP is lower. In one study, it was reported that purified PCP was slightly more embryo/fetotoxic than technical PCP, presumably because contaminants induced enzymes that detoxified the parent compound.

PCP is not considered teratogenic, though, in one instance, birth defects arose as an indirect result of maternal hyperthermia. The NOAEL in rat reproduction studies is 3 mg/kg body weight per day. This value is remarkably close to the NOAEL mentioned in the previous paragraph, but there are no corroborating studies in other mammalian species.

PCP has also proved immunotoxic to mice, rats, chickens, and cattle; at least part of this effect is caused by the parent molecule.

Neurotoxic effects have also been reported, but the possibility that these are due to microcontaminants has not been excluded.

PCP is not considered carcinogenic for rats. Mutagenicity studies support this conclusion in as much as pure PCP has not been found to be highly mutagenic. Its carcinogenicity remains questionable because of shortcomings in these studies. The presence of at least one carcinogenic microcontaminant (H_6CDD) suggests that the potential for technical PCP to cause cancer in laboratory animals cannot be completely ruled out.

1.8 Effects on Man

The effects of PCP on man are very similar to those reported in experimental animals. Human data have been obtained primarily from accidental exposures and from the work-place. Unfortunately, there are few precise estimates of exposure, hence dose-response relationships are difficult to establish in human beings.

It is clear that the use of PCP may pose a significant hazard with regard to specific aspects of the health of workers employed in the production or use of PCP. Chloracne, skin rashes, respiratory diseases, neurological changes,

headaches, nausea, and weakness have been documented in workers at numerous production and manufacturing sites. Similar symptoms have been reported in some inhabitants of houses treated internally with PCP. Acute intoxications leading to hyperpyrexia and death have been clearly associated with exposure to the chlorophenol molecule itself, whereas chloracne appears to be an effect of the PCDD and PCDF micro-contaminants. Changes in industrial practice have resulted in fewer high-dosage, acute exposures, but deaths due to occupational overexposure to PCP are still being reported.

Studies designed to examine biochemical changes in wood-workers exposed to high levels of PCP for extended periods have failed to indicate statistically significant effects on major organs, neural tissues, blood elements, the immune system, or reproductive capacity. However, many of these studies were based on small sample sizes; hence, analyses of trends indicating effects on liver enzymes, kidney function, T-cell suppression, nerve conduction velocity, etc., have not been statistically significant. Others have been non-specific in the search for signs of intoxication in large groups of workers. However, there are mounting indications that long-term exposure to relatively high levels of PCP leading to blood-plasma concentrations as high as 4 ppm is likely to cause borderline effects on some physiological processes. Some of these effects, especially those involving the liver and the immune system, may be caused, in whole or in part, by the microcontaminants of these chlorophenols, especially H_6CDD.

Several epidemiological studies from Sweden and the USA have indicated that occupational exposure to mixtures of chlorophenols is associated with increased incidences of soft tissue sarcomas, nasal and nasopharyngeal cancers, and lymphomas. In contrast, surveys from Finland and New Zealand have not detected such relationships. The major deficiency in all of these studies appears to be a lack of specific exposure data.

There are no conclusive reports of increased incidences of cancers in workers exposed specifically to PCP; however, there have not been any carefully conducted studies of a suitably exposed occupational group large enough to provide the necessary statistical power to identify an increase in cancer mortality. Furthermore, there are few occupational groups that have been exposed to a single chemical, such as PCP. Finally, the various levels of microcontaminants in different formulations make inferences to PCP in general difficult.

Persons non-occupationally exposed to technical PCP in rooms complained about relatively unspecific symptoms (headache, fatigue, hair loss, tonsillitis, etc.); a causative connection with PCP could not be proved or disproved.

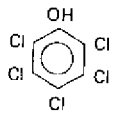
2. IDENTITY, PHYSICAL AND CHEMICAL PROPERTIES, ANALYTICAL METHODS

Pentachlorophenol (PCP) and its salt, sodium pentachlorophenate (Na-PCP), are the most important forms of pentachlorophenol in terms of production and use. Other derivatives such as the potassium salt, K-PCP, and the lauric acid ester, L-PCP are of minor importance. Reflecting this minor role, few data on the physical and chemical properties of K-PCP and L-PCP are reported in the literature. Hence, this section primarly concerns PCP and its sodium salt.

2.1 Identity

2.1.1 Pentachlorophenol (PCP)

Chemical structure:



Molecular formula: C_6HCl_5O

CAS chemical name: Pentachlorophenol

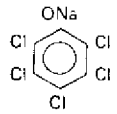
Common synonyms: chlorophen; PCP; penchlorol; penta; pentachlorofenol; pentachlorofenolo; pentachlorphenol; 2,3,4,5,6-pentachlorophenol

Common trade names: Acutox; Chem-Penta; Chem-Tol; Cryptogil ol; Dowicide 7; Dowicide EC-7; Dow Pentachlorophenol DP-2 Antimicrobial; Durotox; EP 30; Fungifen; Fungol; Glazd Penta; Grundier Arbezol; Lauxtol; Lauxtol A; Liroprem; Moosuran; NCI-C 54933; NCI-C 55378; NCI-C 56655; Pentacon; Penta-Kil; Pentasol; Penwar; Peratox; Permacide; Permagard; Permasan; Permatox; Priltox; Permite; Santophen; Santophen 20; Sinituho; Term-i-Trol; Thompson's Wood Fix; Weedone; Witophen P

CAS registry number: 87-86-5

2.1.2 Sodium pentachlorphenate (Na-PCP)

Chemical structure:



Molecular formula: C_6Cl_5ONa
$C_6Cl_5ONa \cdot H_2O$ (as monohydrate)

Common synonyms: penta-ate; pentachlorophenate sodium; pentachlorophenol, sodium salt; pentachlorophenoxy sodium; penta-phenate; phenol, pentachloro-, sodium derivative monohydrate; sodium PCP; sodium pentachlorophenate; sodium pentachlorophenolate; sodium penta-chlorophenoxide

Common trade names: Albapin; Cryptogil Na; Dow Dormant Fungicide; Dowicide G-St; Dowicide G; Napclor-G; Santobrite; Weed-beads; Xylophene Na; Witophen N

CAS registry number: 131-52-2 (Na-PCP);
27735-64-4 (Na-PCP monohydrate)

2.1.3 Pentachlorophenyl laurate

The molecular formula of pentachlorophenyl laurate is C_6Cl_5OCOR; R is the fatty acid moiety, which consists of a mixture of fatty acids ranging in carbon chain length from C_6 to C_{20}, the predominant fatty acid being lauric acid (C_{12}) (Cirelli, 1978b).

2.2 Impurities in Pentachlorophenol

Technical PCP has been shown to contain a large number of impurities, depending on the manufacturing method (section 3.2.1). These consist of other chlorophenols, particularly isomeric tetrachlorophenols, and several microcontaminants, mainly polychlorodibenzodioxins (PCDDs), polychlorodibenzo-furans (PCDFs), polychlorodiphenyl ethers, polychlorophenoxy-phenols, chlorinated cyclohexenons and cyclohexadienons, hexachlorobenzene, and polychlorinated biphenyls (PCBs). Table 1 presents analyses of PCP formulations taken from several publications. According to Crosby et al. (1981), the quality of PCP is depends on the source and date of manu-facture. Furthermore, analytical results may be extremely

Table 1. Impurities (mg/kg PCP) in different technical PCP products

Component	Specification, producer, PCP content (%)						
	Technical[a] Monsanto (84.6%)	Technical[b] Dow (88.4%)	Technical[b,c] Dow (98%)	Technical[c,g,h] Dow (90.4%)	Technical[d,i] Dow (ns)[j]	Technical[e] Dyn. Nobel (87%)	Technical[f] Rhône-Poulenc (86%)
Phenols							
Tetrachloro-	30 000	44 000	2700	10 4000	ns	50 000	70 000
Trichloro-	ns	< 1000	500	< 1000	ns	20	ns
Higher chlorinated phenoxyphenols	ns	62 000	5000	ns	ns	ns	70 000
Dibenzo-p-dioxins							
Tetrachloro-	< 0.1	< 0.05	< 0.05	< 0.05	< 0.2[k]	< 0.001	< 0.01
Pentachloro-	< 0.1	ns	ns	ns	< 0.2	ns	ns
Hexachloro-	8	4	< 0.5	1	9	3.5	5
Heptachloro-	520	125	< 0.5	6.5	235	130	150
Octachloro-	1380	2500	< 1.0	15	250	600	600
Dibenzofurans							
Tetrachloro-	< 4	ns	ns	ns	< 0.2	ns	ns
Pentachloro-	40	ns	ns	ns	< 0.2	0.2	ns
Hexachloro-	90	30	< 0.5	3.4	39	10	ns
Heptachloro-	400	80	< 0.5	1.8	280	60	ns
Octachloro-	260	80	< 0.5	< 1.0	230	150	ns
Hexachlorobenzene	ns	ns	ns	400	ns	ns	ns

[a] From: Goldstein et al. (1977).
[b] From: Schwetz et al. (1974).
[c] From: Schwetz et al. (1978).
[d] From: Buser (1975).
[e] From: Umweltbundesamt (1985).
[f] From: Anon (1983b).
[g] Purified.
[h] Dowicide EC-7.
[i] Dowicide 7.
[j] ns = not specified.
[k] < = below detection limit.

variable, particularly with regard to earlier results, which should be considered with caution. Jensen & Renberg (1972) detected chlorinated 2-hydroxydiphenyl ethers, which obviously may transform to dioxins during gas chromatography, thus giving a false indication of a higher level of PCDDs. Unlike these "predioxins", other isomers are not direct precursors of dioxins, and are labelled "isopredioxins".

In Fig. 1, the structures and numbering system for the polychlorinated dibenzodioxins (PCDDs) and dibenzofurans (PCDFs) are illustrated.

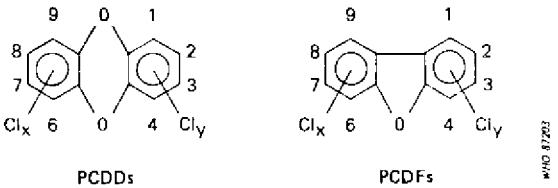


Fig. 1. Structures and numbering systems for the polychlorinated dibenzodioxins (PCDDs) and dibenzofurans (PCDFs). From: Rappe et al. (1979).

Since the toxicity of PCDDs and PCDFs depends not only on the number but also on the position of chlorine substituents, a precise characterisation of PCP impurities is essential. The presence of highly toxic 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-T_4CDD) has only been confirmed once in commercial PCP samples. In the course of a collaborative survey, one out of five laboratories detected 2,3,7,8-T_4CDD in technical PCP and Na-PCP samples at concentrations of 250 - 260 and 890 - 1100 ng/kg, respectively (Umweltbundesamt, 1985). Buser & Bosshardt (1976) found detectable amounts of T_4CDD (0.05 - 0.23 mg/kg) in some samples of different technical PCP products, but on re-analysis were unable to confirm the compound's identity. In other cases, T_4CDD has not been identified at detection limits of 0.2 - 0.001 mg/kg (Table 1).

The higher polychlorinated dibenzodioxins and dibenzofurans are more characteristic of PCP formulations (Table 1). Hexachlorodibenzo-p-dioxin (H_6CDD), which is also considered highly toxic and carcinogenic (section 8), was found at levels of 0.03 - 35 mg/kg (Firestone et al., 1972), 9 - 27 mg/kg (Johnson et al., 1973), and < 0.03 - 10 mg/kg (Buser & Bosshardt, 1976). According to Fielder et al. (1982), the 1,2,3,6,7,9-, 1,2,3,6,8,9-, 1,2,3,6,7,8-, and 1,2,3,7,8,9-isomers of H_6CDD have been detected in technical PCP. The 1,2,3,6,7,8and 1,2,3,7,8,9-H_6CDDs predominated in commercial samples of technical PCP (Dowicide 7) and Na-PCP. Octachlorodibenzo-p-dioxin (OCDD) is present in relatively high amounts in unpurified technical PCP (Table 1).

Recently, the identification of 2-bromo-3,4,5,6-tetrachlorophenol as a major contaminant in three commercial PCP samples (ca. 0.1%) has been reported. This manufacturing by-product has probably not been detected in other analyses because it is not resolved from the PCP peak by traditional chromatographic methods (Timmons et al., 1984).

2.2.1 Formation of PCDDs and PCDFs during thermal decomposition

The thermal decomposition of PCP or Na-PCP yields significant amounts of PCDDs and PCDFs, depending on the thermolytic conditions. For pure PCP, dimerization of PCP has been suggested as an underlying reaction process; in technical PCP, additional reactions, i.e., dechlorination of higher chlorinated PCDDs and cyclization of predioxins are involved in forming various and different PCDD isomers (Rappe et al., 1978b).

Pyrolysis of alkali metal salts of PCP at temperatures above 300 °C results in the condensation of two molecules to produce OCDD. PCP itself forms traces of OCDD only on prolonged heating in bulk and at temperatures above 200 °C (Sandermann et al., 1957; Langer et al., 1973; Stehl et al., 1973).

Although present in original technical PCP products, a number of PCDDs, other than OCDD, are generated during thermal decomposition (290 - 310 °C) in the absence of oxygen (Table 2) (Buser, 1982).

Table 2. PCDDs (mg/kg PCP) in the pyrolysate of technical PCP and Na-PCP[a]

	PCP	Na-PCP
2,3,7,8-T_4CDD	-[b]	-[c]
1,2,3,7,8,9-H_6CDD	53	2.1
1,2,3,6,7,8-H_6CDD	66	0.95
Total H_6CDD	455	10.5
H_7CDD	5200	65
OCDD	15 000	200

[a] From: Buser (1982).
[b] Detection limit (1 mg/kg).
[c] Detection limit (0.25 mg/kg).

2.3 Physical, Chemical, and Organoleptic Properties

Pure pentachlorophenol consists of light tan to white, needlelike crystals. It has a pungent odour when heated (Windholz, 1976). Its vapour pressure suggests that it is relatively volatile, even at ambient temperatures. Since PCP is practically insoluble in water at the slightly acidic pH generated by its dissociation, readily water-soluble salts such as Na-PCP are used as substitutes, where appropriate.

Na-PCP is non-volatile; its sharp PCP odour results from slight hydrolysis (Crosby et al., 1981). Technical PCP consists of brownish flakes or brownish oiled, dustless flakes, coated with a mixture of benzoin polyisopropyl and pine oil. Technical Na-PCP consists of cream-coloured beads (Anon., 1983a,b). Technically pure L-PCP consists of a brown oil that is insoluble in water and alcohols, and soluble in non-polar solvents, oils, fats, waxes, and plasticizers (Cirelli, 1978b).

PCP is non-inflammable and non-corrosive in its unmixed state, whereas a solution in oil causes deterioration of rubber (Mercier, 1981).

Because of the electron withdrawal by the ring chlorines, PCP behaves as an acid, yielding water-soluble salts such as sodium pentachlorophenate. Due to nucleophilic reactions of the hydroxyl group, PCP can form esters with organic and inorganic acids and ethers with alkylating agents, such as methyl iodide and diazomethane (Crosby et al., 1981). This property has been used for analytical purposes (section 2.5.2).

PCP may exist in two forms: the anionic phenolate, at neutral to alkaline pH, and the undissociated phenol at acidic pH. At pH 2.7, PCP is only 1% ionized; at pH 6.7, it is 99% ionized (Crosby et al., 1981). Other relevant properties of pure PCP and Na-PCP are shown in Table 3.

PCDDs and PCDFs may also be formed during the combustion of materials treated with either purified or technical PCP. Smoke from birch leaves impregnated with purified Na-PCP and burnt on an open fire showed considerably increased amounts of PCDDs compared with the original sample (Table 4). The mass fragmentograms revealed 14 of the 22 possible T_4CDD isomers with 1,3,6,8- and 1,3,7,9-T_4CDD as the main and 2,3,7,8-T_4CDD as minor isomers. The formation of PCDFs, including small amounts of 2,3,7,8-T_4CDF, during either combustion or micropyrolysis (280 °C, 30 min) was only observed in technical PCP samples; purified Na-PCP was negative in this respect (Rappe et al., 1978b).

Jansson et al. (1978) observed a very wide range of PCDD concentrations in the smoke from burning wood chips impregnated with a technical PCP formulation (Table 4). The formation of PCDDs was favoured by temperatures below 500 °C,

Table 3. Physical, chemical, and organoleptic properties of PCP and Na-PCP

	PCP	Na-PCP
Boiling point[a]	310 °C (decomposition)	
Relative molecular mass[b]	266.4	288.3 306.3 (mono-hydrate)
Melting point[a]	191 °C	
Density (d_4^{22} in g/ml)[b]	1.987	2
Vapour pressure kPa (mmHg) at 20 °C[c] at 19 °C[d]	2×10^{-6} (1.5×10^{-5}) 6.7×10^{-7} (5×10^{-6})	
Saturation vapour density (μg/m³) (20 °C)[c]	220	
Steam volatility[e] (g/100 g water vapour) (100 °C)	0.167	
Solubility in fat (g/kg) (37 °C)[f]	213	
n-Octanol/water partition coefficient (log P)[g]	4.84 (pH 1.2); 3.56 (pH 6.5); 3.32 (pH 7.2); 3.86 (pH 13.5)	
pK_a (25 °C)[e]	4.7	

oxygen deficit, and lower gas-retention time. The results given in Table 4 are corrected for the very low background values obtained by burning untreated wood chips.

When technical PCP was burnt in a quartz reactor (600 °C, 10 min), Lahaniatis et al. (1985) identified the following thermolytic products: pentachlorobenzene, hexachlorobenzene, octachlorostyrole, octachloronaphthaline, decachlorobiphenyl, H_6CDF, OCDF, and OCDD. 2,3,7,8-T_4CDD was not detected at a detection limit of 1 mg/kg PCP.

Olie et al. (1983) found only slightly higher levels of PCDDs and PCDFs in the fly ash of burned new wood treated with PCP compared with painted wood, which was more than 60 years old. However, because data were missing on PCDD/PCDF levels in the original samples and on the conditions of burning, meaningful interpretation of these results is not possible.

Table 3 (contd).

	PCP	Na-PCP
Solubility in water: (g/litre)[e,h,i]		
0 °C, pH 5	0.005	
20 °C, pH 5	0.014	
30 °C, pH 5	0.020	
20 °C, pH 7	2	
20 °C, pH 8	8	
20 °C, pH 10	15	> 200
25 °C		330
Solubility in organic solvents (g/100 g) (25 °C)[b]:		
acetone	50	35
benzene	15	insoluble
ethanol (95%)	120	65
ethylene glycol	11	40
isopropanol	85	25
methanol	180	25
Odour threshold (mg/litre)[j]:	1.6 (in water)	
Olfactory threshold (mg/litre)[j]:	0.03 (in water)	

[a] From: IRPTC (1983).
[b] From: Cirelli (1978b).
[c] From: Zimmerli (1982).
[d] From: Dobbs & Grant (1980).
[e] From: Crosby et al. (1981).
[f] From: Rippen (1984).
[g] From: Kaiser & Valdmanis (1982).
[h] From: Gunther et al. (1968).
[i] From: Bundesamt für Umweltschutz (1982).
[j] From: Dietz & Traud (1978a).

2.4 Conversion Factors

1 ppm = 10.9 mg PCP/m³ (25 °C, 101.3 kPa)
1 mg PCP/m³ = 0.09 ppm

2.5 Analytical Methods

A number of methods have been used to determine PCP in a variety of media. The earlier procedures were reviewed by Bevenue & Beckman (1967). They were mostly based on colour reactions, which are not very specific and relatively insensitive. For several years, more sophisticated devices have been available to analysts, of which gas chromatography has become the method of choice (Table 5).

Table 4. Amount of PCDDs in the original sample and in the smoke from combusted materials treated with purified Na-PCP or technical PCP

	Birch leaves[a] (mg PCDDs/kg Na-PCP (purified))		Wood chips[b] (mg PCDDs/kg PCP (technical))	
	Original sample	Smoke[c]	Original sample	Smoke[c,d]
T_4CDD	< 0.02	5.2	nd[e]	< 4.7 - 47
P_5CDD	< 0.03	14	nd	< 1.2 - 419
H_6CDD	< 0.03	56	7	< 9.3 - 93
H_7CDD	0.3	172	93	< 4.7 - 279
OCDD	0.9	710	186	< 0.9 - 442

[a] Adapted from: Rappe et al. (1978b).
[b] Adapted from: Jansson et al. (1978).
[c] Smoke trapped on charcoal filter.
[d] Depending on combustion conditions.
[e] nd = not determined.

The determination of PCP is based on the distinctive properties of this substance: steam distillation is possible because of its volatility; its acidic behaviour is used in extracting it into a base and in ion-exchange chromatography; the electro-positive ring reinforces selective chromatographic adsorption and the absorption of ultraviolet radiation; finally, the reactivity of PCP with certain organic compounds to form esters, ethers, and coloured derivatives is of great importance for its detection and measurement (Crosby et al., 1981).

Most of the analytical methods used today involved acidification of the sample to convert PCP to its non-ionized form, extraction into an organic solvent, possible cleanup by back-extraction into basic solution, and analysis by gas chromatography or other chromatographic methods as ester or ether derivatives. In the following section, the sampling and analytical methods is described as reviewed mainly by Bevenue & Beckman (1967), Gebefuegi et al. (1979), and Crosby et al. (1981). In addition, the more recently published methods for PCP determination in various matrices are summarized (Table 5).

2.5.1 Sampling methods

In principle, the sampling techniques summarized by Bevenue & Beckman (1967) are still the methods of choice; more recent methods are included in Table 5.

The first step in preparing a sample consisting of a solid material is a thorough pulverization or homogenization in

Table 5. Analytical methods for the determination of PCP

Medium	Sampling method	Analytical method	Detection	Detection limit	Recovery	Reference
Air						
Air-aerosol	Impinger collection with KOH; hexane extraction	Derivatization with diazomethane; purification in chromatoflex Florisil column; GC[d] analysis	EC[a]	0.22 mg/m³	ns[c]	Hoben et al. (1976a)
Air	Filter and bubbler collection; ethylene glycol extraction	HPLC[e] analysis; column: μ Bondapack C_{18}; mobile phase: methanol/water	UV_{254} [b]	0.27 mg/m³	95.3-100.9%	NIOSH (1978)
Air	Bubbler collection; absorption in K_2CO_3 solution; hexane extraction	Derivatization with acetyl chloride; GC analysis	EC	0.05 μg/m³	ns	Dahms & Metzner (1979)
Air	Adsorption on to filter papers impregnated with adsorbant extraction concentration in ether	GC analysis	EC	0.5 μg/m³	ns	Zimmerli & Zimmermann (1979)
Air	Impinger collection; absorption in K_2CO_3-solution; benzene extraction	HPLC analysis; column: Lichrosorb C_{18}; mobile phase: methanol	UV_{225}	0.5 μg/m³	ns	Woiwode et al. (1980)
Air	Air from wood samples in reactor tube adsorbed on silica gel; desorption with benzene	GC analysis	EC	ns (< 1.5 μg/m³)	89.7-99.9%	Warren et al. (1982)
Air	Impinger collection; absorption in toluene	Derivatization with acetic anhydride in presence of pyridine; GC analysis	EC	ns	ns	Kauppinen & Lindroos (1985)

Table 5 (contd).

Biological tissues and fluids						
Blood (human)	Benzene extraction from acidified solution	Derivatization with diazomethane; GC analysis	EC	20 µg/litre	87–100%	Bevenue et al. (1968)
Blood, urine, tissue (human)	Ethyl ether extraction from acidified solution; NaOH extraction; benzene extraction	No derivatization; GC analysis; column: 3% diethylene glycol succinate + 2% H_3PO_4; confirmation by MS and TLC	EC-^{3}H EC-^{63}Ni	0.1 ng 0.02 ng	90–100%	Barthel et al. (1969)
Organic tissues	Hexane/isopropanol extraction from acidified sample; borax extraction	Der. with acetic anhydride in presence of pyridine; GC analysis	EC	ns	81–91%	Rudling (1970)
Urine (rat)	Ethyl ether extraction from acidified solution	Derivatization with diazoethane; GC analysis	EC	10 µg/litre	92–98%	Shafik et al. (1973)
Adipose tissue (human)	NaOH extraction; diethyl ether extraction from acidified solution	Derivatization with diazomethane; GC analysis	EC	5 µg/kg	75%	Shafik (1973)
Urine, seminal fluid (human)	Acidic hydrolysis (urine); hexane/2-propanol or hexane/ether extraction from acidified solution	No derivatization; negative chemical ionization (NCI) mass spectrometry; internal standard: p-chlorobenzophenone	MS[f]	1 ng	90%	Dougherty & Piotrowska (1976a;b)
Tissue, plasma, urine (rat)	Hexane or benzene extraction	Derivatization with diazoethane (urine) or diazomethane; purification in chromatoflex Florisil column; GC analysis	EC	20 µg/kg	91.4–95.3%	Hoben et al. (1976a)
Tissues (fish)	Acetone extraction	(a) TLC[g] analysis on silica gel UV254; mobile phase: methylene chloride	Radioactive	ns	ns	Glickman et al. (1977)

Table 5 (contd).

Medium	Sampling method	Analytical method	Detection	Detection limit	Recovery	Reference
Tissues (fish) (contd)	Acetone extraction	(b) Derivatization with methyl iodide and K_2CO_3; GC analysis	MS	ns	ns	Glickman et al. (1977)
Urine (human)	Hexane extraction from acidified solution	Derivatization with acetyl chloride in the presence of pyridine; GC analysis	EC	10 µg/litre	ns	Dahms & Metzner (1979)
Urine (human, rat)	Benzene extraction from acidified solution	Derivatization with diazomethane; separation of methylated phenols in acid alumina column; GC analysis; GC-MS confirmation	EC	1 µg/litre	93.2-97.2%	Edgerton et al. (1979)
Plasma (human)	Benzene extraction	Derivatization with acetic anhydride; GC analysis	EC	50 µg/litre	91-102%	Eben et al. (1981)
Urine (human)	Acidic or enzymatic hydrolysis; ethyl ether extraction; benzene extraction	Derivatization with acetic anhydride; GC analysis	EC	20 µg/litre	77-98%	Eben et al. (1981)
Tissues, serum, egg yolk/white	Diethyl ether (ethyl acetate-hexane) extraction from NaOH (hydrochloric acid) solution; concentration by evaporation	Purification on Hypersil-cartridge; mobile phase: methanol; HPLC analysis	UV_{216}	1 µg/kg	62-108%	Mundy & Machin (1981)
Urine (human)	Acidic hydrolysis; distillation; methylene chloride extraction from acidified solution; evaporation and redistillation in acetonitrile	HPLC analysis; column: Spherisorb-ODS; mobile phase: acetonitrile; internal standard: 3,5-dichloro-2,3,6-tribromophenol (DTP)	UV_{313}	10 µg/litre	102%	Drummond et al.(1982)

Table 5 (contd).

Urine (human)	Acidic hydrolysis; hexane/isopropanol extraction; evaporation and redistillation in methanol	LC analysis; column: Spherisorb-ODS; mobile phase: methanol	UV_{254}	0.1 µmol/litre (27 µg/litre)	83.3± 3.7%	Pekari & Antero (1982)
Urine (human)	Acidic hydrolysis; int.standard (4,6-dibromo-o-cresol) added; methylene chloride extraction	Derivatization with acetic or propionic anhydride; GC analysis	SIM-MS[h] (0.27 µg/litre)	1 nmol/litre	ns	Hargesheimer & Coutts (1983)
Food						
Milk (bovine)	Benzene extraction; extraction with K_2CO_3 solution	Derivatization with acetic anhydride; GC analysis	EC	5 µg/litre	80-87.2%	Erney (1978)
Milk (bovine)	Sulfuric acid digestion; hexane extraction	Purification in BioSil A-column; derivatization with diazomethane; GC analysis	EC	10 - 15 µg/litre	80%	Lamparski et al. (1978)
Carrots, potatoes	Soxhlet extraction (carrots) or blending with acidified acetone	Derivatization with diazoethane; purification in Florisil-column; GC analysis	EC	0.2 µg/kg	80-108%	Bruns & Currie (1980)
Canned food and jar lids	Methylene chloride extraction from acidified solution; clean-up by gel permeation chromatography	Derivatization with diazomethane; purification in Florisil column; GC analysis	EC	ns (< 0.3 µg/kg)	92-103%	Heikes & Griffitt (1980)
Edible gelatins	Alkaline hydrolysis; iso-octane extraction from acidified solution	Direct GC analysis on DEGS/phosphoric acid column; confirmation by GC analysis of acetate derivative	EC	5 - 10 µg/kg	83-108%	Stijve (1981)
Plant materials	Maceration with acidified acetone; chloroform extr.; cleanup by automated gel chromatography	Derivatization with diazomethane; purification in Florisil-column; GC analysis	EC	ns	94.2%	Fuchsbichler (1982)

Table 5 (contd).

Medium	Sampling method	Analytical method	Detection	Detection limit	Recovery	Reference
Mushrooms	Steam distillation from acidified sample; dichloromethane extraction	(a) Derivatization with acetic anhydride GC analysis (b) HPLC analysis; column: LiChrosorb RP-8; mobile phase: methanol/o-phosphoric acid	EC UV_{220}	0.5 µg/kg fresh weight 0.5 µg/kg	92%	Schönhaber et al. (1982)
Soil						
Soil	NaOH extraction; clean-up by ion exchanger	Derivatization with diazomethane; GC analysis	EC	0.1 - 1 µg/kg	> 97%	Renberg (1974)
Soil	Nielsen-Kryger steam distillation from acidified soil; toluene-methylene chloride extraction	Direct GC analysis on fused silica SE 54 column	EC	ns	58-95%	Narang et al. (1983)
Water						
Raw and treated water	Petroleum ether extraction from acidified sample; evaporation; drying; evaporation	TLC analysis on Al_2O_3 plates; mobile phase: (a) benzene; (b) NaOH/acetone; chromogenic agent: $AgNO_3$/2-phenoxyethanol	Colorimetric	0.5 µg/litre	75-100%	Zigler & Phillips (1967)
Natural, waste water	Benzene extraction and K_2CO_3-solution	Derivatization with acetic anhydride; hexane extraction; GC analysis	EC	0.01 µg/litre	84-93%	Chau & Coburn (1974)
River water	Hexane/ethyl ether extraction; ethyl acetate extraction from acidified solution	Derivatization with boron trifluoride methanol and trimethylsilyl; GC analysis	MS	0.01 µg/litre	ns	Matsumoto et al. (1977)

Table 5 (contd).

Surface water	Toluene extraction; extraction with K_2CO_3-solution	Derivatization with acetic anhydride; petroleum ether extraction; GC analysis	EC	0.01 µg/litre	85%	Wegman & Hofstee (1979)
Waste water	Chloroform extraction from acidified sample; rotary evaporation	Direct HPLC analysis of chloroform extract; column: silica gel; mobile phase: cyclohexane-acetic acid and other solvents	UV_{254}	10 µg/litre	ns	Ervin & McGinnis (1980)
Surface water	Diethyl ether extraction; evaporation; dissolution in methanol-petroleum	Direct HPLC analysis	UV_{215}	20 µg/litre	> 80%	Ivanov & Magee (1980)
Surface water	Chloroform extraction from acidified sample; NaOH extraction	Direct analysis in double beam UV spectrophotometer	Absorption (320 nm)	5 - 10 µg/litre	92-102%	Carr et al. (1982)
Surface water	Concentration by extraction, adsorption, rotary evaporation	GC analysis (no derivitization); column: Carbowax 20 M plus phosphoric acid; confirmation by MS	EC	0.01 µg/litre	95 ± 3%	Rübelt et al. (1982)
Surface, waste, drinking-water	Addition of Na_2HPO_4 buffer solution (for acid waste water pH adjustment to 7 with NaOH	Extraction and derivitzation by adding hexane containing internal standard (2,6-dibromophenol) and acetic anhydride directly to sample; GC analysis	EC	1 ng/litre	98-100%	Abrahamsson & Xie (1983)
Water	Samples prepared from stock solutions in acetonitrile	HPLC analysis with isocratic elution of various substituted phenols	UV_{280}	21 ng	ns	Buckman et al. (1984)

Table 5 (contd).

Medium	Sampling method	Analytical method	Detection	Detection limit	Recovery	Reference
Wood						
Wood	Chloroform extraction from wood shavings	TLC analysis on silica gel plates; developing solvent: cyclohexane-acetone-paraffin	UV	0.06 µg	ns	Henshaw et al. (1975)
Wood-dust	Soxhlet extraction with ether ether; evaporation; dissolution in acetone; TLC separation; hexane elution	Derivatization with diazomethane; GC analysis	EC	ns	30-70%	Levin & Nilsson (1977)
Lumber (surface-treated)	Pulverization of wood sample; extraction with acetonitrile containing internal standard; ultrasonic bath	HPLC analysis; column: Spherisorb-ODS; mobile phase: water-acetonitrile-acetic acid	UV_{230}	0.1 µg/cm²	ns	Daniels & Swan (1979)
Sawdust, wood-shavings	Extr. with acetic acid-methanol; evaporation; conversion to chloranil in warm nitric acid	TLC analysis; different solvent systems; sprayed with tetrabase reagent	Colour reaction	2 mg/kg	ns	Ting & Quick (1980)
Various materials						
Toy paints	Soxhlet extraction with acetone; concentration by evaporation	Direct GC analysis; confirmation by TLC analysis	FID[i]	1 - 4 mg/litre	70-100%	von Langeveld (1975)
PCP formulations	Dioxane extraction	HPLC analysis; column: BondapakC_{18}; mobile phase: methanol/PIC A (paired ion chromatography A reagent) and water/PIC A	UV_{254}	ns	97%	Hayes (1979)

Table 5 (contd).

Sediment, clams	Homogenization; toluene extraction from acidified sample containing 2,4,6-tribromophenol as internal standard	Derivatization: pyrolytic ethylation with triethyl sulfonium-iodide; GC analysis; confirmation by MS	EC	0.5 - 25 µg/kg	92.8-97.6%	Butte et al. (1983)
Tallow	Vortex mixing; automated gel permeation chromatographic clean-up; rotary evaporation; solution in hexane	Derivatization with diazomethane; Florisil-column; GC analysis; confirmation with MS	EC	1 µg/kg	80-107%	Lee et al. (1984)
Industrial starch, surface water	Hexane extraction (for starch: after steam distillation)	Derivatization with pentafluorobenzyl bromide; GC analysis and negative ion chemical ionization MS (NICI-MS) analysis	EC MS	0.1 pg	ns	Sha & Duffield (1984)

[a] EC = electron-capture detector.
[b] UV = ultraviolet.
[c] ns = not specified.
[d] GC = gas chromatography.
[e] HPLC = high-performance liquid chromatography.
[f] MS = mass spectrometry.
[g] TLC = thin-layer chromatography.
[h] SIM = selected ion monitoring.
[i] FID = flame ionization detector.
[j] NICI = negative ion chemical ionization.

special mills or blenders. Maceration of the sample in a blender with an organic solvent is more rapid than Soxhlet extraction and similar efficiencies can be achieved with both procedures (Bruns & Currie, 1980).

For cellulose materials, adhesives, agricultural commodities, biological tissues, and water, an initial extraction with dilute sodium hydroxide solution at room temperature for several hours, followed by acidification and steam distillation may be preferable. For samples that contain components strongly complexed with PCP, such as soybean oil, treatment with hot concentrated sulfuric acid is recommended prior to steam distillation. Liquid-liquid partitioning or distillation of the filtered extract at the boiling point of water may also be used to isolate PCP (Bevenue & Beckman, 1967).

When alkaline soil extracts are acidified, gel formation can occur at pH values lower than 6, resulting in interference with the extraction of PCP. According to Renberg (1974), proper separation is possible if the acidic substances are bound, under alkaline conditions, to an anion ion exchanger.

When analysing liquid materials, particularly urine samples, the sample should first be hydrolysed by heating the acidified urine to free the PCP moiety of its sulfate and glucuronide conjugates (Edgerton & Moseman, 1979; Drummond et al., 1982; Butte, 1984). Enzymatic hydrolysis is questionable, because the metabolite tetrachlorohydroquinone strongly inhibits the enzyme β-glucuronidase (Ahlborg et al., 1974).

For determining the PCP content of air several possible sampling procedures are described by Gebefuegi et al. (1979) including: absorption in liquids, such as potassium carbonate (K_2CO_3) solution or ethylene glycol; adsorption on activated charcoal or silica gel; freezing and condensing by sucking the air through cooling traps; or derivatization by phenolate formation in alkaline solution. By pumping high volumes of air through the sample-collecting device, PCP is concentrated in the collector, thus enhancing the detection limit.

Concentration is also required for other matrices with relatively low PCP contents. For water samples, procedures used involve the separation of PCP from the water by distillation, sublimation, freeze-drying, adsorption, and extraction (Rübelt et al., 1982). The extraction solvents, in turn, are concentrated by distillation or evaporation.

Only a few investigators have used internal standards, adding specific substances to the samples to check for completeness of recovery during the extensive solvent extractions and manipulative steps required. Drummond et al. (1982) used 3,5-dichloro-2,3,6-tribromophenol, while Needham et al.

(1981) incorporated 2,4,6-tribromophenol, and Hargesheimer & Coutts (1983) spiked the samples with 4,6-dibromo-o-cresol.

Most recovery data given in Table 5 were obtained by spiking samples with known amounts of PCP and carrying them through the entire analytical procedure. Ernst & Weber (1978a) used ^{14}C-PCP for this purpose. To check the efficiency of acetylation, Rudling (1970) compared spiked samples with a pentachlorophenyl acetate standard. According to NIOSH (1978), an appropriate correction factor should be used if recovery of PCP in air samples is less than 95%.

Using the analytical method of Erney (1978) (Table 5), Zimmerli et al. (1980) found that only about 8% of "endogenous" PCP was extractable from raw bovine milk, though 82.5% of known amounts of PCP added had been recovered on average. A complete extraction was only achieved by acid or alkaline pretreatment of the milk (cf., Lamparski et al., 1978) (Table 5), which probably releases the PCP bound to proteins. Zimmerli et al. (1980) concluded from this finding that recovery data may indicate values that do not correspond to the true recovery.

2.5.2 Analytical methods

Earlier methods, which have been thoroughly reviewed by Bevenue & Beckman (1967), were based on the formation of coloured derivatives from the reaction of PCP with either nitric acid or 4-aminoantipyrine. Other reagents commonly used in this respect are p-nitraniline, sulfanilic acid, and 3-methyl-2-benzenethiazoline-hydrazine (Koppe et al., 1977). As already mentioned, these colorimetric or spectrometric methods are not very specific and comparatively insensitive, and therefore only suitable for pure solutions or for production and routine controls. They may be of some importance in determining total phenolics, for example, in the monitoring of levels of phenolics in surface and waste waters. However, comparative studies, in which 45 laboratories within the European Communities participated, revealed that photometric procedures gave rather different results, depending on specific laboratory conditions (Sonneborn, 1976; Rübelt et al., 1982). According to Crosby et al. (1981), colorimetric or spectrophotometric procedures achieve a sensitivity that is, at best, in the low ppb-range ($1:10^9$).

Gas chromatography, particularly when combined with an electron-capture detector, substantially lowers the detection limits to the ppt-range ($1:10^{11}$ - $1:10^{12}$) and is therefore the preferred method today. Very few investigators have applied direct gas chromatography after the extraction procedures. To reduce peak tailing, derivatization of PCP with appropriate compounds prior to analysis is preferred.

Diazomethane is most commonly used to produce the methyl ether. As shown in Table 5, this method, which is based on the work of Bevenue et al. (1966), has been used to determine PCP in a variety of matrices including blood, urine, fish, soil, and water. According to Crosby et al. (1981), it is an official method for regulatory analysis in the USA. The procedure for measuring PCP in blood and urine samples as recommended by the National Institute for Occupational Safety and Health (NIOSH), USA, is described by Eller (1984a,b).

Other alkyl ethers have been produced as derivatives of PCP, including the ethyl, propyl, 1-butyl, isobutyl, amyl, and isoamyl-PCP (Cranmer & Freal, 1970). Besides the potential health risk incurred when using hazardous reagents such as diazomethane or dimethyl sulfate, the alkylation method is subject to interferences from other compounds with active H-atoms, e.g., carboxy acid herbicides such as 2,4-dichloro- and 2,4,5-trichlorophenoxyacetic acid (Chau & Coborn, 1974; Crosby et al., 1981). These drawbacks are avoided by the acetylation of PCP with acetic anhydride to give acetyl-PCP as reported by Rudling (1970), Chau & Coborn (1974), and other research workers (Table 5).

Several techniques, other than gas chromatography, have been used in connection with electron-capture detection. These include thermal conductivity and microcoulometric detectors (Bevenue & Beckman, 1967), thin-layer chromatography (TLC), gas chromatography in connection with mass spectrometry (MS), and high-performance liquid chromatography (HPLC) equipped with UV detectors. In particular, the last two methods have become more and more prevalent as reflected by Table 5. In many cases, mass spectrometry has been used to confirm the identity of PCP peaks determined by EC detectors. Dougherty & Piotrowska (1976a) and Kuehl & Dougherty (1980) screened environmental and tissue samples for PCP using negative chemical ionization (NCI) mass spectrometry. This method provides a sensitivity of detection comparable to GC-ECD analysis. Moreover, it can be used for compound identification. Since both of these methods require an extensive amount of pretreatment, a procedure had to be adopted for PCP determination by which samples could be measured simply and precisely, without the tedious extraction and formation of derivatives needed for the other methods. High-performance liquid chromatography offers these advantages, as using this method direct determination of PCP is possible, giving peaks of constant height and high resolution. Comparative GC-ECD and HPLC analyses of mushrooms, conducted by Schönhaber et al. (1982), resulted in similar detection limits (Table 5).

Detection limits depend not only on the sensitivity of the detection systems, but also, to a great extent, on the volume

of the sample. The detection limits given in Table 5 refer to the smallest amounts of PCP detectable using the procedure and sample size described by the authors. In many cases, it would be possible to lower the detection limit by taking larger samples, particularly in the case of gaseous and fluid matrices.

Analytical interferences may become a problem in PCP analysis for residues, particularly at low measurement levels. Bevenue & Ogata (1971) reported errors during the determination of PCP in the picogram range, because of analytical-grade reagents such as sodium hydroxide. Arsenault (1976) observed an apparent contamination of samples with PCP from the general laboratory atmosphere. However, measuring blank samples as controls and purifying reagents should exclude false data. For example, Dietz & Traud (1978b) distilled the extraction solvent diethyl ether to remove the antioxidant BHT (2,6-di-tert-butyl-4-methyl-phenol). Similarly, the authors recommended the distillation of dioxan prior to its use as extraction solvent; otherwise, some volatile impurities could interfere with the measurement of PCP.

Substances interfering during gas chromatography may cause more of a problem. These include chloronaphthalenes, polychlorinated biphenyls (PCBs), pesticides such as diuron, and p-methoxytetrachlorophenol. Arsenault (1976) therefore questioned the GC-ECD method in the µg range. In a thorough study on phenolics in water (Rübelt et al., 1982), derivatization was omitted because non-specific reactions might occur in complex mixtures, e.g., in polluted waters. The working group achieved best results in terms of separation of chlorophenols with a column of 10% Carbowax 20 M plus 2% phosphoric acid, the mobile phase being nitrogen enriched with formic acid. The latter was found to prevent tailing resulting from adsorption of chlorophenols on the packing material of the column. For quantitative analysis with an unequivocal identification, it has been recommended that after gas chromatographic separation the carrier gas should be split and conducted to both an electron capture detector (ECD), and a flame ionization detector (FID), as well as to a mass spectrometer (MS).

3. SOURCES OF HUMAN AND ENVIRONMENTAL EXPOSURE

3.1 Natural Occurrence

Arsenault (1976) hypothesized the existence of a natural background level of PCP or analytically similar compounds. He suggested this on the basis that paramethoxytetrachlorophenol, a metabolite of a fungus, could interfere with the GC-EC analysis of PCP, because of its similar molecular size, shape, and retention time. The hypothesis of a natural background level of PCP has not been examined further. Unsuccessful attempts to produce higher chlorophenols by enzymatic conversion (Siuda, 1980) suggest that sources of environmental PCP are exclusively related to human activities.

3.2 Man-Made Sources

3.2.1 Industrial production

3.2.1.1 Manufacturing processes

PCP was first synthesized by Merz & Weith (1872) using a similar preparation method to that currently used during commercial production (Prager et al., 1923). The use of PCP as a wood preservative started in the late 1930s (Doedens, 1964).

PCP is produced by one of two methods: direct chlorination of phenols and hydrolysis of hexachlorobenzene. The direct chlorination is carried out in two steps. First, liquid phenol, chlorophenol, or a polychlorophenol is bubbled with chlorine gas at 30 - 40 °C to produce 2,4,6-trichlorophenol, which is then converted to PCP by further chlorination at progressively higher temperatures in the presence of catalysts (aluminum, antimony, their chlorides, and others). The second method involves an alkaline hydrolysis of hexachlorobenzene (HCB) in methanol and dihydric alcohols, in water and mixtures of different solvents in an autoclave at 130 - 170 °C (Melnikov, 1971). In the Federal Republic of Germany, PCP is synthesized by means of stepwise chlorination of phenols. Na-PCP was produced until 1984 using hexachlorobenzene hydrolysis; now, it is produced by dissolving PCP flakes in sodium hydroxide solution (BUA, 1986). In the USA, the general reaction used is the chlorination of phenols (Crosby et al., 1981).

In addition to the formation of PCP, numerous by-products are generated, as reflected by analytical profiles in Table 1. The chlorination procedure yields a technical product that usually contains a considerable amount of tetrachlorophenols

(4 - 12%) due to incomplete chlorination reactions. The formation of microcontaminants is favoured by elevated temperatures and pressure. With both manufacturing methods, toxic by-products, such as chlorinated ethers, dibenzofurans, and dibenzo-p-dioxins, are formed. In addition, the alkaline HCB hydrolysis method can result in the presence of hexachlorobenzene in the resulting PCP (Jensen & Renberg, 1973; Plimmer, 1973; Firestone, 1977; Jones, 1981).

3.2.1.2 Emissions during production

Some data are available concerning the loss of phenolic and nonphenolic compounds into the environment during the normal production of PCP or Na-PCP (Umweltbundesamt, 1985). The following air emission concentrations (mg/m^3) and mass flow values (g/h) were reported: PCP 0.7 mg/m^3, 9 g/h; tetrachlorophenols 0.2 mg/m^3, 0.8 g/h; trichlorophenols 0.02 mg/m^3, 0.04 g/h; hexachlorobenzene 23.9 mg/m^3, 12 g/h; pentachlorobenzene 2 mg/m^3, 15.5 g/h; tetrachlorobenzene 2.8 mg/m^3, 66.5 g/h; OCDD 0.05 mg/m^3, 0.04 g/h; OCDF 0.02 mg/m^3, 0.002 g/h.

The annual air emission values resulting from the production of approximately 2000 tonnes of PCP or Na-PCP, respectively, per annum are given in Table 6.

Table 6. Air emissions of phenolic and non-phenolic compounds during production (maximum values)[a]

	Annual air emissions (kg/year) during production of:	
	2000 tonnes PCP/year	2000 tonnes Na-PCP/year
PCP	18	65
Other chlorophenols	9	5
Hexachlorobenzene	-	105
Other chlorobenzenes	1	700
OCDD	0.2	0.2

[a] Adapted from: BUA (1986).

While no waste water occurs during the production of PCP, the annual loss of various compounds resulting from Na-PCP production into the waste water was as follows: PCP, 60 kg; OCDD, 0.34 g; H_7CDDs, 0.1 g; H_6CDDs, 0.001 g; OCDF, 0.1 g; H_7CDFs, 0.026 g; H_6CDFs, 0.002 g (BUA, 1986).

3.2.1.3 Disposal of production wastes

The volume of contaminated waste water generated during the production of Na-PCP is small, because manufacturers and regulatory agencies have emphasized efficient process design (Jones, 1981).

During the production of approximately 2000 tonnes PCP/year, about 8 tonnes of washing methanol, 4 tonnes of activated charcoal, and 2 tonnes of other wastes occur. These wastes, as well as the filtration sludge resulting from Na-PCP production, contain considerable amounts of hazardous chemicals (Table 7). They are generally disposed of by either storage in underground disposal sites (filtration sludge) or incineration at temperatures above 1200 °C (BUA, 1986).

Table 7. Phenolic and non-phenolic compounds in the combined wastes (PCP production) and filtration sludge (Na-PCP production)

Compound	Combined wastes (kg/year)	Filtration sludge (kg/year)
PCP	1350	900
Other chlorophenols	0.7	ns[b]
Hexachlorobenzene	ns	6000
Decachlorobiphenyl	ns	3400
Decachlorophenoxybenzene	ns	44
OCDD (OCDF)	0.98	0.67 (0.67)
H_7CDDs (H_7CDFs)	0.13	0.17 (0.045)
H_6CDDs (H_6CDFs)	0.013	0.092 (0.015)
P_5CDDs (P_5CDFs)	$0.003 \cdot 10^{-3}$	0.016 (0.005)
T_4CDDs (T_4CDFs)	$0.002 \cdot 10^{-3}$	0.007 (0.001)
2,3,7,8-T_4CDD	ns	0.001

[a] Adapted from: BUA (1986).
[b] ns = not specified.

US EPA (1985) proposed that wastes from the production and manufacturing use of PCP should be classifed as acutely hazardous wastes, on the basis of the presence of substantial concentrations of the carcinogenic congener H_6CDD and the chronic toxicity potential of PCP itself.

3.2.1.4 Production levels

No precise estimates can be made of the total world production of PCP and Na-PCP. According to the data profile of IRPTC (1983), 90 000 tonnes of PCP per year are produced globally. The Economist Intelligence Unit (1981) estimated

world production to be of the order of 50 000 - 60 000 tonnes per year, based on the North American and European Community output. However, the production figures presented in Table 8 indicate a total production of only 30 000 tonnes per year. The production, foreign trade, and consumption figures given in this summary table can give only a rough idea of the true PCP market. Recent restrictions on the use of PCP (section 3.3), a decline in the forestry industry, and the increasing use of alternative means of wood preservation have probably reduced the demand for PCP over the last few years.

The major PCP producers operating in 1980 are shown in Table 9 together with the plant locations and their capacities. Some additional factories exist in which PCP is mixed or formulated to yield special end-use products. There are also chemical producers who sell pure, analytical grade PCP, but do not produce PCP for technical purposes. The Monsanto Company, which had a capacity of 11.8 kilotonnes in the USA, stopped PCP production in their plant at Sauget, Illinois, in 1978 (Jones, 1981). Dow Chemical closed down its manufacturing plant at Midland, Michigan in October 1980 (Jones, 1984). Similarly, the only PCP producing plant in the United Kingdom, also operated by the Monsanto Company, was closed down in the same year (Economist Intelligence Unit, 1981), while Reichhold Chemicals Inc., at Tacoma, Washington, USA ceased PCP production in 1985. In the Federal Republic of Germany, the production of PCP and Na-PCP was stopped in 1986.

3.3 Uses

The main advantages of PCP and its derivatives are that they are effective biocides and soluble in oil (PCP) or water (Na-PCP). Few pesticides show a similarly broad efficiency spectrum at low cost. Therefore, PCP and its salts have a variety of applications in industry, agriculture, and in domestic fields, where they have been used as algicides, bactericides, fungicides, herbicides, insecticides, and molluscicides.

3.3.1 Commercial use

In Table 10, the major registered commercial uses of PCP are broken down for the United Kingdom and the USA. Although PCP and its derivatives have many uses, by far the major application is wood preservation. Cirelli (1978a), Hoos (1978), and Jones (1981) have reported on commercial use patterns in North America. In the USA, about 80% of PCP is used for commercial wood treatment, 6% is in use for slime control in pulp and paper production, and 3% accounts for non-industrial purposes, such as weed control, fence-post treatment and paint preservation (Crosby et al., 1981);

Table 8. Production, foreign trade, and consumption of PCP and Na-PCP (tonnes per year) according to data available from government authorities and producers

	Belgium/ Luxemburg[a]	France[a]	Germany, Federal Republic of[b]		Italy[a]	Nether-lands[a]	United Kingdom[a]	Canada[c]	USA[d]
	(year na)[e]	1979	1979	1984	(year na)[e]	(year na)[e]	(year na)[e]	1981	1977
Production									
PCP	0	1700	2450	1550	0	0	0	1700	20 349
Na-PCP	0	2800	2100	1750	0	0	0	70	
Imports									
PCP	150-	insigni-	0	0	250 -	30 -	na	500	na
Na-PCP	160	ficant	300	0	280	40	na	0	na
Exports									
PCP	0	300-	1950	1360	0	0	300	600	approximately
Na-PCP	0	700	2150	1710	0	0		0	200[f]
Consumption									
PCP	approxi-	1000	500	190	250-	30-	500	1536	na
Na-PCP	mately 150	2500	250	40	280	40		32	na

[a] From: Economist Intelligence Unit (1981).
[b] From: BUA (1986).
[c] From: Jones (1984).
[d] From: Jones (1981).
[e] na = not available.
[f] Approximately 1% of domestic sales.

Table 9. Pentachlorophenol producers and their capacities in 1980

Producer	Country	Plant Location	Capacity (tonnes) (total PCP)
Uniroyal Chemical,[a] Division of Uniroyal, Ltd	Canada	Clover Bar, Alta	1800
Rhône-Poulenc[b]	France	Pont-de-Claix	4500
Dynamit Nobel[b]	Germany, Federal Republic of	Rheinfelden	4000
Dow Chemical, USA[a]	USA	Midland, Michigan	13 500
Reichhold Chemicals[a] Inc.	USA	Tacoma, Washington	8100
Vulcan Material[a] Company Chemical Division	USA	Wichita, Kansas	9000

[a] From: Jones (1981).
[b] From: Economist Intelligence Unit (1981).

however, the last two cases imply wood treatment as well. The remaining 11% is converted to Na-PCP, which in turn is partly used for wood preservation, mainly sapstain control in waterborne conditions, e.g., for treating pressboard. Overall, some 95 - 98% of American PCP production is used directly or indirectly in wood treatment (Economist Intelligence Unit, 1981).

Data from Canada and the Federal Republic of Germany confirm the main use of PCP as a wood preservative. In Canada, about 95% of the PCP is used for this purpose (Jones, 1981). Approximately 61% of the volume of PCP used in the Federal Republic of Germany in 1983 was used for wood preservation, while considerable amounts of PCP were used by the textile (13%), leather (5%), mineral oil (6%), and glue (6%) industries, respectively (Angerer, 1984). No PCP was used in the paint or pulp industry whereas, in 1974, as much as 3% or 7%, respectively, were used in these branches. PCP used on textiles is usually in the form of the PCP ester rather than PCP or Na-PCP.

Pentachlorophenyl laurate (L-PCP) was developed especially for application on fabrics (Hueck & LaBrijn, 1960; Bevenue & Beckman, 1967). The estimates of L-PCP use in the United Kingdom in Table 10 are based on a publication from the year

Table 10. Major commercial (non-agricultural) uses of PCP in the United Kingdom and the USA[a]

Use	Active ingredient
United Kingdom	
Anti-mildew agent in the wool textile industry	L-PCP, Na-PCP
Mothproofing carried out by dyers and cleaners	L-PCP
Wood preservation	PCP, L-PCP, Na-PCP
Paint additives	PCP
Antimicrobial (slimicide) agents in paper and board	PCP
Antifungal agent in textiles other than wool (cotton, flax and jute fabric, ropes, cordage and tentage)	L-PCP
Cable impregnation	L-PCP
Anti-mildew agent in leather	ns[b]
Fungicide in adhesives	Na-PCP
Bactericide in drilling fluids	ns[b]
USA	
Microbiostat for commercial and industrial water cooling	Na-PCP
Microbiocide for leather	K-PCP, PCP
Microbiocide for burlap, canvas, cotton, rope, and twine	PCP
Microbiocide and insecticide for wood treatment	PCP, Na-PCP
Preservative for oil and water-based paint	PCP
Slime control for pulp and paper	PCP
Microbiocide for petroleum drilling mud and flood water	PCP
Fumigant for shipping-van interiors	PCP
Preservative for hardboard and particle-board	PCP

[a] From: Crosby et al. (1981).
[b] ns = not specified.

1974 (HMSO, 1974). According to an unpublished note submitted to the IPCS by Catomance Limited, Hertfordshire, the sole manufacturer of pentachlorophenyl laurate in the United Kingdom, the usage pattern in the United Kingdom has not changed following the cessation of production of PCP in 1978. However, most of the PCP ester used there today is said to be for domestic timber preservation; the use of L-PCP for textile preservation is supposed to be mainly confined to tropical or semi-tropical countries.

In the USSR, PCP is used for the preservation of commercial timber, paints, varnishes, paper, textiles, ropes, and leather (IRPTC, 1984).

Na-PCP is also used to inhibit algal and fungal growth in cooling tower waters at electric generating plants (Hoos, 1978); in 1976, about 30% of the Na-PCP used in Canada was for this purpose (Jones, 1981).

Alterations in the use pattern have taken place during the last few years as a result of the increased concern about the potential health hazards from PCP and its impurities. In Japan, the production of PCP was 14.5 kilotonnes in 1966 and 3.3 kilotonnes in 1971, after which production ceased entirely (IARC, 1979a). In the Federal Republic of Germany, 3300 tonnes of total PCP were produced in the year 1984, of which 93% was exported, leaving 230 tonnes for use in the country (BUA, 1986). Nine years earlier (1974), 4100 tonnes of PCP were produced, 60% of which were exported; in 1979, 84% of the 4503 tonnes produced were sold abroad (Angerer, 1984). These figures indicate a drastic decrease in the consumption of PCP in the Federal Republic of Germany during the last few years. In Canada, the Federal Republic of Germany, and Sweden, where PCP had been heavily used as a slime control agent in the paper mills, the use of chlorinated phenols for this purpose was prohibited in recent years as a consequence of the discharges, which had toxic effects on the aquatic environment. In Sweden, all use of PCP was banned in 1977 (Ahlborg & Thunberg, 1980; Jones, 1981). The US Environmental Protection Agency does not intend to prohibit the use of PCP in oil-well water or in pulp and paper mills, provided that impermeable gloves are worn during application and that the H_6CDD content will be reduced to 1 ppm (US EPA, 1984b). Similarly, the use of PCP (including its salts) for wood protection has not been cancelled in the USA. However, the US EPA (1984a) intends to establish certain changes in the terms and conditions of registration.

3.3.2 Agricultural use

Significant quantities of PCP were previously used in a number of agricultural applications. These resembled industrial uses in that most were to prevent wood decay, in farm buildings, fences, and storage facilities (Jones, 1981). However, PCP or its sodium salt have also been used as a herbicide and dessicant for forage seed crops, a herbicide for non-food vegetation control, a biocide in the post-harvest washing of fruit, and as an insecticide for use in beehives, seed plots, and greenhouses (Crosby et al., 1981). PCP was formerly used as a herbicide in paddy and upland rice fields, particularly in Japan (Kobayashi, 1978; Crosby et al., 1981). In addition, PCP and Na-PCP have been approved for a number of applications in the food industry, such as biocides in packaging materials and glues (Table 11).

In the USSR, PCP is applied as a nonselective herbicide and as a desiccant on cotton plants. At least 10 days should lapse following cotton plant treatment (IRPTC, 1984).

Table 11. Other uses of PCP and its salts as a potential source of food contamination[a]

Use	Specific compound
Slime control on paper and paperboard	K-PCP, Na-PCP
Preservative in can-end cement	Na-PCP
Defoaming agents	Na-PCP
Paper contacting aqueous and fatty food	Na-PCP
Animal glue for containers	Na-PCP
Sealing gaskets for containers	K-PCP, Na-PCP
Preservative for wood products	PCP, Na-PCP
Preservative in coatings	Na-PCP
Rubber antioxidant	Na-PCP
Preservative for ammonium alginate	Na-PCP

[a] Adapted from: Firestone (1973).

Recently, regulations to limit or even ban some uses of PCP have been established in a number of countries. The Canadian government suspended agricultural applications of PCP and Na-PCP in mushroom culture, above-ground interior woodwork of farm buildings, and as herbicides and soil sterilants (Jones, 1984). Japan restricted herbicidal use of PCP because of its high toxicity to fish (Kobayashi, 1979; Crosby et al., 1981). The paper industry of the Federal Republic of Germany and Sweden no longer use PCP in packaging paper (Ahlborg & Thunberg, 1980; Angerer, 1984).

US EPA (1984b) proposed cancelling the registration of pesticide products containing PCP as the active ingredient for non-wood preservative uses, i.e., herbicidal and antimicrobial uses. In addition, PCP-containing wood preservatives for home and farm use must not be applied where there may be direct contact with domestic animals or livestock or close contact with food or feed (US EPA, 1984a).

3.3.3 Domestic use

The largely uncontrolled use of PCP by private individuals is almost exclusively related to the treatment of wood, both outdoors and indoors. PCP is the main active ingredient in certain wood preservatives for home use, and is added to products such as stains and paints. Although this category of products plays only a minor role in the overall PCP market, it has been of particular concern, since cases of apparent PCP intoxication after indoor application in private homes have been reported (section 5). As a consequence of such incidents, the use of PCP for the preservation of interior

timber has been banned in Canada (Jones, 1981) and the Netherlands (Economist Intelligence Unit, 1981). Since 1986, the use of PCP as a biocide for indoor application has been forbidden in the Federal Republic of Germany by government regulatory action (FRG, 1986). Furthermore, there is a gentlemen's agreement between the government and industry to suspend the use of PCP in wood preservatives in general (BUA, 1986). The US EPA (1984a) intends to limit the use of PCP-containing wood preservatives in interiors to certain support structures. This is also true for the indoor use of PCP-treated wood. The sale and use of PCP is restricted to certified applicators. Thus, the domestic use of PCP is not as significant as it was some years ago.

Other reported applications of PCP include health-care products and disinfectants for use in the home, farms, and hospitals. PCP may also be contained in dental-care products (Jones, 1981), bactericidal soaps, laundry products, and medical products for the skin (Crosby et al., 1981).

3.3.4 Use for control of vectors

The application of Na-PCP to control vectors of pathogens has been of some relevance in tropical and subtropical areas. Na-PCP has been used as a herbicide to control Salvinia sp., a host plant of Mansonia mosquitos, which transmit the elephantiasis-causing filarias to man (Chow et al., 1955).

Na-PCP has also been used for control of the intermediate snail hosts of schistosomiasis (Berry et al., 1950; Toledo et al., 1976). After World War II, Hunter et al. (1952) proposed Na-PCP as the molluscicide of choice for use in Japan. In China, Na-PCP is still in use for this purpose today (Xue, 1986)[a].

3.3.5 Formulations

In the treatment of wood, PCP is usually administered as a 5% solution in a mineral spirit solvent, such as No. 2 fuel oil or kerosene (Cirelli, 1978a), or methylene chloride, isopropyl alcohol, or methanol (Ingram et al., 1981a). Since PCP is not very soluble in hydrocarbon solvents, and tends to migrate to, and crystallize on, treated wood surfaces (a phenomenon known as "blooming"), formulations may also contain co-solvents and anti-blooming agents (David, 1985[b]). Most commercial formulations also contain other chlorophenols, mainly tetrachlorophenol (Nilsson et al., 1978). The aim of

[a] Personal communication to the Task Group on Pentachlorophenol.

[b] Personal communication, Catomance Ltd, Welwyn Garden City, Hertfordshire, United Kingdom.

such mixtures is to prevent blooming on treated wood by lowering the melting point of the chlorophenols. An aqueous solution of Na-PCP is used for commercial sapstain control (Konasevich et al., 1983).

Chlorophenols may be combined with other active components such as methylene bisthiocyanate and copper naphthenate in the formulation of PCP pesticides (von Rümker et al., 1974). Conversely, PCP is added to biocides, the primary active ingredient of which is another compound; for example, sodium fluoride formulations for wooden poles and posts may contain up to 10% technical PCP (US EPA, 1973).

4. ENVIRONMENTAL TRANSPORT, DISTRIBUTION, AND TRANSFORMATION

4.1 Transport and Distribution Between Media

Several physical and chemical parameters affect the transport and distribution of PCP in soil, water, and air. Volatilization and adsorption are the major mechanisms; leaching and movements on surfaces and in air are of minor importance (Jones, 1981).

4.1.1 Volatilization

Volatilization can be an important source of loss of PCP from water and soil surfaces as well as from PCP-treated materials. Dip- or brush-treating coniferous wood may lead to a 30 - 80% loss of PCP, due to evaporation, within 12 months (Morgan & Purslow, 1973; Petrowitz, 1981).

Several factors influence the rate of volatilization of PCP from wood. Ingram et al. (1981b) showed that certain solvents or mixtures of solvents may either reduce or increase the volatilization of PCP. Such solvents, as well as resins, are used to achieve a timely release of PCP through solubilization and/or occlusion, e.g., PCP evaporation was decreased by about 20%, when 15% of an alkyd resin was added to a wood preservative containing 5% PCP (Petrowitz, 1981). Temperature appeared to be the external variable that had the greatest effect on volatilization; a rise in temperature from 20 to 30 °C caused a 3- to 4-fold increase in volatilization. Relative humidity and rate of air flow had only a minor influence on PCP volatilization from wood. The loss of PCP from pine-wood samples was half as much as that from spruce wood samples after 21 days, apparently because pine is much more easily impregnated than spruce. Thus, the depth of penetration of PCP in wood, the species of wood, and the process of treatment appear to be other external variables influencing diffusion and volatilization. As an example, immersion of small blocks of pine sapwood with a 5% PCP solution leads to a PCP loss of 20% after 6 months compared with only 4%, 9 months following double vacuum treatment (Morgan & Purslow, 1973).

Evaporation is used for the disposal of PCP in waste water at some wood-preserving plants (section 4.4). Extensive studies on the volatilization of PCP from water or soil have not been carried out, but Klöpffer et al. (1982) studied this process in an aqueous solution in the absence of other pathways of removal. Temperature and pH of the solution were the most important factors influencing the evaporation rate. Since only the un-ionized form of PCP seems to be volatile, at

pH 5.1, when 13.2% of the PCP was present as the free acid, the 50% residence time was 328 h at 30 °C, whereas, at pH 6, with more than 98% PCP dissociated to its phenate, a one-half residence time of 3120 h was measured. These findings suggest that evaporation of PCP from surface waters with a pH above 6 should be quite low.

4.1.2 Adsorption

The extent of adsorption of a pesticide governs its biovailability in soil; hence, both the rate of degradation and the biocidal activity are likely to be reduced by strong adsorption. In addition, though possessing a reduced activity, a highly adsorbed compound would exert a prolonged effect (Su & Lin, 1971; Choi & Aomine, 1972).

pH seems to be the major factor controlling the magnitude of PCP adsorption. Choi & Aomine (1974a) investigated PCP retention in a range of soil types, and determined that adsorption was maximal in strongly acidic soils, relatively minor in moderately acidic soils, and absent in weakly acidic or neutral soils. Other research workers have observed the same relationship between soil pH and PCP retention (Green & Young, 1970; Kaufmann, 1976).

The organic matter content and surface area of soils exert a minor, but significant, effect on PCP adsorption. Choi & Aomine (1974a) found that the magnitude of adsorption decreased in the following order: humusallophanic, allophanic, montmerillonitic, and halloysitic soils. This finding confirms the binding of PCP by organic matter reported by other authors (Su & Lin, 1971; Choi & Aomine, 1972).

Under the weakly acidic to neutral conditions characterizing most soils, adsorption is likely to exert a minor effect on PCP dynamics. In this regard, it is noteworthy that Choi & Aomine (1974b) studied adsorption using hexane as a solvent, because the amount of the pesticide sorbed onto soils from aqueous solution was too small to determine.

4.1.3 Leaching

Leaching of a chemical through the soil is interrelated with factors such as adsorption, water solubility of the substance, soil type, moisture, percolation velocity, and pH (Haque & Freed, 1974). Thus, the leaching behaviour of PCP will vary, depending on the soil under examination.

Leaching is an important means of transport for PCP, in some instances. Kuwatsuka (1972) noted that much of the PCP applied to flooded rice paddies was carried through the soil in solution, and the Weed Science Society of America Herbicide Handbook (WSSA, 1974) reported that Na-PCP also leaches

readily in soil. This is consistent with the observation that leaching of PCP occurs more easily in alkaline soils than in both acidic clay and sandy soils (Kaufman, 1976).

In addition, substantial quantities of PCP are found in waters leaching from contaminated sites. For example, 2.05 and 3.35 mg PCP/litre were detected in groundwater from a wood preservation plant near Lake Superior (Thompson et al., 1978), and PCP in the µg/litre range was detected in water seeping from a landfill (Kotzias et al., 1975).

Some in vitro studies have revealed little or no PCP in soil leachate (Arsenault, 1976; Weiss et al., 1982b), but these are difficult to interpret, as residence times are either extremely long, or not reported. In other percolation tests, PCP did not leach in the profile of a brown earth-Lessivé within one month, but was detected in the water seeping from a podzol (1.5 mg PCP/litre) after two days (Fränzle, 1982).

From the sorption and leaching behaviour of PCP, it can be concluded that organic matter serves as a reversible storage compartment, allowing desorption of PCP at elevated soil-water content and, hence, accumulation of PCP in the soil solution and eventually, in the groundwater (BUA, 1986).

Stranks (1976) stated that PCP does not leach readily from treated wood, particularly if applied via an oil carrier.

4.2 Biotransformation

4.2.1 Abiotic degradation

Both PCP and Na-PCP are subject to abiotic (photochemical) degradation in water, organic solvents, and on solid surfaces. In the photolysis pathway (Fig. 2) suggested by Wong & Crosby (1978), three types of degradation products occur: (a) lower chlorinated phenols, mainly 2,3,4,6- and 2,3,5,6-tetrachlorophenol together with trichlorophenols; (b) chlorinated dihydroxybenzenes, primarly tetrachlororesorcinal and tetrachlorocatechol; and (c) non-aromatic fragments, mostly dichloromaleic acid. Irradiation of the last compound, in turn, yielded carbon dioxide (CO_2) and chloride ions.

Wong & Crosby (1978, 1981) discovered that photolysis of PCP (100 mg/litre) in aqueous solutions took place much faster at pH 7.3 than at pH 3.3. The ionized PCP disappeared completely within 20 h (half-life, 3.5 h), whereas the half-life of the un-ionized form was about 100 h. The increasing rate of photodecomposition with increasing pH, reported also by Wang (1965), provides evidence of an ionic mechanism, the initial and rate-limiting reaction being the photo-nucleophilic replacement of PCP chlorine atoms by hydroxyl groups (Crosby et al., 1972).

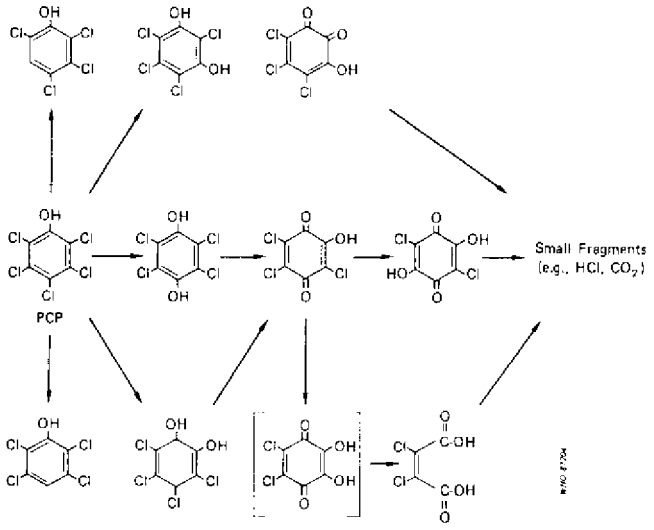


Fig. 2. Proposed photolysis pathway for PCP. Adapted from: Wong & Crosby (1978).

PCP photodegradation proved to be primarily oxidative in the studies described. However, in natural waters, reduction processes seem to prevail in an acid, high organic load environment and under the influence of organic proton-donors. Wong & Crosby (1981) concluded this from the absence of oxidized substances, such as dichloromaleic acid, and the detection of reduced products.

Gäb et al. (1975) and Gäb (1981) simulated photochemical decomposition in, or on, aerosol surfaces, dust particles etc., in the troposphere, using a mercury high-pressure lamp to match tropospherical sunlight. Adsorption of PCP on silica gel resulted in markedly accelerated photodecomposition because of the bathochromic shift of the maxima of absorption from 210 to 310 nm; about 14% of 80 mg solid PCP was mineralized to HCl and CO_2 within 7 days, while, under otherwise identical conditions, 88% of PCP deposited on silica gel was decomposed.

Photodecomposition of PCP is even accelerated if catalysed by semiconductors such as zinc (ZnO) and titanium dioxide (TiO_2) in aqueous suspensions (Barbeni et al., 1985). Under direct summer sunlight, the half-life of PCP was about 8 min (12 mg PCP/litre with 2 TiO_2/litre, pH 3). Under laboratory conditions, the half-life was 15 min at 45 - 50 °C, pH 10.5, and $\lambda > 330$ nm; mineralization of PCP was more than 95%.

Na-PCP, like its parent compound, is readily photolysed. Hiatt et al. (1960) investigated photodecomposition of Na-PCP as a possible factor reducing its efficacy as a molluscicide in South African streamwaters. In vitro exposure to UV radiation (290 - 330 nm) caused chemical degradation of Na-PCP, which was directly proportional to light intensity, and a corresponding loss of molluscicidal activity. Similarly, Na-PCP applied to rice paddies in order to control barnyard grass (Panicum crusgalli L.) was readily decomposed by sunlight (Kuwahara et al., 1966a). Aqueous solutions of Na-PCP exposed to sunlight broke down to form mainly chloroanilic acid and 3,4,5-trichloro-6-(2'-hydroxy-3',4',5',6'-tetrachlorophenoxy)-o-benzoquinone (Kuwahara et al., 1966a), and minor amounts of tetrachlororesorcinol and three benzoquinones (Kuwahara et al., 1966a,b; Munakata & Kuwahara, 1969).

Field evidence indicates that photolysis is an important means of PCP loss in situ. In their study of PCP contamination in the Bay of Quinte, Lake Ontario, Fox & Joshi (1984) found the proportions of 2,3,4,6- and 2,3,5,6-tetrachlorophenol in environmental samples to be enriched relative to PCP. Since these compounds are products of the photodegradation of PCP, they suggested that photolysis was dominating PCP breakdown. Similarly, Yunker (1981) concluded that photolysis was the most important pathway for the removal of pentachlorophenate from enclosed marine pelagic enclosures off the west coast of Canada.

Crossland & Wolf (1985) found evidence that direct phototransformation was mainly responsible for the loss of PCP from experimental outdoor ponds (50 - 100 µg PCP/litre). They observed half-lives for the loss of PCP in the range of 2 - 4.7 days (pH 7.3 - 10.3; 10 - 21 °C); decomposition was most rapid in relatively clear water.

The formation of PCDDs as a result of photochemical reaction has been described. Crosby & Wong (1976) irradiated Na-PCP in aqueous solution. Traces of OCDD were found, while 2,3,7,8-T_4CDD was not detectable, presumably because of its rapid photoreduction (Crosby et al., 1971). The photolysis of OCDD yields a variety of chlorinated dibenzodioxins with decreasing numbers of chlorine atoms (Crosby et al., 1971, 1973; Buser, 1976).

This is consistent with the findings of Lamparski et al. (1980), who observed H_6CDD and H_7CDD in the course of photolysis studies with wood samples treated with PCP in methylene chloride. The OCDD content increased from the initial concentration of 3 mg OCDD/kg Dowicide EC-7 (containing low initial PCDD concentrations) or non-detectable amounts of OCDD/kg purified PCP (Aldrich Chemical Company), respectively, to yield up to about 70 mg OCDD/kg PCP on the surface of wood in both PCP specifications, while controls

stored in the dark showed no increase in OCDD. Use of a hydrocarbon oil as a solvent significantly reduced OCDD formation during irradiation to yield 4.4 mg OCDD/kg Dowicide EC-7 or 2.2 mg OCDD/kg purified PCP, respectively. Moreover, OCDD concentrations only slightly increased in wood samples treated with a technical PCP containing relatively high initial PCDD concentrations (OCDD - 1100 mg/kg).

These results agree with those reported by Cull & Dobbs (1984), who found no evidence of the formation of OCDD in technical PCP (solvent - hydrocarbon oil) or Na-PCP (solvent - water). This has been attributed to the photolytic destruction and volatilisation of OCDD dominating its formation when the initial OCDD concentration is relatively high.

4.2.2 Microbial degradation

The microbial degradation of PCP has been studied using natural and artificial media with mixed or single microbial cultures. Lyr (1963) demonstrated that fungi were able to attack PCP by means of phenol oxidase. Cserjesi (1967) observed PCP decomposition by fungi of the genus Trichoderma in malt extract solution at a concentration of approximately 10 mg/litre. Similar studies have also been carried out with a number of other fungal species (Duncan & Deverall, 1964; Cserjesi, 1972).

Numerous PCP degrading bacterial strains, which are partly capable of using PCP as a sole source of organic carbon, have been isolated (Chu & Kirsch, 1972; Kirsch & Etzel, 1973; Watanabe, 1973; Suzuki, 1977; Reiner et al., 1978; Edgehill, 1982; Stanlake & Finn, 1982; Trevors, 1982a).

Several pathways of PCP degradation have been suggested. Because of the tremendous number of microbial strains, numerous metabolites have been identified as degradation products (Table 12). The possible steps of PCP decomposition as reported by several authors are summarized in Fig. 3. The major metabolic processes degrading PCP or its sodium salt are as follows (Suzuki, 1977; Kaufman, 1978; Reiner at al., 1978; Murthy et al., 1979; Rott et al., 1979):

(a) methylation to yield the methylether of PCP, pentachloroanisole;
(b) acylation of the hydroxyl group resulting in pentachlorophenol acetate;
(c) dechlorination to tetrachlorophenols; and
(d) hydroxylation to tetrachlorodihydroxybenzenes.

The metabolites originating from these initial steps are subject to further transformations as depicted in Fig. 3. Thus, a number of substances may arise, which accumulate to

Table 12. Metabolites formed by the microbial transformation of PCP[a]

	Substance	Reference
(1)	pentachlorophenol acetate	Rott et al. (1979)
(2)	2,3,4,5-tetrachlorophenol	Ide et al. (1972); Kuwatsuka & Igarashi (1975); Murthy et al. (1979)
(3)	2,3,5,6-tetrachlorophenol	Ide et al. (1972); Kuwatsuka & Igarashi (1975); Murthy et al. (1979)
(4)	2,3,4,6-tetrachlorophenol	Ide et al. (1972); Kuwatsuka & Igarashi (1975)
(5)	2,4,5-trichlorophenol	Ide et al. (1972); Kuwatsuka & Igarashi (1975)
(6)	2,3,6-trichlorophenol	Kuwatsuka & Igarashi (1975); Murthy et al. (1979)
(7)	2,3,4-trichlorophenol	Kuwatsuka & Igarashi (1975)
(8)	2,3,5-trichlorophenol	Ide et al. (1972); Kuwatsuka & Igarashi (1975)
(9)	2,4,6-trichlorophenol	Kuwatsuka & Igarashi (1975)
(10)	3,4-dichlorophenol	Ide et al. (1972); Kuwatsuka & Igarashi (1975)
(11)	3,5-dichlorophenol	Ide et al. (1972); Kuwatsuka & Igarashi (1975)
(12)	2,3,4,5-tetrachloroanisole (acetate)	Ide et al. (1972); Rott et al. (1979)[b]
(13)	2,3,5,6-tetrachloroanisole (acetate)	Ide et al. (1972); Rott et al. (1979)[b]
(14)	2,3,4,6-tetrachloroanisole (acetate)	Engel et al. (1966); Ide et al. (1972); Rott et al. (1979)[b]
(15)	2,3,5-trichloroanisole	Ide et al. (1972)
(16)	2,4,5-trichloroanisole	Ide et al. (1972)

different extents; the limiting step is the ring fission to chlorinated aliphatic compounds such as tetrachloromuconic acid (Lyr, 1962). Further dechlorination may result in further transformations of the aliphatic compounds (Janke & Fritsche, 1978) to form low molecular substances such as

Table 12 (contd).

	Substance	Reference
(17)	3,4-dichloroanisole	Ide et al. (1972)
(18)	3,5-dichloroanisole	Ide et al. (1972)
(19)	3-chloroanisole	Ide et al. (1972)
(20)	pentachloroanisole	Cserjesi & Johnson (1972); Ide et al. (1972); Kuwatsuka & Igarashi (1975); Murthy et al. (1979); Rott et al. (1979)
(21)	tetrachlorocatechol (diacetate)	Suzuki (1977); (Rott et al. (1979)[b]
(22)	tetrachlorohydroquinone	Suzuki (1977)
(23)	tetrachlororesorcinol (diacetate)	Rott et al. (1979)[b]
(24)	tetrachlorohydroquinone dimethylether (diacetate)	Rott et al. (1979)
(25)	tetrachlorobenzoquinone	Reiner et al. (1978)
(26)	trichlorohydroxybenzoquinone	Reiner et al. (1978)
(27)	2,3,6-trichlorohydroquinone	Reiner et al. (1978)
(28)	2,6-dichlorohydroquinone	Reiner et al. (1978)
(29)	2-chlorohydroquinone	Reiner et al. (1978)
(30)	$^{14}CO_2$	Chu & Kirsch (1972); Kirsch & Etzel (1973); Suzuki (1977)
(31)	Cl^-	Watanabe (1973); Suzuki (1977)
(32)	tetrachloromuconic acid	Lyr (1962)
(33)	β-hydroxytrichloromuconic acid	Lyr (1962)

[a] -Adapted from: Kaufman (1978).
[b] Reference refers to acetate form.

acetic acid or succinate, which then enter the tricarboxylic acid cycle. Suzuki (1983) reported that 34% of the ^{14}C resulting from ^{14}C-PCP microbial decomposition was recovered as $^{14}CO_2$, the remaining compounds being unidentified ^{14}C-metabolites.

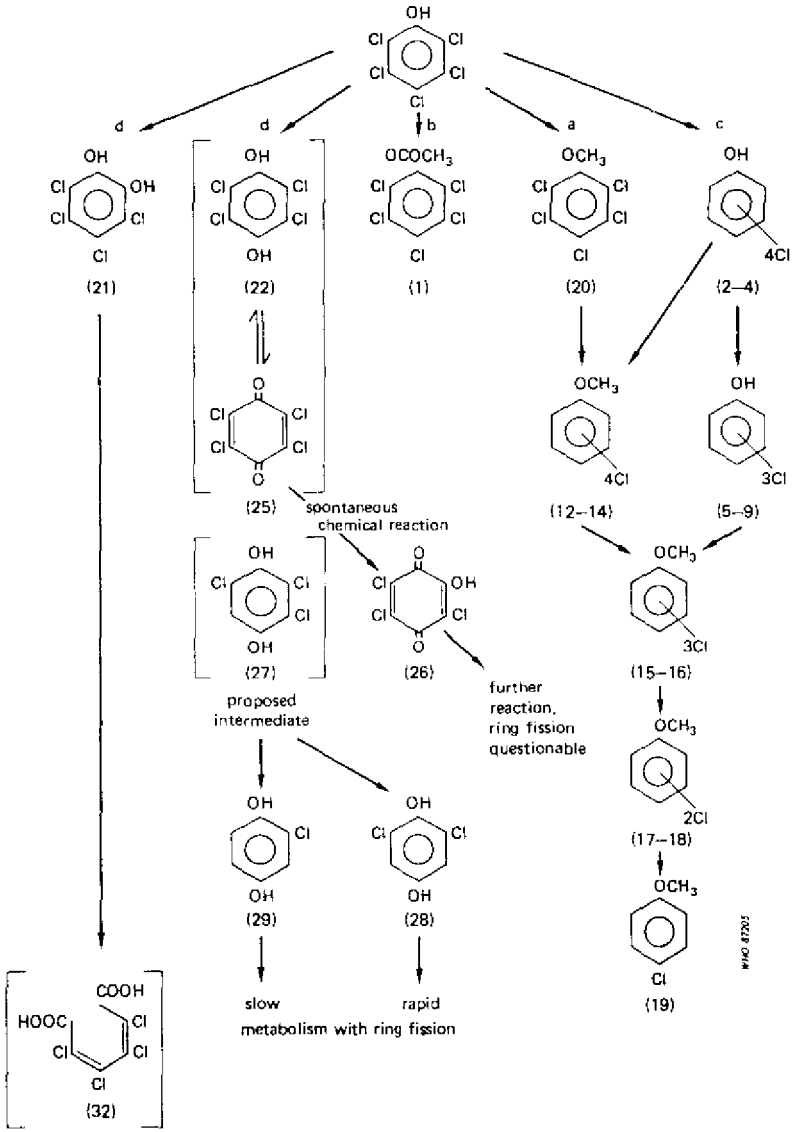


Fig. 3. Metabolic pathways for the biodegradation of PCP. Adapted from: Kaufmann (1978), Reiner et al. (1978), and Rott et al. (1979). For a list of metabolites (numbers in parentheses), see Table 12.

4.2.2.1 Aquatic degradation

Boyle et al. (1980) studied the effects of dissolved oxygen supply, light, pH, and the presence of hydrosoil on the aquatic biodegradation of PCP. Light, high pH, and high oxygen concentrations led to the most rapid and complete breakdown of PCP. PCP disappeared from the pond water of aquaria at differential rates, with half-lives ranging from 12.8 to 18.6 days, except for the anaerobic aquarium without hydrosoil (79.8 days). The absence of light and mud associated with low pH and anaerobic conditions favoured the persistence of PCP, indicating that the phenolic form of PCP is more persistent than the phenate form and that the oxidative pathway is the major mechanism for PCP degradation in simulated lake environments. Thus, PCP may be most persistent in the deoxygenated hypolimnion of stratified lakes.

This effect of oxygen on biotransformation was confirmed by Liu et al. (1981), who calculated the half-lives of PCP in aerobic and anaerobic metabolic fermentors to be 0.36 and 192 days, respectively. These half-lives are much lower than those reported by Boyle et al. (1980), probably because Liu et al. (1981) used an acclimatized culture whereas in the other studies natural pond water was employed. This illustrates how important the preadaptation of microorganisms is for their capacity to degrade PCP.

Pignatello et al. (1983) showed that the aquatic microflora can adapt to PCP and can become the most important factor for clearing contaminated surface water of PCP, particularly in deeper waters where the photolytic contribution is minimized.

Liu et al. (1981) investigated the impact of co-metabolites and of different nitrogen sources on PCP biodegradability. Peptone, glucose, and the sodium salt of 4-chlorophenol suppressed the degradation rate while yeast extracts stimulated PCP decomposition; the basis for these various effects is not clear.

In a report by Pierce & Victor (1978), levels of PCP in a man-made lake in Mississippi increased from background levels (0.3 µg/litre) to 150 - 277 µg/litre, immediately after an accidental overflow from a pole-treatment plant, decreasing to 5 - 16 µg/litre within 4 months. Long-term influx of PCP from the contaminated watershed and persistence in organically rich sediments (4 - 1518 µg/kg dry weight) were thought to provide a source of long-term pollution of the aquatic ecosystem (sections 5.1.4 and 6.5.1).

Since anaerobic biodegradation of PCP is relatively slow, PCP persists in sediments considerably longer than in water. Accordingly, high concentrations of PCP have been measured in river and lake sediments (section 5.1.2).

The fate of PCP in estuarine sediments was investigated following contamination with 11 tonnes of PCP after a ship collision (De Laune et al., 1983). Although the contaminated sediments had been removed by vacuuming 2 weeks after the accident, as much as 1.6 mg/kg (dry weight) could be detected 1 1/2 years later compared with < 5 µg/kg at remote sampling points. Laboratory studies showed a much faster breakdown under aerobic conditions (70% decomposition at pH 8 within 5 weeks) compared with anaerobic conditions (10% decomposition).

The high persistence of PCP in the sediment has been confirmed by studies on the fate of PCP in a bay of Lake Ontario (Canada), which has been contaminated by a wood-preserving plant since the 1940s (Fox & Joshi, 1984). The rather constant T_4CP:PCP ratio throughout the core (depth of 15 cm corresponding to the year 1949) indicates that almost no degradation of these chlorophenols occurred, once they had been incorporated into sediments.

Of the possible PCP metabolites, tetrachlorocatechol seems to be among the most persistent. Compared with all other chlorinated phenols studied, this substance showed the highest levels in the sediment (3.2 - 348 µg/kg dry weight) or plankton (108 µg/kg wet weight) of Finnish lakes contaminated with wood preservatives and chlorobleaching wastes (Paasivirta et al., 1980).

4.2.2.2 Degradation in soil

As in water, the biodegradability of PCP in soil depends on the type and the physiological state of the microorganisms, but several environmental factors also influence this process, such as a high amount of organic matter or high moisture content, which enhance the biodegradation of PCP (Young & Carrol, 1951; Kuwatsuka, 1972). Low temperatures (0 °C, 4 °C) have proved unfavourable for the growth of Pseudomonas species and hence their PCP breakdown activity, while, at 20 °C, PCP (50 mg/litre) was degraded to about 50% within 8 days (Trevors, 1982a). Low pH values also reduced the microbial breakdown of PCP (Stanlake & Finn, 1982).

The effects of oxygen on biodegradation vary: in some instances, anaerobic conditions in soils increase the rate of degradation, apparently as reducing conditions promote reductive dechlorination (Ide et al., 1972). On the other hand, biodegradation in terms of formation of the intermediate pentachloroanisole was significantly greater in aerobic than in anaerobic soil (Murthy et al., 1979). An average loss of 88% of 100 mg PCP/kg from clay soil was detected under aerobic conditions (over 160 days at 23 °C) compared with only 7% loss under anaerobic conditions (Baker & Mayfield, 1980).

The half-life of PCP in moist farm soils (initial concentration, 100 mg/kg) ranged from 7 to 14 days, depending on the soil varieties. PCP degradation was inhibited by certain fungicides and also under submerged conditions (Suzuki, 1983). Other half-lives reported are 10 - 70 days, under flooded conditions, and 20 - 120 days under upland conditions (Kaufman, 1978).

Edgehill & Finn (1983) investigated the use of PCP-degrading bacteria as a prophylactic measure to decontaminate soil after accidental PCP spills or when PCP-treated poles are set up near surface waters. Direct inoculation of acclimated Arthrobacter cells into the soil enhanced the disappearance of PCP at least 10-fold; the half-life of PCP in the soil incubated at 30 °C in the laboratory was reduced from 12 - 14 days to about 1 day. However, outdoor trials demonstrated that the efficacy of this measure was limited under natural conditions, as thorough mixing of the soil at the time of inoculation was required to achieve a 85% reduction of the extractable PCP at 12 days compared with only 15 - 30% without mixing.

4.3 Degradation by Plants

Degradation of PCP may also take place in plants. Rice plants were found to absorb about 3% of the radioactivity of ^{14}C-PCP applied on the soil, of which 50% could be extracted, mainly as unchanged PCP, 9% as unidentified conjugates, and about 1% as a tetrachlorophenol-isomer (Haque et al., 1978).

Weiss et al. (1982a) also studied the metabolism of ^{14}C-PCP (23 kg/ha) in rice plants. Rice roots contained 0.14% of the applied radioactivity as unchanged PCP, 3.95% as unextractable residues, and 1.08% as various metabolites. The influence of soil microorganisms was not excluded, but the authors regarded the detection of hydroxylated and methoxylated tetrachlorobenzenes as evidence of plant metabolism, because these substances were not found in soil (Weiss et al., 1982a,b).

The metabolism of PCP was also investigated under aseptic conditions using soybean (Glycine max L.) and wheat (Triticum aestivum L.) cell suspension cultures in which the isolated conversion products could be attributed to the metabolic activity of the plant cell cultures themselves (Langebartels & Harms, 1984). The β-D-glucoside of PCP was identified as the main conjugate formed by the cell suspensions. Anisoles and lower chlorinated phenols were not detected; however, some PCP was incorporated into a non-extractable fraction. Sandermann et al. (1984) isolated polar conjugates from wheat

and soybean cell cultures, and demonstrated that covalent incorporation of PCP into lignin takes place.

4.4 Ultimate Fate Following Use

4.4.1 General aspects

The amount of PCP entering the environment and its subsequent fate can be controlled at point sources where high amounts of PCP are used, such as preservation plants. However, because of its many applications, PCP is released into the environment from a number of diffuse sources and is subject to transport and transformation in different environmental compartments, as outlined in the previous sections. The evaporation data cited above (section 4.1.1) suggest that a significant fraction of the entire production of PCP will ultimately enter the atmosphere.

4.4.2 Disposal of waste water

As shown in Table 13, municipal sewage discharges contain only low PCP concentrations, whereas effluents from wood-treating factories may contain considerable amounts of PCP, depending on the intensity and efficacy of treatment measures prior to discharge. One method of handling wood preservation effluents in Canada is to store waste water on company property and allow it to evaporate, which obviously contributes to air pollution. The disposal of waste water is also achieved by incineration (section 4.4.3) and by secondary treatment before discharge into the receiving water (Hoos, 1978).

Most small wood-treatment plants handle wastes by incineration or lagooning, while larger manufacturers treat their wastes. Primary treatment is often applied when PCP is dissolved in a carrier oil: gravity separation is used to recover oil and PCP for recycling or treatment, while some plants remove oil droplets or wood particles by filtration (Richardson, 1978).

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). However, in full-scale treatment plants, the treatment efficiency is often reduced. For example, according to a US EPA survey, 8 out of 14 publicly-owned treatment plants could not remove any of the PCP load. Most of the removal efficiency of the remaining plants (6 - 87%) was attributed to adsorption on solids (Feiler, 1980).

Table 13. Levels of PCP in industrial and municipal discharges in different countries

Country	Type of waste water	PCP (µg/litre)	Reference
Canada	Effluents from wood preservation industry at 4 sites in British Columbia	0.6 225 ND[a] 2760	Environment Canada (1979)
Canada	Industrial and municipal discharges in the Greater Vancouver Area: - average from 22 sites - range - drainage ditches	 5.1 (0.2 - 42.5) 6000 2520 1125	Garrett (1980)
Denmark	Municipal sewage - influents - effluents	 0.2 - 0.7 0.1 - 2.4	Folke & Lund (1983)
Germany, Federal Republic of	Effluents from sewage treatment plant receiving waste water from paper mill	20 - 680	Dietz & Traud (1978b)
	Effluents from various industries	1 - 130	
USA	Municipal sewage - influents - effluents	 1.4 - 4.6 1 - 4.4	Buhler et al. (1973)
USA	Samples from wood-treating factories - untreated waste water - treated waste water	 17 000 - 32 000 160 - 75 000	Ervin & McGinnis (1980)
USA	Effluents from wood-treatment factories	25 000 - 15 0000	Thompson & Dust (1971)

[a] ND = not detectable.

Biodegradability strikingly decreases when commercial PCP is introduced unless the input concentrations are reduced (Reiner et al., 1978). In the presence of more readily degradable substrates, PCP degradation is suppressed. Moreover, activated sludge is not usually protected from shock loads, unless acclimatized to PCP (Hickman & Novak, 1984).

Some other treatment systems appear to be appropriate for the treatment of PCP-contaminated waste water, but their suitability has not as yet been demonstrated on a large

scale. Degradation of PCP in a biofilm reactor only occurred when the microflora was attached to solid support material, such as soft-wood bark (Apajalahti & Salkinoja-Salonen, 1984; Salkinoja-Salonen et al., 1983, 1984). PCP concentrations exceeding 1 mmol (266 mg/litre), and also some toxic solvents, such as chloroform, inhibited PCP biodegradation.

Hakulinen & Salkinoja-Salonen (1982) reported on the efficiency of a fluidized bed reactor in removing chlorophenols from pulp and paper industry bleaching effluents. Chlorophenols including PCP were completely mineralized in the anaerobic reactor. The aerobic part of the system served as an after treatment unit to remove the remaining organic load.

Adsorption on to activated carbon has also been used in treating contaminated waste waters; removal of PCP approaches 100% using this method (Richardson, 1978).

4.4.3 Incineration of wastes

As considerably increased amounts of PCDDs can be emitted during the combustion of PCP-treated material compared with untreated samples (section 2.2.1), the incineration of PCP-containing wastes is problematical. Since temperature of burning and the residence time cannot be controlled in the fire-places of private homes, the incineration of wood treated with chlorophenols is a potential source of PCDD/PCDF emission. Moreover, accidental burning of chlorophenols can lead to considerable emissions of these compounds: Kauppinen & Lindroos (1985) estimated that the burning of 100 kg chlorophenol formulation during a saw-mill fire would result in 20 g of PCDDs.

According to Powers (1976), "the complete and controlled high temperature oxidation coupled with adequate scrubbing and ash disposal facilities offers the greatest immediate potential for the safe disposal of concentrated pentachlorophenol". The destruction of PCP in treated wood in a controlled air incinerator was achieved with efficiencies greater than 99.99% at combustion temperatures of between 916 and 1032 °C (Stretz & Vavruska, 1984). The analytical results showed no evidence of T_4CDD or T_4CDF, both in the hot zone between primary and secondary chambers and in the offgas, at detection limits of 1 ppb or 5 ppb, respectively.

There are many other sources of PCDDs and PCDFs from combustion processes. The incineration of municipal waste may be the largest source of PCDD and PCDF emissions into the environment (Ballschmiter et al., 1983; Chiu et al., 1983; Tiernan et al., 1983). The various sources of these compounds are discussed in more detail in the corresponding reviews on PCDDs and PCDFs, e.g., Umweltbundesamt (1985), Karasek & Hutzinger (1986), and in Boddington et al. (1985).

The thermal conversion of organochlorine compounds, e.g., polyvinylchloride and polyvinylidene chloride, can be a source of atmospheric chlorophenols including PCP (Ahlborg et al., 1986; Dougherty, 1986[a]).

Other common methods of waste disposal such as deep-sea or deep-well disposal, landfill sites, or open pits should not be considered as a means for disposing of PCP-containing wastes, because of the mobility of PCP (Powers, 1976; Crosby et al., 1981).

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[a] Personal communication to the Task Group on Pentachlorophenol.

5. ENVIRONMENTAL LEVELS AND HUMAN EXPOSURE

5.1 Environmental Levels

5.1.1 Air

While PCP concentrations in the air at industrial sites and in rooms contaminated with PCP have been reported (section 5.2), there is apparently little information on PCP levels in the ambient air.

Cautreels et al. (1977) sampled airborne particulate matter near La Paz, Bolivia, at an altitude of 5200 m and in a residential city area of Antwerp, Belgium. At a detection limit of 0.02 ng/m^3, the atmosphere of the Bolivian mountain rural area contained 0.25 - 0.93 ng/m^3 and that of the Antwerp urban area 5.7 - 7.8 ng/m^3 air, respectively. More recent analytical results (Bundesamt für Umweltschutz, 1983) showed PCP air concentrations ranging between 0.9 and 5.1 ng/m^3 in Switzerland.

The ubiquitous occurrence of PCP in ambient air can also be shown from rain water and snow analyses. Rain water collected in Canada (Jones, 1981), Hawaii (Bevenue et al., 1972) and West Berlin (Rosskamp, 1982) contained between 0.002 and 0.3 µg PCP/litre. Water melted from snow in southern Finland revealed PCP concentrations of 0.15 and 0.98 µg/litre, respectively. PCP fallout as calculated from Finnish snow samples ranged from 1.49 to 136.0 µg/m^2 (Paasivirta et al., 1985).

5.1.2 Water and sediments

Levels of industrial and municipal discharges in different countries are shown in Table 13 (section 4.4.2). Municipal sewage discharges contain PCP concentrations at levels comparable with those in surface waters. However, wood-treating factories may contribute substantially to the PCP load in surface waters, which ranges from non detectable to 10 500 µg PCP/litre (Table 14), depending on the extent of pollution by different sources.

The majority of the water samples analysed for PCP contained less than 10 µg/litre, most contained less than 1 µ PCP/litre. The extreme PCP levels of up to 10 500 µg/litre reported by Fountaine et al. (1976) were found in a highly polluted stream near an industrial area in the vicinity of Philadelphia, USA.

Ernst & Weber (1978b) calculated the PCP input into the German Bight via the river Weser to be of the order of 1000 kg per year, assuming an average PCP level of 0.1 µg PCP/litre and a water flow of 300 m^3/second. Taking an average

Table 14. PCP concentrations in surface waters of different countries

Country	Surface water and location	PCP (µg/litre) (range, mean)	Reference
Canada	Fresh-water sites in British Columbia (BC)	trace - 0.30	Environment, Canada (1979)
	Marine sites in BC	ND[a] - 7.3	
Germany, Federal Republic of	Weser river and estuary	0.05 - 0.5	Ernst & Weber (1978b)
	German Bight	< 0.002 - 0.026	
	Ruhr river	< 0.1 - 0.2 (0.1)	Dietz & Traud (1978b)
	Rhine river, Cologne	0.1	Fischer & Slemrova (1978)
Japan	Tama river, Tokyo	0.1 - 0.9 0.01 - 0.09	Matsumoto et al. (1977)
	Sumida river, Tokyo	1 - 9	
	River water, Tokyo area	0.18 ± 0.14	Matsumoto (1982)
Netherlands	Rhine river 1976 Rhine river 1977 River Meuse 1976 River Meuse 1977	Max.[b] 2.4 (0.7) Max. 11.0 (1.1) Max. 1.4 (0.3) Max. 10.0 (0.8)	Wegman & Hofstee (1979)
South Africa	124 sampling points	ND - 0.85	Van Rensburg (1981)
Sweden	River water downstream from pulp mill	9	Rudling (1970)
	Lake receiving discharges	3	
USA	Willamette river	0.1 - 0.7	Buhler et al. (1973)
	Highly polluted stream near Philadelphia - factory location - downstream	 4500 - 10 500 49 - 240	Fountaine et al. (1976)
	Estuary in the Galveston Bay, Texas	ND - 0.01	Murray et al. (1981)
	Pond in Mississippi contaminated by waste from pole-treatment plant	< 1 - 82	Pierce et al. (1977)

[a] ND = not detectable.
[b] Max. = maximum values.

concentration of 0.5 µg PCP/litre in the surface waters of the Federal Republic of Germany (Foquet & Theisen, 1981), the total load in all surface waters of the Federal Republic of Germany was estimated by Fischer (1983) to be in the range of 60 tonnes per year, of which 30 - 40 tonnes are transported by the Rhine river.

Wong & Crosby (1981) reported PCP concentrations ranging from 1 to 800 µg/litre (average, 227 µg/litre) in the surface pond water near a local wood-treatment factory and of about 20 µg PCP/litre in agricultural drainage. Elevated PCP concentrations were also found in groundwater (3.03 - 23.3 µg/litre) and surface water samples (0.07 - 31.9 µg/litre) within saw-mill areas. Around these sites, PCP levels ranged between not detectable and 0.6 µg/litre in groundwater and between 0.01 and 0.07 µg/litre in the water of a nearby lake (Valo et al., 1984). PCP in the µg/litre range was detected in the water seeping from a landfill (Kotzias et al., 1975). A level as high as 3.35 mg/litre was found in groundwater from a monitoring well near a wood-preservation factory (Thompson et al., 1978).

A PCP-monitoring study in water was performed by Rahde & Della Rosa (1984, 1986) in a region of the Amazon jungle (Tucurui, Brazil). The construction of a dammed reservoir affected a large area (2430 km^2) with sawmills and PCP-treated wood. Water samples collected from the main river and its affluents before the flooding in 1984 contained between 5 and 14 µg PCP/litre. In 1984-85, after the flooding, the area had been covered with about 46 billions m^3 of water, PCP was not detectable at a detection limit of 4 µg/litre.

In general, the sediments of a water body contain much higher levels of PCP than the overlying waters. At several fresh-water and marine sites in British Columbia, Canada, receiving effluents from the wood-treatment industry, average PCP levels in the sediments ranged from not detectable to 590 µg/kg, while the corresponding range in the overlying waters was from not detectable to 7.3 µg/litre (Table 14). During a 1978 survey of toxic substances in the Great Lakes of Canada, sediment samples from the Thunder Bay, Marathon, and Michipicoten areas of Lake Superior contained averages of 16 900, 7300, and 2300 µg PCP/kg dry sediment, respectively. In another study of contamination from a wood preservation facility on the Bay of Quinte, Lake Ontario, Fox & Joshi (1984) analysed water and sediment samples for PCP. At a site distant from the plant discharge, sediment PCP levels ranged from 1 to 61 µg/kg dry weight, while surface waters contained only 0.015 µg/litre. Sediments from the Mississippi lake monitored by Pierce & Victor (1978) averaged 364 µg/kg dry sediment, compared with levels in the lake water of only 0.1 µg/litre. A similar distribution was

observed in surface waters in the Netherlands (Wegman & van den Broek, 1983); sediment samples from Lake Ketelmeer, a deposition area for Rhine river sediments, contained a median PCP concentration of 8.4 µg/kg dry weight, while the overlying water contained 0.41 µg/litre. PCP concentrations in sediment samples collected in the vicinity of a paper mill discharge pipe in a North Sea bight, two years after going out of use (Butte et al., 1985) and in Finnish lakes contaminated by wood preservatives (Paasivirta et al., 1980) were of the same order of magnitude.

These examples indicate that PCP and Na-PCP adsorb on sediments, which concurs with findings from experimental work. Strufe (1968) reported a study in which 65% of added Na-PCP adsorbed on river mud within 20 h.

5.1.3 Soil

Soil samples, taken at 4 sites in the vicinity of a Swiss PCP-producing facility (Dynamit Nobel), contained between 25 and 140 µg per kg (dry weight) at a depth of 0 - 10 cm and between 33 and 184 µg/kg at 20 - 30 cm. These levels are higher than the PCP concentrations of 35 µg/kg (0 - 10 cm) and 26 µg/kg (20 - 30 cm) determined in soil samples from a "reference site". The simultaneous presence of some PCDDs and PCDFs (maximum values: H_7CDD, 0.6 µg/kg; OCDD, 7.68 µg/kg; P_5CDF, 1 µg/kg at 0 - 10 cm) in sample sites near the chemical factory compared to only one positive sample (H_7CDF, 0.51 µg/kg) at the remote site confirmed the contamination (Bundesamt für Umweltschutz, 1983).

The soil surrounding Finnish sawmills was found to be heavily contaminated with up to 45.6 mg/kg (0 - 5 cm) or 1 mg PCP/kg fresh weight (80 - 100 cm) near the treatment basin, up to 0.14 mg/kg in the storage area for preserved wood and 0.012 mg/kg outside the storage area. The vertical distribution of chlorophenols including PCP explains the ground-water contamination observed (Valo et al., 1984).

In Canada, soil samples from the former site of a pesticide plant contained less than 50 µg PCP/kg (Garrett, 1980). The PCP levels in the leachate and in soil in the vicinity of 3 waste-disposal sites were also in the µg/kg range (Kotzias et al., 1975). Samples of agriculturally used soils in Bavaria (Federal Republic of Germany) contained about 100 µg PCP/kg (Gebefuegi, 1981).

PCP concentrations in soil samples taken at a distance of 2.5, 30.5, and 152.5 cm from poles treated with PCP were 658, 3.4, and 0.26 mg/kg, respectively. Arsenault (1976) considered the last value as a "natural background level", which he derived from the blank of 0.2 - 0.4 ppm found in unexposed soil samples. However, such a level seems very high for a

substance that does not appear to occur naturally. This high level could be the result of the contamination of the soil or of the reagents used for analysis.

5.1.4 Aquatic and terrestrial organisms

5.1.4.1 Aquatic organisms

Levels of PCP in aquatic organisms from various collection sites are listed in Table 15. No data are available on the background levels of PCP in biota. All sampling sites in Table 15 were more or less contaminated with industrial effluents. Relatively low contamination is reflected by residues of PCP in aquatic invertebrate and vertebrate fauna in the low µg/kg-range. For example, Zitko et al. (1974) found a range of < 0.5 - 4 µg PCP/kg wet weight in the muscle tissue of different fish species (Table 15). Higher levels were detected in organisms collected in surface waters that were thought to be contaminated with wood preservatives: up to 2100 µg PCP/kg wet weight were found in marine fish in British Columbia, Canada (Environment Canada, 1979) and up to 6400 µg/kg in fresh-water fish from Finnish lakes (Paasivirta et al., 1981) (Table 15). Some sediment-dwelling organisms showed the highest residues: polychaetes from the Weser estuary contained between 103 - 339 µg PCP/kg wet weight (Ernst & Weber, 1978a). Even higher levels (266 - 133 000 µg/kg) were found in clams from a North Sea bight, near the end of a waste-water pipe from which about 26 tonnes of PCP were discharged into the mud flats until 1978 (Butte et al., 1985).

Residues of PCP in biota associated with toxic PCP water concentrations are in the mg/kg range. Following extensive application of Na-PCP as a molluscicide in rice fields in Surinam, Vermeer et al. (1974) found 8.1 mg PCP/kg wet weight in dead frogs (Pseudis paradoxa) and between 31.2 and 59.4 mg/kg in three species of fish, which were also found dead. Composite samples of snails (Pomacea glauca) contained, on average, 36.8 mg PCP/kg wet weight.

Whole samples of small fish collected from a river in British Columbia, Canada, during an accidental fish kill resulting from the spraying of hydropoles, had levels of 16.3 mg PCP/kg; two large cutthroat trout (Salmo clarki) contained 10.3 mg/kg (Jones, 1981).

5.1.4.2 Terrestrial organisms

As with aquatic plants, almost no data are available on residues of PCP in terrestrial plants. Grass samples taken in the vicinity of a PCP producer at Rheinfelden, Switzerland, contained between 67 - 87 µg PCP/kg dry weight, comparable

Table 15. PCP residues in aquatic animals[a]

Organism	Type of sample	Location of sample	Sample date	Concentration (µg/kg)[a]	Basis	Reference
Invertebrates						
Jellyfish	whole	Gulf of Mexico	1979	0.1 - 1	wet	Kuehl & Dougherty (1980)
Sponge	whole	Finnish lakes contaminated with wood preservatives	Summer 1978	1.9 - 13	wet	Paasivirta et al. (1980)
Sagartia troglodytes (actinian)	whole	Weser estuary and German Bight	1976-77	2.7 - 7	wet	Ernst & Weber (1978a)
Polychaete (Lanice conchilega)	whole		1978	103 - 339	wet	
Mussel	muscle	Finnish lakes contaminated with wood preservatives	Summer 1978	1.7 - 5.6	wet	Paasivirta et al. (1980)
Clam (Macoma sp.)	muscle	Marine sites near wood-preservation factories in British Columbia, Canada	Autumn 1978	ND - 12	wet	Environment, Canada (1979)
Clam (Mya arenaria)	whole (without shells)	Wadden sediment of Jadebusen, bight of the North Sea, PCP discharged area until 1978	1980-81	266 - 133 000 (median: 800)	dry	Butte et al. (1985)
		Reference site		266 - 532		
Crayfish (Pacifastacus sp.)	muscle	Fresh-water sites near wood-preservation factories in British Columbia, Canada	Autumn 1978	ND - trace	wet	Environment, Canada (1979)

Table 15 (contd).

Invertebrates (contd)						
Crab (*Cancer magister*)	muscle	Marine sites near wood-preservation factories in British Columbia, Canada	Autumn 1978	ND - 20	wet	Environment, Canada (1979)
Crab (*Cancer productus*)	muscle	Marine sites near wood-preservation factories in British Columbia, Canada	Autumn 1978	trace - 7	wet	
Brown shrimp (*Penaeus aztecus*)	whole	Estuary of the Galveston Bay area of Texas	1980	4 - 17	wet	Murray et al. (1981)
Blue crab (*Calinectes sapidus*)	soft tissues			1.9 - 4.1	wet	
Dwarf squid (*Lollingnuula brevis*)	whole			1.4 - 4.3	wet	
Vertebrates						
Sculpin (marine) (*Leptocottus armatus*)	muscle liver	Mariue sites near wood-preservation factories in British Columbia, Canada	Autumn 1978	trace - 84 trace - 2100	wet wet	Environment, Canada (1979)
Sculpin (freshwater) (*Cottus asper*)	muscle liver	Fresh-water sites near wood-preservation factories in British Columbia, Canada		5 - 100 trace - 600	wet wet	

Table 15 (contd).

Organism	Type of sample	Location of sample	Sample date	Concentration (µg/kg)	Basis	Reference
Vertebrates (contd)						
Pike (Esox lucius)	muscle	Finnish lakes contaminated with wood preservatives	Summer 1978	6.5 - 8	wet	Paasivirta et al. (1980)
Roach (Rutilus rutilus)	muscle			0.9 - 12.8	wet	
Pike (Esox lucius)	muscle	Finnish lakes contaminated with wood preservatives	May 1980	11.9 - 94.3 (maximum 6400)	wet	Paasivirta et al. (1981)
Pike (Esox lucius)	muscle	Finnish lakes contaminated with wood preservatives	Spring/ Summer 1981	15.9 - 18.9	wet	Paasivirta et al. (1983)
Pike (Esox lucius)	muscle	Finnish lakes contaminated with wood preservatives 1983	Summer 1982	8.2 - 17.3	wet	Paasivirta et al. (1985)
				1.2	wet	
Crab (Rutilus rutilus)	muscle		1982	9.4 - 41.5	wet	
			1983	0.5	wet	
Baltic salmon	muscle		1983	1.8 - 4.7	wet	

Table 15 (contd).

Vertebrates (contd)						
Winter flounder (*Pseudopleuronectus*)	muscle	Estuaries in New Brunswick, Canada	Autumn 1972	1.8 - 4	wet	Zitko et al. (1974)
Cod (*Gadus morhua*)	muscle			0.8	wet	
Sea raven (*Hemipterus americanus*)	muscle			< 0.5	wet	
Atlantic salmon (*Salmo salar*)	whole	Estuaries in New Brunswick, Canada	Autumn 1972	0.5 - 1.3	wet	Zitko et al. (1974)
White shark (*Carcharodon carcharias*)	liver			10.8	wet	
Flounder	whole	Estuary in the Galveston Bay	1980	1.6 - 3.5	wet	Murray et al. (1981)
Longnose killifish (*Fundulus similis*)	whole			4.7 - 5.6	wet	

[a] ND = not detectable.

to the PCP concentration of 87 µg/kg found in grass from a reference site (Bundesamt für Umweltschutz, 1983).

Reported residue levels in terrestrial vertebrates are mainly related to domestic animals exposed to PCP: the tissues and blood of cows and calves of dairy herds in the USA showed unquantified PCP contamination (Hoeting, 1977). One herd housed in a PCP-treated wooden barn had blood-PCP levels of 270 - 570 µg/litre (US EPA, 1978).

Pentachloroanisole, a metabolite of the PCP biodecomposition, causes a musty taint in broiler chicken tissues. It appears that the chloroanisole arises through the microbial methylation of PCP in wood shavings used as chicken litter (Curtis et al., 1972; Parr et al., 1974; Harper & Banave, 1975). Wood shavings have been used as litter not only for broiler chickens, but also for turkeys, ducks, pigs, and cattle.

Neidert et al. (1984) found low residue levels of PCP in all 1072 chicken liver and 723 fat samples examined (most < 0.01 mg/kg), indicating an overall exposure of poultry to PCP. Only 0.75% of the liver samples contained PCP levels higher than 0.1 mg/kg.

In the field study of Vermeer et al. (1974) mentioned earlier, PCP was detected in liver samples of birds (0.06 - 0.19 mg/kg wet weight) residing in the vicinity of PCP-treated rice fields. High PCP residues were found in the brain (mean, 11.3 mg/kg wet weight), liver (46.6 mg/kg), and kidney (20.3 mg/kg) of dead snail kites (Rostrhamus sociabilis), which had probably ingested Na-PCP contaminated snails.

Only a few data on PCP residues in terrestrial animals, apparently not exposed to PCP, have been reported: purple martin fledglings from Alberta, Canada, contained 31 µg PCP/kg (Jones, 1981). The muscle tissue of juvenile starlings, collected from their nests in South Finland in 1982 and 1983, contained PCP levels ranging from not detectable to 59 µg/kg wet weight (mean, 5.9 µg/kg) (Paasivirta et al., 1985). The pectoral muscles of white-tailed eagles, also collected in Finland, contained between 14 and 8571 µg PCP/kg wet weight, while levels in eggs ranged from not detectable to 25 µg/kg. Eggs of osprey contained between 1 and 803 µg PCP/kg.

5.1.5 Drinking-water and food

PCP concentrations ranging from < 1 to 50 µg/litre were detected in domestic well water (Oroville, California) (Wong & Crosby, 1981). Buhler et al. (1973) analysed drinking-water obtained from the Willamette river (USA). They found 0.06 µg PCP/litre in the finished water. PCP was found at a level of 0.1 µg/litre in one water sample

(Dougherty & Piotrowska, 1976b). Concentrations of 0.01 - 0.02 µg PCP/litre were detected in drinking-water in the Ruhr area of the Federal Republic of Germany (Dietz & Traud, 1978b). PCP levels in Florida drinking-water supplies ranged from 0.003 to 0.34 µg/litre (Morgade et al., 1980). Detrick (1977) suggested that the chlorination of phenol in water supplies might be responsible for the wide occurrence of PCP. The chlorination of 1 mg phenol/litre by 10 mg chlorine/litre is said to yield about 0.2 µg PCP/litre, which is comparable with the levels found in drinking-water. However, the odour threshold for phenol is in the µg/litre range, thus low levels of phenol can generally be detected in water.

Most data on PCP residues in food have been collected in the USA, where a number of pesticides, including PCP, have been routinely monitored in the FDA Market Basket Survey. In 1973-74, PCP was found in 10 out of 360 composite food samples, at concentrations ranging from 10 to 30 µg/kg (Manske & Johnson, 1977). In 1975, 5.4% of a total of 240 samples were contaminated with PCP at 10 - 40 µg/kg (Johnson & Manske, 1977). Values for the period 1965-70 are shown in Table 16. PCP concentrations measured in daily diet samples in the Federal Republic of Germany (Gebefuegi, 1981) are similar, averaging 16.3 µg/kg (range, 2.6 - 27.5 µg/kg). Krause (1982) found elevated PCP concentrations in the food-basket samples of persons applying wood preservatives in private homes. Two-thirds of the samples analysed contained between 2 and 13 µg PCP/kg with a median of about 6 µg PCP/kg, whereas the control samples fell between less than 0.1 and 5 µg/kg.

Samples of agricultural produce taken by the Alberta Department of Agriculture (Canada), consisting mainly of potatoes and raw milk, contained PCP levels of less than 10 µg/kg. In isolated samples, PCP levels of up to 2700 µg/kg occurred, as a result of contamination from storage containers made of treated wood (Jones, 1981).

In southern Ontario, Canada, 45 bovine milk samples collected from bulk transports hauling milk were analysed for chlorophenols (Frank et al., 1979). PCP was not detected in whole milk at a detection level of 0.1 µg/litre.

In analysing commercial mushrooms for PCP residues, Meemken et al. (1982) found that levels in 11 out of 17 fresh mushroom samples exceeded the recommended limit of 10 µg/kg set in the Federal Republic of Germany for certain food items. Residues apparently originated from the treated wooden cases used for culturing mushrooms, which contained up to 3900 mg PCP/kg.

PCP can also enter food during processing, transportation, or storage. Heikes & Griffitt (1980) demonstrated that canned fruit and vegetables in Mason jars can be contaminated with

Table 16. Average incidence of PCP residues in food composites and daily dietary intake of PCP in the USA[a]

Year	Number of composites examined	Percent positive composites	Daily PCP intake (µg/person per day)
1965	216	1.4	-[b]
1966	312	3.3	6
1967	360	2.2	1
1968	360	1.9	1
1969	360	2.8	2
1970	360	ns[c]	ns[c]

[a] From: Duggan & Corneliussen (1972).
[b] < detection limit (1 µg).
[c] ns = not specified.

PCP due to PCP residues in sealing gaskets, lids, and enamel. Levels in the jar lid, sealing gaskets, and enamel were as high as 198 µg/lid, 125 mg/kg, and 4.4 mg/kg, respectively. Six fruits and vegetables originally free from PCP, contained between 0.29 and 1.1 µg/litre in the liquid and between 1.4 and 38 µg/kg in the solids, after being canned and stored for 4 days in contaminated jars.

Kroyer et al. (1982) modelled the transfer of PCP from wooden storage containers to flour experimentally. Within 24 h, remarkable quantities of PCP can be adsorbed by flour in contact with PCP-treated wood: applied wood preservative could be detected in the foodstuff at levels ranging from 0.2 to 1 mg PCP/kg.

PCP levels in the range of 240 - 1090 µg/kg were found in the flesh grease from hides treated with PCP. Collagen material derived from hides, pigskin, and decalcified bones is used for the manufacture of edible gelatins, and Stijve (1981) detected PCP in each of 50 samples of commercially available gelatins tested. Products from western Europe and the USA generally contained less than 100 µg/kg, while those from tropical countries contained from 1000 to 5000 µg PCP/kg. The US Food and Drug Administration (FDA) has proposed prohibiting "the use of animal bones, hides, or skins that have been exposed to pentachlorophenol" (Federal Register, 1977).

A calculated daily dietary intake of PCP for the period 1965-70 is shown in Table 16. The values ranging from 1 to 6 µg/person per day were based on a market-basket survey of 117 retail food items. Each market basket represented a 2-week diet, constructed according to consumer behaviour. The foods were prepared as for eating and then analysed (Duggan & Corneliussen, 1972). In another survey (Krause, 1982), in

contrast to the above food collection procedure, samples of complete meals prepared and eaten by different families were collected over a period of 3 - 7 days and pooled. This sampling procedure is more realistic, as it takes into consideration the fact that food may be contaminated during storage in PCP-contaminated rooms. In fact, in households where PCP-containing wood preservatives had been applied, meals averaged 6 µg PCP/kg (2/3 range, 2 - 13 µg/kg), while the meals of a control group were less contaminated (< 0.1 - 5 µg/kg). According to Fischer (1983), the daily dietary intake on the basis of these data is 0.1 - 1 µg/person per day for people without known exposure and 6 µg/person per day for persons exposed to PCP-treated interiors.

5.1.6 Consumer products

On the basis of the diverse applications of PCP, it would be expected that a large number of consumer products contain this compound. Furthermore, PCP from the indoor atmosphere can contaminate a number of household items. However, there are few data on PCP levels in consumer products. In one example, van Langeveld (1975) analysed 65 commercial samples of paints used on children's toys and found that 14% contained PCP in the range of 100 - 2700 mg/kg.

The Swiss Federal Office of Health (Siegwart, 1983) found PCP in various clothes including socks, pantyhose, and insoles, with PCP concentrations between 0.015 and 0.96 mg/kg; one insole contained 13.2 mg PCP/kg (Siegwart, personal communication, 1986).

5.1.7 Treated wood

Obviously, PCP-treated wood contains substantial quantities of the compound itself. The Ontario Ministry of Agriculture detected tetrachlorophenol and PCP in samples of wood shavings used as livestock litter in southern Ontario (Jones, 1981); PCP levels were as high as 628 mg/kg in fresh litter, but fell off sharply, after 56 days use to 96 mg/kg or less. In the United Kingdom, Parr et al. (1974) found an average PCP concentration of 12 mg/kg (range, 1 - 83 mg/kg) in fresh broiler house litter, while spent litter contained an average of 0.3 mg/kg. Curtis et al. (1972) found as much as 40 mg PCP/kg in samples of shavings and sawdust. Levin & Nilsson (1977) assayed for tetrachlorophenol, PCP, and several contaminants in wood dust from a Swedish sawmill. PCP levels

in dust from wood treated with 2% Na-2,3,4,6-tetrachlorophenol ranged from 30 to 100 mg/kg.

Analysis of timber samples taken from homes in the Federal Republic of Germany, several years after it had been recommended to avoid the indoor use of PCP, revealed PCP levels ranging from 0.1 to 615 mg/kg (mean, 35 mg/kg) (Ruh et al., 1984). This means that the timber had either been treated with PCP or that it was contaminated. In this context, it is noteworthy that Ruh & Gebefuegi (1984) also analysed wooden material which, according to consumer information, was supposed to be untreated. Only 30% of the samples were PCP-free, 40% contained from 0.05 to 0.8 mg PCP/kg, and 31% contained from 1 to 20 mg/kg.

Untreated wood samples from furniture in a living room in which panelling had been painted with a wood preservative (6% PCP) according to instructions, were analysed by Gebefuegi et al. (1979). PCP concentrations ranged from 15.5 to 26 mg/kg in the top layer (0 - 1.5 mm) and from 2.5 to 7 mg/kg at 3 - 8 mm. For comparison, treated wood samples contained between 1570 and 2754 mg/kg in the top layer, 612 - 1800 mg/kg in the middle layer (1.5 - 3 mm), and 117 - 340 mg/kg in the bottom layer (3 - 8 mm). Freshly treated wood surfaces showed PCP concentrations of between 4000 and 6000 mg/kg.

5.2 Occupational Exposure

A list of potential sources of occupational exposure to PCP is presented in Table 17. However, the actual PCP concentrations that workers are exposed to during such industrial or commercial activities are rarely measured.

Since PCP is extensively used for wood protection and preservation, most studies of occupational exposure have been conducted in this field of industry. If the pressure treating method is used, respiratory exposure to PCP occurs mainly when the door of the pressure vessel is opened and PCP can escape into the breathing zone of the worker. With non-pressure treatment, continuous evaporation of PCP into the air takes place, since the tanks or vats are open. With both processes, dermal exposure of workers is possible during the handling of the treated wood (Williams, 1982). The polychlorinated impurities in PCP may be enriched relative to freshly prepared PCP solution during the recirculation of the preservatives (Levin et al., 1976; Lamberton et al., 1979). Hence, during the periodic tank and cylinder cleaning processes, much higher exposures to PCP impurities may occur than expected theoretically.

In Table 20 (pp. 87-89), a number of PCP air concentrations as measured in the course of human monitoring studies is shown. In addition, air samples taken at the breathing zone in

Table 17. Potential sources of occupational exposure to PCP or its sodium salt[a]

Manufacture and shipping of industrial chlorophenols
Sawmills
Wood-treatment plants
Carpentry and other timber and wood-working
Termite control
Agricultural pesticide application
Greenhouses
Industrial cooling towers and evaporative condensers
Treatment and handling of wool
Treatment and handling of burlap, canvas, rope, leather
Paper manufacture
Petroleum and other drilling
Paint and adhesive manufacture and use
Telephone and electrical line work
Dyeing and cleaning of garments

[a] Adapted from: Crosby et al. (1981).

11 wood-treating factories in the USA ranged from 10 to 510 µg/m³ (Todd & Timbie, 1983). Most of the data in Table 20 are below the TWA or MAC value of 500 µg PCP/m³ (IRPTC, 1983), which has been established by several countries. However, this value is derived "by analogy with other compounds of similar action and toxicity in addition to the specific available information" (ACGIH, 1980). With lumber treatment, exposure to airborne PCP is generally below 100 µg/m³; concentrations higher than the TWA value commonly occur during PCP or Na-PCP production.

Extremely high occupational exposures have been reported as a result of the agricultural use of PCP. Following PCP application on cotton fields over a 2-year period, Demidenko (1969) reported that unusually high concentrations of up to 38 000 µg PCP/m³ air were found where the sprayers were working and that the workers exhibited typical symptoms of PCP intoxication (eye and nasal irritation, headaches, fatigue). In the breathing zone of the workers formulating the spray, air-PCP levels of 320 µg/m³ were measured. Pilots in spraying aircraft were exposed to an average of 880 µg PCP/m³. Air levels, at a distance of 10 - 50 m from the treated field, varied from 960 to 4400 µg/m³.

The magnitude of PCP exposure depends particularly on the methods used in handling the chemical, and on measures to minimize PCP levels in the work-place. According to Wood et al. (1983), automated processes and closed systems have greatly reduced the exposure level in large-scale manufacturing and wood-treatment factories. However, in small-scale operations, overexposure may occur through inadequate control

measures. In addition to measurements of ambient PCP levels during industrial or agricultural use, several attempts have been made to estimate exposure on the basis of urine-PCP levels in workers involved in the direct and controlled application of PCP (section 5.4).

5.3 General Population Exposure

Because of the widespread use of PCP products, the general population also comes into contact with this substance. PCP has been detected at the µg/litre level in the urine of people, not occupationally exposed, in widely different groups and locations (section 5.4). It is likely that this widespread occurrence of PCP in human populations results from PCP intake or from the metabolism of other chlorinated compounds rather than from the natural occurrence of PCP.

Some possible sources of non-occupational exposure to PCP in the home, work, and outdoor environments are listed in Table 18. In such cases, the general population can be incidentally exposed to PCP-treated items such as textiles, leather, and paper products (Jones, 1981, 1984). In addition, a variety of consumer products including food may contain PCP, though no direct PCP application has been involved, if they are stored in PCP-treated wooden containers or exposed to PCP in the atmosphere of rooms where woodwork has been treated with PCP. This is consistent with the laboratory studies of Morgan & Purslow (1973), Ingram et al. (1981a,b), and Petrowitz (1981) who observed considerable losses of PCP from wood samples (section 4.1.1).

Table 18. Some possible sources of non-occupational exposure to PCP or its sodium salt[a]

Use of retail trade pesticide products containing PCP (for wood preservation, termite control, etc.)
Use of PCP-treated lumber for construction of dwellings
Smoke from sawmills and burning scrap lumber
Sawdust (fuel, floor covering, particle-board, etc.)
Burlap, canvas, and rope
Wool and other textiles
Leather products
Paper products
Contact with adhesives, paint, and painted surfaces
Used telephone poles and railroad ties
Ornamental wood-chips
Fat trimmed from treated hides (used as feed additive)
Water treated for mollusc control
Contaminated food

[a] Adapted from: Crosby et al. (1981).

Wood preservatives containing PCP or its sodium salt have been widely applied in the domestic field both indoors and outdoors. In some countries, the indoor use of PCP-containing wood preservatives has been regulated by government authorities (section 3.3.3). Cases of PCP intoxication in persons residing in treated houses have roused public concern as to whether the general population might be endangered by domestic applications of PCP and have led to investigations of PCP levels in rooms and the evaluation of potential health effects.

In one instance, volatilization of PCP within a room from treated interior wood led to PCP deposition on untreated wood, furniture, and curtains at levels of between 23 and 26 mg/kg and to residues (mg/kg) on other household items such as carpets, books, oil paintings, and cassette tapes. The air levels of PCP varied between 50 and 100 $\mu g/m^3$ in the living room of the house, which had been under examination since 1974, because of reported PCP intoxications (Gebefuegi et al., 1979).

Krause & Englert (1980), Aurand et al. (1981), and Krause (1982) reported the results of a survey in the Federal Republic of Germany, which included the analysis of indoor air samples in 104 homes and of the urine of more than 1000 persons. Depending on the intensity of, and the time elapsed since, indoor PCP application, PCP concentrations in the air ranged from not detectable to about 25 $\mu g/m^3$, frequently from 2 to 10 $\mu g/m^3$. The median value of 5 μg PCP/m^3 is 1000 times higher than the outdoor air levels found in residential areas (section 5.1.1). For comparison, indoor air levels of PCP in houses of a control group without known exposure were generally below the detection limit of 0.1 μg PCP/m^3.

Air concentrations of PCP of between 1 and 10 $\mu g/m^3$ have been reported in the living- and bedrooms of Swiss homes (Zimmerli et al., 1979). Similar levels (1 - 25 $\mu g/m^3$) were found in rooms treated one to several years earlier; levels of 25 and 30 $\mu g/m^3$ were found in rooms a few weeks after treatment (Dahms & Metzner, 1979).

In an unpublished study carried out in the United Kingdom in 1980 and cited by Dobbs & Williams (1983), PCP air concentrations were monitored as a function of time. During the first week after treatment of the roof void of a house, PCP levels were as follows: 16 - 67 $\mu g/m^3$ in the treated roof void, 3.9 - 15 $\mu g/m^3$ in the landing, and 1.6 - 2.8 $\mu g/m^3$ in the bedroom; 5 - 10 weeks after treatment, PCP concentrations in the treated roof void ranged from 1.7 to 6.7 $\mu g/m^3$ compared with 0.6 - 5 $\mu g/m^3$ in the landing and 1.6 - 2.8 $\mu g/m^3$ in the bedroom. Although the PCP air concentration in or near the treated room rapidly decreased,

levels in the untreated bedroom remained stable, perhaps as a result of adsorption and desorption processes.

To follow the volatilization of PCP from treated wood in enclosed environments, studies were conducted in a building with an enclosed swimming pool, the walls and ceiling of which had been treated with PCP (Gebefuegi, 1981; Gebefuegi et al., 1983). Within a fortnight, an estimated 178.5 mg PCP had diffused from the wooden panels (210 m^2), based on detection of 1 µg/litre in the water of the swimming pool, 60 µg/litre in the water condensed from the heat pump, and 4 $µg/m^3$ in the air of the hall housing the swimming pool. Air levels of PCP inside this building ranged from 1 to 160 $µg/m^3$, one year after the application of the wood preservative. Two years later, PCP concentrations in the indoor air averaged 4 $µg/m^3$, and, even after 7 - 8 years, PCP was still present at about 0.4 $µg/m^3$, though, in the interim, the wood panels had been painted with another wood preservative, which undoubtedly reduced the rate of PCP diffusion.

In a study conducted in the USA, PCP vapour levels were measured in the air of treated wooden structures. The highest level detected was 38 $µg/m^3$ in the basement of the building where there was the highest ratio of treated wood surface area to room volume, and no ventilation. PCP levels were higher in the main floor of this house (8.8 $µg/m^3$) and in a warehouse (3.52 $µg/m^3$) than in 11 other rooms of different buildings, which ranged from 0.09 to 1 $µg/m^3$. Variability in PCP concentrations was mainly attributable to ventilation differences (Saur et al., 1982).

Compared with the aforementioned studies, the values (0.06 - 1.6 $µg/m^3$) reported by Dobbs & Williams (1983) from houses in the United Kingdom represent rather low PCP levels. Generally, PCP concentrations of up to about 30 $µg/m^3$ can be expected during the first month following treatment; considerably higher levels (up to 160 $µg/m^3$) may not be excluded under unfavourable conditions. In the long term, values of between 1 and 10 $µg/m^3$ are typical PCP concentrations after extensive treatments.

Krause (1982) considered household dust to be very suitable for screening purposes, because it accumulates PCP and can be easily collected. Household dust collected in the houses of residents using PCP contained about 1000 times more PCP (mean, 15 mg/kg; 2/3 range, 6 - 20 mg/kg) than that of control households (mean, 0.008 mg/kg; 2/3 range, 0.003 - 0.013 mg/kg).

In similar, more recent studies, relatively high PCP levels (range, 0.2 - 217.3 mg/kg; mean, 28.5 mg/kg) were found in household dust samples, indicating indoor air contamination resulting from PCP contaminated surfaces (Ruh et al., 1984).

The concentration of PCDDs or PCDFs in PCP-contaminated interiors has not yet been determined. However, it may be assumed that the ratio of their air concentrations will be proportional to their rates of volatilization. Because of their lower vapour pressure (e.g., H_6CDD, 8.8×10^{-5} Pa), volatilization of PCDDs will be lower than that of PCP. According to Cull et al. (1983), the following PCDD concentrations can be predicted in houses where PCP air concentrations range from 1 to 10 µg/m³: OCDD, 0.2 - 20 ng/m³; H_6CDD, 0.007 - 0.7 ng/m³; H_7CDD, 0.04 - 4 ng/m³.

First reports of indoor air analyses of PCDDs and PCDFs in a house in the Federal Republic of Germany (Eckrich, 1986), which had been treated with PCP-containing wood preservatives several years before, seem to confirm these estimates; however, the data reported are still insufficient for a conclusion to be drawn. Further studies are under way that could be used to characterize the PCDD and PCDF levels in indoor air of PCP-treated homes.

Residues of PCP in the general population may arise not only from oral, dermal, or inhalation uptake of PCP, but also from the metabolic transformation of other chlorinated compounds (Table 19). In studying the biotransformation of hexa- and pentachlorobenzene in the rat, mouse, guinea-pig, laying hen, and rainbow trout, Koss & Koransky (1978) found PCP and other metabolites in both the excreta and tissues of the animals. Considering the substantial residues of hexachlorobenzene in the human body and in human milk, PCP intake arises via this route in both adults and new-born children. Similarly, the continuous low-level PCP excretion from people, who apparently are not exposed to PCP, might be partly due to continuous exposure to hexachlorobenzene and related compounds.

Table 19. Chlorinated compounds metabolized to PCP

Source	Reference
hexachlorobenzene	Mehendale et al. (1975); Engst et al. (1976); Rozman et al. (1977); Sanborn et al. (1977); Koss & Koransky (1978); van Ommen et al. (1985)
pentachloronitrobenzene	Murthy & Kaufman (1978); Koegel et al. (1979)
BHC isomers (i.e., lindane)	Balba & Saha (1974); Engst et al. (1978)

5.4 Human Monitoring Data

Exposure levels as measured in the indoor air or in consumer products may provide indirect indications of exposure to PCP. However, it is not possible to separate oral, respiratory, and dermal exposures, under non-experimental conditions. Thus, the PCP concentrations of the sources do not directly indicate the actual human PCP intake by the different routes.

Several investigations have been carried out to relate the human body burden to the urinary-PCP level. These are summarized in Tables 20, 21, and 22) distinguishing between occupationally exposed workers and the general population. The latter has, in turn, been divided into individuals exposed non-occupationally, such as persons exposed to PCP-containing wood preservatives applied to the interior of private homes, offices, public facilities etc., and people without known exposure.

In many cases, values for populations without known exposure overlap those of exposed populations, perhaps because persons designated as unexposed might unknowingly have been exposed to obscure sources of PCP. In addition, occupational exposure does not always involve high loading, for, as pointed out in section 5.2, both very low and very high air levels of PCP have been found in work-places. Conversely, people exposed non-occupationally, particularly those who apply PCP-containing wood preservatives indoors, may be exposed to air levels of PCP encountered at work-places or even higher levels.

Analytical improvements in the last few years have substantially lowered the detection limits (section 2.5.2) and, combined with different methods, this makes the comparability of analytical data questionable, particularly when urinary-PCP levels have been determined without hydrolysis, as in the survey of Krause & Englert (1980), since, under these conditions, PCP levels will have undoubtedly been underestimated. According to Zimmerli et al. (1979) and Butte (1984), analysis for total PCP yields concentrations about 3 times higher than those for only free PCP.

For these reasons, it is not possible to derive exact ranges of PCP levels in different exposure groups from the data in Tables 20, 21, and 22. However, the mean or median urine-PCP levels are likely to range around 0.01 mg/litre for the general population without known exposure, around 0.04 mg/litre for persons exposed non-occupationally, and around 1 mg/litre for occupationally exposed people.

Only two particularly detailed studies of domestic PCP exposure provide comparative data. Comparing the mean urine-PCP levels, Hernandez & Strassmann-Sundy (1980) (No. 3

Table 20. Levels of PCP in the air, and in the serum or plasma, and urine of individuals exposed occupationally

Number of study	Activity	Sample size (number)	Length of exposure (years)	Air (μg/m³) mean (range)	Serum (mg/litre) mean (range)	Urine (mg/litre) mean (range)	Reference
(1)	Lumber, carpentry	1	ns	na	na	0.024 (0.022 - 0.025)[a]	Cranmer & Freal (1970)
(2)	Lumber, closed tank procedure	11	1	na	na	1.6 (ns)	Casarett et al. (1969)
(3)	Lumber, dipping	11	1	na	na	2.6 (ns)	Casarett et al. (1969)
(4)	Lumber, dipping	ns	ns	19 (3 - 63)	na	2.83 (0.12 - 9.68)	Arsenault (1976)
(5)	Lumber, dipping	18 - 22	ns	na	3.78 (0.15 - 17.4)	0.95 (< 0.01 - 7.80)	Klemmer et al. (1980)
(6)	Lumber, dipping, spraying, or brushing	18	ns	na	5.14 (0.43 - 14)	1.31 (0.09 - 3.3)	Begley et al. (1977)
	- 6th day of vacation	18	ns	na	4.92 (0.50 - 13)	1.36 (0.18 - 3.5)	
	- 20th day of vacation	18	ns	na	2.19 (0.32 - 5.3)	0.59 (0.05 - 1.4)	
	- 51st day of renewed work exposure	13	ns	na	2.61 (0.19 - 8.1)	0.95 (0.03 - 3.6)	
(7)	Lumber, general[b]	3	5 (2 - 11)	1 (< 1 - 15)	1.11 (0.35 - 3)	0.15 (0.044 - 0.47)	Wyllie et al. (1975)
(8)	Lumber industry	20	ns	na	ns (0.4 - 4.8)	ns (0.07 - 0.57)[c]	Gossler & Schaller (1978)

Table 20 (contd).

Number of study	Activity	Sample size (number)	Length of exposure (years)	Air (µg/m³) mean (range)	Serum (mg/litre) mean (range)	Urine (mg/litre) mean (range)	Reference
(9)	Lumber, office[b]	1	10	2 (< 1 - 3)	0.65 (0.42 - 0.75)	0.06 (0.04 - 0.11)	Wyllie et al. (1975)
(10)	Lumber, pressure treatment[b]	1	5	6 (< 1 - 15)	2.29 (1.51 - 3.55)	0.30 (0.09 - 0.76)	Wyllie et al. (1975)
(11)	Lumber, pressure treatment	ns	ns	14 (4 - 1000)[d]	na	1.24 (0.17 - 5.57)	Arsenault (1976)
(12)	Lumber, pressure treatment	23 - 24	ns	na	1.72 (0.02 - 7.70)	0.27 (< 0.01 - 2.40)	Klemmer et al. (1980)
(13)	Lumber, pressure treatment						Embree et al. (1984)
	- Airborne + dermal	10	5 - 10	55.6 (± 89)	0.71 (± 0.38)	0.11 (± 0.02)	
	- Airborne exposure	8	5 - 10	66.7 (± 100)	0.24 (± 0.23)	0.05 (±0.02)	
	- No known exposure	5	5 - 10	ns	0.06 (± 0.02)	ns	
(14)	Lumber, spraying	2	ns	na	na	0.20 (0.13 - 0.27)[d]	Crammer & Freal (1970)
(15)	Lumber, spraying	ns	ns	6 (3 - 69)[d]	na	0.98 (0.13 - 2.58)	Arsenault (1976)
(16)	PCP processing factory	18	12 (0.3 - 31)	ns (2.2 - 55.5)	0.25[e] (0.02-1.5)[f]	0.112[e] (0.013 - 1.224)	Triebig et al. (1981)[g]
(17)	PCP application	23	3[e] (0.5 - 12)	2.4 (0.3 - 8)	1[e] (0.2 - 2.4)[f]	ns	Zober et al. (1981)

Table 20 (contd).

(18)	PCP processing	18	10[e] (0.2-31)	17.5 (2 - 50)	0.25[e] (0.02 - 1.5)[f]	ns	Zober et al. (1981)
(19)	PCP production	8	ns	< 100 - > 500[h]	4.73 ± 3.41	2.38 ± 1.91	Bauchinger et al. (1982)
	Na-PCP production	14	ns	< 100 - > 500[i]	2.23 ± 1.51	0.84 ± 0.65	
(20)	PCP production	18	ns	270 - 4000	na	0.72 ± 0.55	Ning (1984)
	Na-PCP production	50	ns	0 - 50	na	0.35 ± 0.30	
(21)	PCP synthesis, full time activity	9	ns	na	na	1.2 (0.34 - 3.4)	Siqueira & Fernicola (1981)
	- same factory, reduced PCP exposure	12	ns	na	na	0.15 (0.032 - 0.4)	
(22)	Pesticide, spraying	130	ns	na	na	1.80 (0.003 - 35.7)	Bevenue et al. (1967b)
(23)	Farmers and pest control operators	210 - 280	ns	na	0.25 (< 0.01 - 8.4)	0.01 (< 0.01 - 0.040)	Klemmer et al. (1980)

[a] Range of replicate analyses of single urine samples.
[b] Mean concentrations shown are calculated from sampling data collected over a 5-month period. Mean air level for workers listed as "lumber, general", is calculated from data provided for all 11 sites over a 5-month period by Wyllie et al. (1975).
[c] Assuming a daily urine volume of 1.4 litre.
[d] Mean "average exposure levels" encountered by employees. Air at "maximum exposure" sites, next to sources, contained 26 µg/m³ (lumber spraying site) and 297 µg/m³ (pressure treatment site).
[e] Median.
[f] Plasma.
[g] Data partly identical with those from Zober et al. (1981).
[h] From 67 samples, 18 were < 100 and 10 > 500 µg/m³.
[i] From 55 samples, 7 were < 100 and 8 > 500 µg/m³.
na = Not analysed.
ns = Not specified.

Table 21. Levels of PCP in the air, and in the serum or plasma, and urine of individuals exposed non-occupationally

Number of study	Exposure/ comments	Sample size (number)	Length of exposure (months)	Air (μg/m³) mean (range)	Serum (mg/litre) mean (range)	Urine (mg/litre) mean (range)	Reference
(1)	Miscellaneous groups including households and pesticide users	117	ns	na	na	0.04 (nd - 1.84)	Bevenue et al. (1967b)
(2)	Indoor application of PCP solutions	16	ns	ns (1 - 10)	na	ns (0.030 - 0.150)	Zimmerli et al. (1979)
(3)	Residents of log homes treated with PCP solutions	5	ns	0.29 (0.20 - 0.38)[a]	1.126 (0.580 - 1.750)	0.084 (0.047 - 0.216)	Hernandez & Strassmann-Sundy (1980)
		32	ns	na	0.330 (0.116 - 1.084)	0.013 (0.002 - 0.087)	
(4)	"No occupational exposure"; control group for Number 5 in Table 20	32	ns	na	0.32 (0.002 - 7.20)	0.03 (< 0.01 - 1)	Klemmer et al. (1980)
(5)	Indoor application of an average of 40 litre PCP solutions	989	ns	6.1 (nd - 25)[b]	na	0.044	Krause & Englert (1980)
			(< 9 years)	4.9[c] (2.5 - 9.5)		0.029[c] (0.013 - 0.071)	
	- Subgroups:						
	1. m < 18 years	16	ns	≤ 5	na	0.047[c] (0.017 - 0.107)	
	2. m ≥ 18 years	39	ns	≤ 5	na	0.023[c] (0.011 - 0.052)	
	3. f < 18 years	22	ns	≤ 5	na	0.033[c] (0.016 - 0.066)	
	4. f ≥ 18 years	39	ns	≤ 5	na	0.026[c] (0.015 - 0.059)	

Table 21 (contd).

	5. m < 18 years	23	ns	> 5	na	0.079[c] (0.014 - 0.125)	
	6. m ≥ 18 years	31	ns	> 5	na	0.043[c] (0.011 - 0.146)	
	7. f < 18 years	25	ns	> 5	na	0.059[c] (0.011 - 0.103)	
	8. f ≥ 18 years	43	ns	> 5	na	0.039[c] (0.021 - 0.125)	
(6)	Indoor application of about 70 litres PCP solution						Sangster et al. (1982)
	- before ventilation	6	6	0.60 (0.14 - 1.20)	na	0.0032 (0.0007 - 0.0078)	
	- after ventilation	6	-	0.08 (nd - 0.24)	0.080 (0.025 - 0.190)[d]	0.0033 (0.0018 - 0.0080)	
	Indoor application of about 100 litres PCP solution about 75 litres PCP solution	2	0.5	0.15 (nd - 0.40)	0.033 (0.031 - 0.034)[d]	na	
	Indoor application of about 100 litres PCP solution	2	1	0.67 (0.44 - 0.95)	0.565 (0.47 - 0.66)[d]	na	
(7)	"Workers non-occupationally exposed"; control group for Number 21 in Table 20	27	ns	na	na	0.009 (nd - 0.034)	Siqueira & Fernicola (1981)

Table 21 (contd).

Number of study	Exposure/ comments	Sample size (number)	Length of exposure (months)	Air (μg/m³) mean (range)	Serum (mg/litre) mean (range)	Urine (mg/litre) mean (range)	Reference
(8)	Indoor application PCP solutions	80	ns	na	(0.0025 - 0.5)	(0.002 - 0.075)	Janssens & Schepens (1984)
(9)	Residents in buildings with PCP contaminated wood	46	ns	na	(0.001 - 0.110)[c]	na	Ruh et al. (1984)
(10)	Residents in homes treated with PCP	204 (234)	ns	na	0.058[c]	0.014[c]	Grimm et al. (1985)

[a] Air samples taken on the 1st and 2nd floor of a 2-story log house. A sample of interior surface wood contained 1132 mg PCP/kg (0.11%).
[b] 104 air indoor samples taken.
[c] Median (2/3 range).
[d] Plasma.
[e] Whole blood.
na = Not analysed.
nd = Not detectable.
ns = Not specified.
f = Female.
m = Male.

Table 22. Levels of PCP in the serum or urine of individuals without known exposure

Number of study	Comments	Sample size (number)	Indoor air ($\mu g/m^3$)	Serum (mg/litre) mean (range)	Urine (mg/litre) mean (range)	Reference
(1)	ns	6	na	na	0.005 (0.002 - 0.011)[a]	Cranmer & Freal (1970)
(2)	Control group for Number 8 in Table 20	ns	na	0.06[b] (0.03 - 0.2)	ns (0.001 - 0.057)[c]	Gossier & Schaller (1978)
(3)	US National Human Monitoring Program for Pesticides	418	na	na	0.0063 (nd - 0.193)	Kutz et al. (1978)
(4)	Control group for Number 2 in Table 21	12	na	na	0.0135 (0.006 - 0.023)	Zimmerli et al. (1979)
(5)	Control groups for Number 3 in Table 21; January 1980 "conventional" homes	42	na	ns (0.004 - 0.068)	ns (0.0007 - 0.011)	Hernandez & Strassmann-Sundy (1980)
	March 1980; untreated log homes	2	na	0.051 (0.034 - 0.075)	0.0014 (0.001 - 0.002)	
	March 1980; "conventional" homes	11	na	0.048 (0.015 - 0.055)	0.0025 (0.001 - 0.007)	

Table 22 (contd).

Number of study	Comments	Sample size (number)	Indoor air (µg/m³)	Serum (mg/litre) mean (range)	Urine (mg/litre) mean (range)	Reference
(6)	Control group for Number 5 in Table 21	207	nd[d]	na	0.0127 0.0102[b] (0.0038 - 0.0214)	Krause & Englert (1980)
(7)	ns	10	na	na	0.009 (0.003 - 0.016)	Lores et al. (1981)
(8)	Dutch draftees; control group for Number 6 in Table 21	99	na	0.128 (< 0.05 - 1.10) 0.088[b]	na	Sangster et al. (1982)
(9)	Control group for Number 7 in Table 21	12	na	ns	0.0009 (0.0002 - 0.002)	Janssens & Schepens (1984)
(10)	Non-specifically exposed persons	12 30	na	0.025 (0.019 - 0.036)	0.014 (0.007 - 0.034)[c]	Uhl et al. (1986)

[a] Range of replicate analysis of single urine samples.
[b] Median (2/3 range).
[c] Assuming a daily urine volume of 1.4 litre.
[d] Below detection limit of 0.1 µg/m³.
na = Not analysed.
nd = Not detectable.
ns = Not specified.

in Table 21, No. 5 in Table 22) observed that residents of log homes treated with PCP had a body burden that was between 5 and 60 times higher than that of residents of untreated log homes or conventional homes.

The most thoroughly designed survey (Krause & Englert, 1980; Aurand et al., 1981; Krause, 1982) included air analyses in the houses of a control group showing PCP concentrations generally below the detection limit of 0.1 μg/m³ (No. 6 in Table 22). The mean urine-PCP level of this group was about 3.5 times lower than that of the corresponding exposure group (No. 5 in Table 21). Much greater differences are encountered, if the highest concentrations measured are compared with the control levels. No significant correlation was established between the PCP levels in air and in urine, which again casts doubt on the validity of air-PCP levels as an exposure parameter. Nevertheless, on subdividing the exposed persons into 2 groups with PCP exposure either lower and equal to 5 μg PCP/m³ or higher than 5 μg PCP/m³, urinary-PCP levels seem to be elevated at the higher indoor concentrations. In addition, younger residents are obviously more exposed to PCP than older ones, perhaps because, on average, children spend more time at home.

When comparing PCP concentrations in the urine and blood, the levels in serum or plasma generally exceed those in urine, the extent of this difference varying according to the exposed group. The blood-PCP:urine-PCP ratio in people without known exposure or in persons exposed non-occupationally is considerably higher than that in occupationally exposed individuals. For comparison, in most of the cases of lethal intoxication summarized in Table 24 (section 6.2.2), urine-PCP levels even exceeded the corresponding blood levels. This pattern may be the result of heterogenous plasma-protein binding of PCP (section 6.6).

Shafik (1973) detected significant amounts of PCP (mean, 0.025 mg/kg; range, 0.005 - 0.052 mg/kg) in human adipose tissue samples from the general population. Similar values (mean, 0.0145 mg/kg) (Table 25, section 6.3.1) were reported by Grimm et al. (1981), whereas higher PCP contents (mean, 0.14 mg/kg; range, not detectable - 0.57 mg/kg) were found in adipose tissue samples from subjects with "no occupational contacts" (Ohe, 1979).

Samples of human milk were found to contain between 0.03 and 2.8 μg PCP/kg (mean, 0.68 ± 0.05 μg/kg), which is considerably less than the PCP levels usually found in other body fluids or tissues (Gebefuegi & Korte, 1983).

In investigating the apparent decrease in sperm density in US males over the last 30 years, Dougherty et al. (1980) and Kuehl & Dougherty (1980) detected PCP (100 - 200 ppb) in all 50 samples of human seminal plasma analysed. They also

observed that PCP was selectively concentrated by the cellular material.

Only few monitoring data are available on the human body burden of microcontaminants as a result of exposure to PCP. Rappe et al. (1982) analysed urine and blood samples of 9 workers exposed to PCP or L-PCP. In the case of 5 workers in the textile industry, urinary levels of PCDDs (total PCDDs, 3 - 365 ng/kg) and PCDFs (total PCDFs, < 1 - 45 ng/kg) paralleled the urinary-PCP levels (< 0.01 - 3.12 mg/litre). Similar levels of these impurities were found in the blood of 4 tannery workers 8 months after last exposure, but these could not be compared with urinary-PCP levels. However, in both groups, the concentration pattern of the different isomers reflected the different proportions of contaminants in commercial PCP products.

Because of their high fat-solubility and slow metabolic degradation and elimination, impurities of PCP such as HCB, PCDDs, and PCDFs are expected to accumulate in body fat. No data are available concerning the accumulation behaviour of these microcontaminants as a result of human PCP uptake. However, levels of dioxins in the milk- or body-fat of cows orally treated with technical-grade PCP (10 mg/kg body weight per day) were about 1000 times higher than those in blood, indicating a substantial accumulation (Firestone et al., 1979). In addition, the three dioxins detected (1,2,3,6,7,8-H_6CDD, 1,2,3,4,6,7,8 H_7CDD, and OCDD) declined comparatively slowly from about 20, 40, and 25 µg/kg composite milk-fat to 4.3, 6.9, and 3 µg/kg, respectively, 100 days after PCP feeding was stopped. For comparison, the steady-state PCP level of about 40 mg/kg in blood or 4 mg/kg in composite milk dropped to basal levels (0.02 - 0.08 mg/kg) within less than 10 days. Firestone et al. (1979) concluded from their results that "the absence of PCP in milk or biological tissue affords no guarantee of the absence of biologically active dioxins".

6. KINETICS AND METABOLISM

6.1 Absorption

6.1.1 Animal studies

PCP is readily absorbed through the skin as well as through the respiratory and gastrointestinal tracts. Braun & Sauerhoff (1976) administered a single oral dose of 10 mg PCP/kg body weight in corn oil to 3 male and 3 female rhesus monkeys and calculated the half-life for absorption to be 3.6 h in males and 1.8 h in females. After 12 - 24 h, plasma levels peaked in the range of 10 - 30 mg PCP/litre.

In rats given a single oral dose of 10 mg of ^{14}C-PCP/kg body weight, the peak plasma concentration (50 mg/litre) was attained much earlier, after 4 - 6 h. The absorption rate constants were 1.95 and 1.52/h for males and females, respectively (Braun et al., 1977); assuming first order kinetics, the half-life for absorption can be calculated to be 0.36 and 0.46 h, respectively.

Rapid absorption of PCP was also observed in rats during 20-min inhalation of approximately 5.7 mg PCP/kg body weight (Hoben et al., 1976d) and in mice following intraperitoneal and subcutaneous injections of ^{14}C-PCP (Jakobson & Yllner, 1971).

The same holds true for fish. Goldfish exposed to PCP medium (0.4 mg/litre) absorbed PCP rapidly, until a lethal level of approximately 100 mg/kg body weight was reached after about 5 h (Kobayashi & Akitake, 1975a). The apparent route of PCP uptake was via the gills and the skin. Similarly, PCP was rapidly taken up from the water by rainbow trout and assimilated into various tissues (Glickman et al., 1977).

6.1.2 Human studies

Braun et al. (1979) studied 4 healthy male volunteers of normal weight, between 21 and 55 years of age, who ingested a dose of 0.1 mg Na-PCP (> 99% purity)/kg body weight. The observed half-life for absorption was about 1.3 h. The peak plasma level of 0.245 mg PCP/litre occurred 4 h after ingestion of PCP. In the study of Uhl et al. (1986), the PCP level in the plasma of a male volunteer was approximately 0.185 mg/litre, 2 days after a single oral dose of 0.016 mg ^{13}C-PCP/kg body weight in 40% ethanol. This implies that absorption of PCP, when dissolved in alcohol, is much greater than when it is dissolved in water.

For the general population, the uptake of PCP by the oral route is thought to be more significant than that via other

routes of exposure. For individuals exposed to high airborne concentrations of PCP in the work-place or in PCP-treated dwellings, the major routes of exposure are probably via the skin and lungs. No experimental data are available concerning these routes. However, the cases of acute intoxication reported were almost exclusively due to extensive skin contact with PCP or to the inhalation of high doses of PCP, which subsequently led to high PCP levels in the human body.

Bevenue et al. (1967a) reported a case of PCP absorption through the skin. A male individual had skin contact with PCP for 10 min while cleaning a paint brush in a can containing a solution of 4% PCP. Two days later, a urinary-PCP level of 236 µg/litre was measured.

One case of oral uptake has been reported (Haley, 1977). A 71-year-old Japanese male had intentionally ingested an amount estimated at between 113 and 226 g of weed killer containing 12% PCP. Although the patient was treated with gastric aspiration and lavage within the next hour, a substantial amount of PCP must have already been absorbed as indicated by the high serum level of 150 mg PCP/litre, 5 h after the incident.

6.2 Distribution

6.2.1 Animal studies

Available information indicates that usually the highest PCP levels can be found in the urine immediately after exposure, and consequently, the PCP concentrations in the tissues account for only a small fraction of the dose applied. This is reflected by the data on excretion and recovery of radioactivity from groups of rats, 9 and 10 days after oral administration of 10 and 100 mg PCP/kg body weight, respectively (Table 23). It should be noted that the percentages of the dose recovered are to be considered as cumulative over the period of 9 days (10 mg/kg dose) or 8 days (100 mg/kg dose) in the case of the excreta, while the PCP contents of the organs were only analysed 9 days after administration of 10 mg/kg body weight. Thus, PCP is apparently eliminated much more rapidly from the kidney than from the liver (section 6.5.1).

The results of early studies did not show a uniform distribution pattern of PCP in experimental animals but indicated that very high levels of PCP could be found in liver and kidneys (Truhaut et al., 1952b). However, following long-term exposure, most PCP was absorbed by the central nervous system.

Several recent studies on the distribution and elimination of PCP were performed using ^{14}C-labelled PCP, thus making the results more reliable. Larsen et al. (1972) studied the

Table 23. Recovery of radioactivity from rats given a single oral dose of 10 or 100 mg of ^{14}C-PCP/kg body weight[a]

	Percentage of radioactivity (mean ± SD) dose: 10 mg/kg	dose: 100 mg/kg
Excreta		
urine	79.8 ± 2.9	64.0 ± 14.9
faeces	18.6 ± 3.7	33.6 ± 13.7
expired $^{14}CO_2$	0.2 ± 0.1	-[b]
Organs[c]		
liver	0.315 ± 0.137	-[b]
kidneys	0.045 ± 0.014	-[b]
Total body	0.437 ± 0.142	-[b]
Cage rinse	1.4 ± 1.9	-[b]
Total recovery	99.8 ± 4.4	97.6 ± 2

[a] From: Braun et al. (1977).
[b] Samples were not analysed.
[c] Other organs analysed were the stomach, lungs, testes, ovaries, brain, heart, spleen, and adrenals. Each of these organs contained 0.005% of the dose or less and were included with the liver and kidneys in the total body figure.

tissue distribution in rats after administering oral doses between 31 and 40 mg ^{14}C-PCP/kg body weight. The body component containing the highest level appeared to be the liver, followed by the kidney and blood. Low levels of PCP were found in fat, brain, and muscle tissue. More than 99% of the total radioactivity in the blood was contained in the serum, indicating that PCP and/or its metabolites in the blood are not bound to the cellular constituents.

Jakobson & Yllner (1971) examined the distribution of PCP in the mouse after the subcutaneous or intraperitoneal injection of ^{14}C-PCP (15 - 37 mg/kg body weight). Autoradiographic studies showed that the highest specific activity was in the liver, the gall bladder and its contents, the wall of the stomach fundus, the kidney, and the contents of the gastrointestinal tract, while the lung, heart, and brain contained only negligible amounts of PCP.

PCP concentrations were highest in the plasma of rats immediately after a 20-min inhalation exposure to an aerosol of Na-PCP, resulting in a calculated dose of about 5.7 mg/kg body weight (Hoben et al., 1976d). About 35% of the dose was found in the plasma, while the liver contained about 25% and the lung a little less than 2% at time 0. After 24 h, the

liver showed the highest PCP level followed by the plasma and the lung. Other organs were not examined.

Zenzen (1979) administered a daily dose of 15 mg ^{14}C-PCP/kg body weight intraperitoneally to rats for 15 days. On day 1, the highest PCP levels in the organs examined were found in the liver and kidney of male rats, comprising 14.1 and 14.3 %, respectively, of the total activity on a dry weight basis. Similar concentrations were measured in the testicle. However, on a fresh weight basis, the levels in this organ were similar to those in the other endocrine organs.

Preliminary data obtained from a single sheep (Wilson et al., 1982) indicated that PCP is absorbed into the lymphatic system; 47% of the PCP dose (10 mg/kg in corn oil, given by intraruminal injection) remained in the digestive tract 36 h after dosing. Of the absorbed PCP (53% of total dose), approximately 17% was found in the lymph collected through a thoracic duct canula. The remainder was probably absorbed from the digestive tract directly into the blood.

To study the placental transfer of PCP in rats, 60 mg ^{14}C-PCP/kg body weight was orally administered to pregnant rats on day 15 of gestation. The amount of specific radioactivity in the maternal blood-serum was greatest at 8 h (about 1.1% of the administered dose per gram of tissue), but, in the placentas and fetuses, it never exceeded 0.3% and 0.1%, respectively (Larsen et al., 1975). Thus, the amount of PCP that crosses the placental barrier is very low. Contrasting data have been obtained in a preliminary observation of a single pregnant monkey, but no full report has been published (Müller, 1981).

Kobayashi (1979) observed an accumulation of ^{14}C in various organs of goldfish exposed to 0.1 mg ^{14}C-PCP/litre water. The gall bladder contained the highest ^{14}C level after a 24-h exposure. The biliary concentration increased, even after fish had been transferred to clean, running water for 24 h, whereas a decrease was observed in the levels in all other organs examined (Kobayashi & Akitake, 1975b). This characteristic accumulation indicates that conjugated PCP is transferred to the gall bladder and bile due to an enterohepatic circulation (section 6.5.1).

6.2.2 Human studies

Human data concerning tissue distribution following PCP uptake are derived mainly from autopsy results on victims of fatal intoxications (Table 24). No exact conclusions can be drawn from these data with regard to PCP accumulation, though PCP levels in the liver, kidney, and lungs are often elevated. The high levels in the lungs reported in some cases might be related to inhalation uptake of PCP. Similarly, the stomach

Table 24. PCP levels found in human tissues and body fluids after PCP intoxication resulting in death

Reference	Case number	Urine (mg/litre)	Blood (mg/litre)	Liver (mg/kg)	Kidney (mg/kg)	Lung (mg/kg)	Brain (mg/kg)	Supposed routes of uptake
Truhaut et al. (1952b)	1	55	5	10	5	1.5	na	dermal[a]
	2	96	6	52	21	38	6.5	dermal[a]
Gordon (1956)	1	70	50	65	95	145	20	inhalation, dermal[a]
Menon (1958)	1	160	na	na	na	na	na	inhalation, dermal[a]
Blair (1961)	1	na	na	59	41	na	na	dermal, oral[a]
	2	na	na	62	84	76	na	inhalation[a]
	3	na	na	59	63	na	na	oral[b]
Mason et al. (1965)	1	na	79	66	na	na	10	inhalation[a]
	2	365	110	89	86	na	25	inhalation[a]
Burger (1966)	1	na	39	na	na	na	na	oral[d]
Barthel et al. (1969)	1	na	na	na	27.6	na	na	dermal[c]
Cretney (1976)	1	75	173	225	116	na	na	oral(?)[d]
Wood et al. (1983)	1	29	16	52	639	116	na	inhalation, dermal[a]

[a] Occupational exposure.
[b] Accidentally contaminated food.
[c] accidentally contaminated diapers.
[d] Suicide.

na = Not analysed.

of the individual who committed suicide by ingesting PCP contained 750 mg PCP/kg, which highly exceeded the concentrations found in the other body parts examined (Cretney, 1976). An unusually high kidney-PCP level of 639 mg/kg, reported by Wood et al. (1983), might have been due to kidney malfunction. In general, PCP levels in the various tissues do not indicate a clear accumulation of PCP, since blood-PCP levels are often similar to the corresponding tissue concentrations. Levels in urine can vary depending on the actual urine volume in the bladder at the time of poisoning and the pH value. From the data in Table 24, liver and kidney residues associated with acute lethal intoxications can be estimated to be 10 - 225 mg PCP/kg and 5 - 145 mg PCP/kg, respectively.

There is a paucity of data on the distribution of PCP in the tissues and body fluids in the general population. In 2 investigations (Table 25), autopsy samples were collected from human subjects in Northern Bavaria (Federal Republic of Germany) with no known history of PCP exposure. Grimm et al. (1981) concluded from the data that there was only a slight tendency for PCP to accumulate in both liver and kidney. The relatively high level observed in the brain samples was attributed to the fact that most of the persons with high brain-PCP levels had bled to death. In such cases, a cerebral hypoxia preceding the death might have led to the breakdown of the blood-brain barrier and accumulation of PCP in the brain. Löwer (1982) found much lower brain-PCP levels, in conjunction with liver and kidney levels similar to those reported by Grimm et al. (1981). There was no correlation between PCP levels in tissues and the age of the person examined (Löwer, 1982). Moreover, PCP levels in the body fluids were of the same order of magnitude as those in the tissues (Grimm et al., 1981).

6.3 Metabolic Transformation

6.3.1 Animal studies

The first studies on the fate of PCP in the body were conducted by Deichmann et al. (1942), who obtained evidence of metabolic transformation in the rabbit after oral administration and in the rat after intraperitoneal dosing with Na-PCP. The authors did not identify any metabolites.

Later studies using more advanced analytical methods have shown that PCP is metabolized, either to tetrachlorohydroquinone through oxidation or conjugated to PCP glucuronide. Tetrachlorohydroquinone was found in its free form in the urine of mice and rats (Jakobson & Yllner, 1971; Ahlborg et al., 1974); in the rat, it is also conjugated with glucuronic acid (Ahlborg et al., 1978). Traces of trichlorohydroquinone

Table 25. Medians, means, and ranges of PCP concentrations in tissues and body fluids at autopsy from people without known exposure

	Number of cases	Urine (mg/litre)	Blood (mg/litre)	Liver (mg/kg)	Kidney (mg/kg)	Brain (mg/kg)	Body fat (mg/kg)	Spleen (mg/kg)
Median	21[a]	0.0044	0.0233	0.0670	0.0430	0.0470	0.0127	0.0190
5. Percentile		dl[b]	dl	0.0017	0.0240	0.0190	0.0100	0.0070
95. Percentile		0.1603	0.0679	0.1735	0.0950	0.0725	0.0225	0.0325
Mean		0.0297	0.0260	0.0860	0.0641	0.0491	0.0145	0.0208
Median	51[c]	na[d]	na	0.0720	0.0223	0.0180	na	na
Lowest value		na	na	0.0140	nd[e]	nd	na	na
Highest value		na	na	0.4190	0.1040	0.0560	na	na

[a] From: Grimm et al. (1981).
[b] dl = detection limit = 0.001 mg PCP/litre urine; 0.005 mg PCP/litre blood.
[c] From: Löwer (1982).
[d] na = not analysed.
[e] nd = not detected (detection limit = 0.010 mg PCP/kg wet tissue).

formed by the reductive dechlorination of tetrachlorohydroquinone were found in the urine of rats. The formation of tetra- and trichlorohydroquinone as well as total elimination during the first 24 h can be enhanced through pretreatment with 3-methylcholanthrene or 2,3,7,8-T_4CDD. Phenobarbital only increases the metabolism to tetrachlorohydroquinone. These observations were confirmed by in vitro tests on rat liver microsomes (Ahlborg & Thunberg, 1978). Glucuronidation rates were not significantly altered by pretreatment with phenobarbital or 3-methylcholanthrene (Lilienblum, 1985).

In contrast to these rodent species, the rhesus monkey eliminates PCP unchanged in the urine (Braun & Sauerhoff, 1976). This is the only recent study that failed to detect any metabolites of PCP.

Detoxication of PCP has also been observed in fish. While no dechlorination processes have been reported, conjugation and subsequent excretion of the PCP conjugates occurs: PCP glucuronide is formed and excreted into the bile of both goldfish (Kobayashi & Nakamura, 1979b) and rainbow trout (Glickman et al., 1977), while pentachlorophenylsulfate is excreted into the surrounding water through the gills and in the urine of goldfish (Kobayashi & Nakamura, 1979a,b).

6.3.2 Human studies

Most of the human data available consist of analyses of urine samples from people exposed to different uncontrolled PCP regimes.

In the studies of Braun et al. (1979) and Uhl et al. (1986) on male volunteers (section 6.1.2), PCP was eliminated as both the parent compound and glucuronide. No other metabolites could be detected. Ahlborg et al. (1974) found tetrachlorohydroquinone in the urine of 2 occupationally exposed spray operators, who were also exposed to other chlorophenolic compounds.

Recently, the metabolic transformation of PCP to tetrachlorohydroquinone was substantiated by Juhl et al. (1985); human and rat liver homogenates showed similar metabolizing activities. The rate of PCP metabolism depended on the PCP concentration and was 1000 times lower at 1 mmol/litre (266 mg/litre) than at 0.01 mmol/litre (2.66 mg/litre).

6.4 Elimination and Excretion

6.4.1 Animal studies

PCP has been rapidly eliminated by most of the animals examined. It is cleared from the plasma by its distribution

to the tissues and by excretion via the urine and the faeces; the metabolites, when produced, are also rapidly excreted.

The uptake of PCP by the tissues accounts for only a small amount of the total PCP dose taken up by the body (section 6.2.1). Most of it leaves the body immediately after uptake, mainly through the urinary excretion of PCP and its metabolites. The proportions of PCP excreted via the two major excretion routes in the rat, mouse, and monkey are summarized in Table 26. Although the species and the test conditions differed, the excretion patterns were very similar: renal excretion amounted to between 45 and 83% of the total dose applied, while most of the remaining activity appeared in the faeces. Thus, excretion of PCP and its metabolites mainly occurs via the kidneys, and to a lesser extent by the processes of gastric and biliary secretion.

Table 26. Urinary and faecal excretion of ^{14}C activity as a percentage of a single dose of ^{14}C-PCP

Species	Dose (mg/kg body weight)	Time (h)	% recovery in: urine	faeces	Reference
Monkey					
male	10[a]	168	75	12	Braun & Sauerhoff
female	10[a]	360	70	17	(1976)
Monkey	30[a]	144	51.7	4.3	Ballhorn et al.
male	50[a]	144	44.9	11.3	(1981)
Rat	10[a]	216	80	19	Braun et al. (1977)
	100[a]	192	64	34	
Mouse	14.8[b]	96	83	8	Jakobson & Yllner
	18.2[b]	96	62	5	(1971)
	37.2[b]	96	73	4	
	35.2[b]	168	82	10	
	36.8[b]	168	80	12	

[a] Oral (corn oil solutions).
[b] Intraperitoneal.

Only trace amounts of radioisotopes from the metabolism of labelled compounds are expired. Although this route is of minor importance, it could indicate other metabolic processes, provided that analytical errors can be excluded. However, Larsen et al. (1972) questioned whether expired ^{14}C originated from PCP metabolism, attributing it, instead, to impurities in the radiolabelled PCP.

Ahlborg et al. (1974) found that the radioactivity from labelled PCP excreted in the urine of mice treated intra-

peritoneally (10 mg/kg body weight) consisted of about 41% unchanged PCP, 13% conjugated PCP, 24% unconjugated, and 22% conjugated tetrachlorohydroquinone. For rats, the corresponding values were 60%, 9 - 16%, 7%, and 16 - 22%, respectively (Ahlborg et al., 1978).

Following an oral dose of 100 mg/kg body weight, the urinary metabolites of ^{14}C-PCP in rats accounted for 75% unchanged PCP, 9% PCP glucuronide, and 16% tetrachlorohydroquinone. Levels of the last compound were below detectable values in the blood-plasma (Braun et al., 1977). The authors concluded that the rate-limiting step for the elimination of the metabolites of PCP is the rate of metabolism rather than that of urinary excretion and therefore, PCP metabolites were unlikely to accumulate in the body.

The proportions of PCP glucuronide in urine may have been underestimated to date; this metabolite has recently been shown to undergo a partial hydrolysis under weakly acidic conditions in urine (Lilienblum, 1985).

In contrast to the rodents, rhesus monkeys excreted all of the ^{14}C activity in urine as unmetabolized PCP (Braun & Sauerhoff, 1976).

Goldfish, in addition to free PCP, mainly excrete sulfate and glucuronide conjugates via 3 pathways of elimination: the amounts of PCP lost by the branchial, renal, and biliary routes were 52, 24, and 22% of the total amount of PCP excreted by the fish in the 24 h following a 24-h exposure to 0.1 mg PCP/litre water. The excretion of PCP from the body surface was minor. About 30% of the PCP excreted via the gills was in the unchanged form, whereas almost all the PCP excreted in both the bile and urine was conjugated. PCP sulfate was the major conjugate in the branchial and renal routes, while PCP glucuronide was the primary biliary conjugate (Kobayashi & Nakamura, 1979b).

6.4.2 Human studies

The PCP concentration in human urine has been widely used as an indicator of the PCP body burden (section 5.4), based on the fact that renal excretion of PCP is the major elimination route in man. In the study of Braun et al. (1979) (section 6.3.2), within 168 h of ingesting 0.1 mg Na-PCP/kg body weight, volunteers excreted 74% of the total dose in urine as PCP and 12% as PCP glucuronide. About 4% of the total dose was eliminated in the faeces; this amount consisted of equal parts of both free PCP and PCP glucuronide. The fate of the remaining 10% of the dose was not discussed.

Uhl et al. (1986) found that about 30% of PCP was excreted as glucuronide in the urine of a volunteer, up to 4 days after a single dose of 0.31 mg PCP/kg body weight (section 6.5.2).

However, in contrast to the study of Braun et al. (1979), the percentage of PCP glucuronide gradually increased to reach about the normal range determined for people not specifically exposed (65 ± 5% PCP glucuronide) after about 14 days. The findings of Zimmerli et al. (1979) and Janssens & Schepens (1984) also indicated that long-term exposure result in a higher proportion of conjugated PCP than that reported by Braun et al. (1979). On the average, two thirds of the PCP detected in the urine samples of non-occupationally exposed people was conjugated.

6.5 Retention and Turnover

6.5.1 Animal studies

Pharmacokinetic data on the retention and half-life of PCP in the compartments also indicate that most of the PCP absorbed is rapidly eliminated from the body.

The dynamics of elimination of PCP and its metabolites depend on the species and the sex of the test animal. As summarized in Table 27, the monkey differs from other animal species in showing a much slower elimination rate as expressed by the half-life for the clearance from urine and plasma, perhaps because monkeys do not metabolize PCP.

An extensive enterohepatic circulation of PCP is also suggested by the slow but steady elimination of ^{14}C activity in the faeces of the monkeys (Braun & Sauerhoff, 1976). On treating rhesus monkeys with cholestyramine, this enterohepatic circulation was interrupted as the cholestyramine bound the PCP and/or its metabolites and bile acids, thus preventing their reabsorption (Ballhorn et al., 1981). However, the results were derived from only 4 monkeys in single studies.

Apart from the monkey studies, pronounced differences in PCP kinetics that are only in part related to the species or type of application have been observed in different single-dose studies (Table 27). Braun & Sauerhoff (1976) and Braun et al. (1977) observed a monophasic elimination of PCP in monkey, while, in rats, 2 phases could be distinguished (Fig. 4): an α-phase with a rapid elimination rate (elimination half-lives, 13 - 17 h) followed by a β-phase (elimination half-lives for male rats, 40 h (10 mg/kg body weight), 121 h (100 mg/kg body weight)) with a comparatively slow elimination rate. However, the β-phase, is not well defined, as it does not remain constant.

Braun et al. (1977) found that, at a higher dose (100 mg/kg body weight), the female rats followed the monophasic scheme (elimination half-life, 27 h) (Fig. 4). Hoben et al. (1976d) also reported a monophasic elimination in rats,

Table 27. Comparison of PCP elimination kinetics in mammals after administration of single doses

Species	Dose (mg/kg body weight)	Elimination via	Sex	Elimination half-life (h) of phase α	Elimination half-life (h) of phase β	Kinetics	Reference
Mouse[a,b]	15 - 37	urine	female	approximately 24	-	not reported	Jakobson & Yllner (1971)
Rat[c]	37 - 41	urine	female	approximately 10	2448	biphasic	Larsen et al. (1972)
Rat[d]	5.7	urine	male	approximately 24	-	monophasic	Hoben et al. (1976d)
Rat[c]	10	urine and faeces	female	13	33	biphasic	Braun et al. (1977)
			male	17	40	biphasic	
	100	urine and faeces	female	27	-	monophasic	
			male	13	121	biphasic	
Rat[a]	15	all routes	female	6.3 - 9.9	33-374	biphasic	Zenzen (1979)
Monkey[c]	10	urine	female	92.4	-	monophasic	Braun & Sauerhoff (1976)
			male	40.8	-	monophasic	

[a] Intraperitoneal.
[b] Subcutaneous.
[c] Oral.
[d] Inhalation.

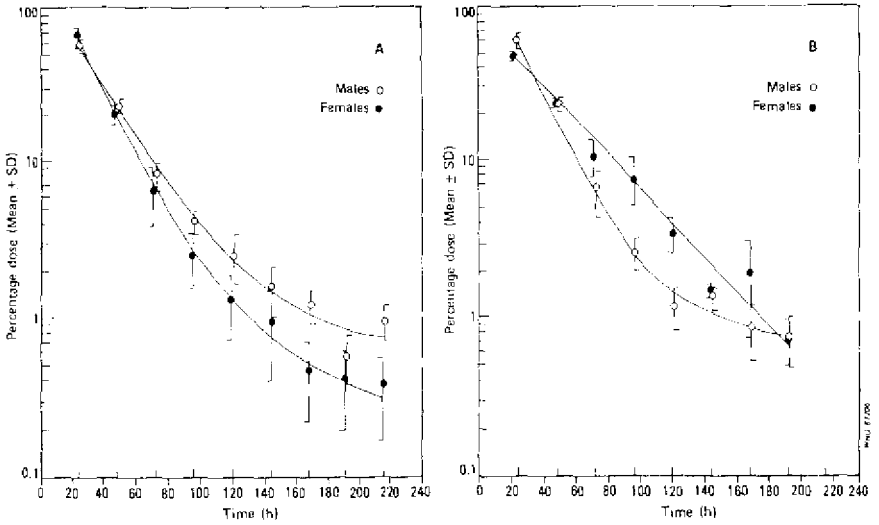

Fig. 4. Elimination of radioactivity via urine and faeces from the body of rats given a single oral dose of 10 (A) and 100 mg of ^{14}C-PCP/kg body weight (B). From: Braun et al. (1977).

while Larsen et al. (1972) and Zenzen (1979) described a distinct biphasic model. The accuracy of the unusually slow β-phase (102 days = 2448 h) reported by Larsen et al. (1972) has been questioned by Braun et al. (1977), since this value was obtained by subtracting the cumulative amount excreted in the urine from the total dose, without knowing the total recovery. On the other hand, the monophasic scheme claimed by Braun et al. (1977) for female rats dosed with 100 mg/kg body weight is not as distinct as it seems to be; for, on omitting the last sample measured at 192 h, a biphasic scheme could be fitted to the points as well (Fig. 4).

The amount of the PCP or ^{14}C activity remaining in the body several days after dosing differs markedly between test species. According to Braun et al. (1977), in each case, 90% or more of the radioactivity had been excreted by rats 3 days after dosing; detectable levels of PCP remained only in liver and kidney, 9 days after the 10 mg/kg dose (see also Table 23). As a result of a slower elimination rate, about 11% of the administered ^{14}C activity remained in the body of rhesus monkeys 15 days after oral application of 10 mg/kg body weight; approximately 80% of this remaining activity was identified in the large and small intestines and liver. Braun & Sauerhoff (1976) calculated that a steady-state concentration of PCP in plasma would be reached by the 10th repeated

daily dose; the approximate plasma concentration at this time was estimated to be 50 mg PCP/litre.

When comparing the turnover of PCP in rats after single and after repeated inhalation exposure, Hoben et al. (1976d) did not find any evidence of accumulation. The clearance rates for urine, plasma, liver, and lung were fairly parallel. After repeated inhalation exposures to about 5.9 mg/kg body weight, the PCP body burden did not increase as expected from the 24-h half-life following a single exposure. On the basis of the increased urinary excretion, the authors concluded that the biotransformation was accelerated and possibly induced by prior exposure to PCP.

6.5.2 Human studies

Braun et al. (1979) observed a time lag in the urinary excretion rate following a single oral dose of 0.1 mg Na-PCP/kg body weight given to 4 volunteers (section 6.1.2). Maximum urinary excretion was reached 40 h after ingestion and 36 h after the maximum plasma level of 0.245 mg PCP/litre. The authors ascribed this delay to a strong enterohepatic circulation similar to that reported in rats and monkeys. The elimination half-life for PCP in plasma was about 30 h. The elimination half-life for PCP and PCP glucuronide in urine was 33 and 13 h, respectively. The elimination of PCP from plasma in these human subjects followed linear kinetics and was monophasic, and resembled the elimination kinetics reported for the monkey. Elimination kinetics in the rat are biphasic; however, the rate constants and half-lives for the absorption and elimination of PCP from rat plasma are more similar to those for men than those for monkeys.

Using the kinetic parameters determined in their single-exposure studies, Braun et al. (1979) calculated that men ingesting 0.1 mg PCP/kg body weight daily (based on 100% uptake of 0.5 mg PCP/m^3 by a man carrying out light work) would attain a steady-state plasma concentration of 0.491 mg/litre, after 8.4 days. This suggests that there is no cumulative effect, even with repeated daily low-level exposure. This conclusion is based on a simulation model for the daily ingestion of PCP using data derived from single-dose studies.

Uhl et al. (1986) studied 3 healthy male volunteers aged 29, 24, and 47 years, exposed to single oral doses of PCP (purity > 99%) in 40% ethanol in 6 different studies. The doses varied from 0.016 to 0.31 mg PCP/kg body weight. Their results are in contrast to those of Braun et al. (1979). Uhl et al. (1986) determined PCP elimination half-lives of 16 days (plasma) and 18 - 20 days (urine), elimination rates being about 13 times slower than those reported by Braun et al.

(1979). Uhl et al. (1986) did not find any evidence for an enterohepatic accumulation mechanism. They ascribed the low elimination rate to the high protein-binding tendency of PCP and the concomitantly low PCP clearance observed (0.07 ml/min). At normal urinary pH (5 - 6), PCP exists in its phenolic form and therefore more than 99% of the filtered PCP is believed to be reabsorbed in the renal tubules. In one study, alkalinization of the urine by administration of sodium bicarbonate considerably enhanced the elimination rate of PCP in urine. Over the pH range 5.4 - 7.8, the rate of PCP elimination varied by a factor of 8; urinary excretion was approximately 2 µg PCP/h at pH 5.4 and about 16 µg PCP/h at pH 7.4.

The differences in the pharmacokinetic profile established in the 2 studies may be explained by the different experimental regimes. Uhl et al. (1986) administered the PCP in ethanol; Braun et al. (1979) administered the sodium salt of PCP in water. The role of the dietary status of the volunteers before and after the PCP ingestion or of any other factors is unknown. According to Uhl et al. (1986), the time lag necessary to attain a steady state after a change in the exposure, as calculated from the elimination half-life, is about 3 months. These authors estimated that the human body burden of PCP at steady state is 10 - 20 times higher than that estimated by Braun et al. (1979).

Reported cases of accidental PCP exposure as well as data from occupationally exposed people seem to confirm the results of Uhl et al. (1986). In the case of an accidental uptake of PCP through the skin (section 6.1.2), the urinary-PCP concentration decreased from 236 µg/litre, 2 days after the accident to 17 µg/litre, 51 days later (Bevenue et al., 1967a). From these data, an elimination half-life of about 15 days can be derived.

In the case of intentional ingestion of PCP (solvent: 82% aromatic petroleums) discussed in section 6.1.2, despite forced diuresis with furosemide and mannitol, the serum-PCP level of the patient decreased from the highest level on day 2 (155 mg PCP/litre) to 12 mg PCP/litre on day 37 (Haley, 1977), suggesting an elimination half-life of approximately 10 days.

Begley et al. (1977) surveyed PCP concentrations in the blood and urine of 18 workers in a wood-treatment factory before and during a 20-day vacation. The blood and urine levels of PCP decreased from an average of 5.14 mg/litre to 2.19 mg/litre and from 1.31 mg/litre to 0.59 mg/litre, respectively, during vacation. Elimination half-lives of about 9 days for both urine and plasma can be derived.

Casarett et al. (1969) calculated an excretion half-life of about 10 h, based on measurements made one day after a single inhalation exposure in 2 wood-treatment workers.

Despite this rapid elimination rate, the PCP concentrations in the urine of workers following a long-term high level exposure (PCP in urine, 1.6 - 2.6 mg/litre) did not decrease by more than 60 - 80% "even after a long absence from exposure" (Casarett et al., 1969). In a comparable survey with a group of woodworkers exposed long-term to Permatox 100 (3% PCP, 21% tetrachlorophenol), no clear elimination pattern could be found during a 16-day vacation (Kalman & Horstman, 1983); half-times for urinary elimination varied from 4 to 72 days, as estimated from the urinary-PCP levels at day 0 and day 16. A number of pre-exposed workers showed an increase in urinary-PCP during the vacation, either as a result of storage of PCP in tissues (section 6.6), additional exposure to PCP independent of work-place exposure, or a continuous biotransformation of hexachlorobenzene and similar compounds to PCP (section 5.2.2). However, the latter can hardly explain an increase in urinary-PCP levels of 53 - 88 µg/litre, as observed by Kalman & Horstman (1983); urinary-PCP levels range around 10 µg/litre for the general population and around 40 µg/litre for people exposed non-occupationally (section 5.2.3).

Since all controlled studies on the metabolism of PCP in mammals have been performed using pure PCP, a judgement of the influence of impurities in commercial PCP on the metabolism of PCP is not possible. In fish, Huckins & Petty (1983) observed a greater conjugation of PCP to its glucoronide with exposure to purified PCP compared with exposure to commercial PCP. Conjugation may be a rate-limiting step in its elimination, in which case the toxic impurities in industrial PCP formulations could alter the turnover pattern.

6.6 Reaction With Body Components

Braun et al. (1977) found that 99% of the PCP in rat plasma was bound to protein. Heterogenous binding has been demonstrated, indicating that, at very low plasma concentrations of PCP, the protein binding becomes even stronger, because of preferential binding to more limited but higher affinity sites. Braun et al. (1977) and Uhl et al. (1986) suggested that this heterogenous plasma-protein binding might be the cause of long-term urinary excretion of PCP. Hoben et al. (1976e) found that human plasma had a much higher capacity for binding to PCP than rat plasma; this could explain the longer retention times observed in human beings compared with that in the rat. The difference in binding capacity could not be accounted for by albumin fraction.

PCP is conjugated *in vitro* to palmitic acid in rat liver incubated with a coenzyme A-fortified microsomal system (Leighty & Fentiman, 1982). Presumably, the binding of PCP to

fatty acids could contribute to PCP retention in lipid-containing tissues.

Weinbach & Garbus (1965) had already discovered the strong affinity of PCP for rat liver mitochondrial protein. In more recent studies of Arrhenius et al. (1977a,b) on the subcellular distribution of PCP, PCP accumulation in microsomes or in the cytosol was approximately 6 and 3 times, respectively, higher than in the mitochondria. On this basis, the authors suggested that the microsomal functions, though 4 times less sensitive than mitochondrial oxidative phosphorylation, were disturbed by PCP concentrated in these organelles, possibly increasing the toxic and carcinogenic action of other xenobiotics.

7. EFFECTS ON ORGANISMS IN THE ENVIRONMENT

The toxic effects of chlorophenols have been studied in a number of organisms. The degree of oil solubility governs the toxicity of phenolic compounds by controlling their binding to lipoid cellular structures, e.g., biological membranes, which probably are the loci of action of PCP. Blackman et al. (1955a,b) showed that, with the duckweed Lemna minor and the mould Trichoderma viride, the lipophilic behaviour and, hence, the toxicity of chlorophenols increased with the degree of chlorination of the aromatic ring, PCP being the most effective chlorophenol. Similar results have been reported from studies on fish (Ingols & Gaffney, 1965), bacteria (Liu et al., 1982), and algae (Huang & Gloyna, 1968; Rowe et al., 1982).

Although there have been some studies on the effects of PCP on ecosystems, most of the toxicity data have been derived from single species trials. Moreover, most bioassays deal with acute rather than long-term toxic effects.

7.1 Microorganisms

The microbiocidal effectiveness of PCP has been the basis of its widespread use as a bactericide and fungicide (section 3.3). For instance, PCP at a concentration of 0.25% and 0.125% (v/v) was used to control the sapstain fungi Trichoderma harzianum and Phialophora sp., respectively (Cserjesi & Roff, 1975). Conkey & Carlson (1963) screened PCP-containing pesticides against 2 bacterial species and 2 species of fungi that are common in pulp and paper mill systems. Depending on the PCP formulation and the microbial species, complete inhibition occurred on agar plates at 4 - 250 ppm.

Ishizawa et al. (1961) found bacterial und fungal growth in soil to be depressed by PCP at 2 g Na-PCP/kg dry soil. Similarly, oxidative phosphorylation and ATPase activity in Micrococcus denitrificans cultures were strongly inhibited by PCP at a concentration of about 130 mg/litre (Imai et al., 1967).

In anaerobic soil containing 10 mg PCP/kg, Murthy et al. (1979) observed reduced soil respiration as PCP directly or indirectly inhibited cellulose degradation. The degradation of PCP itself may also be affected by the toxicity of this compound for degrading microorganisms.

Godsy et al. (1986) studied the effects of PCP on the methanogenic fermentation of phenol in anaerobic laboratory digestors. With PCP concentrations of 0.1 mg/litre or less, PCP was dechlorinated to non-toxic levels allowing for

complete bioconversion of phenol (200 mg/litre) and PCP, presumably to methane and carbon dioxide (CO_2). Higher PCP levels inhibited the methanogenic fermentation; at 5 mg PCP/litre, complete inhibition occurred.

Tam & Trevors (1981a,b) studied the effects of PCP on asymbiotic nitrogen fixation in soil. The EC_{50} values for the inhibition of nitrogenase activity in non-sterile soil, incubated aerobically and anaerobically, and in sterilized soil inoculated with Azotobacter sp. were 49.8 mg Na-PCP/kg, 186.8 mg Na-PCP/kg, and 660.8 mg Na-PCP/kg, respectively. The inhibition of both CO_2 evolution and oxygen uptake by Azotobacter vinelandii was found to be similar to that of nitrogen fixation activity (Tam & Trevors, 1981a). The high concentrations required for inhibition suggest that, at normal field application rates, no adverse effects on nitrogenase activity would be expected.

Na-PCP at 50 and 100 mg/kg had a stimulating effect on soil microbial electron transport activity, while 200 mg Na-PCP/kg caused 5.8% inhibition (Trevors, 1982c). Inhibition by Na-PCP was greater in soil enriched with glucose and yeast extract than in non-amended soil. Concentrations of 25 - 50 mg PCP/litre of nutrient broth delayed the growth of the bacterium Pseudomonas fluorescens, which does not degrade PCP. A 1-h exposure to 75 mg PCP/litre inhibited growth completely. Higher concentrations of PCP were required to produce inhibition of respiration. Oxygen consumption was reduced by 21% at a concentration of 25 mg PCP/litre, while CO_2 evolution was not inhibited (Trevors et al., 1981a; Trevors, 1982b).

Pre-exposure to PCP lowered the sensitivity of Pseudomonas fluorescens to PCP (Trevors et al., 1982). In addition, non-toxic concentrations of the antioxidants butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT), which have also been used as food additives, enhanced the toxicity of PCP for this bacterial species (Trevors et al., 1981b).

Izaki et al. (1981) found gram-negative bacteria to be more resistant to PCP than gram-positive bacteria. Some very resistent Pseudomonas strains tolerated over 500 mg PCP/litre. Studies on various mutants, in which the lipopolysaccharide layers were more or less defective, supported the hypothesis that these layers act as a barrier for PCP and impart resistance to gram-negative bacteria.

7.2 Aquatic Organisms

PCP has been used in aquatic environments as a molluscicide and an algicide. The potential hazard of PCP was recognized early, leading to a number of toxicological studies on aquatic organisms; these have been reviewed by US EPA

(1978) and Buikema et al. (1979). In general, PCP is extremely toxic for aquatic organisms. Apart from very sensitive or resistant species, there is apparently no significant difference in sensitivity to PCP between the different taxonomic groups (Adema & Vink, 1981).

7.2.1. Plants

Most toxicity tests on aquatic plants have been performed on algae, particularly the microscopic, free-floating forms. A selection of these tests is summarized in Table 28. One of the more striking features evident from the Table is the extreme variability in the PCP levels that result in toxic effects. For example, Adema & Vink (1981) determined that a nominal concentration of 7 mg/litre inhibited the growth of Chlorella pyrenoidosa by 50%. In contrast, Huang & Gloyna (1968) found that as little as 7.5 µg/litre caused complete destruction of chlorophyll in the same species.

At least part of this variability reflects different sensitivities to PCP between algal species. Adema & Vink (1981) found that the green alga Scenedesmus quadricauda had an EC_{50} for growth that was 87.5 times lower than that for Chlorella pyrenoidosa. The most sensitive algae were Ankistrodesmus falcatus and Microcystis sp., for which as little as 0.001 mg PCP/litre inhibited photosynthesis by an average of 21%, in semi-continuous cultures.

However, the tremendous variability in susceptibility to PCP presented in the Table cannot be accounted for solely by species-specific differences in sensitivity. They probably also reflect differences in the experimental conditions under which the tests were run, such as the ambient pH, which affects PCP toxicity for invertebrates (section 7.2.2), and presumably algae.

Some aquatic vascular plants have also been used for toxicity studies. The water hyacinth (Crassipes eichhornia) is relatively tolerant to Na-PCP; a concentration of 5 mg/litre was required to affect its appearance, and 80 mg/litre to kill the plant (Hirsch, 1942). Only 7.1×10^{-7} mol PCP/litre (approximately 0.19 mg/litre) were required to induce 50% chlorosis in the fronds of the duckweed (Lemna minor) (Blackman et al., 1955a). In contrast, Huber et al. (1982) noted a 50% decrease in the chlorophyll content of this aquatic macrophyte on exposure to 3 - 4 mg PCP/litre. Photosynthesis as well as the activity of glutamate dehydrogenase and alanine aminotransferase were similarly inhibited, but there was no pronounced effect on dark respiration.

Table 28. The toxicity of PCP and Na-PCP for algae

Test species	Aquatic system	Test type	Test duration (h)	Concentration (mg/litre)	Effects	Reference
Chlorella pyrenoidosa	freshwater	static	72	0.008	complete destruction of chlorophyll	Huang & Gloyna (1968)
Chlorella pyrenoidosa	freshwater	static and flow	96	7[a]	EC_{50}, growth	Adema & Vink (1981)
Scenedesmus quadricauda	freshwater	static and flow	96	0.08[a]	EC_{50}, growth	Adema & Vink (1981)
Microcystis aeruginosa	freshwater	static	96	1	NOEC, growth	Sloof & Canton (1983)
Scenedesmus pannonicus	freshwater	static	96	0.1	NOEC, growth	Sloof & Canton (1983)
Cylindrospermum licheniforme[b]	freshwater	static	72	2	no growth	Palmer & Maloney (1955)
Microcystis aeruginosa[b]	freshwater	static	72	2	no growth	Palmer & Maloney (1955)
Scenedesmus obliquus[b]	freshwater	static	72 - 168	2	growth inhibition	Palmer & Maloney (1955)
Chlorella variegata[b]	freshwater	static	72 - 504	2	no inhibition	Palmer & Maloney (1955)
Monochrysis sp.	marine	static and flow	96	0.2[a]	EC_{50}, growth	Adema & Vink (1981)

Table 28 (contd).

Test species	Aquatic system	Test type	Test duration (h)	Concentration (mg/litre)	Effects	Reference
Chlamydomonas sp.	marine	static and flow	96	1.4[a]	EC_{50}, growth	Adema & Vink (1981)
Phaeodactylum tricornutum	marine	static and flow	96	3[a]	EC_{50}, growth	Adema & Vink (1981)
Dunaliella sp.	marine	static and flow	96	3.6[a]	EC_{50}, growth	Adema & Vink (1981)
Chlorella ovalis	marine	static and flow	96	5.5[a]	EC_{50}, growth	Adema & Vink (1981)
Ankistrodesmus falcatus	marine	semi-continuous flow	216 - 264	0.001	inhibition of photosynthesis	Gotham & Rhee (1982)
Microcystis sp.	marine	semi-continuous flow	216 - 264	0.001	inhibition of photosynthesis	Gotham & Rhee (1982)
Melosira sp.	marine	semi-continuous flow	216 - 264	0.001	inhibition of photosynthesis and growth	Gotham & Rhee (1982)
Selenastrum capricornutum	marine	static	2	0.05 - 0.1	beginning inhibition of carbon assimilation rate	Jayaweera et al. (1982)
Selenastrum capricornutum	marine	static	2	2.66	complete inhibition	Jayaweera et al. (1982)

[a] Average results of static and flow-through tests.
[b] Na-PCP.

7.2.2 Invertebrates

As shown in Table 29, the toxicity of PCP or Na-PCP for invertebrates varies with concentrations ranging from 0.068 mg/litre to 10.39 mg/litre. Most of the reported 50% lethal or effective concentrations are below 1 mg/litre.

In general, developing embryos and larvae are more affected by PCP than the adults (Table 29). The most striking difference was reported by van Dijk et al. (1977), who found that, at the same Na-PCP concentration, the larvae of the marine decapod Palaemon elegans were inhibited (in terms of the 96-h LC_{50}) about 130 times more than the adults.

Dragonfly nymphs (Epicordulia sp.), damsel fly nymphs (Ischnura sp.), isopods (Asellus communis Say), and amphipods (Hyalella knickerbockeri Bate) were resistant to Na-PCP compared with other invertebrate species, and easily survived exposure to 5 mg/litre (Goodnight, 1942). Turner et al. (1948) found that 0.1 mg Na-PCP/litre was ineffective against mussels (Mytilus edulis), anemones, and barnacles, while a concentration of 1 mg/litre prevented attachment and growth in sea water.

The results of more recent studies, mainly conducted on annelids, molluscs, and crustaceans, are mostly based on median lethal or effective concentrations (LC_{50}, EC_{50}, TL_m). However, a comparison of acute toxicity data established within equal test duration may only be appropriate if the various organisms have similar life cycles. It is arbitrary to compare, for instance, the 96-h LC_{50} of copepods, crayfish, and trout. On a basis of the median life span, a 96-h toxicity test with the cladoceran Daphnia would correspond to a test with trout or carp lasting as long as one year.

Very few studies have been carried out to assess chronic or sublethal effects, or the influence of various environmental conditions on the toxicity of PCP. Examining the effect of Na-PCP on the burrowing activity of a lugworm (Arenicola cristata), Rubinstein (1978) noted a significant adverse effect at concentrations of 80 and 156 µg Na-PCP/litre. At both concentrations, no mortality was observed. The reduced lugworm activity could affect the sediment turnover.

At sublethal concentrations (120 µg PCP/litre), coelomic fluid glucose in the marine sandworm Neanthes virens increased to about twice the control levels after 24 h and then gradually decreased (Carr & Neff, 1981; Thomas et al., 1981). Ascorbic acid levels became elevated during exposure, indicating sublethal stress. During the acute lethal exposure (above 365 µg/litre), a significant hypoglycaemic response and ascorbic acid depletion were observed.

Table 29. The toxicity of PCP and Na-PCP for invertebrates

Test species	Life stage	Aquatic system	Test type	Test modifier	Test duration (h)	Concentration (mg/litre)	Effects	Reference
Tubificid worms[a,b]		freshwater	static	pH 7.5	24	0.31	LC_{50}	Whitley (1968)
Tubificid worms[a,b]		freshwater	static	pH 8.5	24	0.67	LC_{50}	Whitley (1968)
Tubificid worms[a,b]		freshwater	static	pH 9.5	24	1.40	LC_{50}	Whitley (1968)
Water flea (Daphnia magna)		freshwater	static		24	0.8	EC_{50}	Bringmann & Kühn (1982)
Fresh-water snail (Lymnaea acuminata)		freshwater	static		96	0.16	LC_{50}	Gupta & Rao (1982)
Fresh-water snail (Lymnaea acuminata)		freshwater	static		96	0.19[b]	LC_{50}	Gupta & Rao (1982)
Eastern oyster (Crassostrea virginica)		marine	static		48	< 0.25	LC_{50}, egg development	Davis & Hidu (1969)
Eastern oyster (Crassostrea virginica)		marine	static		336	0.07	LC_{50}, survival of larvae	Davis & Hidu (1969)
Pacific oyster[b] (Crassostrea gigas)		marine	static		48	0.027	4.3% abnormal embryos	Woelke (1972)

Table 29 (contd).

Pacific oyster (Crassostrea gigas)		marine	static	48	0.069	72.4% abnormal embryos	Woelke (1972)
Pacific oyster (Crassostrea gigas)		marine	static	48	0.11	100% abnormal embryos	Woelke (1972)
Eastern oyster (Crassostrea virginica)		marine	static	48	0.04	EC_{50}, embryo development	Borthwick & Schimmel (1978)
European brown shrimp (Crangon crangon)[b]	adult	marine	static	96	1.79	LC_{50}	van Dijk et al. (1977)
European brown shrimp (Crangon crangon)[b]	larvae	marine	static	96	0.11	LC_{50}	van Dijk et al. (1977)
Marine decapod (Palaemon elegans)[b]	adult	marine	static	96	10.39	LC_{50}	van Dijk et al. (1977)
Marine decapod (Palaemon elegans)[b]	larvae	marine	static	96	0.08	LC_{50}	van Dijk et al. (1977)
Brackish water decapod (Palaemonetes varians)[b]	adult	marine	static	96	5.09	LC_{50}	van Dijk et al. (1977)
Brackish water decapod (Palaemonetes varians)[b]	larvae	marine	static	96	0.36	LC_{50}	van Dijk et al. (1977)
Grass shrimp (Palaemonetes pugio)[b]	inter-molt	marine	static	96	2.63	LC_{50}	Conklin & Rao (1978)

Table 29 (contd).

Test species	Life stage	Aquatic system	Test type	Test modifier	Test duration (h)	Concentration (mg/litre)	Effects	Reference
Grass shrimp (*Palaemonetes pugio*)[b]	early premolt	marine	static		96	2.74	LC_{50}	Conklin & Rao (1978)
Grass shrimp (*Palaemonetes pugio*)[b]	late premolt	marine	static		96	0.44	LC_{50}	Conklin & Rao (1978)
Brown shrimp (*Penaeus aztecus*)[b]		marine	flow		96	> 0.195	LC_{50}	Schimmel et al. (1978)
Copepod (*Pseudodiaptomus coronatus*)[b]		marine	static		96	0.068	LC_{50}	Hauch et al. (1980)
Crayfish (*Astacus fluviatilis*)		marine	semi-continuous flow	pH 7.5	192	53	LC_{50}	Kaila & Saarikoski (1977)
Crayfish (*Astacus fluviatilis*)		marine	semi-continuous flow	pH 6.5	192	9	LC_{50}	Kaila & Saarikoski (1977)

[a] Mixed population of *Tubifex tubifex* and *Limnodrilus hoffmeistori*.
[b] Na-PCP.

The acute toxicity of PCP has been found to be pH dependent (Table 29). The data of Whitley (1968) indicate that the toxicity of PCP for tubificid worms increased up to almost 5-fold, when the pH value decreased from 9.5 to 7.5. This is consistent with the sensitivity pattern of various oligochaete species (Chapman et al., 1982). Similarly, lowering the pH from 7.5 to 6.5 increased the toxicity of PCP for the crayfish (Astacus fluviatilis) by a factor of 5.9 (Kaila & Saarikoski, 1977). The non-ionized form of a compound penetrates biological membranes much more easily than the ionized form, which accounts for the effects of pH on PCP toxicity.

7.2.3 Vertebrates

Most studies on vertebrates have been performed with fish. In short-term studies, the LC_{50} values for PCP or Na-PCP are generally less than 1 mg PCP/litre, and, in many cases, even less than 0.1 mg PCP/litre (Table 30).

The effectiveness of purified PCP and Na-PCP as well as of commercial products has been investigated under comparable conditions in only a few cases. Borthwick & Schimmel (1978) determined that the 96-h LC_{50} for 14-day-old sheepshead minnow fry exposed to analytical grade PCP was similar to that of the commercial formulation Dowicide G (0.392 and 0.516 mg/litre, respectively, corresponding to 1.47 and 1.41 µmol). Similarly, the prolarval pinfish was, on a molar basis, about equally affected by analytical grade Na-PCP (LC_{50}, 0.038 mg/litre = 0.14 µmol) and Dowicide G (LC_{50}, 0.066 mg/litre = 0.18 µmol).

Differences in the toxicity of PCP and Na-PCP for fish have been observed under various test conditions. For example, both the goldfish (Carassius auratus) and the sheepshead minnow (Cyprinodon variegatus) were more affected by PCP in static than in continuous-flow bioassays (Table 30). Ruesinck & Smith (1975) noted that the fathead minnow (Pimephales promelas) was more resistant to Na-PCP at 25 °C than at 15 °C. In contrast, Crandall & Goodnight (1959) observed that higher temperatures increased the toxicity of Na-PCP for the fathead minnow (Pimephales promelas), i.e., the LD_{50} at 10 °C, 18 °C, and 26 °C was 260, 81, and 46 mg/litre, respectively. Temperature was also found to control PCP toxicity for rainbow trout (Salmo gairdneri) (Hodson & Blunt, 1981). Eggs of trout exposed to PCP at 0.01 - 0.1 mg/litre) showed elevated mortality between fertilization and hatch and reduced weight at hatch. The effects on hatch weight were greater at 6 °C than at 10 °C, while growth rates were reduced more at 20 °C than at 12 °C.

Table 30. The toxicity of PCP and Na-PCP for various fish species

Test species	Life stage	Aquatic system	Test type	Test modifier	Test duration (h)	Concentration (mg/litre)	Effect	Reference
Brown trout (Salmo trutta)		freshwater	static		24	0.2	LC_{50}	Hattula et al. (1981)
Bluegill sunfish (Lepomis macrochirus)		freshwater	static	hardness	48	0.03 - 0.04	LC_{50}	Inglis & Davis (1972)
Goldfish (Carassius auratus)		freshwater	static	hardness	48	0.08 - 0.17	LC_{50}	Inglis & Davis (1972)
Fathead minnow (Pimephales promelas)	juvenile	freshwater	flow		48	0.21	LC_{50}	Ruesinck & Smith (1975)
Rainbow trout[a] (Salmo gairdneri)		freshwater	static	laboratory[b]	96	0.05 - 0.10	LC_{50}	Davis & Hoos (1975)
Coho salmon[a] (Oncorhynchus kisutch)		freshwater	static	laboratory[b]	96	0.03 - 0.09	LC_{50}	Davis & Hoos (1975)
Goldfish (Carassius auratus)		freshwater	flow		96	0.22	LC_{50}	Adelmann & Smith (1976)
Fathead minnow (Pimephales promelas)	juvenile	freshwater	static		96	0.6	LC_{50}	Mattson et al. (1976)

Table 30 (contd).

Common carp[a] (Cyprinus carpio)	larvae	freshwater	static	96	0.01	LC_{50}	Verma et al. (1981b)
Guppy (Lebistes reticulatus)		freshwater	static	96	0.97	LC_{50}	Gupta et al. (1982)
Sheepshead minnow (Cyprinodon variegatus)		marine	flow	96	0.44	LC_{50}	Parrish et al. (1978)
Sheepshead minnow (Cyprinodon variegatus)	1-day-old fry	marine	static	96	0.329	LC_{50}	Borthwick & Schimmel (1978)
Sheepshead minnow (Cyprinodon variegatus)	14-day-old fry	marine	static	96	0.392	LC_{50}	Borthwick & Schimmel (1978)
Sheepshead minnow (Cyprinodon variegatus)	28-day-old fry	marine	static	96	0.240	LC_{50}	Borthwick & Schimmel (1978)
Sheepshead minnow (Cyprinodon variegatus)	42-day-old fry	marine	static	96	0.223	LC_{50}	Borthwick & Schimmel (1978)
Pin perch[a] (Lagodon rhomboides)	adult	marine	flow	96	0.053	LC_{50}	Schimmel et al. (1978)
Pin perch[a] (Lagodon rhomboides)	48-h pro-larvae	marine	static	96	0.038	LC_{50}	Borthwick & Schimmel (1978)

[a] Na-PCP.
[b] Results of an inter-laboratory bioassay standardization exercise.

Saarikoski & Viluksela (1981) also demonstrated that the ambient pH influences the toxicity of PCP for fish. The 96-h LC_{50} values for the guppy (Poecilia reticulata) were about 0.04 mg/litre at pH 5, 0.12 mg/litre at pH 6, 0.44 mg/litre at pH 7, and 0.91 mg/litre at pH 8. At pH 5, 33.39% of PCP is in the molecular form, while, at pH 8, more than 99% exists as phenate ion. Since the change in toxicity was substantially smaller than it would be if only the molecular PCP were toxic, the authors concluded that the phenate ion also contributes to the toxic effect.

Dissolved oxygen also plays an important role in modifying the toxicity of PCP for fish. Dissolved oxygen levels of 7.8, 6.5, or 5 mg/litre resulted in 96-h LC_{50} values of 0.107, 0.083, and 0.026 mg PCP/litre, respectively (Gupta et al., 1983a). The increase in toxicity at low levels of dissolved oxygen may be due to enhanced absorption of PCP via gills, as the ventilation rate speeds up under low oxygen regimes.

The size of fresh-water fish may also influence the toxicity of PCP. The toxicity of PCP for Notopterus notopterus decreased with increasing fish length up to 14.5 cm, though larger fish were again more susceptible (Gupta et al., 1982). Similarly, slight differences in sensitivity were observed when Cyprinodon variegatus fry of different ages were exposed to PCP (Borthwick & Schimmel, 1978).

As with invertebrates, larvae of fish seem to be more vulnerable to PCP than adult fish. The lowest value in Table 30 in terms of LC_{50} is based on tests with the larvae of the fresh-water carp (Cyprinus carpio).

Data derived from acute toxicity tests are of limited value in estimating the long-term effects of PCP on fish. Studies dealing with sublethal concentrations of PCP may provide more valuable information, since they involve PCP concentrations approaching ambient levels. Since responses to sublethal concentrations require prolonged periods of time, the continuous-flow method is usually chosen to keep test conditions, particularly the concentration of the toxicant, constant.

In underyearling sockeye salmon (Oncorhynchus nerka) exposed to sublethal concentrations of Na-PCP, Webb & Brett (1973) observed significant reductions in growth rate and food conversion efficiency. The EC_{50} for these processes is about 1.80 µg Na-PCP/litre (approximately 2.8% of the 96-h LC_{50} of 0.063 mg/litre).

Similarly, low concentrations of PCP (13.6 - 60.2 µg/litre) were used to induce physiological stress in the fresh-water fish Notopterus notopterus, as measured by the activity of hepatic acid and alkaline phosphatases and succinic dehydrogenase (Dalela et al., 1980a). The activity of

these 3 enzymes was reduced after 10, 20, and 30 days of exposure. The greatest effect was observed in acid phosphatase after 30 days at a concentration of 60.2 µg PCP/litre caused a 71.09% inhibition of enzyme activity.

In vivo blood variables of Notopterus notopterus (Verma et al., 1981c) were sensitive to PCP concentrations as low as 1/10th, 1/15th, and 1/20th of the 96-h LC_{50} of 0.083 mg PCP/litre. Generally, red and white blood cell counts and packed cell volume were increased after 30 days of exposure, while clotting time, erythrocyte sedimentation rate, levels of haemoglobin and mean corpuscular haemoglobin, and mean cell volume were decreased. In addition, there were significant increases in the activity of transaminases in the blood-serum (Verma et al., 1981a) and in the brain, liver, kidney, and gills (Gupta et al., 1983b). Succinic dehydrogenase and pyruvic dehydrogenase were inhibited, while the activity of lactic dehydrogenase was stimulated, thus indicating the development of anaerobic conditions at the cellular level at these sublethal concentrations (Verma et al., 1982).

Other biochemical responses were observed in juvenile striped mullet (Mugil cephalus), a marine fish (Thomas et al., 1981); environmental stress was indicated by a rapid rise in plasma-cortisol concentrations at 200 µg PCP/litre, accompanied by a marked hyperglycaemia and a depletion of hepatic glycogen reserves.

Cleveland et al. (1982) evaluated the chronic toxicities of commercial PCP, purified PCP, and Dowicide EC-7 in 90-day partial life-cycle studies with fathead minnows (Pimephales promelas). The commercial grade PCP used contained relatively large quantities of hexachlorobenzene, chlorophenoxyphenols, chlorodiphenyloxides, chlorodibenzodioxins, and chlorodibenzofurans. The purified PCP included relatively high amounts of chlorinated phenoxyphenols, and the Dowicide EC-7 contained a broad spectrum of impurities, generally at lower concentrations than the other 2 formulations. The commercial composite PCP formulation was the most toxic preparation; a concentration of 13 µg/litre reduced growth of the fish, and 27 µg/litre also reduced survival. Growth, but not survival, was affected by the purified PCP at concentrations equal to, or greater than, 85 µg/litre. Dowicide EC-7 was the least toxic of the PCPs tested, and at the maximum level tested (139 µg/litre), did not adversely affect growth or survival of fathead minnows. Thus, impurities present in PCP were found clearly to increase toxicity under long-term exposure conditions. Moreover, degeneration of the fins and opercula, as well as malfunction of the anterior regions of the skull were lso noted in fathead minnows exposed to the commercial composite of PCP mixture.

7.3 Terrestrial Organisms

7.3.1 Plants

Previously, PCP was widely used as a herbicide, defoliant, and preharvest desiccant. However, as PCP is not a very specific herbicide in terms of inhibiting special target species (Kozak et al., 1979), non-target crop and wildlife species can also be adversely affected, though no data are available in this respect.

Plants may be damaged by contact with the PCP in treated wooden material as, for example, when fruit trees in the vicinity of freshly-treated wooden support posts or stakes suffered bark lesions and chlorosis (Ferree, 1974). Golden delicious trees (Malus domesticus) were the most sensitive, some even died.

7.3.2 Animals

Data on the toxicity of PCP for terrestrial animals have been obtained almost exclusively from laboratory studies. The results of toxicity tests on experimental animals are presented in section 8. Some fatal cases have been reported in which farm animals were incidentally exposed to PCP. Blevins (1965), for example, described a case of acute and lethal poisoning of baby pigs by PCP. The owners of a newly constructed farrowing house had exceeded the manufacturer's recommendation in treating the floor with a solution of PCP in used crankcase oil. All piglets died within one day after they had been moved into the farrowing house. The sow was moved outside where she recovered. No information was given concerning the PCP levels in the air or in the swine.

A recent case, in Canada, of the mortality of young pigs kept on a PCP-treated wooden floor was reported by Ryan (1983). Although PCP residues of 310 µg/litre were found in sow's milk samples, no PCP could be detected in the liver and stomach of the young pigs. However, µg/kg concentrations of the higher chlorinated dioxins were found in the skin and liver of the young pigs, and Ryan (1983) concluded from these findings that these impurities were responsible for their deaths.

Pesticide poisonings of livestock in the United Kingdom have been reviewed by Quick (1982) for the period 1977-80. Of 38 suspected PCP poisoning incidents, only 9 were confirmed as PCP intoxications. High PCP levels found in wood shavings and sawdust, used as bedding or litter for cats and poultry, apparently caused the death of animals. Quick (1982) suspected that impurities present in the commercial PCP products could have been partly responsible for the deaths.

Hill et al. (1975) reported a study in which the toxicity of PCP was determined in young birds of 4 species after 5 days of feeding PCP in the diet; the relatively high LC_{50} values (3400 - 5204 mg/kg body weight) do not indicate that PCP is highly toxic for birds. However, Vermeer et al. (1974) found 50 dead snail kites after extensive application of Na-PCP as a molluscicide in the rice fields of Surinam (section 5.1.4).

7.4 Population and Ecosystem Effects

Very few studies have addressed the effects of PCP on aquatic or terrestrial communities. Field studies on pesticides have usually been carried out when their accidental release resulted in visible kills of fish, birds, or other organisms. For instance, Pierce et al. (1977) and Pierce & Victor (1978) investigated the fate of PCP in a fresh-water lake after an overflow from a pole treatment waste pond caused extensive fish kills (section 7.5).

More valuable information about the effects of PCP on communities can be obtained from model ecosystem studies, in which the response of portions of the environment placed in a laboratory was observed. Tagatz et al. (1977) designed a test system consisting of constant-flow aquaria containing a layer of sand, and seawater with its plankton as well as animals representing estuarine macrobenthic communities. The averages and ranges of the PCP concentrations in the exposed aquaria were 7 µg/litre (3 - 13 µg/litre), 76 µg/litre (47 - 112 µg/litre), and 622 µg/litre (330 - 964 µg/litre). After the 9-week exposure period, a dose-related decrease was found in the numerically dominant groups. Molluscs in particular were markedly reduced at 7 µg PCP/litre, and annelids and arthropods at 76 µg/litre. Almost no animals occurred at 622 µg PCP/litre, while the total numbers of individuals and species were significantly less in aquaria exposed to 76 µg PCP/litre than in controls or those exposed to 7 µg PCP/litre. These striking changes in the relative abundance and diversity of species are evidence of substantial alterations in the community structure induced by PCP. In nature, the stability of macrobenthic communities could be disrupted.

In a second study conducted with Dowicide G-ST (79% Na-PCP), molluscs were also the most sensitive organisms tested. Levels of 15.8 and 161 µg PCP/litre caused similar reductions in the numbers of individuals and species (Tagatz et al., 1978).

Using the same test procedure, Cantelmo & Rao (1978) studied the effects of PCP on meiobenthic communities.

Meiofauna comprise organisms that pass through a 0.5 mm sieve but are retained on a sieve with mesh widths smaller than 0.1 mm. The Nematoda are generally the most common taxon in marine sediments (83% in this study). PCP at 76 µg/litre caused an increase in the biomass and density of nematodes compared with those in control aquaria, while higher concentrations of PCP (161 and 622 µg/litre) caused a decrease. One of the major effects of PCP on nematodes was a shift from epistrate feeders to deposit feeders at concentrations of 161 and 622 µg PCP/litre. Part of this alteration may have been due to the reduction of algae serving as a food supply.

Tagatz et al. (1981) reported the effects of PCP on field and laboratory estuarine benthic communities. In principle, test apparata were the same as those used in earlier studies, except that already established communities were exposed to PCP. Community structure was significantly altered at a PCP concentration of about 140 µg/litre in both field and laboratory aquaria; the populations of several invertebrate species were significantly reduced. There were slight differences in the effects of PCP on numbers of individuals and species between the field and laboratory systems.

Cook et al. (1980) examined the effects of PCP on the microfungal succession of an estuarine benthic microcosm. Trichoderma sp. was initially the most common fungus isolated from the sediment. The addition of PCP (140 µg/litre) resulted in an alteration in the pattern of species; a different species, probably Penicillium canescens, assumed dominance.

Considerable effects of PCP on the population dynamics of several species were noted by Schauerte et al. (1982) during an outdoor study on a natural pond divided into 6 compartments of about 100 litres each. PCP was applied in the water of 2 compartments at a concentration of 1 mg/litre. Three days after application, the population of Daphnia pulex pulex was eliminated from the treated enclosures. The phytoplankton species showed marked alterations in population dynamics: the autotrophic blue-green alga Chroococcus limneticus decreased, while the mixotrophic flagellate Euglena acus significantly increased. This increase was attributed to the reduced grazing pressure by Daphnia; interspecific competition was also discussed as possible cause. As a further secondary effect, the oxygen concentration significantly decreased, because of the "changed balance between autotrophic and heterotrophic populations" (Schauerte et al., 1982).

The US Environmental Protection Agency examined the effects of PCP on a periphyton community in outdoor experimental streams. Even at the low PCP level corresponding to the water quality criterion (48 µg/litre) (US EPA, 1980), adverse effects were noted in terms of community alterations

and suppressed community metabolism (Yount & Richter, 1986). PCP at this concentration also caused adverse effects on fish growth, larval drift, and larval yield (Zischke et al., 1985).

7.5 Biotransformation, Bioaccumulation, and Biomagnification

7.5.1. Aquatic organisms

Most research on the bioaccumulation of PCP has been carried out in aquatic situations. This presents difficulties in that the bioconcentration factors, which are generally directly related to the partition coefficients, could vary by several orders of magnitude, depending on the pH and, at high pH values, on the ionic strength, the two factors governing the partition coefficient of PCP (Kaiser & Valdmanis, 1982). In addition, exposure time must also be taken into account when interpreting PCP residues in organisms. These influences may, in part, explain the wide range in bioconcentration factors that has been found.

In general, substances with the solubility properties of PCP are predominantly taken up by the surrounding water (Niimi & McFadden, 1982). However, PCP accumulation along the food chains contributes to its overall bioaccumulation as well.

Table 31 shows the bioconcentration factors derived for several fish species along with the ambient levels in water. Fresh-water species seem to accumulate PCP to a much greater extent than marine fish, possibly because the relevant enzyme systems in marine species respond faster than those in fresh-water fish (Trujillo et al., 1982).

Since the ambient concentrations of PCP in the water of natural aquatic environments are usually less than 1 µg/litre (section 5.1.2), the studies of Niimi & McFadden (1982) are of particular importance. The authors applied realistic concentrations in exposing rainbow trout (Salmo gairdneri) to < 10 (control), 35, and 660 ng Na-PCP/litre, and distinguished between PCP content in liver and gall bladder, the remaining tissues, and whole fish. As shown in Table 32, rainbow trout accumulated PCP, even when exposed to concentrations as low as 35 ng Na-PCP/litre over prolonged periods. The percentage of PCP stored was highest in the liver and gall bladder. On the basis of this high bioconcentration at the low waterborne toxicant concentrations, the authors suggested that rainbow trout may be less efficient in eliminating PCP than other species.

On removal from PCP-containing water, fish eliminate previously accumulated PCP. However, a portion of the PCP incorporated is more persistent: residues of 0.32 mg/kg (Trujillo et al., 1982) and 0.03 in the muscle to 0.6 mg/kg in the liver (Pruitt et al., 1977) were still detectable after 18 and

Table 31. Measured bioconcentration factors for PCP for several fish species

Species	Time (days)	Concentration in water (µg/litre)	Bioconcentration factor	Reference
Fresh-water fish				
Carassius auratus	5	100	1000	Kobayashi & Akitake (1975a)
Lepomis macrochirus (various tissues)	1	100	320	Pruitt et al. (1977)
	4	100	5 - 350	
	16	100	4 - 230	
Salmo trutta (whole body)	1	200	100	Hattula et al. (1981)
Salmo gairdneri (whole body)	20	0.035	200	Niimi & McFadden (1982)
		0.660	130	
	65	0.035	600	
		0.660	232	
Leuciscus idus melanotus (whole body)	3	42	1050	Freitag et al. (1982)
Marine fish				
Fundulus similis (unspecified tissues)	4	36 - 306	30	Schimmel et al. (1978)
Mugil cephalus (unspecified tissues)	4	26 - 308	38	Schimmel et al. (1978)
Mugil cephalus (edible tissues)	4	46	6	Faas & Moore (1979)
	4	85	79	
	4	157	56	
Fundulus similus (whole body)	1	57 - 610	8	Trujillo et al. (1982)
	1		49	
	7		64	
	7		47	

16 days of depuration, respectively. Elimination half-lives during depuration phases were 4.7 days in killifish (Trujillo et al., 1982) and 6 - 24 days in rainbow trout (Glickman et al., 1977).

In an ecotoxicological profile analysis, Freitag et al. (1982) determined the bioconcentration of PCP not only in fish (Table 31) but also in the green alga Chlorella fusca var. vacuolata and in activated sludge. The bioaccumulation factor in the 24-h algal test was 1250; in a 5-day activated sludge

Table 32. PCP levels in tissues, organs, and whole body of rainbow trout (Salmo gairdneri) exposed to < 10 (control), 35, and 660 ng Na-PCP/litre[a]

Days	Na-PCP in water (ng/litre)	PCP concentrations (µg/kg) in: liver and gall bladder	remaining tissue	whole body
0	< 10	2.3	1.1	1.1
20	< 10	1.2	1.5	1.5
	35	28	7	7
	660	674	77	86
65	< 10	3.9	3.7	3.6
	35	135	20	21
	660	1984	135	153
115	< 10	3.1	1.9	1.9
	35	63	6	7
	660	2204	128	160

[a] Adapted from: Niimi & McFadden (1982).

assay it was 1100 at a waterborne concentration of 0.05 mg PCP/litre.

Ernst (1979) measured PCP residues in water and benthic invertebrates at steady state in a static marine system. For the common mussel (Mytilus edulis) and the polychaete (Lanice conchilega), bioconcentration factors averaged 390 and 3820 on a wet weight basis, respectively, at an initial PCP concentration in sea water of 0.002 - 0.005 mg/litre. The species studied and the lipid contents of the animals had pronounced effects on the bioconcentration factor, while temperature and metabolic activity did not show any remarkable effects on the bioaccumulation. In a similar study, the polychaete (Neanthes virens) was exposed to 0.1 mg ^{14}C-PCP/litre in sea water (Carr & Neff, 1981). The bioconcentration factor of 280 was 10 times lower than that reported by Ernst (1979) for Lanice conchilega.

Clams from the Jadebusen, a North Sea bight, sampled near the end of a waste-water pipe, accumulated 100 - 1000 times more PCP than the sediments (Butte et al., 1985).

The studies of Pierce et al. (1977) and Pierce & Victor (1978) are some of the few field studies concerning the biotransformation of PCP. The authors followed an accidental discharge into a fresh-water lake near Hattiesburg, Mississippi, USA. Within two months, the initially lethal levels of PCP, which had resulted in an extensive fish kill, decreased to between 6 and 19 µg/litre in the water and

remained near this level throughout the studies, apparently because of the continuous influx of contaminated water from other areas. In a control pond with a low background concentration of 0.5 µg PCP/litre, fish contained only 50 µg PCP/litre, whereas much higher levels were found in fish in the contaminated pond. Two months following the spill, levels in fish averaged 2500 µg PCP/kg dry weight but dropped to 130 µg/kg after 6 months; background levels were achieved within about 10 months.

In a Finnish lake area contaminated through pulp bleaching and with wood preservative wastes, PCP residues in fish and plankton did not indicate a strong accumulation via the food chain, plankton > roach > > pike. However, tetrachlorocatechol, a possible biodegradation product of PCP, was found to be strongly absorbed in plankton (Paasivirta et al., 1980).

In littoral microcosms, ^{14}C-PCP was linearly accumulated by aquatic plants, mainly Potamogeton foliosus and Najos guadalupensis, during the first 35 days, levelling off to concentrations over 700 times the initial concentration in water (41 µg/litre). After 8 weeks, PCP concentration in the macrophytes rapidly decreased (Knowlton & Huckins, 1983).

In an aquatic model ecosystem, the ecological magnification value for PCP in fish was 296, the parent compound representing 74% of the total extractable ^{14}C. The other members had lower bioconcentration factors: algae, 1.5; mosquito larvae, 16; snail, 121; and Daphnia, 165. In a terrestrial-aquatic model ecosystem, the bioconcentration factors were: algae, 5; Daphnia, 205; snail, 21; mosquito, 26; and fish, 132 (Lu et al., 1978). These data indicate that bioaccumulation takes place not only through the surrounding water but also along the food chains.

7.5.2 Terrestrial organisms

The terrestrial model ecosystem established by Lu et al. (1978) simulated a crop-soil interaction and included the following organisms: earthworm (Lumbricus terrestris), slug (Limax maximus), pillbug (Armadillidium vulgare), saltmarsh caterpillar (Estigmene acrea), prairie vole (Microtus ochregaster), and corn (Zea mays). Corn plants grown on the soil of the model system rapidly accumulated radioactivity. After 14 days, they contained 6.3 mg/kg of which 16% was intact PCP, 40% were unknown compounds, and 44% were conjugates. The prairie vole, at the top of the food chain, consumed virtually all the plant and animal material in the system within the 5-day exposure time, and then was found to contain 0.5% of the total dosage applied (25 µg).

Gruttke et al. (1986) investigated the fate of Na-PCP in two different model food chains representing important groups

of organisms commonly present in soils. In food chain 1, contaminated bakers-yeast (0.87 µg ^{14}C-Na-PCP/mg dry weight) was fed to springtails (Folsomia candida), which accumulated up to 0.37 µg PCP/mg fresh weight after 10 days. Carabid beetles (Nebria brevicollis) preying on the contaminated springtails showed a body burden of approximately 4.5 mg PCP/kg fresh weight in the steady state, from day 4 to 12. Four days after offering uncontaminated prey, the PCP content in the beetles dropped to 0.4 mg/kg fresh weight. Similar results were obtained in food chain 2, which consisted of contaminated leaves of poplar (700 mg Na-PCP/kg dry weight), with isopods (Oniscus asellus) as primary consumers, and staphylinid beetles (Ocypus olens) as predators. Because of the low accumulation tendency, a lasting effect on the predators would only be expected in case of long-term contamination.

Apart from these model ecosystem studies, little information is available on the biotransformation of PCP in terrestrial systems. Miller & Aboul-Ela (1969) observed that cottonseed kernels of bolls that were closed during spraying accumulated PCP or its metabolites in quantities of up to 2 mg/kg. No PCP was detected when the bolls were open during spraying.

PCP, applied in nutrient solution to the roots of growing corn plants, was taken up by the roots (Schuppener, 1974). At concentrations of up to 20 mg/litre, roots of sterile hydroponic cultures accumulated as much as 151 mg PCP/kg. Apparently, PCP did not translocate in the corn plants as it was not detected in the upper parts of the plants. The root system of sugarcane treated with 5 mg PCP/litre nutrient solution accumulated ^{14}C-PCP within 4 weeks, retaining over 99% of the total PCP taken up from solution (Hilton et al., 1970): no measurable translocation into stalks or leaves occurred. These findings contrast with the translocation within corn plants described by Lu et al. (1978).

8. EFFECTS ON EXPERIMENTAL ANIMALS AND IN VITRO TEST SYSTEMS

Toxicology data on both purified and commercial PCP are provided in this review because both are relevant for a health assessment. The mode of action of chlorophenol can only be determined using purified chemicals. Furthermore, any decision to remove or reduce the levels of microcontaminants in PCP would have to be based on a clear understanding of the toxicity of these purified products.

8.1 Acute Toxicity

PCP, regardless of the route of administration, is the most acutely toxic of the chlorophenols tested in laboratory animal species. Oral LD_{50} values range between 27 and 205 mg/kg body weight for a variety of species, regardless of the vehicle of administration and the grade of PCP (Table 33). Acute oral exposure of mice and rats to lethal doses of PCP (Deichmann, 1943; Farquharson et al., 1958; Borzelleca et al., 1985; Renner et al., 1986) results in an increase in respiratory rate, a marked rise in temperature (4 - 4.5 °C), tremors or possibly convulsions, and a loss of the righting reflex. Asphyxial spasms and cessation of breathing usually occurs 0.5 - 2 min before cardiac arrest. A rapid and intense rigor mortis is observed within 3 - 5 min of death and approximately 45 min sooner than the onset of rigor mortis in rats given ether. Similar signs are observed with lethal exposure to PCP and its sodium salt, regardless of the route of administration.

In addition to its systemic effects, PCP also induces more localized effects in test organisms. Both dermal and subcutaneous applications have produced swelling, skin damage, and occasionally hair loss in a variety of animals (Kehoe et al., 1939; Baader & Bauer, 1951; Johnson et al., 1973). Localized effects on blood vessels may result in hyperaemia or erythema (Kehoe et al., 1939; Baader & Bauer, 1951). Contact with PCP causes irritation of the eye, skin, or respiratory mucosae in man (section 9). Skin bioassay techniques have shown that technical PCP, but not purified PCP, is acnegenic for rabbits, and that the acnegenic effects are caused by the microcontaminants, particularly H_6CDD (Johnson et al., 1973).

There are far fewer published data on the effects of acute exposure of animals to PCP and Na-PCP via the dermal and pulmonary exposure routes compared with oral exposure, which is surprising considering that the primary exposures in the work-place are via the skin and lung. Kozak et al. (1979) reported that PCP was readily absorbed when applied to the skin of experimental animals. The effects of acute dermal exposure have been examined only in the rat and rabbit. For

Table 33. Acute toxicity of PCP

Species	Parameter[a]	Sex	Dose[b]	Route	Purity/carrier	Reference
Mouse	LD_{50}	F	74	oral	PCP in 40% ETOH	Ahlborg & Larsson (1978)
	LD_{50}	M	36	oral	PCP in 40% ETOH	Ahlborg & Larsson (1978)
	LD_{50}	F	150	oral	PCP in polypropylene glycol	Ahlborg & Larsson (1978)
	LD_{50}	M	177	oral	PCP in 10% Emulphor	Borzelleca et al. (1985)
	LD_{50}	F	117	oral	PCP in 10% Emulphor	Borzelleca et al. (1985)
	LD_{50}	M	129	oral	PCP in corn oil	Renner et al. (1986)
	LD_{50}	F	134	oral	PCP in corn oil	Renner et al. (1986)
	LD_{50}	F	32	intraperitoneal	PCP in 40% ETOH	Ahlborg & Larsson (1978)
	LD_{50}	M	59	intraperitoneal	PCP in polypropylene glycol	Ahlborg & Larsson (1978)
	LD_{50}	M	59	intraperitoneal	PCP in corn oil	Renner et al. (1986)
	LD_{50}	F	61	intraperitoneal	PCP in corn oil	Renner et al. (1986)
	LD_{50}	M/F	82	subcutaneous		Ning et al. (1984)
Rat	LD_{50}		150	oral		Schwetz et al. (1978)
	LD_{50}	F	135	oral	commercial PCP	Schwetz et al. (1974)
	LD_{50}	M	205	oral	commercial PCP	Schwetz et al. (1974)
	LD_{50}		78	oral	1% in olive oil	Deichmann et al. (1942)
	LD_{50} (3- to 4-day-old)		65	oral		Schwetz et al. (1978)
	LD_{50}		27	oral	0.5% in Stanolex fuel oil	Deichmann et al. (1942)
	LD_{50}	M/F	83	oral	reagent grade	Ning et al. (1984)
	LD_{50}	M	146	oral	peanut oil	Gaines (1969)
	LD_{50}	F	175	oral	peanut oil	Gaines (1969)
	MLD	M/F	160	oral	peanut oil	Gaines (1969)
	LD_{50}	F	149	cutaneous	PCP technical 40% w/v solution in glycerol formal	Noakes & Sanderson (1969)
	LD_{50}		320	cutaneous	xylene	Gaines (1969)
	LD_{50}		330	cutaneous	xylene	Gaines (1969)
	MLD	M/F	300	cutaneous	xylene	Gaines (1969)

Table 33 (contd).

Species	Parameter[a]	Sex	Dose[b]	Route	Purity/carrier	Reference
Rat	MDLD	M	56	intraperitoneal	olive oil	Farquharson et al. (1958)
	LD_{50}		100	subcutaneous	4% in fuel oil	Deichmann (1943)
	LD_{50}		90	subcutaneous	4% in fuel oil	Deichmann & Mergard (1948)
	LD_{50}	M/F	40	subcutaneous	reagent grade	Ning et al. (1984)
Rabbit	MLD		100 - 130	oral	11% PCP in olive oil	Kehoe et al. (1939)
	MLD		70 - 90	oral	5% in Stanolex fuel oil No. 1	Deichmann et al. (1942)
	MLD		40 - 170	cutaneous	various carriers	Deichmann et al. (1942)
	MLD		350	cutaneous	11% in olive oil	Kehoe et al. (1939)
	MLD		39	cutaneous	1.8% in pine oil	Kehoe et al. (1939)
	MLD		60	cutaneous	5% in Stanoflex fuel oil No. 1	Kehoe et al. (1939)
	MLD		110	cutaneous	5% in Shell Dione oil	Kehoe et al. (1939)
	MLD		70 - 85	subcutaneous	5% in Olive Oil	Kehoe et al. (1939)
Hamster	LD_{50}		168	oral		Cabral et al. (1979)
	LD_{50}		70 - 85	subcutaneous	5% in olive oil	Kehoe et al. (1939)
Sheep	MLD		120	oral	aqueous suspension of sawdust treated at 20 lb technical PCP/ cu. ft	Harrison (1959)
Calf	MLD		140	oral	aqueous suspension of sawdust treated at 20 lb technical PCP/ cu. ft	Harrison (1959)

[a] MLD = Minimum lethal dose.
MDLD = Median lethal dose.
LD_{50} = Estimated dosage capable of causing 50% mortality of a test population.
LC_{50} = Estimated concentration capable of causing 50% mortality of a test population.

[b] LD_{50} or MLD in mg/kg body weight; LC_{50} in mg/m^3 air.

rats, but not rabbits, PCP is much more toxic when given orally than when applied dermally (Table 33). However, with Na-PCP, toxicity via the 2 routes appears to be similar (Table 34). The only acute inhalation toxicity value reported for Na-PCP is for rats; Na-PCP is at least 10 times more toxic via inhalation than by oral ingestion (Hoben et al., 1976c).

The limited data on other routes of administration (intraperitoneal, intravenous, perhaps subcutaneous), which introduce PCP or Na-PCP directly into the body indicate that these exposures result in a stronger toxic effect on rats, hamsters, and mice than either oral or dermal exposure (Tables 33, 34). These differences probably result from incomplete uptake of the compound via the oral, dermal, and perhaps subcutaneous routes.

PCP is considerably more toxic than its sodium salt when administered orally to rats or rabbits, or dermally to rabbits (Tables 33, 34). However, subcutaneous or intravenous injections of PCP and Na-PCP are almost equally toxic. These patterns may reflect differences in the rate of absorption of the parent compounds when applied to the skin of rats, but this does not appear to be true of PCP.

One sex is not consistently more strongly affected by PCP than the other. For a given combination of organism (rats and mice), vehicle, and exposure route (mostly oral), males are sometimes more, sometimes equally, and sometimes less sensitive than females (Table 33). However, technical PCP is more toxic for female rats than for males (Schwetz et al., 1974) and more toxic for young rats than for adults (Schwetz et al., 1978). This differential toxicity between the sexes is apparent in both short- and long-term studies with technical PCP and with one of its contaminants, hexachlorodibenzo-p-dioxin (H_6CDD).

Although the influence of exposure route, the form of the PCP (sodium salt or parent molecule), and the sex of the experimental animal are evident within a given study, such patterns may be masked by a number of factors. Unfortunately, the type and extent of contamination of PCP tested under acute exposure conditions is rarely described, despite the fact that some of the microcontaminants, especially some congeners of polychlorinated dibenzo-p-dioxin (PCDD) and polychlorinated dibenzofuran (PCDF), are extremely toxic. Furthermore, a variety of solvents is used to administer chemicals tested for acute toxicity, and some of these solvents can enhance or decrease absorption of PCP, thus affecting toxicity. Hence, the variations in the LD_{50}, LD_{LO} and TD_{LO} values reported in Kozak et al. (1979), Ahlborg & Thunberg (1980), Jones (1981), NRCC (1981), and NIOSH (1983) for each animal species and route of exposure may result, in part, from the use of a variety of purified and commercial products

Table 34. Acute toxicity of Na-PCP

Species	Parameter[a]	Dose[b]	Route	Purity/carrier	Reference
Mouse	LD_{50}	83	subcutaneous	reagent grade	Ning et al. (1984)
Rat	LD_{50}	210.6	oral	2% aqueous	Deichmann et al. (1942)
	LD_{50} (F)	125 - 200	oral	commercial (79%); aqueous	Stohlman (1951)
	LD_{50}	71	oral	reagent grade	Ning et al. (1984)
	LD_{50}	104	dermal	reagent grade	Ning et al. (1984)
	LD_{50}	66	subcutaneous	2% aqueous	Deichmann et al. (1942)
	LD_{50}	38	subcutaneous	reagent grade	Ning et al. (1984)
	LC_{50}	294	inhalation	reagent grade; 2-h inhalation	Ning et al. (1984
	LD_{50} [c]	11.7	inhalation	aqueous aerosol	Hoben et al. (1976c)
	LD_{50}	34	intraperitoneal	aqueous	Hoben et al. (1976c)
Rabbit	MLD	218	oral	1% NaCl	Kehoe et al. (1939)
	MLD	250 - 300	oral	5% aqueous	Deichmann et al. (1942)
	MLD	450 - 700	oral	aqueous	McGavack et al. (1941)
	MLD	250	cutaneous	10% aqueous	Deichmann et al. (1942)
	MLD	257	cutaneous	2% aqueous	Kehoe et al. (1939)
	MLD	450 - 600	cutaneous	aqueous	McGavack et al. (1941)
	MLD	100	subcutaneous	10% aqueous	Deichmann et al. (1942)
	MLD	250 - 300	subcutaneous	aqueous	McGavack et al. (1941)
	MLD	50 - 150	intraperitoneal	aqueous	McGavack et al. (1941)
	MLD	22 - 23	intravenous	2% aqueous	Deichmann et al. (1942)
	MLD	22	intravenous	1% aqueous	Kehoe et al. (1939)
Guinea-pig	MLD	266	cutaneous	aqueous	Kehoe et al. (1939)
Dog	MLD	135	subcutaneous	aqueous	McGavack et al. (1941)

[a] MLD = Minimum lethal dose.
LD_{50} = Estimated dosage capable of causing 50% mortality of a test population.
LC_{50} = Estimated concentration capable of causing 50% mortality of a test population.

[b] LD_{50} or MLD in mg/kg body weight; LC_{50} in mg/m³ air.

[c] Inhalation toxicity value expressed by author as LD_{50}, not LC_{50}.

containing several different solvents, as well as possible differences in animal strains, or test design (in this regard, note that some of the earlier studies involved only a small number of animals, sometimes as few as two). Acute toxic effects, other than chloracne, which are due exclusively to the presence of PCDDs or PCDFs, are difficult to identify. PCDDs, in particular, have a delayed toxic effect that is masked by the rapid onset of signs of acute exposure to the PCP molecule.

8.2 Short-Term Toxicity

As discussed in the previous section, some of the acute effects of exposure to commercial PCP are attributable to microcontaminants present in the technical preparation. In addition, signs of exposure to some of these microcontaminants, notably PCDDs, may not appear for weeks. As a consequence, it is particularly important to consider the possible confounding effects of these impurities in reviewing the long-term toxicity of chlorophenols. In this section, studies on the toxicity of purified PCP, technical grade PCP, and comparative studies are discussed separately.

8.2.1 Pure or purified PCP

Debets et al. (1980) studied the effect of 99% pure PCP fed to female rats for 5 weeks. The PCP concentration used was 500 mg/kg feed, which corresponds to an approximate dose of 40 - 50 mg/kg body weight per day. Of several liver microsomal enzymes tested, only ethoxyresorufin O-de-ethylase (20-fold) and glucuronyl transferase (3-fold) increased in activity with exposure. Body weight gain, urine and liver porphyrin concentrations, and liver weights were unaffected by PCP. Interestingly, PCP accelerated the onset of hexachlorobenzene (HCB) porphyria, suggesting that it is the PCP metabolized from HCB that causes the porphyria.

In 6-week-old pigs, Greichus et al. (1979) found no overt signs of toxicosis associated with the oral administration of purified PCP (at 5, 10, and 15 mg/kg body weight per day in capsules) for 30 days. However, at 10 and 15 mg/kg per day, hepatocyte size increased and enlarged livers were observed.

8.2.2 Technical grade PCP

Knudsen et al. (1974) fed rats diets containing 0, 25, 50 and 200 mg commercial PCP/kg for 12 weeks. The 50 mg/kg exposure (corresponding to about 2.3 mg/kg body weight per day) increased liver weights in both sexes, while haemoglobin concentrations, haematocrit, and glucose concentrations in

serum were elevated in the 2 highest dosage groups. The no-observed-adverse-effect level of 25 mg/kg corresponded to an ingested dose of about 1.2 mg/kg body weight per day.

Post-mortem examination of dairy cattle fed 0.2 mg/kg body weight per day, for 75 - 84 days, and 2 mg/kg body weight per day for another 56 - 60 days during lactation, revealed enlargement of the liver, lungs, kidneys, and adrenals, thickening of the urinary bladder walls, chronic interstitial nephritis, and subacute urocystitis in exposed animals (Kinzell et al., 1981). In vitro testing identified a significant loss of renal function associated with exposure.

8.2.3 Comparative studies

Recent studies of between 2 and 8 months duration are useful in discerning differences in the effects of purified and technical grade pentachlorophenol (Table 35). These studies on rats and mice have been summarized by Fielder et al. (1982) and NRCC (1982).

Rats receiving 500 mg technical PCP (Table 1, section 2.2) per kg feed for 8 months had slower growth rates, hepatomegaly, porphyria, and increased hepatic enzyme activities (aryl hydrocarbon hydroxylase, glucoronyl transferase, and cytochrome P-450) (Goldstein et al., 1977). When rats were fed purified PCP under similar conditions, i.e., 500 mg/kg feed for 8 months, only retardation of growth rate and an increase in liver glucoronyl transferase activity were observed. Rats fed 20 mg technical PCP/kg feed for 8 months had elevated liver enzyme activities, while rats fed purified PCP at the same concentrations did not.

These findings have been confirmed by Kimbrough & Linder (1978) using rats exposed to 0, 20, 100, and 500 mg/kg of the same technical and purified PCP and the same protocol as was employed by Goldstein et al. (1977). Male and female rats exposed to either purified or technical PCP gained less weight than controls. Exposure to purified PCP in the diet at 500 mg/kg resulted in slightly enlarged liver cells and caused occasional cytoplasmic inclusions. These effects were not observed in rats fed lower doses. In contrast, exposure of rats to diets containing 500 mg technical PCP/kg increased liver weights and thickened the walls of the hepatic central veins in both sexes, and also caused pleiomorphic hepatocytes with foamy or vacuolar cytoplasm in male rats. The livers of females exposed to 500 mg/kg were characterized by vacuolation and degeneration of hepatocytes and mitotic anomalies. Similar, but less severe, effects were noted in rats exposed to diets containing 100 mg and 20 mg technical PCP/kg.

Wainstok de Calmanovici & San Martin de Viale (1980) determined that technical PCP is more toxic for porphyrin

Table 35. No-observed-adverse-effect-levels (NOAELs) established in rats exposed orally to pure, technical, and purified technical grades of PCP

PCP	Sex	NOAEL (mg/kg body weight per day)	Reference
Short-term toxicity			
Pure		3	Johnson et al. (1973)
Purified technical		3	Johnson et al. (1973)
Technical		< 3	Johnson et al. (1973)
Technical		approximately 1.2	Knudsen et al. (1974)
Teratogenicity/ fetotoxicity[a]			
Technical	male, female (progeny)	5	Schwetz et al. (1974)
Purified technical	male, female (progeny)	< 5	Schwetz et al. (1974)
Reproductive toxicity[b]			
Purified technical	male, female	3	Schwetz et al. (1978)
Long-term toxicity			
Pure		approximately 5	Goldstein et al. (1977)
Technical		< 1	Kimbrough & Linder (1978)
Purified technical	female	< 3	Schwetz et al. (1978)
	male	< 10	Schwetz et al. (1978)

[a] Studies involved exposure of females during days 6 - 15 of gestation and evaluation of progeny.

[b] Studies involved exposure of both sexes for 62 days before mating, for 15 days during mating, and, subsequently, throughout gestation and lactation for females.

metabolism in rats than the purified compound. Dosing with 45 - 90 mg technical PCP/kg body weight per day (the amount given by stomach tube for 18 weeks varied) enhanced the excretion of porphyrins and their precursors, increased the deposition of porphyrins in the spleen, liver, and kidney, and altered the activity of enzymes involved in porphyrin metabolism. Larger doses of purified PCP (100 - 195 mg/kg body weight per day) had similar effects.

In a similar comparative study by Johnson et al. (1973), 99% pure PCP and purified technical PCP (H_6CDD reduced to 1 mg/kg) at 10 and 30 mg/kg body weight per day increased liver weight, but did not affect other variables monitored. In contrast, unpurified PCP increased liver and kidney weights, enhanced serum-alkaline phosphatase activity, and reduced serum-albumin, numbers of erythrocytes, total haemoglobin, and haematocrit.

The toxicity of different grades of PCP has also been studied in cattle (McConnell et al., 1980; Parker et al., 1980; Hughes et al., 1985). These studies have confirmed that effects such as reduced weight gain, anaemia, liver pathology, and a decrease in thymus weight were induced by microcontaminants in the technical PCP. Reductions in serum-thyroid hormones (triiodo-thyronine T_3 and thyroxine - T_4) observed in cows fed either purified or technical PCP were probably due to the chlorophenol itself. Significant levels of octa-, hepta-, and hexachlorodioxins were found in liver, fat, and milk at the conclusion of 160 days of exposure (Parker et al., 1980). Firestone et al. (1979) also reported residues of PCP and related chemicals in cows' milk, body fat, and blood following short-term exposures. Only 3 out of 7 PCDD congeners identified in the technical PCP used were found in tissue and body fluids, i.e., 1,2,3,6,7,8-H_6CDD, 1,2,3,4,6,7,8-H_6CDD, and OCDD. Hexachlorobenzene (HCB) and PCP were also detected. Levels of PCP, HCB, and PCDD in pooled milk fat from 3 cows reached 4 mg/kg, 200 µg/kg, and 85 µg/kg, respectively. PCP levels fell to 100 µg/kg a few days after the cessation of dosing and levels of HCB and total dioxin declined by 50% in 50 days.

8.3 Long-Term Toxicity

The 8-month PCP feeding studies on rats by Goldstein et al. (1977) and Kimbrough & Linder (1978) might be considered by some to be long-term. The results of these studies (section 8.2) indicate that the toxicity of technical PCP preparations is primarily attributable to microcontaminants.

Schwetz et al. (1978) reported a 2-year exposure of rats to purified PCP (Table 35). In females, no toxic effects were observed at levels below 3 mg/kg body weight per day; pigment accumulation was observed at 10 mg/kg body weight per day, and decreased body weight gain, increased serum-glutamic pyruvic transaminase (GPT) activity, and pigment accumulation were observed at 30 mg/kg body weight per day. Fewer changes were observed in male rats; no effects were observed at levels below 10 mg/kg body weight per day, and pigment accumulation and increased GPT activity were reported at 30 mg/kg body weight per day. It is interesting to note that Schwetz et al.

(1978) did not observe any absolute or relative weight increase in kidney and liver at 30 mg/kg body weight per day. In contrast, Johnson et al. (1973) reported increased weights of these tissues in male and female rats after a 90-day exposure to the same purified PCP used by Schwetz et al. (1978) at 30 mg/kg body weight per day (section 8.2). An earlier 90-day rat study with purified PCP containing < 0.5 mg PCDD or PCDF/kg also demonstrated changes in liver and kidney weight at the 30 mg/kg body weight per day dose level (Kociba et al., 1971).

Ning et al. (1984) reported test results for laboratory animals exposed to airborne Na-PCP. Both weanling rats (males) and rabbits (males and females) were exposed to reagent grade Na-PCP at 21.4 mg/m^3 or 3.1 mg/m^3 for 4 h per day, 6 days per week, for 4 months. Rabbits (6 pooled males and females) in the high-dose group showed a statistically significant increase in serum-gamma-globulin but not in alpha- or beta-globulin or serum-albumin. Lung weight increased significantly in the high-dose group and liver weight increased significantly in both dose groups compared with controls. In rats, the lung, kidney, liver, and adrenal gland all increased significantly in weight in the high-dose group compared with the same organs in control animals. Blood-glucose levels in rats from the group exposed to 21.4 mg/m^3 remained higher than those in controls, throughout the study.

These results are consistent with previous observations reported by Demidenko (1969). Rats and rabbits exposed to 28.9 or 2.97 mg PCP/m^3 for 4 h per day and 4 months were significantly adversely affected at the high dose (anaemia, leukocytosis, eosinophilia, hyperglycaemia, dystrophic processes in the liver). At the low dose, only minor effects on liver function, cholinesterase activity, and blood sugar were registered, which returned to normal one month after completion of exposure.

Although the results of these 2 inhalation toxicity studies are only preliminary, they give an indication that short-term inhalation of Na-PCP or PCP at concentrations as low as about 3 mg/m^3 can cause biochemical and gross pathological effects in laboratory mammals. Assessing the data of Demidenko (1969), Kunde & Böhme (1978) calculated from the 3 mg/m^3 concentration a daily dose of 0.3 mg/kg body weight per day for rats, assuming 100% pulmonary uptake and absorption. This dose would indicate that PCP is at least 10 times more toxic with inhalation exposure than with oral exposure. This finding is corroborated by the results of studies comparing acute inhalation and acute oral exposure (section 8.1).

Other long-term studies on animals have been designed specifically to evaluate the carcinogenic properties of PCP and are reported in section 8.6.

8.4 Effects on Reproduction and Fetal Development

There is good agreement that PCP is a fetotoxic agent; however, it does not appear to be teratogenic (Kozak et al., 1979; Ahlborg & Thunberg, 1980; Fielder et al., 1982; NRCC, 1982). These conclusions are based primarily on the studies of Schwetz et al. (1974, 1978) on rats.

Technical grade PCP administered to pregnant female rats from day 6 to day 15 of gestation did not have any effects on the mother or fetus at 5 mg/kg body weight per day (Schwetz et al., 1974). Fetal resorptions and delayed development of fetuses were observed at 15 mg/kg body weight per day, and signs of maternal toxicity, based on weight loss, were observed at 35 mg/kg body weight per day. Reports of delayed ossification of the skull, supernumerary, fused, or missing vertebrae and lumbar spurs are usually considered indicative of delayed development rather than teratogenicity, and are responsible for the differences of opinion between the early position of US EPA, that PCP is teratogenic (Cirelli, 1978b), and most other reviews. Purified PCP induced effects similar to those of technical PCP; however, maternal toxicity and decreased fetal weights occurred at 30 mg/kg body weight per day, and delayed fetal development was observed at the 5 mg/kg body weight per day dose level, which had previously been found to be the no-observed-adverse-effect-level for technical grade PCP. More limited fetotoxic effects were observed in rats exposed to PCP by Courtney et al. (1976).

Na-PCP (> 98% pure) fed to female Wistar rats at 10, 30, or 60 mg/kg body weight during days 8 - 19 of gestation led to statistically significant reductions in body weight in females, decreased litter weights, and dramatic increases in fetal resorption and fetal death in the 2 highest dose groups (Anon, 1981). No birth defects were observed in the control group or in the group fed 10 mg/kg body weight; however, 3/31 pups examined from females in the 30 mg/kg body weight group had major malformations (hare lip, umbilican hernia, exocephalus) and 60% had spine and rib malformations (supernumerary, fused, bifurcated, or short ribs). In addition, retardation of ossification and increased breadth of sagittal fissure were extensive in this group. No pups were born to females in the 60 mg/kg body weight group. The authors concluded that 10 mg/kg body weight was the no-observed-adverse-effect level for teratogenicity, fetotoxicity, and embryotoxicity in rats administered Na-PCP. Considering the linearity of the dose-response curve and the fact that 10 mg/kg body weight was the lowest dose administered, the no-observed-adverse-effect level reported in this study is not substantially different from that determined for PCP.

It is probable that the reduced fetotoxicity of technical PCP relative to the purified material, if not artifactual, is a result of the presence of microcontaminants (NRCC, 1982). Liver enzymes that accelerate the rate of PCP metabolism are known to be activated by phenobarbital, 3-methylcholanthrene, and 2,3,7,8-T_4CDD (Ahlborg & Thunberg, 1978). Other PCDD and PCDF microcontaminants in technical PCP may also activate microsomes and reduce the amount of fetal exposure to PCP, causing a concomitant decrease in toxicity. Indeed, the induction of liver enzymes by technical PCP has been demonstrated in the rat by Goldstein et al. (1977). Purified PCP did not increase the activity of liver enzymes. Technical grade PCP was contaminated with 8 - 1380 mg PCDDs/kg and 4 - 1500 mg PCDFs/kg, while purified PCP contained less than 0.1 mg of these contaminants per kg.

Larsen et al. (1975) reported single instances of dwarfism, exencephaly, macrophthalmia, and taillessness in fetuses after pregnant rats were fed single doses of 60 mg purified PCP per kg body weight per day on days 8, 9, or 10 of gestation. However, these findings were attributed to maternal hyperthermia, which is known to cause teratogenic effects in rats (Edwards, 1968). Hyperthermia is a common outcome of exposure to large, single doses of chlorophenol.

Exon & Koller (1983a) investigated the effects of PCP on rats exposed pre- and postnatally. Females were exposed to technical PCP (95% pure) in the feed from 21 days of age, throughout breeding (at 90 days), gestation, and up to weaning of the pups, 21 days after parturition. Exposure doses were 0, 5, 50, and 500 mg/kg body weight per day. The progeny were exposed to the same levels of PCP in feed as their mothers for a total exposure period of 12 1/2 months. No significant decreases in mean litter size or percentage of still-born pups were recorded in the groups given PCP. There was a significant decrease in survival to weaning in the group fed 5 mg/kg body weight but not in the 2 higher dose groups.

A level of purified technical PCP of 30 mg/kg body weight per day (Schwetz et al., 1978) as well as pure Na-PCP at 26 mg/kg body weight per day (Kunde & Böhme, 1978) fed to male and female rats for 62 days before mating, 15 days during mating, and to females during gestation and lactation, caused reductions in the numbers of offspring, neonatal body weight, neonatal survival, and growth of weanlings. The no-observed-adverse-effect level was 3 mg/kg body weight per day (Table 35). Male fertility did not appear to be affected in this study.

8.5 Mutagenicity

Williams (1982) reviewed the literature and concluded that, although there are deficiencies in the data, the Ames Salmonella typhimurium test (Andersen et al., 1972), a sex-linked lethal test with Drosophila melanogaster (Vogel & Chandler, 1974), and a host-mediated assay (Schwetz et al., 1978) all indicate that PCP probably does not cause point mutations. On the basis of negative findings in an in vivo mammalian dominant lethal test (Buselmaier et al., 1973), PCP does not seem to cause chromosomal aberrations. However, an in vitro study to show primary damage using Saccharomyces cerevisiae demonstrated an increase in mitotic gene conversion (Fahrig, 1974; Fahrig et al., 1978). A mammalian spot-test pointed to weak mutagenic activity (Fahrig et al., 1978). PCP did not cause single-strand breaks in human fibroblast DNA, while its metabolite tetrachlorohydroquinone did (Witte et al., 1985). Lymphocytes taken from workers at a PCP factory showed a small, but significantly higher, incidence of dicentric and acentric mitoses (Bauchinger et al., 1982). Sodium pentachlorophenate (20 mmol) reportedly increased the frequency of both auxotrophic and morphological variations in the fungus Aspergillus niger strain 350 (Roy et al., 1981). However, because of shortcomings in these studies, the information available is still insufficient to assess the mutagenicity of PCP. The host-mediated assay with bacteria (Schwetz et al., 1978) and the sex-linked recessive lethal assay (Vogel & Chandler, 1974) have only been carried with single dose levels. In the Ames test (Andersen et al., 1972), no metabolic activation system was used. The increase in the incidence of offspring with coat discoloration in the mouse spot test (Fahrig et al., 1978) was not statistically significant. The mutagenicity test of sodium pentachlorophenate on Aspergillus niger 350 (Roy et al., 1981) did not include a control group.

8.6 Carcinogenicity

The carcinogenicity of chlorophenols in mammals is a contentious issue. In 1979, the International Agency for Research on Cancer reviewed the data available on the carcinogenic properties of PCP (IARC, 1979a) and concluded that the information was inadequate for a meaningful assessment of carcinogenicity.

Two carcinogenicity bioassays have been carried out using PCP. Innes et al. (1969) exposed 2 hybrid strains of mice to roughly the maximum tolerated dose of PCP for a total of 78 weeks, and did not find any significant increases in tumour incidence in males or females of either strain. Schwetz et

al. (1978) report similar findings in rats exposed to a maximum of 30 mg technical PCP/kg body weight per day, for 24 months. Using these data, the Carcinogenic Assessment Group of the US EPA concluded that PCP was negative with respect to oncogenic effects (Williams, 1982).

PCP (technical and commercial grade) is currently being tested by the National Toxicology Program of the US EPA (NRC, 1986), however, data from this study were not available to the Task Group for evaluation.

Exon & Koller (1983a) investigated the potential for PCP to act as a co-carcinogen by administering ethylnitrosourea (ENU) to female rats exposed pre- and/or postnatally to 0, 5, 50, or 500 mg PCP/kg body weight per day. ENU was administered as ethylurea in drinking-water and nitrite in feed during days 14 - 21 of gestation. The progeny were exposed to the same levels of PCP in feed as their mothers for a total exposure period of 12.5 months. High incidences of tumours in progeny exposed to PCP + ENU could not be separated from those observed in progeny exposed to ENU alone.

Tumour promotion studies on phenol and chlorophenol using dimethylbenzanthracene (DMBA) as the initiator on mouse skin indicated that phenol, 2-MCP, 2,4-DCP, and 2,4,5-T_3CP were probable tumour promoters, but that 2,4,6-T_3CP and higher chlorophenols, including PCP, were not (Boutwell & Bosch, 1959). None of the chlorophenols tested were tumorigenic, when applied alone.

Carcinogenicity bioassays involving oral exposure have been conducted on one other chlorophenol, 2,4,6-trichorophenol (NCI, 1979) and on a mixture of 2 hexachlorodibenzo-*p*-dioxin isomers (NCI, 1980a). 2,4,6-T_3CP caused a significant increase in cancer in a variety of tissues in both male and mice and in male rats.

A mixture of two H_6CDD isomers known to contaminate technical PCP caused a significant increase in cancer in the livers of female rats and mice (Table 36, pp. 152-153).

Thus, animal data indicate that, when PCP is ingested, it does not cause cancer in mice or rats, and that, when applied to the skin or administered orally, it does not act as a tumorigen or a tumour promoter. Nevertheless, there is evidence that one other chlorophenol is an animal carcinogen, the lower chlorinated phenols are tumorigens, and that H_6CDD found in PCP is carcinogenic, when ingested by rodents. In addition, Arrhenius et al. (1977b) suggested that PCP may be able to act as a co-carcinogen, on the basis of its effects on liver microsomes.

8.7 Other Studies

The immunotoxic effects of PCP have been investigated in a variety of animal species. Cows fed technical PCP have shown thymic hypoplasia in one study (McConnell et al., 1980) but no overt differences in immunological function in another (Forsell et al., 1981). Mice exposed to technical grade PCP have shown reduced humoral immunity and an *in vitro* impairment of T-cell cytolytic activity (Kerkvliet et al., 1982a,b). Analytical grade PCP did not have any effect. In the rat, a decrease in humoral immunity and an increase in cell-mediated immunity was demonstrated following exposure to technical PCP (97% pure) (Exon & Koller, 1983b). Hillam & Greichus (1983) reported a suppression of total leukocyte counts, gamma globulins, and IgG in young pigs exposed to technical PCP (95% pure) at dose levels of 5 and 10 mg/kg body weight per day for 30 days. Chickens ingesting 2400 µg/g feed of purified PCP exhibited significantly reduced humoral responses to injections of bovine serum-albumin and lymphoproliferative responses to the mitogens concanavalin and phytohaemaglutinin and lower white blood cell counts (Prescott et al., 1982). Thus, some immunotoxic effects are observed when PCP (pure and technical) is administered to experimental animals. In studies carried out with technical PCP, it is likely that the non-phenolic contaminants such as PCDD are responsible for most of the observed immunotoxic effects.

A neurotoxic effect of PCP (grade not specified) has been reported by Walum & Peterson (1984) on the basis of an *in vitro* assay with cultured mice neuroblastoma cells in which an increase in cell detachments with exposure to PCP was observed. Also, a transient alteration in brain tissue enzyme activity was found in rats given 20 mg technical PCP per litre drinking-water over a period of 3 - 18 weeks (Savolainen & Pekari, 1979). The significance of these findings is unclear.

8.8 Contaminants Affecting Toxicity

The toxicological evaluation of pentachlorophenol is complicated by the presence of several impurities in technical grade formulations of this chemical. Some of these impurities are extremely toxic in their own right. On the other hand, some microcontaminants are capable of inducing liver microsomal enzymes, and in so doing, affect the rates of metabolism and excretion and the fetotoxicity of PCP (Ahlborg & Thunberg, 1978) (section 8.4). Thus, meaningful assessments of toxicological studies on the effects of pentachlorophenol are impossible without an accurate knowledge of the type and extent of contamination of the PCP under investigation.

Concern for the toxic effects of microcontaminants has focused on the dioxins, because of the extreme toxicity of the intensely studied congener 2,3,7,8-T_4CDD. However, it is necessary to emphasize that this congener has not been found frequently in PCP. A brief summary of the toxic properties of the microcontaminants of chlorophenols is provided in section 2.2. Extensive reviews of the toxicology and residue levels of PCDDs and PCDFs are available in Hutzinger et al. (1982), Jones (1981), NRCC (1981), Fielder et al. (1982), Kociba & Schwetz (1982), Umweltbundesamt (1985), and in several articles published in Boddington et al. (1985).

8.8.1 Octachlorodibenzodioxin (OCDD)

Only one congener exists of this fully substituted isomer. It was not acutely toxic for rats, when administered orally at 1 mg/kg body weight or acnegenic for rabbits, when applied to the ear as a 10% solution in chloroform (Fielder et al., 1982). Exposures of approximately 1 mg/kg body weight per day for 3 weeks did not cause any toxic signs. Livers were nominally enlarged, but appeared normal under the light microscope. OCDD does not appear to be mutagenic in the Ames test and has not undergone a carcinogenicity bioassay. Studies of the effects of OCDD on reproduction and fetal development indicate that it is not teratogenic at 500 µg/kg body weight per day or fetotoxic at 100 µg/kg body weight per day, when administered to females on days 6 - 15 of gestation.

8.8.2 Heptachlorodibenzodioxin (H_7CDD)

Few data available on H_7CDD. The LD_{50} value has not been determined accurately for either the 1,2,3,4,6,7,8- or 1,2,3,4,6,7,9-isomers.

An in vitro assessment of the induction of aryl hydrocarbon hydroxylase (AHH) in rat hepatoma cell cultures was used to calculate the biological potency of both H_7CDD isomers relative to 2,3,7,8-T_4CDD. The relative potencies of 1,2,3,4,6,7,8-H_7CDD and 1,2,3,4,6,7,9-H_7CDD were 0.3 - 0.5% and 0.011 - 0.025% respectively (Bradlaw et al., 1980).

8.8.3 Hexachlorodibenzodioxin (H_6CDD)

Commercial PCP and Na-PCP have been found to contain 4 out of 10 possible H_6CDD isomers; however, the 1,2,3,6,8,9- and 1,2,3,6,7,8-isomers predominate (Fielder et al., 1982). Levels have been in the 5 - 10 mg/kg range in recent commercial samples of PCP and Na-PCP. The acute oral toxicity (LD_{50}) of 1,2,3,6,7,8-H_6CDD in the mouse is 1250 µg/kg (Table 36). H_6CDD is more toxic for female rats and mice

Table 36. Summary of toxicology data for hexachlorodibenzo-p-dioxin (H_6CDD)

Species	Toxic for: (sex)	Vehicle[a]	Isomer[b]	Route	Toxicity (μg/kg body body weight per exposure period)	Observations	Reference
Acute toxicity							
Lethality (LD_{50})							
Rat	females males	CO:acetone	B/C mix	oral	800 1800	Observations in all studies included:	NCI (1980a)
Mouse	females males	CO:acetone	B/C mix	oral	500 750	weight loss, skin eruptions, delayed death; Tissues	NCI (1980a)
	females, males	CO	A	oral	825	affected: liver,	McConnell et al.
		CO	B	oral	1250	thymus, spleen,	(1978)
		CO	C	oral	1440	kidney, testes	
Guinea-pig	females, males	CO	A	oral	73		McConnell et al.
		CO	B	oral	70 - 100		(1978)
		CO	C	oral	60 - 100		
Short-term toxicity (NOAEL)							
Rat	female, male	CO:acetone	B/C mix	oral	< 2.5 (per week)	thymic atrophy, splenic hypertrophy, and liver lesions at 10 - 50 μg/kg body weight per week	NCI (1980a)
Mouse	female, male	CO:acetone	B/C mix	oral	1.2 (per week)	only liver damage at higher levels (10 - 50 μg/kg body weight per week	NCI (1980a)
	female, male	acetone		dermal	<< 1.5 (per week)		NCI (1980b)

Table 36 (contd).

Fetal toxicity (NOAEL)							
Rat	females, males	CO:acetone		oral	0.1 (per day during gestation)	fetal oedema at 1 µg/kg body weight; resorptions at 10 µg/kg body weight; teratogenic and maternal toxicty at 100 µg/kg body weight	Schwetz et al. (1973)
Long-term toxicity Carcinogenicity bioassay							
Rat	females	CO:acetone	B/C mix	oral	carcinogen > 1.5 (per week)	Loss of body weight (male and female); hepatocellular carcinomas and neoplastic nodules in females only	NCI (1980a)
Mouse	females (inconclusive in males)	CO:acetone	B/C mix	oral	carcinogen > 2.5 (per week)	hepatocellular carcinomas and adenomas in females only; incidence in males not significant	NCI (1980a)
	inconclusive	acetone	B/C mix	dermal	inconclusive	fibrosarcomas observed in females; incidence not significant	NCI (1980b)

[a] CO = corn oil; CO.acetone = 9:1 mixture of corn oil and acetone.
[b] A = 1,2,3,4,7,8-H_6CDD; B = 1,2,3,6,7,8-H_6CDD; C = 1,2,3,7,8,9-H_6CDD.

than for males. Signs of toxicity include weight loss and deterioration of the skin. The onset of mortality is often delayed for up to 3 weeks. Thymus, liver, spleen, kidney, and testes are affected by H_6CDD. This isomer is also known to be acnegenic.

Oral exposure of rats to H_6CDD isomers indicated that no-observed-adverse-effect levels for the rat were < 2.5 µg/kg body weight per week and, for the mouse, < 1.25 µg/kg body weight per week (NCI, 1980a). Above these levels, weight loss and liver damage were observed. Dermal exposure of mice to H_6CDD also resulted in liver damage and mortality, even at the lowest dose of 1.5 µg/kg body weight per week (NCI, 1980b). Thus, H_6CDD is readily absorbed through the skin and extremely toxic. A mixture of 1,2,3,6,7,8- and 1,2,3,7,8,9-H_6CDD has been shown to be carcinogenic for female mice and rats; however, males did not develop hepatocellular carcinomas or adenomas in excess of the control rate in the same study (NCI, 1980a). Carcinogenicity assays using dermal exposures were inconclusive (NCI, 1980b).

On the basis of the results of exposure of pregnant rats to an unidentified mixture of H_6CDD isomers, this homologue is considered fetotoxic and teratogenic (Schwetz et al., 1973). The no-observed-adverse-effect-level was 0.1 µg/kg body weight. Cleft palate, vertebrae with split or unfused centra, and split sternebrae were observed in the fetuses of females fed 100 µg/kg body weight on days 6 - 15 of gestation. Fetal resorptions were observed at maternal doses of 10 µg/kg body weight and fetal subcutaneous oedema at doses of > 1 µg/kg body weight.

8.8.4 Polychlorinated dibenzofurans (PCDFs)

Little is known of the toxicity of the PCDFs, despite their relatively common occurrence in chlorophenol formulations at concentrations of 1 - 500 mg/kg. Some have considerable acute oral toxicity. For example, the LD_{50} of 2,3,7,8-T_4CDF in guinea-pigs and monkeys is 5 - 10 µg/kg body weight and 1000 µg/kg body weight, respectively (Jones, 1981). Rappe et al. (1982) indicated that 1,2,3,7,8-P_5CDF, 2,3,4,7,8P_5CDF, and 2,3,4,6,7,8-H_6CDF all had LD_{50} values in the 1 - 100 µg/kg body weight range for the most sensitive species tested. As with PCDD, the toxicity of PCDF isomers appears related to the extent of symmetrical positioning of chlorine atoms in the 2, 3, 7, and 8 positions of the molecule. 2,3,7,8-T_4CDF and 2,3,4,7,8-P_5CDF appear to have the longest half-lives of the PCDFs studied (Masuda & Kuroki, 1982). Furthermore, these authors have suggested that PCDFs, especially the tetra- and penta-isomers, may have been largely responsible for the signs of Yusho disease reported in

the Japanese who ingested rice oil contaminated with PCBs, PCDF, and polychlorinated quarterphenyls (PCQs). PCDFs have acnegenic properties, but may not be porphyrinogenic.

8.8.5 Polychlorodiphenyl ethers (PCDPEs)

PCDPEs are common contaminants of chlorophenols and are found almost exclusively in T_4CP and PCP (Jones, 1981). Little is known of their toxicity.

8.8.6 Other microcontaminants

Less common impurities of chlorophenols include polychlorinated phenoxyphenols (PCPP) ("predioxins" or "isopredioxins"), polychlorinated biphenyls (PCBs), and polychlorinated benzenes (Jones, 1981). Extensive toxicology data exist on the effects of PCBs (WHO, 1976) and some members of the chlorinated benzene group, i.e., hexachlorobenzene (IARC, 1979b). Although these 2 groups of chemicals are not acutely toxic, they can affect reproduction and are considered carcinogenic. The levels found in technical formulations of PCP are not likely to increase their toxicity or carcinogenicity.

8.9 Mechanism of Toxicity

PCP is known to be cytotoxic for mammalian cells (Packham et al., 1982). All chlorophenols, especially PCP, are uncouplers of oxidative phosphorylation (Kozak et al., 1979). However, the molecular basis for the uncoupling action is not clear (NRCC, 1981). PCP binds to mitochondrial protein and inhibits mitochondrial ATPase activity. PCP may have 2 independent effects on mitochondria; uncoupling oxidative phosphorylation and also inhibiting mitochondrial ATPase (Stockdale & Selwyn, 1971a,b). Thus, both the formation of ATP and the release of energy to the cell from the breakdown of ATP to ADP are prevented. Electron transport is not inhibited by PCP, though reactions dependent on available high-energy bonds, such as oxidative and glycolytic phosphorylation, are affected. Binding to enzymic protein has been reported and may lead to the observed inhibition of other cellular enzymes (Kozak et al., 1979). An increase in cellular oxygen demand during the uncoupling of oxidative phosphorylation has also been observed, which gives rise to the initial increase in respiration rate reported for individuals poisoned by PCP (Weinbach, 1957; Mitsuda et al., 1963; Wood et al., 1983).

9. EFFECTS ON MAN

There are no studies or case reports of the effects of pure or purified PCP on human beings. Human exposure is nearly always to technical grades of PCP or Na-PCP in a variety of formulations. Reference to "PCP" in this section is to the technical grade.

9.1 Acute Toxicity - Poisoning Incidents

In man, the minimum lethal oral dose (LD_{LO}) of PCP has been estimated to be 29 mg/kg body weight (Ahlborg & Thunberg, 1980). Kozak et al. (1979) report that this value depends on the ambient temperature at the time of exposure, and the general health and renal competence of the individual. PCP is approximately 5 times more toxic than phenol (estimated oral LD_{LO} is 140 mg/kg body weight). The proportional lethality of these 2 chemicals (LD_{LO} phenol:LD_{LO} pentachlorophenol) in man is almost identical to the proportional lethality of the LD_{50} values for these substances in rats.

Numerous accidental or suicidal poisonings with commercial chlorinated phenols have been reported (Nomura, 1954; Menon, 1958; Blair, 1961; Bergner et al., 1965; Mason et al., 1965; Armstrong et al., 1969; Robson et al., 1969; Watanabe & Watanabe, 1970; Haley, 1977; Stevens & Richardson, 1979; Gjovik et al., 1981; Wood et al., 1983), and nearly 60% of these acute exposures have resulted in death. These cases together with the results of animal studies provide a relatively clear picture of the signs and symptoms of acute exposure to technical pentachlorophenol in man.

In contrast to the lower chlorinated phenols, PCP does not cause convulsions. Ataxia, mental and physical fatigue, headaches, dizziness, disorientation, anorexia, nausea, vomiting, dyspnoea, hyperpyrexia, tachycardia, and a rise in metabolic rate are common signs and symptoms of PCP poisoning. Most prominent are extreme weakness, elevated body temperature, and profuse sweating. Death is due to cardiac arrest and poison victims usually show a marked rigor mortis (Truhaut et al., 1952a,b; Nomura, 1954; Mason et al., 1965; Robson et al., 1969; Watanabe & Watanabe, 1970).

The gross pathology and histological lesions associated with acute exposures to PCP are generally consistent between laboratory animals and man. Oral exposures result in gastric and intestinal inflammation; however, the severity can depend on the carrier solvent and the presence of other chemicals (Menon, 1958; Stevens & Richardson, 1979). Pulmonary oedema and congestion have been reported after inhalation exposure, and occasionally oral exposure, if aspiration of ingested PCP

has occurred. Splenomegaly, cardiomegaly, renal congestion, hepatomegaly, and hepatic congestion are also frequently observed at autopsy. Histologically, fatty degeneration, and necrosis in the centrilobular region of the liver have been reported, together with degenerative lesions in renal tubules (Gordon, 1956; Menon, 1958; Blair, 1961; Bergner et al., 1965; Mason et al., 1965; Robson et al., 1969).

It is generally agreed that the signs and symptoms of acute toxicity observed in animals and human beings exposed to chlorophenols result from the effects of the chlorophenol molecule itself rather than the microcontaminants, with hyperthermia, profuse sweating, and the rapid onset of morbidity and early death associated with acute chlorophenol exposures. These signs are not observed in animals exposed only to PCDD and PCDF; death is delayed by up to 3 weeks in acute exposure studies with these microcontaminants.

9.2 Effects of Short- and Long-Term Exposures

Most data on the effects of non-acute exposures to chlorophenols in man come from occupational studies. The clinical outcome of repeated exposure to PCP has been reviewed by Fielder et al. (1982), Williams (1982), and Exon (1984). The high rate of employee turnover and variation in the level and duration of exposure make it difficult to distinguish between subacute, short- and long-term exposures. For this reason, the following studies concerning occupational PCP toxicity in man are not separated on the basis of duration of exposure. Interpretation of these studies is frequently confounded by factors such as age, alcohol consumption, tobacco smoking, and other aspects of life style.

9.2.1 Occupational exposure

Clinical studies have identified a number of toxic effects of short-term PCP exposure in man, some of which are also characteristic of acute intoxication (section 9.1). Symptoms include irritation of the skin, mucous membranes, and respiratory tract, signs of chloracne, neurasthesia, depression, headaches, porphyria cutanea tarda, and liver and kidney functional changes (Fielder et al., 1982). These effects are discussed in greater detail in the following sections. Among workers employed in pressure-treating wood with PCP, insomnia and vertigo have also been reported (Arsenault, 1976).

9.2.1.1 Skin and mucous membranes

Workers exposed to airborne concentrations of 1 mg PCP/m^3 or more have reported painful nasal irritation

(Deichmann & Keplinger, 1981). Variations in the effect level are associated with the historical exposure of the individual to inhaled PCP. Workers accustomed to exposure may have a higher threshold for irritating effects and may tolerate up to 2.4 mg PCP/m^3 air.

As in the case of experimental animals (section 8), persons exposed to large amounts of technical PCP develop chloracne. Fielder et al. (1982) summarized published cases of chloracne in workers at PCP-manufacturing sites in Czechoslovakia, the Federal Republic of Germany, the United Kingdom, and the USSR. Kozak et al. (1979) reported other cases in Japan and the USA. The use of Na-PCP and Na-tetrachlorophenol has also resulted in chloracne in woodworkers (Behrbohm, 1959). Baxter (1984) reported chloracne and minor disturbances of the lipid metabolism among 40 workers from a PCP-manufacturing plant over a 3-year study period. However, the author concluded that the abnormalities observed were due to the PCDD contaminants and could not be attributed to the PCP preparation.

A survey of sawmill workers in British Columbia, Canada, carried out using self-administered questionnaires, indicated that dermatological and respiratory symptoms were significantly higher in a PCP/T_4CP exposed group than in the control group (Sterling et al., 1982). However, no reliable estimates of exposure were provided.

A more detailed study carried out in the same geographical area made use of personal monitors carried by individual workers to determine exposure levels of PCP and T_4CP (Embree et al., 1984). Blood and urine samples were collected and analysed, and health and employment histories were recorded by a trained interviewer. The workers were divided into 3 groups: a high exposure group handling wet-treated lumber; a medium exposure group with no manual contact with treated lumber; and a control group with no exposure to PCP, T_4CP, or related chemicals. Exposure concentrations for PCP are shown in Table 20. The authors reported a correlation between exposure levels and serum- and urine-chlorophenol concentrations. However, they were unable to substantiate the findings of Sterling et al. (1982) of increased incidences of respiratory and dermatological health problems in workers exposed to PCP/T_4CP.

A study on 113 employees at a wood-treatment facility found that workers were in good health overall, but with a greater than expected prevalence of skin pustular eruptions (Flickinger & Lawrence, 1982). Airborne exposures were less than 0.03 mg/m^3.

Klemmer et al. (1980) reported the results of a 7-year study on 400 Hawaiians, many of whom had long-term, high-level exposure to PCP. Concentrations of PCP in blood-serum far

exceeded the 1.05 mg/litre reported in Arsenault's (1976) study; workers treating wood in open-vats had a mean level of 3.78 mg PCP/litre, pressure-tank workers 1.72 mg/litre, and farmers and controls 0.25 and 0.32, mg/litre, repectively. After considering data on 189 individuals of the total of 400, Klemmer et al. (1980) concluded ... "despite high chronic exposures to PCP, individuals in the wood treatment group of workers had not undergone any serious health effects from this exposure. The only evidence of tangible health effects, part of which could have been caused by exposures to chemicals other than PCP, were the low-grade infections or inflammations of the skin and subcutaneous tissue, of the protective membrane of the eye, and of the mucous membrane of the upper respiratory tract. No specific long-term effects could be elicited in the exposed group".

9.2.1.2 Liver and kidney

Indications of significant liver damage have not been found. Elevations in circulating levels of some hepatic enzymes have been reported; however, they are usually transitory and do not suggest severe functional impairment (Kozak et al., 1979; Fielder et al., 1982). These findings are consistent with those reported in studies on rats with short-term exposure to technical PCP (section 8.2).

Kidney functional changes resulting in reductions in creatinine clearance and resorption of phosphorus have been reported by Begley et al. (1977). The spontaneous normalization in kidney function during a 3-week non-exposure period indicated that this effect on kidney is largely reversible.

Jirasek et al. (1974) reported the clinical signs exhibited by workers who suffered intoxication during the manufacture of Na-2,4,5-T_3CP and Na-PCP. These workers displayed abnormal porphyrin metabolism (increased uroporphyrin and delta-aminolevulinic acid in urine, UV fluorescence of liver), and indications of hepatotoxicity (liver enlargement, mild steatosis or fibrosis of liver tissue, elevated levels/activities of bilirubin, serum-glutamic-oxaloacetic transaminase and serum-glutamic-pyruvic transaminase).

Mild dysfunction of the liver has been reported among Soviet workers engaged in the production of Na-PCP (Vinogradova et al., 1973) including, for example, a reduced ability to synthesize protein.

Zober et al. (1981) reported a study on a small group of woodworkers involved in the application of PCP. The average concentration of PCP in the air at the time of the study was 2.4 $\mu g/m^3$, the average exposure period for the cohort was 3 years and the average levels in urine and serum were 46 µg PCP/g creatinine and 1 µg/ml, respectively. Elevations in

serum-aminotransferases and α-glutamyl transpeptidase were observed; however, confounding factors of sample size and alcohol consumption prevented the formation of any conclusions concerning the effects of PCP on liver function.

As part of a similar study (Embree et al., 1984) (section 9.2.1.1), Enarson et al. (1986) found that serum levels of creatinine, bilirubin, glutamic oxaloacetic transaminase, and alkaline phosphatase in sawmill workers exposed to a mixture of Na-PCP and Na-tetrachloropenate did not differ from those measured in the controls.

9.2.1.3 Blood and the haematopoietic system

Aplastic anaemia has been associated with PCP use (Roberts, 1981); however, sample sizes were small and exposures were not quantified. Incidental references to haematological changes in isolated workers in a German chemical plant manufacturing PCP and HCB were made by Baader & Bauer (1951). Effects on the haematopoetic systems of animals have been reported in studies with PCDD contaminated PCP (Johnson et al., 1973; Knudsen et al., 1974; McConnell et al., 1980) and 2,3,7,8-T_4CDD (Allen & van Miller, 1978). Wood (1980) examined the relationship between anaemias (with no established cause) in 128 Canadian woodworkers and exposure to PCP. No significant differences between the haematology values of exposed and unexposed workers were found. Wood (1980) concluded that PCP exposure did not appear to have any significant effects on the prevalence of anaemias in these woodworkers.

In a companion report to that of Embree et al. (1984) (section 9.2.1.1), Enarson et al. (1986) found few exposure effects in sawmill workers exposed to Na-PCP and Na-tetrachlorophenate. Most blood variables monitored were within normal ranges and did not differ between exposed and unexposed workers. A significant decrease in haematocrit and an increase in haematuria were reported in workers handling treated lumber, but not in workers exposed solely through inhalation.

Urinary-PCP values (2.2 mg/litre) reported by Shirakawa et al. (1959) in primarily female workers at several rubber manufacturing factories indicated that these workers were exposed to high levels of Na-PCP (presumably technical grade). Increased blood sugar levels, decreased blood pressure, and dermatoses were reported, but no worker was reported to have missed work through the effects of PCP exposure.

9.2.1.4 Nervous system

Investigation of clinical reports of neuropathy did not indicate any overt significant signs of peripheral neuropathy in a recent study on PCP workers (Triebig et al., 1981). Sensory nerve conduction velocity was significantly reduced in exposed workers, but was not correlated with urinary levels of PCP.

Skin, blood, and neurological disorders have been reported among workers at a Na-PCP manufacturing factory in the USSR (Vinogradova et al., 1973). The workers were exposed to air levels of PCP and Na-PCP ranging between 0.03 and 1 mg/m^3. Readings for 21% of the air samples ranged from 0.21 to 1 mg/m^3, exceeding the maximum permissible concentration in the USSR of 0.1 mg/m^3. Washings taken from clothing and exposed skin yielded PCP and Na-PCP values of 21 - 212 mg/dm^2 and 7.6 - 75 mg/dm^2, respectively. However, concentrations of hexachlorobenzene were also 2 - 3 times higher than the maximum permissible concentration (0.9 mg/m^3) set in the USSR and may have had an influence on the disorders reported.

9.2.1.5 Immunological system

McGovern (1982) suggested that man may suffer an immunotoxic response to phenolic compounds, including chlorinated phenolic compounds. Marked T-cell suppression has been observed in several patients exposed to phenols. Zober et al. (1981) reported that some woodworkers exposed to PCP displayed increased concentrations of immunoglobulins, though this increase was not correlated with exposure. Ning (1984) reported that workers exposed to PCP showed significant decreases in IgG and IgA immunoglobulins. The results of animal studies, while indicating that PCP is not strongly immunotoxic, confirm that PCP exposure can lead to immunological changes (section 8.7).

9.2.1.6 Reproduction

There are few published data on the effects on male or female reproductive capacity of short- or long-term exposure to chlorophenols. Schrag & Dixon (1985) classified PCP as "agents with inconclusive effects" on male reproduction. Corddry (1981) investigated pregnancy outcomes in women married to sawmill workers in Canada. 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" compared with "unexposed" men. There was a slight trend towards more adverse pregnancy outcomes in

the exposed group, but this trend disappeared when the alcohol consumption was considered as a confounding factor. Male fertility was not studied.

9.2.1.7 Cytogenetic effects

There is no evidence to indicate that PCP or other chlorophenols exert cytogenetic effects on human cells. A study of circulating lymphocytes in a small group of workers in Idaho, USA, indicated that individuals exposed to PCP had a slightly higher rate of chromosome breakage than controls, but the increase was not statistically significant (Wyllie et al., 1975). Bauchinger et al. (1982) reported that lymphocytes from 22 workers in a PCP-manufacturing factory had a significantly elevated number of chromosomal aberrations (dicentrics and acentrics). These data are not adequate for assessing the cytogenetic effects of PCP in man.

9.2.1.8 Carcinogenicity

Only 2 reports associating exposure to PCP specifically with human cancer are available. Greene et al. (1978) suggested that there was an association between exposure to wood treatment chemicals (PCP) and the incidence of Hodgkin's disease, on the basis of a family case history (2 of 4 siblings contracting the disease were occupationally exposed to PCP) and a relative risk (RR) of 4.2 (from death certificates, in the USA) for persons employed in carpentry and lumbering. Bishop & Jones (1981) reported 2 cases of non-Hodgkin's lymphoma in PCP workers in the United Kingdom; both cases were associated with chloracne. These data are not adequate for the identification of a positive and statistically sound correlation between lymphomas and PCP.

However, there is some epidemiological evidence that exposure of workers to mixtures of chlorophenols, but not specifically PCP, increases their risk of developing soft-tissue sarcomas and lymphomas. Considerable debate has ensued since the initial report of chlorophenol-related cancer by Hardell (1977) and the subsequent reports of Hardell and his co-workers in Sweden. Case control studies of soft-tissue sarcoma patients in Sweden indicated a relative risk (RR) of 6.6 for those "exposed" to chlorophenols compared to those who did not appear to have been exposed (Hardell & Sandström, 1979). Individuals exposed to 2,4,5-T had an RR of 5.8. A follow-up study in another area of Sweden involving 330 subjects tended to confirm the overall risk of soft-tissue sarcomas in individuals exposed to phenoxyacetic acids and chlorophenols (Erickson et al., 1981). The authors reported RR values of 6.8 for all phenoxyacetic acid exposures and 3.3

for chlorophenol exposures. Exposures to phenoxyacetic acids, assumed by the authors to be free of PCDD and PCDF impurities resulted in an RR of 4.2. Hence, Erickson et al. (1981) concluded that impurities in these chlorinated phenols and phenoxyacids were probably not the sole cause of the elevated cancer rates reported, though they might have played a role in this apparent carcinogenicity.

The validity of the assumption that 2,4-D is free of PCDD and PCDF "impurities" is questionable inasmuch as 2,4-D has been found to be contaminated, in one case, with H_6CDD (IARC, 1977) and, in another, with T_4CDF (Norström et al., 1979). However, it is reasonable to assume that the contamination of the phenoxy-acid herbicides 2,4-D, MCPA, necoprop, and dichlorprop with PCDDs and PCDFs is very low.

Hardell et al. (1981) have also applied their case-referent technique to malignant lymphoma patients (both Hodgkin's disease and non-Hodgkin's lymphomas) in Sweden. They reported RR values in individuals exposed to phenoxy acids, chlorophenols, and other organic solvents to be 4.8, 4.3, and 2.4, respectively. The RR value for high-level exposure to chlorophenols was as high as 8.4. A possible explanation for the lymphomas may rest with the immunological effects (in animals) of the PCDD contaminant, 2,3,7,8-T_4CDD. Some immunosuppressive chemicals have been shown to cause an increase in histiocytic lymphomas in man (Hardell, 1979).

In response to criticisms that recall bias was a significant factor in his studies, Hardell (1981a) applied his case-control method to study colon cancer, a disease that correlates positively with asbestos exposure, but not with chlorophenol exposure. His findings indicated that recall and observer bias were negligible in his earlier studies, since colon cancers correlated significantly only with asbestos exposure, and not with phenoxy acids or chlorophenols exposure. Hardell et al. (1982) also used their technique to demonstrate an increased risk of nasal/nasopharyngeal cancer (RR = 7) among workers exposed to chlorophenols.

Others have not found associations between cancer and human exposure to chlorophenols. In contrast to Hardell et al. (1982), Tola et al. (1980) did not find any relationship between nasal cancer and chlorophenol exposure in Finnish workers. A case-control study in New Zealand (Smith et al., 1984) did not reveal a higher incidence of soft-tissue sarcoma in workers exposed to chlorophenols. Gilbert et al. (1983) conducted a cohort study in Hawaii with workers employed in the wood-treatment industry, in which chromated copper-arsenate, tributyl tin oxide, and PCP were used. They did not find any adverse health effects, but urinary-PCP levels were higher in the exposed group.

In a recent Swedish study on the risks of soft-tissue sarcoma, a cohort of 354 620 men employed in agriculture or forestry was compared to a reference cohort of 1 725 845 men employed in other industries during the period 1961-79 (Wiklund & Holm, 1986). A relative risk of 0.9 (95% confidence interval 0.8 - 1) was found. When the cohort was divided into 6 subgroups, based on assumed exposure to phenoxy acid herbicides, no significant differences in relative risks were found. Despite the increased use of phenoxy acid herbicides in Sweden between 1947 and 1970, no time-related increase in the relative risk of soft-tissue sarcomas was found. The authors concluded that their study did not confirm the results of Hardell (1981b). However, they pointed out that only a small percentage of their total cohort of agricultural and forestry workers in Sweden were possibly exposed to phenoxy acid herbicides (15%) and chlorophenols (2%). Hence, a relative risk of 1.5 observed for sarcomas in these groups, as defined in their study, would be equivalent to an actual 6-fold risk from exposure to these compounds. Thus, it is unlikely that their study would have detected a true increased risk from such exposures, if the risk were less than 6-fold.

Pearce et al. (1986) studied 82 cases of non-Hodgkin's lymphoma in New Zealand with 168 cancer controls and 228 general population controls. They obtained statistically significant odds ratios (OR) of 2.7 and 2, respectively, for workers in the pelt department of meat works with potential exposure to 2,4,6-trichlorophenol and for workers who carried out fencing with potential exposure to both 2,4,6-trichlorophenol and pentachlorophenol. Further examination of the data revealed that: 2 of the 4 lymphoma cases who worked in the pelt department were possibly not exposed to TCP; that a significant proportion of the fencing workers also worked in the meat works; and that no significant risk was found for exposure to chlorophenols as a group. Pearce et al. (1986) concluded that the excess risk observed in these 2 groups of workers might not be due to chlorophenol exposure. In a second study, Pearce et al. (in press) added other lymphoma cases to their previous study sample and found similar relationships. They concluded that, though an association with chlorophenol exposure was unlikely, it could not be ruled out. They proposed that alternative hypotheses, such as exposure to oncogenic zoonotic viruses should be considered to explain their findings.

While there is some evidence that chlorophenols, and in particular trichlorophenols, are associated with elevations in the rates of certain cancers in exposed individuals, there is no clear-cut dose-effect relationship. "Exposure" has been loosely defined in most studies and no quantitative assess-

ments have been published. In addition, it has been suggested that, since other environmental chemicals such as hexachlorobenzene, pentachlorobenzene, and pentachloronitrobenzene, are metabolized to PCP in animals and man, there is no necessary relationship between PCP concentrations in body fluids and exposure to PCP (Renner & Mücke, 1986). Other factors that could have a bearing on the conflicting reports of chlorophenol exposure and cancer incidence include differences in study methods and the diagnosis of soft-tissue sarcoma cases, and inadequacies in death-certificate data. The results of epidemiological studies, currently underway in several countries, could confirm or refute the association between chlorophenol exposure and human cancer (Fingerhut et al., 1984).

9.2.1.9 Other systems

It is not unusual to find few or no signs of toxicity in workers with long-term exposure to low levels of PCP or Na-PCP. Arsenault (1976) reported a prospective clinical evaluation of 21 PCP workers involved in the pressure-treatment of wood, who had been exposed for an average of 9 years and had elevated blood-serum levels of PCP (on average, 1.05 mg/litre, versus 0.1 mg/litre in controls). The only significant clinical findings in the pressure-treatment workers were vertigo and insomnia. Arsenault (1976) also provides information obtained from the health records of 1330 workers in a large wood-processing company. From 1961 to 1971, only 26 cases of health problems related to PCP use and exposure were identified; however, it is probable that this is an underestimate because of under-reporting.

Similarly, in a cohort study comparing 88 wood-treatment workers with 61 controls (Gilbert et al., 1983), no significant effects of exposure (by history or physical examination) to wood preservatives, including PCP, were reported on: skin or mucous membranes of the eyes or upper respiratory tract; mental status; cardiovascular, gastrointestinal, genitourinary, or neuromuscular systems; or reproduction. In the accompanying historical perspective study, calculations of age-specific deaths rates from all causes for 125 workers, over 21 years, showed that observed rates were similar to, or lower than, those expected.

9.2.2 General population exposure

References to non-occupational exposure to chlorophenols, for example from wood in homes, confirm that pulmonary, and, to a lesser extent, dermal exposure to PCP can produce symptoms of poisoning similar to those documented in occupational settings. These studies (section 5.2) may be of

significance in as much as they identify new sources of exposure; however, they add little to the toxicology data base for PCP. Concentrations of PCP in the indoor air of homes and in the urine and serum of their residents are elevated relative to those in the general population (Table 21). The limited effects of this exposure are considered briefly here.

In cases where individuals display symptoms of PCP intoxication, usually as a result of the application of PCP in the interior of houses, typical acute symptoms are observed, but other parameters (haematological, biochemical) may be normal. Sangster et al. (1982) outlined case histories of 3 families in PCP-treated houses who reported experiencing one or more of the following signs or symptoms: generalized itching or burning dermatosis, nausea, vomiting, decreased appetite, headache, dizziness, and fatigue. Haematological, urinary, and biochemical parameters were unaffected by exposure. Similarly, a young girl poisoned by bathwater stored in a PCP-contaminated tank displayed fever, intermittent delirium, rigors, acidosis, and elevated urine levels of ketones and amino acids, but her respiratory rate and other clinical symptoms were normal (Chapman & Robson, 1965). However, longer-term exposure may have more profound effects. Brandt et al. (1977) reported that exposure to PCP for several years in the air of a treated wooden house resulted in liver damage and elevated activities of several liver enzymes in a German woman (Ahlborg & Thunberg, 1980).

A Sacramento woman lost weight, and complained of weakness and tightness in the chest after the interior of her house was treated with PCP (Anon, 1970).

Krause & Englert (1980) examined several medical and laboratory parameters in 250 persons with elevated PCP exposure (section 5.3). No clear relationship could be found between elevated concentrations of PCP in the urine and biochemical parameters related to the liver, kidney, and blood. However, significantly more complaints of headache, fatigue, tonsillitis, hair loss, and bronchitis were reported in persons with PCP exposure. Because the signs and symptoms usually reported in connection with indoor PCP exposure are relatively non-specific, thye cannot be definitively ascribed to PCP. However, the observation that many symptoms disappeared when exposure was reduced (by improving ventilation, sealing wood surfaces, or leaving the premises) is indicative that PCP or the substances included in the formulated product might well be the causative agents. The persistence of some biochemical and dermatological signs, similar to those reported in the work-place, is a further indication that PCP may induce subacute effects in these exposed persons.

In general, however, no adverse effects can be ascribed to the low ambient concentrations of PCP resulting from the diffuse sources to which most people are exposed.

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

10.1 Evaluation of Human Health Risks

In this subsection, PCP and Na-PCP are referred to as PCP.

10.1.1 Occupational exposure

10.1.1.1 Exposure levels and routes

Occupational exposure to technical PCP mainly occurs through inhalation and dermal contact. Virtually all workers exposed to airborne concentrations take up PCP through the lungs and skin. In addition, workers handling treated lumber or maintaining PCP-contaminated equipment would be exposed dermally to PCP in solution, and may take up from one-half (based on urinary-PCP concentrations) to two-thirds (using serum levels) of their total PCP burden through the skin.

The actual concentrations to which workers have been exposed are seldom measured but, where they have been monitored, they are predictably high. Airborne levels at PCP-production and wood-preservation facilities have ranged from several $\mu g/m^3$ to more than 500 $\mu g/m^3$ in some work areas. The outer layer of treated wood can contain up to several hundred mg/kg, though levels are usually less than 100 mg/kg.

These exposures result in concentrations of PCP in the serum and urine that are 1 - 2 orders of magnitude higher than those in the general population without known exposure. Mean/median urinary-PCP concentrations of approximately 1 mg/litre are typical for workers in contact with PCP, compared with urinary concentrations of approximately 0.01 mg/litre for the general population (section 5.4).

Automated processes and the use of closed systems have greatly reduced worker exposure in large-scale manufacturing and modern wood-treatment factories and sawmills. Other improvements in industrial hygiene can significantly reduce exposure, as measured by lower urinary-PCP concentrations.

10.1.1.2 Toxic effects

Past use of PCP has affected workers producing or using this chemical. Chloracne, skin irritation and rashes, respiratory disorders, neurological changes, headaches, nausea, weakness, irritability, and drowsiness have been documented in exposed workers. Work-place exposures are to technical PCP, which usually contains mg/kg quantities of

microcontaminants, particularly H_6CDD. Subacute effects such as chloracne and potential subchronic and chronic effects such as hepatotoxicity, fetotoxicity, and immunotoxicity (as reported in animal studies) are probably mainly caused by microcontaminants. However, the PCP molecule itself appears to play a role in the pathology of the last 3 effects and is likely to be wholly responsible for the reports of skin and mucous membrane irritiation, hyperpyrexia and, in severe cases, coma and death. The toxicity of pure or purified PCP has not been evaluated for human beings, because human exposure has usually been to technical PCP.

Investigations of biochemical changes in woodworkers with long-term exposure to PCP have failed to detect consistently significant effects on major organs, nerves, blood, reproduction, or the immune system. However, the statistical power of these studies has been limited as a result of the small sample sizes used. Overall, the body of research suggests that long-term exposure to levels of PCP encountered in the work-place is likely to cause borderline effects on some organ systems and biochemical processes.

Some epidemiological studies from Sweden and the USA have revealed an association between exposure to mixtures of chlorophenols, especially 2,4,5-T_3CP, and the incidences of soft-tissue sarcomas, lymphomas, and nasal and nasopharyngeal cancers. Other studies have failed to detect such a relationship. None of these studies has managed to address the effects of exposure to PCP itself.

Animal studies designed to assess the carcinogenicity of PCP and reported to date have been negative. Carcinogenicity bioassays with one other chlorophenol (2,4,6-T_3CP) and a mixture of two H_6CDD congeners found in PCP have been positive. Hence, the carcinogenic effects of long-term exposure of animals to technical PCP are not clear.

10.1.1.3 Risk evaluation

It is clear that the levels of PCP found in work-places have adversely affected some aspects of the health of exposed workers. Potentially the most deleterious effect of technical PCP is on the fetus, and pregnant women should avoid exposure, whenever possible. There is limited evidence that PCP may cause hepatotoxicity, neurological disorders, and effects on the immune system. No convincing data for or against a carcinogenic link exists.

The National Academy of Sciences (1977) calculated an acceptable daily intake (ADI) for PCP of 3 µg/kg body weight per day. This ADI is based on data from a feeding study on rats and a 1000-fold safety factor. The results of long-term

studies indicate that the no-observed-adverse-effect level for rats is below 3 mg/kg body weight per day (section 8.2). A recent human study has shown that the steady-state body burden is 10 - 20 times higher than the value extrapolated from rat pharmacokinetic data, suggesting that caution should be applied when extrapolating directly from the rat model to man. Furthermore, the US ADI was not based on an inhalation study, and does not account for the possibly greater toxicity of PCP via inhalation, as indicated by animal studies (sections 8.1 and 8.3). Hence, the safety factor of 1000 used to derive this ADI value is by no means too conservative. The intake for a 60-kg adult exposed to concentrations of PCP at the ADI level would be 180 µg/person per day.

A rough estimate of occupational exposure alone can be calculated, assuming a moderate breathing rate of 1.8 m^3/h for a 60-kg worker, 100% uptake of all inhaled PCP (which takes some account of the often significant dermal uptake), and an 8-h working shift per day, 5 days per week. Hence, an exposure to 500 µg PCP/m^3 per shift (section 5.2) would result in an average daily PCP intake of approximately 5000 µg/person per day, averaged over the entire week. Under these circumstances, the ADI level proposed by the National Academy of Sciences is significantly exceeded, even when consideration is given to the effects of intermittant exposures during the working week and the high health status assumed for workers.

There is a clear need for a reduction in occupational exposure to PCP. Emphasis must be placed on reducing airborne concentrations at production and wood-treatment facilities, as well as dermal contact with solutions containing PCP. In addition, reductions in the concentrations of microcontaminants in technical PCP, particularly PCDDs and PCDFs, would reduce the potential for expression of several effects and would better protect the health of workers in these industries.

10.1.2 Non-occupational exposure

10.1.2.1 Exposure levels and routes

Domestic use of products containing technical PCP, especially the indoor application of wood preservatives and paints based on PCP, has led to elevated concentrations of PCP in indoor air. Indoor exposures have been well documented in houses constructed with PCP-treated wood, or in which interior wood panels or boards have been treated with PCP. PCP concentrations in indoor air can be expected to reach 30 µg/m^3 during the first month after treatment. Considerably higher levels, up to 160 µg/m^3, have been reported in houses with concomitant poor indoor ventilation. Even higher concentra-

tions can be encountered immediately after do-it-yourself applications of PCP-containing wood preservatives.

In the long term, values of between 1 and 10 μg/m³ are typical, though higher levels, up to 25 μg/m³, have been found in rooms treated one to several years earlier. Indoor air concentrations are influenced by a variety of factors, e.g., intensity of treatment, solvents and additives involved, species of wood treated, environmental conditions, and time elapsed since treatment.

In many cases, levels of PCP in the serum and urine of people exposed in the home overlap those for occupationally exposed persons; but, on average, urine-PCP levels are approximately 0.04 mg/litre for non-occupationally exposed persons.

In the long term, exposure to PCP in treated buildings continuously decreases, because of the high volatility of PCP. Because of their lower vapour pressure, the volatilization of PCDDs and PCDFs from the wood surface is much slower than that of PCP. Hence, these microcontaminants are emitted at a low rate, but over a longer period of time. Long-term exposure to these lipophilic contaminants is likely to lead to accumulation of PCDDs and PCDFs in fatty body tissues.

As a result of regulations restricting the use of PCP, and also changing use patterns, indoor exposure to PCP is probably declining in most developed countries.

10.1.2.2 Risk evaluation

Assuming a daily respiratory volume of 20 m³/adult and 100% uptake of all inhaled PCP (a worst case that takes some account of dermal uptake), the exposure of persons living in PCP-treated buildings, shortly after treatment, or, in some cases, after a long period of time, could be expected to range between 600 and 3200 μg/person per day. Long-term exposure to concentrations of 1 - 25 μg PCP/m³ could result in a daily PCP intake of 20 500 μg/person per day. The median value of 5 μg/m³ reported from a survey of 104 homes (section 5.3) corresponds to a daily PCP uptake of 100 μg/person per day. Other potential sources of exposure to PCP including food, drinking-water, and consumer products contribute further to PCP uptake (section 10.1.3.1).

The indoor air data suggest that, at least during the first weeks following indoor treatment, and occasionally for quite prolonged periods of time, the ADI level of 180 μg/person per day is significantly exceeded. Under these circumstances, there is a potential health risk. This conclusion is supported, in part, by reports of signs and symptoms similar to those in persons occupationally exposed to PCP (dermatosis, nausea, headache, dizziness, fatigue). These signs and symptoms are most likely associated with the effects

of the PCP molecule and, in some cases, the solvents associated with the wood treatment chemicals used. The long-term significance of exposure to low levels of PCDDs and PCDFs and their accumulation in human tissues is not entirely clear; however, at least 2 isomeric groups of the PCDDs family are carcinogenic for animals. Animal data indicate that low concentrations of PCP in biological tissues or body fluids do not signify an absence of biologically active PCDDs and PCDFs.

It is worth noting that exposure in the home is frequently for longer periods of time than exposures in the work-place and can affect subpopulations potentially at greater risk than workers, for example, children, the elderly, pregnant women, or those with an existing adverse health condition.

10.1.3 General population exposure

10.1.3.1 Exposure levels and routes

Exposure of the general population to low levels of PCP is common. PCP has been found in air, food, water, and other consumer products. Biotransformation of some chlorinated hydrocarbons (e.g., lindane, hexachlorobenzene) to PCP also contribute to the human body burden.

The ambient air in urban areas typically contains several ng/m^3, while concentrations in less developed areas are roughly an order of magnitude lower (section 5.1.1).

Drinking-water concentrations of PCP rarely exceed several µg/litre, even in highly industrialized regions, and most are less than 1 µg/litre (section 5.1.5).

Fruits, vegetables, and other produce usually contain much less than 10 µg/kg, but may on occasion exceed this level. Most meats contain similar concentrations of PCP (< 10 µg/kg) but, a few samples, particularly liver, can contain over 100 µg/kg. Fish skeletal muscle typically contains PCP levels of 4 µg/kg or less. Overall estimates of PCP intake from all foods, based on total diet samples in the USA and the Federal Republic of Germany, are remarkably similar, i.e., up to 6 µg/person per day (section 5.1.5).

PCP is also present in a wide variety of consumer products, including veterinary supplies, disinfectants, photographic solutions, fabrics, home-care products, and pharmaceutical products. No calculated estimates of the contribution made by consumer products to overall exposure to PCP are available.

10.1.3.2 Risk evaluation

On the basis of the PCP levels in the various compartments, the overall exposure of an average person without known

specific exposure can be estimated to be approximately 6 µg/person per day from food, 2 µg/person per day from drinking-water, and 2 µg/person per day from the ambient air. Thus, the total exposure of the general population could be approximately 10 µg/person per day (exclusive of exposure to consumer products), which is far below the intake based on the ADI proposed by the US National Academy of Science of 180 µg/person per day. On the basis of available data, this exposure is not likely to constitute a health hazard.

However, the diffuse contamination of the environment with technical PCP must be considered as an important source of environmental PCDDs and PCDFs.

10.2 Evaluation of Effects on the Environment

The widespread use of technical PCP and its physical and chemical properties (water solubility, n-octanol/water partition coefficient, volatility) lead to ubiquitous contamination of air, soil, water, sediments, and environmental organisms.

Depending on the soil type, PCP can be very mobile, potentially leading to contamination of groundwater and hence, of drinking-water. Because applications in agriculture have been reduced, soil contamination will, for the most part, be confined to treatment areas.

Photodecomposition and biodegradation processes may not be adequate to eliminate PCP from the different compartments. Unfavourable temperature, pH, and other environmental conditions may retard degradation of PCP allowing it to persist in the environment. Biological decomposition may also be limited in waste-treatment factories resulting in high concentrations in the final effluents. PCP has also been used in aquatic environments as a molluscicide and an algicide.

PCP concentrations in surface waters are usually in the range of 0.1 - 1 µg/litre, though much higher levels can be found near point sources or after accidental spills (section 5.1.2).

PCP is highly toxic for aquatic organisms. Apart from very sensitive or resistant species, there is apparently no difference in the sensitivity to PCP of the different taxonomic groups (section 7.2). Invertebrates (annelids, molluscs, crustaceans) and fish are adversely affected by PCP concentrations below 1 mg/litre in acute toxicity tests. Sublethal concentrations are in the low µg/litre range.

As little as 1 µg PCP/litre can have adverse effects on very sensitive algal species. Moreover, low concentrations (µg/litre) may lead to substantial alterations in community structures, as seen in model ecosystem studies.

10.3 Conclusions

In this subsection, PCP and Na-PCP are referred to as PCP.

1. Human exposure to PCP is usually from technical products that contain several toxic microcontaminants, including PCDDs and PCDFs.

2. The acute health effects of exposure to high concentrations of technical PCP are generally the result of the biological action of the PCP molecule itself. Sub-chronic effects and the effects of long-term exposure to technical PCP are most probably largely related to the biological action of the PCDDs and PCDFs.

3. A dose-effect relationship for the acute or chronic toxicity of technical PCP for human beings cannot be derived from available data. Derivation of this relationship is confounded by variations in individual susceptibility, social and environmental influences, concomitant exposure to other chemical substances, a lack of accurate exposure estimates, and inadequate toxicity data.

4. Occupational exposure to technical PCP can lead to adverse health effects.

5. Non-occupationally exposed persons (using products containing technical PCP and/or those living in buildings treated with wood preservatives or paints containing PCP) can be exposed to concentrations of PCP in air that can have adverse health effects.

6. The exposure of the general population to diffuse sources of PCP (via food, drinking-water, ambient air, consumer products, chlorinated compounds that can be metabolized to PCP) is very low and, on the basis of available data, it is not likely to constitute a health hazard.

7. Epidemiological investigations and animal studies, conducted to date, are insufficient for an evaluation of the carcinogenicity of technical PCP. Uncertainties also exist over the genotoxic and fetotoxic effects of technical PCP.

8. PCP is rather persistent, quite mobile, and found in all environmental compartments. At the higher concentrations found in the surface water near point sources or discharges (mg/litre), aquatic life is adversely affected. Ambient concentrations of PCP commonly found in surface waters (0.1 -

1 µg/litre) may adversely affect very sensitive organisms and may lead to alterations in the ecosystem.

9. Use of technical PCP and its improper disposal (landfill and low-temperature combustion) can contribute significantly to the contamination of the environment with PCP, PCDDs, and PCDFs.

11. RECOMMENDATIONS

In this section, PCP and Na-PCP are referred to as PCP.

11.1 Environmental Contamination and Human Exposure

(a) Concentrations of microcontaminants in technical PCP, especially PCDDs and PCDFs, must be reduced by improving the quality in production processes.

(b) There is a need for specification of a technical PCP.

(c) Disposal of technical PCP and associated waste should preferably involve high-temperature combustion or, where this is not possible, the use of secure land-fill sites.

(d) In order to reduce contamination of surface waters and the hazards for the aquatic ecosystem, manufacturers and users of technical PCP should prevent releases into the environment.

(e) Protective measures should be provided for non-target aquatic organisms in cases where PCP is used as molluscicide or algicide.

(f) Occupational exposure to technical PCP must be reduced to a minimum. Reduction in exposure can be achieved by:

- explicit product labelling;
- employee instruction on product handling;
- lowering airborne concentrations; and
- use of effective protective equipment.

(g) Industries handling technical PCP should ensure adequate routine monitoring and health surveillance of all potentially exposed employees.

(h) The indoor application of PCP-based wood preservatives and wood stains and the use of PCP-treated wood products in the interior of buildings should cease.

(i) The availability and use of consumer products containing PCP should be reduced and controlled.

(k) The following commercial uses of PCP-based products should be eliminated, in order to reduce contamination of food and the environment:

- application as wood preservatives on wooden food containers, horticultural lumber, wood and tools in mushroom houses, and above-ground interior wood of farm buildings;
- application during the curing of hides;
- application as a herbicide or soil sterilant;
- application as a slimicide in wood pulp and paper operations; and
- application as a molluscicide in surface water if another control chemical or measure is available that is less toxic for man and the aquatic ecosystem.

11.2 Future Research

11.2.1 Human exposure and effects

(a) Reliable estimates of human absorption of airborne PCP via the lung and skin are required.

(b) The importance of the biotransformation of hexachlorobenzene and related compounds as contributors to human body burdens of PCP needs to be quantified.

(c) It is necessary to determine the intake and accumulation by human beings of the lipophilic microcontaminants (especially the PCDDs and PCDFs) resulting from exposure to technical PCP.

(d) Development of reliable estimates of biochemical and reproductive no-observed-adverse-effect levels is desirable.

(e) Studies on persons occupationally exposed to technical PCP should be conducted using a large enough cohort or sufficient numbers of cases to provide the statistical power necessary to determine the relationships between exposure to PCP and morbidity, mortality in general, and cancer. Such studies should include quantitative estimates of concentrations and duration of exposure to PCP, whereever possible.

11.2.2 Effects on experimental animals and in vitro test systems

(a) New data on the carcinogenicity of technical and pure PCP in both sexes of 2 mammalian species are required.

(b) There is a need for a long-term inhalation study on the effects of both technical and pure PCP.

(c) Studies should be undertaken to clearly determine the teratogenic effects of pure and technical PCP. The potential effects of PCP induced maternal hyperthermia on embryological development and fetal growth warrant investigation.

(d) More research on the genotoxic and mutagenic activity of pure and technical PCP is required.

11.2.3 Effects on the ecosystem

(a) Studies are needed to clarify the fate of sediment-bound PCP and its effects on the environment.

(b) Studies of the effects of long-term, low-level exposure on fresh-water aquatic communities are required to establish no-observed-adverse-effect levels.

12. PREVIOUS EVALUATIONS BY INTERNATIONAL BODIES

"The WHO Recommended Classification of Pesticides by Hazard" (WHO, 1984) distinguishes between the four hazard classes Ia, Ib, II, and III, based on the toxicity of technical products. In this report, PCP is classified in class Ib, being highly hazardous.

The WHO manual "Prevention, Diagnosis and Treatment of Insecticide Poisoning" (Plestina, 1981) provides practical advice that generally applies to nitro- and chlorophenols.

In the Guidelines for Drinking-Water Quality (WHO, 1985), a guideline value of 10 µg/litre is recommended for PCP.

No evaluation of the carcinogenicity of PCP was made by the International Agency for Research on Cancer (IARC, 1979a), because the available data on the carcinogenic and mutagenic effects of PCP were considered inadequate for a sound evaluation.

Regulatory standards established by national bodies in different countries and the EEC are summarized in the data profile of the International Register of Potentially Toxic Chemicals (IRPTC, 1983).

IRPTC (1984), in its series "Scientific reviews of Soviet literature on toxicity and hazard of chemicals", issued a review on pentachlorophenol.

REFERENCES

ABRAHAMSSON, K. & XIE, T.M. (1983) Direct determination of trace amounts of chlorophenols in fresh water, waste water and sea water. J. Chromatogr., 279: 199-208.

ACGIH (1980) Documentation of the threshold limit values, 4th ed., Cincinnati, Ohio, American Conference of Governmental Industrial Hygienists Inc, p. 323.

ADELMANN, I.R. & SMITH, L.L. (1976) Standard test fish development. I. Fathead minnows (Pimephales promelas) and goldfish (Carassius auratus) as standard fish in bioassays and their reaction to potential reference toxicants, Duluth, Minnesota, US Environmental Protection Agency, 88 pp (Ecology Research Series No. EPA 600/3-76-061A).

ADELMANN, I.R., SMITH, L.L., Jr, & SIESENNOP, G.D. (1976) Acute toxicity of sodium chloride, pentachlorophenol, guthion, and hexavalent chromium to fathead minnow (Pimephales promelas) and goldfish (Carassius auratus). J. Fish. Res. Board Can., 33: 203-208.

ADEMA, D.M.M. & VINK, G.J. (1981) A comparative study of 1,1,2-trichloroethane, dieldrin, pentachlorophenol, and 3,4-dichloroaniline for marine and fresh water organisms. Chemosphere, 10: 533-554.

AHLBORG, U.G. & LARSSON, K. (1978) Metabolism of tetrachlorophenols in the rat. Arch. Toxicol., 40: 63-74.

AHLBORG, U.G. & THUNBERG, T. (1978) Effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the in vivo and in vitro dechlorination of pentachlorophenol. Arch. Toxicol., 40: 55-61.

AHLBORG, U.G. & THUNBERG, T. M. (1980) Chlorinated phenols: occurrence, toxicity, metabolism, and environmental impact. CRC Crit. Rev. Toxicol., 7: 1-35.

AHLBORG, U.G., LINDGREN, J.-E., & MERCIER, M. (1974) Metabolism of pentachlorophenol. Arch. Toxicol., 32: 271-281.

AHLBORG, U.G., LARSSON, K., & THUNBERG, T. (1978) Metabolism of pentachlorophenol in vivo and in vitro. Arch. Toxicol., 40: 45-53.

AHLBORG, U.G., VICTORIN, K., CAMNER, P., NORDBERG, G., & WAERN, F. (1986) [Health effects of waste incineration.] In:

[Energy from waste,] Sweden, National Board for Energy, Appendix 4 (Report No. 1986:6) (in Swedish).

AHLING, B. & JOHANSSON, L. (1977) Combustion experiments using pentachlorophenol on a pilot scale and full-scale. Chemosphere, 6: 425-436.

ALLEN, J.R. & VAN MILLER, J.P. (1978) Health implications of 2,3,7,8-tetrachlorodibenzo-p-dioxin exposure in primates. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 371-379.

ANDERSEN, K.J., LEIGHTY, E.G., & TAKAHASHI, M.T. (1972) Evaluation of herbicides for possible mutagenic properties. J. agric food Chem., 20: 649-656.

ANDO, M., HIRANO, S., & ITOH, Y. (1985) Transfer of hexachlorobenzene (HCB) from mother to new-born baby through placenta and milk. Arch. Toxicol., 56: 195-200.

ANGERER, C. (1984) [Production and use of pentachlorophenol in the Federal Republic of Germany.] In: [Pentachlorphenol - specimen case,] Berlin, Umweltbundesamt, 76 pp (UBA F & E - Bericht No. 106 04 007) (in German).

ANON (1970) Pentachlorophenol poisoning in the home. Californian Health, 27: 13.

ANON (1981) [Studies of the teratogenicity of Na-PCP in the rat.] In: Shanghai Medical College, ed. [Studies on maximal allowable concentration of hazardous substances in surface water.] Beijing, China, People's Medical Publication, pp. 215-224 (in Chinese).

ANON (1983a) Cryptogil Na. Technical documentation, Courbevoie, France, Rhône-Poulenc Specialités chimiques, 3 pp.

ANON (1983b) Cryptogil Ol. Technical documentation, Courbevoie, France, Rhone-Poulenc Specialités chimiques.

APAJALAHTI, J.H.A. & SALKINOJA-SALONEN, M.S. (1984) Absorption of pentachlorophenol (PCP) by bark chips and its role in microbial PCP degradation. Microbiol. Ecol., 10: 359-367.

ARMSTRONG, R.W., EICHNER, E.R., KLEIN, D.E., BARTHEL, W.F., BENNETT, J.V., JONSSON, V., BRUCE, P.H.H., & LOVELESS, L.E. (1969) Pentachlorophenol poisoning in a nursery for newborn

infants. II. Epidemiologic and toxicologic studies. J. Pediatr., 75(2): 317-325.

ARRHENIUS, E., RENBERG, L., & JOHANSSON, L. (1977a) Subcellular distribution, a factor in risk evaluation of pentachlorophenol. Chem.-biol. Interact., 18: 23-34.

ARRHENIUS, E., RENBERG, L., JOHANSSON, L., & ZETTERQVIST, M.A. (1977b) Disturbance of microsomal detoxication mechanisms in liver by chlorophenol pesticides. Chem.-biol. Interact., 18: 35-46.

ARSENAULT, R.D. (1976) Pentachlorophenol and contained chlorinated dibenzodioxins in the environment. A study of environmental fate, stability, and significance when used in wood preservation. Am. Wood Preserv. Assoc., 20: 122-148.

AURAND, K., ENGLERT, N., KRAUSE, CH., ULRICH, D., & WALTER, R. (1981) [Pentachlorophenol containing wood preservatives in rooms.] Schr.-Reihe Ver. WaBoLu, 52: 293-313 (in German).

BAADER, E.W. & BAUER, H.J. (1951) Industrial intoxication due to pentachlorophenol. Ind. Med. Surg., 20: 286-290.

BAKER, M.D. & MAYFIELD, C.I. (1980) Microbial and non-biological decomposition of chlorophenols and phenol in soil. Water Air Soil Pollut., 13: 411-424.

BALBA, M.H. & SAHA, J.G. (1974) Metabolism of lindane-^{14}C by wheat plants grown from treated seed. Environ. Lett., 7: 181-194.

BALLHORN, L., ROZMAN, T. ROZMAN, K., KORTE, F., & GREIM, H. (1981) Cholestyramine enhances fecal elimination of pentachlorophenol in rhesus monkeys. Chemosphere, 10: 877-888.

BALLSCHMITER, K., ZOLLER, W., SCHOLZ, CH., & NOTTRODT, A. (1983) Occurrence and absence of polychlorodibenzofurans and polychlorodibenzodioxins in fly ash from municipal incinerators. Chemosphere, 12: 585-594.

BARBENI, M., PRAMAURO, E., PELIZZENTI, E., BORGARELLO, E., & SERPONE, N. (1985) Photodegradation of pentachlorophenol catalyzed by semiconductor particles. Chemosphere, 14: 195-208.

BARTHEL, W.F., CURLEY, A., TRASHER, C.L., SEDLAK, V.A., & ARMSTRONG, R. (1969) Determination of pentachlorophenol in blood, urine, tissue, and clothing. J. Assoc. Off. Anal. Chem., 52: 294-298.

BAUCHINGER, M., DRESP, J., SCHMID, E., & HAUF, R. (1982) Chromosome changes in lymphocytes after occupational exposure to pentachlorophenol. Mutat. Res., 102: 83-88.

BAXTER, R.A. (1984) Biochemical study of pentachlorophenol workers. Ann. occup. Hyg., 28: 429-438.

BEGLEY, J., REICHERT, E.L., RASHAD, M.N., KLEMMER, H.W., & SIEMSEN, A.W. (1977) Association between renal function tests and pentachlorophenol. Clin. Toxicol., 11: 97-106.

BEHRBOHM, P. (1959) [On the hazards of exposure to chlorinated phenols.] Dtsch. Gesundheitswes., 14: 614-619 (in German).

BERGNER, H., CONSTANTINIDES, P., & MARTIN, J.H. (1965) Industrial pentachlorophenol poisoning in Winnipeg, Canada. Can. Med. Assoc. J., 92: 448-451.

BERRY, E.G., NOLAN, M.O., & GONZALES, J.O. (1950) Field tests of molluscicides against Australorbus glabratus in endemic areas of schistosomiasis in Puerto Rico. US Public Health Rep., 65: 939-950.

BETTS, J.J., JAMES, S.P., & THORPE, W.V. (1955) The metabolism of pentachloronitrobenzene and 2,3,4,6-tetrachloronitrobenzene and the formation of mercapturic acids in the rabbit. Biochem. J., 61: 611-617.

BEVENUE, A. & BECKMAN, H. (1967) Pentachlorophenol: a discussion of its properties and its occurrence as a residue in human and animal tissues. Residue Rev., 19: 83-134.

BEVENUE, A. & OGATA, J.N. (1971) A contributive error from analytical reagents in the analysis of chlorophenoxy acids and pentachlorophenol by electron capture gas chromatography. J. Chromatogr., 61: 147-148.

BEVENUE, A., WILSON, J.R., POTTER, E.F., SONG, M.K., BECKMAN, H., & MALLETT, G. (1966) A method for the determination of pentachlorophenol in human urine in picogram quantities. Bull. environ. Contam. Toxicol., 1: 257-266.

BEVENUE, A., HALEY, T.J., & KLEMMER, H.W. (1967a) A note on the effect of a temporary exposure of an individual to pentachlorophenol. Bull. environ. Contam. Toxicol., 2: 293-296.

BEVENUE, A., WILSON, J.R., CASARETT, L.J., & KLEMMER, H.W. (1967b) A survey of pentachlorophenol content in human urine. Bull. environ. Contam. Toxicol., 2: 319-332.

BEVENUE, A., EMERSON, M.L., CASARETT, L.J., & YAUGER, W.L. (1968) A sensitive gas chromatographic method for the determination of pentachlorophenol in human blood. J. Chromatogr., 38: 467-472.

BEVENUE, A., OGATA, J.N., & HYLIN, J.W. (1972) Organochlorine pesticides in rainwater, Oahu, Hawaii, 1971-72. Bull. environ. Contam. Toxicol., 8: 238-241.

BISHOP, C.M. & JONES, A.H. (1981) Non-Hodgkin's lymphoma of the scalp in workers exposed to dioxins. Lancet, 2: 369.

BLACKMAN, G.E., PARKE, M.H., & GARTON, G. (1955a) The physiological activity of substituted phenols. I. Relationships between chemical structure and physiological activity. Arch. Biochem. Biophys., 54: 45-54.

BLACKMAN, G.E., PARKE, M.H., & GARTON, C. (1955b) The physiological activity of substituted phenols. II. Relationships between physical properties and physiological activity. Arch. Biochem. Biophys., 54: 55-71.

BLAIR, D.M. (1961) Dangers in using and handling sodium pentachlorophenate as a molluscicide. Bull. World Health Organ., 25: 597-601.

BLEVINS, D. (1965) Pentachlorophenol poisoning in swine. Vet. Med., 60: 455.

BODDINGTON, M.J., BARRETTE, P., GRANT, D., NORSTROM, R.J., RYAN, J.J., & WHITBY, L. (1985) Chlorinated dioxins and related compounds, 1984. Proceedings of the Fourth International Symposium, Ottawa, Canada, 16-18 October 1984. Chemosphere, 14(6/7): 571-989.

BORTHWICK, P.W. & SCHIMMEL, S.C. (1978) Toxicity of pentachlorophenol and related compounds to early life stages of selected estuarine animals. In: Rao, K.R. ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 141-146.

BORZELLECA, J.F., HAYES, J.R., CONDIE, L.W., & EGLE, J.L., Jr (1985) Acute toxicity of monochlorophenols, dichlorophenols, and pentachlorophenol in the mouse. Toxicol. Lett., 29: 39-42.

BOUTWELL, R.K. & BOSCH, D.K. (1959) The tumour-promoting action of phenol and related compounds for mouse skin. Cancer Res., 19: 413-424.

BOYLE, T.P., ROBINSON-WILSON, E.F., PETTY, B.D., & WEBER, W. (1980) Degradation of pentachlorophenol in simulated lentic environment. Bull. environ. Contam. Toxicol., 24: 177-184.

BRADLAW, J.A., GARTHOFF, L.H., & HURLEY, N.W. (1980) Comparative induction of aryl hydrocarbon hydroxylase activity in vitro by analogues of dibenzo-p-dioxin. Food Cosmet. Toxicol., 18: 627-635.

BRANDT, M., SCHMIDT, E., & SCHMIDT, F.W. (1977) [Chronic liver disease caused by long term household poisoning with pentachlorophenol.] Verh. Dtsch. Ges. Inn. Med., 83: 1609-1611 (in German).

BRAUN, W.H. & SAUERHOFF, M.W. (1976) The pharmacokinetic profile of pentachlorophenol in monkeys. Toxicol. appl. Pharmacol., 38: 525-533.

BRAUN, W.H. & WAECHTER, J.M., Jr (1983) Sources of uncertainty in pharmacokinetic prediction. J. anim. Sci., 56: 235-243.

BRAUN, W.H., YOUNG, J.D., BLAU, G.E., & GEHRING, P.J. (1977) The pharmacokinetics and metabolism of pentachlorophenol in rats. Toxicol. appl. Pharmacol., 41: 395-406.

BRAUN, W.H., BLAU, G.E., & CHENOWETH, M.B. (1979) The metabolism/pharmacokinetics of pentachlorophenol in man, and a comparison with the rat and monkey. In: Deichmann, W.B., ed. Toxicology and occupational medicine, New York, Amsterdam, Oxford, Elsevier/North-Holland, pp. 289-296.

BRINGMANN, G. & KUHN, R. (1982) [Results of toxic action of water pollutants on Daphnia magna Straus tested by an improved standardized procedure.] Z. Wasser Abwasser Forsch., 15: 1-6 (in German).

BRUNS, G.W. & CURRIE, R.A. (1980) Extraction of pentachlorophenol and tetrachlorophenol residues from field-contaminated carrots and potatoes: comparison of several methods. J. Assoc. Off. Anal. Chem., 63: 56-60.

BUA (1986) In: Ges. Dt. Chemiker, ed. [Pentachlorophenol. Report of the Advisory Group for existing chemicals which are

relevant from an environmental point of view (BUA),] Weinheim, Deerfield Beach, VCH Publishers, 183 pp (in German).

BUCKMAN, N.G., HILL, J.O., MAGEE, R.J., & MCCORMICK, M.J. (1984) Separation of substituted phenols, including eleven priority pollutants using high-performance liquid chromatography. J. Chromatogr., 284: 441-446.

BUHLER, D.R., RASMUSSON, M.E., & NAKANE, H.S. (1973) Occurrence of hexachlorophene and pentachlorophenol in sewage and water. Environ. Sci. Technol., 7: 929-934.

BUIKEMA, A.L., GINNISS, M.J., & CAIRNS, J. (1979) Phenolics in aquatic ecosystems: a selected review of recent literature. Mar. environ. Res., 2: 87-181.

BUNDESAMT FUR UMWELTSCHUTZ (1982) [Impairment of surface waters by pentachlorophenol.] Mitteilung No. 21, Bern, 12 pp. (in German).

BUNDESAMT FUR UMWELTSCHUTZ (1983) [Polychlorinated organic compounds in Rheinfelden (Switzerland). Investigation of dust, soil, and grass samples: results and evaluation.] Schriftenreihe Umweltschutz, 18, Bern, 32 pp (in German).

BUNDESGESETZBLATT (1978) [Regulation of agricultural pesticides in or on foodstuffs of plant origin and tobacco products (regulation of plant-protective pesticides).] In: [Bundesgeseztblatt. Part I,] Bonn, Federal Republic of Germany, Federal Ministry of Youth, Family Affairs and Health, pp. 718-719, 734 (in German).

BUNDESGESUNDHEITSAMT (1983) [On handling wood preservatives,] Berlin, Bundesgesundheitsamt, 36 pp (Information Booklet of the Federal Health Office of Federal Republic of Germany) (in German).

BURGER, E. (1966) Acute fatal poisoning with sodium pentachlorophenol. Dtsch. Z. Gesamt. Gerichtl. Med., 58: 240-247.

BUSELMAIER, W., ROHRBORN, G., & PROPPING, P. (1973) Comparative investigations on the mutagenicity of pesticides in mammalian test systems. Mutat. Res., 21: 25-26.

BUSER, H.R. (1975) Analysis of polychlorinated dibenzo-p-dioxins and dibenzofurans in chlorinated phenols by mass fragmentography. J. Chromatogr., 107: 295-310.

BUSER, H.R. (1976) Preparation of qualitative standard mixtures of polychlorinated dibenzo-p-dioxins and dibenzofurans by ultraviolet and γ-irradiation of the octachloro compounds. J. Chromatogr., 129: 303-307.

BUSER, H.R. (1982) [Report on the formation of PCDDs during pyrolysis of PCP and PCP-Na,] Wädenswil, Switzerland, Eidg. Forschungsanstalt, 2 pp (Unpublished report) (in German).

BUSER, H.R. & BOSSHARDT, H.P. (1976) Determination of polychlorinated dibenzo-p-dioxins and dibenzofurans in commercial pentachlorophenols by combined gas chromatography - mass spectrometry. J. Assoc. Off. Anal. Chem., 59: 562-569.

BUTTE, W. (1984) Determination of free and total pentachlorophenol in urine. Fresenius Z. Anal. Chem., 317: 659.

BUTTE, W., KIRSCH, M., & DENKER, J. (1983) The determination of pentachlorophenol and tetrachlorophenols in Wadden sediment and clams (Mya arenaria) using triethylsulfonium hydroxide for extraction and pyrolytic ethylation. Int. J. environ. anal. Chem., 13: 141-153.

BUTTE, W., DENKER, J., KIRSCH, M., & HOPNER, TH. (1985) Pentachlorophenol und tetrachlorophenols in Wadden sediment and clams Mya arenaria of the Jadebusen after a 14-year period of waste-water discharge containing pentachlorophenol. Environ. Pollut. B, 9: 29-39.

CABRAL, J.R.P., RAITANO, F., MOLLNER, T., BRONCZYK, S., & SHUBIK, P. (1979) Acute toxicity of pesticides in hamster. Toxicol. appl. Pharmacol., 48: A192.

CANTELMO, A.C. & RAO, K.R. (1978) Effects of pentachlorophenol on the meiobenthic nematodes in an experimental system. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 165-174.

CARR, R.S. & NEFF, J.M. (1981) Biochemical indices of stress in the sandworm Neanthes virens (Sars). I. Responses to pentachlorophenol. Aquat. Toxicol., 1: 313-327.

CARR, R.S., THOMAS, P., & NEFF, J.M. (1982) A simple spectrophotometric technique for the determination of pentachlorophenol in water. Bull. environ. Contam. Toxicol., 28: 477-479.

CASANOVA, M. & DUBROCA, J. (1972) Residues of pentachloronitrobenzene and its hexachlorobenzene impurity in soils and lettuce (Fr.). C.R. Séances Acad. Agric. Fr., 58: 990-998.

CASARETT, L.J., BEVENUE, A., YANGER, W.L., & WHALEN, S.A. (1969) Observations on pentachlorophenol in human blood and urine. Am. Ind. Hyg. Assoc. J., 30: 360-366.

CASTERLINE, J.L., Jr (1982) Uptake, translocation, and transformation of pentachlorophenol in soybean and spinach plants. Diss. Abstr. Int. B 1983, 43(8): 2409.

CAUTREELS, W., VAN COUWENBERGHE, K., & GUZMAN, L.A. (1977) Comparison between the organic fraction of suspended matter at a background and an urban station. Sci. total Environ., 8: 79-88.

CHAPMAN, J.B. & ROBSON, P. (1965) Pentachlorophenol poisoning from bath-water. Lancet, 12 June: 1266-1267.

CHAPMAN, J.C., HIGGINS, V.R., SIMPSON, G.R., & SIYALI, D.S. (1981) Pentachlorophenol (PCP) exposure: an occupational health hazard in mushroom growing. In: Mushroom science. XI. Proceedings of the eleventh International Scientific Congress on the Cultivation of Edible Fungi, Sydney, Australia, 18 pp.

CHAPMAN, P.M., FARRELL, M.A., & BRINKHURST, R.O. (1982) Relative tolerances of selected aquatic oligochaetes to combinations of pollutants and environmental factors. Aquat. Toxicol., 2: 69-78.

CHAU, A.S.Y. & COBURN, J.A. (1974) Determination of pentachlorophenol in natural and waste waters. J. Assoc. Off. Anal. Chem., 57: 389-393.

CHIU, C., THOMAS, R.S., LOCKWOOD, J., LI, K., HALMAN, R., & LAO, R.C.C. (1983) Polychlorinated hydrocarbons from power plants, wood burning and municipal incinerators. Chemosphere, 12: 607-616.

CHOI, J. & AOMINE, S. (1972) Effects of soil on the activity of pentachlorophenol. Soil Sci. plant Nutr., 18: 255-260.

CHOI, J. & AOMINE, S. (1974a) Adsorption of pentachlorophenol by soils. Soil Sci. plant Nutr., 20: 135-144.

CHOI, J. & AOMINE, S. (1974b) Mechanism of pentachlorophenol adsorption by soils. Soil Sci. plant Nutr., 20: 371-379.

CHOW, C.Y., THEVASAGAYAM, E.S., & WAMBEEK, E.G. (1955) Control of Salvinia - a host plant of Mansonia mosquitos. Bull. World Health Organ., 12: 365-369.

CHU, J.P. & KIRSCH, E.J. (1972) Metabolism of pentachlorophenol by an axenic bacterial culture. Appl. Microbiol., 23: 1033-1035.

CIRELLI, D.P. (1978a) Patterns of pentachlorophenol usage in the United States of America: an overview. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology. New York, London, Plenum Press, pp. 13-18.

CIRELLI, D.P. (1978b) Pentachlorophenol: position document 1. Fed. Reg., 43: 48446-48477.

CLEVELAND, L., BUCKLER, D.R., MAYER, F.L., & BRANSON, D.R. (1982) Toxicity of three preparations of pentachlorophenol to fathead minnows: a comparative study. Environ. Toxicol. Chem., 1, 205-212.

CONKEY, J.H. & CARLSON, J.A. (1963) Relative toxicity of biostatic agents suggested for use in the pulp and paper industry: 1963 review. Tech. Assoc. Pulp Paper Ind., 46: 23 A-39A.

CONKLIN, P.J. & RAO, K.R. (1978) Toxicity of sodium pentachlorophenate (Na-PCP) to the grass shrimp, Palaemonetes pugio, at different stages of the molt cycle. Bull. environ. Contam. Toxicol., 20: 275-279.

COOK, W.L., FIEDLER, D., & BOURQUIN, A.W. (1980) Succession of microfungi in estuarine microcosms perturbed by carbaryl, methyl parathion, and pentachlorophenol. Bot. Mar., 23: 129-131.

CORDDRY, A.E. (1981) A pregnancy outcome study of the wives of workers exposed to chlorophenate wood preservatives at a sawmill, University of Washington, Department of Environmental Health, 191 pp (Thesis).

COURTNEY, K.D., COPELAND, M.F., & ROBBINS, A. (1976) The effects of pentachloronitrobenzene, hexachlorobenzene, and related compounds on fetal development. Toxicol. appl. Pharmacol., 35: 239-256.

CRANDALL, C.A. & GOODNIGHT, C.J. (1959) The effect of various factors on the toxicity of sodium pentachlorophenate to fish. Limnol. Oceanogr., 4: 53-56.

CRANMER, M. & FREAL, J. (1970) Gas chromatographic analysis of pentachlorophenol in human urine by formation of alkyl ethers. Life Sci., 9: 121-128.

CRETNEY, M.J. (1976) Pentachlorophenol death. Bull. Int. Assoc. Forensic Toxicol., 12: 10.

CROSBY, D.G. & WONG, A.S. (1976) Photochemical generation of chlorinated dioxins. Chemosphere, 5: 327-332.

CROSBY, D.G., WONG, A.S., PLIMMER, J.R., & WOOLSON, E.A. (1971) Photodecomposition of chlorinated dibenzo-p-dioxins. Science, 173: 748-749.

CROSBY, D.G., MOILANEN, K.W., NAKAGAWA, M., & WONG, A.S. (1972) Photonucleophilic reactions of pesticides. In: Matsumura, F., Boush, G.M., & Misato, T., ed. Environmental toxicology of pesticides, New York, London, Academic Press, pp. 423-431.

CROSBY, D.G., MOILANEN, K.W., & WONG, A.S. (1973) Environmental generation and degradation of dibenzodioxins and dibenzofurans. Environ. Health Perspect., 5: 259-266.

CROSBY, D.G., BEYNON, K.I., GREVE, P.A., KORTE, F., STILL, G.G., & VOUK, J.W. (1981) Environmental chemistry of pentachlorophenol. Pure appl. Chem., 53: 1051-1080.

CROSSLAND, N.O. & WOLF, C.J.M. (1985) Fate and biological effects of pentachlorophenol in outdoor ponds. Environ. Toxicol. Chem., 4: 73-86.

CSERJESI, A.J. (1967) The adaptation of fungi to pentachlorophenol and its biodegradation. Can. J. Microbiol., 13: 1243-1249.

CSERJESI, A.J. (1972) Detoxification of chlorinated phenols. Int. Biodeterioration Bull., 8: 135-138.

CSERJESI, A.J. & JOHNSON, E.L. (1972) Methylation of pentachlorophenol by Trichoderma virgatum. Can. J. Microbiol., 18: 45-49.

CSERJESI, A.J. & ROFF, J.W. (1975) Toxicity tests of some chemicals against certain wood-staining fungi. Int. Biodeterioration Bull., 11: 90-96.

CULL, M.R. & DOBBS, A.J. (1984) Long-term changes in polychlorodibenzo-p-dioxin concentrations in wood treated with technical pentachlorophenol. Chemosphere, 13: 1091-1099.

CULL, M.R., DOBBS, A.J., & WILLIAMS, N. (1983) Polychlorodibenzo-p-dioxins (PCDDs) in commercial pentachlorophenol (PCP) used in wood preservation. Chemosphere, 12: 483-485.

CURTIS, R.F., LAND, D.G., GRIFFITH, N.M., GEE, M., ROBINSON, D., PEEL, J.L., DENNIS, C., & GEE, J.M. (1972) 2,3,4,6-tetrachloroanisole association with musty taint in chickens and microbiological formation. Nature (Lond.), 235: 223.

DAHMS, A. & METZNER, W. (1979) [On the analytics of pentachlorophenol and tetrachlorophenol in the air and in urine.] Holz Roh-Werkst., 37: 341-344 (in German).

DALELA, R.C., RANI, S., & VERMA, S.R. (1980a) Physiological stress induced by sublethal concentrations of phenol and pentachlorophenol in Notopterus notopterus: hepatic acid and alkaline phosphatases and succinic dehydrogenase. Environ. Pollut., 21: 3-8.

DALELA, R.C., RANI, S., RANI, S., & VERMA, S.R. (1980b) Influence of pH on the toxicity of phenol and its two derivatives pentachlorophenol and dinitrophenol to some fresh water teleosts. Acta hydrochim. hydrobiol., 8: 623-629.

DANIELS, C.R. & SWAN, E.P. (1979) Determination of chlorinated phenols in surface-treated lumber by HPLC. J. chromatogr. Sci., 17, 628-630.

DAVIS, H.C. & HIDU, H. (1969) Effects of pesticides on embryonic development of clams and oysters and on survival and growth of the larvae. US Fish Wildl. Serv. Fish. Bull., 67: 393-403.

DAVIS, J.C. & HOOS, R.A. (1975) Use of sodium pentachlorophenate and dehydroabiotic acid as reference toxicants for salmonid bioassays. J. Fish. Res. Board Can., 32: 411-416.

DEBETS, F.M.H., STRIK, J.J.T.W.A., & OLIE, K. (1980) Effects of pentachlorophenol on rat liver changes induced by hexachlorobenzene with special reference to porphyria and alterations in mixed-function oxygenases. Toxicology, 15: 181-195.

DEICHMANN, W.B. (1943) The toxicity of chlorophenols for rats. Fed. Proc., 2: 76-77.

DEICHMANN, W.B. & KEPLINGER, M.L. (1981) Phenols and phenolic compounds. In: Clayton, G.D. & Clayton, F.E., ed. Patty's industrial hygiene and toxicology 2A, 3rd revised ed., New York, John Wiley and Sons, pp. 2567-2627.

DEICHMANN, W.B. & MERGARD, E.G. (1948) Comparative evaluation of methods employed to express the degree of toxicity of a compound. J. ind. Hyg. Toxicol., 30: 373-378.

DEICHMANN, W.B., MACHLE, W., KITZMILLER, K.V., & THOMAS, G. (1942) Acute and chronic effects of pentachlorophenol and sodium pentachlorophenate upon experimental animals. J. Pharmacol. exp. Ther., 76: 104-117.

DE LAUNE, R.D., GAMBRELL, R.P., & REDDY, K.S. (1983) Fate of PCP in estuarine sediment. Environ. Pollut. (B), 6: 297-308.

DEMENTI, B.A. (1981) Health hazard alert: pentachlorophenol (news). Am. Ind. Hyg. Assoc. J., 42: A16, A18.

DEMIDENKO, N.M. (1969) [Materials for establishing the maximum permissible concentrations in air.] Gig. Tr. Prof. Zabol., 7: 58-60 (in Russian).

DETRICK, R.S. (1977) Pentachlorophenol: possible sources of human exposure. For. Prod. J., 27: 13-16.

DIETZ, F. & TRAUD, J. (1978a) [Threshold odour and taste concentrations of phenolic compounds.] GWF-Wasser/Abwasser, 119: 318-325 (in German).

DIETZ, F. & TRAUD, J. (1978b) [On the analysis of phenols, particularly chlorophenols, in water by means of gas chromatography - methods and results.] Vom Wasser, 51: 235-257 (in German).

DIJK, J.J., VAN, VAN DER MEER, C., & WIJNANS, M. (1977) The toxicity of sodium pentachlorophenolate for three species of decapod crustaceans and their larvae. Bull. environ. Contam. Toxicol., 17: 622-630.

DOBBS, A.J. & GRANT, C. (1980) Pesticide volatilisation rates: a new measurement of the vapour pressure of pentachlorophenol at room temperature. Pestic. Sci., 11: 29-32.

DOBBS, A.J. & WILLIAMS, N. (1983) Indoor air pollution from pesticides used in wood remedial treatments. Environ. Pollut. (B), 6: 271-296.

DOEDENS, J.D. (1964) Chlorophenols. In: Kirk, R.E. & Othmer, D.F., ed. Encyclopedia of chemical technology, 2nd ed., New York, John Wiley and Sons, Vol. 5, pp. 336-337.

DOUGHERTY, R.C. & PIOTROWSKA, K. (1976a) Multi-residue screening by negative chemical ionization mass spectrometry of organic polychlorides. J. Assoc. Off. Anal. Chem., 59: 1023-1027.

DOUGHERTY, R.C. & PIOTROWSKA, K. (1976b) Screening by negative chemical ionization mass spectrometry for environmental contamination with toxic residues: application to human urines. Proc. Natl Acad. Sci. (USA), 73: 1777-1781.

DOUGHERTY, R.C., WHITAKER, M.J., SMITH, L.M., STALLING, D.L., & KUEHL, D.W. (1980) Negative chemical ionization studies of human and food chain contamination with xenobiotic chemicals. Environ. Health Perspect., 36: 103-117.

DRUMMOND, I., VAN ROOSMALEN, P.B., & KORNICKI, M. (1982) Determination of total pentachlorophenol in the urine of workers. A method incorporating hydrolysis, an internal standard and measurement by liquid chromatography. Int. Arch. occup. environ. Health., 50: 321-327.

DUGGAN, R.E. & CORNELIUSSEN, P.E. (1972) Dietary intake of pesticide chemicals in the United States. III. June 1968 - April 1970. Pestic. monit. J., 5: 331-341.

DUNCAN, C.G. & DEVERALL, F.J. (1964) Degradation of wood preservatives by fungi. Appl. Microbiol., 12: 57-62.

DUST, J.V. & THOMPSON, W.S. (1973) Pollution control in the wood-preserving industry. Part IV. Biological methods of treating waste water. For. Prod. J., 23: 59-66.

EBEN, A., SCHALLER, K.H., & KRAUSE, CH. (1981) [Pentachlorophenol (PCP): analysis of plasma and urine.] In: German Science Foundation, Working Group on Analytical Chemistry, Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, ed. [Analysis of hazardous substances in biological materials,] Weinheim, VCH Publishers, Vol. 2, pp. 1-11 (in German).

ECKRICH, W. (1986) [Levels of PCDDs/PCDFs in indoor air and in human blood.] In: VDI-Kommission Reinhaltung der Luft, ed. [Dioxins. Report of the VDI Meeting, Essen, Federal Republic of Germany, 22-23 April 1986,] Düsseldorf, VDI-Verlag, pp. 70-81 (in German).

ECONOMIST INTELLIGENCE UNIT (1981) Economic implications of abatement measures of water pollution due to hexachlorobutadiene, endosulfan, trichlorophenol, and pentachlorophenol, Brussels, Commission of the European Communities, 134 pp (Report prepared for Environment and Consumer Protection Service).

EDGEHILL, R.U. (1982) Microbial treatment of wastewater and soil to remove pentachlorophenol. Part 1. Diss. Abstr. Int. B, 42: 4871.

EDGEHILL, R.U. & FINN, R.K. (1983) Treatment of soil to remove pentachlorophenol. Appl. environ. Microbiol., 45: 1122-1125.

EDGERTON, T.R. & MOSEMAN, R.F. (1979) Determination of pentachlorophenol in urine: the importance of hydrolysis. J. agric. food Chem., 27: 197-199.

EDGERTON, T.R., MOSEMAN, R.F., LINDER, R.E., & WRIGHT, L.H. (1979) Multi-residue method for the determination of chlorinated phenol metabolites in urine. J. Chromatogr., 170: 331-342.

EDWARDS, M.J. (1968) Congenital malformations in the rat following induced hyperthermia during gestation. Teratology, 1: 173-178.

ELLER, P.M., ed. (1984a) Pentachlorophenol in blood. In: NIOSH manual of analytical methods, 3rd ed., Cincinnati, Ohio, US Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, pp. 8001-1 - 8001-4 (DHHS Publication No. 84-100).

ELLER, P.M., ed. (1984b) Pentachlorophenol in urine. In: NIOSH manual of analytical methods, 3rd ed., Cincinnati, Ohio, US Department of Health and Human Services, Public Health Service, Centers for Disease Control, National Institute for Occupational Safety and Health, pp. 8303-1 - 8303-4 (DHHS Publication No. 84-100).

EMBREE, V., ENARSON, D.A., CHAN-YEUNG, M., DY BUNCIO, A., DENNIS, R., & LEACH J. (1984) Occupatonal exposure to chlorophenates: toxicology and respiratory effects. Clin. Toxicol., 22: 317-329.

ENARSON, D.A., CHAN-YEUNG, M., EMBREE, V., WANG, R., & SCHULZER, M. (1986) Occupational exposure to chlorophenates,

renal, hepatic and other health effects. Scand. J. Work environ. Health, 12: 144-148.

ENGEL, C., DE GROOT, A.P., & WEURMAN, C. (1966) Tetrachloroanisole: a source of musty taste in eggs and broilers. Science, 154: 270-271

ENGST, R., MACHOLZ, R.M., KUJAWA, M., LEWERENZ, H.J., & PLASS, R. (1976) The metabolism of lindane and its metabolites gamma-2,3,4,5,6-pentachlorocyclohexene, pentachlorobenzene, and pentachlorophenol in rats and the pathways of lindane metabolism. J. environ. Sci. Health (B), 11: 95-117.

ENGST, R., MACHOLZ, R.M., & KUJAWA, M. (1978) [Metabolites of hexachlorocyclohexane isomers (HCH) in human blood.] Pharmazie, 33: 109-111 (in German).

ENVIRONMENT, CANADA (1979) Monitoring environmental contamination from chlorophenol contaminated wastes generated in the wood preservation industry, Ottawa, Environmental Protection Bureau, Environmental Protection Service, Pacific and Yukon Region, pp. 74 (Regional Program Report No. 79-24) (Prepared by Can Test Ltd and EVS Consultants Ltd) (DSS File No. 075B, KE 114-8-1935).

ERIKSON, M., HARDELL, L., BERG, N.O., MOELLER, T., & AXELSSON, O. (1981) Soft-tissue sarcomas and exposure to chemical substances: a case reference study. Br. J. ind. Med., 38: 27-33.

ERNEY, D.R. (1978) Gas-liquid chromatographic determination of pentachlorophenol in milk. J. Assoc. Off. Anal. Chem., 61: 214-216.

ERNST, W. (1979) Factors affecting the evaluation of chemicals in laboratory experiments using marine organisms. Ecotoxicol. environ. Saf., 3: 90-98.

ERNST, W. & WEBER, K. (1978a) Chlorinated phenols in selected estuarine bottom fauna. Chemosphere, 7: 867-822.

ERNST, W. & WEBER, K. (1978b) The fate of pentachlorophenol in the Weser estuary and the German Bight. Veröff. Inst. Meeresforsch. Bremerh., 17: 45-53.

ERVIN, H.E. & MCGINNIS, G.D. (1980) Analysis of pentachlorophenol in waste-water using high-performance liquid chromatography. J. Chromatogr., 190: 203-207.

ETZEL, J.E. & KIRSCH, E.J. (1974) Biological treatment of industrial wastewater containing pentachlorophenol. Dev. ind. Microbiol., 16: 287-295.

EXON, J.H. (1984) A review of chlorinated phenols. Vet. hum. Toxicol., 26: 508-520.

EXON, J.H. & KOLLER, L.D. (1982) Effects of transplacental exposure to chlorinated phenols. Environ. Health Perspect., 46: 137-140.

EXON, J.H. & KOLLER, L.D. (1983a) Alternation of transplacental carcinogenesis by chlorinated phenols. In: Jolley, R.L., et al., ed. Water chlorination: environmental impact and health effects, Ann Arbor, Michigan, Ann Arbor Science, Vol. 2, Book 4, pp. 1177-1188.

EXON, J.H. & KOLLER, L.D. (1983b) Effects of chlorinated phenols on immunity in rats. Int. J. Immunopharmacol., 5: 131-136.

FAAS, L.F. & MOORE, J.C. (1979) Determination of pentachlorophenol in marine biota and sea water by gas-liquid chromatography and high pressure liquid chromatography. J. agric. food Chem., 27: 554-557.

FAHRIG, R. (1974) Comparative mutagenicity studies with pesticides, Lyons, International Agency for Research on Cancer, pp. 161-181 (IARC Scientific Publication Vol. 10).

FAHRIG, R., NILSSON, C.-A., & RAPPE, C. (1978) Genetic activity of chlorophenols and chlorophenol impurities. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 325-338.

FARQUHARSON, H.E., CAGE, J.C., & NORTHOVER, J. (1958) The biological action of chlorophenols. Br. J. Pharmacol., 13: 20-24.

FARRINGTON, D.S. & MUNDAY, J.W. (1976) Determination of trace amounts of chlorophenols by gas-liquid chromatography. Analyst, 101: 639-643.

FEDERAL REGISTER (1977) Gelatin; affirmation of GRAS status as a direct and indirect human food ingredient. Fed. Reg., 42(218): 58763-58765.

FEILER, H. (1980) Fate of priority pollutants in publicly owned treatment works, Washington DC, US Environmental Protection Agency (EPA-440/1-80-301).

FERREE, D.C. (1974) Influence of freshly treated posts on growth of newly planted trees. Ohio Agric. Res. Dev. Cent. Res. Summ., 75: 11-12.

FIELDER, R.J., SORRIE, G.S., BISHOP, C.M., JONES, R.B., & VAN DEN HEUVEL, M.J. (1982) Pentachlorophenol. In: Toxicity review, London, Health and Safety Executive, Vol. 5, 20 pp.

FINGERHUT, M.A., HALPERIN, W.E., HONCHAR, P.A., SMITH, A.B., GROTH, D.H., & RUSSELL, W.O. (1984) An evaluation of reports of dioxin exposure and soft-tissue sarcoma pathology among chemical workers in the United States. Scand. J. Work environ. Health, 10: 299-303.

FIRESTONE, D. (1973) Etiology of chick edema disease. Environ. Health Perspect., 5: 59-66.

FIRESTONE, D. (1977) Chemistry and analysis of pentachlorophenol and its contaminants, Washington DC, US Food and Drug Administration, pp. 57-59 (FDA Bylines No. 2).

FIRESTONE, D., REES, J., BROWN, N.L., BARRON, R.P., & DAMICO, J.N. (1972) Determination of polychlorodibenzo-p-dioxins and related compounds in commercial chlorophenols. J. Assoc. Off. Anal. Chem., 55: 85-92.

FIRESTONE, D., CLOWER, M., Jr, BORSETTI, A.P., TESKE, R.H., & LONG, P.E. (1979) Polychlorodibenzo-p-dioxin and pentachlorophenol residues in milk and blood of cows fed technical pentachlorophenol. J. agric. food Chem., 27: 1171-1177.

FISCHER, A. & SLEMROVA, J. (1978) [The contamination of the river Rhine with chlorophenols.] Vom Wasser, 51: 33-46 (in German).

FISCHER, M. (1983) [Pentachlorophenol as model case of a xenobiotic compound,] Berlin, Federal Health Office Institute for Water, Soil and Air Hygiene, 38 pp (Research Report No. 10604007) (in German).

FLEISCHER, M., MEISS, R., ROBENEK, H., THEMANN, H., & ECKHARD, R. (1980) Ultrastructural morphometric investigations on rat liver of young and adult rats after treatment with technical pentachlorophenol. Arch. Toxicol., 44: 243-257.

FLICKINGER, C.W. & LAWRENCE, A.W. (1982) Occupational health experience in the wood preserving industry. In: Am. Wood Preserv. Assoc., 78: 11-30.

FOCQUET, J.P. & THEISEN, R. (1981) Détermination de la réduction de l'hexachlorobutadiène de l'endosulfan, du pentachlorophenol et du trichlorophénol contenue dans les effluents en tenant compte des meilleurs moyens techniques disponsibles, Luxembourg, Commission of the European Communities (Contract No. ENV/723/74-FR) (unpublished report).

FOLKE, J. & LUND, H. (1983) Occurrence of low- and high-chlorinated phenols in municipal sewage before and after passing through biological treatment plants. J. Chromatogr., 279: 189-198.

FORSELL, J.H., SHULL, L.R., & KATELEY, J.R. (1981) Subchronic administration of technical pentachlorophenol to lactating dairy cattle; immunotoxicologic evaluation. J. Toxicol. environ. Health, 8: 543-558.

FOUNTAINE, J.E., JOSHIPURA, P.B., & KELIHER, P.N. (1976) Some observations regarding pentachlorophenol levels in Haverford Township, Pennsylvania. Water Res., 10: 185-188.

FOX, M. & JOSHI, S.R. (1984) The fate of pentachlorophenol in the Bay of Quinte, Lake Ontario (Canada USA). J. Great Lakes Res., 10: 190-196.

FRANZLE, O. (1982) [Modelling the transport of environmental chemicals and their metabolites through the unsaturated zone of natural soil profiles and sludge in laboratory lysimeters and in the field.] In: BMI Environmental Research Plan, pp. XIX + 315 (Research Report No. 10602005/02) (in German).

FRAGIADAKIS, A., KLEIN, W., KORTE, F., MOZA, P.N., SCHEUNERT, I., VOCKEL, D., & WEISS, U. (1979) [Fate of organochlorine compounds in plant-soil systems] In: [Organohalogen compounds in the environment. Project report 1975-78,] Jülich Nuclear Research Plant (Jül-Spez. 45, July 1979) (BMFT Research Report 037118) (in German).

FRANK. R., BRAUN, H.E., HOLDRINET, M., SIRONS, G.J., SMITH, E.H., & DIXON, D.W. (1979) Organochlorine insecticides and industrial pollutants in the milk supply of southern Ontario, Canada, 1977. J. food Prot., 42: 31-37.

FREITAG, D., GEGER, H., KRAUS, A., VISWANATHAN, R., KOTZIAS, D., ASSAR, A., KLEIN, W., & KORTE, F. (1982) Ecotoxico-

logical profile analysis. VII. Screening chemicals for their environmental behaviour by comparative evaluation. Ecotoxicol. environ. Saf., 6: 60-81.

FRG (1986) [Statuary ordinance by dangerous chemicals.] In: Gefahrstoffverordnung, Bonn, Ministry of Labour and Social Affairs (BGBL I), p. 1470 (in German).

FUCHSBICHLER, G. (1982) Automated gel chromatography as clean-up process for determination of ECD-detectable substance, chlorinated hydrocarbons, pentachlorophenol, diphenyl and o-phenylphenol in plant materials. Z. Lebensm.-Unters. Forsch., 174: 9-12.

GAB, F. & PARLAR, H. (1979) [Transformation of organohalogens under abiotic conditions.] In: [Organohalogen compounds in the environment. Project report 1975-78,] Jülich Nuclear Research Plant (Jül.-Spez. 45, July 1979) (BMFT Research Report 037114) (in German).

GAB, S., NITZ, S., PARLAR, H., & KORTE, F. (1975) Photomineralisation of certain aromatic xenobiotica. Chemosphere, 4: 251-256.

GAB, S. (1981) [Decomposition of organic chemicals in adsorbed phase.] In: [Report on the 1980 Symposium of the Institute for Ecological Chemistry,] München, Society for Radiation and Environmental Research (GSF), pp. 61-75 (in German).

GAINES, T.B. (1969) Acute toxicity of pesticides. Toxicol. appl. Pharmacol., 14: 515-534.

GARRETT, C.L. (1980) Fraser River Estuary study. Water quality series. Toxic organic contaminants, Ottawa, Environmental Protection Service, Pacific and Yukon Region, Environment Canada, pp. 123.

GEBEFUEGI, I. (1981) [Our present knowledge of the occurrence of pentachlorophenol in the environment.] In: [Report on the 1980 Symposium of the Institute for Ecological Chemistry,] München, Society for Radiation and Environmental Research (GSF), pp. 25-33 (in German).

GEBEFUEGI, I. & KORTE, F. (1983) Pentachlorophenol contamination of human milk samples. Chemosphere, 12: 1055-1060.

GEBEFUEGI, I. & KORTE, F. (1984) Indoor contamination of household articles through pentachlorophenol and lindane. In: Berglund, B., Lindvall, T., & Sundell, J., ed. Indoor air. IV. Chemical characterisation and personal exposure, Stockholm, Swedish Council for Building Research, pp. 317-322.

GEBEFUEGI, I., PARLAR, H., & KORTE, F. (1979) Occurrence of pentachlorophenol in closed environments. Ecotoxicol. environ. Saf., 3: 269.

GEBEFUEGI, I., OXYNOS, K., & KORTE, F. (1983) [Long-term behaviour of pentachlorophenol in closed rooms.] Chemosphere, 12: 59-63 (in German).

GILBERT, F.I., MINN, C.E., DUNCAN, R.C., ALDRICH, T., LEDERER, W.H., & WILKINSON, J.E. (1983) Effects of chemical preservatives on the health of wood treating workers in Hawaii, 1981. Clinical and chemical profiles and historical prospective study, Honolulu, Hawaii, Pacific Health Research Institute, 233 pp.

GJOVIK, L.R., JOHNSON, D.B., KOZAK, V., WOOLSON, E.A., THOMPSON, W.A., MICKLEWRIGHT, J.T., DOST, W.A., & NICHOLAS, D.D. (1981) The biologic and economic assessment of pentachlorophenol, inorganic arsenicals, creosote. I. Wood Preservatives, Washington DC, US Department of Agriculture, pp. 69-87 (Technical Bulletin No. 1658-1).

GLICKMAN, A.H., STRATHAM, C.N., & LECH, J.J. (1977) Studies on the uptake, metabolism, and disposition of pentachlorophenol and pentachloroanisole in rainbow trout. Toxic. appl. Pharmacol., 41: 649-658.

GODSY, E.M., GOERLITZ, D.F., & EHRLICH, G.G. (1986) Effects of pentachlorophenol on methanogenic fermentation of phenol. Bull. environ. Contam. Toxicol., 36: 271-277.

GOLDSTEIN, J.A., FRIESEN, M., LINDER, R.E., HICKMAN, P., HASS, J.R., & BERGMAN, H. (1977) Effects of pentachlorophenol on hepatic drug-metabolizing enzymes and porphyria related to contamination with chlorinated dibenzo-p-dioxins and dibenzofurans. Biochem. Pharmacol., 26: 1549-1557.

GOODNIGHT, C.J. (1942) Toxicity of sodium pentachlorophenate and pentachlorophenols to fish. Ind. eng. Chem., 34: 868-872.

GORDON, D. (1956) How dangerous is PCP? Med. J. Aust., Sept. 29: 485-488.

GOSSLER, K. & SCHALLER, K.H. (1978) [Quantitative determination of pentachlorophenol in urine and plasma by gas chromatography.] Z. anal. Chem., 290: 111-112 (in German).

GOTHAM, I.J. & RHEE, G.Y. (1982) Effects of a hexachlorobiphenyl and pentachlorophenol on growth and photosynthesis of phytoplankton. J. Great Lakes Res., 8: 328-335.

GREEN, R.E. & YOUNG, R.H.T. (1970) Herbicide and fertilizer movement in Hawaiian sugarcane soils in relation to subsurface water quality. Hawaiian Sugar Technol., 29: 88-96.

GREENE, M.H., BRINTON, L.A., FRAUMENI, J.F., & D'AMICO, R. (1978) Familial and sporadic Hodgkin's disease associated with occupational wood exposure. Lancet, 9: 626-627.

GREICHUS, Y.A., LIBAL, G.W., & JOHNSON, D.D. (1979) Diagnosis and physiologic effects of pentachlorophenols on young pigs. I. Effects of purified pentachlorophenol. Bull. environ. Contam. Toxicol., 23: 418-422.

GRIMM, H.G., SCHALLER, K.H., & VALENTIN, H. (1985) [Results of pentachlorophenol exposure in the workplace and the environment.] Zentralbl. Arbeitsmed., Arbeitsschutz, Prophyl. Ergon., 34: 136-142 (in German).

GRIMM, H.G., SCHELLMANN, B., SCHALLER, K.H., & GOSSLER, K. (1981) [Pentachlorophenol concentrations in tissues and body fluids of normal persons.] Zbl. Bakt. Hyg., I. Abt. Orig. B, 174: 77-90 (in German).

GRUTTKE, H., KRATZ, W., PAPENHAUSEN, U., WEIGMANN, G., HAQUE, A., & SCHUPHAN, I. (1986) [Transfer of ^{14}C-Na-PCP in model-foodchains.] Verhd. Ges. ökol., 14: 451-455 (in German).

GUNTHER, F.A., WESTLAKE, W.E., & JAGLAN, P.S. (1968) Reported solubilities of 738 pesticide chemicals in water. Residue Rev., 20: 56-148.

GUPTA, P.K. & RAO, P.S. (1982) Toxicity of phenol, pentachlorophenol, and sodium pentachlorophenate to a freshwater pulmonate snail Lymnaea acuminata. Arch. Hydrobiol., 94: 210-217.

GUPTA, P.K., MUJUMDAR, V.S., RAO, P.S., & DURVE, V.S. (1982) Toxicity of phenol, pentachlorophenol, and sodium pentachlorophenolate to a freshwater teleost Lebistes reticulatus (Peters). Acta hydrochim. hydrobiol., 10: 177-181.

GUPTA, S., VERMA, S.R., & SAXENA, P.K. (1982) Toxicity of phenolic compounds in relation to the size of a freshwater fish Notopterus notopterus (Pallas). Ecotoxicol. environ. Saf., 6: 433-438.

GUPTA, S., DALELA, R.C., & SAXENA, P.K. (1983a) Influence of dissolved oxygen levels on acute toxicity of phenolic compounds to fresh water teleost Notopterus notopterus (Pallas). Water Air Soil Pollut., 19: 223-228.

GUPTA, S., DALELA, R.C., & SAXENA, P.K. (1983b) Effects of phenolic compounds on in vivo activity of transaminases in certain tissues of the fish Notopterus notopterus. Environ. Res., 32: 8-13.

GUTHRIE, M.A., KIRSCH, E.J., WUKASCH, R.F., & GRADY, C.P.L. (1984) Pentachlorophenol biodegradation. II. Anaerobic. Water Res., 18: 451-461.

HAKULINEN, R. & SALKINOJA-SALONEN, M. (1982) Treatment of pulp and paper industry waste waters in an anaerobic fluidised bed reactor. Process Biochem., 3/4: 18-22.

HALAWANI, A. (1951) Endemic diseases control. J. Egypt. Med. Assoc., 34: 347-358.

HALEY, T.J. (1977) Human poisoning with pentachlorophenol and its treatment. Ecotoxicol. environ. Saf., 1: 343-347.

HALL, L.H. & KIER, L.B. (1984) Molecular connectivity of phenols and their toxicity to fish. Bull. environ. Contam. Toxicol., 32: 354-362.

HAQUE, A., SCHEUNERT, I., & KORTE, F. (1978) Isolation and identification of a metabolite of pentachlorophenol-^{14}C in rice plants. Chemosphere, 7: 65-69.

HAQUE, R. & FREED, V.H. (1974) Behaviour of pesticides in the environment: environmental chemodynamics. Residue Rev., 52: 89-116.

HARDELL, L. (1977) Soft-tissue sarcoma and exposure to phenoxy acids: a clinical observation. Läkartidingen, 74: 2853-2854.

HARDELL, L. (1979) Malignant lymphoma of histiocytic type and exposure to phenoxyacetic acids or chlorophenols. Lancet, 1: 55-56.

HARDELL, L. (1981a) Relation to soft-tissue sarcoma, malignant lymphoma, and colon cancer to phenoxy acids, chlorophenols, and other agents. Scand. J. Work environ. Health, 7: 119-130.

HARDELL, L. (1981b) Epidemiological studies on soft-tissue sarcoma and malignant lymphoma and their relation to phenoxy acid or chlorophenol exposure, Umea, Sweden, Umea University Medical Dissertations (New Series No. 65).

HARDELL, L. & SANDSTROM, A. (1979) Case-control study: soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br. J. Cancer, 39: 711-717.

HARDELL, L., ERIKSSON, M., LENNER, P., & LUNDGREN, E. (1981) Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols, and phenoxy acids: a case-control study. Br. J. Cancer, 43: 169-176.

HARDELL, L., JOHANSSON, B., & AXELSON, O. (1982) Epidemiological study of nasal and nasopharyngeal cancer and their relation to phenoxy acid or chlorophenol exposure. Am. J. ind. Med., 3: 247-257.

HARGESHEIMER, E.E. & COUTTS, R.T. (1983) Selected ion mass spectrometric identification of chlorophenol residues in human urine. J. Assoc. Off. Anal. Chem., 66: 13-21.

HARPER, D.B. & BANAVE, D. (1975) Chloroanisole residues in broiler tissues. Pestic. Sci., 6: 159-163.

HARRISON, D.L. (1959) The toxicity of wood preservatives to stock. Part I. Pentachlorophenol. NZ. Vet. J., 7: 89-98.

HARVEY, W.A. & CRAFTS, A.S. (1952) Toxicity of pentachlorophenol and its sodium salts in three Yolo soils. Hilgardia, 21: 487-490.

HATTULA, M.L., WASENIUS, V.M., REUNANEN, H., & ARSTILA, A.U. (1981) Acute toxicity of some chlorinated phenols, catechols and cresols to trout. Bull. environ. Contam. Toxicol., 26: 295-298.

HAUCH, R.G., NORRIS, D.R., & PIERCE, R.H. (1980) Acute and chronic toxicity of sodium pentachlorophenate to the copepod Pseudodiaptomus coronatus. Bull. environ. Contam. Toxicol., 25: 562-568.

HAYES, E.H. (1979) High-pressure liquid chromatographic determination of pentachlorophenol by using paired ion chromatography reagents. J. Assoc. Off. Anal. Chem., 62: 1004-1006.

HEIKES, D.L. & GRIFFITT, K.R. (1980) Pentachlorophenol in Mason jar lids and home canned food. J. Assoc. Off. Anal. Chem., 63: 1125-1128.

HENSHAW, B.G., MORGAN, J.W.W., & WILLIAMS, N. (1975) The detection of organic solvent preservatives in wood by thin-layer chromatography. J. Chromatogr., 110: 37-41.

HERNANDEZ, C. & STRASSMAN-SUNDY, S. (1980) Pentachlorophenol in log homes - Kentucky. Morb. Mortal. Wkly Rep., 29: 431-432, 437.

HERNBERG, S. & PESSI, T. (1964) Peripheral nervous paralysis due to pentachlorophenate. Int. Arch. Gewerbepathol. Gewerbehyg., 21: 23-26.

HIATT, C.W., HASKINS, W.T., & OLIVIER, L. (1960) The action of sunlight on sodium pentachlorophenate. Am. J. trop. Med. Hyg., 9: 527-531.

HICKMAN, G.T. & NOVAK, J.T. (1984) Acclimation of activated sludge to pentachlorophenol. J. Water Pollut. Control Fed., 56: 364-469.

HILL, E.F., HEALTH, R.G., SPANN, J.W., & WILLIAMS, J.D. (1975) Lethal dietary toxicities of environmental pollutants to birds, Washington DC, US Fish and Wildlife Service, Department of the Interior, 61 pp (Special Scientific Report - Wildlife No. 191).

HILLAM, R.P. & GREICHUS Y.A. (1983) Effects of purified pentachlorophenol on the serum proteins of young pigs. Bull. environ. Contam. Toxicol., 31: 599-604.

HILTON, H.W., YUEN, Q.H., & NOMURA, N.S. (1970) Distribution of residues from atrazine, ametryne, and pentachlorophenol in sugarcane. J. agric. food Chem., 18: 217-220.

HINKLE, D.K. (1973) Fetotoxic effects of pentachlorophenol in the golden Syrian hamster. Toxicol. appl. Pharmacol., 25: 455.

HIRSCH, A.A. (1942) Toxicity of sodium pentachlorophenate and other chemicals on water hyacinth. Bot. Gaz., 103: 620-621.

HMSO (1974) The non-agricultural user of pesticides in Great Britain, London, Her Majesty's Stationery Office, 65 pp (Pollution Paper No. 3).

HOBEN, H.J., CHING, S.A., CASARETT, L.J., & YOUNG, R.A. (1976a) A study of the inhalation of pentachlorophenol by rats. I. A method for the determination of pentachlorophenol in rat plasma, urine, and tissue and in aerosol samples. Bull. environ. Contam. Toxicol., 15: 78-85.

HOBEN, H.J., CHING, S.A., & CASARETT, L.J. (1976b) A study of the inhalation of pentachlorophenol by rats. II. A new inhalation exposure system for high doses in short exposure time. Bull. environ. Contam. Toxicol., 15: 86-92.

HOBEN, H.J., CHING, S.A., & CASARETT, L.J. (1976c) A study of inhalation of pentachlorophenol by rats. III. Inhalation toxicity study. Bull. environ. Contam. Toxicol., 15: 463-465.

HOBEN, H.J., CHING, S.A., & CASARETT, L.J. (1976d) A study of inhalation of pentachlorophenol by rats. IV. Distribution and excretion of inhaled pentachlorophenol. Bull. environ. Contam. Toxicol., 15: 466-474.

HOBEN, J.H., CHING, S.A., YOUNG, R.A., & CASARETT, L.J. (1976e) A study of the inhalation of pentachlorophenol by rats. V. A protein binding study of pentachlorophenol. Bull. environ. Contam. Toxicol., 16: 225-232.

HODSON, P.V. & BLUNT, B.R. (1981) Temperature-induced changes in pentachlorophenol chronic toxicity to early life stages of rainbow trout (Salmo gairdneri). Aquat. Toxicol., 1: 113-128.

HODSON, P.V., DIXON, D.G., & KAISER, K.L.E. (1984) Measurement of median lethal dose as a rapid indication of contaminant toxicity to fish. Environ. Toxicol. Chem., 3: 243-254.

HOETING, A.L. (1977) Penta - another environmental contaminant. In: Proceedings of the Central States Association of Food and Drug Officials Spring Meeting, Mason, Ohio, 4-5 May 1977, pp. 65-71.

HOLMBERG, B., JENSEN, S., LARSSON, A., LEWANDER, K., & OLSSON, M. (1972) Metabolic effects of technical pentachlorophenol (PCP) on the eel Anguilla anguilla L. Comp. Biochem. Physiol., 43B: 171-183.

HOOS, R.A.W. (1978) Patterns of pentachlorophenol usage in Canada - an overview. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 3-11.

HUANG, J.-C. & GLOYNA, E.F. (1968) Effect of organic compounds on photosynthetic oxygenation. I. Chlorophyll destruction and suppression of photosynthetic oxygen production. Water Res., 2: 347-366.

HUBER, W., SCHUBERT, V., & SAUTTER, C. (1982) Effects of pentachlorophenol on the metabolism of the aquatic macrophyte Lemna minor. Environ. Pollut. A, 29: 215-224.

HUCKINS, J.N. & PETTY, J.D. (1983) Dynamics of purified and industrial pentachlorophenol in fathead minnows. Arch. environ. Contam. Toxicol., 12: 667-672.

HUECK, H.J. & LABRIJN, J. (1960) [Mold protection of cotton with pentachlorophenol and laurylpentachlorophenol.] Textil-Rundschau, 15: 467-472 (in German).

HUGHES, B.J., FORSELL, J.H., SLEIGHT, S.D., KUD, S., & SHULL, L.R. (1985) Assessment of pentachlorophenol toxicity in newborn calves: clinicopathology and tissue residues. J. anim. Sci., 61(6): 1587-1603.

HUNTER, G.W., FREYTAG, R.E., RITCHIE, L.S., PAN, C., YOKOGAWA, M., & POTTS, D.E. (1952) Studies on schistosomiasis. VI. Control of the snail host of schistosomiasis in Japan with sodium pentachlorophenate (Santobrite). Am. J. trop. Med. Hyg., 1: 831-847.

HUTZINGER, O., FREI, R.W., MERIAN, E., & POCCHIARI, F. (1982) Chlorinated dioxins and related compounds impact on the environment. In: Proceedings of a Workshop, Rome, 22-24 October, 1980, Oxford, New York, Toronto, Sydney, Paris, Frankfurt, Pergamon Press, Vol. 5, 658 pp (Pergamon Series on Environmental Science).

IARC (1977) Some fumigants, the herbicides 2,4-D and 2,4,5-T, chlorinated dibenzodioxins and miscellaneous industrial chemicals, Lyons, International Agency for Research on Cancer, pp. 111-138 (IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Vol. 15).

IARC (1979a) Pentachlorophenol. In: Some halogenated hydrocarbons, Lyons, International Agency for Research on

Cancer, pp. 303-325 (IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Vol. 20).

IARC (1979b) Hexachlorobenzene. In: Some halogenated hydrocarbons, Lyons, International Agency for Research on Cancer, pp. 155-178 (IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Vol. 20).

IDE, A., NIKI, J., SAKAMOTO, F., WATANABE, J., & WATANABE, H. (1972) Decomposition of pentachlorophenol in paddy soil. Agric. biol. Chem., 36: 1937-1944.

IFEADI, C.N. (1975) Screening study to develop background information and determine the significance of air contaminant emissions from pesticide plants, Washington DC, US EPA Office of Pesticide Programes (EPA Report No. PB-244734).

IMAI, K., ASANO, A., & SATO, R. (1967) Oxidative phosphorylation in Micrococcus denitrificans. I. Preparation and properties of phosphorylating membrane fragments. Biochim. Biophys. Acta, 143: 462-476.

INGLIS, A. & DAVIS, E.L. (1972) Effects of water hardness on the toxicity of several organic and inorganic herbicides to fish. US Bur. Sport Fish. Wildl. tech. Pap., 67: 1-22.

INGOLS, R.S. & GAFFNEY, P.E. (1965) Biological studies of halophenols. Proc. Soc. Water Resour. Pollut. Control Conf., 14: 175-181.

INGOLS, R.S., GAFFNEY, P.E., & STEVENSON, P.C. (1966) Biological activity of halophenols. J. Water Pollut. Control Fed., 38: 629-635.

INGRAM, L.L., MCGINNIS, G.D., & GJOVIK, L.R. (1981a) The relative amount of pentachlorophenol volatilization from treated wood. In: Proceedings of the American Wood Preservers' Association Annual Meeting, April 27-29, Hyatt Orlando, Florida, Florida, Kissimmee, pp. 102-108.

INGRAM, L.L., MCGINNIS, G.D., JASPERSE, G., & GJOVIK, L.R. (1981b) The effect of solvent systems on the volatilization of pentachlorophenol from treated wood. In: Proceedings of the American Wood Preservers' Association Annual Meeting April 27-29, Hyatt Orlando, Florida, Florida, Kissimmee, pp. 105-117.

INNES, J.R.M., ULLAND, B.M., VALERIO, M.G., PETRUCELLI, L., FISHBEIN, L., HART, E.R., PALLOTTA, A.J., BATES, R.R., FALK, H.L., GART, J.J., KLEIN, M., MITCHELL, I., & PETERS, J.

(1969) Bioassay of pesticides and industrial chemicals for tumourigenicity in mice: a preliminary note. J. Natl Cancer Inst., 42: 1101-1114.

IRPTC (1983) Data profile on pentachlorophenol, Geneva, International Register of Potentially Toxic Chemicals, United Nations Environment Programme.

IRPTC (1984) Scientific review of Soviet literature on toxicity and hazards of chemicals Vol. 75. Pentachlorophenol, Moscow, Centre of International Projects (GKNT, no. 75).

ISHIZAWA, S., TOYODA, H., & MATSUGUCHI, T. (1961) Effects of DD, EDB, and PCP upon microorganisms and their activities in soil. Part I. Effects on microflora. Soil Plant Food Tokyo, 6: 145-155.

IVANOV, Z. & MAGEE, R.J., (1980) The determination of trace amounts of chlorophenols by high-performance liquid chromatography. Microchem. J., 25: 543-547.

IZAKI, K., TAKAHASHI, M., SATO, Y, SASAGAWA, Y., SATO, K., & FURUSAKA, C. (1981) Some properties of pentachlorophenol-resistant gram-negative bacteria. Agric. biol. Chem., 45: 765-767.

JAKOBSON, I. & YLLNER, S. (1971) Metabolism of ^{14}C-pentachlorophenol in the mouse. Acta pharmacol. toxicol., 29: 513-524.

JANKE, D. & FRITSCHE, W. (1978) [Microbial dechlorination of pesticides and other xenobiotica.] Z. Allerg. Mikrobiol., 18: 365-382 (in German).

JANSSENS, J.J. & SCHEPENS, P.J.C. (1984) Chronic pentachlorophenol intoxication as a result of the usage of wood protectants. Meded. Fac. Landbouwwet., 49: 1175-1184.

JANSSON, B., SUNDSTROM, G., & AHLING, B. (1978) Formation of polychlorinated dibenzo-p-dioxins during combustion of chlorophenol formulations. Sci. total Environ., 10: 209-217.

JAYAWEERA, R., PETERSEN, R., & SMEJTEK, P. (1982) Induced hydrogen ion transport in lipid membranes as origin of toxic effect of pentachlorophenol in an alga. Pestic. Biochem. Physiol., 18: 197-204.

JENSEN, S. & RENBERG, L. (1972) Contaminants in pentachlorophenol: chlorinated dioxins and predioxins (chlorinated hydroxy-diphenylethers). Ambio, 1: 62-65.

JENSEN, S. & RENBERG, L. (1973) Chlorinated dimers present in several technical chlorophenols used as fungicides. Environ. Health Perspect., 5: 37-39.

JIRASEK, L., KALENSKY, J., KUBEC, K., PAZDEROVA, J., & LUKAS, E. (1974) [Acne chlorina, porphyria cutanea tarda, and other manifestations of general poisoning during the manufacture of herbicides. II.] Cesk. Dermatol., 49: 145-157 (in Czech with English summary).

JOHNSON, R.D. & MANSKE, D.D. (1977) Pesticides in food and feed. Pesticide and other chemical residues in total diet samples (XI). Pestic. monit. J., 11: 116-131.

JOHNSON, R.L., GEHRING, P.J., KOCIBA, R.J., & SCHWETZ, B.A. (1973) Chlorinated dibenzodioxins and pentachlorophenol. Environ. Health. Perspect., 5: 171-175.

JONES, P.A. (1981) Chlorophenols and their impurities in the Canadian environment, Ottawa, Environment Canada, 434 pp. (Report No. EPS 3-EC-81-2)

JONES, P.A. (1984) Chlorophenols and their impurities in the Canadian environment: 1983 supplement, Ottawa, Environment Canada, 93 pp (Report No. EPS 3-Ep-84-3).

JUHL, U., WITTE, I., & BUTTE, W. (1985) Metabolism of pentachlorophenol to tetrachlorohydroquinone by human liver homogenate. Bull. environ. Contam. Toxicol., 35: 596-601.

KAILA, K. & SAARIKOSKI, J. (1977) Toxicity of pentachlorophenol and 2,3,6-trichlorophenol to the crayfish (Astacus fluviatilis L.). Environ. Pollut., 12: 119-123.

KAISER, K.L.E. & VALDMANIS, I. (1982) Apparent octanol/water partition coefficients of pentachlorophenol as a function of pH. Can. J. Chem., 60: 2104-2106.

KALMAN, D.A. & HORSTMAN, S.W. (1983) Persistence of tetrachlorophenol and pentachlorophenol in exposed woodworkers. J. Toxicol. clin. Toxicol., 20: 343-352.

KARASEK, F.W. & HUTZINGER, O. (1986) Dioxin danger from garbage incineration. Anal. Chem., 58: 633A-642A.

KAUFMAN, D.D. (1976) Phenols. In: Kearney, P.C. & Kaufman, D.D., ed. Chemistry, degradation, and mode of action, New York, Marcel Dekker, Vol. 2, pp. 665-707.

KAUFMAN, D.D. (1978) Degradation of pentachlorophenol in soil, and by soil microorganisms. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 27-39.

KAUPPINEN, T. & LINDROOS, L. (1985) Chlorophenol exposure in saw mills. Am. Ind. Hyg. Assoc. J., 46: 34-38.

KEHOE, R.A., DEICHMANN-GRUEBLER, W., & KITZMILLER, K-V. (1939) Toxic effects upon rabbits of pentachlorophenol and sodium pentachlorophenate. J. ind. Hyg. Toxicol. 21(5): 160-172.

KENAGA, E.E. (1972) Guidelines for environmental study of pesticides: determination of bioconcentration potential. Residue Rev., 44: 73-113.

KERKVLIET, N.I., BAECHER-STEPPAN, L., CLAYCOMB, A.T., CRAIG, A.M., & SHEGGEBY, G.G. (1982a) Immunotoxicity of technical pentachlorophenol (PCP-T): depressed humoral immune response to T-dependent and T-independent antigen stimulation in PCP-T exposed mice. Fundam. appl. Toxicol., 2: 90-99.

KERKVLIET, N.I., BAECHER-STEPPAN, L., & SCHMITZ, J.A. (1982b) Immunotoxicity of pentachlorophenol (PCP): increased susceptibility to tumour growth in adult mice fed technical PCP-contaminated diets. Toxicol. appl. Pharmacol., 62: 55-64.

KIMBROUGH, R.D. & LINDER, R.E. (1978) The effect of technical and purified pentachlorophenol on the rat liver. Toxicol. appl. Pharmacol., 46: 151-162.

KINZELL, J.H., AMES, N.K., SLEIGHT, S.D., KREHBIEL, J.D., KUO, C., ZABIK, M.J., & SHULL, L.R. (1981) Subchronic administration of technical pentachlorophenol to lactating dairy cattle: performance, general health, and pathologic changes. J. dairy Sci. 64: 42-51.

KIRSCH, E.J. & ETZEL, J.E. (1973) Microbial decomposition of pentachlorophenol. J. Water Pollut. Control Fed., 45: 359-364.

KLEMMER, H.W. (1972) Human health and pesticides - community pesticide studies. Residue Rev., 41: 55-63.

KLEMMER, H.W, WONG, L., SATO, M.M., REICHERT, E.L., KORSAK, R.J., & RASHAD, M.N. (1980) Clinical findings in workers exposed to pentachlorophenol. Arch. environ. Contam. Toxicol., 9(6): 715-725.

KLOPFFER, W., KAUFMANN, G., RIPPEN, G., & POREMSKI, H.-J. (1982) A laboratory method for testing the volatility from aqueous solution: first results and comparison with theory. Ecotoxicol. environ. Saf., 6: 545-559.

KNOWLTON, M.F. & HUCKINS, J.N. (1983) Fate of radiolabelled sodium pentachlorophenate in littoral microcosms. Bull. environ. Contam. Toxicol., 30: 206-213.

KNUDSEN, I., VERSCHUUREN, H.G., DEN TONKELAAR, E.M., KROES, R., & HELLEMAN, P.F.W. (1974) Short-term toxicity of pentachlorophenol in rats. Toxicology, 2: 141-152.

KOBAYASHI, K. (1978) Metabolism of pentachlorophenol in fishes. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 89-105.

KOBAYASHI, K. (1979) Metabolism of pentachlorophenol in fish. In: Khan, M.A.Q., Lech, J.J., & Menn, J.J., ed. Pesticide and xenobiotic metabolism in aquatic organisms, Washington DC, Americal Chemical Society, Vol. 99, pp. 131-143 (ACS Symposium Series).

KOBAYASHI, K. & AKITAKE, H. (1975a) Studies on the metabolism of chlorophenols in fish. I. Absorption and excretion of PCP by goldfish. Bull. Jpn. Soc. Sci. Fish., 41: 87-92.

KOBAYASHI, K. & AKITAKE, H. (1975b) Studies on the metabolism of chlorophenols in fish. II. Turnover of absorbed PCP in goldfish. Bull. Jpn. Soc. Sci. Fish., 41: 93-99.

KOBAYASHI, K. & NAKAMURA, N. (1979a) Isolation and identification of a conjugated PCP excreted in the urine of goldfish. Bull. Jpn. Soc. Sci. Fish., 45: 1001-1004.

KOBAYASHI, K. & NAKAMURA, N. (1979b) Major detoxification pathways for pentachlorophenol in goldfish. Bull. Jpn. Soc. Sci. Fish., 45: 1185-1188.

KOCIBA, R.J. & SCHWETZ, B.A. (1982) A review of the toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) with a comparison of the toxicity of other chlorinated dioxin isomers. Assoc. Food Drug Off. Q. Bull., 46: 168-188.

KOCIBA, R.J., GEHRING, P.J., MCCOLLISTER, S.B., WADE, C.E., LISOWE, R.W., & MEINECKE, B. (1971) Results of 90-day toxicological study in male rats maintained on diets containing production grade or "purified" pentachlorophenol, Midland, Michigan, Dow Chemical Company, 23 pp.

KOEGEL, W., MUELLER, W.F., COULSTON, F., & KORTE, F. (1979) Biotransformation of pentachloronitrobenzene-^{14}C in rhesus monkeys after single and chronic oral administration. Chemosphere, 8: 97-105.

KONASEWICH, D.E., HENNING, F.A., WILE, K.H., & GERENCHER, E. (1983) Chlorophenate wood protection, Canada, British Columbia Ministry of Environment (ISBN 0-7719-9371-4).

KOPPE, P., DIETZ, F., TRAUD, J., & RUEBELT, C. (1977) [Detection and photometric determination of 126 phenolic compounds in water using four group-specific reagents.] Z. anal. Chem., 285: 1-19 (in German).

KOSS, G. & KORANSKY, W. (1978) Pentachlorophenol in different species of vertebrates after administration of hexachlorobenzene and pentachlorobenzene. In: Rao, R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 131-137.

KOTZIAS, D., KLEIN, W., & KORTE, F. (1975) [Occurrence of xenobiotica in seeping waters of landfills.] Chemosphere, 5: 301-306 (in German).

KOZAK, V.P., SIMSIMAN, G.V., CHESTERS, G. STENSBY, D., & HARKIN, J. (1979) Reviews of the environmental effects of pollutants: XI. Chlorophenols, Washington DC, US Environmental Protection Agency, 492 pp (EPA Report 600/1-79-012).

KRAUSE, CHR. (1982) [Active ingredients of wood preservatives used in homes.] In: Aurand, K., Seifert, B., & Wegner, J., ed. [Air quality in interiors,] Stuttgart, New York, Gustav-Fischer-Verlag, pp. 309-316 (in German).

KRAUSE, CHR. & ENGLERT, N. (1980) [Health evaluation of PCP (pentachlorophenol) containing wood preservatives in rooms.] Holz Roh Werkst., 38: 429-432 (in German).

KROYER, G., WASHUTTL, J., SCHOERGMEYER, W., STEINER, I., & WINKER, N. (1982) [Contamination of food with volatile biocide substances from wood preservatives in model experiments.] Lebensm.-Wissen. Technol., 15: 111-112 (in German).

KUEHL, D.W. & DOUGHERTY, R.C. (1980) Pentachlorophenol in the environment. Evidence for its origin from commercial pentachlorophenol by negative chemical ionization mass spectrometry. Environ. Sci. Technol., 14: 447-449.

KUNDE, M. (1982) [Experience in the evaluation of wood preservatives.] In: Aurand, K., Seifert, B., & Wegner, J., ed. [Air quality in interiors,] Stuttgart, New York, Gustav-Fischer-Verlag, pp. 317-325 (in German).

KUNDE, M, & BOHME, C. (1978) [Toxicology of pentachlorophenol - an overview]. Bundesgesundheitsblatt. 21: 302-310 (in German).

KUTZ, F.W., MURPHY, R.S., & STRASSMAN, S.C. (1978) Survey of pesticide residues and their metabolites in urine from the general population. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 363-369.

KUWAHARA, M., KATO, N., & MUNAKATA, K. (1966a) The photochemical reaction of pentachlorophenol. Part I. The structure of the yellow compound. Agric. Biol. Chem. Jpn, 30: 232-238.

KUWAHARA, M., KATO, N., & MUNAKATA K. (1966b) The photochemical reaction of pentachlorophenol. Part II. The chemical structure of minor products. Agric. biol. Chem. Jpn, 30: 239-245.

KUWATSUKA, S. (1972) Degradation of several herbicides under different conditions. In: Matsumura, F., Boush, G., & Misato, T., ed. Environmental toxicology of pesticides, New York, Academic Press, pp. 385-400.

KUWATSUKA, S. & IGARASHI, M. (1975) Degradation of PCP in soils. II. The relationship between the degradation of PCP and the properties of soils, and the identification of the degradation products of PCP. Soil Sci. Plant Nutr., 21: 405-414.

LAHANIATIS, E.S., CLAUSEN, E., BIENIEK, D., & KORTE, F. (1985) Formation of 2,3,7,8-tetrachlorodibenzofuran during thermolysis of selected chlorinated organic compounds. Chemosphere, 14: 233-238.

LAMBERTON, J., GRIFFIN, B., ARBOGAST, B., INMAN, R., DEINZER, M., & GRIFFIN, D. (1979) The determination of polychlorodibenzo-p-dioxins in pentachlorophenol and wood treatment solutions. Am. Ind. Hyg. Assoc. J., 40: 816-822.

LAMPARSKI, L.L., MAHLE, N.H., & SHADOFF, L.A. (1978) Determination of pentachlorophenol, hexachlorodibenzo-p-dioxin, and octachlorodibenzo-p-dioxin in bovine milk. J. agric. food Chem., 26: 1113-1116.

LAMPARSKI, L.L., STEHL, R.H., & JOHNSON, R.L. (1980) Photolysis of pentachlorophenol-treated wood. Chlorinated dibenzo-p-dioxin formation. Environ. Sci. Technol., 14, 196-200.

LANGEBARTELS, C. & HARMS, H. (1984) Metabolism of pentachlorophenol in cell suspension cultures of soybean and wheat: pentachlorophenol glucoside formation. Z. Pflanzenphysiol., 113: 201-212.

LANGER, H.G., BRADY, T.P., DALTON, L.A., SHANNON, T.W., & BRIGGS, P.R. (1973) Thermal chemistry of chlorinated phenols. In: Blair, E.H., ed. Chlorodioxins: origin and fate, Washington DC, American Chemical Society, pp. 26-32 (Advances in Chemistry Series No. 120).

LANGEVELD, VAN, H.E.A.M. (1975) Determination of pentachlorophenol in toy paints. J. Assoc. Off. Anal. Chem., 58: 19-22.

LARSEN, R.V., BORN, G.S., KESSLER, W.V., SHAW, S.M., & VAN SICKLE, D.C. (1975) Placental transfer and teratology of pentachlorophenol in rats. Environ. Lett., 10: 121-128.

LARSEN, R.V., KIRSCH, L.E., SHAW, S.M., CHRISTIAN, J.E., & BORN, G.S. (1972) Excretion and tissue distribution of uniformly labelled ^{14}C-pentachlorophenol in rats. J. Pharm. Sci., 61: 2004-2006.

LAUWERYS, R. (1970) Biological criteria for selected industrial toxic chemicals: a review. Scand. J. Work. environ. Health, 1: 139-172.

LEE, B.E., LACROIX, M.D., DUPONT, G.A.J., & SCOTT, J.A. (1984) Capillary gas chromatographic determination of pentachlorophenol residues in tallow following automated gel permeation clean-up. J. Assoc. Off. Anal. Chem., 67: 546-548.

LEIGHTY, E.G. & FENTIMAN, A.F., Jr (1982) Conjugation of pentachlorphenol to palmitic acid by liver microsomes. Bull. environ. Contam. Toxicol., 28(3): 329-333.

LEVIN, J.-O. & NILSSON, C.-A. (1977) Chromatographic determination of polychlorinated phenols, phenoxyphenols,

dibenzofurans, and dibenzodioxins in wood-dust from worker environments. Chemosphere, 6: 443-448.

LEVIN, J.-O., RAPPE, C., & NILSSON, C. (1976) Use of chlorophenols as fungicides in sawmills. Scand. J. Work environ. Health, 2: 71-81.

LILIENBLUM, W. (1985) Formation of pentachlorophenol glucuronide in rat and human liver microsomes. Biochem. Pharmacol., 34: 893-894.

LIU, D., THOMSON, K., & STRACHAN, W.M.J. (1981) Biodegradation of pentachlorophenol in a simulated aquatic environment. Bull. environ. Contam. Toxicol., 26: 85-90.

LIU, D., THOMSON, K., & KAISER, K.L.E. (1982) Quantitative structure-toxicity relationship of halogenated phenols on bacteria. Bull. environ. Contam. Toxicol., 29: 130-136.

LOWER, M. (1982) [Studies on the pentachlorophenol content of human organs.] Friedrich-Alexander- University Erlangen-Nürnberg (Thesis) (in German).

LORES, E.M., EDGERTON, T.R., & MOSEMAN, R.F. (1981) Method for the confirmation of chlorophenols in human urine by LC with an electrochemical detector. J. chromatogr. Sci., 19, 466-469.

LU, P.Y. & METCALF, R.L. (1975) Environmental fate and biodegradability of benzene derivatives as studied in a model aquatic ecosystem. Environ. Health Perspect., 10: 269-284.

LU, P.Y., METCALF, R.L., & COLE, L.K. (1978) The environmental fate of ^{14}C-pentachlorophenol in laboratory model ecosystems. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 53-63.

LYR, H. (1962) [On the oxidative decomposition of chlorinated phenols.] Holztechnologie, 3: 201-208 (in German).

LYR, H. (1963) [Enzymatic detoxification of chlorinated phenols.] Phytopathol. Z., 47: 73-83 (in German).

MCCONNELL, E.E., MOORE, J.A., HASEMANN, J.K., & HARRIS, M.W. (1978) The comparative toxicity of chlorinated dibenzo-p-dioxins in mice and guinea-pigs. Toxicol. appl. Pharmacol., 44: 335-356.

MCCONNELL, E.E., MOORE, J.A., GUPTA, B.N., RAKES, A.H., LUSTER, M.I., GOLDSTEIN, J.A., HASEMAN, J.K., & PARKER, C.E. (1980) The chronic toxicity of technical and analytical pentachlorophenol in cattle. I. Clinicopathology. Toxicol. appl. Pharmacol., 52: 468-490.

MCGAVACK, T.H., BOYD, L.J., PICCIONE, F.V., & TERRANOVA, R. (1941) Acute and chronic intoxications with sodium pentachlorophenate in rabbits. J. ind. Hyg. Toxicol., 23(6): 239-251.

MCGOVERN, J.J. (1982) Apparent immunotoxic response to phenolic compounds. Food Chem. Toxicol., 20: 496.

MANSKE, D.D. & JOHNSON, R.D. (1977) Residues in food and feed. Pesticide and other chemical residues in total diet samples. X. Pest. monit. J., 10: 134-148.

MASON, M.F., WALLACE, S.M., FOERSTER, E., & DRUMMOND, W. (1965) Pentachlorophenol poisoning: report of two cases. J. Forensic Sci., 10: 136-147.

MASUDA, Y. & KUROKI, H. (1982) Polychlorinated dibenzofurans and related compounds in patients with "Yusho". In: Hutzinger, O., Frei, R.W., Merian, E., & Pocchiari, F., ed. Chlorinated dioxins and related compounds: impact on the environment, Oxford, Pergamon Press, Vol. 5, pp. 561-570 (Pergamon Series on Environmental Science).

MATSUMOTO, G. (1982) Comparative study on organic constituents in polluted and unpolluted inland aquatic environments. III. Phenols and aromatic acids in polluted and unpolluted waters. Water Res., 16: 551-557.

MATSUMOTO, G., ISHIWATARI, R., & HANYA, T. (1977) Gas chromatographic-mass spectrometric identification of phenols and aromatic acids in river waters. Water Res., 11: 693-698.

MATTSON, V.R., ARTHUR, J.W., & WALBRIDGE, C.T. (1976) Acute toxicity of selected organic compounds to fathead minnows, Duluth, Minnesota, US Environmental Protection Agency, 13 pp (Ecological Research Series No. EPA 600/3-76-097).

MEEMKEN, H.-A., FUERST, P., & HABERSAAT, K. (1982) [Analysis of pentachlorophenol in cultured champignons.] Dtsch. Lebensm. Rundsch. 78: 282-287 (in German).

MEHENDALE, H.W., FIELDS, M., & MATTHEWS, H.B. (1975) Metabolism and effects of hexachlorobenzene on hepatic microsomal enzymes in the rat. J. agric. food Chem., 23: 261-264.

MELNIKOV, N.N. (1971) Chemistry of pesticides. Residue Rev., 36: 104-107.

MENON, J.A. (1958) Tropical hazards associated with the use of pentachlorophenol. Br. med. J., 11: 1156-1158.

MERCIER, M. (1981) Criteria (dose/effect relationships) for organochlorine pesticides, Oxford, Pergamon Press, 381 pp.

MERZ, V. & WEITH, W. (1872) [On the characteristics of pentachlorophenol.] Ber. Dtsch. Chem. Ges., 5: 458-463 (in German).

MILLER, C.S. & ABOUL-ELA, M.M. (1969) Fate of pentachlorophenol in cotton. J. agric. food Chem., 17: 1244-1246.

MITSUDA, H., MURAKAMI, K., & KAWAI, F. (1963) Effect of chlorophenol analogues on the oxidative phosphorylation in rat liver mitochondria. Agric. biol. Chem., 27: 366-372.

MORGADE, C., BARQUET, A., & PFAFFENBERGER, C.D. (1980) Determination of polyhalogenated phenolic compounds in drinking-water, human blood-serum, and adipose tissue. Bull. environ. Contam. Toxicol., 24: 257-264.

MORGAN, J.W.W. & PURSLOW, D.F. (1973) Volatile losses of wood preservatives. In: Proceedings of the 23rd Annual Convention of the BWPA, British Wood Preservers Association, pp. 173-193.

MOOS, L.P., KIRSCH, E.J., WUKASCH, R.F., & GRADY, C.P.L. (1983) Pentachlorophenol biodegradation. I. Aerobic. Water Res., 17: 1575-1584.

MULLER, W.F. (1981) [Metabolism and pharmacokinetics of selected chemicals in rhesus monkey and chimpanzee,] Society for Radiation and Environmental Research (GSF), Munich, pp. 120-128 (Report 6/599) (in German).

MUNAKATA, K. & KUWAHARA, M. (1969) Photochemical degradation products of pentachlorophenol. Residue Rev., 25: 13-23.

MUNDY, D.E. & MACHIN, A.F. (1981) Determination of pentachlorophenol and related compounds in animal materials by

high-performance liquid chromatography and gas chromatography. J. Chromatogr., 216: 229-238.

MUNRO, I.B., OSTLER, D.C., MACHIN, A.F., & QUICK, M.P. (1977) Suspected poisoning by pentachlorophenol in sawdust. Vet. Rec., 101(26/27): 525.

MURRAY, H.E., RAY, L.E., & GIAM, C.S. (1981) Analysis of marine sediment, water, and biota for selected organic pollutants. Chemosphere, 10: 1327-1334.

MURTHY, N.B.K. & KAUFMAN, D.D. (1978) Degradation of pentachloronitrobenzene (PCNB) in anaerobic soils. J. agric. food Chem., 26: 1151-1156.

MURTHY, N.B.K., KAUFMAN, D.D., & FRIES, G.F. (1979) Degradation of pentachlorophenol (PCP) in aerobic and anaerobic soil. J. environ. Sci. Health, B14: 1-14.

NARANG, A.S., VERNOY, C.A., & EADON, G.A. (1983) Evaluation of Nielsen-Kryger steam distillation technique for recovery of phenols from soil. J. Assoc. Off. Anal. Chem., 66: 1330-1334.

NCI (1979) Bioassay of 2,4,6-trichlorophenol for possible carcinogenicity, Bethesda, Maryland, National Cancer Institute, 115 pp (Technical Report No. PC A06/MF, PB 293-7700).

NCI (1980a) Bioassay of a mixture of 1,2,3,6,7,8-hexachlorobenzo-p-dioxin and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin (gavage) for possible carcinogenicity, Bethesda, Maryland, National Cancer Institute (Carcinogenesis Technical Report Series No. 198) (US Department of Health and Human Services Publication No. (NIH) 80-1754).

NCI (1980b) Bioassay of a mixture of 1,2,3,6,7,8-hexachlorodibenzo-p-dioxin and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin (dermal) for possible carcinogenicity, Bethesda, Maryland, National Cancer Institute (Carcinogenesis Technical Report Series No. 202) (US Department of Health and Human Services Publication No. (NIH) 80-1758).

NEEDHAM, L.L., CLINE, R.E., HEAD, S.L., & LIDDLE, J.A. (1981) Determining pentachlorophenol in body fluids by gas chromatography after acetylation. J. anal. Toxicol., 5: 283-286.

NEIDERT, E., SASCHENBRECKER, P.W., & PATTERSON, J.R. (1984) Detection and occurrence of pentachlorophenol residues in chicken liver and fat. J. environ. Sci. Health B, 19: 579-592.

NIIMI, A.J. & MCFADDEN, L.A. (1982) Uptake of sodium pentachlorophenate (NaPCP) from water by rainbow trout (Salmo gairdneri) exposed to concentrations in the ng/litre range. Bull. environ. Contam. Toxicol., 28(1): 11-19.

NILSSON, C.-A., NORSTROM, A., ANDERSSON, K., & RAPPE, C. (1978) Impurities in commercial products related to pentachlorophenol. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 313-324.

NING, H.S. (1984) [Investigation of the chronic intoxication of pentachlorophenol.] Chin. J. Ind. Hyg. Occup. Dis., 4: 24-28 (in Chinese).

NING, H.S., ZHEN, H.-Q., LI, L.-S., XU, H., WANG, J.-J., WU, S.-S., LIANG, T.-Z., JAN, J.-Q., ZHU, B.-H., HUANG, W.-W., CHEN, W.-Y., & WANG, G.-F. (1984) [Study of the toxicity of pentachlorophenol and recommendations of the maximum allowable concentration in air.] J. Commun. ind. Hyg. (Rail Transp. Syst.), 4: 7-16 (in Chinese).

NIOSH (1978) Manual of analytical methods, Cincinatti, Ohio, US Department of Health, Education, and Welfare, Vol. 4, pp. S297-1-S297-8 (DHEW Publication No. 78-175).

NIOSH (1983) In: Tatken, R.L. & Lewis, R.J., ed. Registry of toxic effects of chemical substances, Cincinnati, Ohio, US National Institute for Occupational Safety and Health, pp. 74-75.

NOAKES, D.N. & SANDERSON, D.M. (1969) A method for determining the dermal toxicity of pesticides. Br. J. ind. Med., 26: 59-64.

NOMURA, S. (1954) Studies on chlorophenol poisoning. I. A clinical examination of workers exposed to pentachlorophenol. Bull. Hyg., 29: 294.

NORSTROM, A., RAPPÉ, C., LINDAHL, R., & BUSER, H.-R. (1979) Analysis of some older Scandinavian formulations of 2,4-dichlorophenoxy acetic acid and 2,4,5-trichlorophenoxy acetic acid for contents of chlorinated dibenzo-p-dioxins and dibenzofurans. Scand. J. Work environ. Health, 5: 375-378.

NRC (1986) In: Thomas, R.D., ed. Drinking water and health, Washington DC, National Research Council, National Academy Press, Vol. 6, pp. 407-421.

NRCC (1981) Polychlorinated dibenzo-p-dioxins: criteria for their effects on man and his environment, Ottawa, Ontario, National Research Council of Canada, Associate Committee on Scientific Criteria for Environmental Quality (No. 18574), 251 pp.

NRCC (1982) Chlorinated phenols: criteria for environmental quality, Ottawa, Ontario, National Research Council of Canada, Associate Committee on Scientific Criteria for Environmental Quality, (No. 18578) 191 pp.

OHE, T. (1979) Pentachlorophenol residues in human adipose tissue. Bull. environ. Contam. Toxicol., 22: 287-292.

OLIE, K., BERG, M.V.D., & HUTZINGER, O. (1983) Formation and fate of PCDD and PCDF combustion processes. Chemosphere, 12: 627-636.

OWEN, J.W. & ROSSO, S.W. (1981) Effects of sublethal concentrations of pentachlorophenol on the liver of bluegill sunfish, epomis machrochirus. Bull. environ. Contam. Toxicol., 26: 594-600.

PAASIVIRTA, J., SORKKO, J., LESKIJORVI, T., & ROOS, A. (1980) Transportation and enrichment of chlorinated phenolic compounds in different aquatic food chains. Chemosphere, 9: 441-456.

PAASIVIRTA, J., SORKKO, J., AHO, M., SURMA-AHO, K., TARHANEN, J., & ROOS, A. (1981) Recent trends of biocides in pikes of the lake Päijänne. Chemosphere, 10: 405-414.

PAASIVIRTA, J., SORKKO, J., SURMA-AHO, K., HUMPPI, T., KUOKKANEN, T., & MARTTINEN, M. (1983) Food chain enrichment of organochlorine compounds and mercury in clean and polluted lakes of Finland. Chemosphere, 12: 239-252.

PAASIVIRTA, J., HEINOLA, K., HUMPPI, T., KARJALAINEN, A., KNUUTINEN, J., MANTYKOSKI, K., PAUKKU, R., PIILOLA, T., SURMA-AHO, K., TARHANEN, J., WELLING, L., & VIHONEN, H. (1985) Polychlorinated phenols, guaiacols and catechols in the environment. Chemosphere, 14: 469-491.

PACKHAM, E.D., DUXBURY, C.L., MAYFIELD, C.I., INNISS, W.E., KRUUV, J., & THOMPSON, J.E. (1982) Quantitative analysis of

pollutant-induced lethal and sublethal damage in cultured mammalian cells. Bull. environ. Contam. Toxicol., 29: 739-746.

PALMER, C.M. & MALONEY, T.E. (1955) Preliminary screening for potential algicides. Ohio J. Sci., 55: 1-8.

PARKER, C.E., JONES, W.A., MATTHEWS, H.B., MCCONNELL, E.E., & HASS, J.R. (1980) The chronic toxicity of technical and analytical pentachlorophenol in cattle. II. Chemical analysis of tissues. Toxicol. appl. Pharmacol., 55: 359-369.

PARR, L.J., GEE, M.G., LAND, D.G., ROBINSON, D., & CURTIS, R.F. (1974) Chlorophenols from wood preservatives in broiler house litter. J. Sci. Food Agric., 25: 835-841.

PARRISH, P.R., DYAR, E.E., ENOS, J.M., & WILSON, W.G. (1978) Chronic toxicity of chlordane, trifluralin, and pentachlorophenol to sheepshead minnows (Cyprinodon variegatus), Washington DC, US Environmental Protection Agency 67 pp (Report No. EPA 600/3-78-010).

PAULI, O. & FRANKE, G. (1972) Behaviour and degradaton of technical preservatives in the biological purification of sewage. In: Walters, A.H. & Hueck-Van der Plas, E.H., ed. Biodegradaton of materials. II, New York, John Wiley and Sons, pp. 52-60.

PEARCE, N.E., SMITH, A.H., HOWARD, J.K., SHEPPARD, R.A., GILES, H.J., & TEAGUE, C.A. (1986) Non-Hodgkin's lymphoma and exposure to phenoxyherbicides, chlorophenols, fencing work, and meat works employment: a case control study. Br. J. ind. Med., 43: 75-83.

PEARCE, N.E., SHEPPARD, R.A., SMITH, A.H., & TEAGUE, C.A. (in press) Non-Hodgkin's lymphoma and farming: an expanded case-control study. Int. J. Cancer.

PEKARI, L. & ANTERO, A. (1982) A simple liquid chromatographic method for the analysis of penta- and tetrachlorophenols in urine of exposed workers. J. Chromatogr. biomed. Appl., 232: 129-136.

PETROWITZ, H.J. (1981) [Volatilisation of the active ingredients of wood preservatives from chemically protected timber.] In: [Research report of the Expert Group on Biological Materials Research,] Berlin, Federal Institute for Materials Research, 32 pp (in German).

PIERCE, R.H., Jr & VICTOR, D.M. (1978) The fate of pentachlorophenol in an aquatic ecosystem. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 41-52.

PIERCE, R.H., BRENT, C.R., WILLIAMS, H.P., & REEVES, S.G. (1977) Pentachlorophenol distribution in a fresh water ecosystem. Bull. environ. Contam. Toxicol., 18: 251-258.

PIGNATELLO, J.J., MARTINSON, M.M., STEIERT, J.G., CARLSON, R.E., & CRAWFORD, R.L. (1983) Biodegradation and photolysis of pentachlorophenol in artificial freshwater streams. Appl. environ. Microbiol., 46: 1024-1031.

PLESTINA, R. (1984) Prevention, diagnosis and treatment of insecticide poisoning, Geneva, World Health Organization, 69 pp (unpublished report VBC/84.889).

PLIMMER, J.R. (1973) Technical pentachlorophenol: origin and analysis of base-insoluble contaminants. Environ. Health Perspect., 5: 41-48.

POWERS, P.W. (1976) How to dispose of toxic substances and industrial wastes, Park Ridge, New Jersey, Noyes Data Corporation, p. 373.

PRAGER, B., JACOBSON, P., SCHMIDT, P., & STERN, D., ed. (1923) [Beilstein's handbook of organic chemistry.] 4th ed., Berlin, Springer-Verlag, Vol. 6, (Syst. No. 522) pp. 194-197 (in German).

PRESCOTT, C.A., WILKIE, B.N., HUNTER, B., & JULIAN, R.J. (1982) Influence of a purified grade of pentachlorophenol on the immune-response of chickens. Am. J. vet. Res., 43: 481-487.

PRUITT, G.W., GRANTHAM, B.J., & PIERCE, R.H. (1977) Accumulation and elimination of pentachlorophenol by the bluegill Lepomis macrochirus. Am. Fish. Soc., 106: 462-465.

QUICK, M.P. (1982) Pesticide poisoning of livestock: a review of cases investigated. Vet. Rec., 111: 5-7.

RAHDE, A.F. & DELLA ROSA, H.V. (1984) [Evaluation of ecotoxicological impact of the hydroelectric dam of Tucurui, Brazil,] 45 pp (unpublished report presented to Eletronorta (Eletrobras)) (in Portuguese).

RAHDE, A.F. & DELLA ROSA, H.V. (1986) Pentachlorophenol - an evaluation of the ecotoxicological impact of the hydroelectric

dam of tucurui, Brazil, 6 pp (unpublished report presented to Eletronorte (Eletrobras)).

RAPPE, C., GARA, A., & BUSER, H.R. (1978a) Identification of polychlorinated dibenzofurans (PCDFs) in commercial chlorophenol formulations. Chemosphere, 12: 981-991.

RAPPE, C., MARKLUND, S., BUSER, H.R., & BOSSHARDT, H.-P. (1978b) Formation of polychlorinated dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) by burning or heating chlorophenates. Chemosphere, 3: 269-281.

RAPPE, C., BUSER, H.R., & BOSSHARDT, H.-P. (1979) Dioxins, dibenzofurans, and other polyhalogenated aromatics: production, use, formation, and destruction. Ann. NY Acad. Sci., 320: 1-18

RAPPE, C., NYGREN, M., BUSER, H.R., & KAUPPINEN, T. (1982) Occupational exposure to polychlorinated dioxins and dibenzofurans. In: Hutzinger, O. et al., ed. Chlorinated dioxins and related compounds: impact on the environment, Oxford, Pergamon Press, Vol. 5, (Pergamon Series on Environmental Science) pp. 495-514.

REINER, E.A., CHU, J.P., & KIRSCH, E.J. (1978) Microbial metabolism of pentachlorophenol. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 67-81.

RENBERG, L. (1974) Ion exchange technique for the determination of chlorinated phenols and phenoxy acids in organic tissue, soil, and water. Anal. Chem., 46: 459-461.

RENNER, G. & MUCKE, W. (1986) Transformations of pentachlorophenol. I. Metabolism in animals and man. Toxicol. environ. Chem., 11: 9-29.

RENNER, G., HOPFER, C., & GOKEL, J.M. (1986) Acute toxicities of pentachlorophenol, pentachloroanisole, tetrachlorohydroquinone, tetrachlorocatechol, tetrachlororesorcinol, terachlorodimethoxybenzene diacetates administered to mice. Toxicol. environ. Chem., 11: 37-50.

RICHARDSON, N.G. (1978) Wood preserving effluents and their treatment. In: Proceedings of the Technical Transfer Seminar Timber Processing Industry, March 10-11 1977, Toronto, Environment Canada, pp. 40-62 (Econ. Technical Review No. EPS 3-WP-78-1).

RIPPEN G. (1984) [Pentachlorophenol.] In: [Handbook of environmental chemicals: physicochemical and ecotoxicological data of selected chemicals,] Landsberg/Lech, Ecomed, pp. 1-13 (in German).

ROBERTS, H.J. (1981) Aplastic anemia due to pentachlorophenol. New Engl. J. Med., 305: 1650-1651.

ROBERTS, H.J., (1983) Aplastic anemia and red cell aplasia due to pentachlorophenol. South. Med. J., 76(1): 45-48.

ROBSON, A.L., KISSANE, J.M., ELVICK, N.H., & PUNDAVELA, L. (1969) Pentachlorophenol poisoning in a nursery for newborn infants. I. Clinical features and treatment. J. Pediatr., 75(2): 309-316.

ROSSKAMP, E. (1982) [Pentachlorophenol as a model case of a xenobiotic compound: PCP in the environment.] Berlin, Federal Health Office Institute for Water, Soil and Air Hygiene, 22 pp (Research Report No. 10604007) (in German).

ROTT, B., NITZ, S., & KORTE, F. (1979) Microbial decomposition of sodium pentachlorophenolate. J. agric. food Chem., 27, 306-310.

ROWE, E.L., ZIOBRO, R.J., WANG, C.J.K., & DENCE, C.W. (1982) The use of an alga Chlorella pyrenoidosa and a duckweed Lemna perpusilla as test organisms for toxicity bioassays of spent bleaching liquors and their components. Environ. Pollut. (Ser. A), 27: 289-296.

ROY, P., KUNDU, P., & DAS, A. (1981) Sodium pentachlorophenate as a mutagenic agent. Biotechnol. Lett., 3: 401-404.

ROZMAN, K., MUELLER, W., COULSTON, F., & KORTE, F. (1977) Long-term feeding study of hexachlorobenzene in rhesus monkeys. Chemosphere, 2/3: 81-84.

RUBINSTEIN, N.I. (1978) Effects of sodium pentachlorophenate on the feeding activity of the lugworm Arenicola cristata Stimpson. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 175-179.

RUDLING, L. (1970) Determination of pentachlorophenol in organic tissues and water. Water Res., 4: 533-537.

RUBELT, C., DIETZ, F., KICKUTH, R., KOPPE, P., KUNTE, H., PESCHEL, G., & SONNEBORN, M. (1982) [Pollutants in ambient

water. Vol. II. Phenols.] Boppard, Harald Boldt Verlag, 168 pp (DFG Report) (in German).

RUMKER, VON, R., LAWLESS, E.W., & MEINERS, A.F. (1974) Production, distribution, use, and environmental impact potential of selected pesticides. Washington DC, US Environmental Protection Agency, pp. 308-319 (EPA Production Report No. EPA 540/1-74-001).

RUSINK, R.G. & SMITH, L.L. (1975) The relationship of the 96-hour LC_{50} to the lethal threshold concentration of hexavalent chromium, phenol, and sodium pentachlorophenate for fathead minnows (Pimephales promelas Rafinesque). Trans. Am. Fish. Soc., 104: 567-570.

RUH, C. & GEBEFUEGI, I. (1984) [Sources for indoor space contamination: presence of pentachlorophenol and lindane in untreated wood samples.] Chemosphere, 13: 919-925 (in German).

RUH, C., GEBEFUEGI, I., & KORTE, F. (1984) The indoor biocide pollution: occurrence of pentachlorophenol and lindane in homes. In: Berglund, B., Lindvall, T., & Sundell, J., ed. Indoor air. IV. Chemical characterization and personal exposure, Stockholm, Swedish Council for Building Research, pp. 309-322.

RYAN, J.J. (1983) Higher chlorinated dioxins implicated in the mortality of young pigs kept on a pentachlorophenol-treated wooden floor. Can. vet. J., 24: 72-75.

SAARIKOSKI, I. & VILUKSELA, M. (1981) Influence of pH on the toxicity of substituted phenols to fish. Arch. environ. Contam. Toxicol., 10: 747-753.

SALKINOJA-SALONEN, M.S., HAKULINEN, R., VALO, R., & APAJALAHTI, J. (1983) Biodegradation of recalcitrant organochlorine compounds in fixed film reactors. Water Sci. Tech., 15: 309-319.

SALKINOJA-SALONEN, M.S., VALO, R., APAJALAHTI, J., HAKULINEN, R., SILAKOSKI, L., & JAAKKOLA, T. (1984) Biodegradation of chlorophenolic compounds in wastes from wood-processing industry. In: Klug, M. & Reddy, C., ed. Current perspectives in microbial ecology, Washington DC, American Society for Microbiology, pp. 668-676.

SANBORN, J.R., CHILDERS, W.F., & HANSEN, L.G. (1977) Uptake and elimination of ^{14}C-hexachlorobenzene (HCB) by the green

sunfish, Lepomis cyanellus Raf., after feeding contaminated food. J. agric. food Chem., 25: 551-553.

SANDERMANN, H., Jr, SCHEEL, D., & V.D. TRENCK, T. (1984) Use of plant cell cultures to study the metabolism of environmental chemicals. Ecotoxicol. environ. Saf., 8: 167-182.

SANDERMANN, H.S., CASTEN, R., & STOCKMANN, H. (1957) Pyrolysis of pentachlorophenol. Chem. Ber., 90: 690-692.

SANGSTER, B., WEGMAN, R.C.C., & HOFSTEE, A.W.M. (1982) Non-occupational exposure to pentachlorophenol: clinical findings and plasma-PCP-concentrations in three families. Hum. Toxicol., 1: 123-133.

SAUR, J.M., WALCHESKI, P.J., NICHOLAS, D.-D., & GJOVIK, L.R. (1982) The concentration of airborne pentachlorophenol within treated wood structures. Proc. Ann. Meet. Am. Wood Preserv. Assoc., 78: 169-173.

SAVOLAINEN, H. & PEKARI, K. (1979) Neurochemical effects of peroral administration of technical pentachlorophenol. Res. Commun. chem. Pathol. Pharmacol., 23(1): 97-105.

SCHAUERTE, W., LAY, J.P., KLEIN, W., & KORTE, F. (1982) Influence of 2,4,6-trichlorophenol and pentachlorophenol on the biota of aquatic systems. Outdoor experiments in compartments of a natural pond. Chemosphere, 11: 71-79.

SCHIMMEL, S.C., PATRICK, J.M., Jr, & FAAS, L.F. (1978) Effects of sodium pentachlorophenate on several estuarine animals: toxicity, uptake and depuration. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 147-155.

SCHONHABER, R., SCHWARZ, A., & KRANL, D. (1982) Comparative studies on the high-pressure liquid chromatographic and gas chromatographic determination of pentachlorophenol in mushrooms. Dtsch. Lebensm. Rundsch., 78: 254-257.

SCHRAG., S.D. & DIXON, R.L. (1985) Occupational exposures associated with male reproductive dysfunction. Ann Rev. Pharmacol. Toxicol., 25: 567-592.

SCHUPPENER, H. (1974) [Uptake of pentachlorophenol (PCP) by corn plants from culture media - a methodological study on the ecological chemistry of lipophilic toxic compounds,] University of Göttingen, 105 pp, (Dissertation) (in German).

SCHWETZ, B.A., NORRIS, J.M., SPARSCHU, G.L., ROWE, V.K., GEHRING, P.J., EMERSON, J.L., & GERBIG, C.G. (1973) Toxicology of chlorinated dibenzo-p-dioxins. Environ. Health Perspect., 5: 87-99.

SCHWETZ, B.A., KEELER, P.A., & GEHRING, P.J. (1974) The effect of purified and commercial grade pentachlorophenol on rat embryonal and fetal development. Toxicol. appl. Pharmacol., 28: 151-161.

SCHWETZ, B.A., QUAST, I.F., KEELER, P.A., HUMISTON, C.G., & KOCIBA, R.J. (1978) Results of two-year toxicity and reproduction studies on pentachlorophenol in rats. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 301-309.

SHA, S.Z. & DUFFIELD, A.M. (1984) Negative ion chemical ionization gas chromatography-mass spectrometry of some derivatives of tri-, tetra-, and pentachlorophenols. J. Chromatogr., 284: 157-166.

SHAFIK, T.M. (1973) The determination of pentachlorophenol and hexachlorophene in human adipose tissue. Bull. environ. Contam. Toxicol., 10: 57-63.

SHAFIK, T.M., SULLIVAN, H.C., & ENOS, H.R. (1973) Multi-residue procedure for halo- and nitrophenols. Measurement of exposure to biodegradable pesticides yielding these compounds as metabolites. J. agric. food Chem., 21: 295-298.

SHEN, S., VILLENEUVE, D.C., CHU, I., KELLY, J., & GILMAN, A.P. (1983) The acute dermal toxicity of tetrachlorophenols in the rat. Bull. environ. Contam. Toxicol., 31: 680-685.

SHIRAKAWA, M., NAGATOSHI, H., & HIRAKAWI, M. (1959) Hygienic investigation on workers dealing with pentachlorophenol (PCP) in a rubber manufacturing industry. Kurume Med. J., 6(1): 24-35.

SIEGWART, Y. (1983) [Control of foodstuff in Switzerland in the year 1982.] Mitt. Geb. Lebensm. Hyg., 74: 179-319 (in German).

SIQUEIRA, M.E.P.B. & FERNICOLA, N.A.C.G. (1981) Determination of pentachlorophenol in urine. Bull. environ. Contam. Toxicol., 27: 380-385.

SIUDA, J.F. (1980) Natural production of organohalogens. In: Jolley, R.L., Brungs, W.A., Cumming, R.B., & Jacobs, V.A., ed. Water chlorination - environmental impact and health effects, Ann Arbor, Michigan, Ann Arbor Science Publishers Inc, Vol. 3, pp. 63-72.

SLOOF, W. & CANTON, J.H. (1983) Comparison of the susceptibility of 11 freshwater species to 8 chemical compounds. II. (Semi) chronic toxicity tests. Aquat. Toxicol., 4: 271-282.

SMITH, A.H., PEARCE, N.F., FISHER, D.O., GILES, H.J., TEAGUE, C.A., & HOWARD, J.K. (1984) Soft-tissue sarcoma and exposure to phenoxyherbicides and chlorophenols in New Zealand. J. Natl Cancer Inst., 73: 1111-1117.

SONNEBORN, M. (1976) A study to determine the comparability of chemical analyses for drinking-water quality within European communities, Luxembourg, Commission of European Communities, 97 pp (EUR 5542e).

STANLAKE, G.J. & FINN, R.K. (1982) Isolation and characterization of a pentachlorophenol-degrading bacterium. Appl. environ. Microbiol., 44: 1421-1427.

STEHL, R.H., PAPENFUSS, R.R., BREDEWEG, R.A., & ROBERTS, R.W. (1973) The stability of pentachlorophenol and chlorinated dioxins to sunlight, heat, and combustion. Adv. Chem. Ser., 120: 119-125.

STERLING, T.D., STOFFMAN, L.D., STERLING, D.A., & MATE, G. (1982) Health effects of chlorophenol wood preservatives on sawmill workers. Int. J. Health Serv., 12: 559-571.

STEVENS, H.M. & RICHARDSON, A. (1979) The rapid screening of body tissues for pentachlorophenol (PCP) with special reference to poisoning fatality. J. Forensic Sci. Soc., 19: 125-129.

STIJVE, T. (1981) Determination of pentachlorophenol and 2,3,4,6-tetrachlorophenol in edible gelatins. Dtsch. Lebensm. Rundsch., 77: 249-253.

STOCKDALE, M. & SELWYN, M.J. (1971a) Influence of ring substituents on the action of phenols on some dehydrogenases, phosphokinases, and the soluble ATPase from mitochondria. Eur. J. Biochem., 21: 416-423.

STOCKDALE, M. & SELWYN, M.J. (1971b) Effects of ring substituents on the activity of phenols as inhibitors and uncouplers of mitochondrial respiration. Eur. J. Biochem., 21: 565-574.

STOHLMAN, E.F. (1951) The toxicity of some related halogenated derivatives of phenols, Bethesda, Maryland, US Public Health Service, pp. 1303 (Public Health Reports No. 66).

STRANKS, D.W. (1976) Wood preservatives: their depletion as fungicides and fate in the environment, Ottawa, Environment Canada, Canadian Forestry Service, pp. 1-35 (Forestry Technical Report No. 10).

STRETZ, L.A. & VAVRUSKA, J.S. (1984) Controlled air incineration of pentachlorophenol-treated wood, Washington DC, US Environmental Protection Agency, 4 pp (EPA-600/S2-84-089).

STRUFE, R. (1968) Problems and results of residue studies after application of molluscicides. Residue Rev., 24: 80-168.

SU, Y.H. & LIN, H.C. (1971) Influence of soil physicochemical characteristics on the efficacy of herbicide pentachlorophenol. Chung. Kuo Nung Yeh Hua Hsueh Hui Chih, 8(3-4): 99-104 (Chem. Abstr. 110707, 74: 301).

SUZUKI, T. (1977) Metabolism of pentachlorophenol by a soil microbe. J. environ. Sci. Health, B12: 113-127.

SUZUKI, T. (1983) Metabolism of pentachlorophenol (PCP) by soil microorganisms, Nippon Noyaku Gakkaishi, 8, 385-394.

TAGATZ, M.E., IVEY, I.M., MOORE, I.C., & TOBIA, M. (1977) Effects of pentachlorophenol on the development of estuarine communities. J. Toxicol. environ. Health, 3: 501-506.

TAGATZ, M.E., IVEY, I.M., & TOBIA, M. (1978) Effects of Dowicide® G-ST on development of experimental estuarine macrobenthic communities. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 157-163.

TAGATZ, M.E., IVEY, J.M., GREGORY, N.R., & OGLESBY, J.L. (1981) Effects of pentachlorophenol on field- and laboratory-developed estuarine benthic communities. Bull. environ. Contam. Toxicol., 26: 137-143.

TAM, T.Y. & TREVORS, J.T. (1981a) Toxicity of pentachlorophenol to Azotobacter vinelandii. Bull. environ. Contam. Toxicol., 27: 230-234.

TAM, T.Y. & TREVORS, J.T. (1981b) Effects of pentachlorophenol on asymbiotic nitrogen fixation in soil. Water Air Soil Pollut., 16: 409-414.

THOMAS, P., CARR, R.S., & NEFF, J.M. (1981) Biochemical stress responses of mullet Mugil cephalus and polychaete worms Neanthes virens to pentachlorophenol. In: Vernberg, F.J., Calabrese, A., Thurnberg, F.P., & Vernberg, W.B., ed. Biological monitoring of marine pollutants, New York, Academic Press, pp. 73-103.

THOMPSON, G.E., HUSAIN, H., PARRY, J., WARDROP, W.L., & GILBRIDE, P.J. (1978) Hydrogeological control and clean-up of soil and groundwater contaminants at Northern Wood Preservers, Ltd. In: Proceedings of the Ontario Industrial Waste Conference, Toronto, June 18-21, Winnipeg, Manitoba, Engineering Consultants, 18 pp.

THOMPSON, W.S. & DUST, J.V. (1971) Pollution control in the wood preserving industry. I. Nature and scope of the problem. For. prod. J., 21: 70-75.

TIERNAN, T.O., TAYLOR, M.L., GARRETT, J.H., VAN NESS, G.F., SOLCH, J.G., DEIS, D.A., & WAGEL, D.J. (1983) Chlorodibenzodioxins, chlorodibenzofurans and related compounds in the effluents from combustion processes. Chemosphere, 12: 595-606.

TIMMONS, L., STEELE, D., CANNON, M., GRESE, R., BROWN, R., MURRIL, E., & JAMESON, C.W. (1984) Identification of bromotetrachlorophenol in commercial pentachlorophenol samples. J. Chromatogr., 314: 476-481.

TING, H.H. & QUICK, M.P. (1980) Simple thin-layer chromatography method for detection of pentachlorophenol in sawdust and woodshavings. J. Chromatogr., 195: 441-444.

TODD, A.S. & TIMBIE, C.Y. (1983) Industrial hygiene surveys of occupational exposure to wood preservative chemicals, Cincinatti, Ohio, US Department of Health, Education, and Welfare, National Institute for Occupational Safety and Health.

TOLA, S., HANBERG, S., COLLAN, Y., LINDERBORG, H., & KORKALA, M.L. (1980) A case-control study of the etiology of nasal cancer in Finland. Int. Arch. occup. environ. Health, 46: 79-85.

TOLEDO, J.V., MONTEIRO DA SILVA, C.S., BULHOES, M.S., PAES LEME, L.A., DA SILVA NETTO, J.A., & GILBERT, B. (1976) Snail control in urban sites in Brazil with slow-release hexabutyldistannoxane and pentachlorophenol. Bull. World Health Organ., 54: 421-425.

TREVORS, J.T. (1982a) Effect of temperature on the degradation of pentachlorophenol by Pseudomonas spp. Chemosphere, 11: 471-475.

TREVORS, J.T. (1982b) Differences in the sensitivity of short-term bioassays. Bull. environ. Contam. Toxicol., 28: 655-659.

TREVORS, J.T. (1982c) Effect of pentachlorophenol on electron transport system activity in soil. Bull. environ. Contam. Toxicol., 29: 727-730.

TREVORS, J.T., MAYFIELD, C.I., & INNISS, W.E. (1981a) A rapid toxicity test using Pseudomonas fluorescens. Bull. environ. Contam. Toxicol., 26: 433-439.

TREVORS, J.T., MAYFIELD, C.I., INNISS, W.E., & THOMPSON, J.E. (1981b) Effect of phenolic antioxidants on the toxicity of pentachlorophenol in short-term bacterial bioassays. Bull. environ. Contam. Toxicol., 27: 433-439.

TREVORS, J.T., MAYFIELD, C.I., & INNISS, W.E. (1982) Effect of sequence of exposure to chlorophenols in short-term bacterial bioassays. Arch. environ. Contam. Toxicol., 11: 203-207.

TRIEBIG, G., KREKELER, H., GOSSLER, K., & VALENTIN, H. (1981) [Investigations into neurotoxicity of work-related materials. II. Motor and sensory nerve conduction velocity in pentachlorophenol-exposed persons.] Int. Arch. occup. environ. Health, 48: 357-367 (in German).

TRUHAUT, R., VITTE, G., & BOUSSEMART, E. (1952a) Recherches sur la toxicologie du pentachlorphénol. I. Propriétés. Caractérisation et dosage dans les milieux biologiques. Arch. Mal. prof. Méd. Trav. Sécur. soc., 13: 561-567.

TRUHAUT, R., L'EPEE, P., & BOUSSEMART, E. (1952b) Recherches sur la toxicologie du pentachlorophénol. II. Intoxications professionelles dans l'industrie du bois. Observations de deux cas mortels. Arch. Mal. prof. Méd. Trav. Sécur. soc., 13: 567-569.

TRUJILLO, D.A., RAY, L.E., MURRAY, H.E., & GIAM, C.S. (1982) Bioaccumulation of pentachlorophenol by killifish (Fundulus similis). Chemosphere, 11: 25-32.

TURNER, H.J., Jr, REYNOLDS, D.M., & REDFIELD, A.C. (1948) Chlorine and sodium pentachlorophenate as fouling preventives in sea water conduits. Ind. eng. Chem., 40: 450-453.

UHL, S., SCHMID, P., & SCHLATTER, C. (1986) Pharmacokinetics of pentachlorophenol in man. Arch. Toxicol., 58: 182-186.

UMWELTBUNDESAMT (1985) [State of the art: dioxins,] Berlin, Erich Schmidt Verlag, 353 pp (in German).

US EPA (1973) EPA compendium of registered pesticides, Washington DC, US Environmental Protection Agency, Vol. II. pp. S-59-001 - S-59-003.

US EPA (1978) Ambient water quality criteria. Pentachlorophenol, Washington DC, US Environmental Protection Agency (PB-292439).

US EPA (1980) Ambient water quality criteria for pentachlorophenol, Washington DC, Office of Water Regulations and Standards, US Environmental Protection Agency, 98 pp (EPA-440/5-80-065).

US EPA (1984a) Creosote, pentachlorophenol, and inorganic arsenicals; notice of intent to cancel; notice of determination of availability of position document. Fed. Reg., 49(136): 28666-28689.

US EPA (1984b) Pentachlorophenol: preliminary notice of determination concluding the rebuttable presumption against registration of pesticide products containing pentachlorophenol for non-wood preservative uses; proposed notice of intent to cancel such registrations; notice of availability of position document 2/3. Fed. Reg., 49(240): 48367-48372.

US EPA (1985) Hazardous waste management system: dioxin-containing wastes. Fed. Reg., 50: 1978-2006.

US NATIONAL ACADEMY OF SCIENCES (1977) Drinking-water and health, Washington DC, Safe Drinking Water Committee, National Academy of Sciences, pp. 583.

VALLEJO-FRIERE, A., RIBEIRO, O.F., & RIBEIRO, I.F. (1954) Quaternary ammonium compounds as molluscicides. Science, 119(3093): 470-472.

VALO, R., KITUNEN, V., SALKINOJA-SALONEN, M., & RAISANEN, S. (1984) Chlorinated phenols as contaminants of soil and water in the vicinity of 2 Finnish sawmills. Chemosphere, 13: 835-844.

VAN OMMEN, B., VAN BLADEREN, P.J., TEMMINK, J.H.M., & MUELLER, F. (1985) Formation of pentachlorophenol as the major product of microsomal oxidation of hexachlorobenzene. Biochem. biophys. Res. Commun., 126: 25-32.

VAN RENSBURG, J.F.J. (1981) Health aspects of organic substances in South African waters - opinions and realities. Water S.Afr., 7: 139-149.

VERMA, S.R., RANI, S., & DALELA, R.C. (1981a) Responses of serum transaminases in Notopterus notopterus chronically exposed to phenolic compounds and their combinations. Environ. Res., 24: 218-223.

VERMA, S.R., TONK, I.P., & DALELA, R.C. (1981b) Determination of the maximum acceptable toxicant concentration (MATC) and the safe concentration for certain aquatic pollutants. Acta hydrochim. hydrobiol., 9: 247-254.

VERMA, S.R., RANI, S., & DALELA, R.C. (1981c) Effects of phenolic compounds on in vivo blood parameters of a fish Notopterus notopterus. J. environ. Sci. Health B, 16: 273-282.

VERMA, S.R., RANI, S., & DALELA, R.C. (1982) Effects of sodium pentachlorophenate on enzymes of energy metabolism in tissues of Notopterus notopterus. Toxicol Lett., 10: 297-302.

VERMEER, K., RISEBROUGH, R.W., SPAANS, A.L., & REYNOLDS, L.M. (1974) Pesticide effects on fish and birds in rice fields of Surinam, South America. Environ. Pollut., 7: 217-236.

VINOGRADOVA, V.K., KALYAGANOV, P.I., SUDONINA, L.T., & ELIZAROV, G.P. (1973) [Industrial hygiene and the health condition of workers engaged in the production of sodium pentachlorophenolate.] Gig. Tr. Prof. Zabol., 8: 11-13 (in Russian).

VOGEL, E. & CHANDLER, J.L.R. (1974) Mutagenicity testing of cyclamate and some pesticides in Drosphila melanogaster. Experientia (Basel), 30(6): 621-623.

WAINSTOCK DE CALMANOVICI, R. & SAN MARTIN DE VIALE, L.C. (1980) Effect of chlorophenols on porphyrin metabolism in rats and chick embryo. Int. J. Biochem., 12: 1039-1044.

WALUM, E. & PETERSON, A. (1984) On the application of culture neuroblastoma cells in chemical toxicity screening. J. Toxicol environ. Health, 13: 511-520.

WANG, M. (1965) [Stability and molluscciidal activity of Na-PCP in the environment.] Chin. J. Hyg., 10: 243-245 (in Chinese).

WARREN, J.S., LAMPARSKI, L.L., JOHNSON, R.L., & GOOCH, R.M. (1982) Determination of pentachlorophenol volatilized from wood via collection on silica gel. Bull. environ. Contam. Toxicol., 29: 719-726.

WATANABE, I. (1973) Isolation of pentachlorophenol decomposing bacteria from soil. Soil Sci. plant Nutr., 19: 109-116.

WATANABE, I. (1978) Pentachlorophenol (PCP) decomposing activity of field soils treated annually with PCP. Soil Biol. Biochem., 10: 71-75.

WATANABE, S. & WATANABE, S. (1970) [Contact dermatitis due to herbicide (PCP and MCPB): a fatal case.] Rinsho Hifugaku, 24(10): 945-949 (in Japanese).

WEBB, P.W. & BRETT, J.R. (1973) Effects of sublethal concentrations of sodium pentachlorophenate on growth rate, food conversion efficiency, and swimming performance in underyearling sockeye salmon (Oncorhynchus nerka). J. Fish. Res. Board Can., 30: 499-507.

WEBER, K. & ERNST, W. (1978) Levels and patterns of chlorophenols in water of the Weser estuary and the German bight. Chemosphere, 11: 873.

WEGMAN, R.C.C. & HOFSTEE, A.W.M. (1979) Chlorophenols in surface waters of the Netherlands. Water Res., 13: 651-657.

WEGMAN, R.C.C. & VAN DEN BROEK, H.H. (1983) Chlorophenol in river sediment in the Netherlands. Water Res., 17: 227-230.

WEINBACH, E.C. (1957) Biochemical basis for the toxicity of pentachlorophenol. Proc. Natl Acad. Sci. (USA), 43: 393-397.

WEINBACH, E.C. & GARBUS, J. (1965) The interaction of uncoupling phenols with mitochondria and with mitochondrial protein. J. biol. Chem., 240: 1811-1819.

WEISS, U.M., KORTE, F., HAQUE, A.U., MOZA, P., & SCHEUNERT, I. (1982a) Fate of pentachlorophenol-^{14}C in rice plants under controlled conditions. J. agric. food Chem., 30: 1186-1190.

WEISS, U.M., SCHEUNERT, I., KLEIN, W., & KORTE, F. (1982b) Fate of pentachlorophenol-^{14}C in soil under controlled conditions. J. agric. food Chem., 30: 1191-1194.

WHITLEY, L.S. (1968) The resistance of tubificid worms to three common pollutants. Hydrobiologia, 32: 193-205.

WHO (1976) EHC 2: Polychlorinated biphenyls and terphenyls, Geneva, World Health Organization, 85 pp.

WHO (1984) The WHO recommended classification of pesticides by hazard. Guidelines to classification 1984-1985, Geneva, World Health Organization (Unpublished report VBC/84.2).

WHO (1985) Guidelines for drinking-water quality: health criteria and other supporting information, Geneva, World Health Organization, Vol. 2, pp. 237-239.

WIKLUND, K. & HOLM, L.E. (1986) Soft-tissue sarcoma risk in Swedish agricultural and forestry workers. J. Natl Cancer Inst., 76: 229-234.

WILLIAMS, P.L. (1982) Pentachlorophenol: an assessment of the occupational hazard. Am. Ind. Hyg. Assoc. J., 43: 799-810.

WILSON, R.D., ZIPRIN, R.L., CLARK, D.E., & ELISSALDE, M.H. (1982) Absorption of pentachlorophenol by the ovine lymphatic system: a technical note. Vet. hum. Toxicol., 24: 12-14.

WINDHOLZ, M., ed. (1976) The Merck index, 9th ed., Rahway, New Jersey, Marck & Co., p. 921.

WITTE, I., JUHL, U., & BUTTE, W. (1985) DNA-damaging properties and cytotoxicity in human fibroblasts of tetrachlorohydroquinone, a pentachlorophenol metabolite. Mutat. Res., 145: 71-75.

WOELKE, C.E. (1972) Development of a receiving water quality bioassay criterion based on the 48-h Pacific oyster (Crassostrea gigas) embryo. Wash. Dep. Fish. Techn. Rep., 9: 93 pp.

WOLWODE, W., WODARZ, R., DRYSCH, K., & WEICHARDT, H. (1980) Determination of free pentachlorophenol in air and in blood by efficient chromatographic procedures. Int. Arch. occup. environ. Health, 45: 153-162.

WONG, A.S. & CROSBY, D.G. (1978) Photolysis of pentachlorophenol in water. In: Rao, K.R., ed. Pentachlorophenol: chemistry, pharmacology, and environmental toxicology, New York, London, Plenum Press, pp. 19-25.

WONG, A.S. & CROSBY, D.G. (1981) Photodecomposition of pentachlorophenol in water. J. agric. food Chem., 29: 125-130.

WOOD, K.M. (1980) Prevalence of unexplained anaemias associated with occupational exposures to pentachlorophenol used as a wood preservative, University of Washington, Department of Environment and Health, 74 pp (Thesis).

WOOD, S., ROM, W.N., WHITE, G.L., & LOGAN, D.C. (1983) Pentachlorophenol poisoning J. occup. Med., 25(7): 527-530.

WSSA (1974) Herbicide handbook of the Weed Science Society of America, Champaign, Illinois, Weed Science Society of America.

WYLLIE, J.A., GABICA, J., BENSON, W.W., & YODER, J. (1975) Exposure and contamination of the air and employees of a pentachlorophenol plant, Idaho - 1972. Pestic. Monit. J., 9: 150-153.

YOUNG, H.C. & CARROL, J.C. (1951) The decomposition of pentachlorophenol when applied as a residual pre-emergence herbicide. Agron. J., 43: 504-507.

YOUNT, J.D. & RICHTER, J.E. (1986) Effects of pentachlorophenol on periphyton communities in outdoor experimental streams. Arch. environ. Contam. Toxicol., 15: 51-60.

YUNKER, M.B. (1981) A pelagic marine ecosystem study of the behaviour, pathways, residence time and toxicity of pentachlorophenol, Sidney, Institute of Ocean Sciences (DSS file No. 07sb.fp833-9-09043, contract rpt. Dobrocky Seatch. Ltd).

ZENZEN, C. (1979) [Pentachlorophenol. Studies on the distribution kinetics after single and repeated dosing,] University of Düsseldorf, 149 pp (Thesis) (in German).

ZIGLER, G.M. & PHILLIPS, W.F. (1967) Thin-layer chromatographic method for estimation of chlorophenols. Environ. Sci. Technol., 1: 65.

ZIMMERLI, B. (1982) [Modelling the transfer of pollutants from painted surfaces in the surrounding air.] In: Aurand, K., Seifert, B., & Wegner, J., ed. [Air quality in closed rooms,] Stuttgart, New York, Gustav Fischer Verlag, pp. 235-267 (in German).

ZIMMERLI, B. & ZIMMERMANN, H. (1979) [Simple procedure to estimate the concentrations of toxic chemicals in the indoor atmosphere.] Mitt. Geb. Lebensmittelunters Hyg., 70: 429-422 (in German).

ZIMMERLI, B., MARSCHALL, T., & MAREK, B. (1979) [Preliminary studies on occurrence of pentachlorophenol in human urine.] Mitt. Geb. Lebensmittelunters. Hyg., 70: 443-450 (in German).

ZIMMERLI, B., MARSCHALL, T., & MAREK, B. (1980) [On the excretion of pentachlorophenol in cow milk.] Mitt. Geb. Lebensmittelunters. Hyg., 71: 404-414 (in German).

ZISCHKE, J.A., ARTHUR, J.W., HERMANUTZ, R.O., HEDTKE, S.F., & HELGAN, J.C. (1985) Effects of pentachlorophenol on invertebrates and fish in outdoor experimental channels. Aquat. Toxicol., 7: 37-58.

ZITKO, V., HUTZINGER, O., & CHOI, P.M.K. (1974) Determination of pentachlorophenol and chlorobiphenyls in biological samples. Bull. environ. Contam. Toxicol., 12: 649-653.

ZOBER, A., GOSSLER, K., MANKE, G., & SCHALLER, K.H. (1979) [Studies on pentachlorophenol loading in the wood industry.] Ber. Jahrestag. Dtsch. Ges. Arbeitsmed., 19th, 1979: 447-454 (in German).

ZOBER, A., SCHALLER, K.H., GOSSLER, K., & KREKELER, H.J. (1981) [Pentachlorophenol and liver function: a pilot study of occupationally exposed groups.] Int. Arch. occup. environ. Health, 48: 347-356 (in German).

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