PENTACHLOROPHENOL
POSITION DOCUMENT 1

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Pentachlorophenol
Position Document 1

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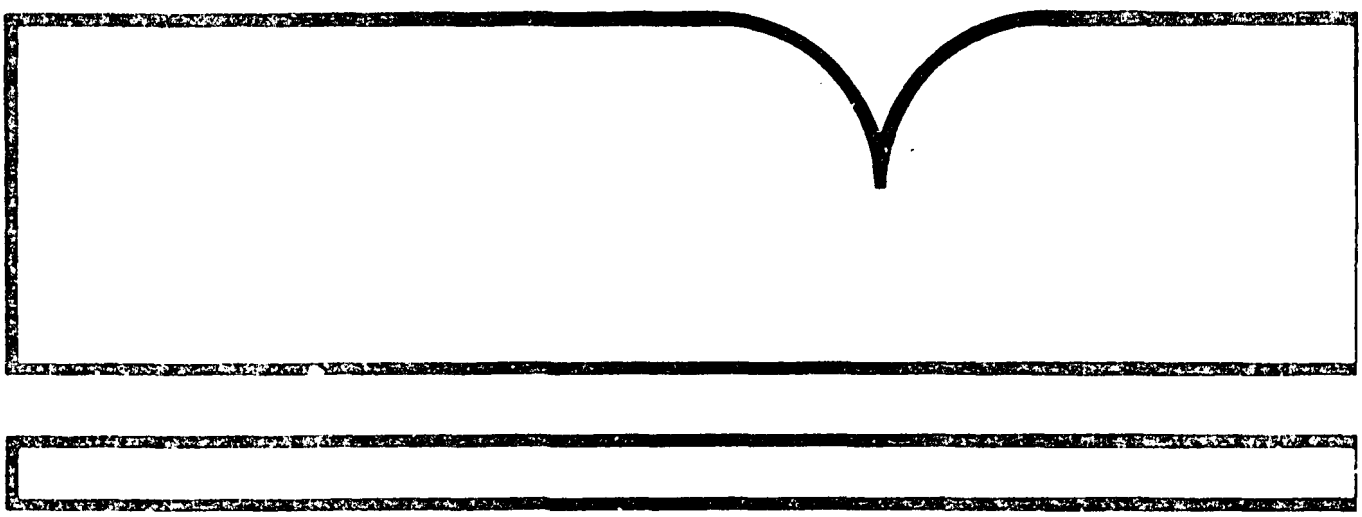

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PENTACHLOROPHENOL

POSITION DOCUMENT 1

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I. Background

A. Chemistry

1. General

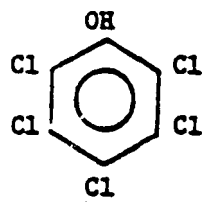
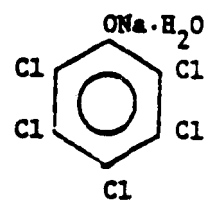
Pentachlorophenol (PCP or PENTA)[1/] is a buff-colored crystal which is produced in the United States by chlorination of molten phenol in the presence of a catalyst. Derivatives of PCP which are registered for use as pesticides are the sodium and potassium salts (Na-PCP and K-PCP, respectively), and the lauric acid ester (L-PCP). The structures and physical properties of PCP and Na-PCP are given in Figure I. K-PCP is produced as *in situ* formulations by dissolving PCP in potassium hydroxide solutions. The physical and chemical properties of pure K-PCP are not available from standard chemical references or from EPA files. L-PCP is produced by esterification of PCP with mixtures of alkyl carboxylic acids, the most predominant of which is lauric acid. Technically pure L-PCP is a brown oil having a specific gravity of 1.28 at room temperature. It is soluble in non-polar solvents, oils, fats, waxes and plasticizers, and insoluble in water and alcohols.

Industrial production of PCP is a two-stage process. In the first stage, isomers of tri- and tetrachlorophenols are formed when the reaction temperature is about 105 °C. In the second stage, the temperature is progressively increased to 130 °C to keep the reaction mixture molten, and the tri- and tetrachlorophenols are further chlorinated to form PCP. This reaction is not quantitative; tetrachlorophenols persist during the reaction and are carried with PCP during subsequent processing. The result is that

1/ PCP will be used as an abbreviation for pentachlorophenol in this document.

Figure I

Physical properties of pentachlorophenol and sodium pentachlorophenate

Structural Formula		
Name	Pentachlorophenol	Sodium Pentachlorophenate
Formula	C_6Cl_5OH	$C_6Cl_5ONa \cdot H_2O$
Molecular Weight	266.4	306.3
Description	Buff-colored crystal	Buff-colored crystal
Specific Gravity	1.9	2.0
Density	1.987	-
Vapor Pressure	0.00015 (25 °C)	-
Solubility, g/100 g, 25 °C		
Water	< 0.01	33
Acetone	50	35
Benzene	15	-
Diacetone Alcohol	190	45
Ethanol (95%)	120	65
Methanol	180	25
Isopropanol	85	30
Ethylene glycol	11	40

technical grade PCP contains from 4 to 12% tetrachlorophenols. These tetrachlorophenols are listed on the product labels as active ingredients. One of the three possible tetrachlorophenol isomers, 2,3,4,6-tetrachlorophenol, was registered by the Dow Chemical Company as Dowicide 6, a fungicide; this chemical is no longer produced as a separate product. It is, however, listed as an active ingredient in some PCP products.

The elevated temperatures required for the second stage of PCP production favor condensation of the tri- and tetrachlorophenols to form hexa-, hepta-, and octa-chlorodibenzo-p-dioxins (dioxins) and various chlorinated dibenzofurans (furans). These impurities are also carried forward with PCP and will be discussed in greater detail in Section I.C.

2. Environmental Residues

The amount of PCP produced in the United States, approximately 50,000,000 pounds/year, and its widespread use as a pesticide strongly indicate its potential as an environmental pollutant. Possible sources of PCP in the environment are: runoff from manufacturing or wood preserving processes, leaching or vaporization from preserved wood, and from its use as a termiticide and herbicide. Although there is evidence that PCP could be found in the environment, the ambient monitoring programs for air, water, and soils do not routinely test for PCP.

a. Air

The vapor pressure of PCP, 0.00017 torr at 20 ^{o}C and 0.0031 torr

at 50°C, suggests that it can volatilize from treated surfaces (torr: pressure required to support 1 mm of mercury at 0°C). Gebefugi et al. (1976) measured PCP vapors in a closed test area in which wall paneling was covered according to label instructions with a wood-protecting agent containing PCP. Air samples were taken every day for 9 days at 25°C, and then for 6 days at 28°C. Samples were taken in the morning, and the sampling period was not specified. Gas chromatographic measurements showed PCP measurements ranging from 1 microgram/cubic meter (ug/m^3) on the first day to 160 ug/m^3 on the fourth day. There were wide fluctuations in PCP concentrations during the course of the experiment. In a separate experiment, an increase in the amount of water vapor in the test area decreased the PCP levels in the air.

Bevenue et al. (1972) measured PCP in rain water in Hawaii [2-284 parts per trillion (ppt)], in snow samples taken from Mauna Kai Summit (14 ppt), and in lake water fed by this snow (10 ppt). The authors did not determine whether this airborne PCP was in gaseous form or adsorbed on dust particles. Because of the heavy use of PCP in Hawaii to protect wooden surfaces against termites, both physical forms are likely to occur in the air.

There is indirect evidence that PCP vapors can be toxic. An article that appeared in California Health in 1970 (Anon. "Pentachlorophenol Poisoning in the Home") described the effects on the inhabitants of painting interior wood paneling with PCP-containing paint. House plants within the

home died in 3 or 4 days. Over a 3-month period, the housewife became progressively weaker while losing 20 pounds. She recovered after hospitalization. Her condition was diagnosed as PCP poisoning by a California State Department toxicologist.

Ferguson in 1959 showed that PCP vapors were toxic to conifer seedlings grown in greenhouses on wood flats whose sideboards had been treated with PCP. Leaching of PCP into the soils of the flats was not implicated since transfer of these soils to untreated flats supported normal seedling growth. He observed toxic effects, to a lesser extent, on seedlings in untreated flats, which he attributed to air movement from treated to the untreated flats. PCP has been found in the blood and urine of workers in wood-preserving factories; in one report this was attributed, in part, to respiratory exposure (Casarett et al., 1969).

The American Conference of Government Industrial Hygienists has established a PCP Threshold Limit Value-Time Weighted Average of 0.5 mg/m^3 for a normal 8-hour workday or 40-hour workweek, and a Threshold Limit Value-Short Term Exposure Limit of 1.5 mg/m^3 for a 15-minute period.

b. Water

PCP can be released into water as an effluent from manufacturing or wood-preserving plants, by leaching from treated wood exposed to rain, and by runoff from its uses as a herbicide, fungicide, and molluscicide. In spite of its wide production and variety of uses, PCP is not routinely monitored by the National Water Monitoring Program, which measures contami-

nants in rivers and streams in the United States. This program reported fifteen measurements of PCP along the California Aqueduct between 1974 and 1976. There was no sampling previous to 1974. Values reported from five sites along the Aqueduct ranged from 0.01 to 16.0 ug/liter PCP in whole water samples.

Buhler et al. (1973) measured PCP in sewage treatment plant effluent collected simultaneously from three Oregon cities. He reported PCP levels between 1 and 4 parts per billion (ppb). The same workers found PCP concentrations between 0.10 and 0.70 ppb in water sampled from the Willamette River, and 0.6 ppb in drinking water from a water treatment plant. In unpublished data, the EPA Drinking Water Program has found PCP in the water of 86 of the 108 cities sampled; the mean concentration of the positives was 0.07 ug/liter. The median concentration for all cities was 0.051 ug/liter (Kutz, 1977).

In 1976 Fountaine et al. analysed samples from a stream which originated in an area containing several manufacturing plants, including a wood-preserving installation. The highest measurement of PCP, 5,450 parts per million (ppm), was in surface oil slicks; water samples ranged from 0.082 to 10.5 ppm. The authors noted that these PCP levels are not necessarily due to discharge from the wood-preserving factory outlet into the stream. The factory had been in business for 20 years. Gross spillage of PCP occurred in the factory area, particularly in the early years of operation, and this PCP seeped into the ground. There is, therefore, the possibility that the PCP levels in the stream were due to runoff from PCP-contaminated soil, rather than direct discharge from

the factory. Measurements of PCP in the factory discharge were not reported.

c. Soils

Because the National Soils Monitoring Program does not routinely analyze soil samples for PCP, ambient levels in soils are not available.

In a series of papers, Choi and Aomine (1972, 1974a, 1974b) studied the adsorption properties of PCP on various soil types and under a variety of environmental conditions in the laboratory. They found that PCP was adsorbed to some extent on all soil types. Soil acidity was a major factor in determining the amount of PCP adsorbed; strongly acidic soils (pH 5) adsorbed more than less acid soils (pH 6). There was less adsorption by weakly acidic or neutral soils. However, increased organic matter or temperature or both increased PCP adsorption at the pH-values tested. In a series of experiments using different soil types and ion concentrations, the authors demonstrated competition between inorganic ions and PCP for adsorption sites on soil colloids. They concluded from their experiments that PCP is adsorbed on soil through ion exchange reactions as well as molecular adsorption due to van der Waals forces.

The fate of PCP in soils has been extensively studied. The primary factor in the degradation of PCP in soils is microbiological activity; other contributing factors include soil type, moisture content, and temperature. Kuwatsuka and Igarashi (1975) demonstrated a positive correlation between the proportion of organic matter and the degradation

rate of PCP in soils, observing that soils devoid of organic matter did not degrade PCP. Ide et al. (1972) found that PCP did not degrade in sterilized soil samples; Young and Carroll (1951) showed that PCP decays most rapidly in soil containing a large proportion of organic matter and at temperatures which are optimal for microbiological activity. Kuwatsuka and Igarashi (1975) compared the PCP degrading characteristics of upland (i.e., aerated) soil with flooded (i.e., rice paddy) soil. They found that soil microorganisms degraded PCP most rapidly when they were maintained in the environment to which they are adapted, e.g. flooding upland soil and aerating flooded soil decreased the rate of PCP decay. Using a gas chromatograph with an electron-capture detector the authors identified tri- and tetrachlorophenols as degradation products of PCP and indicated that, at least as a first step, PCP degrades by dechlorination. Ide et al. (1972) found tri- and tetrachloroanisoles as PCP degradation products. This indicated that methylation is also involved in the degradation process.

The persistence of PCP in soils ranges between 21 days and 5 years, depending primarily on the microbial population. Watanebe (1973) reported complete degradation in paddy soil in 21 days. Hetrick (1952) claimed that PCP persisted for over 5 years in an unspecified soil type.

d. Plants and Animals

i. Plants

There are no data available on PCP residues in higher plants resulting from its use as a pesticide.

ii. Animals

In 1974 Vermeer et al. reported the death of wildlife caused by application of Na-PCP to a rice field in Surinam, South America. The Na-PCP was applied at the rate of 4 kg/hectare to control water snails which damaged young rice plants. PCP residues were measured in snails (36.8 mean wet-weight ppm), frogs (8.1 mean wet-weight ppm), fishes (31.2, 41.6 and 59.4 mean wet-weight ppm for three species), and snail kites, a bird which feeds on water snails. The dead kites showed mean PCP residues of 11.25 ± 1.11 ppm in brain tissue, 45.56 ± 2.18 ppm in liver, and 20.34 ± 1.25 ppm in the kidneys, all on a wet weight of tissue basis. These PCP levels were 53, 74, and 166 times greater, respectively, than those in kites collected from an untreated marsh. The investigators attributed the death of the kites from the treated field to their feeding on water snails containing PCP. In addition, when other bird species which frequented the treated fields were examined, PCP was detected at levels ranging from 0.04 to 0.24 wet-weight ppm in the liver and 0.08 to 0.49 wet-weight ppm in the brain.

Early in 1977 PCP was detected in the blood of dairy cattle and calves on eight Michigan farms. These herds all showed signs of sickness and had high calf mortality rates. The levels of PCP found in one herd ranged from 270 to 570 ppb. This herd was housed in a total-confinement barn which had been constructed, in part, of PCP-treated wood. In another herd the dioxins found in PCP were detected in fat and liver tissue in the parts per billion and parts per trillion ranges,

respectively. As a result of this incident, the Animal and Plant Health Inspection Service of the Department of Agriculture (USDA) instituted a nationwide survey of beef fat and liver for the presence of the hexa- and octachlorodioxins found in PCP. In the first group of 238 beef samples collected in seventeen States, 70 (29.4%) showed positive levels using low resolution mass spectrometry. Of these 70 samples, 4 had been confirmed using high resolution mass spectrometry. Detection levels were in fractional nanograms/gram for both hexa- and octa-chlorodibenzo-p-dioxins. The determination of the signficance of these residues awaits the completion of the survey and its subsequent statistical and methodological analysis.

e. Humans

PCP appears to be ubiquitous in human urine. In 1970 Cranmer and Freal found PCP in urine at concentrations ranging from 2 to 11 ppb in the general population. In 1967 Bevenue et al. found PCP in the urine of 130 Hawaiians occupationally exposed to PCP at levels ranging from 0.03 to 35.7 mg/liter. In the same study, PCP was found in the urine of all but one of 117 unexposed subjects; these values varied from 0 to 0.44 mg/liter. In a recent study, preliminary data from a joint U.S. Public Health Service - EPA effort disclosed that 86% of the urine samples taken from subjects within the continental United States showed positive PCP values averaging 6.3 ppb, with a maximum observed value of 193 ppb. The limit of detection was 5 ppb (Kutz et al., 1978).

Arsenault (1976) reported the mean blood serum level of PCP in twenty-one workers in pressure treatment plants to be 1.05 ppm; there

were about 0.1 ppm in the controls (unspecified). Data for the general population are not available. In another study Shafick (1973) reported PCP levels ranging from 12 to 52 ppb in the adipose tissue of eighteen subjects who were not occupationally exposed to PCP. Dougherty and Piotrowska (1976) detected PCP in seminal fluid from seven sexually active men. Levels detected averaged 50 ppb (range: 20-70 ppb).

The sources and exposure routes of PCP residues in human tissues have not been conclusively established. Possible routes are inhalation of vaporized PCP and ingestion of PCP in water and food. In addition, PCP forms as a metabolic product of hexachlorobenzene (HCB). Lui and Sweeney (1975) fed rats 0.25% HCB, which amounted to about 50 to 100 mg HCB daily. Analysis of urine by gas-liquid chromatography showed a level of 12.5 ug/ml PCP in a daily urine output of about 15 ml. The analyses were confirmed by gas-liquid chromatography/mass spectrometry.

The Food and Drug Administration Market Basket Survey has estimated the amount of pesticides in foodstuffs since 1965. The estimates are based on the average daily intake of an 18-year-old male, whose food consumption is the highest of any age group of either sex. The most recent data from this survey (Johnson and Manske, 1977) are available from food samples collected from August 1974 to July 1975. PCP was assayed in twelve food commodities collected in twenty cities in the United States, so that there were twenty measurements for each commodity. The results are summarized in Table 1.

TABLE 1. Pentachlorophenol in food commodities[1/]

Commodity	Average, ppm[2/]	Positive Composites	Range, ppm
Dairy Products	0.0005	1	0.01
Meat, Fish, and Poultry	-	0	-
Grain and Cereal Products	0.001	2	0.01-0.013
Potatoes	-	0	-
Leafy Vegetables	T[3/]	1	T
Legume Vegetables	-	0	-
Root Vegetables	0.001	2	0.010
Garden Fruits	T	1	T
Fruits	T	1	0.011
Oils, Fats, and Shortening	-	0	-
Sugars and Adjuncts	0.006	5	0.01-0.04
Beverages	-	0	-

1/ Data from Johnson and Manske (1977).
2/ Averages based on twenty composite samples; trace residues were not included in calculating the average.
3/ T = trace.

These low levels of PCP in food are a constant means of exposure to humans. However, the connection between this route of exposure and the presence of PCP in blood, urine, and adipose tissue is not clear.

B. Metabolism

1. Plants

As described earlier, microorganisms are capable of degrading PCP in soils. Certain bacterial strains have been isolated which are capable of growing on media containing PCP (Horton et al., 1969) and of using PCP as the sole source of carbon (Chu and Kirsch, 1972). The metabolic mechanisms of bacterial action on PCP are, however, unknown. Certain species of fungi, some of which are present in wood, have been found to tolerate PCP. Several of these fungi depleted PCP in treated wood blocks, but lost their ability to cause wood decay (Duncan and Deverall, 1964). As is the case with bacteria, metabolic pathways of PCP degradation by fungi have not been identified. There are no data available on the metabolism of PCP by higher plants.

2. Animals

There have been two studies on PCP metabolism in aquatic animals. Each of these papers demonstrated the same metabolic pathway. In 1970 Kobayashi et al. reported that the short-necked clam (Tapes phillippinarium) converts PCP to pentachlorophenyl sulfate in sea water. The level of PCP in the shellfish reached a plateau after about 24 hours of exposure. After 50 hours, 80% of the PCP had been converted to the sulfate conjugate. The same detoxification mechanism was demonstrated by Akitake and Kobayashi

(1975) in goldfish cultured in fresh water containing PCP. Whether this detoxification mechanism is common to other aquatic animals is not known.

Mammals are known to excrete PCP in unchanged form after exposure by various routes. In 1974 Ahlborg et al. administered ^{14}C-PCP orally and intraperitoneally to rats and mice (10 to 25 mg/kg). Approximately 40% was excreted as PCP in the urine. ^{14}C-tetrachlorohydroquinone was also detected at levels equal to 5% of the excreted radioactivity in rats, and 24% of the activity in mice. The authors also found PCP and tetrachlorohydroquinone in the urine of workers occupationally exposed to PCP. Larsen et al. (1972) orally administered ^{14}C-PCP to rats, and found that 50% of the radioactivity was excreted in the urine in 24 hours, 68% was excreted in 10 days; between 9.2 and 13.2% was excreted in the feces. Tissue analyses 40 hours after exposure showed small amounts of ^{14}C activity in the adrenal glands, blood, brain, fat, heart, kidneys, liver, lungs, muscles, ovaries, spleen, stomach and intestine, and testes. Highest levels were found in liver (0.23% of administered radioactivity), kidney (0.18%), and blood (0.15%). In blood, 99% of the radioactivity detected was in the serum.

Larsen et al. (1972) postulated a two-component urinary excretion pattern that has a 10-hour half-life for the first 2 days, followed by a 102-day half-life. In 1969 Casarett et al. measured PCP concentrations in the urine of two subjects after respiratory exposure and determined that after 24 hours, the half-life is approximately 10 hours. They found a blood-to-urine PCP ratio of between 1.5 and 2.5 in occupationally ex-

posed individuals. At about 10 ppm, PCP in blood plasma reached a plateau while urine levels continued to increase. They postulated that PCP binds to plasma protein, and is subsequently distributed to the tissues. The work of Larsen et al. (1972) seems to confirm this.

Tashiro et al. (1970) demonstrated an additional metabolic pathway for PCP. They collected and analysed the urine of three rabbits fed 10 g of unlabeled PCP over 30 days. They identified a sugar conjugate of PCP, pentachlorophenyl-beta-glucuronide, in the urine which led them to propose a three-way excretory pathway for PCP in mammals: unchanged PCP; the oxidation product "chloranil", which is actually tetrachloroquinone, and the conjugate PCP-beta-glucuronide.

C. Pentachlorophenol Contaminants

As stated previously, commercial production of PCP results in the formation of dioxin and furan contaminants. Figure 2 shows the structural formula of the basic molecules. Substitution of chlorine atoms at one or more of the numbered positions results in the chlorinated dibenzo-p-dioxin (dioxin) and chlorinated dibenzofuran (furan) chemical families. There are 75 members of the dioxin family and 135 furans. Members of these families differ not only in the number of chlorine atoms on the molecule, but also in the positioning of these atoms (isomerism). Thus the dioxin that has six chlorine atoms on its molecule has ten possible isomers.

The dioxins which are found in PCP are the hexa- (HCDD), hepta- (HeCDD), and octa-chlorodibenzo-p-dioxins (OCDD); the furans found are

FIGURE 2. Structure of dioxin and furan

the tetra-, penta-, hexa-, hepta-, and octa-dibenzofurans (Buser and Bosshardt, 1976). The amount of these chemicals in PCP varies with each industrial batch produced, even when produced by the same manufacturer. Analytical methods for measuring individual isomers require sophisticated and expensive analytical instrumentation, and standards for the isomers are not generally available. Until recently, both the dioxins and furans in PCP have been measured as isomeric groups. Table 2 shows the composition of typical commercial PCP.

The physical, chemical, and toxicological properties of individual dioxins and furans are, with one exception, relatively unknown. The exception is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), which has been shown to be one of the most toxic compounds known. TCDD is not found in PCP at a limit of detection less than 0.05 ppm (Johnson et al., 1973). However, the dioxins in PCP have been shown by Johnson et al.

TABLE 2. Composition of commercial pentachlorophenol[1/]

Component	Dowicide 7	Dowicide EC-7[2/]
Pentachlorophenol	88.4%	89.8%
Tetrachlorophenol	4.4%	10.2%
Trichlorophenol	< 0.1%	< 0.1%
Chlorinated Phenoxyphenols	< 6.2%	-
Hexa-dioxins	4 ppm	1.0 ppm
Hepta-dioxins	125 ppm	6.5 ppm
Octa-dioxin	2500 ppm	15.0 ppm
Hexa-furans	30 ppm	< 1 ppm
Hepta-furans	80 ppm	1.8 ppm
Octa-furan	80 ppm	< 1 ppm

1/ Data from Dow Chemical Company.
2/ Total greater than 100% because numbers are rounded off.

(1973) to cause chloracne in rabbits and edema in chicks. The only data available comparing the toxic effects of individual dioxin isomers were reported by McConnel et al. (1977), and these are shown in Table 3. These data indicate that the hexa- and hepta-dioxin isomers tested were less toxic than TCDD in mice and guinea pigs; however, they would be classified as Category I poisons (oral LD-50 less than 50 mg/kg).

TABLE 3. Single oral LD-50-30 of dioxin isomers [1/]

Isomer	LD-50-30, ug/kg	
	Guinea Pigs	Mice
1,2,3,4,7,8-HCDD	72.5	825
1,2,3,6,7,8-HCDD	70-100 [2/]	1250
1,2,3,7,8,9-HCDD	60-100 [2/]	1440
1,2,3,4,6,7,8-HpCDD	7180	-
TCDD [3/]	2	283.7

1/ Data from McConnell et al. (1977).
2/ Estimated range represents variability among replicates.
3/ TCDD values are shown for comparative purposes.

Firestone (1977) detected PCP, individual hexa- and hepta-dioxin isomers, and octa-dioxin in samples of commercial gelatin procurred from supermarkets and in bulk. Gelatin is produced from pork skins and cattle

bones and hides, which may be preserved with PCP during processing both in this country and abroad. According to Firestone, the annual consumption of gelatin in the United States is 57 million pounds of domestic production and 13 million pounds of imports.

Highest levels of PCP and total dioxins were found in bulk gelatin that was imported from Mexico and produced by a single company. Three measurements of this gelatin averaged 6.4 ppm of PCP, and six measurements averaged 26.8 ppb of total dioxins. In contrast, bulk domestic porkskin gelatin had no PCP and 0.1 ppb of total dioxins (octadioxins) in one of two sample measurements. Three consumer packages of unflavored gelatin purchased in a supermarket showed 0.2, 0.8, and 3.6 ppb of total dioxins.

D. Registered Uses and Production

Pentachlorophenol and its derivatives are among the most versatile pesticides now in use in the United States. This versatility is due first to their efficacy against a wide variety of pests (bacteria, yeast, slime molds, algae, fungi, plants, insects, snails), and second to their solubility in both organic solvents and water. Thus, PCP can be applied to a wide spectrum of materials. In various concentrations, solvents, and formulations, pentachlorophenols are registered for use on beans (for replanting purposes only), wood, leather, burlap, masonry, cordage, paints, petroleum, pulp and paper mill systems, weeds on seed crops (preharvest desiccant), secondary oil recovery injection waters, and commercial and industrial water cooling towers and evaporation condensers (Na-PCP).

Approximately 50,000,000 pounds of PCP is produced annually in the United States. The major use of PCP in the United States is as a wood preservative. This use consumes approximately 80% of all PCP produced. About 11% of the PCP produced is formulated as Na-PCP and used in the production of pressed and insulation board, and in cooling towers. Approximately 6% is used in pulp and paper mills to control the growth of slime-forming bacteria and fungi in paper production; 3% is used for farm treatment of fence posts, home protection against termites, and as a herbicide and pre-harvest desiccant.

The number of Federally-registered products containing PCP and the number of registrants is given in Table 4. In addition, there are 75 State-registered products formulated by 60 registrants.

TABLE 4. Federal registration of pentachlorophenol[1/]

	No. Products	No. Registrants
PCP	578	240
Na-PCP	196	88
K-PCP	5	4
L-PCP	6	2

1/ Data from computerized Registration Division files.

E. Regulatory History

Technical PCP was registered for use as a wood preservative in 1948 by Dow Chemical Company and Monsanto Agricultural Products Company. Subsequently, registrations were granted for a wide variety of uses, including agricultural uses such as pre- or postharvest weed treatment and preharvest dessication of seed crops. Until 1970, regulatory actions against PCP were confined to these kinds of uses. For example, in the "USDA Summary of Registered Agricultural Pesticide Uses" issued on August 31, 1968, PCP was registered as a weed killer on alfalfa, cotton, pineapples, and sugarcane. These registrations were cancelled by Pesticide Regulation (PR) Notices 69-4 (February 1, 1969) and 70-4 (February 26, 1970) when the concept of zero tolerance was abandoned by the Department of Agriculture. Currently, PCP is registered for agricultural use only as a seed treatment for nonfood uses on beans, alfalfa, clover, lespedeza, and vetch.

On September 28, 1970, USDA published PR Notice 70-22. Although PCP was not mentioned by name, the Notice stated "Appropriate regulatory action will be taken under the provisions of the Act (FIFRA) if these chlorodioxins are found in any economic poison." The notice was directed toward the presence of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in the herbicides 2,4,5-trichlorophenoxyacetic acid and silvex; PCP and its chlorodioxins were not mentioned. The Dow Chemical Company, however, interpreted the Notice to apply to PCP and took action to reduce chlorodioxin levels in its technical PCP.

At the time the Notice was issued, methodologies for the analysis of dioxins in PCP were not totally reliable. Therefore, there was disagreement within the industry on the actual levels of dioxins in their products. There were no toxicological studies on PCP dioxins, and toxic effects were inferred from chloracne and chick edema effects of commercial PCP. These same effects are caused by TCDD. In the absence of such evidence, regulatory action on dioxin levels in PCP was not possible. This situation continued until 1974, when research involving purified PCP (i.e., relatively free of dioxins), in contrast to commercial PCP, began to appear in the literature.

II. Summary of Scientific Evidence Relating to Rebuttable Presumption Criteria

A. Reproductive and Fetotoxic Effects in Mammalian Species

40 CFR 162.11(a)(3)(ii)(B) provides that "a rebuttable presumption shall arise if a pesticide's ingredient(s)... Produces any other chronic or delayed toxic effect in test animals at any dosage up to a level, as determined by the Administrator, which is substantially higher than that to which humans can reasonably be anticipated to be exposed, taking into account ample margins of safety." This section reflects concern that chronic exposure to chemicals may result in injury to the reproductive system and/or the fetus and provides that a rebuttable presumption shall arise if chronic chemical exposure in test animals produces such results, and if human exposure to the chemicals exceed an ample margin of safety.

In the studies summarized below, fetotoxic and teratogenic effects have been reported in rats exposed to purified and commercial grade PCP. These same effects were observed in rats exposed to a mixture of two unspecified isomers of HCDD. Specifically, exposure to PCP and these HCDD isomers resulted in statistically significant increases in the incidence of skeletal and soft tissue anomalies, growth-retarded fetuses and of embryonic resorption in the litters of treated dams.

1. Fetotoxicity

a. Studies with PCP

Schwetz et al. (1974) studied the effects of purified and commercial grade PCP on rat embryonal and fetal development. The compositions of the two types of PCP are given in Table 5. Dosages of 5, 15, 30, and 50 mg/kg/day of both PCP types were administered by gavage on gestation days 6 through 15 inclusive. Their results, shown in Table 6, may be summarized as follows: both purified and commercial PCP caused statistically significant increases in fetal resorptions at the two higher doses, as well as among litters exposed to 15 mg/kg/day of commercial PCP. Specifically, the resorption rate ranged from 27.2% (64/235) to 100% (229/229) in the two highest (commercial and purified) dose groups, compared to 4.2% (15/358) in the control group. At 30 and 50 mg/kg day, purified PCP had a more pronounced effect than commercial PCP. For example, at 50 mg/kg/day, purified PCP caused 100% fetal resorbtion, while commercial

TABLE 5. Composition of pentachlorophenol materials used by Schwetz et al. (1974)

	Commercial Grade	Purified
Identification	Lot No. MM06210-9822A	Ref. No. 27-91-1
Phenolics, %[1]		
Pentachlorophenol	88.4	98+
Tetrachlorophenol	4.4	0.27
Trichlorophenol	< 0.1	0.05
Higher Chlorinated Phenoxyphenols	6.2	0.5
Nonphenolics, ppm[2]		
Dibenzo-p-dioxins		
2,3,7,8-tetrachlorodibenzo-p-dioxin	< 0.05	< 0.05
Hexachlorodibenzo-p-dioxin	4	< 0.5
Heptachlorodibenzo-p-dioxin	125	< 0.5
Octachlorodibenzo-p-dioxin	2500	< 1.0
Dibenzofurans		
Hexachlorodibenzofuran	30	< 0.5
Heptachlorodibenzofuran	80	< 0.5
Octachlorodibenzofuran	80	< 0.5

1/ Determined by gas-liquid chromatography.
2/ Determined by use of an LKB 9000 gas chromatograph-mass spectrometer.

TABLE 6. Effect of pentachlorophenol on the incidence of fetal resorptions and on the sex ratio of survivors[1/]

Test Material and Dose, mg/kg/day	Resorptions Among Fetuses %	Resorptions Among Fetuses No.	Resorptions Among Litters %	Resorptions Among Litters No.	Sex Ratio M	Sex Ratio F
Vehicle Control[2/]	4.2	15/358	30.3	10/33	50	50
Pentachlorophenol[3/]						
Commercial						
5.8[4/]	7.1	15/212	55.6	10/18	50	50
15	8.8	17/194[5/]	64.7	11/17[5/]	52	48
34.7[6/]	27.2	64/235[5/]	94.7	18/19[5/]	60	40
50	58.1	108/186[5/]	93.3	14/15[5/]	79	21[5/]
Purified						
5	4.2	8/189	46.7	7/15	48	52
15	5.9	13/221	38.9	7/18	50	50
30	97.5	233/239[5/]	100.0	20/20[5/]	83	17[5/]
50	100.0	229/229[5/]	100.0	19/19[5/]	-	-

1/ Adapted from Schwetz et al. (1974)
2/ 2.0 ml/kg body weight corn oil per day.
3/ Dosages administered in 2.0 ml corn oil/kg body weight.
4/ Equivalent to 5.0 mg/kg/day purified PCP.
5/ Indicates values significantly different from control values by the binomial expansion test, $p < 0.05$.
6/ Equivalent to 30.0 mg/kg/day purified PCP.

PCP caused 58% resorption. At 30 (purified) and 50 (commercial) mg/kg/day, there were statistically significant differences in the sex ratio of surviving fetuses; males were heavily predominant. Schwetz et al. found that administration of PCP during early organogenesis (days 8 through 11 of gestation) had more pronounced effects on fetal resorption than did its administration during late organogenesis (days 12 through 15) (Table 7).

The no-effect dose for fetal resorptions was 5.8 commercial grade PCP/kg/day and 15 mg purified PCP/kg/day. Measurements were also taken on fetal body weight and crown-rump length, both of which decreased with the increase in dosage. The no-effect dose for these parameters was 15 mg commercial grade or purified PCP/kg/day.

Larsen et al. (1975) fed 60 mg ^{14}C-PCP/kg body weight to pregnant Charles River CD strain rats on day 15 of gestation. They detected negligible amounts of ^{14}C-PCP in the placentas and fetuses up to 32 hours after dosage. This indicated that the amount of PCP that passes through the placental barrier on day 15 is negligible. In a separate experiment that used unlabeled PCP and was reported in the same paper, single oral doses of 60 mg/kg administered to separate groups of animals on days 8, 9, 10, 11, 12, or 13 of gestation had no statistically significant effect on the rate of resorption of the test animals as compared to controls. However, statistically significant reductions in fetal weight were reported in days 9 and 10.

TABLE 7. Effect of administration of pentachlorophenol during early or late organogenesis on the incidence of fetal resorptions and on the sex ratio of offspring[1/]

Test Material and Dose, mg/kg/day	Resorptions: Among Fetuses %	Resorptions: Among Fetuses No.	Resorptions: Among Litters %	Resorptions: Among Litters No.	Sex Ratio M	Sex Ratio F
DAYS 8-11 OF GESTATION						
Vehicle Control	7.6	13/172	53.3	8/15	53	47
Pentachlorophenol						
Commercial 34.7[2/]	45.3	105/232[3/]	94.7	18/19[3/]	55	45
Purified 30.0	91.1	163/179[3/]	100.0	16/16[3/]	62	38
DAYS 12-15 OF GESTATION						
Vehicle Control	4.2	11/259	40.9	9/22	46	54
Pentachloropnenol						
Commercial 34.7[2/]	6.1	13/213	58.8	10/17	52	48
Purified 30.0	4.5	11/244	45.0	9/20	49	51

1/ Adapted from Schwetz et al. (1974).
2/ Equivalent to 30.0 mg/kg/day purified PCP.
3/ Values significantly different from control values by the binomial expansion test, $p < 0.05$.

Hinkle (1973) reported on the fetotoxic effects of PCP in the Golden Syrian hamster. After doses of 1.25, 2.5, 5, 10, and 20 mg/kg were administered by gavage on days 6 through 10 of gestation, he reported no differences between control and test animals in these parameters: maternal body weight, fetal weight, litter size, and number of resorptions. Increased toxicity was noted at the two highest doses, but these increases were "minimal in number." The author stated that PCP was found in detectable amounts (unspecified) in the untreated animals as well as in their diet.

Fahrig (1978), in a study to be described in more detail in Section III. B., observed decreases in litter size after injection of 50 and 100 mgms PCP/kg body weight into the peritoneal cavity of pregnant mice at day ten of gestation. Control mice, on the average, produced 6.4 fetuses/dam. Litter size was reduced at the 50 mg/kg dose to 3.67 fetuses/dam, and to 3.92 fetuses/dam at the 100 mg/kg dose. PCP was administered in a 10% solution of dimethylformamide; a vehicle control was not reported. Litter size calculations included dams that had no litters.

The Schwetz et al. study cited earlier establishes that ingestion of PCP by pregnant rats during organogenesis produces lethal and toxic effects such as fetal resorption and reduced body size. Comparable effects were not observed when larger but single doses were administered to rats during organogenesis (Larsen, 1975), nor when single doses were administered to hamsters (Hinkle, 1973).

Table 8. Effect of treatment with chlorinated dibenzo-p-dioxin on maternal and fetal body measurements and the incidence of fetal resorption[1/]

Test Compound[2/]	No. litters	Maternal weight gain, g[3/] Days 6-13	Days 13-21	Days 6-21	Fetal body weight, g[4/]	Fetal crown-rump length, mm[4/]	Fetal Resorption, %[4/] Population[5/]	Litter[6/]
Control	30	36 ± 2	101 ± 6	137 ± 8	5.68 ± 0.05	44.5 ± 0.1	7(22/337)	47(14/30)
Hexachlorodibenzo-p-dioxin (4)								
0.1 ug/kg/day	19	28 ± 2	102 ± 5	130 ± 5	5.73 ± 0.04	43.8 ± 0.1	5(10/217)	47(9/19)
1 ug/kg/day	19	27 ± 3	99 ± 5	126 ± 6	5.93 ± 0.16	45.7 ± 0.5	9(20/218)	74(14/19)
10 ug/kg/day	18	22 ± 3[7/]	97 ± 5	119 ± 6	5.12 ± 0.05[7/]	42.6 ± 0.2[7/]	25(57/229)[7/]	94(17/18)[7/]
100 ug/kg/day	19	6 ± 2[7/]	13 ± 7[7/]	19 ± 9[7/]	3.65 ± 0.28[7/]	35.2 ± 0.7[7/]	85(194/227)[7/]	100(19/19)[7/]
Octachlorodibenzo-p-dioxin (5)								
100 mg/kg/day	12	32 ± 2	100 ± 8	131 ± 7	5.73 ± 0.09	43.6 ± 0.4	8(11/131)	42(5/12)
500 mg/kg/day	17	35 ± 3	115 ± 4	150 ± 5	5.69 ± 0.05	44.5 ± 0.2	5(9/199)	41(7/17)

1/ Adapted from Schwetz et al. (1973).
2/ Hexachlorodibenzo-p-dioxin sample: purity = >99%; two unspecified isomers in ratio of 89:11. All samples administered on days 6-15 of gestation as a corn oil:acetone (9:1) solution. Octachlorodibenzo-p-dioxin samples: purity = 98.86%.
3/ Mean ± standard error for various gestation times.
4/ Mean of litter means ± standard error.
5/ % (number resorptions/number implantations).
6/ % (number litters with at least one resorption/number litters).
7/ Significantly different from control by an analysis of variance and Tukey's test or the 2 x 2 contingency table (resorptions), $p < 0.05$.

b. Studies with Dioxins

Schwetz et al. (1973) administered purified hexachloro-p-dibenzo-dioxins (HCDD) (two unspecified isomers) and octachloro-p-dioxin (OCDD) by gavage to pregnant Sprague-Dawley rats on days 6 through 15 of gestation. Doses were 0.1, 1, 10, or 100 mg/kg/day HCDD and 100 or 500 mg/kg/day OCDD.

The results of these studies are shown in Table 8. For HCDD, there were statistically significant increases over controls in fetal resorptions at the 10 and 100 mg/kg/day doses, as well as decreases in fetal body weight and fetal crown-rump length. In contrast, OCDD at both dose levels (100 and 500 mg/kg/day) produced no fetal resorptions or other effects except for an increase in the incidence of subcutaneous edema at the high dose level.

The HCDD used in this experiment was reported by the authors to have a purity in excess of 99%, and to consist of two isomers in the ratio 89:11. The presence of HCDD in PCP and the low HCDD doses producing fetotoxic effects in pregnant rats strongly suggests that exposure to HCDD via exposure to PCP can cause chronic effects as defined in 40 CFR 162.11(a)(3)(ii)(B).

2. Teratology

a. Studies with PCP

Schwetz et al. (1974a) also investigated the teratogenic effects of PCP on rats. In this study they observed fetal anomalies produced by oral administration (gavage) of 5.8, 15, 34.7, and 50 mg/kg/day of commercial grade PCP, and 5, 15, and 30 mg/kg/day of purified PCP. In one experiment, they administered these amounts of PCP during days 6 through

TABLE 9. Effect of pentachlorophenol on the incidence of fetal anomalies

	Vehicle Control	Pentachlorophenol (mg/kg/day) Commercial Grade 5.8	15	34.7	50	Purified Grade 5	15	30
SOFT TISSUE ANOMALIES								
No. of Litters	33	18	16	19	13	15	18	2
		Percent of Litters Affected						
Subcutaneous Edema	18	11	50[2/]	84[2/]	62[2/]	0	78[2/]	100[2/]
Dilated Ureters	0	0	0	21[2/]	0	0	0	0
SKELETAL ANOMALIES								
No. of Litters	31	18	16	19	12	15	18	
		Percent of Litters Affected						
Skull (delayed ossification)	19	39	31	37	8	60[2/]	72[2/]	0
Lumbar Spurs	13	28	88[2/]	37[2/]	83[2/]	20	78[2/]	0
Ribs (supernumerary, lumbar, or fused)	0	0	0	95[2/]	83[2/]	0	33[2/]	100[2/]
Vertebrae (supernumerary, abnormal shape, delayed ossification, missing or unfused centers of ossification)	19	0	19	95[2/]	100[2/]	13	78[2/]	100[2/]
Sternebrae (supernumerary, delayed or unfused centers of ossification, fused or staggered)	16	11	13	89[2/]	83[2/]	33	39[2/]	100[2/]

1/ Administered po in corn oil on days 6-15 of gestation. The doses of 5.8 and 34.7 mg commercial grade PCP/kg/day are equivalent to 5 and 30 mg/kg/day purified PCP, respectively.

2/ Incidence significantly different from control (binomial expansion test, $p < 0.05$).

Modified from Schwetz et al. (1974)

TABLE 10. Effect of administration of pentachlorophenol during early or late organogenesis on the incidence of fetal anomalies

Anomalies	Days 8-11 of Gestation			Days 12-15 of Gestation		
	Pentachlorophenol [1]					
	Vehicle Control	Commercial 34.7 mg/kg/day	Purified 30 mg/kg/day	Vehicle Control	Commercial 34.7 mg/kg/day	Purified 30 mg/kg/day
SOFT TISSUE ANOMALIES						
No. of Litters	15	17	4	22	17	20
	Percent of Litters Affected					
Subcutaneous edema	7	82 [2]	100 [2]	59	35	95 [2]
SKELETAL ANOMALIES						
No. of Litters	15	18	6	22	17	20
	Percent of Litters Affected					
Skull (delayed ossification)	33	33	17	36	41	70 [2]
Ribs (supernumerary or fused)	0	100 [2]	100 [2]	0	0	0
Vertebrae (supernumerary, abnormal shape, delayed ossification, fused, missing or unfused centers of ossification)	27	100 [2]	100 [2]	9	0	0
Sternebrae (delayed or unfused centers of ossification, fused or staggered)	47	94 [2]	100 [2]	50	82 [2]	85 [2]

1/ Administered po in corn oil during early or late organogenesis. The dose of 34.7 mg/kg/day commercial grade PCP is equivalent to 30 mg/kg/day purified PCP.

2/ Incidence significantly different from control (binomial expansion test, $p < 0.05$).

Adapted from Schwetz et al. (1974)

15 of gestation; statistically significant increases in skeletal defects of the ribs, sternebrae and vertebrae were observed in both treatment groups (Table 9). In a second experiment, they gave 30.0 (purified) and 34.7 (commercial grade) mg/kg/day PCP on days 8 through 11 of gestation to one group of animals, and on days 12 through 15 to a second group; statistically significant increases in abnormal sternebrae and skulls were observed in animals treated with purified PCP and abnormal sternebrae in animals treated with commercial PCP (Table 10).

These results establish that the higher doses of PCP produce fetal anomalies in the rat. At the 30 mg/kg/day dose the effects of purified PCP were more pronounced than those of the equivalent of commercial grade PCP.

b. Studies with Dioxins

In the 1973 paper cited above, Schwetz et al. reported teratogenic effects from the dioxins found in PCP. They administered doses of 0.1, 1, 10, and 100 ug HCDD/kg/day to pregnant Sprague-Dawley rats on days 6 through 15 of gestation. They found statistically significant increases over the controls in all of the teratogenic parameters observed at 100 ug/kg. For example, cleft palate was observed in 47% (8/17) of the fetuses exposed to HCDD, compared to none (0/156) in the controls; 12% (2/17) of the treated fetuses had dilated renal pelvis compared to 0.6% (1/56) in the controls; and 31% (5/16) of the treated fetuses had abnormal vertebrae compared to 6% (9/158) in the controls. Subcutaneous edema was observed at all doses except 0.1 ug/kg/day, which was considered the no-effect dose. In contrast, OCDD did not cause teratogenicity at 100 ng/kg/day; doses of 500 ng/kg/day caused subcutaneous edema, but no other effects.

Table 11 summarizes the results of treatment with HCDD.

3. Exposure Analysis

In order to determine whether a presumption should be issued based on reproductive and fetotoxic effects, pursuant to Section 162.11(a)(3)(ii)(B), the Agency must determine whether or not an ample margin of safety exists between the levels of PCP which produce reproductive and fetotoxic effects, and the level(s) to which the population at risk (women of child-bearing age) can reasonably be anticipated to be exposed.

This section presents estimates of dietary, inhalation and dermal exposure to PCP and HCDD on a "worst case" basis. These estimates are based on the exposure of a pregnant woman in the home and at work at major PCP and Na-PCP use work sites, i.e., wood preserving plants, cooling towers, tanneries, and construction sites. This approach to PCP exposure analysis is taken because of the fetotoxic and teratogenic effects of PCP described in Section II.A.1 and II.A.2 and because of the continued movement of women into all areas of the labor force. Estimates are computed on the basis of 60 kg pregnant woman, 100% absorption via dietary and inhalation exposure, and 10% adsorption via dermal contact for both PCP and Na-PCP. There is no data available on dermal absorption of PCP by pregnant women; the 10% estimate is based on the penetration value of 7-15% of several chlorinated hydrocarbons, reported by Maibach and Feldman (1974). A normal breathing rate is defined as 1.8 m^3/hour at work, and 1.0 m^3/hour in the home.

Inhalation of water vapor containing Na-PCP is an exposure route for workers in industrial cooling towers, paper pulp mills and tanneries. Appendix I shows the calculations used to derive estimates of PCP in water vapors at these sites.

TABLE 11. Effect of treatment with hexachlorodibenzo-p-dioxin on the incidence of fetal anomalies [1]

		Incidence of Anomalies After Treatment on Days 6-15 of Gestation				
		Control	0.1 ug/kg/day	1 ug/kg/day	10 ug/kg/day	100 ug/kg/day
SOFT TISSUE ANOMALIES						
Cleft Palate	P [2]	0 (0/156)	1 (1/104)	0 (0/99)	0 (0/86)	47 (8/17) [4]
	L [3]	0 (0/28)	5 (1/19)	0 (0/19)	0 (0/18)	73 (8/11) [4]
Dilated Renal Pelvis	P	0.6 (1/156)	0 (0/104)	2 (2/99)	6 (5/86) [4]	12 (2/17) [4]
	L	4 (1/28)	0 (0/19)	5 (1/19)	17 (3/18)	18 (2/11)
Subcutaneous Edema	P	5 (8/156)	6 (6/104)	55 (54/99) [4]	100 (86/86) [4]	100 (17/17) [4]
	L	21 (6/28)	32 (6/19)	100 (19/19) [4]	100 (18/18) [4]	100 (11/11) [4]
SKELETAL ANOMALIES						
Split Vertebral Centra	P	6 (9/158)	2 (2/103)	1 (1/99)	7 (6/86)	31 (5/16) [4]
	L	19 (5/27)	5 (1/19)	6 (1/18)	29 (5/17)	56 (5/9) [4]
Split Sternebrae	P	0.6 (1/158)	1 (1/103)	2 (2/99)	2 (2/86)	31 (5/16) [4]
	L	4 (1/27)	5 (1/19)	11 (2/18)	12 (2/17)	56 (5/9) [4]
Delayed Ossification of Sternebrae	P	11 (18/158)	28 (29/103)	12 (12/99)	34 (29/86)	56 (9/16) [4]
	L	44 (12/27)	74 (14/19)	50 (9/18)	71 (12/17)	56 (5/9)

1/ Adapted from Schwetz et al. (1973).
2/ Incidence among fetal population: % (number of affected fetuses/number fetuses examined).
3/ Incidence among litters: % (number of affected litters/number litters examined).
4/ Significantly different from control by 2 x 2 contingency table, $p < 0.05$.

Exposure to HCDD is developed using the same bases as for PCP. In addition these assumptions are made: that the HCDD content of most technical PCP and Na-PCP in the market place is 4 ppm (Table 2) and that assimilation of HCDD is identical to that of PCP and Na-PCP. Using these assumptions, exposure to HCDD is equal to the exposure to PCP times the factor 4×10^{-6} (4 ppm).

a. Dietary Exposure

Although PCP has no registered uses on any food commodity, PCP residues have been measured in foodstuffs (Table 1), and therefore there is exposure to PCP in the diet. Using the data in Table 1 and the average daily intake of the commodities which have been found to contain PCP, it is possible to obtain an estimate of PCP exposure from foodstuffs. Table 12 displays these results, computed for average and maximum PCP intake per day. For a 60 kg pregnant woman, the intake would be:

0.0015 mg/day/60 = 0.025 ug/kg/day average,

or 0.0181 mg/kg/day/60 = 0.302 ug/kg/day maximum.

For HCDD, intake would be:

0.1×10^{-6} ug/kg/day average, or 1.21×10^{-6} ug/kg/day maximum.

b. Dermal Exposure

i. Homeowners

PCP is sold in retail stores for treatment of wood to prevent rot and decay in boats, masonry, fences, and other sites. Common directions call for two coats of 5% PCP in mineral oil or a 3 to 30 minute soak. Assuming that a 60 kg applicator spills enough of the solution to cover one hand (10 ml or about 10 grams), the exposure would be:

(10 gms x 0.05 x 0.1)/60 = 0.833 mg/kg/day.

For HCDD, exposure would be 3.33×10^{-6} mg/kg/day.

Table 12. Estimated Average and Maximum Daily Intake of PCP in the Diet

Commodity	Average Intake kg/day [1]	Average PCP Residue mg/kg [2]	Maximum PCP Residue mg/kg	Average PCP Intake mg/day	Maximum PCP Intake mg/day
Dairy Products	0.477	0.0005	0.01	0.0002	0.0048
Grains and Cereals	0.181	0.001	0.013	0.0002	0.0024
Root Vegetables	0.261	0.001	0.010	0.0003	0.0026
Fruits	0.261	Trace	0.011	–	0.0029
Sugars and Adjuncts	0.135	0.006	0.04	0.0008	0.0054
Totals				0.0015	0.0181

1 From Agricultural Handbook No. 62, August 1961, p. 42

2 From Table 1 (Johnson and Manske, 1977)

ii. Construction Workers

PCP-treated wood is used to construct platforms, fences, porches, and other structures. It is estimated that 6 months after treatment, PCP will be present on the wood surface at about 0.5 mg/ square foot (Koppers Chemical Company, 1978). Dermal exposure occurs if workers handle wood without wearing gloves. Assuming that the worker actually handles wood 40 times during an 8-hour period, and that the area of the hands averages 0.25 sq. ft., then exposure would be:

(40 x 0.5 mg/sq.ft. x 0.25 sq.ft./operation x 0.1)/60 = 8.3 ug/kg/day.

For HCDD, exposure would be 33.2×10^{-6} ug/kg/day.

iii. Cooling Tower Workers

Na-PCP is used to control the growth of algae, bacteria and fungi in water cooling systems. Formulations typically contain 80% Na-PCP, and are added to the system at concentrations of 60 ppm for initial cleaning, then reduced to 30 ppm to maintain control. A worker could be exposed dermally to 100 ml of cooling water containing 80% x 60 ppm formulation, or 48 ppm (48 mg/liter), of Na-PCP. (Shamaiengar, 1978). Exposure would then be:

(48 mg/l x 0.1 liter x 0.1)/60 kg = 0.008 mg/kg/day.

During routine maintenance, this would drop to 0.004 mg Na-PCP/kg/day. For HCDD, exposure would be 0.032×10^{-6} mg/kg/day for initial cleaning, and 0.016×10^{-6} mg/kg/day during routine maintenance.

iv. Paper/Pulp Mill Workers

To control slime, algae and bacteria, Na-PCP is added to the paper-pulp slurry during the manufacturing process. A typical product contains 45% active ingredients of which 25% is Na-PCP. The concentration of the product used is 450 ppm, of which 113 ppm (113 mg/l) is Na-PCP.

During the process, samples of pulp slurry are taken periodically. If a worker takes samples hourly (8 times/day) and wets one hand with 10 ml of the slurry (International Paper Company, 1978), the exposure would be:

(8 x 0.01 liter x 113 mg/l x 0.1)/60 kg =

0.015 mg PCP/kg/day

For HCDD, exposure would be 0.060×10^{-6} mg/kg/day.

v. Tannery Workers

A typical product used to control growth of slime and fungi contains 12.9% PCP. With a use concentration of 1:4,000, the solution would contain 1 gm/4,000 gm water or 250 ppm of product. If a worker were exposed during normal operations, she could dermally receive about 1400 ml of solution daily on her exposed arms and neck (Shamaiengar, 1978). Exposure here would be:

(1.4 liter x 250 mg/l x 0.129 x 0.1)/60 kg =

0.075 mg Na-PCP/kg/day

For HCDD, exposure would be 0.3×10^{-6} mg/kg/day.

vi. Workers in Pressure-Treatment Plants

Although data is not available on dermal exposure at these sites, it can be assumed that this exposure is at least equal to exposure at construction sites. Freshly treated wood can be expected to contain more PCP on its surface than wood used at construction sites, the latter having been subjected to weathering, i.e., leaching, vaporization, etc., in the interval between pressure treatment at the plant and use at construction sites. Therefore, dermal exposure at pressure treatment plants is taken to be at least the same as that at construction sites.

Table 13. [1/] Pentachlorophenol Concentrations in Air at a Pressure Treatment Plant.
Koppers Company, Incorporated
North Little Rock, Arkansas
February 24, 1976

Sample No.	Operation	Sampling Period (min)	*Type of Sample	**Concentrations mg/M^3
A1	Hand Mix Oper.	112	GA	0.004
A3	Hand Mix Oper.	112	GA	0.004
A5	Sampling Man		EQUIPMENT FAILURE - VOID	
A6	Asst. Treater	442	P	0.001
A7	Laborer	445	P	0.001
A8	Laborer	438	P	0.006
A9	Treating Oper.	437	P	0.001
A10	Locomotive Oper.	339	P	<0.001
A2/12	Hand Mixer	110	P	0.008
A4/14	Hand Mix Oper.	112	GA	0.003

American Conference on Governmental Industrial Hygienists,
Threshold Limit Value Committee 0.5

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* GA - General Area; P - Personal

** mg/M^3 = milligrams of substance per cubic meter of air sampled

1/ Source: Health Hazard Evaluation Determination Report No1. 75-117-371, DHEW, Center for Disease Control, National Institute for Occupational Safety and Health, Cincinnati, Ohio. March, 1977.

Table 11 summarizes the results of treatment with HCDD.

3. Exposure Analysis

In order to determine whether a presumption should be issued based on reproductive and fetotoxic effects, pursuant to Section 162.11(a)(3)(ii)(B), the Agency must determine whether or not an ample margin of safety exists between the levels of PCP which produce reproductive and fetotoxic effects, and the level(s) to which the population at risk (women of child-bearing age) can reasonably be anticipated to be exposed.

This section presents estimates of dietary, inhalation and dermal exposure to PCP and HCDD on a "worst case" basis. These estimates are based on the exposure of a pregnant woman in the home and at work at major PCP and Na-PCP use work sites, i.e., wood preserving plants, cooling towers, tanneries, and construction sites. This approach to PCP exposure analysis is taken because of the fetotoxic and teratogenic effects of PCP described in Section II.A.1 and II.A.2 and because of the continued movement of women into all areas of the labor force. Estimates are computed on the basis of 60 kg pregnant woman, 100% absorption via dietary and inhalation exposure, and 10% adsorption via dermal contact for both PCP and Na-PCP. There is no data available on dermal absorption of PCP by pregnant women; the 10% estimate is based on the penetration value of 7-15% of several chlorinated hydrocarbons, reported by Maibach and Feldman (1974). A normal breathing rate is defined as 1.8 m^3/hour at work, and 1.0 m^3/hour in the home.

Inhalation of water vapor containing Na-PCP is an exposure route for workers in industrial cooling towers, paper pulp mills and tanneries. Appendix I shows the calculations used to derive estimates of PCP in water vapors at these sites.

the daily exposure of a 60 kg worker at a moderate breathing rate (1.8 m^3/hr) would be:

$$(8\ ug/m^3 \times 1.8\ m^3/hr \times 8\ hours)/60 = 1.92\ ug/kg/day.$$

For HCDD, exposure would be 7.68×10^{-6} ug/kg/day.

In the absence of data on PCP concentrations in the air at construction sites, these values for PCP and HCDD are taken as worst case estimates at these sites.

iii. Cooling Towers

Some persons working near cooling towers can be exposed by inhalation of vapors and drift containing Na- PCP. The relative amounts of Na-PCP and water evaporating from the cooling water is a function of their molecular weights and vapor pressures, and is estimated to be 0.02 ug PCP/m^3 (Appendix 1). Exposure therefore would be:

$$(0.02\ ug/m^3 \times 1.8\ m^3/hr \times 8\ hr)/60 = 0.004\ ug\ Na\text{-}PCP/kg/day.$$

For HCDD, exposure would be 0.016×10^{-6} ug Na-PCP/kg/day.

Drift is the entrained water carried from the tower by the exhaust air. In an average cooling tower, approximately 1% of the cooling fluid is lost to drift. For a properly functioning cooling tower, the ratio of water to air weight should be unity in order to insure maximum heat exchange. At an average cooling rate of 300 gallons/minute, this weight of water is equivalent to the weight of 880 m^3 of air. The drift (3 gallons or 11.355 liters), distributed in this volume of air, gives an Na-PCP concentration of:

$$(11.355\ l \times 48\ mg/l)/880\ m^3 = 0.6\ mg\ Na\text{-}PCP/m^3.$$

Exposure would then be:

$$(0.6\ mg/m^3 \times 1.8\ m^3/hr \times 8\ hrs)/60 = 0.15\ mg\ Na\text{-}PCP/kg/day$$

For HCDD, exposure would be 0.60×10^{-6} mg/kg/day.

iv. Paper/Pulp Mills

Inhalation exposure is based on a concentration of 0.047 ug Na-PCP/m^3 (see Appendix 1), which computes to:

$$(0.047\ ug/m^3 \times 1.8\ m^3/hr \times 8\ hrs)/60 = 0.01\ ug\ Na\text{-}PCP/kg/day.$$

For HCDD, exposure would be 0.04×10^{-6} ug/kg/day.

v. Tanneries

Inhalation exposure is based on a concentration of 0.013 ug/m^3 (see Appendix 1) so that exposure is:

$$(0.013\ ug/m^3 \times 1.8\ m^3/hr \times 8\ hrs)/60\ kg = 0.003\ ug\ Na\text{-}PCP/kg/day$$

For HCDD, exposure would be 0.012×10^{-6} ug/kg/day.

4. Conclusions

Table 14 summarizes the exposure estimates for PCP and HCDD developed in Section II.A.3. Table 15 gives the ratios of the no effect dose level to total exposure to PCP and HCDD of the major use sites.

The foregoing discussion establishes that PCP and possibly its HCDD contaminants cause teratogenic and fetotoxic effects in test animals. The adverse effects observed among the injured fetuses include distorted sex ratios, increased incidences of resorbed embryos, skeletal anomalies and subcutaneous edema. The no-effect levels are 5.8 mg/kg/day for PCP and 1 ug/kg/day for HCDD. In addition, PCP contains other dioxin contaminants which have not been fully characterized toxicologically, and which vary quantitatively from batch to batch.

TABLE 14. Estimates of Human Exposure to PCP and HCDD [1/]

Site	PCP ug/kg/day				HCDD $\times 10^{-6}$ ug/kg/day			
	Dietary	Dermal	Inhalation	Total	Dietary	Dermal	Inhalation	Total
Home	0.025 av	833	53.3	886.32	0.1 av	3330	213.3	3543.40
	0.302 max			886.60	1.21 max			3544.51
Construction Sites	0.025 av	8.33	1.92	10.28	0.1 av	33.2	7.68	40.98
	0.302 max			10.55	1.21 max			42.09
Cooling Towers	0.025 av	8 [2/]	0.004	158.03 [5/]	0.1 av	32 [2/]	0.016	632.02 [5/]
	0.302 max	4 [3/]	150 [4/]	154.31 [5/]	1.21 max	16 [3/]	600 [4/]	617.23 [5/]
Paper Pulp Mills	0.025 av	15	0.01	15.04	0.1 av	60	0.04	60.14
	0.302 max			15.31	1.21 max			61.25
Tanneries	0.025 av	75	0.003	75.03	0.1 av	300	0.012	300.11
	0.302 max			75.31	1.21 max			301.22
Pressure Treatment Plants	0.025 av	8.33	1.92	10.28	0.1 av	33.2	7.68	40.98
	0.302 max			10.55	1.21 max			42.09

1/ Based on a 60 kg pregnant woman
2/ Initial Treatment
3/ Routine Treatment
4/ Cooling Tower Drift
5/ Inhalation of cooling tower drift + PCP vapors + dermal and dietary exposure

Data available to the Agency indicate that the physical and chemical properties of PCP, and its commercial uses and distributions lead to substantial human and environmental exposure to this pesticide. In this regard, several factors are significant:

- Current PCP production approximates 50,000,000 pounds per year and production is expected to increase to 80,000,000 pounds per year in the near future (Josephson, 1977). If PCP is equally distributed among the total U.S. population, assuming 60 kg body weight for each individual exposed, the theoretical exposure potential for each person in the general population is 5 mg/kg/day.

- Although PCP is registered mainly for non-agricultural uses, the chemical is widely distributed in the environment and in human tissues. It is present in the blood and urine of persons not known to be exposed to the pesticide. It has been found in the drinking water of 80% of 108 cities sampled, in rainwater in Hawaii, and at low levels in food commodities such as sugars, root vegetables, and grain and cereal products (Table 1).

- PCP is registered for home and industrial uses. As a result, homeowners, workers using PCP in leather, wood, and paper processing plants, and others using products containing PCP are exposed to the chemical. The Agency estimates that user exposure levels range from approximately 0.9 mg/kg/day for home uses to less than 0.01 mg/kg/day at construction sites (Table 14).

- Homes, tanneries, wood pressure treatment plants, paper pulp mills, and cooling towers are major use sites presenting significant exposure potential, particularly since PCP has been shown to be absorbed through the skin. These uses may involve dermal as well as inhalation contact with the pesticide. Further, since 80% of the annual PCP production is used for wood preservatives, substantial numbers of people who spray, dip, and pressure-treat wood at plants may be exposed to the pesticide. In addition, workers using PCP-treated wood at construction sites can be exposed.

The Agency's pre-RPAR review of pesticide exposure is based on data about the chemical under review, other pesticides, general assumptions, and other relevant information. The Agency recognizes that the exposure data available is sketchy and incomplete. The Agency supplemented this data with reasonable worst case assumptions, which by

Table 15. Ratio of No Effect Dose [1] to Total Exposure Estimates [2] for PCP and HCDD

Site	PCP	HCDD
Home	6.55	282
Construction Sites	557	24073
Cooling Towers	37.2	1602
Paper Pulp Mills	382	16477
Tanneries	77.2	3327
Pressure Treatment Plants	557	24073

1) No Effect Doses are 5.8 mg/ug/day for PCP and 1 ug/kg/day for HCDD.

2) Averages of Total Exposures from Table 14.

their nature are conservative. Nevertheless, uncertainty remains as to the validity of the preliminary exposure estimates derived from the data and the assumptions. Therefore, in determining whether an adequate margin of safety exists, the Agency considers it prudent public policy to utilize greater safety factors for PCP than it would in situations where it had greater confidence in the underlying exposure data and assumptions.

40 CFR 162.11(a)(3)(ii)(B) provides that a rebuttable presumption shall arise if a pesticide produces any "chronic or delayed toxic effect in test animals at any dosage up to a level. . . which is substantially higher than that to which humans can reasonably be anticipated to be

exposed, taking into account ample margins of safety . . . ." PCP produces teratogenic and fetotoxic effects in test animals, and workers using PCP in connection with tannery, home, pressure treatment, paper pulp processing, cooling tower and all other uses may be exposed to PCP, with levels at major use sites ranging from 0.01 to 0.9 mg/kg/day. The Agency has concluded that the difference between these human exposure levels and the no-effect level in test animals may not constitute an ample margin of safety. Accordingly, the Agency has concluded that all PCP registrations exceed this risk criterion.

The Agency invites registrants to provide data and information to confirm, refine, or rebut the information upon which the exposure estimates are based. The Agency will use the new data to determine whether or not the presumption has been rebutted and in assessing the risks which PCP uses may present to health and the environment.

III. Studies Relating to Possible Adverse Effects

This section describes studies on PCP which do not meet the criteria outlined in 40 CFR Section 162.11. It is intended to provide information on other toxic effects of PCP, including those resulting from misuse. With the exception of the discussion of oncogenicity and mutagenicity, the studies presented were chosen as examples of these effects; other reports are available in the scientific literature.

A. Oncogenic Effects in Test Animals

In 1969, Innes et al. administered PCP (Dowicide 7) by gavage to mice at doses of 46.4 mg/kg on days 7-28 of age and at 130 ppm (17 mg/kg/day) in the diet for the following 17 months. They reported that this regime caused no significant increase in tumor incidence in test animals as compared to the control animals. In 1976 Schwetz et al. in an

unpublished study submitted to EPA, reported that dietary regimes of Dowicide EC-7 at 1, 3, 10, and 30 mg/kg/day for 22 and 24 months for male and female rats, respectively, did not increase tumor incidence over control animals. The composition of the PCP products used in these studies was similar to those shown in Table 2.

Boutwell and Bosch (1959) tested a series of phenolic chemicals for their ability to induce skin tumors in mice. In these experiments a simple application of 0.3% dimethylbenzanthracene (DMBA) in benzene was first applied to shaved back skin as an initiator. Subsequently, 20% PCP, the promoter, was applied in benzene to the back skin of each test animal twice weekly for 15 weeks. In this short-term study the investigators reported a survival rate of 82.9% (29/35) in the test animals and a rate of 75% (15/20) in control animals treated with benzene only after the initial exposure to DMBA. The average number of papillomas per survivor in the test group was 0.04, slightly less than the 0.07 observed in the controls; the percent of survivors with papillomas was 4.0% as compared to 7% in the control group.

These papers have been reviewed by the EPA Carcinogen Assessment Group and were found to be negative with respect to oncogenic effects of PCP (Albert, 1978).

B. Mutagenic Effects

Fahrig (1974) induced mitotic gene conversion at the ade 8 and trp 5 loci of Saccharomyces cerevisiae. Using a concentration of 0.19 millimoles (50 ppm) PCP in 1% dimethyl sulfoxide for 6 hours, he found 6.62 ade 2 convertants per 10^5 survivors

(control: 0.45 per 10^5 survivors) and 4.31 trp 5 convertants per 10^5 survivors (control: 0.36 per 10^5 survivors). Fahrig did not report on the statistical reliability of these data.

In a later report, Fahrig (1978) studied the mutagenic properties of certain chlorophenols, including PCP, in yeast and mice ("mammalian spot test"). He used S. cerevisiae MP-1, a diploid multipurpose strain for screening intergenic recombination (mitotic crossing over), intragenic recombination (mitotic gene conversion) and forward mutation. He incubated cell suspensions at 25 C with 400 mg/liter PCP for 3.5 hours. He spread aliquots of the suspensions, approximately 3×10^7 cells, on solid nutrient-deficient (intragenic recombinants and mutants) or complete (intergenic recombinants) media and incubated at 25 C for 4 and 8 days respectively. Fahrig reported statistically significant ($p<0.001$) increases is foward mutation and mitotic gene conversion. Table 16 contains the results of this experiment.

In the mammalian spot test, he mated females of inbred C57BL/6JHan strain mice to males of rotation bred T-stock. The progeny of this combination are susceptible to color spots in the adult coat if a mutagenic agent is injected into the peritoneal cavity of the dam during the tenth day of fetal development. The incidence of color spots in untreated mice bred as described was 0.1%. A dosage of 50 mg/kg PCP to pregnant mice produced color spots in 0.6% of the progeny; a dosage with 100 mg/kg resulted in a 1.3% incidence of spots. Fahrig did not give the statistical significance of these data.

TABLE 16. Induction of forward mutation, intragenic and intergenic recombination in S. cerevisiae MP-1 in vitro with pentachlorophenol at a treatment time of 3.5 hours [1]

	Experiment				Control		
Genetic Alteration	# of Experiments	Concentration (mg/l)	Survival [2]	Colonies [3] of Genetically Altered Cells Per Survivor	# of Experiments	Colonies [3] of Genetically Altered Cells Per Survivor	Significance
Mutation	4	400	59 ± 8 (10813)	2.00 ± 0.22 (216)	4	0.61 ± 0.07 (113)	< 0.001
Intergen. Rec.				0.47 ± 0.14 (50)		0.49 ± 0.08 (91)	> 0.8
Intragen. Rec.				5.64 ± 0.45 (542)		2.93 ± 0.10 (542)	< 0.001

1. Adapted from Fahrig et al. (1977)

2. Control Survival = 100%

3. Mutants, Convertants (Intragenic Recombination)/10^7 survivors, Recombinants (Intergenic Recombination)/10^2 survivors

The numbers in parenthesis give the actual numbers of colonies counted.

A geneticist and statistician assigned to EPA have reviewed the Fahrig et al. paper (1978). In the opinion of the geneticist, this study does not provide evidence of the mutagenicity of PCP. This opinion was based on the fact that the experiment has certain shortcomings. Among these are absence of information on the controls as well as on maternal toxicity (Mauer, 1978). Only two animals were affected at each dose level; the EPA statistician has found that this response is not statistically significant at the 0.05 level (Rossi, 1978) using the chi-square test.

For these reasons, the reviewers did not consider the mammalian spot test to be sufficient evidence of mutagenicity, and the criteria of multitest evidence of 40 CFR Section 162.11 (a)(3)(ii)(A) are not met.

It should be noted that mutagenicity tests on PCP were negative with the Ames test (Andersen et al. 1972), the host-mediated assay (Buselmaier et al. 1973), and the sex-linked recessive lethal test on Drosophila (Vogel and Chandler, 1974).

C. Chloracne

Chloracne ("chlorine acne") is a human skin disorder characterized by distention of hair follicles by horny cutaneous tissue, and by a decrease or absence of the sebaceous glands in the area of infection. This condition has been observed in workers in PCP manufacturing plants and wood preserving operations (Baader and Bauer, 1951). Chloracne can arise in these workers weeks or months after exposure, and at first was

thought to be due to PCP itself. However, using the rabbit ear test, Jones et al. showed in 1962 that the acnegenic agent in the herbicide 2,4,5-T was its contaminant TCDD. Further study of the acnegenic effects of pure and commercial grade PCP identified its dioxin contaminants as the causative agent (Johnson et al., 1973).

D. Hepatic Effects

Goldstein et al. (1976) fed pure and technical grade PCP to female Sherman rats for 8 months at dosages of 20, 100, and 500 ppm. Technical PCP produced hepatic porphyria at 100 and 500 ppm, and all doses caused increased hepatic aryl hydrocarbon hydroxylase activity, glucuronyl transferase activity, liver weight, cytochrome P-450, and microsomal heme. N-demethylase activity was not affected. In contrast, pure PCP had no significant effect on these parameters, except for increasing glucuronyl transferase at 500 ppm. Both PCP types decreased the rate of body weight gain at 500 ppm. The technical PCP used contained 8 ppm hexa-, 520 ppm hepta-, and 1380 ppm octachlorodibenzodioxin. Pure PCP contained less than 0.1 ppm each of these contaminants.

Kimbrough and Linder (1975) fed 1000 ppm "relatively pure" PCP and technical PCP to male rats for 3 months. All of the animals were reported to have statistically significant enlargement of the liver when compared to the controls. Histological examination of the liver using the light microscope showed that the rats fed technical PCP had foamy cytoplasm or pronounced vacuolation of the hepatocytes, inclusions, single hepatocellular necrosis, interstitial fibrosis, and a brown pigment in macrophages and Kupffer cells.

Examination with the electron microscope showed an increase in smooth endoplasmic reticulum, many lipid vacuoles, and atypical mitochondria. Livers of rats fed the relatively pure PCP showed enlarged hepatocytes, and many cells contained inclusions in their cytoplasm. Electron microscope studies showed a slight increase in smooth endoplasmic reticulum, atypical mitochondria, and some lipid vacuoles. Livers of control rats were normal. Kimbrough and Linder did not report the amount of dioxin contaminants in the pure and technical PCP which was used in the study.

In 1976, Schwetz et al. observed discoloration of the liver in female rats fed 10 or 30 mg/kg/day PCP. Histological examination revealed pigmented material in the hepatocytes surrounding the central veins with smaller amounts present in the reticuloendothelial cells. Hepatocytes in the centrilobular region also contained pigmented material but were not necrotic. The PCP used in this study was representative of Dow's product and contained approximately 30 ppm total dioxins.

E. Toxicity to Humans

There are reports of deaths caused by industrial or accidental exposure to PCP. In most cases exposure occurred by dermal contact, either to PCP in solution or to materials treated with PCP. Bergner et al. (1965) described five cases of PCP intoxication in Winnipeg in 1963. The one fatality involved a worker in a wood treating plant who, using his bare hands, dipped wood into a vat containing a solution of 4.1% PCP in petroleum solvent. A similar incident had previously been reported in 1952 in France by Truhaut et al. In this case two workers were immersing wooden planks in a 3% aqueous solution of a

mixture of 80% Na-PCP and 20% sodium tetrachlorophenate. The workers plunged their hands and forearms into the liquid bath to remove the planks. After 6 days of this work, both men became ill and ultimately died. In all three cases, the initial symptoms of intoxication were profuse sweating and elevated temperatures.

These same symptoms were observed in an incident involving nine neonates in a nursery for newborn infants in St. Louis. Robson et al. (1969) reported these and other symptoms in these infants, two of whom died. Other symptoms reported were increased pulse rate (> 150/minute), hepatomegaly, and respiratory distress. Of the seven survivors, six received exchange blood transfusions, and one received only supportive therapy. Exposure was proven to be via percutaneous absorption of Na-PCP which had been mistakenly used to launder the infants' diapers and bed linens.

In a followup paper, Armstrong et al. (1969) measured PCP levels in samples of these diapers and linens, in autopsy tissues, and in the serum of a surviving infant. They detected the following PCP residues: six diapers, 2.64 to 17.20 mg/100 g; two shirts, 7.38 and 7.90 mg/100 g; two shirt backs, 22.40 and 195 mg/100 g; two crib pads, 4.89 and 176.70 mg/100 g; one mattress pad, 14 mg/100 g; one pillow case, 6.25 mg/100 g; and two muslins, 1.15 and 2.80 mg/100 g. In autopsy tissues, PCP measurements were: kidney, 2.8 mg/100 g; adrenal, 2.7 mg/100 g; heart and blood vessel, 2.1 mg/100 g; fat, 3.4 mg/100 g; and connective tissue, 2.7 mg/100 g. An infant who survived through exchange transfusion, had PCP levels of 11.8 mg/100 ml before, 6.5 mg/100 ml during, and 0.2 mg/ml after the transfusion.

F. Toxicity to Animals

Toxicological data on PCP are complicated by the presence of varying quantities of tetrachlorophenols, dioxins, and furans in the technical material. Table 17 summarizes the available toxicity data for PCP on various mammalian species.

There are reports of fatalities to farm animals following exposure to PCP. Spencer, in 1957, described the deaths of two Hereford cows within 24 hours after drinking a 5% solution of PCP in kerosene. Blevins (1965) reported on the death of a litter of ten pigs kept in a farrowing house whose floor had been overly treated with PCP dissolved in used crankcase oil. They theorized that the pigs were triply exposed by direct adsorption through the skin, from the milk of the gilt, and through inhalation of PCP "aerosol." The gilt recovered when it was moved outside the farrowing house.

Adelman et al. (1976) established the LC-50's for Na-PCP as 0.21 mg/liter for fathead minnows, and 0.22 mg/liter for goldfish. Holmberg et al. (1972) found that the eel (Anguilla anguilla L) did not survive 5 days of exposure to 0.1 ppm Na-PCP in fresh water. Hanes et al. (1968) found that the LC-50 for coho salmon (Onchorynchus kisutch) is 0.15 mg/liter of K-PCP.

The Public Health Service of DHEW has reports on numerous fish kills from 1964 to 1970 that were caused by effluents from wood treatment plant washing into fresh water. Since 1970, the Pesticide Episode Review System (PERS) has recorded only four incidents involving fish kills. This indicates either that wood preserving practices with effluents have become more stringent, or that incidents are not being reported to PERS.

TABLE 17. Toxicity of pentachlorophenol to mammals [1/]

Organism (Sex, Strain)	Route of Administration	Dose or Concentration	Reference
Wistar Rats	Oral (0.5% in Stanoflex fuel oil)	27.3 mg/kg	Deichmann et al. (1942)
	Subcutaneous (2% in water)	66.3 mg/kg	Deichmann et al. (1942)
	Oral (1% in olive oil)	77.9 mg/kg	Deichmann et al. (1942)
	Oral (2% in water)	210.6 mg/kg	Deichmann et al. (1942)
Albino Rats (M)	Intraperitoneal	56 mg/kg	Furquharson et al. (1942)
Albino Sprague-Dawley Rats (M,F)	Intraperitoneal 8 °C	620 mg/kg (LD-100)	Keplinger et al. (1969)
	Intraperitoneal 26 °C	420 mg/kg (LD-100)	Keplinger et al. (1969)
	Intraperitoneal 36 °C	120 mg/kg (LD-100)	Keplinger et al. (1969)
Albino Wistar Rats (F)	Percutaneous (dermal) 40% w/v in glycerol formaldehyde	149 mg/kg	Noakes and Sanderson (1969)
Sherman Rats (M,F)	Oral (in peanut oil)	146 mg/kg	Gaines (1969)
(F)	Oral "	175 mg/kg	Gaines (1969)
(M)	Dermal "	320 mg/kg	Gaines (1969)
(F)	Dermal "	330 mg/kg	Gaines (1969)

TABLE 17. Toxicity of pentachlorophenol to mammals 1/ (Continued)

Organism (Sex, Strain)	Route of Administration	Dose or Concentration	Reference
Sprague-Dawley Rats (M)	Inhalation 80 ml/min	11.7 mg/kg	Hoben et al (1976)
White Mice	Intraperitoneal	29 mg/kg	Pleskova and Bencze (1959)
	Subcutaneous	63 mg/kg	Pleskova and Bencze (1959)
	Oral	130 mg/kg	Pleskova and Bencze (1959)
	Percutaneous	261 mg/kg	Pleskova and Bencze (1959)
Rabbits	Cutaneous	512.5 mg/kg (LD-100)	McCavack et al. (1941)
	Subcutaneous	275.0 mg/kg (LD-100)	McCavack et al. (1941)
	Intraperitoneal	135.5 mg/kg (LD-100)	McCavack et al. (1941)
	Oral	550.0 mg/kg (LD-100)	McCavack et al. (1941)
Sheep	Oral (5% PCP in sawdust)	120 mg/kg (LD-100)	Harrison (1959)
Calves	Oral (5% PCP in sawdust)	140 mg/kg (LD-100)	Harrison (1959)

1/ All values represent the LD_{50} unless otherwise noted.

G. Effects of Tetrachlorophenol

As stated previously, the presence of tetrachlorophenols in all PCP products raises the possibility that adverse effects of PCP could be attributed to these compounds. The toxicological properties of tetrachlorophenols have not been studied extensively. The "Registry of Toxic Effects of Chemical Substances," published by the National Institute of Occupational Safety and Health, DHEW, lists the oral LD_{50} for the rat as 140 mg/kg, both for tetrachlorophenol (presumably mixed isomers) and for 2,3,4,6-tetrachlorophenol.

Schwetz et al. (1974a) evaluated the effects of purified and commercial grade tetrachlorophenol on rat embryonal and fetal development. They fed pregnant Sprague-Dawley rats 10 and 30 mg/kg/day on days 6-15 inclusive of gestation. These doses had no effect on resorptions, fetal body weight, or fetal crown-rump length. At 30 mg/kg/day, there were statistically significant increases in delayed ossification of the skull bones for both tetrachlorophenol types. Schwetz et al. observed subcutaneous edema at 10 mg/kg/day with both compounds, but not with the 30 mg/kg/day doses. Since this effect was not dose-related, the authors speculate that it may have been due to chance.

Appendix 1

Na-PCP Content in Water Vapor

Na-PCP is registered for use as a slimicide in cooling towers, paper pulp mills and tanneries. In these uses, Na-PCP is normally found in water at concentrations of 48, 113 and 32 mg/liter respectively. The humidity in the work areas at these sites can approach 100%, due to vaporization from the large volumes of water required. Na-PCP can also vaporize from solution, and the amounts of Na-PCP in the vapor can be estimated. In the following calculations, it is assumed that the Na-PCP/water solution is an ideal binary system. The following constants will be required:

At 100% humidity and 20°C,

weight of water vapor = 17.3 gms/m^3

vapor pressure of water = 17.54 mm

Vapor pressure of Na-PCP (assuming same volatility as PCP) = 4.7×10^{-4} mm

Molecular weight of water = 18

Molecular weight of Na-PCP = 289

In 1 liter of solution, at 48 mg/l Na-PCP, there are approximately $.048/289 = 1.7 \times 10^{-4}$ moles Na-PCP and 1000 gms/18 = 55.5 moles water. According to Raoult's Law, the partial pressure (p°) of each component in a binary system equals the mole fraction M_f (moles of component/total moles present) multiplied by the vapor pressure of the component (VP_c):

$$p^\circ = M_f \times VP_c$$

Then:

$$P^{\circ}\ \text{Na-PCP} = (1.7 \times 10^{-4}/55.5)\ (4.7 \times 10^{-4}) = 1.4 \times 10^{-9}\ \text{mm}$$

$$P^{\circ}\ \text{Water} = (55.5/55.5)\ (17.54) = 17.54\ \text{mm}$$

The mole fraction of Na-PCP vapor in the air can be calculated using the formula:

$$\text{mole fraction Na-PCP} = \frac{p^{\circ}\ \text{Na-PCP}}{p^{\circ}\ \text{Water} + p^{\circ}\ \text{Na-PCP}}$$

$$= \frac{1.4 \times 10^{-9}}{17.54 + 1.4 \times 10^{-9}}$$

or $\frac{\text{moles Na-PCP in vapor}}{\text{moles water in vapor}} = 8 \times 10^{-11}$

The moles of water on the vapor is

$$\frac{17.3\ \text{gms/m}^3}{18} = 0.96\ \text{moles water/m}^3$$

Therefore

$$\text{moles Na-PCP} = 0.96\ \text{moles water/m}^3 \times 8 \times 10^{-11}$$

$$= 7.7 \times 10^{-11}\ \text{moles/m}^3$$

and

$$\text{Grams Na-PCP} = 7.7 \times 10^{-11}\ \text{moles/m}^3 \times 298$$

$$= 0.02 \times 10^{-3}\ \text{ug/m}^3$$

These same calculations apply for vapors in pulp mills and tanneries, and using the concentrations of Na-PCP specified earlier, these calculate to:

Pulp mills: Na-PCP = 0.047 ug/m^3

Tanneries: Na-PCP = 0.013 ug/m^3

List of References [1/]

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