18 #541 DRAFT 4/7/80

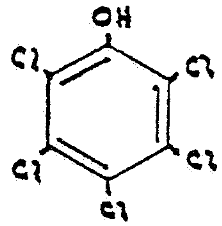
PENTACHLOROPHENOL FUNGICIDE/HERBICIDE SI CLASS II

CFR Reference: No direct food uses; indirect food additive regulations pertaining to pentachlorophenol or its sodium salt are found in 21 CFR 175.105, 176.200, 176.210, 176.300, 177.2800, 178.3120, 178.3900.

Chemical Name: pentachlorophenol

Trade Names: Dowicide*EC-7[1][2] Penchlorol, Pentacon*, Penwar*, Priltox, Sinituko*, many others

Common Names: pentachlorophenol, PCP, penta



C_6Cl_5OH

Molecular Weight: 266.4

Physical State: Crystalline solid.

Melting Point: 174°C [2]

I. Exposure and Use Factors

A. Production or Usage Volume: Approximately 50 million pounds of pentachlorophenol are produced annually in the U.S. The major portion of this is used as a wood preservative. Additional uses include its incorporation in herbicide formulations, its use as a slimicide in paper manufacture, and its many uses as a preservative in diverse products ranging from animal hides to paint.[1]

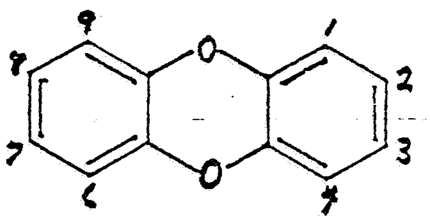
B. Chemistry

1. Solubilities: Pentachlorophenol is slightly soluble in water (18 ppm at 25°C), but its sodium and potassium salts are very soluble in water. Both pentachlorophenol and its alkali salts are very soluble in polar organic solvents. Esterification with alkyl carboxylic acids (lauric acid predominating) yields esters which are more suitable for formulation in hydrocarbon solvents.[1]

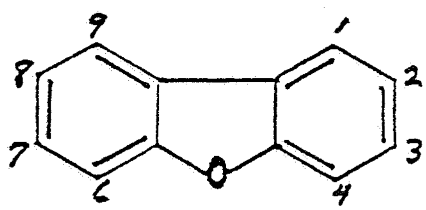
*Registered Trade Names

2. Stability: Pentachlorophenol is stable under normal storage conditions.

3. Manufacturing Process/Impurities: Phenol is chlorinated in the presence of an aluminum chloride catalyst at progressively increasing temperatures sufficient to keep the reaction mixture molten. The technical material is generally about 85-90% pentachlorophenol with the primary impurity (about 10%) being 2,3,4,6-tetrachlorophenol. Hexachlorobenzene (HCB) has been found in some samples. The other impurities include chlorophenoxy chlorphenols, chlorodioxins, chlorofurans, and chlorodiphenyl ethers. The dioxins and furans which have been encountered are the octa-, hepta-, and hexachloro dioxins and furans(3); no TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) has been reported in pentachlorophenol.(4) The hexa-and hepta-chlorodioxins tested are less acutely toxic than TCDD, but are in an extremely toxic range(1) (LD_{50}(mice): 0.8-1.4 mg/kg vs. 0.28 mg/kg for TCDD).



dibenzo-dioxin



dibenzofuran

4. Degradation/Alteration: Photolysis of pentachlorophenol produced octachloro- and heptachloro-dibenzo-p-dioxins. In other studies, photolysis of solid PCP in an oxygen stream produced some CO_2 and HCL.

5. Environmental Stability

   a. Foliar Degradation/Plant Metabolism: No data were found which characterize the alteration products in plants.

   b. Aqueous Degradation: No data were found which indicate the persistence of pentachlorophenol or identify its alteration products in water. EPA's findings of pentachlorophenol in the drinking water of 86 of the 108 cities sampled, at a median concentration of 0.05 ug/liter indicates some persistence and widespread distribution.(1)

c. Soil Degradation: Dechlorination and methylation reactions appear to be routes of microbial degradation; tri- and tetra-chlorophenols and chloroanisoles are reported products. Reported soil persistence of pentachlorophenol ranges from 2 days to 5 years.[1]

d. Animal Metabolism: Mammals excrete pentachlorophenol primarily in the urine. In addition to unchanged pentachlorophenol, tetrachlorohydroquinone (chloranil) and a glucuronide conjugate have been found in the urine. Clams and goldfish convert pentachlorophenol to its sulfate conjugate.[1]

Pentachloroanisole has been found in the tissues and eggs of poultry and in the milk and blood of cattle fed pentachlorophenol.[6][7]

6. Bioaccumulation Potential: The available evidence indicates that in both aquatic species and mammals, residues of pentachlorophenol plateau within a few days of initial exposure and rapidly decline after removal from exposure.[1]

Administration of pentachlorophenol at 20 mg/kg b.w./day to cattle resulted in plateau levels of approximately 4 ppm of pentachlorophenol in milk and 40 ppm in blood. Residues declined to basal levels within a few days after PCP feeding was stopped.[6]

Bioaccumulation of the impurities, HCB and chlorodioxins, in milk fat and body fat during the above cattle feeding study, was much greater proportionately than that of pentachlorophenol.[6]

7. Soil Mobility: The mobility varies widely depending on soil type; strongly acidic soils and high organic matter soils show strong adsorbtion of pentachlorophenol.[1]

8. Systemic Plant Activity: Limited data indicate some translocation of foliar applications but little uptake of soil residues.[8]

9. Summary of Significant Terminal Residues: Tri- and tetra-chlorophenols and tetra- and penta- chloroanisoles may arise as environmental alteration products or animal metabolites of pentachlorophenol. Tetrachlorohydroquinone may also arise as an animal metabolite. Pentachlorophenol and the above metabolites may be present in either free or conjugated form, particularly in animal products.

The hexa-, hepta-, and octa-chlorodioxins and chlorofurans, and HCB often are present as impurities in pentachlorophenol and are of special toxicological concern.[1][3][6]

10. Related Pesticides/Common Metabolites: Tetrachlorohydroquinone, an animal metabolite of pentachlorophenol, is also the fungicide, chloranil, which has registered "non-food" uses as a seed treatment. The various chlorophenols and chloroanisoles may also arise as metabolites of other pesticides, e.g., PCNB, 2,4-D, 2,4,5-T, HCB.

    The impurity, HCB, is also an impurity in other pesticides, e.g., PCNB and Dacthal, a registered fungicide for seed treatments, and is an environmental pollutant arising in the manufacture of various chlorinated compounds such as perchloroethylene.

    The higher chlorodioxin and chlorofuran impurities in pentachlorophenol may also arise from other sources, but the widespread manufacture and use of pentachlorophenol marks it as a major source of these contaminants.

C. Uses and Potential Exposure

1. Registered Uses: Various formulations of pentachlorophenol are registered for use on beans (seed treatment), wood, leather, burlap, masonry, cordage, paints, petroleum, pulp and paper mill systems, seed crops (pre-harvest desiccant) and cooling towers. About 80% of the pentachlorophenol production is used in wood treatment, 11% in insulation board and cooling towers, 6% in pulp and paper mills, and 3% for farm uses including termite protection. The only currently registered agricultural uses are seed treatment or seed crop uses on beans, alfalfa, clover, lespedeza, and vetch.[1]

2. Tolerances: There are no tolerances for pentachlorophenol residues. Various indirect food additive regulations (see CFR references, p.1) allow the use of pentachlorophenol or its sodium salt: as a preservative in packaging adhesives, glues, polymer ingredients, and textiles contacting food; as a defoaming agent in coating and paper manufacture; and as a slimicide in paper and paperboard manufacture.

3. Known Foreign Uses: No data, but wood treatment uses are believed to be worldwide.

4. Exposure Via Foods: Even though there are no uses registered for the direct use of pentachlorophenol on food, residues are being found in various foods. The variety of uses of pentachlorophenol and the volume used provide many opportunities for contaminating foods.

SI: not all info here is on one-liners.

Findings of pentachlorophenol in gelatin (from treated hides), in drinking water, milk, various other food commodities, and the contamination of samples (and therefore presumably home canned and possibly commercially canned foods) from jar seals illustrate the variety of exposures encountered.

Adult dietary intakes of 1.6, 1.2, 0.07 ug/day and none detectable were found respectively in the FY-75, 76, 77, and 78 Adult Total Diet Studies. In the FY 79 survey of fresh whole milk samples, 39 of 198 samples contained pentachlorophenol at or above 0.005 ppm. The highest residue was 0.23 ppm. Some of these results may be suspect due to the jar seal contamination problem mentioned above. None of the positive pentachlorophenol samples were positive for the higher chlorinated dioxins.

Since pentachlorophenol treated wood may be used extensively in barns, wood shavings in poultry shelters, etc., livestock may be subject to exposure from dermal contact, inhalation in tightly enclosed structures, and ingestion from licking or chewing treated wood or feed contact with treated wood. Residues in milk, meat, and eggs may result from these exposures.

5. Other Exposure Routes: Pentachlorophenol formulations are available to the homeowner and cases of reported illness from dermal and inhalation exposure from such uses have been reported.[1]

II. Toxicity

A. Acute Oral LD_{50} (rats): 27 to 80 mg/kg b.w.[9]
The reported oral LD_{50} in guinea pigs for 3 isomers of hexachlorodibenzodioxin ranged from 0.07 to 0.1 mg/kg b.w.; corresponding oral LD_{50}'s in mice ranged from 0.8 to 1.4 mg/kg b.w.[1]

B. Oncogenicity: Studies in mice have been reviewed by the EPA Carcinogen Assessment Group and were found to be negative with respect to oncogenic effects of pentachlorophenol.[1]

C. Mutagenicity: Negative results for pentachlorphenol have been obtained with the Ames test, host-mediated assay, and sex-linked recessive lethal test on *Drosophila*.[1]

D. Teratogenicity and Reproductive Effects: Fetotoxic and teratogenic effects have been reported in rats exposed to purified and commercial grade pentachlorophenol. The same effects were observed in rats exposed to a mixture of two unspecified isomers of hexachlorodibenzodioxins.[1]

E. Other Chronic or Acute Effects:

1. Chloracne, a skin disorder known to be caused by dioxins, has been observed in workers in pentachlorophenol manufacturing plants and wood preserving operations.(1)

2. Hepatic effects, including changes in various enzyme activities and enlargement of the liver have been found in rats fed pentachlorophenol for periods of three to eight months.(1)

3. Human deaths have resulted from occupational and accidental excessive dermal exposure to pentachlorophenol.(1)

F. ADI (EPA): None established.

G. ADI (FAO/WHO): None established.

H. Acute and Chronic Effects Triggering RPAR: Teratogenicity and Fetotoxicity (See D above).

I. Current RPAR Status: The Position Document (PD) 1 comment period closed 2/12/79. Analysis of rebuttal information and development of PD 2/3 is still in progress.

III. Overall Appraisal:

- The present data do not well delineate which toxic effects are due to the associated impurities, particularly various associated chlorodioxins and chlorofurans. Furthermore, the various congeners of the chlorodioxins and chlorofurans vary in their toxic effects and in the levels present in various manufacturer's lots of pentachlorophenol. Full evaluation of the toxicity risks of pentachlorophenol exposure must await the completion of EPA's RPAR analysis; however, the widespread use and potential for contamination of food indicates that a potential hazard may exist.

IV. Surveillance Index Classification: Class II "A high health hazard has not been demonstrated, but there is evidence of possible high risk toxicity effects combined with the potential for significant human dietary exposure. The potential hazard is sufficient to warrant a temporary inclusion of the compound in the monitoring program as soon as possible, and to continue until exposure to the compound is more clearly defined or until additional toxicity data, exposure data, or EPA actions indicate assignment to a different class."

Justification: Many data gaps exist in the knowledge of the overall toxicity of pentachlorphenol and the impurities commonly associated with it. Monitoring of foods and drinking water indicates that some dietary exposure is occurring but the extent of the exposure is not well defined. The widespread use of pentachlorophenol provides many routes for potential contamination of food ranging from dermal, dietary, and inhalation exposure of livestock, and consequent residues in meat, milk, and eggs; migration of residues into food from paper, paperboard, sealants, jar seals, etc., where sodium pentachlorophenate is allowed as an indirect additive; carryover into gelatin from uses on treated hides; and possible contamination of water and fish in the vicinity of woodtreating or paper manufacturing plants.

Necessary Action: In addition to the present FDA pentachlorophenol monitoring (and associated dioxin and furan analysis of positive samples) of milk and Total Diet Samples, consideration should be given to monitoring eggs and other foods where local intelligence indicates contamination is likely.

In areas where wood treatment or paper manufacturing plants utilizing pentachlorophenol may lead to water contamination, District intelligence efforts should also focus on fish, and water used for food processing.

Although negative findings for pentachlorophenol do not necessarily indicate the absence of chlorodioxins or chlorofurans (because of the greater persistence and bioaccumulation properties of these compounds), positive findings are of value in selecting samples for the more complex analyses. The same approach may be of value in the case of using 2,4,5-trichlorophenol as an indicator for tetrachlorodibenzodioxin analysis.

Since di-, tri-, tetra-, and penta-chlorophenols are common alteration products of many pesticides (PCNB, HCB, ronnel, 2,4,5-T, silvex, 2,4-D, and many others containing a chlorinated benzene ring), positive findings of chlorophenols may indicate the need for more specific analysis of such samples for dioxins, furans or parent pesticide.

References

(1) EPA, "Notice of Rebuttable Presumption Against Registration and Continued Registration of Pesticide Products Containing Pentachlorophenol", Federal Register, 43, pp. 48443-48617, 10/18/78.

(2) Berg, G.L. (Editor), Farm Chemicals Handbook, p. D-192, Meister Publishing Co., Willoughby, Ohio, (1976).

(3) Firestone, D., "Chemistry and Analysis of Pentachlorophenol and Its Contaminants", FDA Papers, 8, pp. 57-89, (1977).

(4) American Wood Preservers Institute, Subcommittee No. 6, "Pentachlorophenol - A Wood Preservative", Memorandum for OPP, EPA, 3/1/77.

(5) Menzie, C. M., "Metabolism of Pesticides - Update II", p. 221, USDI Fish and Wildlife Service, Special Scientific Report - Wildlife No. 212, (1978).

(6) Firestone, D., et al., J. Agric. Food Chem., 27, pp. 1171-1177 (1974).

(7) Bemelmans, J.M.H., J. Agric. Food Chem., 22, pp. 1137-1138 (1969).

(8) Miller, C.G., et al., J. Agric. Food Chem., 17, pp. 1244-1246 (1969).

(9) von Rumker, R, et al., "Production, Distribution, Use and Environmental Impact Potential of Selected Pesticides", p. 308-319, EPA 540/1-74-001, EPA (1975).

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