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Pesticides

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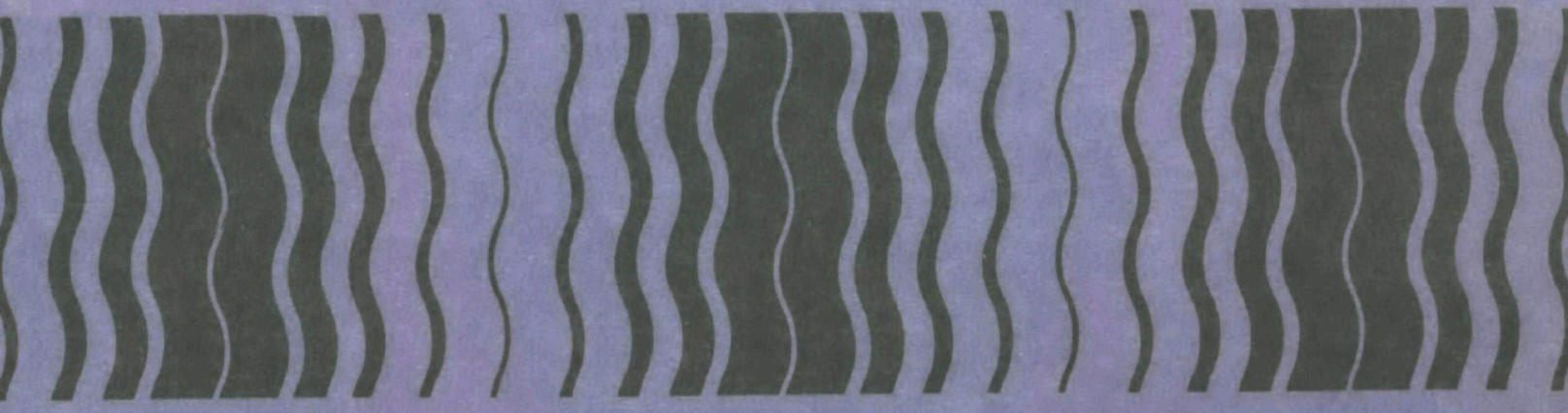
Pentachlorophenol
(Non-Wood Uses)
Special Review Position Document 2/3



PENTACHLOROPHENOL

NON-WOOD USES

POSITION DOCUMENT 2/3

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EXECUTIVE SUMMARY

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Non-Wood Uses

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On October 18, 1978, EPA issued Notices of Rebuttable Presumption Against Registration and Reregistration (RPAR) of pesticide products containing pentachlorophenol (43 FR 48443). The presumption against pentachlorophenol was based on validated studies indicating its fetotoxicity.

In January, 1981, a Position Document 2/3 was issued that addressed the risks and benefits and proposed regulatory action of the wood preservative uses of pentachlorophenol, as well as the inorganic arsenical compounds, creosote, coal tar, and coal tar neutral oils (46 FR 13020).

Studies indicating the oncogenicity of the pentachlorophenol contaminants, chlorinated dibenzo-p-dioxins (HxCDD) and hexachlorobenzene (HCB), were also detailed thereby adding the presumption of oncogenicity for pentachlorophenol.

In July, 1984 a Position Document 4 (PD-4) was issued on the wood preservative uses of pentachlorophenol, the inorganic arsenical compounds, creosote, coal tar, and coal tar neutral oils. It set forth the Agency's final position on the regulation and use of these chemicals as wood preservatives.

This document addresses the risks and benefits of the non-wood uses of pentachlorophenol and its sodium and potassium salts.

The non-wood uses of pentachlorophenol can be divided into these general categories: herbicides, antimicrobial agents, disinfectants, mossicides, and defoliants. Pentachlorophenol is registered for use on the following sites as a non-specific, non-residual contact herbicide: greenhouses, ornamental lawns, rights-of-way, commercial and industrial non-crop areas, domestic dwellings, medical facilities, schools, golf courses, wasteland areas, aquatic areas, and drainage ditch banks.

Uses of pentachlorophenol as an antimicrobial agent to control bacterial and fungal growth include: working solutions (oil well flood waters, evaporative condenser cooling waters, cooling tower waters, air washers); finished product preservatives

(adhesives and sealants, latex paints, rubber articles, defoaming agents, paper coatings, polyvinyl chloride emulsions in food related products, zinc-silicone dioxide matrix coatings in reusable bulk food storage containers, and water-based gasketing compounds for food applications, photographic developing solutions, cements in food can ends and seams, feathers); working fluids and process chemicals in the textile industry; pulp and paper mill solutions and products; leather tannery solutions and products; and marine anti-fouling agents

Pentachlorophenol is also used as a disinfectant in mushroom houses and a mildewicide in a variety of construction materials.

As a mossicide, pentachlorophenol is used to control moss on lawns and roofs.

Pentachlorophenol is also registered for use to treat soil to control subterranean termites. This use is not considered in this document. The subterranean termite control use of pentachlorophenol is under review by the Agency along with other chemicals registered for this use.

In reaching a proposed regulatory decision regarding the non-wood uses of pentachlorophenol, the Agency evaluated rebuttal comments submitted in response to the PD-1 and public comments submitted in response to the PD-2/3 published on the wood uses of these chemicals.

The exposure data indicate that applicators of products containing pentachlorophenol used for non-wood uses are subject to primarily dermal exposure to hands. Some uses would result in inhalation exposure as well.

Three of the currently registered uses have been identified as food uses and require the establishment of tolerances under Section 408 of the Federal Food, Drug and Cosmetic Act. These uses are for mushroom houses, canning/sealing gaskets, and on seed crops. There exists a potential for dietary exposure as a result of these uses. Additionally, the use of pentachlorophenol in the leather tanning industry could result in dietary exposure. Fleshings from penta-treated hides are sold to renderers who then in turn sell the fleshings for incorporation into animal/poultry feed. The use of this feed has resulted in penta residues being found in eggs and poultry.

The Agency has determined that the use of products containing pentachlorophenol and its sodium and potassium salts for non-wood uses poses a risk of fetotoxicity and, due to the presence of the contaminants HxCDD and HCB, the risk of oncogenicity to applicators. There are also potential risks to the general population as a result of the uses that could result in penta-residues in foods as described above.

An analysis of the benefits associated with each registered

use concludes that for the majority of uses viable, effective alternatives are available and in use. Actual usage data are not available for several uses.

The following regulatory options were considered by the Agency in reaching the proposed regulatory decisions.

(1). Continuation of registration without changes.

(2). Continuation of registration with modification to terms and conditions of registration.

(3). Cancellation of registration.

Specific risk reduction modifications selected for further consideration under Option 2 are:

(1). Require protective clothing: impermeable gloves, coveralls, respirators; require proper disposal of protective clothing.

(2). Prohibit eating, drinking, and smoking during application

(3). Restricted use classification

(4). Reduce contaminants in pentachlorophenol

Having evaluated the fetotoxic and oncogenic risks associated with the non-wood uses of pentachlorophenol, the Agency has determined that the benefits outweigh the risks for the use of pentachlorophenol in oil well flood water and pulp and paper mill solutions. The Agency proposes to continue the registration for the use of pentachlorophenol as an anti-fungal agent in oil well flood waters and in pulp and paper mill solutions but amend the terms and conditions of registration to require that impermeable gloves be worn during the handling of pentachlorophenol and that the HxCDD content be required to be reduced to 1 ppm.

Having evaluated the fetotoxic and oncogenic risks associated with the non-wood uses of pentachlorophenol, the Agency has determined that the continued, unrestricted registrations of the uses listed below is unjustifiable and that the risks outweigh the benefits for both Options 1 and 2. Therefore, the Agency proposes to cancel the use of the products for all uses listed below:

<u>Herbicidal uses</u>

- Greenhouses
- Ornamental lawns and edging
- Rights-of-way
- Commercial and industrial non-crop areas

- Domestic dwellings
- Public facilities
- Golf courses and sand traps
- Wasteland areas
- Aquatic areas

Antimicrobial Uses

- Working solutions including evaporative condensers, air washers, cooling towers
- Finished product preservatives including adhesives/sealants, canning and sealing cements, gaskets, photographic developing solutions, and other uses including latex paint/rubber, defoaming agents, paper coatings, polyvinyl chloride emulsions, zinc-silicone dioxide coatings, and feathers
- Working solutions and finished products preservatives including textile/cordage, leather tannery, marine caulking/ marine paint

Disinfectant uses

- Mushroom houses
- Construction materials

Mossicide uses

- Roofs and lawns

Defoliant uses

- Seed crops

I. Introduction

A. General Background and Organization

The Federal Insecticide, Fungicide, and Rodenticide Act, as amended, (FIFRA) and its regulations require the Environmental Protection Agency (EPA) to review the risks and benefits of uses of pesticides. On October 18, 1978, EPA issued Notices of Rebuttable Presumption Against Registration and Reregistration (RPAR) of pesticide products containing creosote, coal tar and coal tar neutral oils, inorganic arsenical compounds, and pentachlorophenol (43 FR 48443). The presumption against pentachlorophenol was based on validated studies indicating its fetotoxicity. Position Document 1 (PD 1) issued with that Notice described these studies in detail.

In January, 1981, a Position Document 2/3 (PD 2/3) addressed the risks and benefits of the wood preservative uses of creosote, coal tar and coal tar neutral oils, the inorganic arsenical compounds and pentachlorophenol (46 FR 13020). Studies indicating the oncogenicity of the pentachlorophenol contaminants, chlorinated dibenzo-p-dioxins (HxCDD) and hexachlorobenzene (HCB) were also detailed thereby adding the presumption of oncogenicity for pentachlorophenol.

In July, 1984 a Position Document 4 (PD 4) was issued on the wood preservative uses of creosote, coal tar and coal tar neutral oils, the inorganic arsenical compounds and pentachlorophenol (46 FR 13020). It set forth the Agency's final position on the regulation and use of these chemicals as wood preservatives.

The Agency's final decision on the wood preservative uses of pentachlorophenol presented in the PD 4 required for all wood preservative uses: an intermediate upper limit of 15 ppm HxCDD and TCDD below the limits of detection and, in 18 months, a 1 ppm HxCDD upper limit; a teratogenicity/fetotoxicity label warning; disposal of protective clothing and unused formulations; statements regarding personal hygiene during and after application.

Modifications to the terms and conditions of registration for pressure treatment, groundline, treatment of poles, home and farm, sapstain control- millwork, plywood, and particle board included: restricted use classification (all uses); protective clothing, gloves, respirators (all uses); FIFRA Mandatory Consumer Awareness Program (pressure treatment); prohibitions on applying wood intended for use in interiors or for use in contact with food, feed, or drinking water (pressure treatment, home and farm); closed mixing and emptying system (pressure treatment, sapstain control, millwork, plywood, particle board); prohibit application indoors (home and farm).

This Position Document 2/3 addresses the risks and benefits of the non-wood preservative uses of pentachlorophenol. The non-wood preservative uses of creosote, coal tar and coal tar neutral oils were discussed in Position Document 2/3 issued in August, 1984. The non-wood preservative uses of the inorganic arsenical compounds will be considered in a future Position Document 2/3.

This document contains five parts. Part I is this introductory section. Part II evaluates the potential risks associated with the non-wood preservative uses of pentachlorophenol. Part II also includes descriptions and evaluations of the risk evidence, exposure data, rebuttal submissions, and the Agency's risk assessment. Part III estimates and summarizes the economic benefits of the non-wood uses of pentachlorophenol for each use category and describes the assumptions and limits of these estimates. Part IV describes the range of possible regulatory options and modifications to reduce the risks so that they are exceeded by the benefits of pentachlorophenol products and explains the Agency's selection of some of these options for further consideration. Part V presents the Agency's proposed regulatory decision for each of the non-wood uses of pentachlorophenol.

B. Legal Background

To obtain a registration for a pesticide under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended, an applicant for registration must show that the pesticide satisfies the statutory standard for registration. That standard requires, among other things, that the pesticide perform its intended function without causing "unreasonable adverse effects on the environment" FIFRA §3(c)(5).

The term "unreasonable adverse effects on the environment" is defined as "any unreasonable risk to man or the environment, taking into account the economic, social and environmental costs and benefits of the use of any pesticide" FIFRA §2(bb). To register a pesticide, the Administrator must find that the benefits of each use of the pesticide exceed the risks of use, when the pesticide is used in accordance with commonly recognized practice and in compliance with the terms and conditions of registration.

The burden of proving that a pesticide satisfies the registration standard is on the proponents of registration and continues as long as the registration remains in effect. Under section 6 of FIFRA, the Administrator may cancel the registration of a pesticide or modify the terms and conditions of registration whenever it is determined that the pesticide causes unreasonable adverse effects on the environment. The

Agency created the RPAR process to facilitate the identification of pesticide uses which may not satisfy the statutory standard for registration and to provide an informal procedure to gather and evaluate information about the risks and benefits of these uses.

The regulations governing the RPAR process are set forth in 40 CFR 162.11. (The RPAR process has been recently named the Special Review Process). Among other things, this section provides that a rebuttable presumption against registration shall arise if a pesticide meets or exceeds any of the risk criteria set out in the regulations. The Agency announces the commencement of the RPAR process by publishing a notice in the Federal Register. After an RPAR is issued, registrants and other interested persons are invited to review the data and information to rebut the presumption by showing that the Agency's initial determination of risk was in error, or by showing that use of the pesticide is not likely to result in any significant exposure to humans or the environment with regard to the adverse effects in question. In addition to submitting evidence to rebut the risk presumption, respondents may submit evidence as to whether the economic, social and environmental benefits of the use of the pesticide outweigh the risks of use.

In determining whether the use of a pesticide poses risks which are greater than the benefits, the Agency considers possible changes to the terms and conditions of registration which can reduce risks, and the impacts of such modifications on the benefits of use. If the Agency determines that such changes sufficiently reduce risks to the level where the benefits outweigh the risks, it may conclude the RPAR process. The Agency announces this type of conclusion to an RPAR review by publication of a Notice of Determination in the Federal Register. That Notice states and explains the rationale for the Agency's regulatory position, provides that the registrant may avoid cancellation by implementing the modifications to the terms and conditions of registration set forth in the Notice, and sets forth the hearing rights of the affected parties.

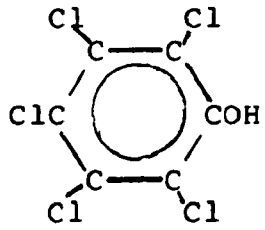
C. Chemical Background

1. Chemical and Physical Characteristics

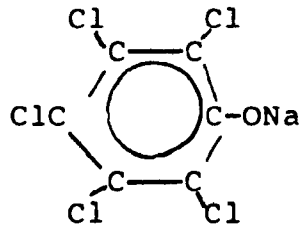
Pentachlorophenol is commonly called "penta". It is a buff colored crystal which is produced in the United States by chlorination of molten phenol in the presence of a catalyst. The major commercial forms of penta are the unmodified phenol and the sodium salt. The potassium salt is used to a lesser extent. Figure 1 shows the structural formulae of these forms of penta, while Table I-1 contains the chemical and physical properties of these compounds.

FIGURE 1

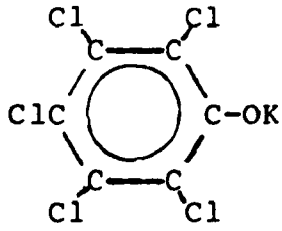
Structure of Pentachlorophenol in its Various Forms



Pentachlorophenol



Sodium Pentachlorophenate



Potassium Pentachlorophenate

TABLE I-1

Physical Properties of Pentachlorophenol and Sodium Pentachlorophenate

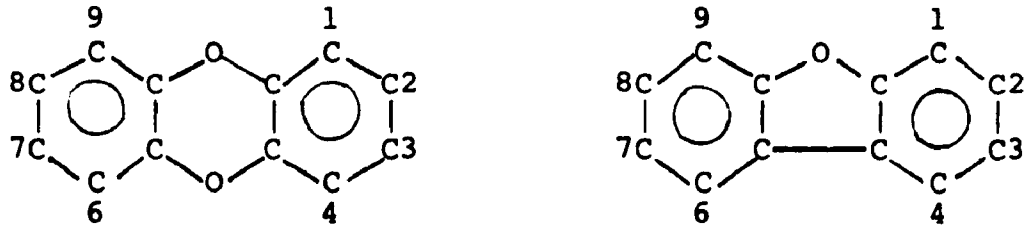
Type	Pentachlorophenol	Sodium Pentachlorophenol
Formula	C_6Cl_5OH	$C_6Cl_5ONaH_2O$
Molecular Weight	266.4	306.3
Specific Gravity	1.9	2.0
Density	1.987	--
Vapor Pressure	0.00015 (25°C)	--
Solubility (g/100 g, @ 25°C)		
o Water	<0.01	33
o Acetone	50	35
o Benzene	15	--
o Diacetone Alcohol	190	45
o Ethanol (95%)	120	65
o Methanol	180	25
o Isopropanol	85	30
o Ethylene Glycol	11	40

Industrial production of penta is a two-stage process. In the first stage, phenol is chlorinated at 105°C to yield isomers of tri- and tetrachlorophenols. In the second stage, the temperature is gradually increased to 130°C to keep the reaction mixture molten, and the tri- and tetrachlorophenols are further chlorinated to form pentachlorophenol. However, not all of these precursor compounds react in the process; some of the tetrachlorophenols survive and remain with the penta through later processing. Technical grade penta, therefore, contains from 4 to 12% tetrachlorophenols; in fact, one of the three possible tetrachlorophenol isomers, 2,3,4,6-tetrachlorophenol, is listed as an active ingredient in some penta products.

Dioxin and furan contaminants also form in the commercial production of penta. The higher temperatures of the second stage of penta production are favorable to the condensation of the tri-and tetrachlorophenols to form hexa-, hepta-, and octachlorodibenzo-p-dioxins (dioxins) and various chlorinated dibenzofurans (furans). Figure 2 shows the structural formulae of the basic molecules of these contaminants. Substitution of chlorine atoms at one or more of the numbered positions produces a member of the chlorinated dibenzo-p-dioxin (dioxin) or chlorinated dibenzofuran (furan) chemical families.

FIGURE 2

Structure of Dioxin and Furan



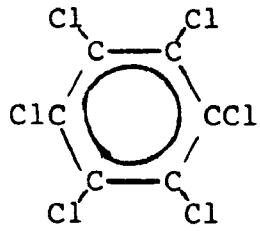
Dibenzo-p-dioxin Dibenzofuran

Buser and Bosshardt (1976) reported the dioxins most prevalent in commercial penta are hexa-, hepta-, and octa-, chlorodibenzo-p-dioxins (HxCDD, HpCDD, and OCDD, respectively). A small amount of tetrachlorodibenzo-p-dioxin (TCDD) has also been found in penta (Buser, 1976), although this proved not to be the extremely toxic 2,3,7,8-isomer. The furans found in penta are the tetra-, penta-, hexa-, hepta-,and octa-, chlorodibenzofurans (Buser and Bosshardt, 1976).

Hexachlorobenzene (HCB) is another contaminant in pentachlorophenol products. It is thought to arise from decomposition of decachlorodiphenyl (Kulka, 1961) in the pyrolytic conversion of penta salt to OCDD (Sanderman et al., 1957). Figure 3 shows the structural formula of this contaminant.

FIGURE 3

Structure of Hexachlorobenzene



2. Use and Production

Pentachlorophenol has a long history of use as a wood preservative, disinfectant, herbicide, and antifungal agent. As of 1977, about 50 million pounds of penta were produced annually in the United States and production was expected to increase to 80 million pounds annually in the near future (Josephson, 1977). Approximately 80% of the pentachlorophenol produced is used for wood preservative uses.

The registered non-wood uses of pentachlorophenol include use as a herbicide, antimicrobial agent, disinfectant, mossicide, and defoliant. Pentachlorophenol is also registered for use to treat soil to control subterranean termites. This use is not considered in this document. The subterranean termite control use of pentachlorophenol is under review by the Agency along with other chemicals registered for this use.

Pentachlorophenol is registered for use on the following sites as a non-specific, non-residual contact herbicide: greenhouses, ornamental lawns, rights-of-way, commercial and industrial non-crop areas, domestic dwellings, medical facilities, schools, golf courses, sand traps, wasteland areas, aquatic areas and drainage ditch banks.

Uses of pentachlorophenol as an antimicrobial agent to control bacterial and fungal growth include: working solutions (oil well flood waters, evaporative condenser cooling waters, cooling tower waters, air washers); finished product preservative (adhesives and sealants, latex paints, rubber articles, defoaming agents, paper coatings, polyvinyl chloride emulsions in food related products, zinc-silicone dioxide matrix coatings in reusable bulk food storage containers, and water-based gasketing compounds for food applications, photographic developing solutions, cements in food can ends and seams, feathers); working fluids and process chemicals in the textile industry; pulp and paper mill solutions and products; leather tannery solutions and products; marine anti-fouling agents; disinfectant in mushroom houses; mildewicides in a variety of construction materials.

As a mossicide, pentachlorophenol is used to control moss on lawns and roofs.

Pentachlorophenol is registered as a defoliant aid in seed crop harvesting of alfalfa, clover, birds foot trefoil, and lespedeza.

3. Tolerances

The Agency has established no tolerances or exemptions from the requirement of a tolerance and the FDA has not established action levels for pentachlorophenol in or on raw agricultural commodities.

The FDA has several regulations permitting the use of penta and/or its salts in wood and non-wood packaging materials as an indirect food additive.* Pentachlorophenol and its sodium and potassium salts are cited in 21 CFR, Part 165.105 as approved for use as an adhesive component. The salts are limited to use as a preservative. In 21 CFR, Part 178.3120, the potassium and sodium penta salts are designated for use as optional adjuvant substances used in the production of animal glue. Animal glue is used as a component of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food. Sodium pentachlorophenate may also be used as a component of paper and paperboard in contact with aqueous and fatty foods, with the restriction of its being used only as a preservative for coating formulations (21 CFR, Part 176.170).

* According to CFR 21, Part 170, Section 170.3, "food additive" includes all substances in which the intended use of which results, or may reasonably be expected to result, directly or indirectly, either in their becoming a component of food, or otherwise affecting the characteristics of food. Material used in the production of containers and packages is subject to the definition if it may reasonably be expected to become a component, or to directly or indirectly affect the characteristics of food packed in the container. The general provisions applicable to "indirect food additives" (Part 174, Section 174.5) are regulations prescribing conditions under which food additive substances may be safely used and predicate usage under conditions of good manufacturing practice. The quantity of any food additive substance that may be added to food as a result of use in articles that contact food shall not exceed, where no limits are specified, that which results from use of the substance in an amount not more than reasonably required to accomplish the intended physical or technical effect in the food-contact article; shall not exceed any prescribed limitations; and shall not be intended to accomplish any physical or technical effect in the food itself.

II. RISK ANALYSIS AND ASSESSMENTS

This portion of the Position Document is divided into five sections. The first two sections discuss the basis for the Agency's presumption, the rebuttal comments received in response to PD 1 and the public comments received in response to the Wood Preservatives Position Document 2/3, as they apply to the non-wood uses of these chemicals.

The third and fourth sections address human exposure for the various non-wood preservative uses of pentachlorophenol. The final section presents the risk assessment.

In assessing the risks, two factors are considered: the toxic effect (or effects) of the pesticide and whether the amount of exposure is sufficient to cause the toxic effect(s). The toxic effects of concern for pentachlorophenol were described in the PD 1 as the basis for the rebuttable presumption.

A. Analysis of Rebuttal Comments and Public Comments Concerning Fetotoxic and Teratogenic Effects

1. Basis of Presumption

In the studies summarized in the PD 1 on pentachlorophenol and the PD 2/3 and PD 4 on the wood uses of pentachlorophenol, fetotoxic effects were reported in rats exposed to purified and commercial grade penta. Teratogenic effects were reported in rats exposed to a mixture of two unspecified isomers of hexachlorodibenzo-p-dioxin (HxCDD). Specifically, exposure to penta contaminated with these HxCDD isomers resulted in statistically significant increases in the incidence of skeletal and soft tissue anomalies, growth retarded fetuses, and embryonic resorptions in the litters of treated dams. Teratogenic effects were also reported in mice exposed to hexachlorobenzene (HCB). Exposure to this penta contaminant produced significantly elevated maternal liver-to-body weight ratios, decreased fetal body weights and caused a significant increase in the number of abnormal fetuses per litter.

The results of these studies are summarized below.

Studies with Pentachlorophenol

Schwetz et al. (1974) studied the effects of purified and commercial grade penta on rat embryonal and fetal development. Doses of 5, 15, 30, and 50 mg/kg/day of purified penta and 5.8, 15, 34.7, and 50 mg/kg/day of commercial penta were administered by gavage on gestation days 6 through 15 inclusive. (Note that 5.8 and 34.7 mg/kg/day of commercial penta are equivalent to 5 and 30 mg/kg/day of purified penta). Both purified and commercial penta caused statistically significant increases in fetal resorptions at the two higher doses (Table II-1).

It is interesting that at 30 and 50 mg/kg/day, purified penta had a more pronounced effect than the two highest doses of commercial penta. For example, at 50 mg/kg/day purified penta caused 100% incidence of fetal resorptions, while commercial penta caused 58% resorptions. At 30 (purified) and 50 (commercial) mg/kg/day, there were statistically significant differences in the sex ratio of surviving fetuses: in both cases, males were heavily predominant. These investigators also found that administration of penta during early organogenesis (days 8 through 11 of gestation) had a more pronounced effect on fetal resorption than did its administration during late organogenesis (days 12 through 15).

In this study, the no-observable-effect level (NOEL) for fetal resorption was 5.8 mg/kg/day for commercial grade penta and 15 mg/kg/day for purified penta. Measurements were also taken on fetal body weight and crown-rump length, both of which decreased with increasing dose. The NOEL for these parameters was 15 mg/kg/day for both commercial grade and purified penta.

TABLE II-1

Effect of Pentachlorophenol
on the Incidence of Fetal Resorptions[a]

Test Material & Dose (mg/kg/dy)	Resorptions			
	Among Fetuses		Among Litters	
	%	No.	%	No.
Vehicle Control[b]	4.2	15/358	30.3	10/33
Pentachlorophenol[c]				
Commercial				
5.8	7.1	15/212	55.6	10/18
15	8.8	17/194[d]	64.7	11/17[d]
34.7	27.2	64/235[d]	94.7	18/19[d]
50	58.1	108/186[d]	93.3	14/15[d]
Purified				
5	4.2	8/189	46.7	7/15
15	5.9	13/221	38.9	7/18
30	97.5	233/239[d]	100.0	20/20[d]
50	100.0	229/229[d]	100.0	19/19[d]

a. From Schwetz et al. (1974).
b. 2.0 ml/kg body weight corn oil per day.
c. Dosages were administered in corn oil (2.0 ml/kg).
d. Significantly different from control values by the binomial expansion test, $p<0.05$.

Schwetz et al. (1974) also investigated the fetal anomalies in rats caused by penta. They studied the effects produced by gavage of 5.8, 15, 34.7, and 50 mg/kg/day of commercial grade penta, and 5, 15, and 30 mg/kg/day of purified penta. In one experiment, they administered these amounts of penta during days 6 through 15 of gestation; significant increases in skeletal defects of the ribs, sternebrae, and vertebrae were observed in the two highest dose groups of both purified and commercial penta. The lowest dose of purified penta (5 mg/kg/day) caused an increase in delayed skull ossification. In a second experiment, they gave 30.0 (purified) and 34.7 (commercial) mg/kg/day penta on days 8 through 11 of gestation to one group of animals, and on days 12 through 15 to a second group; significant increases in abnormal sternebrae and skulls were observed in animals treated with purified penta, and abnormal sternebrae were observed in animals treated with commercial penta.

Larsen et al. (1975) fed 60 mg/kg ^{14}C-penta to pregnant Charles River rats (CD strain) on day 15 of gestation. They detected negligible amounts (<0.3% of administered dose) of ^{14}C-penta in the placentae and fetuses up to 32 hours after dosing. This indicated that the amount of penta that passes through the placental barrier on day 15 is negligible. In a separate experiment reported in the same paper, a single oral dose of 60 mg/kg of unlabeled penta administered to separate groups of animals on days 8, 9, 10, 11, 12, or 13 of gestation had no significant effect on the rate of fetal resorptions in the test animals as compared with controls. However, significant reductions in fetal weight, another fetotoxic effect, were reported on days 9 and 10.

Hinkle (1973) reported the absence of observed fetotoxic effects of penta in the Golden Syrian hamster. Administration of 1.25, 2.5, 5, 10, and 20 mg/kg of penta by gavage on days 6 through 10 of gestation caused no differences between control and test animals in these parameters: maternal body weight, fetal weight, litter size, and number of resorptions. There was some (unspecified) increase in maternal toxicity at the two highest doses. The author stated that penta was found in detectable amounts (unspecified) in the untreated animals as well as in their diet.

Fahrig (1978) observed decreases in litter size after intraperitoneal injection of pregnant mice at day 10 of gestation with 50 to 100 mg/kg penta. Control mice, on the average, produced more than 6 fetuses/dam, whereas litter sizes in the treated groups were about 4 fetuses/dam. Penta was administered in a 10% solution of dimethylformamide; a vehicle control was not reported. Litter size calculations included dams that had no litters.

It is clear from the above discussion that the higher doses of penta can cause fetotoxic effects in experimental animals. Based on the results of Schwetz et al. (1974), the Agency, in PD 1, used 5.8 mg/kg/day of commercial penta as the NOEL for fetotoxicity.

Schwetz et al. (1978), in a dietary study, randomly separated 7-week-old Sprague-Dawley (Spartan substrain) SPF derived rats into test groups and allowed them to acclimatize for 1 week. There were 10 male and 20 female rats in each treatment group and in the control group. The investigators mixed penta (dissolved in anisole) with Purina Lab Chow to make a 1% premix, from which test diets were prepared weekly and fed to the treatment groups. (Table II-2 shows the composition of the penta used in this study.) When adjusted weekly for changing food consumption and body weights, this diet resulted in doses of 3 and 30 mg/kg/day penta. All rats were observed daily. Body weights were recorded on days 0, 29, and 62 of the study, as well as 21 days after parturition. After 62 days on the test diet, each male was placed with two females from the same treatment regimen for 15 days, which is three estrus cycles in normal female rats. After the 15-day period, the males were returned to individual cages and given the appropriate dose-level diet. Females were maintained in individual cages with ground corn-cob litter for nesting. Treatment diets for females continued through 21 days following parturition. After 21 days of lactation, the females and their young were killed and necropsies were performed. One male and one female of each litter were prepared for skeletal examination. The adult male rats were sacrificed and examined at the end of the study.

TABLE II-2

Composition of Dowicide® EC-7[a]

Component	Amount
Phenols	(as percent)
Trichlorophenol	<0.1
Tetrachlorophenol	10.4 ± 0.2
Pentachlorophenol	90.4 ± 1.0
Dibenzo-p-dioxins	(as ppm)
2,3,7,8-Tetrachloro-	<0.05
Hexachloro-	1.0 ± 0.1
Heptachloro-	6.5 ± 1.0
Octachloro-	15.0 ± 3.0
Dibenzofurans	(as ppm)
Hexachloro-	3.4 ± 0.4
Heptachloro-	1.8 ± 0.3
Octachloro-	<1

a. From Schwetz et al. (1978).

Indices of reproduction were evaluated by the Fisher exact probability test, and body weights were analyzed by Dunnett's test. The level of significance in all cases was $P<0.05$.

Statistically significant depression of parental body-weight gain was reported at the 30 mg/kg/day dose for males at all measurement periods, and for females at the last (62nd day) period. At the 3 mg/kg/day dose, there was an apparent trend toward decreased weights in both sexes at all periods reported. This trend exists in the absence of significant depression at any specific period.

At the 30 mg/kg/day dose, the neonatal weights of both sexes compared to controls were significantly lower at all four periods reported. The data for the 3 mg/kg/day dosage shows a trend toward decreased weight (consistent with the high dosage) which continues as the animals age. However, this weight decrease at 3 mg/kg/day is not statistically significant at any individual day.

Measured either as absolute weights or as liver-to-body weight ratios, changes in maternal liver weight at either dosage were not significant compared to controls. Daily inspection revealed no treatment-related effects on demeanor or physical appearance in either adults or young.

Among the reproduction indices reported, neither the fertility index nor the 24-hour survival index was significantly different from controls at either dose. By Dunnett's test four indices at 30 mg/kg/day were significantly less than control: gestation survival, and 7-day, 14-day, and 21-day survival. Average litter sizes were significantly less than controls on days 7, 14, and 21 at the 30 mg/kg/day dose. Gestation-period length showed no significant treatment related effect.

At this 30 mg/kg/day dose there was also a general trend toward increased frequency of abnormalities in all parameters reported. Statistically significant increases at this dose were reported for lumbar spurs and for vertebrae with split centrum. At the 3 mg/kg/day level there was neither a trend toward increased abnormalities nor any statistically significant increases in any of the parameters reported.

Schwetz et al. (1978) is adequate to establish 3 mg/kg/day as a provisional fetotoxicity NOEL for the penta analyzed.* The test material (see Table II-2) was reported in the study to contain 10-fold less hexachloro-, 30-fold less heptachloro-, 200-fold less octachlorodibenzo-p-dioxin, and 6- to 300-fold less of the dibenzofurans than at least one of the currently manufactured technical pentas.

* The term "provisional" is used because a teratogenicity study which adequately demonstrating a fetotoxic no-effect level for penta is not available at this time.

Goldstein et al. (1977) fed female rats 20, 100, and 500 ppm of either technical or purified penta for 8 months. The technical penta used for this study was reported to contain only slightly less HxCDD and hexachlorodibenzofuran than the levels reported for currently manufactured commercial penta.

Dosing at 20 ppm (about 1.5 mg/kg/day as interpolated from food consumption data) resulted in a 15-fold increase over the control in the activity of aryl hydrocarbon hydroxylase (AHH). Purified penta, on the other hand, had no significant effect on AHH induction at any dose tested. Glucuronyl transferase activity was also significantly elevated at the 20 ppm treatment level by the technical penta used in this study. The Agency is not aware of a meaningful toxic state which can be associated, in this case, with the reported levels of enzyme induction or elevation. However, elevated AHH activity has been used as a "biochemical correlate" (Goldstein, 1980) for the presence in biological samples of some of the nonphenolic contaminants of technical penta. At a level of 20 ppm neither technical nor purified penta in this study affected the excretion of urinary porphyrins or their precursors. The liver-to-body weight ratio was not affected significantly at 20 ppm by either grade of penta.

Additional assessment of parental chronic toxicity allows comparison of penta dose levels causing fetotoxicity with those doses causing significant effects in adult animals. A 2-year chronic feeding and oncogenicity study of penta in rats (Schwetz et al., 1978) shows a NOEL of 3 mg/kg/day for bodyweight change and food consumption of the adults. In addition, this study was unable to demonstrate a significant increase of either benign or malignant tumors in either sex.

The 8-month rat (male and female) feeding study of Kimbrough and Linder (1978), using the technical penta of the Goldstein study (Goldstein et al., 1977), showed only "mild" histological alterations (unspecified) in the liver at the 20 ppm dietary concentration.

The results of 90-day feeding studies are also useful for comparison with fetotoxic effects, which may occur with relatively short exposure duration. In a 90-day rat feeding study, Kociba et al. (1973) used doses of 1, 3, 10, and 30 mg/kg/day. Several of the adult body weight gains were significantly different from controls: males were higher, females were lower. A comparison of the pooled dose mean body weights with controls, however, failed to show a treatment effect. The testes-to-body-weight ratios were lower than controls at all doses and significantly lower at 10 and 1 mg/kg/day. Also, there was no clearly established NOEL for serum glutamic pyruvic transaminase or alkaline phosphatase elevations.

The 90-day rat feeding study of Knudsen et al. (1974), performed with an inadequately described technical penta, showed significantly elevated alkaline phosphatase levels in females at 1.1 mg/kg/day. Liver and kidney weights appeared to show a dose-related increasing trend in both sexes. The liver weight increase in females was significant at 2.5 and 10 mg/kg/day. Liver histopathology, specifically centrilobular vacuolization, was present in both sexes at 10 mg/kg/day. At 2.5 mg/kg/day, this effect was marginally elevated in females but absent in males.

A third 90-day rat feeding study (Johnson et al., 1973) also was performed with an incompletely described technical penta. The NOEL was 3 mg/kg/day, based on increased liver weight at higher doses.

Studies with Dioxins

Commercial penta contains several forms of chlorinated dibenzo-p-dioxins (see Part I.C.2). Schwetz et al. (1973) administered purified HxCDD (two unspecified isomers) and octachlorodibenzo-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 ug/kg/day HxCDD and 100 or 500 mg/kg/day OCDD.

In these experiments with HxCDD, there were significant increases over controls in fetal resorptions at the 10 and 100 ug/kg/day doses, as well as decreases in fetal body weight and fetal crown-rump length. Subcutaneous edema was observed at all doses except 0.1 ug/kg/day, which was considered the no-effect dose. At the two highest doses, dilated renal pelvis (at 10 and 100 ug/kg/day) and cleft palate (at 100 ug/kg/day) were also observed. 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.

Significant increases over the controls in all of the teratogenic parameters were observed at 100 ug/kg. For example, cleft palate was observed in 47% (8/17) of the fetuses exposed to HxCDD, compared with none (0/156) in the controls. Of the treated fetuses, 12% (2/17) had dilated renal pelvis compared with 0.6% (1/156) in the controls, and 31% (5/16) of the treated fetuses had abnormal vertebrae, compared with 6% (9/158) in the controls. In contrast, OCDD did not cause teratogenicity at 100 mg/kg/day; although 500 mg/kg/day caused subcutaneous edema, it produced no other observable effects. Because of the extremely high doses of OCDD required to produce an effect, the margins of safety for this dioxin isomer are much greater than those for HxCDD.

As the fetotoxicity NOEL (0.1 ug/kg/day) for HxCDD is lower than that for teratogenicity for HxCDD, the Agency will use the NOEL for fetotoxicity in the quantitative assessment of risk. (Note that errors on pages 43 and 46 of PD 1 mistakenly expressed this NOEL as 1.0 ug/kg/day.)

HxCDD is also responsible for some of the immunosuppressive character of technical penta. In Holsapple et al. (1984), daily exposure of adult female mice for 14 days to technical grade penta at 10, 30, and 100 mg/kg (p.o.) suppressed the peak (day 4) IgM antibody (Ab) response to sheep red blood cells (sRBC) by 44%, 53%, and 72%, respectively. In contrast, similar exposure to pure (dioxin-free) penta had no effect, thereby suggesting that the suppression by technical penta was due to the dibenzodioxins. Similar exposure to 1,2,3,6,7,8-HxCDD at 0.2, 1.0, and 4.0 ug/kg concentrations, corresponding to those found in technical grade penta, indeed suppressed the peak IgM Ab response to sRBC by 30%, 47%, and 62%, respectively. Direct addition of 0.1 ug of either 1,2,3,6,7,8-HxCDD or 1,2,3,7,8,9-HxCDD to spleen-cell suspensions of untreated mice was able to suppress by greater than 80% the Ab response to sRBC.

Among the dioxin isomers, those chlorinated at the 2,3,7, and 8 positions are recognized as the isomers particularly toxic to several species. Holsapple et al. (1984) showed that subchronic (14-day) exposure of their mice to 1,2,3,6,7,8-HxCDD (the major dioxin in penta) produced significant elevations in liver weight, microsomal protein, cytochrome P450, and in the activity of aryl hydrocarbon hydroxylase (AHH). The induction of AHH is a well-known biochemical response associated with exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), which, for several species is the most toxic dioxin isomer. Furthermore, the significantly decreased thymus weights among the mice corresponds to the thymic atrophy observed in almost all species exposed to 2,3,7,8-TCDD.

The immunosuppression by the hexadioxins is thought to be due to the parent compound, as indicated by Holsapple et al., which showed that preincubation with crude liver homogenate preparation (which readily activated cyclophosphamide) abolished the activity of the hexadioxins, possibly by a metabolic deactivation process.

Studies with Furans

As discussed in the chemical background section of this document, chlorinated dibenzo-furans have also been shown to be contaminants of pentachlorophenol products. The chemical structures of the chlorinated dibenzo-furans and chlorinated dibenzo-p-dioxins are similar and levels of contamination of

the two chemicals parallel each other. Although no fetotoxic studies have been done on the furans, because of their functional similarity in short term testing (McConnel and Moore, 1979 and Poland et al., 1979), the chlorinated dibenzo-furans are presumed to be fetotoxic and teratogenic as are the dibenzo-p-dioxins.

Studies with Hexachlorobenzene (HCB)

Courtney et al. (1976) reported a teratogenic effect caused by HCB in mice. Oral administration to CD-1 mice on days 7 to 16 of gestation showed that HCB at 100 mg/kg/day produced significantly elevated maternal liver-to-body weight ratios and decreased fetal body weights. The number of abnormal fetuses per litter increased significantly. In one of the litters the abnormalities included some cleft palates.

Khera (1974) reported fetotoxic effects, which were limited to dose-related sternal defects at doses of 40 mg/kg (days 6 to 21 of gestation) and to a significantly increased incidence of uni- or bilateral fourteenth ribs. This latter effect was dose- and duration-dependent and commenced at the lower dose (10 mg/kg/day) during either days 6 to 16 or days 10 to 13 of gestation. There were no HCB-related effects on external morphology. Khera did not observe visceral deformities and histological examination was negative. The parameters of a concurrent dominant lethal assay were all within the control range. There was a NOEL of 60 mg/kg/day for maternal toxicity (weight loss and convulsions) when HCB was administered on gestation days 6-21 or for shorter periods.

Simon et al. (1979) also observed that HCB, when administered at either 70 or 221 mg/kg/day for 5 days, would not induce dominant-lethal mutations in rat. At these two doses, however, HCB showed a dose-dependent decrease in the number of females inseminated and impregnated.

Grant et al. (1977), in a four-generation rat reproduction study, found that pregnancy, viability, lactation indices, neonatal weight gain, and relative liver weight all had a NOEL of 1.0 mg/kg/day dietary HCB. At a 4-fold higher dose, several of the maternal animals died. No gross abnormalities were observed in the young rats.

In several mammalian species penta is one of the metabolites of hexachlorobenzene (HCB). Koss et al. (1978) dosed female rats with HCB on alternate days at 50 mg/kg. These researchers found a blood ratio of penta (as a metabolite of HCB) to HCB of about 1:10 at steady-state. The mean blood concentration of HCB in the general population is reported to be less than 1 ppb (Strassman-Sundy, 1980).

2. Analysis of Specific Rebuttal and Public Comments Concerning Fetotoxicity

The rebuttal and public comments that follow are rebuttals submitted in response to the PD 1 on pentachlorophenol and public comments submitted in response to the PD 2/3 on the wood preservative uses of pentachlorophenol. The Agency responses to each comment are also provided. These rebuttals were previously published in the PD 2/3 (EPA, 1981) and the PD 4 (EPA, 1984) on wood uses of pentachlorophenol respectively, and are included in this document for completeness. The number in parentheses after the title of each comment is an internal number assigned to each comment received.

The following rebuttal comments were submitted in response to the Position Document 1 on creosote, pentachlorophenol, and the inorganic arsenicals.

Rebuttal Comment 1: Blood Concentrations of Penta After Dosing (18)

Dow Chemical Company believes that the NOEL of 5.8 mg/kg/day used in PD 1 is too low. In support of this opinion, the rebutter provides calculations from a simulation model to show that the theoretical average daily blood concentration of penta after a single NOEL-dose of 60 mg/kg (Larsen et al., 1975), when averaged over 4 days, is very close to the theoretical average after 4 days of dosing at 15 mg/kg/day. The rebutter states that:

> Based on the similarity of these average blood concentrations during the 4 critical days of gestation, and the fact that 60 mg/kg administered singly is a no-effect-dose, the actual no-effect-dose for repeated administration is probably closer to 15 mg/kg per day than to 5 mg/kg per day.

Agency Response: Although the hypothetical calculations submitted by the rebutter are interesting, the Agency is not convinced that the results calculated from a simulation model of a single dose (Larsen et al., 1975) can rebut the empirical results of experiments based on chronic administration.

Schwetz et al. (1974) clearly showed that doses of commercial penta greater than 5.8 mg/kg/day are capable of producing fetotoxic effects in rats. In addition to other possibly relevant variables, the time-course of penta blood concentration (which is very different in the two experiments) may partially account for the difference in NOEL values.

Rebuttal Comment 2: Terminology of Fetotoxic and Teratogenic Effects (1, 18)

The American Wood Preservers Institute and Dow Chemical Company state that the sole reference (Schwetz et. al., 1974) cited in PD 1 as evidence for the teratogenicity of penta in rats does not, in fact, support the conclusion of teratogenic effects from this chemical in either humans or rats. The rebutters claim that the distinctions between teratogenicity, embryotoxicity, embryolethality, and fetotoxicity are critical in the interpretation of the effects of penta. They state that 1) teratogenic effects are typically irreversible changes of a serious nature, 2) fetotoxic changes are typically reversible and are of lesser toxicological significance, and 3) embryolethality is a significant toxic end-point, but does not result in the birth of a malformed infant and is, therefore, not considered to be evidence of teratogenicity.

Agency Response: Generally the term "teratogenic" is defined as the tendency to produce physical and/or functional defects in offspring exposed in utero. The term "fetotoxic" has traditionally been used to describe a wide variety of embryonic and/or fetal divergences from the norm which cannot be classified as gross terata (birth defects), or which are of unknown significance. Types of effects which fall under the very broad category of fetotoxic effects are death, reductions in fetal weight, enlarged renal pelvis, and increased incidence of supernumary ribs. It should be emphasized, however, that the phenomena of terata and fetal toxicity as currently defined are not separable into precise categories. Rather, the spectrum of adverse embryonic/fetal effects is continuous, and all deviations from the norm must be considered as examples of developmental toxicity. Gross morphological terata represent but one aspect of this spectrum, and while the significance of such structural changes is more readily evaluated, such effects are not necessarily more serious than certain effects which are ordinarily classified as fetotoxic (fetal death being the most obvious example).

In view of the spectrum of effects at issue, the Agency suggests that it might be useful to consider developmental toxicity in terms of three basic subcategories. The first subcategory would be embryo or fetal lethality. This is, of course, an irreversible effect and may occur with or without the occurrence of gross terata. The second subcategory would be teratogenesis and would encompass those changes (structural and/or functional)

which are induced prenatally, and which are irreversible. Teratogenesis includes structural defects apparent in the fetus, functional deficits which may become apparent only after birth, and any other long-term effects (such as carcinogenicity) which are attributable to in utero exposure. The third category would be embryo or fetal toxicity as comprised of those effects which are potentially reversible. This subcategory would therefore include such effects as weight reductions, reduction in the degree of skeletal ossification, and delays in organ maturation.

Two major problems with a definitional scheme of this nature must be pointed out, however. The first is that the reversibility of any phenomenon is extremely difficult to prove. An organ such as the kidney, for example, may be delayed in development and then appear to "catch up." Unless a series of specific kidney function tests are performed on the neonate, however, no conclusion may be drawn concerning permanent organ function changes. This same uncertainty as to possible long-lasting after effects from developmental deviations is true for all examples of fetotoxicity. The second problem is that the reversible nature of an embryonic/fetal effect in one species might, under a given agent, react in another species in a more serious and irreversible manner. The Agency must therefore consider all such deviations from normal development in its risk assessment process, regardless of any appearance of reversibilty.

The Agency agrees that the data of Schwetz et al. (1974) should be cited as evidence for fetotoxic effects, rather than for teratogenic effects. The Agency recognizes the value of making distinctions between teratogenicity, embryotoxicity, embryolethality, and fetotoxicity in order to scientifically categorize the effects of a toxic chemical. However, from a regulatory standpoint, a fetotoxic effect may represent as unacceptable a risk to the human fetus as would a teratogenic effect. The studies reported in PD 1 described terata (malformations), fetal resorptions, and increased incidences of normal variants over controls. Any of these adverse effects may engender concern that a sufficient margin of safety may not exist between the test doses in animals and the exposure levels in humans.

In the case of technical penta, when the NOEL for the fetotoxicity of penta is considered in light of the exposure values, the margins of safety (MOS's) are lower than those obtained with the respective exposure figures and NOEL for the fetotoxicity of HxCDD. Consequently, the MOS's for the fetotoxicity of penta will be used in Part V to develop the proposed regulatory decisions.

Rebuttal Comment 3: Distinctions betwen Teratogenicity and Embryotoxicity (1, 18)

The American Wood Preservers Institute and Dow Chemical Company state the Agency is mistaken in using the study of Schwetz et al. (1973) to establish the teratogenicity of HxCDD because of the Agency's failure to distinguish between teratogenic effects and reversible, less severe anomalies. They claim these anomalies should be characterized only as embryotoxic effects.

These rebutters state that the only finding in this study indicative of a teratogenic event was the induction of cleft palate. The rebutters point out that the other findings of dilated renal pelvis, subcutaneous edema, and abnormal vertebral development are evidence of embryotoxicity rather than teratogenicity.

Agency Response: The 1973 paper of Schwetz et al. states that, "By previously described definitions of teratogenicity and embryotoxicity, HxCDD is teratogenic in the rat at 100 ug/kg dose level...." At this dose on days 6 through 15 of gestation, cleft palate was produced in 47% (8/17) of the rat fetuses. The rebutters offer no evidence that any of the dose-related fetal anomalies described are reversible. This study adequately demonstrates that HxCDD is a potential cause of teratogenicity and other symptoms of developmental toxicity. Discussions of the categories of developmental toxicity (teratogenicity, embryotoxicity, fetotoxicity, etc.) do not diminish the Agency's concern about a chemical or its contaminants causing symptoms of developmental toxicity.

Rebuttal Comment 4: Relationship of Maternal Toxicty to Fetotoxicity (1, 18)

The American Wood Preservers Institute and Dow Chemical Company state that a 90-day toxicity study, a 2-year feeding study, and a 1-generation reproduction each show a NOEL of 3 mg/kg/day. This correspondence of the NOEL values cited for fetotoxicity and maternal toxicity is presented as evidence of a low hazard of fetotoxicity from penta. The rebutters suggest that the observed fetal anomalies result indirectly from toxicity to the mother, and not from direct toxicity to the fetus. Thus, margins of safety which would protect the mother against other toxicological manifestations would also protect the developing embryo and fetus against adverse effects.

Agency Response: The rebutters have not demonstrated that maternal toxicity is the cause of the observed fetotoxicity. The concept that the fetotoxic effects of penta do not occur at doses lower than those causing maternal toxicity is refuted by the study of Schwetz et al. (1974). In this study there was a significant increase in percent of fetal resorptions at 15 mg/kg/day (commercial penta), a level which produced

no maternal toxicity. Maternal toxicity did not appear until a dose of 34.7 mg/kg/day was achieved. In addition, it should be noted that the duration of exposure required to manifest fetoxicity in an animal may be considerably less than the time to demonstrate a chronic or life-time effect. For this reason, a proper comparison of hazards involves consideration of the duration and timing of exposure in addition to the NOEL value comparison. The Agency believes that the analysis of hazard to the fetus should be considered in terms of an analysis of fetal exposure vs. fetotoxocity, rather than exclusively in terms of a comparison of the fetal hazard to that of some other hazard, such as maternal toxicity.

Rebuttal Comment 5: Interpretation of Reduced Mouse Litter Size (1, 18)

The American Wood Preservers Institute and Dow Chemical Company contend that the study of Fahrig et al. (1978), reporting decreases in litter size of female mice after intraperitoneal injection of 50 and 100 mg/kg penta, cannot be relied upon for three reasons: 1) evidence of pregnancy was not obtained, i.e., the absence of a litter may have been due to lack of pregnancy, 2) a vehicle control was not used, and 3) the route of administration (intraperitoneal injection) bears no relationship to the routes of human exposure to penta wood preservatives or to treated wood.

Agency Response: The Agency agrees that the Fahrig et al. (1978) study is not primarily concerned with fetotoxic or teratogenic effects. Indeed this study is basically an examination of the mutagenic potency of the chlorophenols and chlorophenol impurities. The conclusions of the study are based upon the observed frequencies of various color spots in the coats of mice. As such, the authors' comment of "decreased litter size" is unaccompanied by supporting data or procedural information which would normally be essential to a study in which litter-size observation was part of the formal protocol. Therefore, the Agency agrees that "decreased litter size" should be considered an ancillary comment rather than as supporting data.

The Agency also agrees that the lack of a vehicle control makes accurate interpretation of the results of this study difficult, as the toxicity of vehicle (dimethylformamide) was not characterized by the authors.

Although the Agency generally does not use the results of intraperitoneal experiments as the sole basis for an RPAR notice, studies of this kind (e.g., Fahrig et al., 1978) can provide valuable supporting information.

The following comments were submitted to the Agency in response to the Position Document 2/3 on the wood preserving uses of creosote, inorganic arsenicals, and pentachlorophenol.

Comment Issue #1: Pentachlorophenol teratogenicity - evidence of reproductive effects

The Dow Chemical Company (32) questions the Agency's use of data concerning "decreased litter size" (Fahrig et al. 1978) to provide supporting information on pentachlorophenol reproductive effects when the Agency has also concluded this observation (on litter size) should only be considered as an ancillary comment.

The Dow Chemical Company (32) also states that the degree of dilation of renal pelvis observed in fetuses treated with HxCDD (Schwetz et al., 1973) was consistent with retardation of kidney development (a reversible effect). Thus, HxCDD should not be considered teratogenic on the basis of its effect on the developing kidney (The Dow Chemical Company, 32).

Agency Response:

The Agency maintains that taking the Schwetz et al. (1973) study into account, regardless of Fahrig et al. (1978), establishes the teratogenicity of HxCDD. That is, the reversibility of dilated renal pelvis can be properly ascertained only upon postnatal examination, particularly for hydronephrosis, an irreversible effect with which dilated renal pelvis may be associated. Postnatal data were not included in the Schwetz et al. (1973) study. However, production of cleft palate (47% at 100 ug/kg/day) is evidence of HxCDD teratogenicity (Van Ormer, 1982a).

The Agency reiterates the conclusion that "decreased litter size" is an ancillary issue and has not used this data in developing the current regulatory position.

Comment Issue #2: Pentachlorophenol teratogenicity/fetoxicity - choice of proper NOEL

The Dow Chemical Company (32), the American Wood Preservers Institute (AWPI) (36B) and The National Forest Products Association (NPFA) (36B) contend that EPA's reduction of the pentachlorophenol NOEL from 5.8 mg/kg/day (Schwetz et al., 1974) to 3.0 mg/kg/day (Schwetz et al., 1978) is unjustified. These commenters state that the data used to establish this fetotoxicity/teratogenicity NOEL utilized pentachlorophenol which varied in purity from one set of animal data to another; they argued that data based on "purified" pentachlorophenol are not relevant to regulation of commercial pentachlorophenol. They point out that although Schwetz et al. (1978) indicate a NOEL between the two doses of 3.0 and 30.0 which were tested, the Agency has identified 3.0 as the proper NOEL.

Agency Response:

The Agency considers all relevant available data. Purified pentachlorophenol data are not irrelevant to the regulation of commercial pentachlorophenol. Because the Agency is not aware of any teratogenicity study conducted according to Agency guidelines on any current commercial pentachlorophenol, such data provide the only basis for regulation.

The provisional NOEL value of 3.0 mg/kg/day was chosen from a one-generation reproduction study (Schwetz et al.,1978), which reports a trend toward decreased neonatal weight at 3.0 mg/kg/day of purified pentachlorophenol, which is consistent with the effects produced by the 30.0 mg/kg/day dosage, but is not statistically significant at 3.0 mg/kg/day (Van Ormer, 1982b). A thorough discussion of the Agency's rationale for the selection of a NOEL value of 3.0 mg/kg/day is presented in the Wood Preservatives PD 2/3 (pages 347-353).

The teratogenicity study of Schwetz et al. (1974) is inadequate to establish a fetotoxicity NOEL for either the commercial or purified pentachlorophenol. There was a statistically significant increase in skull bone delayed ossification at the lowest dose of purified pentachlorophenol (5 mg/kg/day). The study also lists increased incidence of delayed skull ossification at the low dose (commercial grade pentachlorophenol, 5.8 mg/kg/day); lumbar spurs (commercial and purified pentachlorophenol at 5.8 and 5.0 mg/kg/day, respectively); and anomalous sternebrae (purified pentachlorophenol, 5.0 mg/kg/day). Also, the commercial grade pentachlorophenol produces some exencephaly (dose and incidence not listed) which was reported in a public meeting as not significant (Van Ormer, 1982a).

Comment Issue: #3: Pentachlorophenol - concern for the fetus in utero

The Dow Chemical Company (32) disagrees with the Agency's PD 2/3 p. 257 contention that, from a regulatory standpoint, a fetotoxic effect may represent as unacceptable a risk to the human fetus as would a teratogenic effect.

Agency Response:

The Dow Chemical Company's (32) claim concerning the difference between reversible (fetotoxic) and irreversible (teratogenic) effects would mandate a difference in the required margin of safety for the two effects, and implies that fetotoxic effects have been shown to be reversible based on adequate postnatal observation. The claim also implies that data exist on the relative variability of the thresholds for these two types of effects. The Agency is not aware of data on pentachlorophenol which show either the reversibility or the variability of the measured fetotoxic effects, which (in any case) could

appear in another species as a different type of functional or behavioral deficit, e.g., retardation. Above all, the Agency has concern for health of the embryo and fetus in utero, as well as concern that no reversible or irreversible effects manifest after birth (Van Ormer, 1982a). Therefore, a fetotoxic effect may represent as unacceptable a risk to the human fetus as would a teratogenic effect.

Comment Issue #4: Pentachlorophenol fetotoxicity/teratogenicity margin of safety

The AWPI (36B and 36F), the NFPA (36B and 36F) and the Dow Chemical Company (32) state that the EPA's requirement for a fetotoxic margin of safety (MOS) of 400 is unsupported and excessive. They argue that there are data available on the reversible nature of the fetotoxic effects of pentachlorophenol; they claim that it is highly unlikely that any fetotoxic effects would be evidenced if permissible exposures were limited to one-tenth of the NOEL. Without submitting pentachlorophenol postnatal data, the commentors reiterate the claim that fetotoxic effects such as delayed ossification found in Schwetz et al. (1974) can be reversible. An MOS as low as 100 is suggested as appropriate.

Agency Response:

The assignment of an acceptable MOS is largely a risk/benefit question. A fetotoxic effect such as delayed skull ossification (reversible or irreversible) is merely the indication of an effect in one species (A) which may extrapolate in another species (B) into another type of effect, such as retardation. In the field of teratogenicity, there is a relative lack of ability to make qualitative extrapolation. Since the type of response in species (B) cannot easily be predicted, regulation must be based upon the absence of fetotoxic effects in the species in question (A) by applying an MOS which reflects this lack of qualitative correspondence between species (i.e., by applying a margin of safety which includes components for both qualitative and quantitative uncertainty). The Agency is unaware of any pentachlorophenol data bearing on the reversibility of effects such as delayed ossification or dilated renal pelvis (Van Ormer, 1982a).

The Agency did not require an MOS of 400 for fetotoxic effects in the PD 2/3 for pentachlorophenol. The measures proposed in the PD 2/3 to reduce the oncogenic risk from pentachlorophenol to an Agency-acceptable level would provide "margins of safety greater than 400 for fetotoxicity." The assignment of an acceptable MOS must be determined on a case by case, use by use basis by weighing risks and benefits.

The Scientific Advisory Panel (SAP) held an open meeting on June 17-19, 1981, in Arlington, Virginia, to review the Preliminary Notice of Determination concluding the RPAR for the wood preservative chemicals. At this meeting the SAP heard presentations by the Agency, the registrants, and other interested members of the public. The Agency requested the SAP to review several issues relating to the wood preservatives. The SAP submitted its comments on the Preliminary Notice of Determination and its recommendations on July 15, 1981. A summary of the SAP comment relevant to the fetotoxicity of pentachlorophenol and the Agency's response to that comment is as follows:

Issue #1:

The Agency stated in the PD 2/3 that a no-observed effect level (NOEL) for teratology could not be accurately determined and asked the SAP if the occurrence of delayed skull ossification at 5.0 mg/kg/day would preclude the establishment of a NOEL at that level. The SAP commented that the establishment of a NOEL is precluded both by the litter loss phenomenon and by the delayed skull ossification at 5.0 mg/kg/day.

Agency Response

Although the Agency agrees with the SAP that an accurate teratogenicity/fetotoxicity NOEL for pentachlorophenol cannot be determined, in order to estimate the margins of safety for teratogenicity/fetotoxic effects, the Agency has chosen a provisional NOEL of 3 mg/kg/day based on a one-generation reproduction study by Schwetz et al. (1978). Schwetz reported a trend toward decreased neonatal weight at a dose of 3 mg/kg/day (Van Ormer, May 21, 1982). The margins of safety (MOS) for pentachlorophenol were calculated on the basis of the provisional NOEL of 3 mg/kg/day.

Issue #2:

On pages 273-274 of PD-2/3, the Agency addresses the role of the wood preserving industry as a source of ambient background levels of penta in the environment. In the absence of data to the contrary the Agency's commonsense approach assumed that the amount of ambient penta levels contributed by an industry is related to the amount of penta used by that industry. The wood preserving industry uses about 80% of the penta produced in the U.S. Does the Panel agree with this approach? If not, can the Panel suggest a feasible/appropriate method of more accurately addressing the question of the source of environmental penta?

Panel Response

The Panel believes that it is essentially the Agency's responsibility to develop a method of determining the source of environmental penta. In general, the Agency's reasoning appears to be sound. However, the Panel wishes to stress the need for determining the use(s) of the remaining 20 per cent of the penta produced in the U.S., in order that an accurate exposure assessment can be made.

3. Summary of Rebuttal Comments Concerning Fetotoxic and Teratogenic Effects

The rebuttal comments received do not rebut the presumption of fetotoxicity for pentachlorophenol, nor the teratogenicity and fetotoxicity caused by the contaminants HxCDD and HCB. The one-generation study of Schwetz et al. (1978) has been used to establish a provisional NOEL of 3.0 mg/kg/day for the fetotoxicity of pentachlorophenol.

B. Basis of Presumption and Analysis of Rebuttal and Public Comments Concerning Oncogenicity

1. Basis of Presumption

The Agency reviewed three studies concerning penta's possible oncogencity in the PD 1.

Innes et al. (1969) administered (by gavage) 46.4 mg/kg penta to mice on days 7 through 28 of age, followed by 130 ppm (17 mg/kg/day) in the diet for 17 months. They reported that this regimen caused no significant increase in tumor incidence in the test animals when compared with controls.

In 1976, Schwetz et al. reported that 1, 3, 10, and 30 mg/kg/day of purified penta in the diet for 2 years did not increase tumor incidence over control animals.

Boutwell and Bosch (1959) applied 0.3% dimethylbenzanthracene in benzene as an initiator to the shaved backs of mice. As a promoter, a solution of 20% penta in benzene was applied similarly twice weekly for 15 weeks. The average number of papillomas per survivor was 0.04 in the test group, slightly less than the 0.07 observed in the controls. The number of survivors with papillomas was 4% in the test group and 7% in the control group.

These papers were reviewed by the Agency's Carcinogen Assessment Group and were found to be negative with respect to oncogenic effects of penta.

Studies with Dioxins

In March 1980, the Agency received from the National Cancer Institute (NCI) the final draft reports of two bioassay studies dealing with the possible carcinogenicity of two isomers of HxCDD. The results of one study, on the dermal application of HxCDD to mice, were negative. The second study involved oral administration of HxCDD to both rats and mice. The doses ranged from 1.25 ug/kg/week to 10 ug/kg/week. Under the conditions of this study, HxCDD increased the incidences of benign and neoplastic liver tumors in mice of both sexes and in females rats.

Squire Associates (1983) reviewed the NCI feeding study and based on Dr. Squire's histopathological evaluations, reported lower incidences of neoplastic nodules and carcinomas in high dose female rats than the incidence reported by NCI (1980).

At the request of EPA, the National Toxicology Program (NTP) then reviewed the histopathology slides to reexamine the lesions in the liver tissues of the female rats. NTP (Hildebrandt, 1983) concluded that HxCDD administered to female rats causes a toxic hepatitis and an increase in the incidence of neoplastic nodules. The toxicity effects were characterized by cytomegalia, karyomegaly, bile duct proliferation, and varying degrees of cytoplasmic vacuolization (fatty change). In determining the incidence of neoplastic nodules, Dr. Hildebrandt found that although the cells in neoplastic nodules were often very similar to foci of cellular alteration, two differentiating features could be used; a) the degree of compressing adjacent tissue (sometimes bulging from the surface), and b) perhaps more importantly the degree of bile duct proliferation within the focus of proliferating cells. A nodule (focus) of proliferating cells compressing adjacent tissue and not containing bile ducts was diagnosed as a neoplastic nodule. A similar focus of cells that contained small bile ducts and/or small proliferating bile ducts was diagnosed as a focus of cellular alteration.

The nodules, or foci which Dr. Hildebrandt called neoplastic nodules, were either devoid of bile ducts, contained a bile duct at the periphery which was interpreted as entrapment, or had only a hint of bile duct proliferation in one small region of the nodule. Dr. Hildebrandt stated that there is some subjectivity in the criteria he used to determine the number of neoplastic nodules in the liver tissues. For example, a few neoplastic nodules would have been diagnosed as foci of cellular alterations if a reviewer was of the opinion that neoplastic nodules have no bile ducts whatsoever.

Dr. Hildebrandt found that two livers had a lesion that was compatible with hepatocellular carcinoma.

The incidences of neoplastic nodules and carcinomas reported by Dr. Hildebrandt as compared with the findings by NCI (1980) and Squire Associates (1983) are summarized below.

TABLE II-3

Summary of Incidences of Neoplastic Nodules and Carcinomas in Livers of Female Rats

Laboratory	Effect and Dose (ug/kg/wk)					
	Neoplastic Nodules			Carcinomas		
	Low 1.25	Mid 2.5	High 5.0	Low 1.25	Mid 2.5	High 5.0
NCI, 1980	10/50	12/50	30/50	0/50	0/50	4/50
Squire Associates, 1983	4/50	7/50	7/50	0/50	0/50	0/50
Hildebrant	5/50	7/50	16/50	0/50	0/50	2/50

The NTP reevaluation (Hildebrant, 1983) shows incidences of liver tumors in the range of 50% less than that of the original 1980 analysis (30 vs. 16 neoplastic nodules and two vs. four hepatocellular carcinomas at the highest dose).

The Agency's Carcinogen Assessment Group (CAG) evaluated and accepted the findings of NTP (Hildebrandt, 1983) and used those data of incidences of neoplastic nodules and carcinomas in female rats as part of the assessment of the carcinogenic potency of HxCDD.

Other data which were used were contained in the original report of the NCI (1980) bioassay and include incidences of tumors for male rats male mice, and female mice. These data and the data from the NTP reevaluation (Hildebrandt, 1983) are presented in Tables II-4 and II-5.

The Carcinogen Assessment Group (McGaughy, 1984) summarized and evaluated the results of the NCI bioassay. In the evaluation it was stated that the bioassay showed positive results for male and female rats (combined liver neoplastic nodules or hepatocellular carcinomas) with the greater response in the females. In the females, carcinomas appeared only in the high-dose group, with a significant dose-response trend for both neoplastic nodules and nodules and carcinomas combined. In the male rats, there was also a trend for neoplastic

nodules and carcinomas combined, but this was only marginally significant. These results are presented in Table II-3, which includes the recent NTP reevaluation of the female rat liver slides. The review shows responses in the range of 50% less than that of the original analysis. The responses for neoplastic nodules and combined nodules and carcinomas are statistically significant.

In female mice, there was a dose-related trend in hepatocellular carcinomas, but only the combined adenomas and carcinomas were significant. In male mice, there was a minor trend in hepatocellular adenomas, but no increase, statistical or otherwise, in hepatocellular carcinomas (Table II-5).

Although no statistically significant increase in carcinomas occurred in mice or rats of either sex, when neoplastic nodules in the rats and hepatocellular adenomas in the rats and hepatocellular adenomas in the mice were included in the data, the results became significant for all groups. The neoplastic nodules in the rats are viewed as evidence of a progression response for cancer development; hepatocellular adenomas in mice are interpreted as indications of potential cancer, though the adenomas may be reversible.

Studies with Furans

Chlorinated dibenzofurans have been shown to be contaminants of pentachlorophenol products. The chemical structures of chlorinated dibenzofurans and chlorinated dibenzo-p-dioxins are similar and levels of contamination of the two chemicals parallel each other. Short term testing (McConnel and Moore, 1979 and Poland et al., 1979) of the furans indicated a functional similarity with the dioxins. Although there are no chronic long term studies, because of the structural similarity and because of their functional similarity in short term testing, chlorinated dibenzofurans could be potential human oncogens as are the chlorinated dibenzodioxins.

Studies with Hexachlorobenzene (HCB)

In Cabral et al. (1977), six-week-old Syrian golden hamsters were fed a diet containing 50, 100 or 200 ppm HCB (99.5% pure) ad libitum for life. Although no hepatomas were observed in the control group, the incidence of hepatomas in the treated hamsters increased from 47% in the 50 ppm female group to 85% in the 200 ppm female group. Similar results were found in the male hamsters.

Cabral et al. (1979) studied the effects of the same dietary levels in Swiss mice. Again, the treated groups (both male and female) had significantly greater incidences of hepatomas when compared to the controls. (See Section II-E for the quantitative risk assessment.)

2. Analysis of Specific Public Comments Concerning Oncogenicity

No comments relevant to oncogenicity were received in response to the PD 1 on pentachlorophenol since it was not a basis of presumption in the PD 1. The comment that follows is a comment submitted in response to the PD 2/3 on the wood preservative uses of pentachlorophenol. The Agency response to each comment are also provided. This comment was previously published in the PD 4 (EPA, 1984) on wood uses of pentachlorophenol and included in this document for completeness. The number in parentheses after the title of the comment is an internal number assigned to each comment received.

Comment Issue #1: Pentachlorophenol oncogenicity and dioxin contamination

The American Wood Preservers Institute (AWPI) (36B) and the National Forest Products Association (NFPA) (36B) claim that the EPA's contention that technical pentachlorophenol presents an oncogenic risk due to hexachlorodibenzo-p-dioxin (HxCDD) and hexachlorobenzene (HCB) is incorrect. The AWPI and the NFPA remark that pentachlorophenol does not contain the 2,3,7,8 TCDD dioxin, most frequently associated with adverse human health effects; and pentachlorophenol's toxic effects are manifested before any such evidence from HxCDD's presence, so that regulatory measures for pentachlorophenol will prevent HxCDD exposure.

AWPI (36B) further contends that the oncogenic risk analysis should be adjusted for the Science Advisory Board's (SAB) (1978) report that 25% of total HxCDD is comprised of isomers most likely to promote tumors. AWPI (36B) and NFPA (36B) comment that typically the HxCDD content in technical pentachlorophenol is well below the 15 ppm listed in the PD 2/3.

The AWPI (36B) and the NFPA (36B) also contend that the EPA's use of the one-hit model to determine the carcinogenicity of HxCDD based on the National Cancer Institute (NCI) gavage assay (1980) is inappropriate because HxCDD is a "promoter" rather than an "initiator" of cancer. They further comment that Schwetz et al. (1978) and other investigators, including Kimbrough and Linder (1978), indicate pentachlorophenol is not an oncogen; any oncogenic potential of HxCDD is through tumor promotion, not initiation. Thus, any HxCDD-related carcinogenic activity would operate through a dose-response mechanism, i.e., the greater the toxic dose above the NOEL, the greater the promotion response. In addition, they claim the absence of positive epidemiological data, together with negative animal test results, support the "promoter" conclusion (AWPI, 36B and NFPA, 36B).

Agency Response: The regulation of both pentachlorophenol and HxCDD is necessary because both pentachlorophenol and HxCDD exposure can cause acute and chronic toxic effects (PD 2/3 on wood preservative uses, pp. 247-367). The oncogenic risks associated with HxCDD exposure have been estimated in the PD 4 on wood uses (Appendix B) to be of the order of magnitude of 10^{-3} based on 15 ppm HxCDD in technical pentachlorophenol even with the protective measures required. Because the required protective measures (e.g., gloves, protective clothing, respirators, etc.) which reduce the acute toxicity and potential teratogenic/fetotoxic risks from pentachlorophenol exposure do not reduce the potential oncogenic risk from long-term exposure to HxCDD to levels where benefits of use outweigh risks, this contaminant must be regulated concurrently and independently. The Agency is requiring an immediate upper limit of 15 ppm HxCDD, a level cited by Rakshpal (1980), SAB (1978), and AWPI (1979) as representative in technical pentachlorophenol, and requiring that this contaminant be further reduced to an upper limit of 1 ppm. The potential oncogenic risk associated with pentachlorophenol results from exposure to the contaminant HxCDD and was discussed in the Wood Preservatives, PD 2/3 (pp.347-363).

Although HCB has also been shown to be an oncogen in laboratory animals (PD 2/3 on wood uses, p. 345) the potential risks from the HCB contaminant in technical pentachlorophenol are negligible compared to those of HxCDD. The quantitative oncogenic risk (PD 4 on wood uses) from pentachlorophenol is based on the HxCDD contaminant alone, because the HCB slope (potency) is significantly lower than the HxCDD slope, such that including the HCB-related risk estimate would have only a negligible effect on the total risk. This was also true for the risk estimates calculated in the PD 2/3 on wood uses (p. 363).

Buser and Bosshardt (1976) report that the forms of dioxins most prevalent in commercial pentachlorophenol are hexa-, hepta-, and octachlorodibenzo-p-dioxins (HxCDD, HpCDD and OCDD, respectively). A small amount of tetrachlorodibenzo-p-dioxin (TCDD) has also been found in pentachlorophenol (Buser and Bosshardt, 1976) but proved not to be the extremely toxic 2,3,7,8-isomer. Because the principal contaminants of pentachlorophenol are the higher order dioxins, the oncogenic potential of pentachlorophenol has been estimated using information which includes the NCI bioassay of 1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxins (Litt, May 24, 1982).

TABLE II-4

HxCDD (Gavage) BIOASSAY (NCI, 1980):
OSBORNE-MENDEL RATS (2 years)-INCIDENCES OF NEOPLASTIC NODULES
AND HEPATOCELLULAR CARCINOMAS

Tumor	Vehicle Control	Untreated Control	Low-Dose 1.25	Mid-Dose 2.5	High-Dose 5	Estimates[a] of q_1^* $(ug/kg/day)^{-1}$
MALE (700g)[b]						
Number of animals examined	74	75	49	50	48	----------
Hepatocellular carcinoma (HC)	0	0	0	0	1(2%)	----------
Neoplastic nodule (NN)	0	2(3%)	0	1(2%)	3(6%)	5.6×10^{-1}
HC + NN combined	0	2(3%)	0	1(2%)	4(8%)[c]	5.9×10^{-1}
Human equivalent dose (ug/kg/dy)	0	0	0.04	0.08	0.15	----------
FEMALE (450g)[d]						
Number of animals examined	75	73	50	50	50	----------
Hepatocellular carcinoma (HC)	0	0	0	0	2(4%)	3.2×10^{-1}
Neoplastic nodule (NN)	2(3%)	1(1%)	5(10%)	7(14%)[c]	16(32%)[e]	3.3
HC + NN combined	2(3%)	1(1%)	5(10%)	7(14%)[c]	18(36%)[e]	3.5
Human equivalent dose (ug/kg/dy)	0	0	0.03	0.06	0.12	----------

a. 95% upper-limit estimate of linear term in the multistage model based on human equivalent dosages using surface area correction.
b. Analysis by NCI (1980)
c. $p < 0.05$ versus vehicle-control
d. Reevaluation by Hildebrandt (1983)
e. $p < 0.001$

TABLE II-5

HxCDD (Gavage) BIOASSAY (NCI, 1980):
B6C3F1 MICE (2 years) - INCIDENCES OF HEPATOCELLULAR CARCINOMAS AND HEPATOCELLULAR ADENOMAS

Tumor	Vehicle Control	Untreated Control	Low-Dose 1.25	Mid-Dose 2.5	High-Dose 5	Estimates[a] of q_1^* $(ug/kg/day)^{-1}$
(MALES)						
Number of animals examined	73	75	50	49	48	----------
Hepatocellular carcinoma (HC)	8(11%)	12(16%)	9(18%)	5(10%)	9(19%)	3.71
Hepatocellular adenoma (HA)	7(10%)	15(20%)	5(10%)	9(18%)	15(31%)[b]	6.99
Combined HA and HC	15(21%)	27(36%)	14(29%)	14(29%)	24(50%)[c]	11.00
Human equivalent dose (ug/kg/dy)	0	0	0.014	0.027	0.054	----------
(FEMALES)						
Animal dose (ug/kg/wk)	0	0	2.5	5.0	10	----------
Number of animals examined	73	74	48	47	47	----------
Hepatocellular carcinoma (HC)	1(1%)	0	0	2(4%)	2(4%)	9.15×10^{-1}
Hepatocellular adenoma (HA)	2(3%)	2(3%)	4(8%)	4(9%)	9(19%)[b]	2.61
Combined HA and HC	3(4%)	2(3%)	4(8%)	6(13%)	10(23%)[b]	2.94
Human equivalent dose (ug/kg/dy)	0	0	0.027	0.054	0.107	----------

a. 95% upper-limit estimate of linear term in the multistage model based on human equivalent dosages using surface area correction.
b. $p < 0.01$ versus vehicle-control
c. $p < 0.001$

Although it may be that only 25% of the isomers of HxCDD have been shown to cause tumors in laboratory animals, the Agency assumes, for the purpose of developing regulations, that there may be a structure-function relationship for isomers of the same chemicals and takes a conservative regulatory position in the absence of data to the contrary. The HxCDD oncogenic risk estimate therefore reflects this position; i.e., that 100% of the isomers of HxCDD which are contaminants of pentachlorophenol and sodium pentachlorophenate are potential human carcinogens.

Regarding AWPI's (36B) comment that the HxCDD content is typically below 15 ppm, the Agency received data from several manufacturers which indicated that the HxCDD concentration in technical pentachlorophenol could be as high as 23 ppm but was usually approximately 15 ppm. The Agency chose 15 ppm as representative level for purpose of risk estimation in the Wood Preservatives PD 2/3 as well as in the PD 4. The Agency has received no data on HxCDD to the contrary.

The issue of whether the isomers of HxCDD are promoters rather than initiators is not germane to model fitting. Seven low-dose extrapolation models were used and the one with the best data fit is the multistage model (Litt, May 24, 1982). The multi-stage model has proven to be an appropriate choice based on mathematical, theoretical and biological grounds (Appendix to Water Quality Criteria Document; November 28, 1980 [45 FR 79318]). Further discussion of the multistage model is provided in Section II-E of this document.

The Agency agrees that pentachlorophenol itself has not been shown to be oncogenic in laboratory animals (PD 2/3 on wood uses p. 344), but this does not negate the findings by NCI (1980) that HxCDD, a contaminant in pentachlorophenol, has been shown to cause tumors in laboratory animals. It is the Agency's position that exposure to pentachlorophenol containing HxCDD presents a potential oncogenic risk to humans.

Epidemiological data submitted by AWPI (#81:30000/28C) indicated no increased deaths or cases of cancer occurred from exposure to pentachlorophenol (or inorganic arsenic) in workers at a wood-treating plant in Hawaii. The Agency reviewed these data and concluded the study was inadequate to assess whether a cancer risk existed among the wood treaters (Gibbs, 1983). Section V.A.2 (Comment #10) of the PD 4 on wood uses discusses this evaluation more fully.

In the absence of adequate epidemiological data, the Agency continues to assume that pentachlorophenol containing HxCDD poses a potential unreasonable adverse effect. Animal data exist which allow the quantitation of risks and provide an adequate basis for regulation.

A recent reevaluation of the NCI (1980) study showed liver lesions from HxCDD dosed rats confirming that HxCDD is oncogenic in laboratory animals. When compared to historical controls, neoplasia incidence is increased among female rats exposed to the highest dose [NTP (Hildebrant), 1983]. There is a clear indication that liver neoplasia in the female rats was associated with HxCDD exposure (Moore, Nov. 4, 1983). Therefore, based on these findings, the Agency has concluded that technical pentachlorophenol presents a potential oncogenic risk to humans due to the HxCDD that is present.

3. Summary of Public Comments Concerning Oncogenicity

The comments received do not rebut the presumption of oncogenicity of commercial pentachlorophenol. The presumption of oncogenicity is based on the determination of oncogenicity for the contaminants HxCDD and HCB.

C. Analysis of Rebuttal Comments Concerning Human Exposure

The rebuttal comments that follow were submitted in response to the PD 1 on pentachlorophenol. The Agency responses to each comment are also provided.

Rebuttal Comment 1: Distinguish Between Cooling Tower Use and Agriculture Use of Penta

The Cooling Tower Institute comments ask EPA to distinguish between cooling tower use and agriculture use of penta. They point out that penta-containing biocides are not consumer products, only small quantities are used, personnel are well trained, and little exposure to the public is likely. They conclude EPA's registration requirements for cooling towers should be different from agricultural use. They believe restricted use classification should not apply to the use of penta products in cooling towers.

Agency Response: EPA agrees that use of penta-containing products for cooling tower use does not lead to public exposure. However, the commentors did not present a conclusive reason for not restricting the use of penta-containing products. In some cases, penta products are added by a metering device, but in most cases they are added by hand. Dermal exposure is potentially high, particularly if gloves are not worn.

Rebuttal Comment 2: Penta in Ionic Form (Non-Volatile) has Insignificant Inhalation Exposure

Dr. Donald Crosby of the University of California at Davis comments that much of the penta in cooling tower water is in

the ionic form and does not volatilize: also, people are not in direct proximity to the cooling towers during their operation. With regard to tanneries and pulp mills, he states the penta is in a non-volatile form and could not directly contribute to significant inhalation exposure.

Agency Response: EPA agrees that penta in cooling tower water and pulp mill slurries is mostly non-volatile and would not contribute to significant inhalation exposure. The personnel who add the penta-containing biocide, would,however, be subject to potentially dermal exposure, particularly if gloves are not worn.

Rebuttal Comment 3: Non-Volatility of Penta in Ionic Form and Concern over Exposure Numbers (Assumptions)

Betz Laboratories echoed Dr. Crosby's comments on the non-volatility of penta in its ionic form and its resulting in insignificant inhalation exposure. Betz also claims exposure to 100 ml of cooling water is excessive as is exposure to air containing penta for two hours/day. The same remarks apply to the use of penta in pulp/paper mills.

Agency Response: The Agency agrees that two hours/day may be excessive. The Agency is basing penta exposure on actual use time rather than time spent in the area. Regardless, the actual penta available for volatilization is low.

Rebuttal Comment 4: O.M. Scott & Son's Co. Granular 2% Penta Lawn Treatment Product

O.M. Scott & Son's Company comment that their granular penta-containing (2%) lawn treatment product to remove moss from lawns is safe as directed and does not lead to significant exposure.

Agency Response: Because of the low concentration and the granular form of the lawn treatment product, the Agency expects minimal exposure if used as directed. The particles are large and dermal contact would not be expected to result in significant dermal absorption. However, there is concern about exposure to children and animals playing in the treated yard.

Rebuttal Comment 5: Use in Drilling Muds, Cooling Towers, Pulp Industry, Joint Compounds

Dow Chemical Company claims that penta use in drilling muds, as a biocide, is safe and effective. Similarly, they contend that penta use in cooling towers and the pulp industry is safe. Dow also claims that use of penta in joint compounds is necessary to prevent mildew during drying.

Agency Response: Use of penta in pulp mills and oil well waters results in negligible human exposure. However, the use of penta in cooling towers, condensers, and air washers may result in high dermal exposure. The use of penta in wall and joint adhesives could result in volatilization of penta into interiors resulting in inhalation exposure.

Rebuttal Comment 6: Blumberg Co., Inc. Product for Tanning Presents No Inhalation Hazard

The Blumberg Company, Inc. states that use of their penta-containing product in the tanning industry does not present an inhalation hazard.

Agency Response: EPA agrees that the inhalation hazard is low because penta is in an ionic form in the tannery baths used. However, dermal exposure, particularly in the handling of hides in solution, can be high. There have been instances where penta entered the food chain from fleshings taken from hides and sold to rendering plants. Renderers then sold the fleshings for incorporation into animal/poultry feed. The use of this feed resulted in penta contamination of eggs and poultry.

Rebuttal Comment 7: Exposure time in Cooling Tower Use

The Chapman Chemical Company claims the time of exposure to penta from cooling towers has been overestimated. Minimal possible contact time is the actual case.

They also claim exposure from home use of penta-containing products can be lessened by more appropriate warning labels.

Agency Response: As mentioned in the Agency's response to Rebuttal Comment 3, the Agency agrees that the possible time of contact with penta in a cooling tower area is less than two hours/day. The Agency is basing penta exposure on an actual use time rather than time spent in the area. Inhalation exposure is not significant.

D. Human Exposure Analysis

1. Introduction

The PD-1 on pentachlorophenol provided exposure estimates for wood and non-wood uses. The non-wood uses addressed in the PD-1 included cooling towers, pulp/paper mills, and tanneries. This exposure assessment will address these uses as well as several others not included in the PD-1. Also, additional information obtained since publication of the PD-1 is used to improve the exposure assessment, particularly with regard to the estimates of the number of applicators/persons exposed to penta and sodium pentachlorophenol (Na-penta) and their current use patterns.

Information presented below discusses how the exposure figures for each use were derived. The exposure estimates as well as the assumptions used in calculating the estimates are summarized in Table II-6.

2. Herbicidal

The use of pentachlorophenol as a herbicide has been discontinued though current registrations still exist. Exposure would be considered high because penta is applied by hand spray.

Exposure during mixing/loading and spraying is very high because of the high concentration of penta. Also, the absorption will be high when mixing/loading because it usually is in solvent which leads to high dermal absorption.

3. Anti-Microbial

a. Working Solutions

Oil Well Water

The application of sodium penta (Na-penta) is made with a metering pump. The final concentration of Na-penta is about 40 ppm, but the user of the product applies Na-penta at the rate of 1000 ppm. Because no dermal or inhalation exposure is expected, exposure from this use is negligible.

Evaporative Condensors

For this site, Na-Penta is applied as a solution. No information on concentration of the product was available, but a similar use concentration of 2,4,5-trichlorophenol contains 17.5 %A.I. (Reese, 1978). Assuming a similar concentration, and the fact that it is added by hand, a worker could be exposed to 6 ml* of concentrate/use. The Na-Penta is generally added

* The 6 ml value represents a mean value from an experiment by Dow Chemical in which liquid pick-up on the skin was measured.

once/week. The exposure estimate is calculated as follows:

6 ml x 0.175 (% AI) x 1000 mg/gm/70kg=

15 mg/kg/day x 50 days =750 mg/kg/yr

The desired concentration in the water is about 150 ppm. It is not anticipated that further contact with the water or significant vaporization will take place. There are an estimated 500 applicators.

Air Washers, Cooling Towers

The exposure estimated for both of these sites was calculated to be identical to those for the evaporative condenser use. There are an estimated 10,000 applicators exposed due to the use of Na-Penta in air washers and 100,000-1,000,000 applicators due to the use in cooling towers.

b. Finished Product Preservative

Adhesive/Sealants

Pentachlorophenol is used as a component in the formulation of sealers and adhesives as a preservative. A formulation containing 90% Na-Penta including isomers is added to the adhesive/sealer to the extent of .25 - 1% weight for weight (w/w). There are an estimated 20 workers involved in formulations of these products and gloves/dust masks are used. For the formulators involved in adding penta, an exposure estimate can be made assuming no inhalation exposure and an applicator will have both hands (no gloves) covered with dust. The exposure estimate is calculated as follows:

200* mg x 0.9 (% AI)/70kg = 2.6mg/kg/day X 250 days = 650 mg/kg/yr

Canning/Sealing and Gaskets

Na-Penta is formulated into cements for use in canning and sealing food and other containers. The Food and Drug Administration (FDA) allows a maximum of 0.05% (w/w) Na-penta in the sealing materials.

The formulation used contains 90% Na-Penta, including 11 isomers. It is added to sealing or gasket material by the applicator. There are an estimated 20 workers directly involved in this use of penta.

*This value was taken from an experiment conducted by Zoecon Corporation. The experiment showed that 200 mg completely whitened all surfaces of the hands of an adult male with a fine powder.

Assuming an applicator will cover both hands (no gloves) with dust daily and no inhalation exposure, the dermal exposure would be (Noren, 1983):

200 mg x .9 (%AI)/70 kg =

2.6 mg/kg/day x 250 days =650 mg/kg/yr

Photographic Solutions

Pentachlorophenol is not currently used in photographic solutions. No exposure figures are available for this use. However, a qualitative assessment would indicate the potential dermal exposure could be high due to the film developing process.

c. Working Solutions and Finished Product Preservatives

Textile/Cordage

Solid Na-Penta is manually added to textile processing solutions. The exposure estimates for this use are calculated similar to that for the adhesives/sealant use. Approximately 10-15 workers would be exposed to this use of penta. Estimates of dermal exposure to users of penta-treated rope are not available.

Pulp/Paper Mills

Na-Penta is added to pulp slurry to inhibit slime and bacteria growth. It is added with a metering pump directly to the slurry (white water) and the usual concentration is 100 ppm. There are 4000-5300 workers who could be potentially exposed to penta from this use. However, since the addition of penta is with a metering device and workers do not usually contact the slurry, there is little opportunity for exposure. Exposure is considered negligible.

Leather Tannery

Na-Penta is used as an antimicrobial agent in various stages of leather production. It is assumed that a worker on the average is exposed dermally to 100 ml/day of penta diluted in solution. The solid concentrate ranges up to 90%, but the diluted solutions are much less.

For the soak, pickle/tan, fat liquor, and finish operations, 100 ml of daily dermal contact is assumed. The exposure estimate calculation is as follows for the soak operation:

100 ml x 300 ppm conc. /70kg = .0004 mg/kg/day

The calculations are the same for the pickle/tan, fat liquor, and finish operations except that the concentrations in ppm are 150, 85, 400 and the daily dermal exposures are .0002, .0001, and .0005 mg/kg, respectively.

For the biocide application, the daily dermal contact is assumed to be 200 mg of formulation/day. The calculation for exposure for this operation is:

200 mg x .9(% AI)/70 kg = 2.6 mg/kg

There is a potential for dietary exposure to penta as a result of its use in the tanning industry. Fleshings from penta-treated hides are sold to renderers who then in turn sell the fleshings for incorporation into animal/poultry feed.

Marine Anti-Fouling Agents

Pentachlorophenol is added to marine caulking/sealer. The concentration of penta for this use is 5%. Approximately 1650 gallons of penta-containing marine sealer are produced in the United States annually, involving about 6-8 workers.

It is estimated that plant workers will contact 100% penta as dust and that 200 mg will cover the hands (Noren, 1983). Assuming 1650 gallons are produced annually at 70 gallons/batch, there are 24 batches made per year. The exposure estimate is calculated as follows:

200 mg/70 kg = 2.8 mg/kg/day x 24 batches = 67 mg/kg/yr

Since manufacturing is done using a fume hood, inhalation exposure is considered negligible.

Approximately 850 gallons of penta-containing marine sealer are used in the U.S. Assuming contact with 6000 mg of 5% (AI) penta product/yr, the estimated exposure is:

6000 mg(0.05)/70kg = 4.2 mg/kg/yr

The use of pentachlorophenol in marine paints was discontinued in 1981, but the use is still registered. No exposure estimates are available.

d. Mushroom Houses

Dry 100% AI Na-Penta is used in a 1700 ppm solution for spray application for mushroom house exteriors, as a tool disinfectant dip, and around the grounds of mushroom houses. Spraying is done 0.5 hr/day from 15-52 days/yr.

Assuming dermal contact with 200 mg of dry Na-Penta, the dermal exposure estimate is:

200 mg/70kg = 3 mg/kg/day x 50 days/yr = 150 mg/kg/yr

Because the solution is only sprayed or used outside and in a salt solution, inhalation exposure is expected to be negligible because in the salt form vaporization is negligible. However, spray application does produce inhalable particles which can be inhaled or swallowed. In the Wood Preservative, Position Document 2/3, it was determined that the Na-Penta air concentration near a sapstain operation was 70 ug/m^3. Since the sapstain solution is about three times the mushroom house use rate (5000 ppm vs. 1700 ppm), the air concentration near the spraying can be estimated at about 24 ug/m^3. The inhalation exposure estimate is:

24 ug/m^3 x 1.8 m^3/hr x .5 hr/day/70kg =

0.3 mg/kg/day x 50 days = 15 mg/kg/yr

e. Mossicide

Pentachlorophenol is commonly used in the Pacific Northwest to control moss growth on roofs. Two different penta products are used: Na-Penta (28.2% AI) and pentachlorophenol (40% AI). The penta products, 28.2% and 40%, are made-up into solutions of 2.1% and 4%, respectively.

For mixing/loading, dermal contact is assumed to be 6 ml of concentrate. The exposure estimates are as follows:

Penta: 6 ml (.04) x 1000 mg/gm/70kg = 34 mg/kg/use

Na-Penta: 6 ml (.282) x 1000 mg/gm/70kg = 24 mg/kg/use

For brush or spray application, dermal contact is assumed to be 12 ml of concentrate. The exposure estimates are as follows:

Penta: 12 ml (.04) x 1000 mg/gm/70kg = 8 mg/kg/use

Na-Penta: 12 ml (.021) x 1000 mg/gm/70kg = 4 mg/kg/use

For spray application, there will be some inhalation exposure. The roof spraying operation will take 2 hours. Inhalation exposure is estimated to be:

Penta: 560 ug/m^3 x 1.8 m^3/hr/1000ug/mg x 2 hr/70kg =

.02 mg/kg/use

Na-Penta: .02 x 300/560 = 0.01 mg/kg/use

Penta is added to granular formulations containing fertilizer/filler, and applied with a lawn spreader. The concentration of penta used is 1%. Since little handling of the formulation takes place, exposure is estimated to be negligible.

f. Defoliant

Alfalfa grown for seed production is treated with pentachlorophenol, which acts as a dessicant. The single formulation for this use is a 40% AI product to be diluted at the rate of 2-3 quarts/5-10 gallons of oil per acre. Penta is not currently used on alfalfa. Therefore, no applicator exposure information is available. Potential dietary exposure to pentachlorophenol as a result of this use may occur. There are no established tolerances for this use.

TABLE II-6

SUMMARY OF EXPOSURE ANALYSIS FOR NON-WOOD USES OF PENTACHLOROPHENOL

USE	ASSUMPTIONS USED IN ANALYSIS	PERSONS EXPOSED	EXPOSURE (ug/kg/) DAILY DERMAL	DAILY INHALATION	YEARLY DERMAL	YEARLY INAHALATION
HERBICIDE USE [1/]						
1. Greenhouses	Low Usage	----	------- no exposure data available ------			
2. Ornamental lawns and edging						
3. Rights-of-Way						
4. Commercial and industrial non-crop areas						
5. Domestic dwellings, public facilities, golf courses and sand traps						
6. Wasteland areas						
7. Aquatic Areas						

1/Pentachlorophenol use as a herbicide has been essentially discontinued because more effective substitutes are available.

TABLE II-6

SUMMARY OF EXPOSURE ANALYSIS FOR NON-WOOD USES OF PENTACHLOROPHENOL

USE	ASSUMPTIONS USED IN ANALYSIS	PERSONS EXPOSED	EXPOSURE (ug/kg)* DAILY DERMAL	DAILY INHALATION	YEARLY DERMAL	YEARLY INAHALATION
ANTI-MICROBIAL						
Working Solutions 1. Oil Well Water	a. 15-39 ppm use conc. NA-Penta b. metering pump used in application c. Estimated Application Frequency: 2 hr/day, 25 day/yr	-------	-------NEGLIGIBLE EXPOSURE----------			
2. Evaporative Condensers	a. 17.5% use conc. NA-Penta (similar to 2,4,5 Trichlorophenol (Reese, 1978)) b. applied as solution c. concentrate added by hand d. 6 ml concentrate/use e. 150 ppm desired concentration f. Estimated Application Frequency: 1 hr/day, 50 day/yr	500	15,000	--------	750,000	-------
3. Air Washers	a. 17.5% use conc. NA-Penta (similar to 2,4,5 Trichlorophenol (Reese, 1978)) b. applied as solution c. concentrate added by hand d. 6 ml concentrate/use e. 150 ppm desired concentration f. Estimated Application Frequency: 1 hr/day, 50 day/yr	10,000	15,000	-------	750,000	--------
4. Cooling Towers	a. 17.5% use conc.. NA-Penta b. applied as solution c. concentrate added by hand, some sites use pump device d. 6 ml concentrate/use e. 150 ppm desired concentration f. Estimated Application Frequency: 1 hr/day, 50 day/yr	100,000	15,000	-------	750,000	--------

*dermal absorption factors not incorporated

TABLE II-6

SUMMARY OF EXPOSURE ANALYSIS FOR NON-WOOD USES OF PENTACHLOROPHENOL

USE	ASSUMPTIONS USED IN ANALYSIS	PERSONS EXPOSED	EXPOSURE (ug/kg) DAILY DERMAL	DAILY INHALATION	YEARLY DERMAL	YEARLY INAHALATION
ANTI-MICROBIAL						
Finished Product Preservatives						
1. Adhesives/Sealants	a. 90% NA-Pentsa and isomers b. .25-1% w/w in product c. negligible end use exposure d. formulators use gloves and dust masks e. formulators: 200 mg to cover hands f. Estimated application frequency: 1/6 hr/day, 250 day/yr	20	2,600	-----	650,000	------
2. Canning/Sealing	a. 90% NA-Penta and isomers b. .05% max w/w in product (FDA) c. no gloves d. formulators: 200 mg to cover hands e. Estimated application frequency: 1/6 hr/day, 250 day/yr	20	2,600	-----	650,000	------
3. Gaskets		----------low usage----no exposure data available---				
4. Photo Developing Solutions		---------- no exposure data available ----------				
5. Latex paint/Rubber, Defoaming agents, Paper coatings, polvinyl chloride emulsions, zinc-silicone dioxide coatings, feathers.		----------low usage----no exposure data available---				

*dermal absorption factors not incorporated

TABLE II-6

SUMMARY OF EXPOSURE ANALYSIS FOR NON-WOOD USES OF PENTACHLOROPHENOL

USE	ASSUMPTIONS USED IN ANALYSIS	PERSONS EXPOSED	EXPOSURE (ug/kg)* DAILY DERMAL	DAILY INHALATION	YEARLY DERMAL	YEARLY INHALATION
ANTI-MICROBIAL						
Working Solutions and Finished Product Preservatives						
1. Textile/Cordage	a. Solid beads 100% NA-Penta b. Manually added to treating solution c. Rope content: .3% NA-Penta d. formulators: 200 mg to cover hands e. Estimated application frequency: 1/20 hr/day, 250 day/yr	15	2,600	-----	650,000	------
2. Pulp/Paper Mills	a. 1-700 ppm NA-Penta use conc. b. metering pump used	5,000	---------NEGLIGIBLE EXPOSURE---------			
3. Leather Tannery Soak	a. 300 ppm Na-Penta b. daily contact with 100 ml c. Estimated application frequency: 7 hr/day, 250 day/yr	35	.4	-----	100	------
Pickle/Tan	a. 150 ppm Na-Penta b. daily contact with 100 ml c. Estimated application frequency: 7 hr/day, 250 day/yr	700	.2	-----	50	------
Fat Liquor	a. 85 ppm Na-Penta b. daily contact with 100 ml c. Estimated application frequency: 7 hr/day, 250 day/yr	160	.1	-----	25	------
Finish	a. 400 ppm Na-Penta b. daily contact with 100 ml c. Estimated application frequency: 7 hr/day, 250 day/yr	300	.5	-----	125	------
Biocide/ Application	a. 900,000 ppm Na-Penta b. daily contact with 200 mg c. Estimated application frequency: 1/6 hr/day, 250 day/yr	100	2,600	-----	650,000	------

*dermal absorption factors not incorporated

TABLE II-6

SUMMARY OF EXPOSURE ANALYSIS FOR NON-WOOD USES OF PENTACHLOROPHENOL

USE	ASSUMPTIONS USED IN ANALYSIS	PERSONS EXPOSED	EXPOSURE (ug/kg)* DAILY DERMAL	DAILY INHALATION	YEARLY DERMAL	YEARLY INAHALATION
ANTI-MICROBIAL						
Marine Anti-Fouling Agents						
1. Marine Calking						
a. Manufacturing	a. 100% Penta b. product conc. is 5% c. 200 mg 100% penta can cover hands d. Estimated application frequency: 1.5 hr/day, 4 day/yr e. Manufacturing addition uses fume food	8	2,800	-------	67,000	--------
b. Use	a. 5% Penta b. Applied with brush or towel c. 6 gms/yr d. Estimated application frequency: 4 hr/day, 1 day/yr	850	4,200	------	4,200	--------
2. Marine Paints	Low Usage	---------low usage------no exposure data available----				
Mushroom Houses	a. 1700 ppm Na-Penta b. sprayed on house exterior, tool disinfectant dip, around grounds of houses c. 200 mg dry Na-Penta d. air concentration near spraying: 24 ug/m^3 (comparing to sapstain operation) e. Estimated application frequency: .5 hr/day, 50 day/yr	500	3,000	300	150,000	15,000
Construction Materials	Low Usage	----------low usage-----no exposure data available----				

*dermal absorption factors not incorporated

TABLE II-6

SUMMARY OF EXPOSURE ANALYSIS FOR NON-WOOD USES OF PENTACHLOROPHENOL

USE	ASSUMPTIONS USED IN ANALYSIS	PERSONS EXPOSED	EXPOSURE (ug/kg)* DAILY DERMAL	DAILY INHALATION	YEARLY DERMAL	YEARLY INHALATION
MOSSICIDE						
1. Roofs						
Mix 1	a. 40% Na-Penta in organic solvent	N.A.	34,000	----	34,000	------
Mix 2	a. 28.2% Na-Penta in water b. contact w/ 6 ml conc. for mixing/ loading c. Estimated application frequency: 1 day/yr,	N.A.	24,000	----	24,000	------
Application 1	a. 4% Na-Penta in organic solvent	N.A.	8,000	20(spray)	8,000	20(spray)
Application 2	a. 2.1% Na-Penta in water b. can brush or spray c. spray has inhalation exposure d. dermal contact with 12 ml e. roof spraying--2 hr f. Estimated application frequency: 1 day/yr	N.A.	4,000	10(spray)	4,000	10(spray)
2. Lawns	a. 1% granular Penta b. applied with lawn spreader	----------NEGLIBIBLE EXPOSURE----------				
DEFOLIANT						
Seed (non-food): Alfalfa, Clover, Bird foot trefoil, and Lespedeza	Low Usage	---------- no exposure data available --------				

*dermal absorption factors not incorporated
N.A. = data not available

E. Risk Assessment for Fetotoxic and Oncogenic Effects

1. Risk Assessment for Fetotoxic Effects

The Agency has calculated individual values of the Margin of Safety (MOS) for the fetotoxicity risk assessment of penta and its major contaminants for the population sub-groups exposed. The MOS value is the ratio of the NOEL for fetotoxicity in animal experiments to the appropriate sub-group exposure value.

The following absorption factors are assumed in calculating the MOS values (Zendzian, 1982):

Dermal absorption

penta and its salts	= 1%
penta in organic solvent	= 50%
HxCDD	= 50%

Inhalation Absorption = 100%

The following NOEL values have been used in the MOS calculations for penta and two of its major contaminants:

Penta: 3,000 ug/kg/day = 3 mg/kg/day (Schwetz et al., 1978)

HxCDD: 0.1 ug/kg/day (Schwetz et al., 1973)

HCB: 1,000 ug/kg/day = 1 mg/kg/day (Grant et al., 1977)

MOS Values based on the accompanying exposure values are presented in the Table II-7 assuming no protective clothing (gloves). MOS values for HxCDD are given for both 15 ppm and 1 ppm because technical penta generally contains 15 ppm HxCDD but as required by the PD 4 on the wood preservative use of pentachlorophenol the HxCDD contamination will be required to be reduced to 1 ppm. Exposures to the HCB in penta have been determined by the Agency to range below 3.4×10^{-3} ug/kg/day and thus HCB MOS values are all above 10,000. Therefore, the MOS values for exposure to HCB in penta are not tabulated.

TABLE II-7

Margins of Safety for Fetotoxic Effects of Penta and HxCDD

Use	Penta MOS	HxCDD MOS 15 ppm	HxCDD MOS 1 ppm
HERBICIDAL	-------no exposure data available------		
ANTI-MICROBIAL			
Working Solutions			
1. Oil Well Water	----------negligible exposure----------		
2. Evaporative Condensers	20	0.87	13
3. Air Washers	20	0.87	13
4. Cooling Towers	20	0.87	13
Finished Product Preservatives			
1. Adhesives/Sealant	120	5.1	77
2. Canning/Sealing	120	5.1	77
3. Gaskets	---low usage---no exposure data available--		
4. Photo Developing Solutions	---low usage---no exposure data available--		
5. Latex paint/Rubber, defoaming agents, paper coatings emulsions, zinc-silicone dioxide coatings, feathers	---low usage--no exposure data available--		
Working Solutions and Finished Product Preservatives			
1. Textile/Cordage	120	5.1	77
2. Pulp/Paper Mills	----------negligible exposure----------		
3. Leather Tannery			
Soak	>10,000	>10,000	>10,000
Pickle/Tan	>10,000	>10,000	>10,000
Fat Liquor	>10,000	>10,000	>10,000
Finish	>10,000	>10,000	>10,000
Biocide/ Application	120	5.1	77

TABLE II-7

Margins of Safety for Fetotoxic Effects of Penta and HxCDD

Use	Penta MOS	HxCDD MOS 15ppm	HxCDD MOS 1ppm
4. Marine Anti-Fouling Agents			
Marine Caulking			
Manufacturing	110	4.8	72
Use	71	3.2	48
Marine Paints	---low usage----no exposure data available---		
Mushroom Houses	9.1	3.7	56
Construction Materials	---low usage----noe exposure data available---		
MOSSICIDE			
Roofs			
Mix 40%	.18	0.39	5.9
Mix 28.2%	13.0	0.56	8.3
Application			
4%	.75(brush)	1.7(spray)	25(spray)
	.75(spray)	1.7(brush)	25(brush)
2.1%	75(brush)	3.3(spray)	50(spray
	60(spray)	3.3(brush)	50(brush)
Lawns	---------negligible Exposure----------		
DEFOLIANT			
Alfalfa	----low usage---no exposure data-available---		

2. Risk Assessment for Oncogenic Effects

The National Cancer Institute bioassay study (1980) indicated that HxCDD is oncogenic. HxCDD administered to female rats caused a toxic hepatitis and an increase in the incidences of neoplastic nodules and liver tumors. The chlorinated dibenzofurans could also be potential human oncogens as are the chlorinated dibenzodioxins because of the structural similarity and functional similarity in short term testing. In the Cabral et al. 1977 and 1979 studies, the HCB treated groups had significantly greater incidences of hepatomas when compared to the controls thereby indicating HCB's potential oncogenicity.

The oncogenicity risk assessment for penta on the HxCDD Rodent Bioassays follows the method and model developed in the Position Document 4 on the wood uses of pentachlorophenol. The "multi-stage model" was used in calculating the risk and the carcinogenic potency of HxCDD was taken to be the geometric mean of the 95% upper-limit estimates from the male mouse and the female rat. The carcinogenic potency is estimated to be $q_1^* = 6.2\ (ug/kg/day)^{-1}$. To estimate the potential risk (R) to humans from exposure to the HxCDD contamination in pentachlorophenol and its salts, the Agency used the following equation:

$$R = 6.2\ (ug/kg/day)^{-1} \times \text{HxCDD exposure}$$

where the exposure is expressed in ug/kg/day averaged over a lifetime. This exposure value does include the appropriate assumed absorption factors of 1% for penta and its salts, 50% for penta in organic solvent, and 100% of inhalation. The Agency assumes that the average work life is 30 years and that the average life span is 70 years. When q_1^* is multiplied by individual exposures an upper bound risk estimate of carcinogenicity is obtained. Under the assumption of a linear extrapolation model, the values derived are upper bound estimates for which the true risk would not likely exceed the upper bound value and may be lower.

The upper bound estimates of the cancer risks to unprotected workers exposed to penta are presented in Table II-8.

Risk estimates are presented for: worst case daily estimates assuming 15 ppm and 1 ppm HxCDD contamination and average daily lifetime estimates for the 15 and 1 ppm HxCDD contaminant.

The computations involved in calculating the risks are shown below; recall that exposure is multiplied by the potency estimate $q_1^* = 6.2\ (ug/kg/day)^{-1}$.

$$\text{WCE (15 ppm)} = q_1^* \times (50\% \text{ absorption} \times \text{Daily Dermal} + \text{Inhal.}) \times \frac{15 \text{ parts HxCDD}}{1{,}000{,}000}$$

$$\text{WCE (1 ppm)} = q_1^* \times (50\% \text{ absorption} \times \text{Daily Dermal} + \text{Daily Inhal.}) \times \frac{1 \text{ part HxCDD}}{1{,}000.000}$$

$$\text{ADL (15 ppm)} = q_1^* \times (50\% \text{ absorption} \times \text{Yearly Dermal} + \text{Yearly Inha.}) \times \frac{30 \text{ work Yr.}}{70 \text{ yr. lifetime}} \times \frac{1 \text{ Yr.}}{365 \text{ day}} \times \frac{15 \text{ parts HxCDD}}{1{,}000{,}000}$$

$$\text{ADL (1 ppm)} = q_1^* \times (50\% \text{ absorption} \times \text{Yearly Dermal} + \text{Yearly Inhal.}) \times \frac{30 \text{ work Yr.}}{70 \text{ yr. lifetime}} \times \frac{1 \text{ Yr.}}{365 \text{ day}} \times \frac{1 \text{ part HxCDD}}{70 \text{ yr. lifetime}}$$

TABLE II-8

Risk Estimates for Oncogenic Effects of HxCDD

Use	Risk Estimates Using Daily HxCDD Exposure Risk		Using Average Daily Lifetime HxCDD Exposure	
	15 ppm	1 ppm	15 ppm	1 ppm
HERBICIDAL	---low usage--no exposure data available------			
ANTI-MICROBIAL				
Working Solutions				
1. Oil Well Water	----------negligible exposure----------			
2. Evaporative Condensers	7×10^{-1}	5×10^{-2}	3×10^{-2}	2×10^{-3}
3. Air Washers	7×10^{-1}	5×10^{-2}	3×10^{-2}	2×10^{-3}
4. Cooling Towers	7×10^{-1}	5×10^{-2}	3×10^{-2}	2×10^{-3}
Finished Product Preservatives				
1. Adhesives/Sealant	1×10^{-1}	8×10^{-3}	3×10^{-2}	2×10^{-3}
2. Canning/Sealing	1×10^{-1}	8×10^{-3}	3×10^{-2}	2×10^{-3}
3. Gaskets				
4. Photo Developing Solutions	---low usage--no exposure data available------			
5. Latex paint/Rubber, defoaming agents, paper coatings emulsions, zinc-silicone dioxide coatings feathers	---low usage--no exposure data available------			
Working Solutions and Finished Product Preservatives				
1. Textile/Cordage	1×10^{-1}	8×10^{-3}	4×10^{-2}	2×10^{-3}
2. Pulp/Paper Mills	----------negligible exposure----------			

TABLE II-8

Risk Estimates for Oncogenic Effects of HxCDD

Use	Risk Estimates Using Daily HxCDD Exposure Risk		Using Average Daily Lifetime HxCDD Exposure	
	15 ppm	1 ppm	15 ppm	1 ppm
3. Leather Tannery				
Soak	2×10^{-5}	1×10^{-6}	5×10^{-6}	3×10^{-7}
Pickle/Tan	9×10^{-6}	6×10^{-7}	2×10^{-6}	2×10^{-7}
Fat Liquor	5×10^{-6}	3×10^{-7}	1×10^{-6}	8×10^{-8}
Finish	2×10^{-5}	2×10^{-6}	6×10^{-6}	4×10^{-7}
Biocide/ Application	1×10^{-1}	8×10^{-3}	3×10^{-2}	2×10^{-3}
4. Marine Anti-Fouling Agents				
Marine Caulking				
Manufacturing	1×10^{-1}	9×10^{-3}	3×10^{-3}	2×10^{-4}
Use	2×10^{-1}	1×10^{-2}	2×10^{-4}	1×10^{-5}
Marine Paints	---low usage--no exposure data available------			
Mushroom Houses	2×10^{-1}	1×10^{-2}	8×10^{-3}	8×10^{-4}
Construction Materials	---low usage--no exposure data available------			
MOSSICIDE				
Roofs				
Mix 40%	1.6	1×10^{-1}	2×10^{-3}	1×10^{-4}
Mix 28.2%	1.1	7×10^{-2}	1×10^{-3}	7×10^{-5}
Application				
40%	4×10^{-1}	3×10^{-2}	4×10^{-4}	3×10^{-5}
2.1%	2×10^{-1}	1×10^{-2}	2×10^{-4}	1×10^{-5}
Lawns	----------negligible exposure----------			
DEFOLIANT				
Alfalfa	---low usage--no exposure data available-------			

F. Alternatives

This section provides a brief discussion of the toxicological characteristics of the available alternatives of the non-wood uses of penta. The objective of this section is to present an overview of toxicology data derived from literature reviews.

The chemicals considered as possible alternatives to penta are presented below according to use. The suitability and use of the alternatives is discussed in the Benefits Analysis, Part III of this document.

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
DEFOLIANTS/HERBICIDES			
	Glyphosate	Primary Eye Irrit. (rabbit)	Score*= 27/110
		Primary Derm. Irrit. (rabbit)	Score= 0.0/8.0, (Tox Cat IV)
		Mutagenicity	(-) Dominant lethal, (-) host mediated rat & mouse assay, (-) Ames test, (-) recomb. assay
		Teratology (rabbit)	NOEL= 1000 mg/kg (feto-tox & maternal), LEL= 3500 mg/kg (death, wght gain, stomach hemorrhage), no terata at 3500 mg/kg
		Neutoxicity (hens)	IBT study, no neurotox signs or treatment-related leasons, body wght depression
		21-Dy Dermal Study (rabbit)	NOEL= 1000 mg/kg, LEL= 5000 mg/kg (slight erythema/edema)
		26-Mo Feeding Study (rat)	NOEL= 31 mg/kg, no increased tumor incid.
		3-Gen. Repro. Study (rat)	NOEL= 10 mg/kg, LEL= 30 mg/kg (renal focal tubule dilation in F_3b gen.)
		Risk Assessment	Thyroid C-cell tumor
	Endothall	Primary Eye Irrit. (rabbit)	Severe corneal involve. some animals died, 1-4% A.I. caused mod. irrit.

* The term "score" refers to a standardized system to measure the severity of the effect being tested for.

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
DEFOLIANTS/HERBICIDES (cont'd)	Endothall (cont'd)	Primary Derm. Irrit. (rabbit)	1% A.I. caused minimal skin lesions, 10% A.I. caused necrosis, formulated product caused some deaths
		Acute Dermal Study (rabbit)	All animals died at 200 mg/kg, (Tox Cat I)
	Sodium Chlorate	Primary Eye Irrit. (28% A.I.)(rabbit)	Transcient conjunctival irritation
		Subchronic Drinking Water Study (monkey)	No adverse hematological or clinical effects to 400 ppm
	Cacodylic Acid	Primary Eye Irrit. (1.26% A.I.) (rabbit)	No irritation
		Primary Derm. Irrit. (1.26% A.I.) (rabbit)	Score= 0.9/8.0
	s,s,s-Tributylphos-phorotrithioate (DEF)	2-Yr Feeding Study (rat)	NOEL= 25 ppm, LEL= 100 ppm (decreased body wght, liver cell vacuolation), NOEL< 5 ppm (rcb ChE inhibition)
		2-Yr Feeding Study (dog)	NOEL= 50 ppm, NOEL< 5 ppm (plasma/rbc ChE inhibition)
		3-Gen. Repro. Study (mouse)	NOEL> 100 ppm

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
DEFOLIANTS/HERBICIDES (cont'd)	Ametryne	Primary Eye Irrit. (rabbit)	Mild Irrit.(Tox Cat IV)
		Primary Derm. Irrit. (rabbit)	Score=0.0/8.0 (Tox Cat IV)
		Mutagenicity	(-) Reverse mutation, (-) Recomb. assay
		90-Dy Feeding Study (rat)	NOEL= 1000 ppm
		90-Dy Intubation Study (rat)	NOEL= 100 ppm
	Zinc Chloride	Subchronic Feeding (rats)	NOEL= 660 ppm
		Injection Studies (rats/chickens)	Testicular tumors by injection, no oncogenic effects by other routes
		Chronic Feeding (rats)	NOEL= 1500 ppm
		Use Experience	Chemical burns, TWA for zinc chloride fumes= 1 ppm
	Paraquat	Teratogenicity, (mouse)	Not teratogenic at 10 mg per ion/mg (HDT)
		Teratogenicity, (rat)	Not teratogenic at 10 mg per ion/mg.
			NOEL (fetotoxicity) = 1.0 mg/kg
			LEL (fetotoxicity) = 5.0 mg/kg (reduced wt. and retarded ossification)

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
	Paraquat		NOEL (maternal tox) = 1.0 mg/kg
		Acute dermal (rabbit)	LD_{50} = 60 mg per ion/kg
		Primary Eye Irrit.	Opacity, severe pannus (Category I)
		Primary Skin Irrit.	PIS = 2.1 (Category III)
		90-day feeding (dog)	NOEL = 0.5 mg per ion/kg LEL = 1.5 mg per ion/kg (alveolas collapse)
		Oncogenicity (mouse)	Not oncogenic up to 19.0 mg par. ion/kg NOEL = mg per ion/kg LEL = 5.6 mg/kg (renal tubular degeneration and weight loss).
		Mutagenicity Reverse mutation in R. typhimurium	Negative up to 5000 ug/plate
		Cytogenetic (bone marrow), rat	Negative up to 19.0 mg/kg/day
		Dominant lethal (mouse)	Negative up to 4.0 mg per ion/kg
	Zinc Sulfide	Pertinent data not available	
	Ferric Sulfate	Pertinent data not available	
	Zinc Sulfate	Pertinent data not available	

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS			
Working Solutions-Oil Well Flood Waters	Chlorine Dioxide	Acute Inhalation (rat)	No irritation or death after 4 hrs.
		Primary Derm. Irrit. (rabbit)	Score= 6.6/8.0
		Primary Eye Irrit.	Score=10.5/110
	Chlorine Gas	1977 NIOSH Ceiling	Max.conc.$_{15min}$= 0.5 ppm
Working Solutions-Cooling Towers	4-Chloro-2-phenylphenol	Primary Eye Irrit. (rabbit)	Conc.: severe corneal irrit., 1% A.I.: slght irrit.
		Primary Derm. Irrit. (rabbit)	0.1% A.I.: no irrit., >1% A.I.: dose related irritation
		Human Sensitization	No irritation or sensit.
	2-benzyl-4-chlorophenol	Primary Eye Irrit. (9.7% A.I.)(rabbit)	Score= 104/110
		Primary Derm. Irrit. (9.7% A.I.)(rabbit)	Severe irritant
		Human Sensitization (9.7% A.I.)	None
		90-Dy Feeding Study (rat)	Organ wght changes at all doses, LDT= 30 ppm
	dichloro-s-triazine-trione	Primary Eye Irrit. (rabbit)	Corneal damage, no irrit. at 310 ppm
		30-Dy Eye Irrit. (rabbit)	No irrit. at 100 ppm
		Subchronic Oral (dog) (dog)	NOEL= 6.8% diet

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Finished Product Preservatives-Adhesives & Sealants	o-Phenylphenol	Primary Eye Irrit. (18% A.I.)(rabbit)	Corneal damage
		Primary Derm. Irrit. (18% A.I.)(rabbit)	Skin damage
		Human Derm. Irrit. (18% A.I.)	No irritation
		2-Yr. Feeding Study (rat)	No dose related tumor incidence between 0.02-2.0% of diet. Renal damage & increased testes at high dose.
		Japanese Study	Possible tumor incidence
		1-Yr.Feeding (dog)	No dose related histopathology between 0.02-0.5 gm/kg, but elevated kidney damage at high dose.
		Mutagenicity	Negative Ames test with & without activation
	Copper-8-quinolinate	Acute Dermal (rabbit)	LD_{50}> 2000 mg/kg, no dermal irrit. or signs (Tox Cat III)
		Primary Eye Irrit. (rabbit)	Slight reversible conjunctival irrit. (Tox Cat III)

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Finished Product Preservatives-Adhesives & Sealants (cont'd)			
		Acute Inhalation (rat)	LC_{50}= 0.82 mg/L (Tox Cat II)
		2-Yr. Feeding Study (rat)	No effects on behavior, mortality, hematology, blood chemistry or organ weights at dose between 5-2000 ppm in diet. NOEL= 500 ppm
		2-Yr. Feeding Study (dog)	Dose between 10-3000 ppm in diet. NOEL= 200 ppm, changes in liver & lungs
		2 Gen. Reproduction (rat)	Not teratogenic, NOEL>500 ppm
		Mutagenicity	Weak (+) Ames test, (+) mitotic recomb., (-) DNA repair test, (-) micronucleus test
	Formaldehyde	Teratogenicity (dog)	Not teratogenic, HDT= 375 ppm, NOEL> 375 ppm
		Teratogenicity (mouse)	Not teratogenic, HDT= 185 ppm, maternal NOEL= 148 mg/kg, LEL= 185 mg/kg (mortality)

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Finished Product Preservatives-Adhesives & Sealants (cont'd)		90-Dy Inhalation (rat)	NOEL= 0.028 ppm, LEL= 0.82 ppm (proliferation of lung lymphocytes & histocytes, perivascular hyperemia
		18-Mo. Onco. Inhal. (rat)	Carcinomas at 15 ppm
		Mutagenicity	(+) in E.coli & P.fluorescens, (-) S.typhimurium
		Primary Eye Irrit. (37% A.I. & 7% methanol) (rabbit)	Corneal burn/opacity
		Primary Derm. Irrit. (37% A.I. & 7% methanol) (rabbit)	Vesicle formation with superficial necrosis or nodules
	Copper Sulfate	Primary Eye Irrit. (18% A.I.) (rabbit)	Score= 10/110
		Primary Eye Irrit. (99% A.I.) (rabbit)	Corrosive

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Finished Product Preservatives-Adhesives & Sealants (cont'd)			
		Primary Derm. Irrit. (18% A.I.) (rabbit)	Score= 0.0/8.0
		Potable Water Toler.	1.0 ppm copper residue in water from lakes, reserviors, etc.
	p-Chloro-m-cresol	Primary Eye Irrit. (rabbit)	Corneal cauterized
		Primary Eye Irrit. (17% A.I.) (rabbit)	Corneal opacity
		Primary Derm. Irrit. (17% A.I.) (rabbit)	Score= 8.0/8.0
		Sensitization (G. pig)	Positive
		21-Dy Derm. Study (rabbit)	NOEL> 10 mg/kg/dy (LDT) (slight erythema), NOEL= 40 mg/kg/dy (liver)
		90-Dy Feeding Study (rat)	NOEL= 150 ppm, LEL= 500 ppm (depressed weight gain)
		Mutagenicity	(-) Micronucleus test, (-) Ames test

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Finished Product Preservatives-Adhesives & Sealants (cont'd)	Na-trichlorophenate	Primary Derm. Irrit. (85% A.I.)(rabbit)	Severe irritation
		Primary Eye Irrit. (85% A.I.)(rabbit)	Corneal injury
	Boric Acid	Primary Derm. Irrit. (100% A.I.)(rabbit)	Irritation cleared after 4 dys
		Primary Eye Irrit. (100% A.I.)(rabbit)	No irritation
Working Solution & Finished Product Preservatives-Pulp and Paper	Methylbisthiocyanate	Acute Derm. Study (10% A.I.) (rabbit)	LD_{50}= 1.6 gm/kg
		Primary Eye Irrit. (rabbit)	Corneal opacity, (Tox Cat I)
		Primary Derm. Irrit. (10% A.I.) (rabbit)	Score= 7.6/8.0, (Tox Cat I)
		Sensitization (10% A.I.) (g.pig)	Strong, (Tox Cat I)
	Nabam (sodium dimethyl-dithiocarbamate & ethylenediamine)	Primary Eye Irrit. (rabbit)	IBT data, corneal opacity
		Primary Derm. Irrit. (rabbit)	IBT data, Score= 2.1/8.0

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Working Solution & Finished Product Preservatives- Pulp & Paper			
		Note: Formulation may contain ETU (ethylene thiourea)	ETU is an oncogen
	2,2-Dibromo-3-nitrilo-propioamide	Primary Eye Irrit. (5% A.I. in poly-glycol E-200) (rabbit)	Corneal injury
		Primary Derm. Irrit. (rabbit)	Necrosis, (Tox Cat I)
		90-Dy Drinking Water (rat)	NOEL=500 ppm
Working Solution & Finshed Product Preservatives- Tanneries	Diiodomethyl-p-tolyl sulfone (Amical 48)	Mutagenicity	Negative
	2-thiocyanmethylthio-benzothiazole (TCMTB, Busan 44)	Primary Eye Irrit. (Busan 44)(rabbit)	Corrosive
		Primary Derm. Irrit. (Busan 44)(rabbit)	Necrosis
		Sensitization (10% A.I. TCMTB)(rabbit)	Strong sensitizer
		Mutagenicity	(+) with E.coli

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Working Solution & Finshed Product Preservatives- Tanneries (cont'd)			
		90-Dy Feeding Study (rat)	IBT study/NOEL> 500 ppm
		90-Dy Feeding Study (dogs)	IBT Study/NOEL> 500 ppm
		90-Dy Feeding Study (rats)	NOEL= 278 ppm, LEL= 448 ppm (gastric ulceration)
	Alkyl dimethyl benzyl ammonium chloride (Hyamine 3500)	Primary Derm. Irrit. (rabbit)	Score= 6.5/8.0
		Primary Eye Irrit. (rabbit)	Corrosive
		Teratology (80% A.I.) (rabbit)	Not a teratogen, NOEL= 10 mg/kg/dy(fetotox), LEL= 30 mg/kg/dy (fetotox), NOEL< 10 mg/kg/dy (maternal)
		6-Mo. Drinking Water Study (dogs)	NOEL= 1:5000 dilution in water
		6-Mo. Feeding Study (dogs)	NOEL= 200 ppm, (single dose tested)
		1-Yr. Feeding Study (g.pig)	NOEL= 625 ppm, (single dose tested)
		2-Yr. Feeding Study (rats)	NOEL= 5000 ppm, LEL= 10,000 ppm

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Working Solution & Finshed Product Preservatives-Tanneries (cont'd)			
	p-Nitrophenol	Primary Eye Irrit. (rabbits)	Severe corneal injury
		Primary Derm. Irrit. (rabbits)	Score= 1.6/8.0
		Sensitization (g.pig)	Negative
		Human Patch Test	Mild irritation from treated leather applied directly to skin
		Mutagenicity	(-) Ames and yeast tests
		Teratology (rats)	Negative
	1-(3-Chloroallyl)-3,5,7-triaza-1-azoniaadamantane chloride	Primary Eye Irrit. (rabbit)	Minimal Irritation
		Primary Derm. Irrit. (10% Aqueous soln) (rabbit)	Irritatant
		Human Irrit. & Sensitization (0.5% A.I.)	Non-irritant & non-sensitizer
		Sensitization (10% A.I. in Dowanol®/Tween 80)(g.pig)	Moderate Sensitizer

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Working Solution & Finshed Product Preservatives-Tanneries (cont'd)			
		Mutagenicity	(-) Ames test
		21-Dy & 30-Dy Dermal Study (20% A.I. Aqueous soln) (rabbit)	NOEL= 25 mg/kg, LEL= 50 mg/kg (depressed liver wght), LEL= 80 mg/kg (decreased spermatogenesis)
		90-Dy Feeding Study (rat)	NOEL= 2 mg/kg, LEL= 4 mg/kg (cerebral edema)
		90-Dy Feeding Study (dog)	NOEL= 7.5 mg/kg, LEL= 15 mg/kg (decreased heart wght)
	6-Acetoxy-2,4-dimethyl-m-dioxane	No data available (rat)	Liver tumors after oral administration
	Potassium Sorbate	Food & Drug Admin.	GRAS List
	Dichlorophene	Acute Dermal	LD_{50}> 10,000 mg/kg
		Primary Derm. Irrit.	Score= 0.3/8.0
		Human Patch Test	No irritation or sensitization
		Teratology (rat)	NOEL= 5.0 mg/kg (terata, fetotox, maternal), LEL= 25.0 mg/kg (terata microphthatmia), LEL= 75.0 mg (fetotox wght, length, resorption), LEL= 25.0 mg/kg (maternal wght gain & food consumption)

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Working Solution & Finshed Product Preservatives-Tanneries (cont'd)			
	2,3,4,6-tetrachloro-phenol	Human Eye Irrit.	Irritating & injurious
		Primary Derm. Irrit. (10% A.I.)(rabbit)	Minor Irritant, chemical burn from repeated contact
		Human Sensitization	Mild Irritant, no sensit.
		20-Dy Oral Toxicity (rabbit)	NOEL= 1.0 mg/kg, LEL= 10.0 mg/kg (liver dmg)
		Possible Dioxin Contamination	
	2-(hydroxymethyl)-2-nitro-1,3-propanediol	Primary Eye Irrit. (rabbit)	Mild irritation
		Human Sensitization	No irritation or sensit.
	Hexahydro-1,3,5-tris-(2-hydroxyethyl-s-triazine)	Primary Derm. Irrit. (rabbit)	Severe irritant with necrosis
		Primary Eye Irrit. (rabbit)	Severe irritant with opacity
		Acute Derm. Study (rabbit)	LD_{50}= 854 mg/kg (Tox Cat II)
		Sensitization (g.pig)	(+) Sensitizer
	Bioban P-1487	Sensitization	Strong irritant & sensitizer
Finished Product Preservatives-Marine Paints	Cuprous Oxide	Acute Dermal (57% A.I.)(rabbit)	LD_{50}= 8600 mg/kg
		Primary Eye Irrit. (36% A.I. +	No corneal opacity

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd)			
Finished Product Preservatives-Marine Paints		0.5% tributyltin fluoride)(rabbit)	
		Primary Derm. Irrit. (36% A.I. + 0.5% tributyltin fluoride)(rabbit)	Score= 0.05/8.0 (Tox Cat IV)
	Bis(tributyltin) Oxide	Acute Dermal (rabbit)	LD_{50}= 11.7 gm/kg (Tox Cat III)
		Acute Inhalation (rat)	LC_{50}= 0.48 ppm (Tox Cat II)
		Primary Eye Irrit. (rabbit)	Extreme irritant with corneal damage
		Primary Derm. Irrit. (rabbit)	Desquamation, slight fissuring, atonia, edema
		Derm. Sensit.(g.pig)	Sensitizer
		21-Day Dermal (rabbit)	Not irritating at 1200 ppm
		30-Day Feeding (rat)	Growth suppression at 32, 100 & 320 ppm, 40% survival at 320 ppm
		Mutagenicity	Negative Ames test with E.coli & S.cervisiae
		Clinical Studies	
		Draize-Shelanski	Negative
		Schwartz-Peck	No "untoward" reaction at 1200 ppm

TABLE II-9

PENTACHLOROPHENOL ALTERNATIVES

Use Site	Alternative	Available Data	Data Result
ANTI-MICROBIALS (cont'd) Finshed Product Preservatives- Marine Bedding & Double Planking	Copper Naphthenate	Acute Dermal (rabbit)	LD_{50}= 16 ml/kg (Tox Cat III)
		Primary Derm. Irrit. (rabbit)	Moderate irrit. & erythema (Tox Cat III)
MOSSICIDES	Ferrous Sulfate Heptahydrate	Primary Eye Irrit. (10.9% A.I.) (rabbit)	Corneal Opacity
		Primary Derm. Irrit. (10.9% A.I.) (rabbit)	Score= 0.0/8.0
	Ferrous Ammonium Sulfate	Primary Eye Irrit. (15.35% A.I.) (rabbit)	Iritis, chemosis
		Primary Derm. Irrit. (15.35% A.I.) (rabbit)	Score= 0.5/8.0
	Zinc Chloride	Subchronic Feeding (rats)	NOEL= 660 ppm
		Injection Studies (rats/chickens)	Testicular tumors by injection, no oncogenic effects by other routes
		Chronic Feeding	NOEL= 1500 ppm (rats)
		Use Experience	Chemical burns, TWA for zinc chloride fumes= 1 ppm
	Ferric Sulfate	Pertinent data not available	
	Zinc Sulfate	Pertinent data not available	
	Copper Sulfate	See P. II-58	

III. BENEFITS ANALYSIS

A. Introduction

Part III contains the benefit analysis for the non-wood preservative uses of pentachlorophenol and its sodium and potassium salts. This analysis is based on material presented in the following reports: Biological Data Base for Exposure Analysis and Preliminary Benefits Analysis of Pentachlorophenol and Sodium Pentachlorophenol (March 30, 1984); An Overview of the Use of Pentachlorophenol at Various Industrial Sites (MTR-81W258) prepared by the Mitre Corporation; The Biologic and Economic Assessment of Pentachlorophenol, Inorganic Arsenicals and Creosote, Volume II: Non-Wood Preservatives (Technical Bulletin 1658-II) prepared by the United States Department of Agriculture; Preliminary Benefit Analysis of 2,4,5-Trichlorophenol and Pentachlorophenol in Rayon Spinning and Textile Finishing (MTR-79W00295) prepared by the Mitre Corporation; Preliminary Benefit Analysis of 2,4,5-Trichlorophenol and Pentachlorophenol in Tanneries (MTR-79W00264) prepared by the Mitre Corporation; Use Profile and Exposure Assessment of Pentachlorophenol at Industrial Sites (MTR-81W213) prepared by the Mitre Corporation; Preliminary Benefits Analysis of 2,4,5-Trichlorophenol and Pentachlorophenol for Industrial Water Treatment (MTR-79W00311) prepared by the Mitre Corporation; Use Profiles and Alternatives Assessment for 2,4,5-Trichlorophenol and Pentachlorophenol in Adhesives and Polyvinyl Acetate Emulsions (Working Paper 80W00042) prepared by Mitre Corporation).

Pentachlorophenol and its salts, formed by direct chlorination of phenol, are broad-spectrum pesticides. These chemicals are used as herbicides, antimicrobials, mossicides, and defoliants. The following information is presented for each specific use within each category: usage information, alternative chemicals (each chemical and comparative efficacy, where available), and a qualitative assessment of the economic impact if that specific use of penta were cancelled by the Agency.

B. Herbicidal Uses

Pentachlorophenol is a non-specific, nonresidual contact herbicide used for control of broadleaf weeds, grasses, algae and moss. Most herbicidal formulations are not used to control larger woody plants such as trees and brush sprouts. Pentachlorophenol offers no residual control because it is not translocated into roots and stems of wood and perennial plants. The combination of residual herbicides with pentachlorophenol overcomes this problem and provides control of vegetation.

1. Greenhouses

Pentachlorophenol is sprayed by hand on walkways, under benches and canned plant areas to control weeds.

2. Ornamental Lawns

Pentachlorophenol is used to control weeds in dormant ornamental grass lawns (bent, blue, fineleaf fescue, tall fescue and bermuda) by spray application. Pentachlorophenol is also used to control moss on ornamental lawns and turf. Turf edging around driveways and house foundations is usually accomplished with handheld equipment.

3. Rights-of-Way

Pentachlorophenol is used only when total vegetation control is desired along rights-of-way such as roadways, firebreaks, pipelines, etc. Pentachlorophenol, which provides a quick burn of vegetation, is usually applied in an oil spray with other herbicides to provide full season weed and grass control. Perennial plants usually require repeated treatments unless other longer lasting herbicides are used.

4. Commercial and Industrial Non-Crop Areas

Pentachlorophenol is sprayed as a herbicide in areas such as lumber yards, oil refineries, around fences and buildings, etc. Pentachlorophenol has been used in herbicidal mixtures on tank farms and other industrial areas where no vegetation is permitted due to fire hazard. This chemical is also sprayed in areas prior to paving. These products are applied by railroad tankcars by fixed booms calibrated to deliver a specific volume of spray at a given speed. Truck mounted tanks and sprayers, another method of application, are also equipped with fixed booms or handguns with attached hoses. Knapsack spraying is used for small areas.

5. Domestic Dwellings, Medical Facilities, Schools, Golf Courses and Sand Traps

Pentachlorophenol is used to control weeds in golf course sand traps, home areas (driveways, patios, paths, etc.) and established paved and unpaved parking lots and ornamentals. The use of suitable soil sterilants in this latter use site is necessary as pentachlorophenol alone does not kill perennial plants.

6. Wasteland Areas

Pentachlorophenol controls weeds on wasteland areas by spray application.

7. Aquatic Areas (Adjacent to Water) and Drainage Ditch Banks

Pentachlorophenol is used to control weeds in these areas.

8. Alternatives and Economic Impacts

The herbicidal uses of pentachlorophenol have numerous, less costly alternatives of equal or greater efficacy. Alternatives include: chloropicrin, diquat dibromide, sodium chlorate, sodium metaborate, dicamba, paraquat and paraquat dichloride, siduron, sodium cacodylate, ammonium sulfamate, cacodylic acid, disodium methane arsenate, monuron and monuron-tca, picloram, bromacil, tebuthion, dimethylamine, 2,4-D, dinoseb, amitrole, diuron, sodium chlorate, etc. The Agency does not expect the cancellation of the herbicidal uses to cause significant economic impact.

C. Antimicrobial Uses

Antimicrobial use of pentachlorophenol has generally declined between the 1978-1981 survey period. Reductions in use have primarily resulted from efforts to reduce operating costs. The major 1981 industrial use sites, in order of decreasing usage, were: water treatment, adhesives, textiles, tanneries and all other uses.

1. Working Solutions

Pentachlorophenol products are used to control microorganism growth in solutions used in industrial situations.

a. Usage

Sodium pentachlorophenol controls microorganism growth in oil well flood waters, evaporative condenser cooling waters, cooling tower waters and air washers. Application in oil well flood waters is by injection pump. Application at evaporative condensors is by hand, drip-fed, or pumped continuously or intermittently into recirulating waters. Application at cooling towers is by hand, drip feed, continuously or intermittently pumped into recirculating waters. Applications of briquets containing this chemical into air washer systems are by hand.

b. Alternatives

There are 35 alternatives for the oil well flood water use, including organonitrogen and carbonyl compounds as well as compounds containing chlorine and chlorine dioxide. Comparative on-site efficacy data are not readily available for the well flood water use. Data indicate, though, that pentachlorophenol is more effective against fungi than bacteria. Some alternatives for this use have disadvantages such as foaming and corrosion of surfaces.

Alternatives for cooling tower use include: chlorine, 4-chlor-2-phenylphenol, 2-benzyl-4-chlorophenol, 6-chloro-2-phenylphenol, 2,4,6-trichlorophenol, methylene bisthiocyanate, 2,2-dibromo-3-nitrilopropionamide, dichloro-s-triazinetrione, and manual cleaning of systems. Comparative efficacy data of cooling tower alternatives are not readily available because evaluation is qualitative rather than quantitative, and water treatment companies consider this information to be proprietary.

Alternatives for air washer systems include those for cooling tower systems plus carbamates. Manual cleaning and hosing is also an alternative. Comparative efficacy data are not readily available for the air washer use. Disadvantages of some of these alternatives include the tendency of quaternary compounds to foam, and the corrosiveness of chlorine-related compounds.

Alternatives for the evaporative condenser water use include carbamate compounds, quaternary ammonium compounds, and biocides commonly used in cooling tower water. Manual cleaning and hosing is also an alternative. Alternative chemicals are not as effective as sodium pentachlorophenol.

c. Economic Impact

The oil well flood water use of this compound is not considered to be extensive. No breakdown of the amount of pentachlorophenol evaporative condenser usage is available at this time. Evaporative condenser usage is combined with usage in cooling towers and air washers. For 1981, the usage data indicate that only 12,000 pounds of this chemical was used at all three sites. The Agency believes the economic impacts of cancellation of this use to be small based on low usage and the availability of substitutes.

2. Finished Product Preservatives

a. Usage

Pentachlorophenol is used as a fungicide and preservative in adhesives and sealants (sodium and potassium salts), latex paints, rubber articles (sodium salt), defoaming agents (sodium salt), paper coatings (sodium salt), polyvinyl chloride emulsions in food related products (sodium salt), zinc-silicone dioxide matrix coatings in reusable bulk food storage containers (sodium salt) and water-based gasketing compounds for food applications (sodium salt). Pentachlorophenol is incorporated directly to the products during their manufacture. Sodium pentachlorophenol, and some other salts, are used as preservatives in photographic developing solutions. Sodium pentachlorophenol is used as a preservative for cements used in food can ends and seams. Pentachlorophenol is also registered as a preservative of feathers.

The 1979 usage estimates indicate that less than one million pounds of pentachlorophenol is used as a finished product preservative. Data indicate that pentachlorophenol is not extensively used in polyvinyl chloride emulsions. Pentachlorophenol is not used in paper coatings (sodium and potassium salts), zinc-silicone dioxide coatings in reusable bulk food storage containers (sodium and potassium salts), rubber articles (sodium salt), defoamers (sodium and potassium salts). Annual use information for the can and end seal cements is proprietary. No viable alternatives for the gasket use appear to be available. Data indicate that only 9 pounds of pentachlorophenol were used in photographic solutions in 1981. No production of pentachlorophenol containing products is indicated for the feather use.

b. Alternatives

Alternatives for the use of this chemical in adhesives and latex paint include o-phenylphenate, sodium o-phenylphenate, ammonium benzoate, boric acid, tetrahydro-3,5-dimethyl-2H-1,3,5-thiadiazine-2-thione. Alternatives for casein adhesives include esters of p-hydroxybenzoate, sodium fluoride and borax. Alternatives for protein adhesives include phenylphenols, copper naphthenate, tributyltin oxide and copper-8-quinolinolate. Alternatives for starch adhesives are borax, formaldehyde, copper sulfate, zinc sulfate, zinc benzoate and zinc fluoride. Many of these chemicals are approved by FDA for use in food packaging materials (21 CFR 175.105). Comparative efficacy data are generally unavailable for adhesives. No critical use for pentachlorophenol can be identified at this time.

Alternatives for latex paints include mercurial biocides, carbon disulfide-derived compounds, chlorinated alkylthio compounds, and a quaternary salt of 1,3-dichloropropene. The following compounds provide mildewcidal protection on painted surfaces: barium metaborate, cuprous oxide, copper-8-quinolinolinate, bis(tri-n-butyltin)oxide and several phthalimides. Comparative efficacy data are generally unavailable for paint applications. No critical use for pentachlorophenol can be identified at this time.

Alternatives for the defoamer uses (in paper manufacturing chemicals) include: formaldehyde, b-naphthol, parachlorometacresol, potassium trichlorophenate, o-phenylphenol, sodium 2-mecaptobenzothiazole, sodium o-phenylphenate, sodium trichlorophenate.

There are no registered alternatives for photographic solution preservation. Control measures generally involve good housekeeping practices, filtration of process solutions and use of chlorinating agents. Eastman Kodak exports a formaldehyde releasing compound for this use.

Paraformaldehyde, sodium orthophenol tetrahydrate, and zinc dibutyldithiocarbamate are alternatives which are permitted by FDA for food related products (21 CFR 175.300 and 177.1210). The only registered alternative for paper and paper board is barium metaborate. Other non-registered alternatives for paper coatings that are approved by FDA (21 CFR 176.170 and 176.180) include: bis-(trichloromethyl)-lauramide, borax, boric acid, 2-bromo-4'-hydroxyacetophenone, copper-8-quinolinate, dihydroxy dichlorodiphenyl methane, formaldehyde and sodium o-phenylphenate. FDA-approved alternatives for use in can end and seam cements include paraformaldehyde, sodium o-phenolphenate tetrahydrate, and zinc dibutyldithiocarbamate. Data indicate that FDA-approved alternatives are not as effective as pentachlorophenol in the gasket use. Substitution of plastisol and other gasketing material for natural rubber latex precludes the need for biocides in certain applications.

c. Economic Impact

The Agency believes that the cancellation of these uses will not result in significant economic impacts based on the low usage and the small cost differences between alternatives and pentachlorophenol.

3. Working Solutions and Finished Product Preservatives

Pentachlorophenol controls microorganisms in working solutions and imparts a preservative action on finished products.

a. Usage

Pentachlorophenol and its sodium salt is used to control bacterial and fungal growth in working fluids and process chemicals in the textile industry, including the production of rope and cordage. These chemicals preserve starch-sized goods in storage, starch-sized kraft cord and natural fibers in carpeting, and textile finishing for temporary and long term mildew protection (pentachlorophenol only) protection. These chemicals are manually or mechanically added to process solutions and are mechanically applied to finished products.

Sodium pentachlorophenol controls microbial growth in pulp and paper mill solutions and in the final product. This chemical is applied by continuous feed, intermittent feed, slug feed, drip feed or chemical pump feed into the pulp or white water slurry. Dry powder and briquette formulations are applied by hand.

Pentachlorophenol and its sodium salt control microorganisms in leather tannery solutions and final products. While it may be used alone, these chemicals are most commonly used in

combination with 2,4,5-trichlorophenol to provide greater biocidal activity, although either may be used alone. These biocides are applied by slug dosing, gravity feeding or metered pumping, or poured directly into various tannery industrial process solutions. Workers, who usually wear protective clothing in the workplace, are exposed to working tannery solutions containing dilute concentrations of these biocides.

Textile use of sodium pentachlorophenol dropped from 150,000 pounds in 1978 to 40,000 pounds in 1981. No data are available to indicate that pentachlorophenol is used on rope and cordage, while pentachlorophenol and its laurate salt are utilized on tentage, awnings and tarpaulins. Data indicate that leather usage has dropped dramatically between 1978 and 1981.

b. Alternatives

Alternatives for the textile use include sodium-o-phenylphenate (tetrahydrate), and 1-(3-chlorallyl)-3,5,7-triaza-1-azoniadamantane chloride. Alternatives for process fluids include 6-acetoxy-2,4-dimethyl-m-dioxane, and potassium sorbate. Short-term mildew protective alternatives include sodium-o-phenylphenate (tetrahydrate), and potassium sorbate. Long term protective alternatives include copper-8-quinolinolate, dichlorophene, copper naphthenate, mercurials, copper-zirconia, alkyl ammonium naphthenate, benzimidazole, and isothiazolinone.

Limited data indicate that the textile process fluid alternatives are not as effective as sodium pentachlorophenate. Chlorinated phenols and dichlorophene provide effective microorganism control but do not have the broad spectrum activity of the mercurials. Copper-8-quinolinolate is a suitable alternative only for dark fabrics. Dichlorophene has a disadvantage of crystalizing and leaching out of the treated material.

Methylene bisthiocyanate is a widely used registered alternative which is cleared by the Food and Drug Administration for contact with food. Nabam and 2,2 dibromo-3-nitrilopropionamide are also alternatives for use in pulp and paper mills.

The most frequently used alternatives for the tannery use are Amical 48, Busan 30, Busan 72, Kathon LP and Kito 40. Other alternatives, which may or may not be adequate replacements for all uses within the industry include alkyl dimethyl benzyl ammonium chloride, Cyncal®, Hyamine 3500®, paranitrophenol, sodium silicoflouride, nitrobenzene and chlorine. Comparative efficacy data suggest that no single alternative provides equivalent efficacy against bacteria and fungi as the pentachlorophenol/2,4,5-trichlorophenol combination.

c. Economic Impact

Short term annual estimates in control costs are estimated to range from $120,000 to $1,000,000 for the textile finishing industry and $350,000 for the tannery industry. Data indicate that tannery usage has dramatically dropped between 1978 and 1981. Neither industry would experience a major impact by cancellation of pentachlorophenol.

4. Marine Anti-Fouling Agents

These products contain pentachlorophenol not for preservation of the product, but for microorganism control on the treated surface to which the product is applied.

a. Usage

Pentachlorophenol is currently registered for use in marine anti-fouling paints and marine bedding/double planking compounds. These formulations are applied as a coating on treated surfaces. Usage information indicates that very small quantities of pentachlorophenol, approximately 2800 pounds A.I., were used in the U.S. in 1981 for both marine uses.

b. Alternatives

Chemicals which may be substituted in the anti-fouling paint uses of these products include arsenic trioxide and bis (tributyltin) oxide. Alternatives which may be used in the planking compounds include copper naphthenate, bis (tributyltin) oxide, calcium carbonate, diiodomethyl para-tolyl sulfone and cuprous oxide. No precise data is available on the comparative efficacy of these compounds with pentachlorophenol. Some industrial representatives indicate that biocides are not needed in caulking compounds.

c. Economic Impact

There will be little to no economic impact for the affected industries if pentachlorophenol were cancelled based on the low usage and availability of alternatives.

5. Mushroom Houses

a. Usage

Sodium pentachlorophenate is used to control microorganisms in mushroom houses, lofts, compost wharfs, tools and sheds of the mushroom industry. Due to its phytotoxicity, care must be observed in this use to avoid contact with mushrooms. Exposure is primarily inhalation and dermal, resulting from spraying of facilities and dipping of tools, respectively.

b. Alternatives

Alternatives include sodium chloride for non-corrosive sites, broad spectrum disinfectants for tools and steam for interiors, but not lofts.

Sodium chloride is highly corrosive to equipment and metal parts of buildings. Sodium chloride does not have the broad spectrum activity of sodium pentachlorophenol.

Current estimates of pentachlorophenol usage in the mushroom industry range from 7,000 to 9,000 pounds.

c. Economic Impact

Cancellation of this use would affect one-third of the U.S. mushroom production. Both the quality and quantity of a small portion of the mushroom crop would be affected by cancellation. Estimates by the United States Department of Agriculture in 1980 indicate that yield and quality losses would amount to only 0.00045 percent of the $120 million revenue from the affected production. The majority of the mushroom crop is produced without this chemical. The loss of revenue would probably have a minor impact, relative to the value of affected produce.

6. Construction Materials

a. Usage

Pentachlorophenol and its sodium salt are currently registered for use as a mildewicide on a variety of construction materials. These materials include: construction boards, insulation construction paper products, brick and concrete surfaces, caulks and sealants, polyvinyl and acrylic latex products (spackling), and polysulfide grouts. Construction material usage appears to be low.

b. Alternatives

Alternatives to these uses are limited. The alternative for sodium pentachlorophenol in the construction board use is Amical 50. This chemical is incorporated into the construction board. Alternatives for pentachlorophenol in insulation include boric acid. Boric acid, while used as a fire retardant in insulation, does have some biocidal properties.

Information available to the Agency indicates that construction roofing products contain unspecified biocides other than pentachlorophenol and that one manufacturer uses a mildewicidal zinc-copper based paint. No alternatives for pentachlorophenol are available for use on brick and concrete surfaces. Alternatives to pentachlorophenol use in caulks and sealants

include: Troysan 174, Amical 50, and Dowicide A. No alternatives are available for the spackling compound, caulking or polysulfide grout uses of pentachlorophenol. No comparative evaluation of the efficacy of these compounds has been made at this time.

c. Economic Impact

The Agency has no data indicating any usage of pentachlorophenol, or its salts, for the above uses. Therefore, there is no basis for assuming that there would be any economic impact to this industry.

D. Mossicide Use

Areas of the northwestern United States are especially susceptable to growth of moss because the conditions of high humidity and low sunlight favor the growth of these organisms in these geographic areas. The "moss" which infests roofs is a lichen and the moss which infests lawns is a true plant.

1. Usage

A granular form of this chemical is applied by hand spreader to control moss on dormant lawns. Moss lawn control formulations usually contain fertilizer plus pentachlorophenol. The sodium salt of pentachlorophenol is also applied by knapsack spray and brush to control lichens on roofs, masonry and wooden structures.

2. Alternatives

The most likely alternative for lawn moss control to the present penta-ferrous ammonium sulfate fertilizer (FAS) formulation are FAS-fertilizer combinations. These combinations require an additional application, though, to obtain equivalent effectiveness of moss control. Additional alternatives include: ferric sulfate, ferrous sulfate heptahydrate, zinc chloride, zinc sulfate, and copper sulfate. Alternatives are not as efficaceous as pentachlorophenol. There are few data on relative efficacy for non-lawn sites.

3. Economic Impact

Pentachlorophenol is still used for moss control. The extent of use of these chemicals is believed to be limited to western Washington and Oregon. Lawn use in these areas may be substantial because climatic conditions favor growth of this pest. United States Department of Agriculture (USDA) estimated in 1980 that the maximum total additional labor cost would not exceed $1.375 million per year. The impacts of cancellation would be greatest in the northwestern States where infestations are most severe. Considering the limited number of alternatives,

cancellation of these uses may result in a locally significant economic impact.

E. Defoliant

1. Usage

Pentachlorophenol is a seed crop harvesting aid for alfalfa (nonfood). This chemical is also registered on clover (alsike, ladino, red and sweet), birdsfoot trefoil, and lespedeza. This chemical is applied with low volume tractor booms.

2. Alternatives

Alternatives include: endothall, sodium chlorate, cacodylic acid, s,s,s-tributylphosphorotrithioate, ametryn, and paraquat. The alternatives are as effective as pentachlorophenol.

3. Economic Impact

Several alternatives are less expensive than pentachlorophenol. Little to no economic impact is expected from cancellation of this use.

IV. Development of Regulatory Options

A. Introduction

In parts II and II, the Agency identified the risks and benefits of the non-wood uses of pentachlorophenol. As explained in Part I, FIFRA requires the Agency to determine if the use of a pesticide meets the statutory standard for registration by balancing the risks and benefits of use. To carry out this mandate, the Agency has developed a range of regulatory measures which are intended to reduce the risks of use for the pesticide under review. This part discusses the factors which have been taken into account in developing the regulatory options for the non-wood preservative uses of pentachlorophenol and describes in detail those measures selected for further consideration in Part V.

B. Basis and Rationale for Developing Options and Modifications

There are three basic options for regulating all pesticides:

Option 1 - Continuation of Registration without Changes

Option 2 - Continuation of Registration with Modifications to the Terms and Conditions of Registration

Option 3 - Cancellation of Registration

The two extreme options, Option 1, Continuation of Registration without Change and Option 3, Cancellation of Registration, are at the opposite ends of the risk/benefit spectrum. Adoption of Option 1 would be appropriate when the Agency has concluded that the level of risk is acceptable in light of the pesticide's benefits and that further risk reduction measures are not necessary to assure that the use of the pesticide meets the statutory standard for continued registration.

Adoption of Option 3, cancellation, would be appropriate when the Agency has concluded that the risks from a use outweigh the benefits of that use, and that these risks cannot be mitigated to an acceptable level, in light of the benefits, by any other measures short of cancellation. Cancellation prohibits the sale or the distribution of a pesticide for a particular use or uses. The effect of cancellation is to entirely eliminate the risks of a pesticide's use or uses as well as the benefits. Cancellation may affect all uses of a compound, only specific uses or specific formulations, or specific application methods.

The middle option, Option 2, is appropriate when the risks of a pesticide use can be reduced to an acceptable level

while preserving the benefits of the use. This risk reduction is accomplished by modifying the terms and conditions of the pesticide's registration. These modifications, which are expressed through the pesticide's labeling are, for the most part, changes in the way the pesticide is used. These changes are designed to reduce exposure to the pesticide, and thereby reduce or even eliminate the risk from the pesticide.

C. Discussion of Option 2, Modifications to the Terms and Conditions of Registration

The specific risk reducing modifications which the Agency has selected for further consideration are presented in this section.

a. Require Protective Clothing: Impermeable Gloves

To reduce the risk caused by dermal exposure for the non-wood uses of pentachlorophenol, the Agency would require that all applicators using pentachlorophenol must wear gloves impervious to this pesticide in all situations where dermal contact with pentachlorophenol is possible.

This modification would require applicators to wear gloves made of material impervious to pentachlorophenol when involved in the mixing and application of pentachlorophenol. Applicators would also wear gloves when cleaning application equipment such as brushes. This protective clothing modification would apply to all non-wood uses of pentachlorophenol and all applicators where dermal contact is expected. Acceptable materials for gloves include polyvinyl chloride, polyvinyl acetate, neoprene, NBR (Buna-N), and nitrile.

b. Require Protective Clothing: Coveralls

This modification would require persons applying pentachlorophenol to wear protective clothing, such as disposable coveralls, to reduce risks to a greater degree than the risk reduction from gloves alone. This modification would apply to all non-wood uses of pentachlorophenol.

c. Disposal of Protective Clothing

This modification would require applicators of pentachlorophenol to: change protective clothing showing obvious signs of contamination; launder non-disposable clothing separately from other household clothing; clothing and workshoes or boots must be disposed of in any general landfill, in the trash, or in any other manner approved for pesticide disposal.

d. Require Protective Clothing: Respirators

This modification would require that applicators involved in spraying pentachlorophenol products wear respirators. Use sites where these products can be applied by spray are: mushroom houses and mossicide (application to roofs).

Proper use of respirators would be expected to reduce high inhalation exposure during application. The use of a half-mask canister or cartridge respirator capable of trapping pesticide particulates and vapors would reduce potential inhalation by about 90%.

e. Prohibit Eating, Drinking and Smoking During Application

This modification would prohibit eating, drinking, and smoking during the application of pentachlorophenol products registered for non-wood uses.

f. Restricted Use

The Agency is concerned about the possibility of high exposure to applicators who have not been properly trained in the safe handling procedures for formulations of pentachlorophenol products which could be obtained "over-the-counter." Of concern to the Agency is the potential for high exposure to products requiring spraying and to products requiring mixing and/or diluting where there could be some splashing of the formulation resulting in dermal and inhalation exposure.

To protect the applicator from these potentially high exposures to pentachlorophenol products, the Agency would require that the sale and use of pentachlorophenol products be restricted to certified applicators or by persons under their direct supervision and only for those uses covered by the certified applicator's certification.

g. Reduce Contaminants in Penta

This modification would require reduction in the level of the hexachlorodibenzo-p-dioxin (HxCDD) contaminants in all penta products. The HxCDD contaminant, which has been shown to be teratogenic and oncogenic in test animals, is formed in technical penta and its salts during the manufacturing process.

The Agency also would require, as it did in the PD-4 of the Wood Preservatives document of July, 1984, that the method used by registrants to lower the HxCDD contamination must not increase the HCB contamination.

The Agency believes that it is prudent and reasonable to require that registrants reduce HxCDD, and not increase the chlorinated dibenzofurans and HCB contaminants in pentachlorophenol and sodium pentachlorophenate products to protect the public from potential unreasonable adverse effects. Theoretically, these three impurities can be reduced by the same purification or extraction process during manufacturing (Dodd, 1984). By reducing the HxCDD from 15 ppm to 1.0 ppm, the potential oncogenic risks to applicators would be reduced by more than an order of magnitude.

The most highly toxic dioxin is 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) (Nicholson and Moore, 1979). Although it has not been found in analyses of samples of pentachlorophenol (Buser and Bosshardt, 1976; SAB, 1978; Rakshpal, 1980), the Agency would require registrants to amend the confidential statements of formula to indicate that 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is not found in pentachlorophenol products or products containing salts of pentachlorophenol.

V. Proposed Regulatory Decision

As stated in Part IV, the Agency has developed three basic regulatory options to be considered with respect to the non-wood uses of pentachlorophenol:

1. Continuation of registration without changes.

2. Continuation of registration with modification to terms and conditions of registration.

3. Cancellation of registration.

A. Herbicidal Uses

Pentachlorophenol products are registered for a variety of herbicidal uses: greenhouses, ornamental lawns and edging, rights-of-way, commercial and industrial non-crop areas, domestic dwellings, public facilities, golf courses and sand traps, wasteland areas and aquatic areas.

If registrations of pentachlorophenol products were continued without restriction both commercial applicators as well as homeowners would continue to be exposed via spray treatments and at risk to cancer and possible fetotoxic effects. The benefits associated with this use are inconsequential because of the numerous alternatives available, some of which are less costly than pentachlorophenol and of equal or greater efficacy.

If registrations of pentachlorophenol products were continued with amended terms and conditions the following provision would apply: all applicators would be required to be certified and to wear respirators and impermeable gloves. Also, HxCDD content would be required to be reduced to 1 ppm. Exposure and subsequent health risks would be reduced but the risks would still outweigh the benefits for this use.

If registrations of pentachlorophenol products for this use were cancelled, all risks to the applicators and homeowners from these products would be eliminated. Cancellation of this use would have no economic impact.

Although the risks cannot be quantified, they are considered to be high based on the method of application. Although the risks could be reduced for applicators by requiring respirators and impermeable gloves, the virtual absence of benefits supports the finding that the benefits are outweighed by the risks of continued use in either Option 1 or 2. Therefore, the Agency proposes to cancel the use of pentachlorophenol for use as a herbicide in greenhouses, ornamental lawns and edging, rights-of-way, commercial and industrial non-crop areas, domestic dwellings, public facilities, golf courses and sand traps, wasteland areas and aquatic areas.

B. Antimicrobial Uses

1. Working Solutions

a. Oil Well Water

Sodium pentachlorophenate controls microorganism growth in oil well flood waters. Application into oil well flood waters is by injection pump. There is negligible exposure from this use. There are numerous alternatives to pentachlorophenol for this use but comparative on-site efficacy data for the alternatives are not available.

Having evaluated the cancer and fetotoxic risk associated with this use of pentachlorophenol products, the Agency has determined that the benefits outweigh the risks. The Agency proposes to continue the registration for use of pentachlorophenol as an anti-fungal agent in oil well flood waters but amend the terms and conditions of the registration to require that impermeable gloves be worn during the handling of pentachlorophenol and that the HxCDD content be required to be reduced to 1 ppm.

b. Evaporative Condensers, Air Washers, Cooling Towers

Sodium pentachlorophenate controls microorganism growth in evaporative condensers, cooling waters, air washers, and cooling towers. Application for evaporative condensers is by hand or pump system. Penta-containing briquets are applied by hand into air washer systems while application at cooling towers is by hand, drip feed, continuously or intermittently pumped into recirculating waters.

Continued registration of penta for these uses without restriction would result in dermal exposure to applicators. The MOS for fetotoxic effects for penta is 20 and for HxCDD the MOS values are .87 (15 ppm HxCDD) and 13 (1 ppm HxCDD). The oncogenic risk estimates are: using daily lifetime HxCDD exposure, 7×10^{-1} (15 ppm HxCDD) and 5×10^{-2} (1 ppm HxCDD); using average daily lifetime HxCDD exposure, 3×10^{-2} (15 ppm HxCDD), and 2×10^{-3} (1 ppm HxCDD). Usage data from 1981 indicate the only 12,000 lbs. of penta were used at all three sites. The Agency has determined that the economic impacts of cancellation of this use to be small based on low usage and the availability of alternatives.

Amending the registration of these uses to require applicator certification and impermeable gloves would reduce exposure and subsequent risks by 90%. Also, the HxCDD content would be required to be reduced to 1 ppm. Even with this reduction, the risks would remain significant.

If registrations of pentachlorophenol products for this use were cancelled, all risks to the applicators would be eliminated. Cancellation of this use would have no economic impact.

Although the risks could be reduced for applicators, the virtual absence of offsetting benefits requires a finding that the

benefits are outweighed by the risks of continued use in either Option 1 or 2. Therefore, the Agency proposes to cancel the use of penta products as antimicrobial agents in evaporative condensers, cooling towers, and air washers.

2. Finished Product Preservatives

a. Adhesives/Sealants; Canning/Sealing

Products containing pentachlorophenol are used as fungicides and preservatives in adhesives/sealants, and canning/sealing operations. If registration of these products were continued without restriction, applicators would continue to be exposed dermally to this chemical. The MOS for fetotoxic effects for penta is 120 and for HxCDD the MOS values are 5.1 (15 ppm) and 77 (1 ppm). The oncogenic risk estimates using daily HxCDD exposure are 1×10^{-1} (15 ppm) and 8×10^{-3} (1 ppm); using average lifetime HxCDD exposure the respective risk estimates are: 3×10^{-2} and 2×10^{-3}. Also, there is potential dietary exposure to pentachlorophenol from this use since the adhesives and sealants are used in food packaging materials.

The Agency has determined that the economic impacts of cancellation of this use are insignificant based on low usage and the numerous alternatives available.

Amending the registration of these uses to require applicator certification and impermeable gloves would reduce dermal exposure and subsequent risks by 90%. Also, the HxCDD content would be required to be reduced to 1 ppm. However, potential dietary exposure would remain a concern.

If registrations of these products were cancelled for this use, all risks to applicators would be eliminated and there would be no potential dietary exposure. Cancellation of this use would not have a significant economic impact.

Although the risks could be reduced for applicators and the dietary risks are not capable of quantitation, the virtual absence of offsetting benefits requires a finding that the benefits are outweighed by the risks of continued use in either Option 1 or 2. Therefore, the Agency proposes to cancel the use of the pentachlorophenol products for use in adhesives and sealants.

b. Gaskets

If unrestricted registration of this use were continued applicators would be exposed dermally to pentachlorophenol. Also, there is potential dietary exposure to pentachlorophenol

from this use since the penta-treated gaskets are used in food related products. Although exposure and risk estimates have not been determined for this use, the Agency assumes they would be similar to those for adhesives/sealants and the canning/sealing use. The benefits associated with this use are inconsequential because substitution of plastisol and other gasketing material for natural rubber latex precludes the need for biocides (i.e. penta). Alternatives exist and there is a low usage of penta products in gaskets.

Amending registration of this use to require applicator certification and impermeable gloves would reduce exposure and subsequent risks by 90%. Also, the HxCDD content would be required to be reduced to 1 ppm. The risks would still be very high and would outweigh the benefits for this use.

If registrations of these products were cancelled for this use, all risks to applicators would be eliminated. Cancellation of this use would not have a significant economic impact based on low usage.

Although the risks could be reduced for applicators and the dietary risks are not capable of quantitation, the virtual absence of offsetting benefits requires a finding that the benefits are outweighed by the risks of continued use in either Option 1 or 2. Therefore, the Agency proposes to cancel this use of pentachlorophenol.

c. Photographic Developing Solutions

If unrestricted registration of this use were continued applicators would be exposed dermally to pentachlorophenol. Although exposure and risk estimates have not been determined for this use, potential user exposure and subsequent risk could be high due to the film developing process and closed room environment. The benefits associated with this use are not siginificant because of the low usage. Only 9 pounds of pentachlorophenol were used in photographic solutions in 1981, the last year for which data are available.

Amending registration of this use to require applicator certification and impermeable gloves would reduce exposure and subsequent risks by 90%. Also, the HxCDD content would be required to be reduced to 1 ppm. The risks would still be high and outweigh the benefits for this use.

Cancellation of this use would eliminate all risks associated with this use without significant economic impact.

Although the risks could be reduced for applicators through the use of impermeable gloves, the virtual absence of offsetting benefits requires a finding that the benefits are outweighed by the risks of continued use in either Option 1 or 2.

The Agency proposes to cancel the use of pentachlorophenol in photographic developing solutions.

d. Other Uses

There is negligible usage for the remaining registered penta uses (latex paint/rubber, defoaming agents, paper coatings, polyvinyl chloride emulsions, zinc-silicone dioxide coatings, and feathers). The benefits associated with the continued use of these products are insignificant. Exposure and risk estimates have not been determined for these uses due to a lack of usage data. However, it is believed that there is a potential for significant risk to applicators and users is based on the exposure patterns for other industrial uses of penta. In view of the absence of significant benefits, the Agency proposes to cancel the uses of penta in or on latex paints/rubber, defoaming agents, paper coatings, polyvinyl chloride emulsions, zinc-silicone dioxide coatings, and feathers.

3. Working Solutions and Finished Product Preservatives

a. Textile/Cordage

Pentachlorophenol and its sodium salt is used to control bacterial and fungal growth in working fluids and process chemicals in the textile industry. If registrations of these products were continued without restriction, applicators would continue to be exposed dermally to this chemical. The MOS for fetotoxic effects for penta is 120 and for HxCDD the MOS values are 5.1 (15 ppm) and 77 (1 ppm). The oncogenic risk estimates using daily HxCDD exposure are 1×10^{-1} (15 ppm) and 8×10^{-3} (1 ppm); using average lifetime HxCDD exposure the respective risk estimates are 4×10^{-2} and 2×10^{-3}.

Amending the registration of this use to require applicator certification and impermeable gloves would reduce exposure and subsequent risks by 90%. Also, the HxCDD content would be required to be reduced to 1 ppm.

The benefits associated with this use are not significant since usage is low and there are available alternatives. No data are available to indicate that penta is used on rope and cordage; however, it is utilized on tentage, awnings and tarpaulins.

Cancellation of this use would eliminate all risks and result in short term annual increases in control costs from $120,000-$1,000,000 for the entire textile finishing industry.

Although the risks could be reduced for applicators through the use of impermeable gloves, the virtual absence of offsetting benefits requires a finding that the benefits are outweighed by the risks of continued use in either Option 1 or 2. Therefore, the Agency proposes to cancel the use of pentachlorophenol products for use in the textile/cordage industry.

b. Pulp/Paper Mills

Sodium pentachlorophenol controls microbial growth in pulp and paper mill solutions and in the final products. This chemical is applied by continuous feed, intermittent feed, slug feed, drip feed, or chemical pump feed into the pulp or white water slurry. There is negligible exposure from this use. Alternatives to this use are available.

Having evaluated the cancer and fetotoxic risk associated with this use of pentachlorophenol products, the Agency has determined that the benefits outweigh the risks. The Agency proposes to continue the registration of pentachlorophenol for use to control microbial growth in pulp and paper mills but amend the terms and conditions of the registration to require that impermeable gloves be worn during handling of pentachlorophenol and that the HxCDD content be required to be reduced to 1 ppm.

c. Leather Tannery

Pentachlorophenol and its sodium salts are used to control microorganism in leather tannery solutions and final products. Unrestricted registration of this use of pentachlorophenol would result in dermal exposure to applicators during the various operations in the leather tanning process. There is also a potential for dietary exposure to penta as a result of its use in the tanning industry. Fleshings from penta-treated hides are sold to renderers who then in turn sell the fleshings for incorporation into animal/poultry feed.

If unrestricted registration of this use were to continue, applicators would be dermally exposed to pentachlorophenol throughout the various operations in the leather tanning process. The MOS values for both penta and HxCDD are greater than 10,000 for all operations except the biocide/application step. For this process the MOS values are 120 for penta and 5.1 and 77 for 15 ppm and 1 ppm HxCDD, respectively. The oncogenic risks range from 10^{-5} to 10^{-8} for all operations except the biocide/applicatin step using daily lifetime exposure and average daily lifetime exposure of HxCDD. For the biocide/application step in the tanning process, the oncogenic risks are: using daily lifetime HxCCD exposure, 1×10^{-1} (15 ppm) and 8×10^{-3} (1 ppm); using average daily lifetime HxCDD exposure, 3×10^{-2}(15 ppm) and 2×10^{-3} (1 ppm).

If the registration of the products were amended to require that all applicators would be required to be certified and persons working in the tanneries wear impermeable gloves, the exposure would be reduced by 90%. Also, the HxCDD content would be required to be reduced to 1 ppm. However, dietary exposure would still be a concern.

If this use of pentachlorophenol were cancelled, all exposure and subsequent risk would be eliminated.

Cancellation of this use would eliminate all exposure and subsequent risk. Tannery use of sodium pentachlorophenol dropped from 150,000 lbs in 1978 to 40,000 in 1981. Alternatives are available and in use. Short term annual estimates in control costs are estimated at $350,000 for the tanning industry.

Having evaluated the fetotoxic and oncogenic risks associated with this use of pentachlorophenol, the Agency has determined that the risks outweigh the benefits in Options 1 and 2. The Agency proposes to cancel the use of pentachlorophenol for use in the tanning industry.

4. Marine Anti-Fouling Agents

Marine Caulking/Marine Paints

Pentachlorophenol is registered for microorganism control on the treated surface to which the product is applied. These formulations are used in marine anti-fouling paints and marine bedding/double planking compounds. These formulations are applied as a coating on treated surfaces. Approximately 2800 pounds AI were used in 1981 for use in both marine caulking and marine paints.

If registration of pentachlorophenol products were continued without restriction, applicators would continue to be exposed dermally during the manufacturing and use of marine caulking compounds. The MOS values for marine caulking are: 110 for manufacturing of caulking (penta), 4.8 and 3.2 (15 ppm HxCDD), 72 and 48 (1 ppm HxCDD). No exposure information is available from the marine paint use. The oncogenic risks associated with the manufacture of marine caulking are: using daily HxCDD exposure, 1×10^{-1} (15 ppm) and 9×10^{-3} (1 ppm); using average daily HxCDD exposure, 3×10^{-3} (15 ppm) and 2×10^{-4} (1 ppm). The oncogenic risks associated with the use of marine caulking are: using daily HxCDD exposure, 2×10^{-1} (15 ppm) and 1×10^{-2} (1 ppm); using average daily lifetime HxCDD exposure, 8×10^{-3} (15 ppm) and 8×10^{-4} (1 ppm).

Amending the registration of this use would require applicators to be certified and wear impermeable gloves. Exposure and subsequent health risks would be reduced by 90%. Also, the HxCDD content would be required to be reduced to 1 ppm.

If registration of these products were cancelled for this use, all risks to applicators would be eliminated. Alternative chemicals are available and in use. The economic impact would be insignificant.

Having evaluated the fetotoxic and oncogenic risks associated with this use of pentachlorophenol, the Agency has determined that the risks outweigh the benefits in Options 1 and 2. The Agency proposed to cancel the use of penta in marine caulking and marine paints.

5. Mushroom Houses

Sodium pentachlorophenate is used to control microorganisms in mushroom houses, lofts compost wharfs, tools and sheds in the mushroom industry. Exposure is primarily inhalation and dermal, resulting from spraying facilities and dipping of tools, respectively. Alternatives include sodium chloride for non-corrosive sites, and broad spectrum disinfectants for tools and steam for interiors, but not lofts. Sodium chloride is highly corrosive to equipment and metal parts of building nor does it have broad spectrum control activity of sodium pentachlorophenate. Current usage estimates of sodium pentachlorophenate in the mushroom industry range from 7000 to 9000 pounds.

If current registrations were allowed to continue, applicators would be exposed to sodium penta dermally and through inhalation as well. Also, potential dietary exposure to the general population is possible through residues on mushrooms. The MOS values for fetotoxic effects are: 9.1 (penta); 3.7 (15 ppm HxCDD); and, 56 (15 ppm HxCDD). The oncogenic risks from exposure to HxCDD are: using daily HxCDD exposure, 2×10^{-1} (15 ppm) and 1×10^{-2} (1 ppm); using average daily lifetime HxCDD exposure, 8×10^{-3} (15 ppm) and 8×10^{-4} (1 ppm).

If registration of these products were continued with amended terms and conditions, the following provisions would apply: applicators would be required to be certified and wear impermeable gloves and a respirator. Also, the HxCDD content would be required to be reduced to 1 ppm. Exposure and subsequent health risks would be reduced but potential dietary exposure would remain a concern.

Cancellation of this use would eliminate all potential exposure and subsequent risks and would affect one-third of the U.S. mushroom production. However, estimates by the United States Department of Agriculture in 1980 indicate that yield and quality losses would amount to only 0.00045% of the $120 million revenue from the affected population.

Having evaluated the fetotoxic and oncogenic risks associated with this use of pentachlorophenol, the Agency has determined that the risks outweigh the benefits in Options 1 and 2. Therefore, the Agency proposes to cancel the mushroom house use of pentachlorophenol.

6. Construction Materials

Pentachlorophenol and its sodium salt are currently registered for use as a mildewicide on a variety of construction materials. The Agency has no data indicating any usage of pentachlorophenol, or its salts, for any of the following uses in construction materials: constructions boards, insulation construction paper products, brick and concrete surfaces, caulks and sealants, polyvinyl and acrylic latex products (spackling) and polysulfide grouts. Due to a lack of usage data, exposure cannot be evaluated. A qualitative assessment of exposure indicates potential for high exposure. Several

alternatives for use in the various construction materials are available.

Cancellation of the use of pentachlorophenol in construction materials would eliminate all fetotoxic and oncogenic risk and would have no economic impact.

Having evaluated the fetotoxic and oncogenic risks associated with this use of pentachlorophenol, the Agency has determined that the risks outweigh the benefits in Options 1 and 2. Therefore, the Agency proposes to cancel the use of pentachlorophenol as a mildewicide in construction materials.

7. Mossicide

a. Roofs

The sodium salt of pentachlorophenol is applied by knap sack spray and brush to control on roofs, masonry and wooden structures. The extent of use of this chemicals is believed to be limited to western Washington and Oregon. If registration of the pentachlorophenol products were allowed to continue without restriction, applicators would continue to be exposed dermally and through inhalation. Risk estimates are high with a MOS range of .18-13.0 for the formulator and .75-75.0 for the applicator (fetotoxic effects). Oncogenic risk estimate ranges for formulators are: using daily lifetime HxCDD exposure, $1.1 - 7 \times 10^{-2}$; using average daily lifetime, $1 \times 10^{-3} - 7 \times 10^{-5}$. The oncogenic risk estimate ranges for applicators are: using daily lifetime HxCDD exposure, $1 \times 10^{-2} - 3 \times 10^{-2}$; using average daily lifetime, 2×10^{-4}-3×10^{-5}.

If registration of these products were continued with amended terms and conditions, the following provisions would apply: all for formulators and applicators to be certified and wear impermeable gloves and respirators. This would reduce exposure by 90%. Also, the HxCDD content would be required to be reduced to 1 ppm.

Cancellation of this use would eliminate all risk but could result in a significant economic impact on the north-western U.S. A limited number of alternatives all available.

Having evaluated the fetotoxic and oncogenic risk and benefits associated with the use of pentachlorophenol, the Agency has determined that in the absence of quantified economic benefits, the risks outweigh the benefits. Therefore, the Agency proposes to cancel this use of pentachlorophenol.

b. Lawns

A granular form of pentachlorophenol is applied by spreader to control moss on dormant lawns. Moss lawn control formulations usually contain fertilizer plus pentachlorphenol. The extent of use of this chemical is believed to be limited to western Washington and Oregon.

If registration of the pentachlorophenol products were allowed to continue without restriction exposure to applicators would be negligible due to the granular of the product and application via a lawn spreader. Exposure and subsequent risk to homeowners using a treated yard is also thought to be negligible, although no exposure data are available.

Alternative are available but are not as efficacious as pentachlorophenol. Cancellation of this use would eliminate all risk but could result in a significant economic impact in the northwestern U.S.

Having evaluated the risks and benefits associated with this use of pentachlorophenol, the Agency has determined that the risks, in the absence of quantifiable economic benefits, are significant and outweigh the benefits. The Agency proposes cancellation of the registration of this use of pentachlorophenol.

8. Defoliant

Pentachlorophenol products are registered for use as a seed crop harvesting aid for alfalfa (non-food), clover, (aslike, ladino, red, and sweet), birdsfoot trefoil, and lespedza. The benefits for this use are insignificant because less expensive alternatives of equal or greater efficacy are available and its low usage. Dietary exposure as a result of this use of pentachlorophenol may result.

Cancellation of this use would eliminate exposure and subsequent risk of fetotoxic and oncogenic effects. The Agency proposes to cancel the use of pentachlorophenol as a defoliant.

Having evaluated the risks and benefits associated with this use of pentachlorophenol, the Agency has determined that the risks outweigh the benefits in Options 1 and 2.

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U.S. EPA, Position Document PD 2/3 for Wood Preservatives, January, 1980.

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LISTING OF REBUTTAL COMMENTS-PENTACHLOROPHENOL

Rebuttal No.	Source	Date of Comment	Date Received
1	Steptoe and Johnson, Atts. (Rep. American Wood Preservers Inst.) Washington, D.C.	10/23/78	11/2/78
See 1A, 1B	Steptoe & Johnson Washington, D.C.	4/27/79	5/1/79
2	Reichhold Chemicals, Inc. White Plains, N.Y.	11/7/78	11/13/78
3	Cooperative Ext. Service Fitzgerald, Ga.	11/3/78	11/13/78
4	Chapman Chemical Co. Memphis, Tn.	11/6/78	11/15/78
5	Emerald Turfgrass Farms Seattle, Washington	11/16/78	11/20/78
6	Department of the Navy Alexandria, Va.	11/17/78	11/20/78
7	Agro-West, Inc. Wilder, Idaho	11/10/78	11/20/78
8	Link Noe, Wilder Bldg. Ctr. Wilder, Idaho	11/10/78	11/20/78
9	Consolidated Companies Cleveland, Ohio	11/21/78	11/24/78
10	George Brown Idaho Falls, Idaho	11/16/78	11/27/78
11	Howard Larson Emmett, Idaho	11/13/78	11/29/78
See 11 11A	Howard Larson Emmett, Idaho	1/22/79	2/13/79
12	Chas. H. Lilly Co. Portland, Oregon	11/15/78	11/29/78
13	L.A. Tephson	UNDATED	11/29/78
14	Edward Hener	11/17/78	11/24/78
15	Ray S. Buker Teton, Idaho	11/18/78	11/24/78

43A	Bryan Ravenscroft Tuttle, Idaho	11/29/78	12/6/78
44	Vernon Ravenscroft Tuttle, Idaho	11/29/78	12/6/78
45	Kansas Department of Transportation Topeka, Kansas	12/1/78	12/6/78
46	Industrial Water Chemicals Chattanooga, Tenn.	12/4/78	12/7/78
47	Public Service Electric & Gas Company Newark, N.J.	12/1/78	12/6/78
48	Henry J. Ellis Manchester, N.H.	12/4/78	12/8/78
49	Fla. Power & Light Co. Miami, Fla.	11/30/78	12/8/78
50	Osborne A. Goetz Idaho Falls, Idaho	UNDATED	12/8/78
51	Midland Research Labs. Houston, Texas	12/4/78	12/8/78
52	Lester Labs., Inc. Atlanta, Georgia	12/5/78	12/8/78
53	Herman Ratner Atlantic City, N.J.	12/4/78	12/8/78
54	Jewel Hansen Rexburg, Idaho	UNDATED	12/11/78
55	Tullio Gabos Vineland, N.J.	12/5/78	12/11/78
56	Chemical Treatment Co. Ashland, N.J.	12/5/78	12/11/78
57	Industrial Maintenance Corp., Charlotte, N.C.	12/6/78	12/11/78
58	Reliance Brooks Inc. Cleveland, Ohio	12/5/78	12/11/78
59	Arkansas State Plant Board Little Rock, Arkansas	12/5/78	12/11/78

60	Harris Chemical Co., Inc. Knozville, Tenn.	12/5/78	12/11/78
61	Chem-Masters Corp., Chagrin Falls, Ohio	12/4/78	12/11/78
62	Water Services, Inc. Knoxville, Tenn.	12/5/78	12/11/78
63	Dept. of Agriculture Atlanta, Gerogia	12/5/78	12/11/78
64	Dept. of Highways & Transportation Richamond, Virginia	12/1/78	121178
65	Kor-Chem Atlanta, Georgia	12/8/78	12/13/78
66	Branchemco Inc. Jacksonville, Fla.	12/5/78	12/13/78
67	A.W. Williams Inspection Company Mobile, Alabama	12/7/78	12/13/78
68	Allegheny Power System Greensburg, Pa.	12/7/78	12/13/78
69	Arkansas Power & Light Company Littie Rock, Arkansas	12/4/78	12/13/78
70	University of Illinois at Urbana-Champaign Urbana, Illinois	12/5/78	12/13/78
71	Dayton Power & Light Co. Dayton, Ohio	12/1/78	12/13/78
72	Department of Transportation Dover, Delaware	12/7/78	12/13/78
73	Blumberg Co. Peabody, Mass.	12/8/78	12/13/78
74	Watcon, Inc. South Bend, Indiana	12/7/78	12/13/78
75	Long Chemical Inc. Los Angelas, California	12/6/78	12/13/78
76	Mac Gillis & Gibbs Co. Milwaukee, Wisconsin	12/8/78	12/13/78

108	American Water Treatment, Inc. St. Louis, Missouri	12/19/78	12/29/78
109	Bonners Ferry Post Co. Bonners Ferry, Idaho	12/19/78	12/29/78
110	Omaha Public Power District Omaha, Nebraska	12/19/78	12/29/78
111	Tri-Copunty Electric Cooperative Rushford, Minnesota	12/22/78	12/29/78
111A	Tri-County Electric Cooperative Rushford, Minnesota		4/11/79
112	Otter Tail Power Co. Fergus Falls, Minnesota	12/22/78	12/29/78
113	Southern Wood Piedmont Co. Spartanburg, S.C.	12/19/78	12/29/78
See 113 113A	Southern Wood Piedmont Co. Spartanburg, S.C.	2/6/79	2/13/79
114	Ohio Dept. of Agriculture Columbus, Ohio	12/22/78	1/5/79
115	Department of the Army Engineering Res. Ctr., Fort Belvoir, Va.	12/22/78	1/5/79
116	Public Service Co. of New Hampshire Manchester, New Hampshire	12/21/78	1/4/79
117	Indiana State Highway Indianapolis, Indiana	12/27/78	1/5/79
118	Consumers Power Company Jackson, Michigan	12/29/78	1/5/79
119	Dept. of Transportation Sacramento, California	12/28/78	1/5/79
120	Ohio Department of Transportation Columbus, Ohio	12/26/78	1/5/79
121	Dept. of Transportation Federal Aviation Administrarton Washington, D.C.	1/3/79	1/5/79

122	Maine Department of Transportation Augusta, Maine	12/26/78	1/5/79
123	Conroe Creosoting Company (J.A. Ramey) Conroe, Texas	12/30/79	1/10/79
123A	Conroe Creosoting Company (Charline H. Muller) Conroe, Texas	12/30/78	1/10/79
123B	Conroe Creosoting Company (James P. Lumpkin) Conroe, Texas	12/30/78	1/10/79
123C	Conroe Creosoting Company (Elmer Weisinger)	12/30/78	1/10/79
123D	Conroe Creosoting Company (W.E. Kolbe) Conroe, Texas	12/30/78	1/10/79
123E	Conroe Creosoting Company (George B. Brodnax) Conroe, Texas	12/30/78	1/10/79
123F	Conroe Creosoting Company (Marie Henry) Conroe, Texas	12/30/78	1/10/79
123G	Conroe Creosoting Company (Charline Hawthorne) Conroe, Texas	12/30/78	1/10/79
124	Fla. Dept. of Agriculture & Consumer Services Tallahassee, Fla.	12/22/78	1/10/79
125	N.C. Dept. of Agriculture (Commissioner) Raleigh, N.C.	12/29/78	1/10/79
126	Dept. of Transportation (Pa. Ofc. of Secretary) Harrishurg, Penna.	1/2/79	1/10/79
127	City Public Service Board San Antonio, Texas	12/29/78	1/10/79
128	G. Carl Baton (C&B Timber) Ashton, Idaho.	12/31/78	1/10/79

159	Haberman Supplies Owatonna, Minn.	1/19/79	1/24/79
160	Lyle H. Guggishery St. Cruix, Wi.	1/19/79	1/24/79
161	Koppers Company Inc. Denver, Col.	1/11/79	1/25/79
162	John J. Pennington Eugene, Oregon	1/14/79	1/25/79
163	Gordon A. MacGregor Boise, Idaho	1/15/79	1/25/79
164	Interstate Power Co. Dubuque, Iowa	1/18/79	1/25/79
See 164 A	Interstate Power Co., Dubuque, Iowa	8/2/79	8/16/79
165	Edison Sault Electric Co. Sault Ste. Marie, Michigan	1/16/79	1/25/79
166	Oregon State University (Theodore C. Scheffer) Corvallis, Oregon	1/16/79	1/25/79
166A	Oregon State University (R.D. Graham) Corvallis, Oregon	1/17/79	1/25/79
167	Indiana Farm Bureau Cooperative Assn., Inc.	1/15/79	1/25/79
168	Lake States Wood Preserving Inc. Munising, Michigan	1/16/79	1/25/79
169	C.K. Peck Lexington, Oregon	1/7/79	1/24/79
170	Houston Wood Treating Co., Inc. Houston, Missouri	1/18/79	1/29/79
171	Decorator Supply Inc. (J.F. Schellien) Rice Lake, Wi.	UNDATED	1/26/79
172	Fleet Distribution Supply Thief River Falls, Minn.	1/20/79	1/26/79
173	Anderson Glass Co., Inc. Grand Rapids, Minn.	1/18/79	1/26/79

174	G.F. Nemitz' Sons Hutchison, Minn.	1/19/79	1/26/79
175	Kenneth P. Strube Rochester, Minn.	1/19/79	1/26/79
176	Gordon A. Peterson Dresser, Wi.	1/20/79	1/26/79
177	Jan J. Don Grandview, Washington	1/22/79	1/30/79
178	Wayne W. Roundy Boise, Idaho	1/23/79	1/30/79
179	Vepco Richmond, Va.	1/18/79	1/30/79
179A	Vepco Richmond, Va.	1/18/79	8/9/79
See 179 179A	Vepco Richmond, VA.	7/12/79	8/10/79
180	Koppers Company Inc. (194) Pittsburgh, Pa. (See 161, 183, 188, 189, 192, 193 & 194)	1/25/79	1/30/79
180A	Koppers Co. Inc., (Gerald L. Daugherty) Pittsburgh, Pa. (See 180)	2/12/79	2/12/79
180B	Koppers Company Inc. (194) Pittsburgh, Pa. (See 161. 183, 188, 189, 192, 193 & 194)	1/25/79	2/12/79
181	Kansas Gas & Electric Co Witchita, Kansas	1/23/79	1/30/79
182	New England Log Homes Inc. Hamden, Conn.	1/22/79	130/79
183	Koppers Company Inc. Superior, Wi.(See 161, 180, 188, 189, 192, 193, 194)	UNDATED	1/29/79
184	Julian Ochrymowych New Providence, N.J.	1/23/79	1/29/79

215	J.A. Jones Construction, Co. Charlotte, N.C.	1/29/79	2/9/79
216	R.O. Watson Wilmington, Delaware	2/1/79	2/9/79
217	Avco New Idea (Farm Equipment Division) Coldwater, Ohio	2/1/79	2/9/79
218	Rogers Post & Lumber Co. Steelville, Missouri	1/29/79	2/9/79
219	Cleveland Electric Illuminating Co. Cleveland, Ohio	1/23/79	2/1/79
220	Robert K. Hastings Harbor, Oregon	1/29/79	2/12/79
221	Friends of the Earth (Erik Jansson) Washington, D.C.		
222	Texas Forest Service Lufkin, Tx.	2/6/79	2/12/79
223	Web & Sons Inc. Sherburne, N.Y.	UNDATED	2/12/79
224A	Dallas Power & Light Co. Dallas, Texas	2/6/79	2/12/79
See 224 224 A	Dallas Power & Light Dallas, TX.	6/3/79	6/10/79
225	American Electric Power Service Corp.	2/6/79	2/12/79
226	Public Service Co., of New Mexico Albuquerque, N.M.	2/9/79	2/12/79
227	W.C. Timber Products, Inc. (T.F. Clitten) Rexburg, Idaho	2/8/79	2/13/79
228	Idaho Power Co. Boise, Idaho	2/9/79	2/13/79
229	Public Service Co. of OK. Tulsa, OK.	2/8/79	2/13/79

230	Carolina Power & Light Co. Raleigh, N.C.	2/8/79	2/13/79
231	Roof Surgeon Inc. Honolulu, Hawaii	2/9/79	2/13/79
232	Texas Forestry Assoc. Lufkin, Tx.	2/7/79	2/13/79
233	Portland General Electric Co. Portland, Oregon	2/8/79	2/13/79
234	Morton Buildings, Inc. Morton, Ill.	2/7/79	2/13/79
235	Middle South Services Inc. New Orleans, La.	2/8/79	2/13/79
236	Central Vermont Public Service Corp. Rutland, Vt.	2/9/79	2/13/79
237	Texas Electric Service Co. Fort Worth, Tx.	2/5/79	2/13/79
238	Upper Peninsula Power Co. Houghton, Michigan	2/8/79	2/13/79
239	Duke Power Co. (Legal Dept.) Charlotte, N.C.	2/9/79	2/13/79
240	Union Electric Co. St. Louis, Mo.	2/8/79	2/13/79
241	Bill Deveny Riggins, Idaho	1/22/79	2/13/79
242	Everett Van Seyke Wilder, Id.	UNDATED	2/13/79
243	Mark Johnson, Idaho	1/21/79	1/13/79
244	Reuben H. Babcock Moore, Idaho	2/1/79	2/13/79
245	Picabo Livestock Co. Picabo, Idaho	1/18/79	1/13/79
246	Don Heckman White Bird, Idaho	UNDATED	2/13/79

259	Pa. Electric Co. Johnstown, Pa.	2/12/79	2/15/79
260	Nixon, Hargrave, Devans & Doyle(Rep: Rochester Gas & Elec. Corp.) Rochester, N.Y.	2/12/79	2/15/79
261	Indianapolis Power & Light Company Indianapolis, Indiana	2/12/79	2/15/79
262	Ill. Power Co. Decatur, Ill.	2/9/79	2/15/79
262A	Illinois Power Company Decatur, Ill.	3/14/79	3/20/79
263	Tampa Electric Co. Tampa, Fla.	2/9/79	2/15/79
264	Jersey Central Power & Light Co. Morristown, N.J.	2/6/79	2/15/79
265	Central & South West Services, Inc. Dallas, Tx.	2/8/79	2/15/79
266	New York State Electric & Gas Corporation Binghamton, N.Y.	2/8/79	2/15/79
267	Pa. Power & Light Co. Allentown, Pa.	2/9/79	2/15/79
268	Canal Electric Co. Sandwich, Mass.	2/9/79	2/15/79
269	Cambridge Electric Light Cambridge, Mass.	2/9/79	2/15/79
270	New Bedford Gas & Edison Light Co. Duluth, Minn.	2/9/79	2/15/79
271	Southern States Cooperative Richmond, Va.	2/5/79	2/15/79
272	Niagra Mowhawk Power Corporation Syracuse, N.Y.	2/6/79	2/15/79
273	Minnesota Power & Light Co. Duluth, Mn.	2/8/79	2/15/79

273A	Minnesota Power & Light Co. Duluth, Minn.	2/28/79	3/7/79
274	Boston Edison Co. Boston, Mass.	2/5/79	2/15/79
275	American Paper Institute Washington, D.C.	2/12/79	2/15/79
275A	Lumber River Elec. Membership Corp.		4/17/79
276	Dept. of Transportation Raleigh, N.C.	2/12/79	2/15/79
277	Delsea Exterminators Camden, N.J.	2/7/79	2/16/79
278 278A	Forshaw Chemicals Charlotte, N.C.	2/8/79	2/16/79
279	The Washington Water Power Co. Spokane, Washington	2/12/79	2/22/79
280	Kansas Power & Light Co. Topeka, Ks.	2/12/79	2/22/79
281	Iowa-Illinois Gas & Electric Co. Davenport, Iowa		
282	National Solvent Corp., Medina, Ohio	2/11/79	2/22/79
283	Lincoln Electric Coopera- tive Inc. Davenport, Washington	2/12/79	2/22/79
284	Ron Frei Grangeville, Idaho	UNDATED	2/22/79
285	Long Island lighting Co. Hicksville, N.Y.	-2/13/79	2/22/79
286	University of Idaho, Coll. of Agriculture Dept. of Agri., Moscow, Idaho	1/31/79	2/22/79
287	Public Service Co. of Colorado Denver, Colorado	2/9/79	2/23/79

317	Liz Vanleeuwen Halsey, Oregon	2/12/79	3/7/79
318	Bowater Carolina Corp. Catawba, S.C.	2/23/79	3/7/79
319	Yampa Valley Electric Association, Inc. Steamboat Springs, Col.	3/7/79	3/13/79
320	Sonford Products Corp., (Southern Div.) Jackson, Miss.	2/8/79	3/13/79
321	Public Utility District No. 1 of Klickitat Cty Goldendale, Washington	3/9/79	3/13/79
321A	Public Utility District No. 1 of Okanogan Cty. Okanogan, Washington	3/9/79	3/13/79
See 321, A 321 B	Public Util. Distr. No. 1 No. 1 Okanogan, WA.	7/2/79	7/9/79
322	Wasco Electric Cooperative, Inc. Dalles, Oregon	3/12/79	3/20/79
323	Nebraska Public Power Columbus, Nebraska	3/12/79	3/20/79
324	Port Authority of New York & New Jersey New York, N.Y.	3/14/79	3/22/79
325	Savannah Electric & Power Company Savannah, Georgia	UNDATED	3/22/79
326	Orcas Power & Light Company Eastsound, Washington	3/19/79	3/26/79
327	Thyrald H. Finn Rigby, Idaho	3/16/79	3/26/79
328	Dixie Electric Power Assoc. Laurel, Ms.	3/19/79	3/29/79
329	Memphis Light, Gas and Water Division Memphis, Tenn.	3/20/79	3/30/79

330	Columbus and Southern Ohio Electric Co. Columbus, Ohio	3/19/79	3/30/79
331	Poudre Valley Rural Electric Association Fort Collins, Colorado	3/23/79	3/30/79
332	Public Utility District No. 1 of Chelan County Wenatchee, Washington	3/23/79	3/30/79
333	Carbon Power & Light Inc. Saratoga, Wyoming	3/21/79	4/3/79
334	Eugene Water & Electric Board Eugene, Oregon	3/26/79	4/3/79
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337	Dearborn Chemical Chemed Corp., Lake Zurich, Ill.	3/30/79	4/10/79
338	Inter County Rural Elec. Coop. Corp., Danville, Kentucky	4/3/79	4/10/79
339	Craig-Cotetourt Elec. Coop. New Castle, Penna.	4/4/79	4/10/79
340	Crow Wing Coop. Power & Light Co. Brainerd, Minn.	UNDATED	4/10/79
341	Delaware County Electric Coop. Delhi, New York	UNDATED	4/10/79
342	Harkers Island Elec. Corp. Harkers, Island, N.C.	4/3/79	4/10/79
343	Roanoke Electric Corp. Rich Square, N.C.	4/3/79	4/10/79
344	Flint Hills Rural Elec. Coop. Assoc. Inc. Council Grove, Kansas	UNDATED	4/10/79

373	Waynw-White Counties Electric Cooperative Farifield, Ill.	4/4/79	4/13/79
374	Douglas Electric Coop., Inc. Roseburg, Oregon	4/6/79	4/13/79
375	Missouri Public Service Company Kansas City, Mo.	3/27/79	4/13/79
376	RSR Elec. Co-op Inc. Milnor, N.D.	4/9/79	4/17/79
377	The Victory Elec. Coop. Assoc., Inc. Dodge City, Kansas	4/9/79	4/17/79
378	United Elec. Coop. Inc. Dubois, Iowa	4/10/79	4/17/79
379	Howard Elec. Coop. Fayette, Mo.	4/9/79	4/17/79
380	Glacier Elec. Coop., Inc. Cut Bank, Montana	4/10/79	4/17/79
381	Okefenoke Rural Elec., Membership Corp., Nahunta, GA.	4/9/79	4/17/79
382	Kandiyohi Coop., Elec., Power Association Willmar, MN	4/9/79	4/17/79
383	Planters Elec., Membership Corp., Millen, GA.	4/5/79	4/17/79
384	Golden Valley Elec., Assoc., Inc. Fairbanks, Alaska	4/5/79	4/17/79
385	Re Sand Mountain Elec., Coop., Rainsville, Alabama	4/9/79	4/17/79
386	Lake Region Elec., Coop., Inc., Hulbert, Oklahoma	4/9/79	4/17/79
387	EMC Haywood Elec., Membership Corp., Waynesville, N.C.	4/11/79	4/17/79

388	Grand Elec., Coop., Inc., Bison, S.D,	4/9/79	4/17/79
389	Union Rural Elec., Association, Inc.,Brighton, Colorado	4/10/79	4/18/79
390	Kotzebue Elec., Assoc., Inc., Kotzebue, Alaska	4/9/79	4/18/79
391	Alger Delta Coop., Elec., Association Inc., Gladstone, MI	4/12/79	4/18/79
392	TRI-County Elec., Assoc., Inc., Plankinton, S.D.	4/12/79	4/18/79
393	C&W Rural Elec., Coop., Association Clay Center, Kansas	4/13/79	4/18/79
394	Slope Elec., Coop., Inc., New England, N.D.	4/12/79	4/18/79
395	Moreau-Grand Elec., Coop., Inc., Timber Lake S.D.	4/3/79	4/20/79
396	Valley Elec., Membership Corp., Natchitoches, LA.	Undated	4/20/79
397	York Country Rural Public Power District York, Nebraska	4/13/79	4/20/79
398	Carroll Elec., Membership Corp., Carrollton, GA.	4/12/79	4/20/79
399	San Luis Valley Rural Elec., Coop., Inc. Monte Vista, Colorado	4/9/79	4/20/79
400	Mitchell Elec., Membership Corp., Camilla, GA.	4/11/79	4/20/79
401	Flathead Elec., Coop., Inc., Power & Light Kalispell, Montana	4/12/79	4/20/79
402	East Central Elec., Assoc., Braham, MN	4/11/79	4/20/79
403	North-Central Elec., Coop., Inc. Attica, Ohio	4/12/79	4/20/79
404	Wells Rural Elec., Co., Wells, Nevada	4/12/79	4/20/79

439	Harrison County Rural Elec., Membership Corp., Corydon, Indiana	4/20/79	5/1/79
440	Edgecombe-Martin County Elec., Membership Corp., Tarboro, N.C.	4/26/79	5/4/79
441	Kosciusko County Rural Elec., Membership Corp., Warsaw, Indiana	4/30/79	5/4/79
442	Jackson Electric Membership Corp., Jefferson, GA.	4/27/79	5/4/79
443	Fairfield Elec., Coop., Inc., Winnsboro, S.C.	4/27/79	5/4/79
444	Barc Electric Coop., Millsboro, VA.	4/30/79	5/4/79
445	Habersham Electric Membership Corp., Clarkesville, GA.	4/24/79	5/4/79
446	Western Illinois Elec., Coop., Carthage, IL	4/24/79	5/4/79
447	Hickman-Fulton Counties Electric Coop., Corp., Hickman, KY	4/30/79	5/4/79
448	United Power Association Elk River, MN.	4/23/79	5/4/79
449	Blue Grass Recc Nicholasville, KY.	Undated	5/4/79
450	Rural Elec., Convenience Coop., Co., Auburn, IL.	4/26/79	5/4/79
451	Meriwether Lewis Elec., Coop., Centerville, TN	4/27/79	5/8/79
452	Washington State Univ. Pullman, Washington	5/3/79	5/9/79
453	American Institute of Timber Construction Englewood, Colorado	5/2/79	5/9/79
454 454A	National Rural Elec., Coop., Accoc., Washington, D.C.	3/29/79	5/11/79

455	Joe Wheeler Elec., Membership Corp., Hartselle, Alabama	4/30/79	5/11/79
456	Oliver B. Wilbers Umpqua, OR	4/7/79	5/17/79
457	Dairyland Power Coop., LA Croose, WI	5/10/79	5/17/79
458	Oliver-Mercer Elec., Coop., Inc., Hazen, ND	5/9/79	5/17/79
459	Petit Jean Elec., Clinton, Arkansas	5/7/79	5/17/79
460	Eastern Iowa Light & Power Corp., Wilton, Iowa	5/9/79	5/21/79
461	Cookson Hills Elec., Coop., Inc., Stigler, OK	4/26/79	5/2/79
462	Coos Curry Elec., Coop., Inc., Coquille, Oregon	5/9/79d	5/23/79
463	Navopache Elec., Coop., Inc., Lakeside, Arizona	Undated	5/24/79
464	Betz Labs, Inc., Trevose, PA.	5/9/79	6/5/79
465	Green River Elec., Corp. Owensboro, KY	6/5/79	6/14/79
466	Northern Lights, Inc., Sandpoint, Idaho	6/7/79	6/15/79
467	Dow Chemical Co., Midland, MI	6/5/79	6/22/79
468	Concordia Elec., Coop., Inc., Ferriday, LA.	6/11/79	6/22/79
469	Alabama Power Co., birmingham, ALA.	6/15/79	6/22/79
470	U.S. Dept. of Agri. Forest Serv., Asheville, N.C.	6/15/79	6/28/79
471	MS. Power Co., Gulfpost, MS.	6/20/79	6/28/79