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Ambient Water Quality Criteria for Pentachlorophenol

AMBIENT WATER QUALITY CRITERIA FOR

PENTACHLOROPHENOL

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FOREWORD

Section 304 (a)(1) of the Clean Water Act of 1977 (P.L. 95-217), requires the Administrator of the Environmental Protection Agency to publish criteria for water quality accurately reflecting the latest scientific knowledge on the kind and extent of all identifiable effects on health and welfare which may be expected from the presence of pollutants in any body of water, including ground water. Proposed water quality criteria for the 65 toxic pollutants listed under section 307 (a)(1) of the Clean Water Act were developed and a notice of their availability was published for public comment on March 15, 1979 (44 FR 15926), July 25, 1979 (44 FR 43660), and October 1, 1979 (44 FR 56628). This document is a revision of those proposed criteria based upon a consideration of comments received from other Federal Agencies, State agencies, special interest groups, and individual scientists. The criteria contained in this document replace any previously published EPA criteria for the 65 pollutants. This criterion document is also published in satisifaction of paragraph 11 of the Settlement Agreement in Natural Resources Defense Council, et. al. vs. Train, 8 ERC 2120 (D.D.C. 1976), modified, 12 ERC 1833 (D.D.C. 1979).

The term "water quality criteria" is used in two sections of the Clean Water Act, section 304 (a)(1) and section 303 (c)(2). The term has a different program impact in each section. In section 304, the term represents a non-regulatory, scientific assessment of ecological effects. The criteria presented in this publication are such scientific assessments. Such water quality criteria associated with specific stream uses when adopted as State water quality standards under section 303 become enforceable maximum acceptable levels of a pollutant in ambient waters. The water quality criteria adopted in the State water quality standards could have the same numerical limits as the criteria developed under section 304. However, in many situations States may want to adjust water quality criteria developed under section 304 to reflect local environmental conditions and human exposure patterns before incorporation into water quality standards. It is not until their adoption as part of the State water quality standards that the criteria become regulatory.

Guidelines to assist the States in the modification of criteria presented in this document, in the development of water quality standards, and in other water-related programs of this Agency, are being developed by EPA.

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CRITERIA DOCUMENT

PENTACHLOROPHENOL

CRITERIA

Aquatic Life

The available data for pentachlorophenol indicate that acute and chronic toxicity to freshwater aquatic life occurs at concentrations as low as 55 and 3.2 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for pentachlorophenol indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 53 and 34 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Human Health

For comparison purposes, two approaches were used to derive criterion levels for pentachlorophenol. Based on available toxicity data, for the protection of public health, the derived level is 1.01 mg/l. Using available organoleptic data, for controlling undesirable taste and odor qualities of ambient water, the estimated level is 30 µg/l. It should be recognized that organoleptic data as a basis for establishing a water quality criterion have limitations and have no demonstrated relationship to potential adverse human health effects.

INTRODUCTION

Pentachlorophenol (PCP) is a commercially produced bactericide, fungicide, and slimicide used primarily for the preservation of wood, wood products, and other materials. As a chlorinated hydrocarbon, its biological properties have also resulted in its use as an herbicide, insecticide, and molluscicide.

Pentachlorophenol is prepared by the chlorination of phenol in the presence of a catalyst. PCP has the empirical formula C_6Cl_5OH, a molecular weight of 266.35, a density of 1.978, and a vapor pressure of 0.12 mm Hg at 100°C (Stecher, 1968; Natl. Fire Prot. Assoc., 1973; Sax, 1975; Spector, 1956). The melting point of pentachlorophenol ranges between 190 and 191°C for the anhydrous form (Stecher, 1968; Weast, 1975). PCP decomposes at its boiling point of 309 to 310°C (Stecher, 1968).

PCP is slightly soluble in water (14 mg/l at 20°C), while its alkaline salts, such as sodium pentachlorophenate (Na-PCP), are highly soluble in water (Weast, 1975). The log of the octanol/water partition coefficient is 5.01 (Leo, et al. 1971).

It has been shown that commercial preparations of PCP contain certain "caustic insolubles" or "nonphenolic, neutral impurities," such as tetra-, penta-, hexa-, hepta-, and octachlorodibenzofurans and the octachlorodibenzo-p-dioxins (Johnson, et al. 1973), as well as hexachlorobenzene and hexachlorodibenzo-p-dioxin (Schwetz, et al. 1978). The chemically pure PCP used in comparative studies had no detectable concentrations of any chlorinated dioxins.

PCP is known to undergo photochemical degradation in solution in the presence of sunlight, with the subsequent formation of several chlorinated benzoquinones, 2,4,5,6-tetrachlororesorcinol, and chloranilic acid (Mitchell, 1961; Hanadmad, 1967). Na-PCP is decomposed directly by sunlight, with the formation of numerous products, including oxidized monomers, dimers, a trimer, and chloranilic acid (Munakata and Kuwahara, 1969; Haitt, et al. 1960). Wong and Crosby (1977) reported the degradation by sunlight or ultraviolet light of dilute solutions of pentachlorophenol to lower chlorophenols, tetrachlorodihydroxybenzenes, and nonaromatic fragments, such as dichloromaleic acid. The irradiation of Na-PCP in relatively high concentrations in aqueous solutions has been reported to form octachlorodibenzo-p-dioxin (Wong and Crosby, 1977).

Although PCP and Na-PCP are disseminated in the environment, there is a paucity of data on their environmental concentration, fate, and effects. Their principal use as a wood preservative results in point source water contamination at both manufacturing and wood preservation sites and, conceivably, non-point source water contamination through runoff wherever there are PCP-treated lumber products exposing PCP or Na-PCP to soil. Harvey and Crafts (1952) noted that PCP persisted in warm, moist soils for a period of 12 months.

REFERENCES

Haitt, C.W., et al. 1960. The action of sunshine on sodium pentachlorophenate. Am. Jour. Trop. Med. Hyg. 9: 527.

Hanadmad, N. 1967. Photolysis of pentachloronitrobenzene, 2,3,5,6-tetrachloronitrobenzene and pentachlorophenol. Ph.D. dissertation. University of California, Davis.

Harvey, W.A. and A.S. Crafts. 1952. Toxicity of pentachlorophenol and its sodium salt in three yolo soils. Hilgardia. 21: 487.

Johnson, R.L., et al. 1973. Chlorinated dibenzodioxins and pentachlorophenol. Environ. Health. Perspect. 5: 171.

Leo, A., et al. 1971. Partition coefficients and their uses. Chem. Rev. 7: 525.

Mitchell, L.C. 1961. Effect of ultraviolet light (2537A) on 141 pesticide chemicals by paper chromatography. Jour. Off. Anal. Chem. 44: 643.

Munakata, K. and M. Kuwahara. 1969. Photochemical degradation products of pentachlorophenol. Residue Rev. 25: 13.

National Fire Protection Assoc. 1973. Fire protection guide on hazardous materials. 5th ed. Boston.

Sax, N.I. 1975. Dangerous Properties of Industrial Materials. 4th ed. Van Nostrand Reinhold Co., New York.

Schwetz, B.A., et al. 1978. Results of Two-year Toxicity and Reproduction Studies on Pentachlorophenol in Rats. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology, and Environmental Toxicology. Plenum Press, New York. p. 301.

Spector, U.S. 1956. Handbook of Toxicology. W.B. Saunders Co., Philadelphia.

Stecher, P.G. (ed.) 1968. The Merck Index. 8th ed. Merck and Co., Inc., Rahway, New Jersey.

Weast, R.C. (ed.) 1975. Handbook of Chemistry and Physics. 5th ed. CRC Press, Cleveland, Ohio.

Wong, A.S. and D.G. Crosby. 1977. Photodecomposition of pentachlorophenol (PCP). Proc. Symp. on Pentachlorophenol, June 27-29. U.S. Environ. Prot. Agency and Univ. West Florida.

Aquatic Life Toxicology*

INTRODUCTION

Pentachlorophenol (PCP) is one of the most widely used pesticides in the United States. Commonly available as either the phenol or its sodium phenate salt, PCP is used as an algicide, bactericide, fungicide, herbicide, molluscicide, and insecticide.

Prior to 1960 the high toxicity of PCP to aquatic organisms was generally recognized, but few toxicity tests had been conducted with aquatic organisms. Almost all currently available toxicity test data for PCP have been obtained from acute tests conducted in the past 20 years, although results from several recent chronic toxicity tests and long-term growth tests are available for assessing subacute responses. In spite of a possible high degree of phytotoxicity, there are few studies on the toxicity of PCP to aquatic plants. There is almost no information on the bioconcentration of pentachlorophenol by freshwater organisms; however, bioconcentration factors are available for a variety of saltwater organisms.

One likely reason for the paucity of chronic toxicity and freshwater bioconcentration data is the relatively low environmental persistence of PCP as compared to DDT and similar chlorinated hydrocarbon insecticides. Pentachlorophenol also appears to be rapidly excreted by fishes following formation of PCP-glucuronide and PCP-sulfate conjugates, with half-lives in tissue of less than 24 hours (Lech, et al. 1978; Akitake and Kobayashi, 1975).

*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life and Its Uses in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of the appropriate table are calculations for deriving various measures of toxicity as described in the Guidelines.

Pentachlorophenol (PCP) and its sodium salt (Na-PCP) occur in a wide variety of products that can cause contamination of the saltwater environment. Pentachlorophenol behaves as a weak acid that is readily dissociated to form its corresponding salt in an alkaline solution (Bevenue and Beckman, 1967).

Pentachlorophenol contains variable amounts of a number of other chemicals present as impurities, with the quantity of impurities greater in commercial technical grade PCP than in more purified laboratory grade PCP. Most of the impurities in PCP are lower chlorinated phenols (e.g., tetra- and trichlorophenol) and condensation products of two chlorinated phenol molecules (e.g., dibenzo-p-dioxins, dibenzofurans, and diphenyl ethers). At least 19 such condensation products have been identified in various samples of PCP (Jensen and Renberg, 1972; Firestone, et al. 1972; Plimmer, 1973; Buser and Bosshardt, 1976).

The contribution of each or all of these impurities to the toxicity of PCP is difficult to assess. Because of the relatively low concentrations of impurities, any impurity would have to be several orders of magnitude more toxic than PCP, or produce profound synergistic effects, in order to influence the toxicity of PCP appreciably. Although the lower chlorinated phenols are unlikely to produce appreciable toxicity in this regard, the condensation products may. The sum of the concentrations of the various condensation products ranges from 10 to perhaps as high as 1,500 ppm in various batches and grades of PCP.

Unless any highly toxic impurities of PCP are identified and specifically addressed by aquatic life criteria, the criteria should treat PCP, including the impurities and their toxicities, as a single entity.

If future commercial PCP is consistently shown to contain significantly lower concentrations of toxic impurities, then the PCP toxicity data base

may have to be reassessed and new data provided updating the criteria to reflect the changed toxicity resulting from the greater purity.

A parallel effort should be made to obtain data for aquatic and mammalian species to determine the toxicity of the various chlorinated dioxins, furans, and diphenyl ethers, for if they do contribute significantly to the toxicity of PCP, they are likely to be toxic to aquatic organisms at extremely low concentrations.

EFFECTS

Acute Toxicity

Throughout the following aquatic life section, the convention has been adopted to express pentachlorophenol concentrations as molecular PCP (MW 266.34) with toxicity data on other forms, e.g., Na-PCP, converted to equivalent PCP concentrations.

Pentachlorophenol is reported to be acutely toxic to freshwater fish species with 96-hour LC_{50} values from 34 to 600 µg/l; salmonid LC_{50} values ranged from 34 to 128 µg/l, and non-salmonid LC_{50} values ranged from 60 to 600 µg/l (Table 1).

Freshwater invertebrate species are poorly represented in the data base, but standard acute toxicity tests with cladocerans produced 48-hour EC_{50} values of 240 to 800 µg/l for *Daphnia magna* and 2,000 µg/l for *Daphnia pulex* (Table 1). Acute toxicity tests with the worm, *Tubifex tubifex*, yielded 24-hour LC_{50} values of 286 to 1,294 µg/l (Table 6). Based on these limited data, invertebrate species appear to be about as sensitive as non-salmonid fish species to PCP.

The wide range in PCP toxicity to *Tubifex* (Table 6) is apparently due to the effects of pH, since the 24-hour LC_{50} values were 286, 619, and 1,294 µg/l at pH values of 7.5, 8.5, and 9.5, respectively. A similar response was observed in the guppy, *Poecilia reticulata*, where the time to 50

percent mortality at a single concentration (924 µg/l) was 21-38 minutes, 72-93 minutes, and 1,440 minutes at pH values of 6.0, 7.6, and 9.0, respectively (Table 6).

These findings are consistent with the frequently demonstrated result that, in aqueous solutions, molecular forms of substituted phenols are more toxic than ionized forms. Thus, lower pH values favor the formation of molecular PCP while higher pH values favor the ionization of PCP into phenate and hydrogen ions. Unfortunately, no data on the effects of pH on PCP toxicity are available from tests of longer than 24-hour duration. While it is inadvisable to extrapolate quantitatively from these very short-term tests to PCP toxicity in general, it is probable that PCP will be less toxic in alkaline waters than in acidic waters.

The LC_{50} values available for four saltwater invertebrate species (Table 1) indicate that the Eastern oyster is the most sensitive, 40 µg/l (Borthwick and Schimmel, 1978), then a polychaete worm, 435 µg/l (U.S. EPA, 1980), and least sensitive are grass shrimp and pink shrimp, 436-5,600 µg/l (Borthwick and Schimmel, 1978; Conklin and Rao, 1978a, Bentley, et al. 1975). Studies by Conklin and Rao (1978a) indicate that the sensitivity of grass shrimp to pentachlorophenol varies with stage of the molt cycle. In flow-through tests, Schimmel, et al. (1978) found no significant mortality among juvenile grass shrimp or juvenile brown shrimp after 96-hour exposures to 515 and 195 µg/l, respectively (Table 6).

Table 1 also lists data for three species of saltwater fishes. The 96-hour LC_{50} values for sheepshead minnows, pinfish and striped mullet ranged from 38 to 442 µg/l (Borthwick and Schimmel, 1978; Parrish, et al. 1978; Schimmel, et al. 1978). No significant mortality of the longnose killifish occurred after a 96-hour exposure to 306 µg/l (Table 6) (Schimmel, et al. 1978).

Although the sensitivity of tested saltwater invertebrate and fish species was very similar, pentachlorophenol appears to be most toxic to molluscs (Tables 1 and 6), which is consistent with the known molluscicidal application of PCP (Bevenue and Beckman, 1967). Most Pacific oyster embryos developed abnormally to the straight-hinged stage when exposed to 55 µg/l for 48 hours (Table 6) (Woelke, 1972), whereas the 48-hour EC_{50} based on abnormal embryonic development of the Eastern oyster was 40 µg/l (Table 1) (Borthwick and Schimmel, 1978). Also, the 192-hour EC_{50} based on reduced shell deposition in the Eastern oyster (Schimmel, et al. 1978) was 34 µg/l (Table 6).

Chronic Toxicity

Chronic toxicity tests have been reported for two freshwater species, the cladoceran, Daphnia magna, and the fathead minnow, and one saltwater species, the sheepshead minnow. Chronic values were 57 and 64 µg/l for the fathead and sheepshead minnows, respectively, whereas the chronic value for Daphnia magna was 240 µg/l (Table 2).

Survival and growth were adversely affected by PCP, but reproduction did not appear to be particularly sensitive. Adema (1978) reported 21-day chronic mortality of Daphnia magna at 320 µg/l but not at 180 µg/l with PCP. Reproduction was not affected at these levels. PCP caused mortality of sheepshead minnows at 88 µg/l, but neither growth nor fecundity was affected at concentrations up to 195 µg/l (Parrish, et al. 1978). With fathead minnows, growth in an early life stage test was impaired at 73 µg/l but not at 45 µg/l, whereas survival was adversely affected at 128 µg/l (Holcombe, et al. manuscript).

The acute-chronic ratios for Daphnia magna, sheepshead minnow, and fathead minnow are 2.5, 6.9, and 3.9, respectively (Table 2).

Species mean acute values and acute-chronic ratios are summarized in Table 3.

Plant Effects

Huang and Gloyna (1968) studied the effect of PCP and 40 other substituted phenols and herbicides on chlorophyll destruction and photosynthesis of the alga, Chlorella pyrenoidosa. Pentachlorophenol was by far the most toxic compound tested, producing complete destruction of chlorophyll in 72 hours at 7.5 µg/l (Table 4). Since no detailed results of the PCP test were given, it is not possible to evaluate this result fully or determine a general dose-response relationship. Another study of PCP-induced chlorosis in plants (Lemna minor) yielded a 48-hour EC_{50} of 800 µg/l (Blackman, et al. 1955).

In the absence of additional freshwater plant data, it is difficult to assess the relative sensitivity of aquatic plants and animals to PCP because the 7.5 µg/l plant value is lower than the lowest fish or invertebrate 96-hour LC_{50} of 34 µg/l, and the 800 µg/l plant value is higher than any fish or invertebrate LC_{50} except the 2,000 µg/l 48-hour EC_{50} for Daphnia pulex.

Data on the toxicity of pentachlorophenol to three species of saltwater algae are also listed in Table 4. An EC_{50} as low as 17 µg/l for Skeletonema costatum (U.S. EPA, 1980) indicates that pentachlorophenol may be more toxic to some plants than to molluscs. Values for Thalassiosira pseudonana and Dunaliella tertiolecta were as low as 179 and 170 µg/l, respectively; a 12-day exposure of the alga, Monochrysis lutheri, to 293 µg/l caused a 58 percent decrease in cell numbers (Table 6) (Woelke, 1965).

Based on the species tested, sensitivities of invertebrate, fish, and plant species to PCP appear to be similar, and concentrations protective of one group would be expected to protect the other groups.

Residues

Reports of two freshwater studies were found which provided reasonable assurance that steady-state levels of PCP were attained in the tissues of freshwater organisms (Table 5). Both studies used renewed PCP concentrations of 100 µg/l. The data of Kobayashi and Akitake (1975) indicated that steady-state was attained after 96 hours and that goldfish had a whole body bioconcentration factor of approximately 1,000. The data of Pruitt, et al. (1977) indicated that bioconcentration was maximal after 8 days in the bluegill and declined thereafter. The bioconcentration factor for the muscle was 13 after 8 days. Pentachlorophenol was rapidly lost from the body when the fish were placed in PCP-free water.

As was true for freshwater species, steady-state bioconcentration factors for saltwater organisms were also low (390 or less) for the sheepshead minnow (Parrish, et al. 1978) and for two molluscs, Eastern oyster (Schimmel, et al. 1978) and blue mussel (Ernst, 1979) (Table 5). However, pentachlorophenol in water was accumulated appreciably by the polychaete worm, Lanice conchilega, with a bioconcentration factor of 3,830 (Ernst, 1979). A temperature range of 5 to 15°C had no discernible effect on the bioconcentration factor of blue mussel.

Eastern oysters exposed to 25 and 2.5 µg/l for 28 days accumulated the chemical in their tissues to an average of 41 and 78 times, reaching steady-state in tissues within 4 days, and when held in PCP-free water, depurated the chemical to nondetectable concentrations in 4 days (Schimmel, et al. 1978). Bioconcentration factors for 96-hour exposures indicate that shrimp bioconcentrate PCP less than do fishes (Table 6). In 96-hour tests, Schimmel, et al. (1978) determined bioconcentration factors of 1.7 for grass shrimp and 0.26 for brown shrimp compared to 30 for longnose killifish and 38 for striped mullet.

The absence of a maximum permissible tissue concentration makes it impossible to calculate a Residue Limited Toxicant Concentration for pentachlorophenol.

Miscellaneous

Additional data regarding the toxicity of PCP to freshwater organisms are listed in Table 6. The most significant results are from a number of studies of 3- to 13-week duration showing that the primary subacute effect of PCP on fish is a reduction in growth rate. Ten studies with salmonid fish species showed growth inhibition of 10 to 27 percent at PCP concentrations ranging from 3.2 to 28 µg/l (Chapman, 1969; Matida, et al. 1970; Webb and Brett, 1973; and Chapman and Shumway, 1978).

The ten percent growth reduction observed by Webb and Brett (1973) for sockeye salmon occurred at a concentration (3.2 µg/l) which was 6 percent of the 96-hour LC_{50} (58 µg/l) for the test fish. Using the 6 percent factor with the lowest 96-hour LC_{50} for freshwater fish species (coho salmon, 34 µg/l) would predict reduced growth at a PCP concentration of 2.0 µg/l.

Additional studies indicate that PCP is very toxic to saltwater invertebrate species, particularly to molluscs (Table 6). No larvae of the Eastern oyster survived a 14-day exposure to 100 µg/l (Davis and Hidu, 1969). Laboratory tests that assess the impact of toxicants that alter the structure of settling benthic communities support the conclusion reached from acute tests, namely, that molluscs are highly sensitive to PCP (Table 6). As little as 7 µg/l significantly decreased the number of molluscs that developed from larvae in unfiltered saltwater during a 9-week exposure. A PCP concentration of 76 µg/l significantly reduced the total number of benthic macrofauna (Tagatz, et al. 1977).

Summary

Pentachlorophenol (PCP) is reported to be acutely toxic to freshwater organisms at concentrations ranging from 34 to 2,000 µg/l. Fish species appear to be more sensitive to PCP than invertebrate species and salmonid fish species more sensitive than non-salmonid fish species. However, the invertebrate data base consists of tests with only two species of cladocerans, so the fish-invertebrate comparison is tenuous. Interspecific comparisons are further complicated by the apparent effect of pH on PCP toxicity. Data from two 24-hour acute studies strongly suggest that PCP is considerably more toxic at acidic pH values than at alkaline pH values.

Chronic toxicity studies with Daphnia magna, the fathead minnow, and the saltwater sheepshead minnow indicated that chronic toxicity does not occur below about 15-40 percent of the 96-hour LC_{50} concentrations. However, several growth studies with salmonid fish species demonstrated that PCP inhibited growth at concentrations between 3.2 and 28 µg/l, concentrations as little as 6 percent of the 96-hour LC_{50}.

The toxicity of PCP to freshwater aquatic plants has been studied very little; the only studies available report chlorosis in algae and in duckweed at PCP concentrations of 7.5 and 800 µg/l, respectively. Pentachlorophenol is rapidly absorbed by fishes, but bioconcentration is relatively low because PCP is rapidly conjugated and excreted.

The toxicity of PCP may be due in part to one or more of the possible contaminants reported to occur in some batches of PCP, especially in older, technical grade PCP. Most common among these contaminants are lower chlorinated phenols (which are less toxic) and higher chlorinated condensation products including dioxins, diphenyl ethers, and dibenzofurans (which may be more toxic). However, their concentrations in PCP, although variable, are usually extremely low.

The lowest concentrations of PCP reported to cause adverse effects in aquatic organisms are 3.2, 7.4, and 9.2 µg/l which inhibited growth in salmon and trout and 7.5 µg/l which produced total chlorosis in algae. The lowest reported acute toxicity value is 34 µg/l for coho salmon, and the lowest reported chronic value is 57 µg/l for the fathead minnow.

Saltwater fish and invertebrate species have similar sensitivities to PCP. The range of EC_{50} and LC_{50} values is from 40 µg/l for Eastern oyster embryos to 5,600 µg/l for juvenile pink shrimp. The range for fish species is from 38 µg/l for the pinfish to 442 µg/l for juvenile sheepshead minnows. In general, however, molluscan species appear to be the most sensitive of those species tested. An early life stage test with PCP and the sheepshead minnow resulted in mortality at 88 µg/l, but no effects on growth or fecundity at concentrations as high as 195 µg/l. Ninety-six-hour EC_{50} values for three saltwater algal species indicate that PCP may be more toxic to some plants then to molluscs. The bioconcentration factor for a polychaete worm was 3,830. Most factors for two mollusc and one fish species were within the range of 13 to 390.

Only a few additional data for both freshwater and saltwater organisms are needed to provide the minimum data base requirements specified in the Guidelines for developing criteria. However, because PCP is very toxic, and effects commonly occur over a relatively wide range of concentrations, these few tests need to be conducted.

CRITERIA

The available data for pentachlorophenol indicate that acute and chronic toxicity to freshwater aquatic life occur at concentrations as low as 55 and 3.2 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

The available data for pentachlorophenol indicate that acute and chronic toxicity to saltwater aquatic life occur at concentrations as low as 53 and 34 µg/l, respectively, and would occur at lower concentrations among species that are more sensitive than those tested.

Table 1. Acute values for pentachlorophenol

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
		FRESHWATER SPECIES		
Cladoceran, Daphnia magna	S, U	680	-	U.S. EPA, 1978
Cladoceran, Daphnia magna	S, U	260	-	Canton & Adema, 1978
Cladoceran, Daphnia magna	S, U	240	-	Canton & Adema, 1978
Cladoceran, Daphnia magna	S, U	400	-	Canton & Adema, 1978
Cladoceran, Daphnia magna	S, U	400	-	Canton & Adema, 1978
Cladoceran, Daphnia magna	S, U	790	-	Canton & Adema, 1978
Cladoceran, Daphnia magna	S, U	800	-	Canton & Adema, 1978
Cladoceran, Daphnia magna	S, M	600	475	Adema, 1978
Cladoceran, Daphnia pulex	S, U	2,000	-	Canton & Adema, 1978
Cladoceran, Daphnia pulex	S, U	2,000	2,000	Canton & Adema, 1978
Coho salmon, Oncorhynchus kisutch	S, U	89	-	Davis & Hoos, 1975
Coho salmon, Oncorhynchus kisutch	S, U	34	55	Davis & Hoos, 1975
Sockeye salmon, Oncorhynchus nerka	S, U	120	-	Davis & Hoos, 1975
Sockeye salmon, Oncorhynchus nerka	S, U	46	-	Davis & Hoos, 1975

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Sockeye salmon, Oncorhynchus nerka	FT, U	58	68	Webb & Brett, 1973
Chinook salmon, Oncorhynchus tshawytscha	FT, U	72	72	Iwama & Greer, 1979
Rainbow trout, Salmo gairdneri	S, U	75	-	Bentley, et al. 1975
Rainbow trout, Salmo gairdneri	S, U	92	-	Bentley, et al. 1975
Rainbow trout, Salmo gairdneri	S, U	85	-	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S, U	89	_	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S, U	46	-	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S, U	92	-	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S, U	44	-	Davis & Hoos, 1975
Rainbow trout, Salmo gairdneri	S, U	69	71	Davis & Hoos, 1975
Brook trout, Salvelinus fontinalis	FT, M	128	128	Cardwell, et al. 1976
Goldfish, Carassius auratus	FT, M	210	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	220	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	230	-	Adelman & Smith, 1976

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Goldfish, Carassius auratus	FT, M	210	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	170	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	170	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	220	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	230	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	240	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	240	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	200	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	190	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	290	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	300	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	200	-	Adelman & Smith, 1976
Goldfish, Carassius auratus	FT, M	250	220	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	200	-	Adelman & Smith, 1976

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Fathead minnow, Pimephales promelas	FT, M	180	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	220	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	180	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	190	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	210	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	220	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	180	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	190	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	190	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	240	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	200	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	200	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	190	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	270	-	Adelman & Smith, 1976

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Fathead minnow, Pimephales promelas	FT, M	230	-	Adelman & Smith, 1976
Fathead minnow, Pimephales promelas	FT, M	263	-	Cardwell, et al. 1976
Fathead minnow, Pimephales promelas	S, U	600	-	Mattson, et al. 1976
Fathead minnow, Pimephales promelas	FT, M	221	-	Holcombe, et al. Manuscript
Fathead minnow, Pimephales promelas	FT, M	194	-	Ruesink & Smith, 1975
Fathead minnow, Pimephales promelas	FT, M	314	212	Ruesink & Smith, 1975
Guppy, Poecilia reticulata	FT, M	217	217	Anderson & Weber, 1975
Bluegill, Lepomis macrochirus	S, U	60	-	Bentley, et al. 1975
Bluegill, Lepomis macrochirus	S, U	77	-	Bentley, et al. 1975
Bluegill, Lepomis macrochirus	R, M	260	-	Pruitt, et al. 1977
Bluegill, Lepomis macrochirus	R, M	305	138	Pruitt, et al. 1977
		SALTWATER SPECIES		
Polychaete worm (adult), Neanthes arenaceodentata	S, U	435	435	U.S. EPA, 1980
Eastern oyster (adult), Crassostrea virginica	FT, M	77	-	Schimmel, et al. 1978

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Eastern oyster, Crassostrea virginica	S, U	40	77	Borthwick & Schimmel, 1978
Grass shrimp (larva), Palaemonetes pugio	S, U	649	-	Borthwick & Schimmel, 1978
Grass shrimp (intermolt), Palaemonetes pugio	R, U	2,632	-	Conklin & Rao, 1978a
Grass shrimp (early premolt), Palaemonetes pugio	R, U	2,743	-	Conklin & Rao, 1978a
Grass shrimp (late premolt), Palaemonetes pugio	R, U	436	1,200	Conklin & Rao, 1978a
Pink shrimp (juvenile), Penaeus duorarum	S, U	5,600	5,600	Bentley, et al. 1975
Sheepshead minnow (juvenile), Cyprinodon variegatus	FT, M	442	-	Parrish, et al. 1978
Sheepshead minnow (1-day fry), Cyprinodon variegatus	S, U	329	-	Borthwick & Schimmel, 1978
Sheepshead minnow (2-wk fry), Cyprinodon variegatus	S, U	392	-	Borthwick & Schimmel, 1978
Sheepshead minnow (4-wk fry), Cyprinodon variegatus	S, U	240	-	Borthwick & Schimmel, 1978
Sheepshead minnow (6-wk fry), Cyprinodon variegatus	S, U	223	442	Borthwick & Schimmel, 1978
Pinfish (prolarvae), Lagodon rhomboides	S, U	38	-	Borthwick & Schimmel, 1978

Table 1. (Continued)

Species	Method*	LC50/EC50 (µg/l)	Species Mean Acute Value (µg/l)	Reference
Pinfish (juvenile), Lagodon rhomboides	FT, M	53	53	Schimmel, et al. 1978
Striped mullet (juvenile), Mugil cephalus	FT, M	112	112	Schimmel, et al. 1978

* S = static, FT = flow-through, R = renewal, U = unmeasured, M = measured

Table 2. Chronic values for pentachlorophenol

Species	Test*	Limits (µg/l)	Chronic Value (µg/l)	Reference
		FRESHWATER SPECIES		
Cladoceran, Daphnia magna	LC	180-320	240	Adema, 1978
Fathead minnow, Pimephales promelas	ELS	45-73	57	Holcombe, et al. Manuscript
		SALTWATER SPECIES		
Sheepshead minnow, Cyprinodon variegatus	LC	47-88	64	Parrish, et al. 1978

* ELS = early life stage; LC = life cycle or partial life cycle

Acute-Chronic Ratios

Species	Acute Value (µg/l)	Chronic Value (µg/l)	Ratio
Cladoceran, Daphnia magna	600	240	2.5
Fathead minnow, Pimephales promelas	221	57	3.9
Sheepshead minnow, Cyprinodon variegatus	442	64	6.9

Table 3. Species mean acute values and acute-chronic ratios for pentachlorophenol

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
	FRESHWATER SPECIES		
11	Cladoceran, *Daphnia pulex*	2,000	-
10	Cladoceran, *Daphnia magna*	475	2.5
9	Goldfish, *Carassius auratus*	220	-
8	Guppy, *Poecilia reticulata*	217	-
7	Fathead minnow, *Pimephales promelas*	212	3.9
6	Bluegill, *Lepomis macrochirus*	138	-
5	Brook trout, *Salvelinus fontinalis*	128	-
4	Chinook salmon, *Oncorhynchus tshawytscha*	72	-
3	Rainbow trout, *Salmo gairdneri*	71	-
2	Sockeye salmon, *Oncorhynchus nerka*	68	-
1	Coho salmon, *Oncorhynchus kisutch*	55	-
	SALTWATER SPECIES		
7	Pink shrimp, *Penaeus duorarum*	5,600	-

Table 3. (Continued)

Rank*	Species	Species Mean Acute Value (µg/l)	Species Mean Acute-Chronic Ratio
6	Grass shrimp, *Palaemonetes pugio*	1,200	-
5	Sheepshead minnow, *Cyprinodon variegatus*	442	6.9
4	Polychaete worm, *Neanthes arenaceodentata*	435	-
3	Striped mullet, *Mugil cephalus*	112	-
2	Eastern oyster, *Crassostrea virginica*	77	-
1	Pinfish, *Lagodon rhomboides*	53	-

* Ranked from least sensitive to most sensitive based on species mean acute value.

Table 4. Plant values for pentachlorophenol

Species	Effect	Result (µg/l)	Reference
	FRESHWATER SPECIES		
Alga, *Chlorella pyrenoidosa*	Chlorosis, 72-hr EC100	7.5	Huang & Gloyna, 1968
Duckweed, *Lemna minor*	Chlorosis, 48-hr EC50	800	Blackman, et al. 1955
	SALTWATER SPECIES		
Alga, *Skeletonema costatum*	Cell numbers 96-hr EC50	20	U.S. EPA, 1980
Alga, *Skeletonema costatum*	Cell numbers 96-hr EC50	17	U.S. EPA, 1980
Alga, *Skeletonema costatum*	Cell numbers 96-hr EC50	18	U.S. EPA, 1980
Alga, *Thalassiosira pseudonana*	Cell numbers 96-hr EC50	205	U.S. EPA, 1980
Alga, *Thalassiosira pseudonana*	Cell numbers 96-hr EC50	189	U.S. EPA, 1980
Alga, *Thalassiosira pseudonana*	Cell numbers 96-hr EC50	179	U.S. EPA, 1980
Alga, *Dunaliella tertiolecta*	Cell numbers 96-hr EC50	206	U.S. EPA, 1980
Alga, *Dunaliella tertiolecta*	Cell numbers 96-hr EC50	170	U.S. EPA, 1980

Table 5. Residues for pentachlorophenol

Species	Tissue	Bioconcentration Factor	Duration (days)	Reference
		FRESHWATER SPECIES		
Goldfish, *Carassius auratus*	Whole body	1,000	5	Kobayashi & Akitake, 1975
Bluegill, *Lepomis macrochirus*	Edible portion	13	8	Pruitt, et al. 1977
		SALTWATER SPECIES		
Polychaete worm, *Lanice conchilega*	Whole body	3,830	8	Ernst, 1979
Blue mussel, *Mytilus edulis*	Soft parts	390	8	Ernst, 1979
Blue mussel, *Mytilus edulis*	Soft parts	326	8 (5 C)	Ernst, 1979
Blue mussel, *Mytilus edulis*	Soft parts	304	8 (10 C)	Ernst, 1979
Blue mussel, *Mytilus edulis*	Soft parts	324	8 (15 C)	Ernst, 1979
Eastern oyster (adult), *Crassostrea virginica*	Soft parts	78	28 steady-state in 4	Schimmel, et al. 1978
Eastern oyster (adult), *Crassostrea virginica*	Soft parts	41	28 steady-state in 4	Schimmel, et al. 1978
Sheepshead minnow (juvenile), *Cyprinodon variegatus*	Whole body	34*	28	Parrish, et al. 1978
Sheepshead minnow (adult), *Cyprinodon variegatus*	Whole body	13*	151	Parrish, et al. 1978

* Average of all concentrations

Table 6. Other data for pentachlorophenol

Species	Duration	Effect	Result (µg/l)	Reference
		FRESHWATER SPECIES		
Tubificid worm, Tubifex tubifex	24 hrs	LC50, pH = 7.5	286	Whitley, 1968
Tubificid worm, Tubifex tubifex	24 hrs	LC50, pH = 8.5	619	Whitley, 1968
Tubificid worm, Tubifex tubifex	24 hrs	LC50, pH = 9.5	1,294	Whitley, 1968
Cladoceran, Daphnia magna	21 days	LC50	480	Adema, 1978
Cladoceran, Daphnia magna	21 days	LC50	510	Adema, 1978
Cladoceran, Daphnia magna	21 days	LC50	400	Adema, 1978
Cladoceran, Daphnia magna	21 days	LC50	470	Adema, 1978
Cladoceran, Daphnia magna	21 days	LC50	430	Adema, 1978
Cladoceran, Daphnia magna	21 days	LC50	490	Adema, 1978
Cladoceran, Daphnia magna	21 days	LC50	170	Adema, 1978
Cladoceran, Daphnia magna	21 days	LC50	190	Adema, 1978
Cladoceran, Daphnia magna	14 days	LC50	440	Adema, 1978
Cladoceran, Daphnia magna	14 days	LC50	460	Adema, 1978
Sea lamprey, Petromyzon marinus	4 hrs	LC100	924	Applegate, et al. 1957

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Sockeye salmon, Oncorhynchus nerka	6 wks	10% growth inhibition	3.2	Webb & Brett, 1973
Rainbow trout, Salmo gairdneri	48 hrs	LC50	157	Alabaster, 1957
Rainbow trout, Salmo gairdneri	4 hrs	LC100	924	Applegate, et al. 1957
Rainbow trout, Salmo gairdneri	5 days	LC25	92	Chapman, 1969
Rainbow trout, Salmo gairdneri	20 days	11% growth inhibition	28	Chapman, 1969
Rainbow trout, Salmo gairdneri	20 days	18% growth inhibition	28	Chapman, 1969
Rainbow trout, Salmo gairdneri	21 days	19% growth inhibition	28	Chapman, 1969
Rainbow trout, Salmo gairdneri	28 days	12% growth inhibition	28	Chapman, 1969
Rainbow trout, Salmo gairdneri	38 days	18% growth inhibition	28	Chapman, 1969
Rainbow trout, Salmo gairdneri	41 days	LC100	46	Chapman, 1969
Rainbow trout, Salmo gairdneri	41 days	13% growth inhibition	9.2	Chapman, 1969
Rainbow trout, Salmo gairdneri	92 days	9% growth inhibition	18	Chapman & Shumway, 1978
Rainbow trout, Salmo gairdneri	28 days	27% growth inhibition	7.4	Matida, et al. 1970
Brown trout, Salmo trutta	48 hrs	LC50	157	Alabaster, 1957

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Atlantic salmon, *Salmo salar*	24 hrs	Altered temperature preference	46	Peterson, 1976
Brook trout, *Salvelinus fontinalis*	336 hrs	LC50	109	Cardwell, et al. 1976
Goldfish, *Carassius auratus*	336 hrs	LC50	175	Cardwell, et al. 1976
Fathead minnow, *Pimephales promelas*	336 hrs	LC50	141	Cardwell, et al. 1976
Guppy, *Poecilia reticulata*	24 hrs	LC40	333	Crandall & Goodnight, 1959
Guppy, *Poecilia reticulata*	21-38 mins	LC50, pH = 5.9-6.0	924	Crandall & Goodnight, 1959
Guppy, *Poecilia reticulata*	72-93 mins	LC50, pH = 7.5-7.6	924	Crandall & Goodnight, 1959
Guppy, *Poecilia reticulata*	24 hrs	LC50, pH = 8.9-9.0	924	Crandall & Goodnight, 1959
Guppy, *Poecilia reticulata*	90 days	LC45	462	Crandall & Goodnight, 1962
Bluegill, *Lepomis macrochirus*	336 hrs	LC50	174	Cardwell, et al. 1976
		SALTWATER SPECIES		
Alga, *Monochrysis lutheri*	12 days	58% decrease cell numbers	293	Woelke, 1965
Pacific oyster (embryo), *Crassostrea gigas*	48 hrs	61.6% embryos abnormal	55	Woelke, 1972
Eastern oyster (embryo), *Crassostrea virginica*	48 hrs	No embryos developed	250	Davis & Hidu, 1969

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Eastern oyster (larva), *Crassostrea virginica*	14 days	No larvae survived	100	Davis & Hidu, 1969
Eastern oyster (adult), *Crassostrea virginica*	192 hrs	Reduced shell deposition EC50	34	Schimmel, et al. 1978
Bay mussel (larva), *Mytilus edulis*	48 hrs	22.1% abnormal larvae salinity 28 g/kg	400	Dimick & Breese, 1965
Bay mussel (larva), *Mytilus edulis*	48 hrs	69.1% abnormal larvae salinity 24 g/kg	400	Dimick & Breese, 1965
Carpet shell *Tapes* (= *Venerupis*) *philippinarum*	120 hrs	Lethal	100	Tomiyama, et al. 1962
Carpet shell *Tapes philippinarum*	24 hrs	Bioconcentration factor about 20	-	Kobayashi, et al. 1969
Grass shrimp (juvenile), *Palaemonetes pugio*	96 hrs	No significant mortality	515	Schimmel, et al. 1978
Grass shrimp (juvenile), *Palaemonetes pugio*	96 hrs	Bioconcentration factor = 1.7	-	Schimmel, et al. 1978
Grass shrimp (adult), *Palaemonetes pugio*	9 days	50% reduction in limb regeneration	473	Rao, et al. 1978
Grass shrimp (adult), *Palaemonetes pugio*	1 hr	Bioconcentration factor = 6.5	-	Conklin & Rao, 1978b
Brown shrimp (juvenile), *Penaeus aztecus*	96 hrs	No significant mortality	195	Schimmel, et al. 1978
Brown shrimp (juvenile), *Penaeus aztecus*	96 hrs	Bioconcentration factor = 0.26	-	Schimmel, et al. 1978
Meiobenthic nematodes	9 wks	Decrease in biomass and density	622	Cantelmo & Rao, 1978

Table 6. (Continued)

Species	Duration	Effect	Result (µg/l)	Reference
Benthic macrofauna	9 wks	Significantly reduced number of individuals	76	Tagatz, et al. 1977
Benthic macrofauna	9 wks	Significantly reduced molluscs	7	Tagatz, et al. 1977
Longnose killifish (juvenile), *Fundulus similis*	96 hrs	No significant mortality	306	Schimmel, et al. 1978
Longnose killifish (juvenile), *Fundulus similis*	96 hrs	Bioconcentration factor = 30	-	Schimmel, et al. 1978
Striped mullet (juvenile), *Mugil cephalus*	96 hrs	Bioconcentration factor = 38	-	Schimmel, et al. 1978

REFERENCES

Adelman, I.R. and L.L. Smith, Jr. 1976. Standard test fish development. Part I. Fathead minnows (Pimephales promelas) and goldfish (Carassius auratus) as standard fish in bioassays and their reaction to potential reference toxicants. Ecol. Res. Ser. EPA 600/3-76-061a. U.S. Environ. Prot. Agency, Duluth, Minn.

Adema, D.M.M. 1978. Daphnia magna as a test animal in acute and chronic toxicity tests. Hydrobiologia 59: 125.

Akitake, H. and K. Kobayashi. 1975. Studies on the metabolism of chlorophenols in fish - III. Isolation and identification of a conjugated PCP excreted by goldfish. Bull. Jap. Soc. Sci. Fish. 41: 322.

Alabaster, J.S. 1957. Toxicity of weedkilling, algicides and fungicides to trout. In: Proc. 4th Brit. Weed Cont. Conf., Brighton. p. 84.

Anderson, P.D. and L.J. Weber. 1975. Toxic response as a quantitative function of body size. Toxicol. Appl. Pharmacol. 33: 471.

Applegate, V.C., et al. 1957. Toxicity of 4,346 chemicals to larval lampreys and fishes. U.S. Fish Wildl. Ser. Spec. Sci. Rep. Fish. No. 207.

Bentley, R.E., et al. 1975. Acute toxicity of pentachlorophenol to bluegill (Lepomis macrochirus), rainbow trout (Salmo gairdneri), and pink shrimp (Penaeus duorarum). Order No. WA-6-99-1414-B. Criteria Branch, U.S. Environ. Prot. Agency.

Bevenue, A. and H. Beckman. 1967. Pentachlorophenol: A discussion of its properties and its occurrence as a residue in human and animal tissues. Res. Rev. 19: 83.

Blackman, G.E., et al. 1955. The physiological activity of substitute phenols. I. Relationships between chemical structure and physiological activity. Arch. Biochem. Biophys. 54: 45.

Borthwick, P.W. and S.C. Schimmel. 1978. Toxicity of pentachlorophenol and related compounds to early life stages of selected estuarine animals. In: K.R. Rao, (ed.), Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. Plenum Press, N.Y. p. 141.

Buser, H.R. and H.P. Bosshardt. 1976. Determination of polychlorinated dibenzo-p-dioxins and dibenzofurans in commercial pentachlorophenols by combined gas chromatography - mass spectrometry. Jour. Assoc. Off. Agri. Chem. 59: 562.

Cantelmo, F.R. and K.R. Rao. 1978. Effects of pentachlorophenol on the meiobenthic nematodes in an experimental system. In: K.R. Rao, (ed.), Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. Plenum Press, N.Y. p. 165.

Canton, J.H. and D.M.M. Adema. 1978. Reproducibility of short-term and reproduction toxicity experiments with Daphnia magna and comparison of the sensitivity of Daphnia magna with Daphnia pulex and Daphnia cucullata in short-term experiments. Hydrobiol. 59: 135.

Cardwell, R.D., et al. 1976. Acute toxicity of selected toxicants to six species of fish. U.S. Environ. Prot. Agency Ecol. Res. Ser. EPA 600/3-76-008. U.S. Environ. Prot. Agency, Duluth, Minn. 117 pp.

Chapman, G.A. 1969. Toxicity of pentachlorophenol to trout alevins. Ph.D. dissertation. Oregon State University, Corvallis, Oregon. 87 pp.

Chapman, G.A. and D.L. Shumway. 1978. Effects of sodium pentachlorophenate on survival and energy metabolism of embryonic and larval steelhead trout. In: K. R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. Plenum press, New York. p. 285.

Conklin, P.J. and K.R. Rao. 1978a. 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.

Conklin, P.J. and K.R. Rao. 1978b. Toxicity of sodium pentachlorophenate to the grass shrimp, Palaemonetes pugio, in relation to the molt cycle. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. Plenum Press, N.Y. p. 181.

Crandall, C.A. and C.J. Goodnight. 1959. The effect of various factors on the toxicity of sodium pentachlorophenate to fish. Limnol. Oceanog. 4: 53.

Crandall, C.A. and C.J. Goodnight. 1962. Effects of sublethal concentrations of several toxicants on growth of the common guppy, Lebistes reticulatus. Limnol. Oceanog. 7: 233.

Davis, H.C. and H. Hidu. 1969. Effects of pesticides on embryonic development of clams and oysters and on survival and growth of the larvae. U.S. Fish Wild. Ser. Fish. Bull. 67: 393.

Davis, J.C. and R.A. Hoos. 1975. Use of sodium pentachlorophenate and dehydroabietic acid as reference toxicants for salmonid bioassays. Jour. Fish. Res. Board Can. 32: 411.

Dimick, R.E. and W.P. Breese. 1965. Bay mussel embryo bioassay. In: Proc. 12th Pacific Northwest Industrial Waste Conf., Univ. Wash., Seattle. p. 165.

Ernst, W. 1979. Factors affecting the evaluation of chemicals in laboratory experiments using marine organisms. Ecotoxicol. Environ. Safety. 3: 90.

Firestone, D., et al. 1972. Determination of polychlorodibenzo-p-dioxins and related compounds in commercial chlorophenols. Jour. Assoc. Off. Agri. Chem. 59: 85.

Holcombe, G.W., et al. (manuscript) Effects of phenol, 2,4-dimethylphenol, 2,4-dichlorophenol and pentachlorophenol on embryo, larval, and early juvenile fathead minnows (Pimephales promelas). U.S. Environ. Prot. Agency, Duluth, Minn.

Huang, J. and E.F. Gloyna. 1968. Effect of organic compounds on phytosynthetic oxygenation. I. Chlorophyll destruction and suppression of photosynthetic oxygen production. Water Res. 2: 347.

Iwama, G.K. and G.L. Greer. 1979. Toxicity of sodium pentachlorophenate to juvenile chinook salmon under conditions of high loading density and continuous-flow exposure. Bull. Environ. Contam. Toxicol. 23: 711.

Jensen, S. and L. Renberg. 1972. Contaminants in pentachlorophenol: chlorinated dioxins and predioxins (chlorinated hydroxy-diphenylethers). Ambio 1: 62.

Kobayashi, K. and H. Akitake. 1975. Studies on the metabolism of chlorophenols in fish. I. Absorption and excretion of PCP by goldfish. Bull. Jap. Soc. Sci. Fish. 41: 87.

Kobayashi, K., et al. 1969. Studies on the metabolism of pentachlorophenate, a herbicide, in aquatic organisms. I. Turnover of absorbed PCP in Tapes philippinarum. Bull. Jap. Soc. Sci. Fish. 35: 1179.

Lech, J.J., et al. 1978. Studies on the uptake, disposition and metabolism of pentachlorophenol and pentachloroanisole in rainbow trout (Salmo gairdneri). In: K. R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. Plenum Press, New York. p. 107.

Matida, Y., et al. 1970. Study on the toxicity of agricultural control chemicals in relation to freshwater fisheries management. No. 5. Some effects of sodium pentachlorophenate to freshwater fishes. Bull. Freshwater Fish. Res. Lab. 20: 127.

Mattson, V.R., et al. 1976. Acute toxicity of selected organic compounds to fathead minnows. Ecol. Res. Ser. EPA 600/3-76-097. U.S. Environ. Prot. Agency, Duluth, Minn. 13 pp.

Parrish, P.R., et al. 1978. Chronic toxicity of chlordane, trifluralin, and pentachlorophenol to sheepshead minnows (Cyprinodon variegatus). Report No. EPA 600/3-78-010: 1.

Peterson, R.H. 1976. Temperature selection of juvenile Atlantic salmon (Salmo salar) as influenced by various toxic substances. Jour. Fish. Tes. Board Can. 33: 1722.

Plimmer, J.R., et al. 1973. Mass spectrometric identification of the hepta- and octa- chlorinated dibenzo-p-dioxins and dibenzofurans in technical pentachlorophenol. Jour. Agri. Food Chem. 21: 90.

Pruitt, G.W., et al. 1977. Accumulation and elimination of pentachlorophenol by the bluegill, Lepomis macrochirus. Trans. Am. Fish. Soc. 106: 462.

Rao, K.R., et al. 1978. Inhibition of limb regeneration in the grass shrimp, Palaemonetes pugio, by sodium pentachlorophenate. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. Plenum Press, N.Y. p. 193.

Ruesink, R.G. and L.L. Smith, Jr. 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.

Schimmel, S.C., et al. 1978. Effects of sodium pentachlorophenate on several estuarine animals: Toxicity, uptake, and depuration. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology an Environmental Toxicology. Plenum Press, N.Y. p. 147.

Tagatz, M.E., et al. 1977. Effects of pentachlorophenol on the development of estuarine communities. Jour. Toxicol. Environ. Health. 3: 501.

Tomiyama, T., et al. 1962. The toxic effect of pentachlorophenate, a herbicide, on fishery organisms in coastal waters. IV. The effect on Venerupis philippinarum of PCP which was constantly supplied or absorbed on estuary mud. Bull. Jap. Soc. Sci. Fish. 28: 422.

U.S. EPA. 1978. In-depth studies on health and environmental impacts of selected water pollutants. U.S. Environ. Prot. Agency, Contract No. 68-01-4646.

U.S. EPA. 1980. Unpublished laboratory data. Environmental Research Laboratory - Gulf Breeze.

Webb, P.W. and J.R. Brett. 1973. Effects of sublethal concentrations of sodium pentachlorophenate on growth rate, food conversion efficiency, and swimming performance in underyearling sockeye salmon (Oncorhynchus nerka). Jour. Fish. Res. Board Can. 30: 499.

Whitley, L.S. 1968. The resistance of tubificid worms to three common pollutants. Acta Hydrobiol. 32: 193.

Woelke, C.E. 1965. Development of a bioassay method using the marine algae, Monochrysis lutheri. Wash. Dep. Fish. Shellfish Progress Rep. 9 p.

Woelke, C.E. 1972. Development of a receiving water quality bioassay criterion based on the 48-hour Pacific oyster (Crassostrea gigas) embryo. Wash. Dep. Fish. Tech. Rep. No. 9: 1.

Mammalian Toxicology and Human Health Effects

INTRODUCTION

Residues of pentachlorophenol (PCP) have been found in food, water, and human tissues (Bevenue and Beckman, 1967; Johnson and Manske, 1977; Buhler, et al. 1973; Shafik, 1973; Kutz, et al. 1978). It does not follow, however, that in each instance the total residue results directly from PCP applications. Yang, et al. (1975) suggested the formation of PCP in the Rhesus monkey following administration of hexachlorobenzene (HCB). Hexachlorobenzene is a registered pesticide and is used as a fungicide. It is also a frequent contaminant in commercial PCP and chlorinated solvents. HCB is the most commonly found chlorinated hydrocarbon in meat (Conklin and Fox, 1978). Consequently, the degradation of HCB to PCP may account for part of the PCP residue present in certain commodities. Lui and Sweeney (1975) and Mehendale, et al. (1975) reported the isolation of PCP from the urine of rats that had been dosed with HCB. Microsomal preparations from rat liver were able to produce one or more chlorophenols, including PCP from HCB (Mehendale, et al. 1975). Koss and Koransky (1978) administered labeled HCB to rats and collected urine and feces for four weeks. HCB was metabolized to PCP, tetrachlorohydroquinone, and pentachlorothiophenol. Twenty-eight percent of the HCB was recovered as PCP in the urine and 16 percent was recovered as PCP in the feces. These results suggest that metabolism of HCB to PCP can be a significant consideration. Karapally, et al. (1973) obtained tentative gas chromatographic identification of PCP in the urine of rabbits receiving ^{14}C-labeled lindane (γ-1,2,3,4,5,6-hexachloro-

cyclohexane). Rats given 8 mg HCB/kg for 19 days had tissue residues of HCB and metabolites consisting of PCP and small amounts of 2,3,4,6-tetrachlorophenol, 2,3,5,6-tetrachlorophenol, 2,4,6-trichlorophenol, and pentachlorobenzene (Engst, et al. 1976a). PCP, tetrachlorophenol, and trichlorophenols are also metabolites of lindane in the rat (Engst, et al. 1976b). Lindane applied to lettuce growing outdoors degraded to free trichlorophenol, 2,3,4,6-tetrachlorophenol, pentachlorophenol, conjugates of the latter two compounds, and unidentified water-soluble products (Kohli, et al. 1976).

The results of these studies suggest several possible sources for the residues of PCP in foods and tissues, in addition to residues resulting from the direct use of PCP.

EXPOSURE

Ingestion from Water and Food

Buhler, et al. (1973) reported pentachlorophenol levels of 0.06 µg/l in finished drinking water prepared from raw water containing 0.17 µg/l. The calculated daily dietary exposure is from 1 to 6 µg/person/day (Duggan and Corneliussen, 1972).

Pentachlorophenol is absorbed from the digestive tract. Pentachlorophenol was detected at levels of 0.01 to 0.04 mg/kg in 13 of 240 food composites collected from August, 1974 to July, 1975 (Johnson and Manske, 1977). The highest residue (0.04 mg/kg) reported was in the food category of sugars and adjuncts.

A bioconcentration factor (BCF) relates the concentration of a chemical in aquatic animals to the concentration in the water in which they live. The steady-state BCFs for a lipid-soluble com-

pound in the tissues of various aquatic animals seem to be proportional to the percent lipid in the tissue. Thus the per capita ingestion of a lipid-soluble chemical can be estimated from the per capita consumption of fish and shellfish, the weighted average percent lipids of consumed fish and shellfish, and a steady-state BCF for the chemical.

Data from a recent survey on fish and shellfish consumption in the United States were analyzed by SRI International (U.S. EPA, 1980). These data were used to estimate that the per capita consumption of freshwater and estuarine fish and shellfish in the United States is 6.5 g/day (Stephan, 1980). In addition, these data were used with data on the fat content of the edible portion of the same species to estimate that the weighted average percent lipids for consumed freshwater and estuarine fish and shellfish is 3.0 percent.

A measured steady-state bioconcentration factor of 13 was obtained for pentachlorophenol using sheepshead minnows (Parrish, et al. 1978). Similar sheepshead minnows contained an average of about 3.6 percent lipids (Hansen, 1980). An adjustment factor of 3.0/3.6 = 0.83 can be used to adjust the measured BCF from the 3.6 percent lipids of the fathead minnow to the 3.0 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average BCF for pentachlorophenol and the edible portion of all freshwater and estuarine aquatic organisms consumed by Americans is calculated to be 13 x 0.83 = 11.

Inhalation

Data concerning exposure of the general public by inhalation of pentachlorophenol are not available. However, some exposure data and criteria are available for industrial situations. The threshold limit value is 0.5 mg/m^3, and levels greater than 1.0 mg/m^3 cause respiratory irritation in unacclimated persons [American Industrial Hygiene Association (AIHA), 1970]. This value of 0.5 mg/m^3 provides a moderate margin of safety for an 8 hr/day, 5 day/week exposure.

Wyllie, et al. (1975) sampled air five times at 11 sites in a plant treating 2.5 million board feet of lumber annually. Average air PCP levels ranged from 0.263 to 1.888 $\mu g/m^3$. The highest PCP level reported was 15 $\mu g/m^3$ in an air sample from the pressure treating room. The air samples were collected for an average of six hours. Air PCP levels in storage areas ranged from 0.009 to 9.0 ug/m^3. Serum PCP levels in six workers averaged 1-2 mg/l. Urine PCP levels were 0.08 to 0.3 mg/l. The highest serum PCP level found was 3.9 mg/l. PCP levels in the one control reported were 0.04 to 0.07 mg/l in serum and 0.002 to 0.004 mg/l in urine.

The resulting inhalation exposure can be estimated using the above maximum air level of 15 ug/m^3 as follows. With an average minute respiratory volume of 26 l/minute, approximately four times resting volume, a worker would inhale 12 m^3 of air during an 8-hour work period. This ventilation rate includes hard work periods, as well as less strenuous activity and rest. Because there is no reliable information available on the pulmonary deposition of PCP vapor or particles, the inhalation dose calculations assume 100

percent deposition and retention. The resulting pentachlorophenol exposure at an air level of 15 $\mu g/m^3$ is 0.180 mg/person/day. For a 70 kg individual, the resulting exposure rate is 0.0026 mg/kg/day. Under steady-state conditions the same amount of chemical will be excreted as is absorbed per day. Assuming a daily urinary void of 1.4 l/day, the predicted urine level resulting from the air exposure level of 15 $\mu g/m^3$ would be 0.180 mg/1.4 l = 0.13 mg/l. The resulting value of 0.13 mg/l falls between the observed urine levels of 0.08 to 0.3 mg/l reported by Wyllie, et al. (1975). Consequently, all of the inhalation exposure can be accounted for by the PCP levels in the urine. At the same time, since the calculations maximized inhalation doses and the range of urine values actually measured exceeded the calculated urine level, it is reasonable to assume that there was also exposure from oral or dermal routes.

Measured air and urine PCP levels associated with three types of wood treating operations in an Oregon wood treating plant are shown in Table 1 (Arsenault, 1976). The maximum air level of 0.297 mg/m^3 (Table 1) is considerably higher than the 0.015 mg/m^3 maximum level reported by Wyllie, et al. (1975). Rapp (1978), in presenting data obtained by industrial hygiene surveys conducted by Dow Chemical Company scientists at 28 users' sites, reported an unusually high PCP level of 65 mg/m^3.

The above data can be used to estimate inhalation exposure (Table 2). The assumptions used include: resting minute respiratory volume (tidal volume times respiratory rate) = 6 l, moderate exercise minute respiratory volume = 24 l, heavy exercise minute respiratory volume = 100 l; pulmonary deposition and retention of 100 percent; 70 kg person; 8-hour exposure.

TABLE 1

Air and Urine PCP Concentration from Plants and Mill Workers in Oregon*

Operation	Air Level - mg/m^3		Urine - mg/l	
	Average	Maximum	Average	Range
Dip	0.019	0.019	2.83	0.12 - 9.68
Spray	0.006	0.026	0.98	0.09 - 2.58
Pressure	0.014	0.297	1.24	1.24 - 5.57

*Source: Arsenault, 1976

TABLE 2

Estimated Exposures from Reported Air PCP Concentrations

	Condition		
	Resting	Moderate Exercise	Heavy Exercise
Minute respiratory volume:	6 l/min	24 l/min	100 l/min
m^3 air/8 hr:	2.88 m^3	11.52 m^3	48 m^3
Air Level:	Estimated Exposure		
0.006 mg/m^3/day	0.00025 mg/kg/day	0.001 mg/kg/day	0.0041 mg/kg/day
0.014	0.00058	0.0023	0.00958
0.015	0.00062	0.0025	0.0103
0.019	0.00078	0.0031	0.0130
0.026	0.00107	0.0043	0.0178
0.297	0.0122	0.0489	0.2037

The important variable in this approach to estimating exposure is the amount of air inhaled, which is directly related to the amount of muscular work. It is unlikely that a typical worker is represented by either the resting or heavy exercise breathing rates for the entire 8-hour work period. Consequently, a reasonable assumption would be to use the moderate exercise values, which represent respiratory values equal to four times the resting rates.

The next step is to compare total inhalation exposure with the amount of PCP found in the urine in the study reported by Arsenault (1976). For the dip treaters, the average urine PCP concentration value of 2.83 mg/l multiplied by the assumed daily urine volume of 1.4 l results in an approximate overall exposure of 3.96 mg PCP/person. This calculation assumes 100 percent excretion in the urine, which is not the case as pointed out later in this document; nonetheless, this assumption will suffice for the purpose of making the following calculations. The corresponding inhalation exposure, assuming moderate exercise and an average air level of 0.019 mg/m^3, is 0.0031 mg/kg, or 0.217 mg/person. In this instance, inhalation accounts for 5.5 percent of the dose for workers in a dipping operation. The pressure treaters had an average urine level of 1.24 mg/l, which results in an estimated total exposure of 1.74 mg/person. The average air level of 0.014 mg/m^3 yields an inhalation exposure of 0.0023 mg/kg, or 0.16 mg/person. The resulting estimated inhaled dose is 9.2 percent of the calculated total body dose.

In a simple two-subject inhalation trial, 76-88 percent of a calculated respired dose was eliminated within seven days. Peak

urine PCP levels occurred within 48 hours post-exposure (Casarett, et al. 1969).

Dermal

Pentachlorophenol can be absorbed through the intact skin. Pentachlorophenol dissolved in oil solvents has an acute dermal lethal dose of 60 to 200 mg/kg in rabbits (Deichmann, et al. 1942). Quantitative dermal absorption data for man are not available.

While it is not possible to separate oral, respiratory, and dermal exposures, except experimentally, it is possible to establish estimates of total body exposures. Pentachlorophenol is primarily excreted in the urine and has a half-life in man of 1.25 days. Simulated repeated daily ingestion of 0.1 mg PCP/kg indicated that an uptake-elimination equilibrium is reached after nine days of exposure (Braun, et al. 1978). Therefore, the urine PCP concentration can be used to estimate total body exposure. The accuracy of the calculations is limited by the care with which urine samples are collected. The most useful data would be based on 24-hour urine collections or on levels reported based on mOsmols of urine solute. In the absence of these data, the urine levels may range by a factor of 2 to 3 in either direction, depending on volume of fluid intake, perspiration, and presence or absence of renal tubular disease. Even with these restrictions, the calculated exposures are of value in estimating the probable exposure magnitude. The calculated exposures in Table 3 assume a daily urine volume of 1.4 l for a 70 kg adult, steady-state conditions, and 90 percent elimination of the dose in urine and 10 percent in feces. In addition to the studies on occupational exposures cited above,

TABLE 3

Comparison of PCP Biotransformation in Mammals

Species and Reference	Dose & Route	Peak Blood Level	Time To Peak Level	Plasma Half-Life	Excretion in Urine and Feces	Metabolites Found, Comments
Man: Braun, et al. (1977)	0.1 mg/kg Oral	0.248 ppm	4 hr	30.2 hr	Peak at 42 hr; half-life for PCP was 33 hr; half-life for PCP glucuronide was 12.7 hr	74% in urine as PCP; 12% in urine as PCP glucuronide; 4% in feces as PCP and PCP glucuronide.
Rat: Braun, et al. (1977)	10 mg/kg Male Oral	45 ppm (plasma)	4-6 hr		80% in urine 19% in feces	Excretion kinetics: total body half-life males: α =17 hr, β =40 hr; females: α =13 hr, β =33 hr
	10 mg/kg Female Oral	45 ppm (plasma)	4-6 hr		78% in urine 19% in feces	
	100 mg/kg Male Oral			13 hr - α; 121 hr - β	72% in urine 24% in feces	Urine: 75% as PCP; 9% as PCP-glucuronide; 16% as TCH*. Half-lives were 24 hr for PCP, 25 hr for PCP-glucuronide, and 32 hr for TCH.
	100 mg/kg Female Oral			27 hr - α; No D- β	54% in urine 43% in feces	See 100 mg/kg male data above. Urine was pooled.

TABLE 3 (Continued)

Species and Reference	Dose & Route	Peak Blood Level	Time To Peak Level	Plasma Half-Life	Excretion in Urine and Feces	Metabolites Found, Comments
Monkey: Braun and Sauerhoff (1976)	10 mg/kg Male Oral	10-30 ppm	12-24 hr	72 hr	Urine half-life 41 hr	In urine as unchanged PCP; no metabolites.
	10 mg/kg Female	10-30 ppm	12-24 hr	84 hr	Urine half-life 92 hr 360 hr after single dose: 70% in urine; 18% in feces; 11% remained in tissues.	
Mouse: Jakobson and Yllner (1971)	15-37 mg/kg i.p. or s.c.	NR	NR	NR	72-83% excreted in urine in 4 days; about half in 24 hr; 5-7% in feces.	About 45% as unchanged PCP; 14% as PCP conjugate; 40% as TCH.
Rat: Ahlborg, et al. (1974)	25 mg/kg i.p.	NR	NR	NR	70% in urine in 24 hr	43% as unchanged PCP; 5% as TCH; 38% as TCH conjugate; 14% as PCP conjugate.
Mouse: Ahlborg, et al. (1974)	25 mg/kg	NR	NR	NR	70% in urine in 24 hr	41% as unchanged PCP; 24% as TCH; 22% as TCH conjugate; 13% as PCP conjugate.

*TCH - Tetrachlorohydroquinone
NR - Not reported
i.p. - Intraperitoneal
s.c. - Subcutaneous

Kutz, et al. (1978) found an arithmetic average of 6.3 ug PCP/l in 354 of 418 urine samples (84.0 percent) analyzed. Cranmer and Freal (1970) reported urine levels ranging from 2 to 11 µg/l for the general population in a small number of samples.

Exposure estimates based on reported urine PCP levels are given in Table 4. These represent total body exposures from all sources and routes.

Duggan and Corneliussen (1972), using dietary levels, calculated daily exposures of 0.001 to 0.006 mg PCP/person/day. Using the reported urine values and calculated exposures in Table 4, the exposure appears to be in the range of 0.010 to 0.017 mg/person/day for the general population and 1.5 to 4.4 mg for occupational settings.

PHARMACOKINETICS

Absorption

The pharmacokinetic characteristics for PCP are summarized in Table 3.

The half-life for absorption in man following ingestion of a single dose of 0.1 mg PCP/kg was found to be 1.3 $\pm$ 0.4 hour, with a peak plasma concentration of 0.248 mg/l occurring four hours after ingestion (Braun, et al. 1978). Braun, et al. (1978) further reported that a simulation of repeated daily ingestion of 0.1 mg PCP/kg indicated that pentachlorophenol would reach 99 percent of steady-state in 8.4 days with a plasma concentration maximum of 0.491 mg/l.

Braun and Sauerhoff (1976) administered single oral doses of 10 mg PCP/kg in corn oil to three male and three female Rhesus mon-

TABLE 4

Estimated Total Body PCP Exposures for a 70 kg Person Based on Reported Urine PCP Levels and Assumed Daily Urine Void of 1.4 l with 90% Urinary Excretion

Urine Level (mg/l)	Reference	Estimated Exposure mg/person/day	mg/kg/day
0.0063	Kutz, et al. 1978	0.0098	0.00014
0.011	Cranmer and Freal, 1970	0.017	0.00024
2.83	Arsenault, 1976	4.40	0.0629
0.98	Arsenault, 1976	1.52	0.0218
1.24	Arsenault, 1976	1.93	0.0276
2.6	Casarett, et al. 1969	4.04	0.0578
1.6	Casarett, et al. 1969	2.49	0.0356

keys. The half-lives for absorption were 3.6 hours (males) and 1.8 hours (females). Monkeys given a single dose of 10 mg PCP/kg attained peak plasma levels of 10 to 30 ppm in 12 to 24 hours. Braun, et al. (1977) found that rats administered single oral doses of 10 mg PCP/kg had peak plasma concentrations of 45 ppm in 4 to 6 hours.

Distribution

The quantity of PCP in fat has been investigated in many studies. Larsen, et al. (1975) examined the tissue distribution of PCP in rats following oral administration, and found low levels in fat relative to other tissues.

Braun and Sauerhoff (1976) recovered 11.7 and 11.2 percent, respectively, of the 10 mg/kg dose in the tissues of two female monkeys 360 hours after administration. The largest amount of the PCP recovered, 65 to 83 percent, was found in the liver and small and large intestines combined (Table 5). All of the other tissues, including brain, fat, muscle, bone, and remaining soft tissues, contained only 2 to 3.5 percent of the dose.

In rats, nine days after a single 10 mg/kg dose, 0.44 percent of the dose remained in the body, with 82 percent of the residue located in the liver and kidney (Braun, et al. 1977). In a study in which rats were necropsied at 4, 24, 48, 72, and 120 hours postdosing, the highest levels among ten selected tissues were found in liver and kidney. The lowest levels were found in brain, spleen, and fat. Except for liver in female rats, and liver and kidney in male rats, the plasma PCP levels were higher than organ levels.

A study by Casarett, et al. (1969) of blood and urine PCP concentrations of occupationally exposed individuals suggests a ratio

TABLE 5

Tissue Concentrations of ^{14}C Activity from Two Female Monkeys Administered 10 mg ^{14}C PCP/kg*

Tissue	Percentage of Dose	
	Female 1	Female 2
Liver	1.38	0.81
Small Intestine	7.06	2.94
Large Intestine	1.28	3.91
Other[a]	1.98	3.54
TOTAL	11.70	11.20

*Source: Braun and Sauerhoff, 1976

[a]Other tissues = adrenals, brain, gall bladder, kidney, lung, ovaries, pancreas, spleen, stomach, urinary bladder, uterus, vagina, heart, bone, skin, fat, muscle, meat, carcass.

of plasma to urine PCP concentrations of 1.5 to 2.5. Wyllie, et al. (1975) reported that the PCP levels in the urine of six chronically exposed workers in a small wood treatment plant were much lower than those in serum. Levels of PCP in the urine averaged 163.8 ppb for the exposed individuals, while serum PCP levels averaged 1,372 ppb over the same period of time.

Reported cases of acute intoxication frequently present higher PCP concentrations in the urine than in the plasma. Animal studies with single doses also show this pattern. Plasma and urine PCP concentrations were linearly related up to about 1.0 mg/l; above 1.0 mg/l the plasma levels reached a plateau approaching 10 mg/l with increasing levels of PCP in the urine.

Data for tissue distribution following uptake of PCP by man is derived mainly from autopsy results of fatal cases of PCP intoxication (Mason, et al. 1965; Gordon, 1956; Armstrong, et al. 1969). Cretney (1976) reported PCP residues from a suicide as: blood, 173 mg/l; urine, 75 mg/l; liver, 225 mg/kg; and kidney, 116 mg/kg. From available data, levels associated with acute lethal toxicosis can be estimated. Levels in blood, liver, and kidney are most meaningful. Levels in urine can be variable, depending on how much urine was in the bladder at the time of ingestion. Residues associated with acute toxicosis and death are: blood, 50 to 176 mg/l; liver, 62 to 225 mg/kg; and kidney, 28 to 123 mg/kg.

Armstrong, et al. (1969) reported analysis of fat tissue obtained from an infant exposed to a lethal concentration of Na-PCP in diapers and hospital linen. Residues were: kidney, 2.8 mg/kg; adrenal, 2.7 mg/kg; heart and blood vessel, 2.1 mg/kg; and fat, 3.4

mg/kg. Shafik (1973) found an average of 26.3 µg PCP/kg in 18 human fat samples of unspecified origin.

Metabolism

Braun, et al. (1978) determined the metabolism and pharmacokinetics of PCP in four male volunteers ingesting 0.1 mg PCP/kg. Approximately 74 percent of the dose was eliminated in the urine as PCP, and 12 percent was eliminated in urine as PCP-glucuronide. Additionally, 4 percent of the dose was eliminated in the feces as PCP and PCP-glucuronide.

PCP in mice is detoxified by conjugation and metabolism (Jakobsen and Yllner, 1971). Approximately 21 percent of the injected ^{14}C activity was found to consist of ^{14}C-labeled tetrachlorohydroquinone (TCH), which was possibly conjugated in the urine. Rats excrete 75 percent of the PCP in the urine as unchanged PCP, 16 percent as TCH, and 9 percent as PCP-glucuronide (Braun, et al. 1977). In the plasma most of the PCP is unchanged, with a small amount of PCP-glucuronide present. TCH was not detected in rat blood plasma.

Ahlborg (1978) found that rats dechlorinate PCP to form TCH and trichloro-p-hydroquinone, but not tetrachlorophenol or trichlorophenol. Ahlborg found the TCH to be conjugated in the urine, while Braun, et al. (1977) reported TCH was unconjugated in their study. The Rhesus monkey was found to eliminate PCP unchanged in the urine, with no metabolites detected (Braun and Sauerhoff, 1976).

Excretion

In man and experimental animals the primary mode of excretion for PCP is urinary (Deichmann, et al. 1942; Jakobsen and Yllner, 1971; Larsen, et al. 1975; Braun, et al. 1978).

In man the plasma PCP half-life is 30.2 ± 4.0 hours. The half-lives for elimination of PCP and PCP-glucuronide from urine are 33.1 ± 4.5 hr and 12.7 ± 5.4 hr, respectively. The dynamics of elimination in man are described by a one-compartment, open-system model with first-order absorption, enterohepatic circulation, and first-order elimination (Braun, et al. 1978).

Braun and Sauerhoff (1976) found that the monkey eliminated PCP more slowly than other animals. In two monkeys, 360 hours after a single oral dose of 10 mg/kg, 70 percent of the dose was eliminated in the urine, 18 percent in the feces, and 11 percent remained in the carcass. Excretion by the kidney was a first-order process, characterized by half-lives of 40.8 hr (males) and 92.4 hr (females). Plasma levels decreased by a first order process with half-lives of 72 hr (males) and 83.5 hr (females).

The pharmacokinetics of PCP in rats given oral doses of 10 mg/kg are summarized in Table 6, taken from Braun, et al. (1977). The rat eliminates PCP more rapidly than the Rhesus monkey and appears to be more similar to man in the rate of PCP elimination.

It is difficult to draw reliable conclusions from most of the previously reported human urinary excretion data, except for the Braun, et al. (1978) study, for the following reasons: (1) the exposures were accidental or occupational, with the quantity unknown; and (2) the reports do not account for continued background exposure.

TABLE 6

Pharmacokinetics of PCP in Rats Given
Single Oral Dose of 10 mg/kg*

Parameter	Males	Females
K_e (hr^{-1})	0.0343	0.0478
K_{12} (hr^{-1})	0.0046	0.0032
K_{21} (hr^{-1})	0.0061	0.0100
α (hr^{-1})	0.0398	0.0518
β (hr^{-1})	0.0173	0.0213
$t_{1/2}$ (α) (hr)	17.4	13.4
$t_{1/2}$ (β) (hr)	40.2	32.5
V_1 (ml/kg)	136	127

*Source: Braun, et al. 1977

There is speculation that there may be long-term tissue binding and limited storage of PCP. This has resulted from consideration of the long-term fat storage of chlorinated hydrocarbon insecticides such as DDT and dieldrin and the inference that PCP may act accordingly. The other factor generating this speculation is based on the study by Casarett, et al. (1969), where urine and blood of occupationally exposed workers were analyzed for PCP. Casarett observed a decline in urine and blood PCP levels in workers during vacation periods when the individuals were not occupationally exposed. However, the urine PCP levels did not decline to zero. Other studies by Casarett, et al. (1969), Bevenue, et al. (1967a), and Kutz, et al. (1968) report finding low levels of PCP in the urine of nonoccupationally exposed individuals. The Casarett study of occupationally exposed workers did not measure PCP exposure during the vacation period. Consequently, the levels observed during the vacation period could represent evidence of long-term tissue binding or continuing background exposure. Long-term, low level tissue binding has not been adequately studied.

EFFECTS

Acute, Subacute, and Chronic Toxicity

Pentachlorophenol solutions can cause skin irritation. Immersion of hands for 10 minutes in a 0.4 percent solution of PCP can cause pain and inflammation (Bevenue, et al. 1967a).

Dust and mist concentrations greater than 1.0 mg/m^3 cause painful irritation in the upper respiratory tract accompanied by violent sneezing and coughing in persons newly-exposed to PCP. Concentrations as high as 2.4 mg/m^3 can be tolerated by conditioned individuals (AIHA, 1970).

The oral lethal dose of PCP in several species of animals ranges from 70 to 300 mg/kg (Bevenue and Beckman, 1967; Deichmann, et al. 1942). The mechanism of action involves the uncoupling of oxidative phosphorylation (Weinbach and Garbus, 1965). Fuel oil-type solvents reduce the lethal dose, while aqueous solutions of the sodium salt are less toxic.

PCP exposure has resulted in death in man through occupational and accidental exposures and suicide attempts (Gordon, 1956; Bergner, et al. 1965; Armstrong, et al. 1969). Symptoms following fatal exposures include general weakness, fatigue, dizziness, headache, anorexia, profuse sweating, nausea, vomiting, hyperpyrexia of 106 to 108^{o}F, dyspnea, tachycardia, abdominal pain, terminal spasms, and death three to 25 hours after onset of symptoms. Lesions include inflamed gastric mucosa, pulmonary congestion, pulmonary edema, fatty metamorphosis of the liver, and degeneration of renal tubules and myocardium.

Nonfatal acute exposure can result in skin irritation, nasal and respiratory tract irritation, sneezing and coughing, and eye irritation.

One unique poisoning episode involved babies wearing diapers rinsed in an antimicrobial laundry neutralizer containing sodium pentachlorophenate. Babies wearing the diapers an average of eight days became ill and some died. Some were less severely affected and recovered spontaneously (Armstrong, et al. 1969; Robson, et al. 1969). Six of the nine severely affected had hepatomegaly and two of the nine had splenomegaly in addition to profuse sweating hyperpyrexia.

A review of the U.S. EPA Pesticide Episode Response Branch report of September 14, 1976, revealed 47 cases of human exposures ranging from direct eye contact to more serious intoxications involving systemic effects. Significant cases included five situations where PCP was used inside homes and resulted in headache, eye irritation, dyspnea, malaise, and in one case chronic weight loss (U.S. EPA, 1976).

One chronic health effect associated some years ago with certain types of commercial PCP exposure is chloracne, a type of acneform dermatitis similar to juvenile acne. It is characterized by folliculitis and comedones with secondary infections. Chloracne results from exposure to a variety of substances including chlorinated biphenyls, chlorinated naphthalenes, and tetra- and hexachlorodioxins. Baader and Bauer (1951) reported acne, skin, and respiratory tract irritation in workers in a German plant producing PCP from HCB. In addition, eight of ten workers reported pain of the lower extremities that occurred with the onset of the chloracne. Nomura (1953) reported two cases of acneform skin eruptions in workers in a PCP plant in Japan. It was not reported whether the PCP was produced from HCB or by the chlorination of phenol.

Johnson, et al. (1973) found that commercial PCP containing higher levels of chlorodioxins produced chloracne in the rabbit ear test. Using pure PCP or PCP with reduced dioxin content did not cause chloracne.

Symptoms in chronic toxicity, in general, are similar to those seen in acute intoxications. PCP does not accumulate in body tissues to the extent of the chlorinated hydrocarbon insecticides such

as DDT and dieldrin. Consequently, chronic intoxications result from relatively high levels of continuous exposure. Symptoms in nonfatal chronic exposures include muscle weakness, headache, anorexia, abdominal pain, and weight loss in addition to skin, eye, and respiratory tract irritation.

A group of wood treaters in Hawaii has been studied medically for a number of years. Physiopathologic changes were minimal. Klemmer (1972) noted that the levels of the serum enzymes SGOT, SGPT, and LDH were highest in the occupationally exposed group, but were still within normal limits.

Workers chronically exposed to PCP demonstrated significantly elevated levels of total bilirubin and creatinine phosphokinase, although the levels were within normal limits. Workers chronically exposed to PCP showed a significantly higher prevalence of gamma mobility C-reactive protein (CRP) in the sera. The clinical significance of these elevated levels of CRP in individuals exposed to PCP is not known. CRP levels are often elevated in acute states of various inflammatory disorders or tissue damage (Takahashi, et al. 1976).

Begley, et al. (1977) determined plasma and urine PCP, renal creatinine, phosphorus clearance, and phosphorus reabsorption in 19 workers before and after a 20-day vacation. Plasma PCP decreased from 5.14 to 2.19 mg/l at the end of the vacation. Following vacation, both the depressed creatinine clearance values and the phosphorus reabsorption values improved.

Caution is required in interpreting the human epidemiological data since some of the occupationally exposed group were exposed to other wood-preserving chemicals and solvents.

Chronic animal studies have been reported which aid in the evaluation of long term health effects. A complicating factor in such studies is the presence of varying amounts of nonphenolic contaminants in the PCP used in the various studies. Some of the effects are related to the nonphenolic constituents. Oral doses of 1 and 3 mg technical PCP/kg for 90 days did not produce signs of intoxication in rabbits (Machle, et al. 1943).

Male and female rats fed 25 ppm (equivalent to 1.5 mg/kg) technical PCP for 12 weeks did not show significant toxic effcts. A level of 50 ppm (approximately 3 mg/kg) resulted in decreased hemoglobin and RBC numbers in male, but not female, rats. A level of 200 ppm (approximately 12.5 mg/kg) increased liver aniline hydroxylase activity in male and female rats and decreased hemoglobin and RBC numbers in male rats (Knudsen, et al. 1974).

Goldstein, et al. (1977) fed rats 20, 100, or 500 ppm technical and pure PCP (equivalent to 1.2, 6, and 30 mg/kg, respectively) for eight months. At 20 ppm, liver aryl hydrocarbon hydroxylase and glucuronyl transferase were increased in female rats fed technical PCP as compared to controls fed pure PCP. At 100 ppm technical PCP increased excretion of uroporphyrin and delta-aminolevulinic acid. Feeding 20 or 100 ppm of pure PCP had no effect. Body weight gain was reduced at 500 ppm with both types of PCP. The no-observable-adverse-effect-level (NOAEL) for pure PCP from this study was 6 mg/kg (i.e., the 100 ppm diet group).

Kociba, et al. (1971) compared the toxicity of purified versus technical grade PCP. In their study, rats were fed either 3, 10, or 30 mg technical grade or purified PCP/kg body weight/day. They

noted a relative increase in liver weight at all three dosages of the technical PCP, but only at the 10 and 30 mg/kg dosages of purified PCP sample. The technical grade also caused an increase in the absolute liver weights at the 10 and 30 mg/kg dosages, while in the pure sample this was observed at only the 30 mg/kg dosage. Increased relative kidney weights were found at all three dosage levels in the technical grade recipients, while this was noted only at the 30 mg dosage level of the purer sample. Increased absolute kidney weights were found at the top dosage level (30 mg/kg) of the technical grade sample, but this alteration was not noted at any dosage level of the purified sample. No other organ weight alterations were considered to be related to treatment. In the same study, these investigators observed no gross toxicologic effects in the groups of animals fed 3 and 10 mg purified PCP/kg/day. Minimal focal hepatocellular degeneration and necrosis were observed upon microscopic examination of liver from animals maintained on the top dosage level of technical grade PCP. These changes were not observed in animals maintained on a diet containing the purified PCP which provided a similar dosage of PCP.

Toxicological effects observed by Kociba, et al. (1971) in the rats receiving the technical grade PCP sample were as follows: slight increases in preterminal hemoglobin levels, packed cell volumes and total erythrocytes, and elevated serum glutamic-pyruvic transaminase activity with minimal focal hepatocellular degeneration and necrosis at the 30 mg/kg/day dosage level; decreased serum albumin levels at the 10 and 30 mg/kg/day dosage level; and slightly elevated levels of serum alkaline phosphatase activity at all

three dosage levels. Purified PCP was believed to have minimal toxicological properties at the levels used in this feeding study.

Kociba, et al. (1971) concluded that the observed treatment-related alterations, which were more evident in rats maintained on diets containing the technical grade sample than those receiving similar levels of the purified sample, could be attributed to some degree to the presence of nonphenolics, chlorinated dibenzo-p-dioxins, and dibenzofurans in the technical sample (Dowicide 7®).

In a similar supportive study, Johnson, et al. (1973) reported that male rats fed diets containing 10 and 30 mg/kg/day and females receiving 30 mg/kg/day of the test material underwent minimal increases in liver weights which were more apparent in the male than in the female rats. In males, both the absolute and body weight-relative liver weights were increased, while only the relative weight was increased in the females. Minimal increases in kidney weights were observed in both males and females receiving only the 30 mg/kg dosage of technical grade PCP. In the male rats, both the absolute and body weight-relative kidney weights were increased, while in the females only the relative weight was increased. No other alterations in terminal body and organ weights were considered related to treatment. Gross and microscopic examinations of rats and tissues, respectively, revealed no lesions related to treatment. Although some tissue lesions were observed in the 30 mg/kg/day rats, those lesions were considered spontaneous in nature and unrelated to treatment.

In a 12-week chronic study, Knudsen, et al. (1974) fed weanling rats 0, 25, 50, and 200 mg PCP/kg diet. The serum alkaline

phosphatase activity was found to be significantly higher in the 25 and 200 mg/kg groups. A relative increase in liver weight was observed at the 200 mg/kg (both sexes) and 50 mg/kg (females only) doses. No other significant dose-related effects were observed in the animals fed 25 mg PCP/kg diet in this 90-day study.

Kociba, et al. (1973) fed rats 1, 3, 10, or 30 mg/kg of a PCP containing low amounts of nonphenolic impurities for 90 days. The no-effect level was 10 mg/kg in females and 3 mg/kg in males. The effect in males at 10 mg/kg was limited to a change in liver weight. There were no treatment-related histopathologic changes.

The NOAEL in Sprague-Dawley rats fed a PCP containing low amounts of nonphenolic impurities for 22 to 24 months was 3 mg/kg in females and 10 mg/kg in males (Schwetz, et al. 1978). The feeding levels were 1, 3, 10, or 30 mg/kg. The highest dose (30 mg/kg) resulted in decreased body weight gain, increased SGPT, and increased urine specific gravity.

Teratogenicity

Information on teratogenic studies is limited. No information was encountered suggesting pentachlorophenol is a human teratogen.

Hinkle (1973) found fetal deaths and/or resorptions in three of six test groups using Golden Syrian hamsters. Dose-response data and statistical analysis were not provided. Dose range was from 1.25 to 20 mg/kg.

A single 60 mg/kg dose on day 9 or 10 of gestation reduced fetal weights in Charles River CD strain rats, but had no effect when given on days 11, 12, or 13. A total of four abnormalities out of 97 fetuses were found. One of 46 fetuses from day 8 exposure was

a dwarf, and 3 of 51 fetuses from day 9 exposure had malformations consisting of exencephaly, macropthalmia and taillessness. No skeletal abnormalities were found. An increase in maternal deep body temperature of 0.5 to 0.8°C was reported, which indicates systemic toxicity. A dose of 60 mg/kg is about 75 percent of the LD_{50}. The authors concluded that the number of malformations was minimal and could have been due to toxic effects on the maternal rat (Larsen, et al. 1975).

Schwetz, et al. (1974) provided more complete data from a rat study using purified and commercial grade PCP. Dosages ranged from 5 to 50 mg/kg daily and exposure was during days 6 to 15 of gestation. The NOAEL based on incidence of fetal resorption was 5.8 mg/kg (adjusted dose to provide 5 mg PCP/kg) for commercial and 15 mg/kg for purified grade PCP. At 50 mg purified PCP/kg fetal resorption was 100 percent. The NOAEL level for reducing fetal body weight was 15 mg/kg for both grades. Fetal anomalies consisting of subcutaneous edema and dilated ureters were observed in soft tissues at doses of 15 mg/kg or above for both grades of PCP. The NOAEL for soft tissue anomalies was 5 mg commercial grade PCP/kg/day. Delayed ossification of the skull was noted at 5 mg/kg with purified PCP. The NOAEL for skeletal anomalies with commercial PCP was 5.8 mg/kg. At higher dosages, skeletal anomalies consisted of lumbar spurs, supernumerary or fused ribs, or supernumerary, abnormally shaped, missing, or unfused centers of ossification of vertebrae or sternebrae. These effects were more readily produced when dosing occurred on days 8-11 rather than days 12-15 of gestation. The authors considered the effects by PCP to be evidence of embryotoxicity and fetotoxicity, not teratogenicity.

Schwetz, et al. (1978) also reported a reproduction study. Male and female rats were fed 0, 3, or 30 mg PCP/kg for 62 days before mating, during 15 days of mating, and during gestation and lactation. No evidence of toxicosis in the males was reported. The females on the highest dose gained less weight. The 3 mg/kg dose was the NOAEL. At 30 mg/kg the following indices were decreased: percentage of liveborn pups; 7, 14, 21 day post-birth survival; 1, 7, 14, 21 day pup body weight; and 7, 14, 21 day litter size. Since the LD_{50} of PCP in 3- to 4-day-old rats is 65 mg/kg compared to 150 mg/kg in adult rats, the observed effects on offspring may be the result of fetal toxicity.

Mutagenicity

Sodium PCP was not mutagenic to male germ cells of Drosophila when tested at a concentration of 7 mM (Vogel and Chandler, 1974). PCP was not mutagenic in the mouse host-mediated assay or in in vitro spot tests (Buselmaier, et al. 1973).

Anderson, et al. (1972) also reported that PCP did not produce mutagenic effects when tested in vitro using histidine-requiring mutants of Salmonella typhimurium as the test organism. The purity of the PCP used in the three studies cited was not specified.

Fahrig, et al. (1978) tested recrystallized PCP in two mutagenic test systems. In the first system Saccharomyces cerevisiae was used. The PCP concentration used was 400 mg/l, which resulted in a 59 percent survival of test organisms and increased the frequency of mutations and mitotic gene conversion compared to controls. In the second system change in hair coat color (spots) in mice was studied by injecting dams on the tenth day of gestation

with an intraperitoneal dose of either 50 or 100 mg/kg. Four out of 473 offspring were reported to have spots of genetic relevance.

Carcinogenicity

Dermal application of a 20 percent solution of PCP dissolved in benzene did not increase the rate of papillomas in mice pretreated with dimethylbenzanthracene (DMBA) (Boutwell and Bosch, 1959). The initiator (DMBA) was applied once and the pentachlorophenol applied twice weekly for 15 weeks. Seven percent of the controls and 4 percent of the PCP group developed papillomas. Neither group developed carcinomas. The exposure rate was 5 mg PCP per treatment applied in one drop to an unspecified skin area.

Mice dosed with commercial PCP at 46.4 mg/kg from 7 to 28 days of age, and then fed 130 ppm PCP in the diet for the remainder of their life span (approximately 18 months), did not have a significant increase in tumors (Innes, et al. 1969). Detailed results were not published. The study used 18 male and female mice of each of two strains for a total of 72 mice.

PCP containing low amounts of nonphenolic impurities was noncarcinogenic when male and female Sprague-Dawley rats were fed 0, 1, 3, 10, or 30 mg/kg for 22 months (males) or 24 months (females) (Schwetz, et al. 1978). Each sex dose group contained 25 animals. The results, summarized in Table 7, reveal no evident dose-response relationship. (In this study, a NOAEL based on clinical chemistry and hematology determinations, routine histopathology, and organ weight changes was determined to be 3 mg/kg in females and 10 mg/kg in males. The NOAEL of 3 mg/kg was used to calculate the toxicity-based criterion shown later in this document.)

TABLE 7

Incidence of Primary Tumors (Based on Histopathological Diagnosis) in Rats Fed Pentachlorophenol (PCP) for 22 Months (Males) and 24 Months (Females)*

	Males					Females				
Dose: mgPCP/kg/day	0	1	3	10	30	0	1	3	10	30
Number of rats examined:	27	26	27	27	27	27	27	27	27	27
Number of rats with tumors:	11	13	13	12	11	27	26	25	25	25
Number of tumors:	17	14	17	15	61	62	67	42	63	63
Number of tumors/ rats with tumors:	1.6	1.1	1.3	1.4	2.3	2.6	1.7	1.7	2.5	2.5
Number of morphologic malignant tumors:	1	3	2	1	0	2	7	2	3	2

*Source: Schwetz, et al. 1978

Other Effects

An organoleptic threshold for pentachlorophenol in water has been reported by at least two investigators. Hoak (1957) reported the odor threshold of phenol and 19 phenolic compounds. In a study conducted at the Mellon Institute in Pittsburgh, Pennsylvania, a panel of two or four persons sniffed samples of pure phenolic compounds in odor-free water, which had been heated to either 30 or 60°C. A flask of plain odor-free water was provided for comparison. The various samples were placed in random order before the test persons, and the flask with the lowest perceptible odor was noted by each individual sniffer. The lowest concentration detected was considered to be the threshold. Chlorinated phenols were the compounds most easily detected. The odor thresholds for PCP at 30 and 60°C were 857 µg/l and 12,000 µg/l, respectively. Hoak had speculated that odor should become more noticeable as temperature increases; however, when a series of chlorophenols and cresols were evaluated, it was found that some compounds had higher odor thresholds at 30°C, while others had higher thresholds at 60°C.

Dietz and Traud (1978) used a panel composed of 9 to 12 persons of both sexes and various age groups to test the organoleptic detection thresholds for 126 phenolic compounds. To test for odor thresholds, 200 ml samples of the different test concentrations were placed in stoppered odor-free glass bottles, shaken for approximately five minutes, and sniffed at room temperature (20-22°C). For each test, water without the phenolic additive was used as a background sample. The odor tests took place in several individual rooms in which phenols and other substances with intense

odors had not been used previously. Geometric mean values were used to determine threshold levels. To determine taste threshold concentrations of selected phenolic compounds, a panel of four test individuals tasted water samples containing various amounts of phenolic additives. As a point of comparison, water without phenolic additives was tasted first. Samples with increasing phenolic concentrations were then tested. Between samples, the mouth was rinsed with the comparison water and the test person ate several bites of dry white bread to "neutralize" the taste. Geometric mean detection level values for both tests provided threshold levels of 30 µg/l for taste and 1,600 µg/l for odor for the chemical pentachlorophenol.

Neither of these studies, however, indicated whether the determined threshold levels made the water undesirable or unfit for consumption.

CRITERION FORMULATION

Existing Guidelines and Standards

The maximum air PCP concentration established by the American Industrial Hygiene Association (1970) is 0.5 mg PCP or 0.5 mg NaPCP/m^3 for an 8-hour exposure (TLV). The Code of Federal Regulations 21, part 121, paragraph 121:2556 allows up to 50 ppm PCP in wood used in contact with food.

A tolerance for PCP in food has not been established.

A no-adverse-effect-level in drinking water of 0.021 mg PCP/l is suggested by the National Research Council (1977). The recommendation is based on a NOAEL of 3 mg/kg in the 90-day to 8-month rat studies. A safety or "uncertainty factor" of 1,000 and a water consumption of 2 l/day were used in arriving at the level.

Current Levels of Exposure

Based on an assumed food consumption of 1.5 kg/day and a water intake of 2 l/day (2.0 kg), a food PCP residue of 10 µg/kg, and a water PCP residue of 60 ng/kg, the resulting maximum total daily exposure for a 70 kg person would likely be 15 µg from food and 120 ng from water. The exposure rate would be 0.21 ug/kg/day from food and 1.7 ng/kg/day from water. The estimated food residue level (15 µg) is higher than the 1 to 6 µg/day intake calculated by Manske and Corneliussen (1974) where the calculations took into consideration dietary consumption by food class.

An alternative approach to estimating human exposure is extrapolation from urine residue data, since PCP is primarily eliminated in the urine, and at equilibrium excretion equals daily intake. In Hawaii, where exposure for the general population may be higher

than that for persons living in colder climates due to differences in the use of PCP-treated wood in home construction, Bevenue, et al. (1967a) reported an average PCP urine value of 40 µg/l. Assuming a daily urine void of 1.4 l the total daily PCP excretion would be 56 µg, an amount equal to the intake. Cranmer and Freal (1970) found an average of 5.8 µg/l in six general population urine samples, and Kutz, et al. (1978) reported an average of 6.3 µg/l for 416 samples. Consequently, location of residence may influence PCP exposure. Based on available data, the exposure for the general population is estimated to range from 1 to 50 µg/person/day.

Exposure will increase sharply if an individual works with the material and inhales vapors (Casarett, et al. 1969) and/or experiences dermal absorption (Bevenue, et al. 1967a). Casarett, et al. (1969) studied two subjects working in a room in which PCP is applied by brush to lumber and found that the urine PCP concentration peaked at 30 to 50 µg/l.

Occupationally exposed individuals excrete more PCP in the urine than do persons from the general population. Reported urine values include an average of 1.8 mg/l for 130 pest control operators (Bevenue, et al. 1967b), 1 to 10 mg/l for wood treaters (Casarett, et al. 1969), 2.8 mg/l for dip treaters, 0.98 mg/l for spray treaters, and 1.24 mg/l for pressure treaters (Arsenault, 1976). Using the same assumption of 1.4 l of urine per day, the estimated occupational exposures would range from 1.37 to 14 mg/person/day.

Special Groups at Risks

Two groups can be expected to encounter the largest exposures. One group consists of employees involved in the manufacture of PCP;

this cohort is presently under industrial health surveillance programs.

The second and larger group is comprised of formulators and wood treaters. Exposure, hygiene, and industrial health practices can be expected to vary from the small wood treaters to the larger companies. Health related data in general are not available for this group. Employees of two Hawaii wood-treating companies have been studied for a number of years, and although exposures have resulted in blood and urine levels of 1 to 10 mg/l, adverse health effects have been minimal.

Basis and Derivation of Criterion

Based on available and cited literature, PCP is not considered to be carcinogenic.

A health effects criterion can be calculated using the data from the chronic toxicity studies. Using a NOAEL of 3 mg/kg (Schwetz, et al. 1978) for purified PCP containing only low amounts of nonphenolic impurities and applying a 0.01 animal-to-human uncertainty factor, the upper limit for nonoccupational daily exposure is 0.03 mg/kg or 2.10 mg/70 kg person. Satisfactory 90-day (Kociba, et al. 1973) and 22 to 24 month (Schwetz, et al. 1978) studies have defined both a NOEL and a NOAEL, respectively, based on micropathologic effects and biochemical indices. These data, in addition to the limited available human data, justify the selection of a safety factor of 100.

For the purposes of calculating a water quality criterion, human exposure to PCP is considered to be based on daily ingestion of 2 liters of water and 6.5 g of fish. The amount of PCP contained

in ingested water is approximately 100 times greater than the amount of PCP in consumed fish. However, fish bioaccumulate PCP from water by a factor of 11 and thus contain about half as much PCP per gram as water.

With these considerations in mind, the following equation has been established:

$$(2\ l\ C) + (0.0065\ kg\ 11\ C) = ADI = 2.10\ mg$$

where:

2.10 mg = acceptable daily intake (ADI) for a 70 kg person

2 l = amount of drinking water consumed daily

0.0065 kg = amount of fish consumed daily

11 = bioconcentration factor

Solving for C, the water quality criterion, gives:

$$C = 1.01\ mg/l$$

This criterion can alternatively be expressed as 29.4 mg/l if exposure is from consumption of fish and shellfish only.

Present residues of PCP are reported to be 0 to 10 ug/kg in food, and one report indicates 0.06 µg/kg in water. These levels are well below the above criterion, and total daily general population exposures are less than 1 percent of the calculated maximum value based on toxicologic considerations.

It should be noted that this calculated toxicity criterion is based on a NOAEL for a purified grade PCP containing only low amounts of nonphenolic compounds. PCP containing low amounts of nonphenolic impurities has been found to be noncarcinogenic at the dosages tested. However, NCI is presently conducting studies on the carcinogenicity of the PCP contaminants hexachlorodibenzo-p-

dioxin and octachloro-p-dioxin, the results of which are not yet available. The results of these studies should be evaluated before any EPA regulatory standards are established. It should be noted, however, that criteria presented in this document are recommended levels for the pure compound only and not for any contaminants or metabolites of PCP.

Since the taste and odor detection threshold concentrations for pentachlorophenol are below the derived toxicity-based criterion level, the ambient water quality criterion is based on organoleptic data. It should be emphasized that this criterion is based on aesthetic qualities rather than health effects. However, to the extent that this criterion is below the level derived from the chronic toxicity studies of Schwetz, et al. (1978) and Kociba, et al. (1973), it is likely to also be protective of human health.

The data of Hoak (1957) and Dietz and Traud (1978) indicated that high microgram concentrations of pentachlorophenol in water are capable of producing a discernable odor. Neither of these studies indicated a range of responses, but it is certainly possible that at least some of the "sniffers" in the Dietz and Traud group could detect concentrations of PCP down near the 857 µg/l value of Hoak; similarly, it is possible that some of the "sniffers" in the Hoak group would be able to initially detect the presence of PCP at concentrations near the geometric mean threshold value of Dietz and Traud. Dietz and Traud (1978) further observed a distinct flavor alteration of water at low microgram levels of PCP. The taste threshold (30 µg/l) determined by Dietz and Traud for PCP in water is used to arrive at the criterion level for this chemical.

Therefore, based on the prevention of undesirable organoleptic qualities, the criterion level for pentachlorophenol in water is 30 µg/l. This level should be low enough to prevent detection of objectionable organoleptic characteristics by most people and far below minimal no-effect concentrations determined in laboratory animals.

REFERENCES

Ahlborg, U.G. 1978. Dechlorination of Pentachlorophenol *in vivo* and *in vitro*. *In*: K. Rango Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology, and Environmental Toxicology. Plenum Press, New York. p. 115.

Ahlborg, U.G., et al. 1974. Metabolism of pentachlorophenol. Arch. Toxicol. 32: 271.

American Industrial Hygiene Association. 1970. Hygienic guide series: Pentachlorophenol and sodium pentachlorophenate. Am. Ind. Hyg. Assoc. Jour. 31: 521.

Anderson, K.J., et al. 1972. Evaluation of herbicides for possible mutagenic properties. Jour. Agric. Food Chem. 20: 649.

Armstrong, R.W., et al. 1969. Pentachlorophenol poisoning in a nursery for newborn infants. II. Epidemiologic and toxicologic studies. Jour. Pediatr. 75: 317.

Arsenault, R.D. 1976. Pentachlorophenol and contained chlorinated dibenzoidioxins in the environment: A study of environmental fate, stability, and significance when used in wood preservation. Presented at the American Wood-Preservers' Assoc. Annu. Meet., Atlanta, Georgia, April 25-28. p. 1.

Baader, E.W. and H.J. Bauer. 1951. Industrial intoxication due to pentachlorophenol. Ind. Med. Surg. 20: 286.

Begley, J., et al. 1977. Association between renal function tests and pentachlorophenol exposure. Clin. Toxicol. 1: 97.

Bergner, H., et al. 1965. Industrial pentachlorophenol poisoning in Winnipeg. Can. Med. Assoc. Jour. 92: 448.

Bevenue, A. and H. Beckman. 1967. Pentachlorophenol: A discussion of its properties and its occurrence as a residue in human and animal tissues. Residue Rev. 19: 83.

Bevenue, A., et al. 1967a. A note on the effects of a temporary exposure of an individual to pentachlorophenol. Bull. Environ. Contam. Toxicol. 2: 293.

Bevenue, A., et al. 1967b. A survey of pentachlorophenol content in human urine. Bull. Environ. Contam. Toxicol. 2: 319.

Boutwell, R.K. and K.K. Bosch. 1959. The tumor-promoting action of phenol and related compounds for mouse skin. Cancer Res. 19: 413.

Braun, W.H. and M.W. Sauerhoff. 1976. The pharmacokinetic profile of pentachlorophenol in monkeys. Toxicol. Appl. Pharmacol. 38: 525.

Braun, W.H., et al. 1977. The pharmacokinetics and metabolism of pentachlorophenol in rats. Toxicol. Appl. Pharmacol. 41: 395.

Braun, W.H., et al. 1978. The metabolism/pharmacokinetics of pentachlorophenol in man, and a comparison with the rat and monkey model. Toxicol. Appl. Pharmacol. 45: 135.

Buhler, D.R., et al. 1973. Occurrence of hexachlorophene and pentachlorophenol in sewage and water. Environ. Sci. Technol. 7: 929.

Buselmaier, et al. 1973. Comparative investigations of the mutagenicity of pesticides in mammalian test systems. Mutat. Res. 21: 25.

Casarett, L.J., et al. 1969. Observations on pentachlorophenol in human blood and urine. Am. Ind. Hyg. Assoc. Jour. 30: 360.

Conklin, P.J. and F.R. Fox. 1978. Environmental Impact of Pentachlorophenol and Its Products - A Round Table Discussion. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology, and Environmental Toxicology. Plenum Press, New York. p. 393.

Cranmer, M. and J. Freal. 1970. Gas chromatographic analysis of pentachlorophenol in human urine by formation of alkyl ethers. Life Sci. 9: 121.

Cretney, M.J. 1976. Pentachlorophenol death. Bull. T.I.A.F.T. 12:10. In: T.J. Haley, 1977. Human poisoning with pentachlorophenol and its treatment. Ecotoxicol. Environ. Safety. (In press)

Deichmann, W., et al. 1942. Acute and chronic effects of pentachlorophenol and sodium pentacholorophenate upon experimental animals. Jour. Pharmacol. Exp. Therap. 76: 104.

Dietz, F. and J. Traud. 1978. Geruchs- und Geschmacks-Schwellen-Konzentrationen von Phenolkorpera. Gas-Wasserfach. Wasser-Abwasser. 119: 318.

Duggan, R.E. and P.E. Corneliussen. 1972. Dietary intake of pesticide chemicals in the United States (III). June 1968-April 1970. Pestic. Monitor. Jour. 5: 331.

Engst, R., et al. 1976a. The metabolism of hexachlorobenzene (HCB) in rats. Bull. Environ. Contam. Toxicol. 16: 248.

Engst, R., et al. 1976b. 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. Jour. Environ. Sci. Health. 2: 95.

Fahrig, R., et al. 1978. Genetic Activity of Chlorophenols and Chlorophenol Impurities. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology, and Environmental Toxicology. Plenum Press, New York. p. 325.

Goldstein, J.A., et al. 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.

Gordon, D. 1956. How dangerous is pentachlorophenol. Med. Jour. Aust. 2: 485.

Hansen, D.J. 1980. Memorandum to C.E. Stephan. U.S. EPA.

Hinkle, D.K. 1973. Fetotoxic effects of pentachlorophenol in the Golden Syrian hamster. Toxicol. Appl. Pharmacol. 25: 455. (Abst.)

Hoak, R.D. 1957. The causes of tastes and odors in drinking water. Water Sewage Works. 104: 243.

Innes, J.R.M., et al. 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice. A preliminary note. Jour. Natl. Cancer Inst. 42: 1101.

Jakobson, I. and S. Yllner. 1971. Metabolism of ^{14}C-pentachlorophenol in the mouse. Acta. Pharmacol. Toxicol. 29: 513.

Johnson, R.D. and D.D. Manske. 1977. Pesticides in food and feed: Pesticide and other chemical residues in total diet samples (XI). Pestic. Monitor. Jour. 11: 116.

Johnson, R.L., et al. 1973. Chlorinated dibenzodioxins and pentachlorophenol. Environ. Health Perspect. Exp. Issue. 5: 171.

Karapally, J.C., et al. 1973. Metabolism of lindane-^{14}C in the rabbit: Ether-soluble urinary metabolites. Jour. Agric. Food Chem. 21: 811.

Klemmer, H.W. 1972. Human health and pesticides - community pesticide studies. Residue Rev. 41: 55.

Knudsen, I., et al. 1974. Short-term toxicity of pentachlorophenol in rats. Toxicol. 2: 141.

Kociba, R.J., et al. 1971. Results of 90-day toxicological study in male rats maintained on diets containing production grade or purified pentachlorophenol. November 24, 1971. Dow Chemical Co., Midland, Michigan.

Kociba, R.J., et al. 1973. Toxicological evaluation of rats maintained on diets containing pentachlorophenol sample XD-8108 OOL for 90 days. March 2, 1973. Chem. Biol. Section, Dow Chemical Co.

Kohli, J., et al. 1976. Contributions of ecological chemistry CVII - fate of lindane-^{14}C in lettuce, endives, and soil under outdoor conditions. Jour. Environ. Sci. Health Bull. 1: 23.

Koss, G. and W. Koransky. 1978. Pentachlorophenol in Different Species of Vertebrates after Administration of Hexachlorobenzene and Pentachlorobenzene. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology, and Environmental Toxicology. Plenum Press, New York. p. 131.

Kutz, F.W., et al. 1978. Survey of Pesticide Residues and their Metabolites in Urine from the General Population. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology, and Environmental Toxicology. Plenum Press, New York. p. 363.

Larsen, R.V., et al. 1975. Placental transfer and teratology of pentachlorophenol in rats. Environ. Lett. 10: 121.

Lui, H. and C.D. Sweeney. 1975. Hepatic metabolism of hexachlorobenzene in rats. FEBS Lett. 51: 225.

Machle, W., et al. 1943. Observations on the fate of pentachlorophenol in the animal organism. Jour. Ind. Hyg. Toxicol. 25: 192.

Manske, D.D. and P.E. Corneliussen. 1974. Pesticide residues in total diet samples (VII). Pestic. Monitor. Jour. 8: 110.

Mason, J.F., et al. 1965. Pentachlorophenol poisoning: Report of two cases. Jour. Forensic Sci. 10: 136.

Mehendale, H.M., et al. 1975. Metabolism and effects of hexachlorobenzene on hepatic microsomal enzymes in the rat. Jour. Agric. Food Chem. 23: 261.

National Research Council. 1977. Drinking Water and Health. Natl. Acad. Sci., Washington, D.C.

Nomura, S. 1953. Studies on chlorophenol poisoning. Podo Kaguku Jour. Sci. Labor. 29: 474.

Rapp, D.E. 1978. Industrial hygiene study: Pentachlorophenol users' plants. Industrial Hygiene Laboratory, Health and Environmental Research, Dow Chemical USA, Midland, Michigan. (Unpubl.)

Robson, A.M., et al. 1969. Pentachlorophenol poisoning in a nursery for newborn infants. I. Clinical features and treatment. Jour. Pediatr. 75: 309.

Schwetz, B.A., et al. 1974. The effect of purified and commercial grade pentachlorophenol on rat embryonal and fetal development. Toxicol. Appl. Pharmacol. 28: 151.

Schwetz, B.A., et al. 1978. Results of Two-year Toxicity and Reproduction Studies on Pentachlorophenol in Rats. In: K.R. Rao (ed.), Pentachlorophenol: Chemistry, Pharmacology, and Environmental Toxicology. Plenum Press, New York. p. 301.

Shafik, T.M. 1973. The determination of pentachlorophenol and hexachlorophene in human adipose tissue. Bull. Environ. Contam. Toxicol. 15: 57.

Stephan, C.E. 1980. Memorandum to J. Stara. U.S. EPA. July 3.

Takahashi, W., et al. 1976. Acute phase proteins and pesticide exposure. Life Sci. 19: 1645.

U.S. EPA. 1976. Summary of reported episodes involving pentachlorophenol. Pesticide episode review system. Report No. 60. Sept. 14, 1976. Pestic. Episode Response Branch, Operations Div. Off. Pestic. Programs.

U.S. EPA. 1980. Seafood consumption data analysis. Stanford Research Institute International, Menlo Park, California. Final report, Task 11, Contract No. 68-01-3887.

Vogel, E. and J.L.R. Chandler. 1974. Mutagenicity testing of cyclamate and some pesticides in Drosophila melanogaster. Experientia. 30: 621.

Weinbach, E.C. and J. Garbus. 1965. The interaction of uncoupling phenols with mitochondria and with mitochondrial protein. Jour. Biol. Chem. 240: 1811.

Wyllie, J.A., et al. 1975. Exposure and contamination of the air and employees of a pentachlorophenol plant, Idaho 1972. Pestic. Monitor. Jour. 9: 150.

Yang, R.S.H., et al. 1975. Chromatographic methods for the analysis of hexachlorobenzene and possible metabolites in monkey fecal samples. Jour. Assoc. Off. Anal. Chem. 58: 1197.