REPORT OF THE AD HOC STUDY GROUP ON

PENTACHLOROPHENOL CONTAMINANTS

DECEMBER 29, 1978

ENVIRONMENTAL HEALTH ADVISORY COMMITTEE
SCIENCE ADVISORY BOARD
U.S. ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA NOTICE

This report has been written as part of the activities of the Environmental Health Committee of the Science Advisory Board, a public advisory group providing extramural scientific information to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide a balanced expert assessment of the scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency, hence its contents do not necessarily represent the views and policies of the Environmental Protection Agency, nor does mention of trade names or commerical products constitute endorsement or recommendation for use.

TABLE OF CONTENTS

List of Tables

List of Tables (Cont.)

1. SUMMARY and CONCLUSIONS

1.1 Background

In the fall of 1970, the U.S. Department of Agriculture (USDA) expressed concern about the presence of certain chlorodioxins in some "economic poisons." In January 1971, the USDA held a meeting with industry officials to discuss the problems of these chlorodioxins in pentachlorophenol (PCP). At that time the hexa- and heptachlorodibenzo-p-dioxins (dioxins) were identified as the contaminants of major concern in PCP. Since that time the intensity and breadth of concern about the health implications of polychlorinated dibenzo-p-dioxins have increased. This concern has no doubt been stimulated by the development and widespread publication of knowledge of the extremely high toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Although TCDD is or has been a contaminant of great concern in several well publicized cases, it should be noted that TCDD has not been identified as a contaminant of pentachlorophenol manufactured in the United States. Frequent references to TCDD in subsequent discussions are because it is the only polychlorinated dibenzo-p-dioxin that has been the object of comprehensive toxicologic research. Several other polychlorinated dibenzo-p-dioxins and related polychlorinated dibenzofurans have now, however, been identified as contaminants of commercial samples of pentachlorophenol. A commercial process has been developed and patented which enables production of pentachlorophenol with greatly reduced concentrations of these contaminants. This development, as well as the scheduled reregistration procedures required under the amended Federal Insecticide, Fungicide, Rodenticide Act (FIFRA), stimulated the EPA to give extensive consideration to whether or not the polychlorinated dibenzodioxins present in PCP have contributed to increased health hazards or environmental degradation associated with PCP use.

The EPA requested that the Science Advisory Board (SAB) consider this issue. The request was referred to the Environmental Health Advisory Committee of the SAB. On January 12, 1977, the Chairman of the Environmental Health Advisory Committee appointed an Ad Hoc Study Group on Pentachlorophenol Contaminants and charged it to review and report on available information about the chemistry and toxicology of the chlorinated dibenzodioxins and

dibenzofurans. Additionally, to the extent possible, the study group was asked to comment on the potential hazard to humans which could be attributed to registered uses of PCP and the extent to which this hazard might be mitigated by use of a commercial process which results in lower levels of chlorinated dibenzodioxins and related contaminants (see Charge to Study Group--Appendix B).

Early in its deliberations the Study Group recognized that the breadth of the charge, as well as the relative paucity of information on the chemistry and toxicology of polychlorinated dibenzo-p-dioxins and dibenzofurans, precluded an early or comprehensive response. By consensus, the Study Group agreed to respond to the charge by attempting to identify the areas of information needs required to evaluate the problem of PCP contamination with dioxins and related compounds. The Study Group would supply specific information when possible and would attempt to identify the information gaps which limit conclusions regarding both specific regulatory questions concerning PCP and the broad issues of total environmental contamination by chemically and toxicologically related halogenated dioxin-like substances.

1.2 Discussion

Pentachlorophenol is produced and used extensively. Production in the U.S. is estimated at approximately 50 million pounds per year; the vast majority of which is used as a wood preservative. However, there are other uses including use as an herbicide, a fungicide, a bacteriocide, a slimicide and as a preservative for leather.

Numerous contaminants have been identified and quantified in samples of pentachlorophenol from several major commercial producers. The quantity and proportions of the contaminants differ somewhat from batch-to-batch of the technical grade product and are discussed in more detail in Appendix C. The contaminants include tetrachlorophenol (5-10%), trichlorophenol (1%), chlorinated phenoxyphenols (about 5%) and polychlorinated dibenzo-p-dioxins and dibenzofurans ranging in concentration from thousands of ppm in the case of octachlorodibenzo-p-dioxin to tens to hundreds of ppm for the hexa- and heptachlorinated dibenzo-p-dioxins and for the octa-, hepta- and hexachlorodibenzofurans.

While it is technically feasible to produce commercially purified PCP that can meet reasonable regulatory constraints relative to chlorinated dibenzo-p-dioxins and dibenzofurans, the production of this more purified product entails increased production costs and, according to some industry representatives, results in a product that may be more difficult to handle. A patented commercial process exists which enables the production of PCP which contains much lower concentrations of contaminants reducing the hepta- and octachlorodibenzo-p-dioxins to 10 to 20 ppm and most of the other polychlorinated dibenzo-p-dioxin and dibenzofuran concentrations to 1 or 2 ppm. However, the production of the purified product results in another serious problem of how to safely handle and dispose of the concentrated residual waste created in the removal of the contaminants. The matter of disposal has been a subject of serious consideration by a previous advisory committee and by industry representatives. (See Appendix D.) There is no question that the handling, transport and disposal of any residual toxic product from the purification process must proceed under the strictest standards. Possible disposal methods include a suitable licensed disposal site (none is known according to Reichhold, Appendix D) and either land or sea incineration. Presently, the Dow Chemical Company's Midland, Michigan petrochemical complex uses incineration to destroy the wastes associated with PCP purification. (See letter of Robert Johnson to Ernst Linde, Appendix D.)

With regard to the possibility of human exposure to PCP and/or its contaminants, it is useful to consider certain physico-chemical properties of PCP relative to its contaminants. The chlorinated dibenzo-p-dioxin and dibenzofuran contaminants are less volatile and less water-soluble than the un-ionized form of PCP and are, therefore, less readily transported by vaporization and air transfer or by surface water. Furthermore, the dioxins tend to bind strongly to soil and wood, which further limits their transport. On the other hand, the contaminants are generally more persistent than PCP, as they are only slowly biodegradable with half-lives in soil on the order of a year or longer. Although there are considerable data on the environmental persistence of TCDD, for which photodecomposition on surfaces and microbial metabolism are major factors in its environmental degradation, data are very sparse on the environmental persistence and transport of the chlorinated dibenzo-p-dioxin and dibenzofuran contaminants of pentachlorophenol.

A key problem to overcome in order to make an adequate evaluation of the relative hazard of PCP and its contaminants is the lack of ready availability of suitably sensitive and specific analytical methods. Although much progress has been made in developing appropriate analytical capability, routine analysis has been hampered by the unavailability of suitable analytical standards for some of the isomers. In fact, the availability of appropriately specific analytical methods may be the rate limiting factor in assessing the hazard of dioxins and related chemicals. Thus, when there are several isomers with widely differing toxicities, as is the case with hexachlorodibenzo-p-dioxins, analyses of the isomers as a group only permit assessment of hazard based upon the most toxic isomer. This approach may, indeed, lead to overestimates of hazard, but, in the absence of more definitive analyses of specific toxic chemical species, it is necessary to treat contamination data on a toxicologically worst-case basis.

The toxicological information necessary to make the evaluation of relative hazard of purified versus standard commercial PCP is also deficient. Pentachlorophenol Is a toxic chemical in its own right. A set of signs and symptoms characteristic of uncouplers of oxidative phosphorylation has been described in several cases of accidental or suicidal poisonings. The chlorinated dibenzo-p-dioxins and dibenzofurans, on the other hand, have quite a different syndrome in acute poisoning. This syndrome is characterized by a delayed onset and involves widespread degenerative changes in several organs, in particular the liver, thymus, and skin. There are limited data on the acute toxicity (LD_{50}) of the chlorinated dibenzo-p-dioxin and dibenzofuran contaminants of PCP, but there are virtually no data on the chronic toxicity of the contaminants. Although the acute toxicity of purified PCP is generally less than that of contaminated technical samples, there are insufficient data to permit such a comparison for chronic toxicity. Studies of acute toxicity of technical PCP suggest that some of the effects, e.g., liver damage, are more consistent with a dioxin effect than with purely a PCP effect. Induction of aryl hydrocarbon hydroxylase (AHH) activity appears to offer a means of comparing the relative biological activity of poly-chlorinated dibenzo-p-dioxins and dibenzofurans and cor-relates quite well with acute toxicity measurements. How-ever, a problem is that this test has not been validated for assessing relative potential for chronic injury from the contaminants. Recent reports of the induction of

neoplasms by TCDD (Van Miller et al., 1977; Kociba, 1977) raises the specter that the polychlorinated dibenzo-p-dioxin contaminants of PCP may also have this potential. At least some of these contaminants, e.g., octachlorodibenzo-p-dioxin, have been started in the National Cancer Institute's (NCI) carcinogenesis screening program, but no data have yet been made available from NCI on PCP itself. (See section 3.1.4 for discussion of purified PCP.) A paper dealing with long term studies of TCDD and HCDD was recently presented at the New York Academy of Sciences Science Week (Holmes et al., 1978).

A recent incident of illness in a herd of cows housed in a newly constructed barn in Michigan stimulated an investigation into possible contamination of tissue by residues of pentachlorophenol and its dioxin contaminants. Both PCP and some of the polychlorinated dibenzodioxins were found in tissues of these cows (Moore, 1977, see section 3.2.3). This finding of low, but detectable, levels of chlorinated dibenzo-p-dioxins in tissues of these animals is a matter of public health concern; however, the biological significance of this finding is not presently known.

There have been reports of occupational exposure to chlorinated dibenzo-p-dioxins resulting in adverse health effects in man. Usually chloracne has been the predominant sign of toxicity, although signs and symptoms of systemic poisoning (some of which are consistent with dioxin poisoning in laboratory animals) have also been reported in association with these industrial exposures. There is insufficient information concerning the identity and dosage of dioxins involved to allow these observations in man to be useful in a quantitative assessment of the relative hazard of purified PCP versus commercial products containing dioxin contaminants. There are no data that permit an estimate of the relative susceptibility of humans to systemic effects of the dioxins and related contaminants of PCP. The widespread (though of relatively brief duration) exposure of humans to TCDD in Seveso, Italy during an industrial accident in 1976 may yet provide information that will permit some estimates of human dose-response relationships to that dioxin. As yet, there is no quantitative information which permits a comparison of the toxicity of dioxin to humans versus other animals.

1.3 Conclusions

1. Toxic polychlorinated dibenzo-p-dioxin and dibenzofuran isomers are known to be present in commercial, technical pentachlorophenol (PCP). The most toxic dioxin known, TCDD, has not, however, been found in PCP.

2. Analytical methods and preparation of standards for analysis of the various isomers of the hexa-, hepta-, and pentachlorinated dioxins have been developed. The methodology and equipment required, however, have limited their widespread use.

3. Among the chlorinated dioxins there are marked differences in acute toxicity of the isomers; therefore when analysis of a PCP sample is expressed in terms of total isomers, such as hexachlorodibenzo-p-dioxins, evaluation of potential hazard must be based upon the most toxic of the hexachlorinated isomers.

4. The polychlorinated dibenzo-p-dioxin and dibenzofuran contaminants are more stable and persistent, but less mobile, in the environment than PCP.

5. There is evidence that the dibenzo-p-dioxin and dibenzofuran isomers can migrate from PCP-treated wood into animal tissues and products that are consumed by man. The toxicological impact of this exposure cannot be quantified with present data and information, but, conservatively, any exposure by this route must be considered undesirable and attempts should be made to prevent exposure.

6. Numerous cases of acute human poisonings with PCP have occurred, and some occupational exposures to PCP have resulted in chloracne and other signs suggestive of dibenzo-p-dioxin or dibenzofuran poisoning. The data and information related to these reports are inadequate to assess the toxic hazard of PCP and its contaminants to man.

7. The most probable opportunity for human exposure to toxic quantities of PCP and its contaminants is in the PCP production and utilization industries. Any major changes in the application of PCP must consider the implication to this high risk occupational group. Environmental exposures of humans are likely to be limited and most probably would occur from direct contact with PCP-treated wood, from exposures through ingestion of food contaminated by residues, or from occupational exposure from inhalation of off-gassing vapors from improperly treated wood.

8. Certain uses of PCP, e.g., application to wood used in human or animal housing or to wood that may come in contact with foods or feeds, increases the probability of exposure to man. Restrictions on such uses might be a first step in reducing the likelihood of injury from PCP and its contaminants.

9. There are insufficient quantitative data to rank the relative contribution of PCP to the overall environmental contamination with dibenzo-p-dioxins and dibenzofurans. However, because of PCP's extensive use, it may be a major source of chlorinated dioxins in the environment. As regards the dibenzofurans, PCP probably represents a lesser source. However, the similar toxicological effects produced by the polychlorinated dibenzo-p-dioxins, dibenzofurans, and other related compounds (chloroazobenzenes, chloroazoxybenzenes, chlorinated napthalenes, and polyhalogenated biphenyls) suggest the potential for additive hazard from the many sources of these contaminants. Quantitative data on the total environmental contaminants, the fractional contribution of the major sources of these contaminants, and the toxicological response to mixtures of contaminants are urgently needed.

10. Technology is now available which could markedly reduce the levels of dibenzo-p-dioxin and dibenzofuran contaminants in PCP. It would seem prudent, therefore, to control the contaminants to the extent possible by best manufacturing practice. This might best be accomplished by a phasing in of improved processing. This phasing in of the use of the more purified product must take into account the economic impacts as well as the possible trade-offs of occupational hazards related to residue handling, transport and disposal.

Addendum: Coincident with the final review of this report, an article appeared in Science (Vol. 202, p. 1166-1167, December 15, 1978) suggesting that "Dioxins" were produced in trace quantities during the combustion of a wide variety of materials and could be expected to have ubiquitous distribution in the environment. A preliminary review of some data that formed the basis of this report indicated that the quantities produced in most combustion activities would contribute extremely minute quantities or no dioxins to the environment. However, combustion of highly chlorinated materials in improperly fueled incinerators resulted in sufficient quantities of chlorinated dibenzo-p-dioxins to warrant attention and further investigation as to a possible source of environmental contamination.

1.4 References

Holmes, P.A., J.H. Rust, W.R. Richter, and A.M. Shefner (1978). Long term effects of TCDD and HCDD in mice and rats. In: Abstracts of N.Y. Academy of Sciences, Science Week (June 21-30, 1978) on The Scientific Basis for the Public Control of Environmental Health Hazards.

Kociba, R.J., Dow Chemical (1977). Letter and attachments to Thomas Holloway, EPA. September 7, 1977.

Moore, J.A. (1977). Memorandum to Director, NIEHS (March 21, 1977). Subject: Studies on Possible Pentachlorophenol/Dibenzodioxin Intoxication Progress Report #2.

Van Miller, J.P., J.J. Lalich, and J.R. Allen (1977). Increased incidence of neoplasms in rats exposed to low levels of 2,3,7,8- TCDD. Chemosphere 6 (9): 537-544.

2. SUMMARY of CHEMISTRY and ENVIRONMENTAL BEHAVIOR of PENTACHLOROPHENOL and ITS CONTAMINANTS

2.1 Pentachlorophenol and its Uses

Pentachlorophenol (PCP) is a compound of high and diversified biological activity. It has been shown to be an effective contact poison against bacteria, fungi and higher plants and is also toxic to animals. PCP has been registered for a wide variety of uses, including as a wood preservative, an herbicide, a slimicide, a preservative for hardboard and paper, a leather preservative, an additive in paints, and a treatment in greenhouses. The principal use of PCP, however, is in wood treatment as either the free phenol dissolved in a petroleum carrier or as the sodium salt in a water based dip treatment. PCP has been used for over 40 years in wood treatment. The current level of production and use in the United States is probably in excess of 50 million pounds per year. The manufacturing capacity is estimated to be approximately 70 million pounds per year.

2.2 Manufacture of PCP and its Contaminants

PCP in the United States is manufactured from phenol by a catalytic chlorination process. During chlorination, the temperature must be maintained above the melting point of the products formed; this, it is felt, contributes to the side reaction that gives rise to contaminants. Commercial technical PCP contains other chlorinated phenols, among them the 2,3,4,6-tetra isomer, traces of trichlorophenol, chlorinated dibenzo-p-dioxins, chlorinated dibenzofurans, chlorophenoxy phenols, chlorodiphenyl ethers, chlorohydroxydiphenyl ethers, and traces of even more complex reaction products of phenol. Most chlorobenzodioxins are the by-products about which there are the greatest concerns. Analyses of PCP have revealed that the principal chlorodioxin and chlorodibenzofuran contaminants are those containing six to eight chlorines. The highly toxic 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) has not been identified in any sample of PCP that has been analyzed. The compositions of a sample of commercial PCP and of a sample of purified PCP are given in Table 2.1. A representative distribution of isomers is given in Table 2.2.

TABLE 2.1

Comparison of composition of commercial grade and purified grade Pentachlorophenol (PCP)

Component	Analytical Results: Commercial[a] (Dowicide 7)	Purified[b] (Dowicide EC-7)
Pentachlorophenol	88.4%	89.8%
Tetrachlorophenol	4.4%	10.1%
Trichlorophenol	0.1%	0.1%
Chlorinated phenoxyphenols	6.2%	----
Octachlorodioxins	2500 ppm	15.0 ppm
Heptachlorodioxins	125 ppm	6.5 ppm
Hexachlorodioxins	4 ppm	1.0 ppm
Octachlorodibenzofurans	80 ppm	1.0 ppm
Heptachlorodibenzofurans	80 ppm	1.8 ppm
Hexachlorodibenzofurans	30 ppm	1.0 ppm

[a]Sample 9522 A
[b]Technical grade PCP reduced by distillation

TABLE 2.2

Chlorodioxin isomer distributions in commercial grade PCP (Dowicide 7) and PCP-Na samples. (Buser, 1975;1976)

Chlorodioxin	ppm chlorodioxin in PCP	ppm chlorodioxin in PCP-Na
1,2,3,6,7,9-Cl_6D	1	0.5
1,2,3,6,8,9-Cl_6D	3	1.6
1,2,3,6,7,8-Cl_6D	5	1.2
1,2,3,7,8,9-CL_6D	0	0.1
1,2,3,4,6,7,9-Cl_7D	63	16.0
1,2,3,4,6,7,8-Cl_7D	171	22.0
1,2,3,4,6,7,8,9-Cl_8D	250	110.0

2.3 Properties of PCP and its Contaminants

The physical properties of a compound play an important role in how the compound behaves under different conditions. These properties influence the mobility of a compound in air or water, its ability to adsorb to surfaces, and its disappearance due to some type of degradation. This behavior relates to the route and rate of exposure by which a compound might be received by man or other organisms. For these reasons the properties of PCP and its principal contaminants, dioxins and dibenzofurans, so far as possible, were evaluated in this report. (See Tables 2.3-2.5.) From these tables of physical properties it is ascertained that PCP has a higher vapor pressure, a higher water solubility, and a lower capacity for adsorption than the dioxins or dibenzofurans. For these reasons PCP is likely to be far more mobile than the dioxins or the dibenzofurans. The dioxins and dibenzofurans would probably show an enhanced propensity for adsorption and hence a low availability.

2.4 Detection and Quantification of PCP and its Contaminants

There are a number of methods that may be used for analyzing PCP; these include colorimetry, spectrophotometry, and gas chromatography (GC). Gas chromatography is probably the most sensitive and widely used method. It is routinely applied for detection and quantification of PCP down to the parts per billion range. Analytical methods employing gas chromatography and mass spectrometry have been devised for the chlorodibenzodioxins and chlorodibenzofurans. The current state of the art for TCDD provides a reliable analysis down to the low parts per trillion range. Gas chromatography alone is adequate only for the higher concentrations.

2.5 Environmental Chemistry

PCP has been found in a number of different environmental samples such as house dust, air, water and urine of presumably non-exposed humans. Frequently the appearance of PCP in non-biological samples can be explained by the proximity of a source of PCP, but in the case of the urine of presumably non-exposed humans the explanation is more elusive. It may be that exposure to treated wood or the use of PCP as a preservative in certain items affords human exposure, but another possibility that cannot be ruled out is the generation of pentachlorophenol in chlorination of water or perhaps even the generation of PCP by natural processes.

TABLE 2.3

Physical Properties of Pentachlorophenol (PCP)

Molecular Weight	266.35
Melting Point	191°C
Boiling Point	310°C (decomposes)
Density	1.987
Vapor Pressure	1.6×10^{-4} mm Hg (25°)
	1.2×10^{-1} mm Hg (100°C)
	40 mm Hg (211°C)
Solubility H_2O	20 ppm at 30°C
Solubility of sodium salt, H_2O	33g/100g
Partition Coefficient	$1 \times 10^{5.01}$
Molar Refraction	53.5

TABLE 2.4

Physical Properties of Various Chlorodioxins

Chlorodioxin	Mol. Wt.	M.P. C	"P" Value[a]	Estimated Vapor[b] Pressure	Molar Refraction	UV Max (CHCI) nm
2,7,-Cl_2	253.08	--	0.76	6.0×10^{-6}	--	302
2,3,7-Cl_3	287.53	162	0.86	3.6×10^{-6}	--	305
2,3,7,8,-Cl_4	321.87	306	0.51	1.7×10^{-6}	71.4	310
1,2,4,7,8-Cl_5	356.42	206	--	--	72.6	307
1,2,3,7,8-Cl_5	356.42	241	--	--		308
1,2,4,6,7,9-Cl_6	390.86	240	0.94[d]	6.6×10^{-7}	--	310
1,2,3,6,8,9-Cl_6	390.86	--		--	81.1	--
1,2,3,6,7,8-Cl_6	390.86	285	--	--		316
1,2,3,7,8,9-Cl_6	390.86	243	--	--		317
1,2,3,4,6,7,9-Cl_7	425.31	--	0.90	3.0×10^{-7}	85.9	--
1,2,3,4,6,7,8-Cl_7	425.31	--	0.90	--		--
1,2,3,4,6,7,8,9-Cl_8	459.75	331	0.90	1.8×10^{-7}	90.7	318

(a) Beroza, M. and M.C. Bowman, "p" value determined for dioxin between hexane and acetonitrile, J. Assoc. Offic. Anal. Chem. 48:358-370 (1965).

(b) Vapor pressure estimated from data of Woolson (Woolson et al., 1973).

(c) Estimated by summing atomic refractions.

(d) "p" value determined for mixture of hexachlorodioxin isomers.

TABLE 2.5

Solubility of Several Chlorodioxins in Various Solvents[a]

Solvent	Solubility in mg per liter		
	TCDD	HxCDD[b]	OCDD
acetone	90	--	5
anisole	--	2600	1700
benzene	470	1600	1000
chloroform	550	--	560
methanol	10	--	--
toluene	--	1800	1500
o-xylene	--	--	3600
water	0.0002	--	--

-- indicates no data

(a) Firestone observed that 1,2,3,6,7,8-HxCDD is considerably less soluble in organic solvents than other HxCDD isomers. The solubility of the 1,2,3,6,7,8-isomer in isooctane is about 20 mg/l.

(b) Dow standard 82-A, a mixture of 71% 1,2,3,6,7,8-HxCDD and 29% 1,2,3,6,7,9-HxCDD and 1,2,3,6,8,9-HxCDD.

Additionally, expesure to hexachlorobenzene (HCB) results in excretion of significant amounts of PCP in urine. Uptake of PCP by living organisms occurs quite readily, whether by oral, respiratory, or dermal routes. The material is excreted in urine either as free phenol or as conjugated metabolites. The length of time for loss of the ingested amount varies with the species and ranges up to 90 hours.

The distribution of the dibenzo-p-dioxins and dibenzofurans in the environment has been less widely studied. For the most part, in the studies that have been conducted exposure was likely to have occurred through use of materials containing these contaminants. Upon direct exposure, both the chlorinated dibenzodioxins (CDDs) and the chlorinated dibenzofurans (CDFs) are taken up and retained in the bodies of experimental animals. CDDs and CDFs do accumulate in tissues, but not as readily as some other chlorinated organic compounds such as dieldrin, DDT and polychlorinated biphenyls. This would be expected on the basis of the partition coefficients found for one or two members of the series. TCDD, the most toxic of the chlorinated dioxins, has been shown to have a half-life in rats of about 21 days. Analyses of samples of marine organisms for presence of TCDD were negative, but this may have been due to the limitation of the method's sensitivity (parts per billion range).

PCP as a free phenol has been found to adsorb readily on many surfaces, especially on soil. The adsorption is greatest when the molecule is un-ionized and least when it is in the form of a sodium salt or at a higher pH value. It has been found, at least in water, that even the sodium salt is readily adsorbed by suspended particulate matter and carried to the bottom of the water course.

Pentachlorophenol is susceptible to photochemical degradation, particularly in the presence of other substances. PCP photodegrades in water and various solvents to yield a variety of products.

The CDDs and CDFs are relatively less mobile than PCP. Their vapor pressures are substantially lower and their propensity for adsorption greater. Degradation of CDDs and CDFs in the environment, particularly in soil, is substantially slower than for PCP. Whereas PCP degrades in 30-50 days in moist soil, the half-life of TCDD was found to be approximately one year. Photodegradation of TCDD,

on the other hand, was found to be very rapid in the presence of hydrogen donors such as oils and 2,4,5-T.

The principal dioxin contaminant of technical pentachlorophenol is the octachlorodibenzo-p-dioxin, or OCDD. There is concern that this compound and the other chlorodioxins might be generated in burning treated paper or wood. Studies of R.H. Stehl and L.L. Lamparski (1977) and B. Ahling and L. Johansson (1977) indicate that low levels of the chlorodioxins might thus be generated under certain conditions of combustion. The levels are sufficiently low, however, as probably not to be a serious source of exposure.

Further discussion and documentation of the chemistry for PCP and its contaminants may be found in Appendix C, Section 7.

2.6 References

Ahling, B. and L. Johansson (1977). Combustion experiments using pentachlorophenol on a pilot scale and full-scale. Chemosphere 6 (7): 425.

Stehl, R.H. and L.L. Lamparski (1977). Combustion of several 2,4,5-trichlorophenoxy compounds: formation of 2,3,7,8-tetrachloro-dibenzo-p-dioxin. Science 197: 1008.

3. TOXICOLOGY

3.1 Toxicity of Pentachlorophenol in Laboratory Animals

The widespread use of pentachlorophenol (PCP) as an antimicrobial agent and the likelihood of commercial products being contaminated with certain highly toxic polychlorinated dibenzo-p-dioxins and dibenzofurans necessitate a review of the toxicological information currently available. Although this review is primarily concerned with data on PCP per se, available data on commercial samples are included for comparative purposes.

Results of acute toxicity studies by oral, dermal, and injection routes, repeated oral exposures of 3-8 months, a two-year oral test with PCP containing very low levels of contaminants, mutagenic and teratogenic studies, and a recent study on the effects of PCP on metabolizing enzymes are reviewed.

3.1.1 Sample Studies

Table 3.1 lists the composition of the samples used in the long term studies. The PCP content varies from 85% to 99%. There is no evidence of the presence of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), the most toxic of the polychlorinated dibenzo-p-dioxins. The 1,2,3,6,7,8-hexachlorodibenzo-p-dioxin (HxCDD) is the major hexa isomer (Buser, 1975;1976). The 1,2,3,7,8,9-isomer has been reported to produce chick edema. (Cantrell et al., 1969). The octachlorodibenzo-p-dioxin (OCDD) has shown little toxicity, possibly because of its low solubility. The objective in recent years has been to reduce the levels of polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans to a minimum in the commercial samples.

3.1.2 Acute Toxicity

Oral: The LD_{50} for PCP in male rats has been reported as 78 mg/kg (Deichmann et al., 1942), 90 mg/kg (Gabrilevskaya and Laskina, 1964), 146 mg/kg (Gaines, 1969) and 205 mg/kg, the last being Dowicide EC-7 (relatively pure). For the female rat, it was 135 mg/kg (Dow Chemical Co. Summary, 1969) and 175 mg/kg (EC-7) (Gaines, 1969).

The LD_{50} for mice was reported as 130 + 9.5 mg/kg (Pleskova and Bencze, 1959); 100-130 mg/kg for rabbits (Deichmann et al., 1942); for guinea pigs, 250 mg/kg (Gabrilovskaya and Laskina, 1964);and for swine 120 mg/kg

TABLE 3.1

PENTACHLOROPHENOL - COMPOSITIONS REPORTED FOR SOME SAMPLES USED IN TOXICITY TESTING*

	PURIFIED		COMMERCIAL	
	Aldrich (1) (3)	Dowicide EC-7 (2) (4)	Dowicide 7 (6)	Monsanto (1) (3)
Pentachlorophenol	> 99%	90.4 ± 1.0%	85-90%	84.6%
Tetrachlorophenol	< 0.1	10.4 ± 0.2	4-8 %	3 %
Trichlorophenol		< 0.1	< 0.1	
Higher Chlorophenols			2-6%	
Caustic Insolubles (max)			1	
2,3,7,8-Tetrachlorodibenzo-p-dioxins	< 0.1	< 0.05	None	< 0.1
Pentachlorodibenzo-p-dioxins	< 0.1			< 0.1
Hexachlorodibenzo-p-dioxins	< 0.1	1.0 ± 0.1	9.27	8 (5)
Heptachlorodibenzo-p-dioxins	≤ 0.1	6.5 ± 1.0		520
Octachlorodibenzo-p-dioxin	≤ 0.1	15.0 ± 3.0	575-2510	1380
Tetrachlorodibenzofurans	< 0.1			< 4
Pentachlorodibenzofurans	< 0.1			40
Hexachlorodibenzofurans	< 0.1	3.4 ± 0.4	Detected	90
Heptachlorodibenzofurans	< 0.1	1.8 ± 0.3	Detected	400
Octachlorodibenzofuran	< 0.1	< 1	Detected	260

*ppm unless otherwise stated

(1) Analyses by GC-MS - Sensitivity 0.1 ppm

(2) Analyses by GC-MS - Sensitivity 0.05 ppm

(3) J. A. Goldstein et al. (1977)

(4) B. A. Schewtz et al. (1976)

(5) Buser (1975) reported 1,2,3,7,8,9 HxCDD as major isomer (toxic)

(6) R. L. Johnson et al. (1973)

(Harrison, 1959). Dreisbach (1963) has reported an estimated dose for man to be as low as 29 mg/kg.

These data would suggest that PCP has moderate acute oral toxicity, but that the LD_{50} value may vary with the quality and quantity of contaminants. Man would appear to be more susceptible than the rodent and the female to be more susceptible than the male.

Skin Absorption: When PCP in an organic solvent was applied to rabbit skin under occlusion for 24 hours, 200 mg/kg was lethal, but 100 mg/kg and 50 mg/kg were not (Dow, 1969). The LD_{50} for rats has been reported as 96 mg/kg, 105 mg/kg, and 320 mg/kg (Demidenko, 1966; Noakes and Sanderson, 1969; Gaines, 1969) and that for mice as 261 $\pm$ 39 mg/kg (Pleskova and Bencze, 1959).

Subcutaneous Injection: The LD_{50} for the rat was 100 mg/kg, for the rabbit 70 mg/kg (5% in olive oil) (Deichmann et al., 1942), for mice 63 $\pm$ 3.2 mg/kg (Pleskova and Bencze, 1959).

Intravenous Injection: The lowest dose of PCP reported to kill rabbits was 22 mg/kg (Kehoe et al., 1939), when it was instilled as a 1% aqueous sodium pentachlorophenate.

Inhalation: Exposure to 5 mg/l dust for one hour did not kill male and female rats (Reichhold Chemicals, 1974). Demidenko (1969) reported the LD_{50} by inhalation to be 225 mg/kg for rats and 355 mg/kg for mice. The exposure concentration and the calculations to arrive at the LD_{50} dose were not given in the abstract. Workers have reported that the dust is irritating to the mucous membrane of the nose and throat.

Irritancy Tests: Rabbit eyes exposed to solid material showed slight conjunctival and slight iritic congestion in one of four eyes. Exposure of rabbit skin under occlusion caused minimal irritation on intact skin and slightly more on abraded skin (Dow, 1969).

Commercial samples have produced chloracne in the rabbit ear bioassay, whereas the purified material has not. Positive reactions could be produced by topical or oral application (Johnson et al., 1973).

Allergic contact dermatitis has not been a problem in handling the chemical.

Clinical Effects: Acute animal exposures have, in general, caused anorexia, diarrhea, stimulation of the central nervous system, increase in body temperature, anuria, paralysis of the hind legs and functional cardiovascular changes leading to death (Deichmann et al., 1942; Gabrilevskaya and Laskina, 1964; Pleskova and Bencze, 1959; Demidenko, 1966).

3.1.3 Subchronic Feeding Studies

Johnson et al. (1973) compared the toxicity of commercial PCP with improved process PCP and with a purified PCP. (The commercial sample contained 85-90% PCP, 9-26 ppm of HxCDD and 575-2150 ppm OCDD and produced chlorance of rabbit ears and chick edema in bioassays. The improved process PCP contained 88-93% PCP, 30 ppm OCDD and 1.0 ppm HxCDD. Neither the improved process PCP nor the chemically pure PCP produced chloracne or chick edema.) Three, 10 and 30 mg/kg per day (mixed with diet) were fed to Sprague-Dawley, Spartan strain rats for 90 days. The purified and the improved process PCP caused increase in liver weight at 30 mg/kg and 10 mg/kg and increased kidney weight at 30 mg/kg. The commercial sample caused a decrease in hematological values, an increase in alkaline phosphatase, a decrease in serum albumin, and an increase in liver weights at all levels; and focal hepatocellular degeneration and necrosis at the 30 mg/kg level. The authors concluded that the impurities causing toxic effects had been eliminated by the new process.

Knudson et al. (1974) fed PCP (Dynamit-Nobel) containing 200 ppm OCDD, 82 ppm pre-OCDD and no detectable TCDD to rats (SPF-Wistar) at levels of 0, 25, 50 and 200 ppm in the diet. Liver weight was increased in rats fed 50 and 200 ppm PCP and was accompanied by increased activity of microsomal liver enzymes. There were fewer calcium deposits in the kidneys of test rats. Twenty-five ppm was considered the no-effect level.

Kimbrough and Linder (1975) fed purified PCP to one group of ten male rats and commercial PCP to a second group for 90 days. A level of 1000 ppm in the diet, equivalent to approximately 50 mg/kg per day, was chosen for the purpose of examining liver changes by light and electron microscopy. Enlargement of hepatocytes was observed in the livers of rats fed pure PCP, whereas technical grade PCP caused foamy

cytoplasm, vacuoles, inclusions, single hepatocellular necrosis, slight interstitial fibrosis, and prominent brown pigment in macrophages and Kupffer cells. By electron microscopy, there was an increase in the smooth endoplasmic reticulum in the group fed technical PCP with less change in the rats fed pure PCP. There were many lipid vacuoles in the former group and some in the latter. Atypical mitochondria were observed in the livers of both groups.

Goldstein (1977) subsequently studied the differences between the hepatic effects produced by commercial and purified PCP with respect to drug metabolizing enzymes and presence of porphyria. Chemical analyses of the samples used are listed in Table 3.1. The technical grade material contained significant amounts of PCDD's and PCDF's, whereas the purified material contained less than 0.1 ppm of each isomer, the level of sensitivity of the method. Groups of six Sherman female weanling rats were fed pure or technical PCP at levels of 0, 20, 100 or 500 ppm mixed with Purina Chow. Animals were sacrificed after eight months and hepatic enzyme activity and hepatic porphyrins were determined.

Technical pentachlorophenol produced hepatic porphyria and increased hepatic aryl hydrocarbon hydroxylase activity, glucuronyl transferase activity, liver weight, cytochrome p-450, and microsomal heme, but not N-demethylase activity. The peak of the CO-difference spectrum of cytochrome p-450 was shifted to 448 nm, and there was a dramatic increase in the 455/430 ratios of the ethyl isocyanide difference spectrum. The enzyme changes were observed at 20 ppm of technical pentachlorophenol. Porphyria occurred at 100 and 500 ppm. Pure pentachlorophenol had no significant effect on aryl hydrocarbon hydroxylase activity, liver weight, cytochrome p-450, microsomal heme, the ethyl isocyanide difference spectrum, or N-demethylase activity at any dose level, but did increase glucuronyl transferase at 500 ppm. In contrast, both pure and technical pentachlorophenol decreased body weight gain comparably at 500 ppm. It was concluded that technical pentachlorophenol produces a number of liver changes which cannot be attributed to pentachlorophenol itself, but which are consistent with the effects of biologically active chlorinated dibenzo-p-dioxins and dibenzofurans. See Table 3.2.

TABLE 3.2

BIOLOGICAL ACTIVITY
PURIFIED VS TECHNICAL SAMPLES OF PCP

	Pure	Technical Grade
Chick edema	-	+
Chloracne	-	+
Porphyria	-	+
Increase in liver weight/body wt.	-	+
Increase in liver enzyme activity	+	+
Presence of pigment in liver cells	+,-	+
Liver histopathology	less	+
Depressed body weight	+	+
Embryotoxicity	+	+

- indicates no presence

+ indicates presence

3.1.4 Two-year Feeding Study

Schwetz et al. (1976) carried out a two-year oral study with Dowicide EC-7, a substance which the Johnson 90-day study had shown to act more like purified material than commercial preparations. Analyses of the samples used are given in Table 3.1.

Weanling Sprague-Dawley (Spartan-substrain) rats were divided into five groups of 25 males and 25 females each. They were fed a test diet of ground Purina Laboratory Chow mixed with PCP (dissolved in anisole), the amount being adjusted on a monthly basis to provide dose levels of 0, 1, 3, 10 or 30 mg/kg per day. The male rats were terminated after 22 months because of high mortality in both control and test groups. The female groups were terminated after 24 months. Gross and histopathological examinations were performed.

Effects, which the authors attributed to ingestion of PCP at the highest dose level of 30 mg/kg per day, were (1) a significant decrease in body weight among female rats; (2) a significant increase in serum glutamic pyruvic transaminase activity in male and female rats; (3) an increase in the specific gravity of urine among female rats at the end of one year but not at two years; (4) an accumulation of pigment in the liver and kidneys. An accumulation of pigment in the liver and kidneys was also observed in females fed 10 mg/kg per day. There were no other significant differences between test and control groups with respect to clinical observations, hematological changes, blood and urine chemistry, terminal organ weights and pathological changes. There was no evidence of carcinogenic effect, tumors being similar in number and kind in both test and control groups, nor was there a life-shortening effect attributable to the test material.

It was concluded, therefore, that doses of pentachlorophenol as high as 30 mg/kg per day fed throughout the life span produced only mild changes which did not shorten the life span or alter the incidence of tumors.

The results are consistent with those found by Goldstein (1977) when doses of approximately 25 mg/kg per day of purified material fed for eight months caused weight loss. However, dark pigment in the liver reported by Schwetz et al. (1976) was observed by Kimbrough (1972)

in the livers of rats fed technical materials, but not in those fed purified PCP at doses of 50 mg/kg. An 18-month feeding study with mice at 130 ppm did not elevate the incidence of tumors (Innes, 1969).

3.1.5 Chronic Inhalation Exposures

A Russian study has reported that chronic exposure to 3 mg/M^3 caused threshold changes in an unidentified organism, but no details are given in the abstract. Based on this study and on observations in the workplace, maximum allowable concentrations were determined to be 0.1 mg/M^3 (Demidenko, 1969).

The American Conference of Governmental Industrial Hygienists (ACGIH) has established a threshold limit value (TLV) of 0.5 mg/M^3 (0.046 ppm), a level below which irritation to the nose, throat and eyes is minimal (ACGIH, 1971).

3.1.6 Mutagenic-Cytotoxic Potential

PCP has not shown mutagenic activity in the Ames test (Anderson et al., 1972), the host-mediated assay (Buselmaier et al., 1973), or the sex-linked lethal test on drosophila (Vogel and Chandler, 1974).

3.1.7 Teratogenic and Embryotoxic Potential

PCP did not cause deformities, but it was highly embryolethal and embryotoxic following oral administration to rats of 15,30, or 50 mg/kg per day on days 6-15 of gestation. No effects were produced at 5 mg/kg (Schwetz and Gehring, 1973; Schwetz et al., 1974). Purified PCP, with its low nonphenolic content, was slightly more toxic than the commercial grade (Schwetz et al., 1974).

Oral administration of PCP to the golden Syrian hamster at levels ranging from 1.25 to 20 mg/kg daily from days 5 to 10 of gestation resulted in fetal deaths and/or resorptions in three of six test groups. PCP was found in the blood and fat of the fetuses (Hinkle, 1973).

Pregnant rats (Charles River-CD Strain) were given 60 mg/kg of labeled PCP on days 8 through 13 of gestation and were sacrificed on the 20th day. Only a small amount of PCP crossed the placental barrier and only slight teratogenic effects were noted (Larsen et al., 1975).

3.1.8 Summary

Laboratory studies to evaluate the toxicity of PCP as a wood preservative or pesticide began in the 1930's and have continued to the present time. PCP is considered a toxic compound, an economic poison, whose toxicity may vary depending upon the quality and quantity of contaminants which vary with different manufacturing procedures. Samples were not adequately characterized until recently when some insoluble contaminants were recognized to be the highly toxic polychlorinated dibenzodioxins and furans. Due to the difficulty of separating the isomers and in obtaining standards for analyses, there are many gaps in the toxicity data, creating uncertainty in any evaluation of the potential hazard.

An attempt must be made to differentiate between the clinical and pathological effects of PCP, the related phenols, and its likely contaminants, reported as (1) hexa-, hepta- and octachlorodibenzodioxins and (2) hexa-, hepta- and octachlorodibenzofurans. In addition there may be chlorophenoxyphenols and chlorinated diphenyl ethers (reported in European samples) whose identification, amounts, and toxicity have not been evaluated.

The increasing oral LD_{50} values through the years are probably related to improved process procedures, being reported in 1942 as 78 mg/kg and in 1969 as 205 mg/kg for male rats. PCP is easily absorbed through the skin, the LD_{50} for rabbits being similar to that by oral dosing when the material was applied in a lipid solvent under occlusion.

In general, acute exposure of animals has led to rapid development of high body temperature, increased respiratory rate, moderately elevated blood pressure, hyperglycemia, and muscle weakness, terminating in asphyxial convulsions with cardiac arrest, which tends to occur in less than 24 hours. Pathological examinations showed extensive damage to the cardiovascular system. These changes resemble those produced by the related phenolic compound dinitro-orthocresol (DNOC). Barnes (1957) concluded that both DNOC and PCP interfere with production of high energy phosphate compounds essential to cell respiration. This interference causes stimulation of the cell metabolism to the toxic stage with accompanying fever and the other clinical signs described above.

Most chlorinated dibenzodioxins, on the other hand, show a very different clinical picture. Oxidative phosphorylation is not affected. The effects are usually delayed (several weeks to months) and may be accompanied by effects on the liver, the hemopoietic system, and the lymphatic system with thymic atrophy and lymphoid depletion. There is a marked increase in liver microsomal enzyme activity and eventual histological change. There is a striking difference in susceptibility among species, the guinea pig being the most susceptible and the female being more susceptible than the male.

Comparative chronic studies with purified and commercial PCP have been limited. In essence, however, studies show a marked difference in effect on the liver. The no-effect level for the relatively pure material in a 90 day test was 3-10 mg/kg; the no-effect level for commercial material was not established. A life time oral study was done only with new process material at dose levels of 3, 10 and 30 mg/kg. The data showed that at higher levels there were some functional changes which did not result in a shortening of the life span, higher incidence of tumors or significant pathology.

3.1.9 Conclusions

1. Experience has shown that dermal absorption is the primary hazard to man from the use of PCP as a wood preservative.

2. The chemical has a low vapor pressure and is a respiratory irritant which has acted as a warning. No complaints have been noted when the concentration does not exceed the TLV.

3. In the United States there have been no reports of chronic injury to those workers exposed for as long as 35 years while manufacturing this material. This conclusion is supported by Western Electric (Ochrymowych, 1978), whose utility poles were treated with commercial grade PCP, with no reports of injury in over two decades of service. Deaths and injuries have arisen from mishandling of the material in the wood treatment process. There has been a complaint, however, when treated wood was used in a home interior without further finishing, a procedure which is not recommended.

4. Trace contaminants in the form of chlorinated dioxins and chlorinated dibenzofurans are present in biologically active amounts. Due to limited knowledge of the amounts and toxicity of the isomers present, only tentative conclusions as to their contribution to the total toxicity picture and the extent of the hazard to the general public can be made.

3.1.10 References

ACGIH (1971). Documentation of TLV's for Substances in Workroom Air. Third edition.

Amer, S. M. and E.M. Ali (1969). Cytological effects of pesticides. IV. Mitotic effects of some phenols. Cytologia 34(4): 533-40 (CA 73;24223h).

Anderson, K. J., E.G. Leighty, and M.T.Takahashi (1972). Evaluation of herbicides for possible mutagenic properties. J. Agr. Food Chem. 20: 649-56.

Buselmaier, W., G. Roehrborn, and P. Propping (1973). Comparative investigations on the mutagenicity of pesticides in mammalian test systems. Mutat. Research 21(1): 25-6.

Buser, H-R (1975). Polychlorinated dibenzo-p-dioxins, separation and identification of isomers by gas chromatography - mass spectrometry. J. Chromatog. 114: 95-108.

Buser, H.-R (1976). High resolution gas chromatography of polychlorinated dibenzo-p-dioxins and dibenzofurans. Anal. Chem. 48:1553.

Cantrell, J. S., N.C. Webb, and A.J. Mabis (1969). The identification and crystal structure of a hydropericardium-producing factor: 1, 2, 3, 7, 8, 9-hexachlorodibenzo-p-dioxin. Acta Cryst. B25: 150-156.

Deichmann, W. B., W. Machle, K.V. Kitzmiller, and G. Thomas (1942). Acute and chronic effects of pentachlorophenol and sodium pentachlorophenate upon experimental animals. J. Pharm. Exptl. Therap. 76: 104.

Demidenko, N. M. (1966). Toxicological properties of pentachlorophenol. Gig. Toksikol. Pestits. Klin. Otravleni, (4): 234-9.

Demidenko, N. M., (1969). Maximum permissible atmospheric concentration of pentachlorophenol. Gig. Tr. Prof. Zabol. 13 (9): 58-60. (CA 72:47095M).

Dow Chemical Co. (1969) Toxicity Summary for Dowicide 7.

Dreisbach, R. H. (1963). Handbook of Poisoning: Diagnosis and Treatment, p. 256.

Fed. Proc. (1943). Fed. Am. Soc. Exp. Biol. 2:76.

Gabrilevskaya, L. N. and V.P. Laskina (1964). Maximum permissible concentrations of PCP and Na-pentachlorophenolate in water reservoirs. Sanit.Okhrana Vodoemov ot Zagryazneniya Prom.Stochnymi Vodami, (6): 251-272 (CA 62;15304d).

Gaines, T. H. (1969). Acute toxicity of pesticides. Toxicol. Appl. Pharmacol. 14(3): 515-34.

Goldstein, J. A. (1977). Effects of pentachlorophenol on hepatic drug metabolizing enzymes and porphyria related to contamination with chlorinated dibenzo-p-dioxins and dibenzofurans. (In press).

Grant, W. F. (1973). Cytological effects of environmental mutagens - pesticides. Mutat. Res. 21(4): 221-2.

Harrison, D. L. (1959). The toxicity of wood preservatives to stock, Part I: Pentachlorophenol. New Zealand Vet. J. 7: 89-98 (CA 55:23814e).

Hinkle, D. K. (1973). Fetotoxic effects of pentachlorophenol in the golden Syrian Hamster. Tox. and Appl. Pharmacol. 25(3): 455 (abstract).

Innes, J. R. M. et al. (1969). Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: A preliminary note. J. Natl. Canc. Inst. 42: 1101-14.

Johnson, R. L., P.J. Gehring, R.J. Kociba, and B.A. Schwetz (1973). Chlorinated dibenzodioxins and pentachlorophenol. Environ. Health Perspect. 5: 171-5.

Kehoe, R. A., W. Deichmann-Gruebler, K.V. Kitzmiller (1939). Toxic effects upon rabbits of pentachlorophenol and sodium pentachlorophenate. J. Indust. Hyg. & Toxicol. 21: 160-172.

Kimbrough, R. D. (1972). Toxicity of chlorinated hydrocarbons and related compounds. Arch. Environ. Health 25(2): 125-31.

Kimbrough, R. D. and R.E. Linder (1975). The effect of technical and 99% pure pentachlorophenol on the rat liver. Light microscopy and ultrastructure. Toxicol. Appl. Pharmacol. 33: 131-132. (Abstract).

Knudson, I., H.G. Verschuuren, E.M. Den Tonhelaar, R. Kroes, and P.F.W. Helleman (1974). Short-term toxicity of pentachlorophenol in rats. Toxicol. 2: 141-152.

Larsen, R. V., G.S. Born, W.V. Kessler, S.M. Shaw, D.C. Von Sickle (1975). Placental transfer and teratology of pentachlorophenol in rats. Environ. Lett. 10(2): 121-8.

Lehman, H. J. (1951) Quart. Bull. Assoc. Food and Drug Officials 15: 122-33.

Levin, J-O,C. Rappe, and C. -A Nilsson (1976). Use of chlorophenols as fungicides in sawmills. Scand. J. Work Environ. and Health 2: 71-81.

Noakes, D. N. and D.M. Sanderson (1969). A Method for determining the dermal toxicity of pesticides. British J. of Indust. Med. 26: 59-64.

Ochrymowych, J., Western Electric (1978). Personal communication.

Pleskova, A. and K. Bencze (1959). Toxic properties of pentachlorophenol. Pracovni lekerstvi 11: 348-54.

Reichold Chemicals (1974). Report of May 28, 1974.

Schwetz, B. A. and P.J. Gehring (1973). The Effect of tetrachlorophenol and pentachlorophenol on rat embryonal and fetal development. Toxicol. Appl. Pharmacol. 25 (3): 455 (Abstract).

Schwetz, B. A., P.A. Keeler,P.J. Gehring (1974). The Effect of purified and commercial grade pentachlorophenol on rat embryonal and fetal development. Toxicol. Appl. Pharmacol. 28(1): 151-61.

Schwetz, B. A., J.F. Quast,C.G. Humiston,C.E. Wade, G.C. Jersey, R.W. Lisowe, and R.J. Kociba (1976). Results of a toxicological evaluation of pentachlorophenol sample XD 8108.00L administered to rats by the dietary route on a chronic basis. (Dow Chemical Co. Report - unpublished).

Vogel, E. and J.L.R. Chandler (1974). Mutagenicity testing of cyclamate and some pesticides in drosophila melanogaster. Experientia 30(6): 621-3.

3.2 Toxicity of Chlorinated Dioxins and Dibenzofurans

3.2.1 Toxicity of Chlorinated Dibenzo-p-dioxins

It has been reported that hexachlorinated, heptachlorinated, and octachlorinated dibenzo-p-dioxins are found in pentachlorophenol. Of the ten hexachlorodibenzo-p-dioxin isomers theoretically possible, only six are predicted and have been found in pentachlorophenol (Stehl and Crummett, 1977; Vogel 1977). Of these six, two (1,2,3,7,8,9- and 1,2,3,6,7,8-hexachlorodibenzo-p-dioxin) would be expected to have marked toxicity given that the 2,3,7,8, positions are halogenated. Previous toxicity studies have shown that the single oral LD_{50} of these two isomers in guinea pigs ranges between 60 and 100 ug/kg (McConnell et al., 1978). The comparative toxicity of various dibenzodioxin isomers does show a positive correlation between *in vivo* toxicity and the ability of these isomers to induce arylhydrocarbon hydroxylase (AHH) enzyme systems in chick embryos (Poland and Glover, 1973). Utilizing AHH induction data to predict toxicity, one predicts several orders of magnitude decrease in the toxicity of the other four hexachlorodibenzo-p-dioxin isomers (1,2,4,6,7,9-, 1,2,4,6,8,9-, 1,2,3,6,7,9- and 1,2,3,6,8,9-). Specific toxicologic evaluation of the other isomers has not been performed.

Chronic (two year) toxicity studies of a mixture of two hexachlorodibenzodioxins is in progress at the Illinois Institute of Technology Research Institute through an NCI contract. The two isomers present in this mixture are the 1,2,3,6,7,8 and 1,2,3,7,8,9-hexachlorodibenzodioxins. A hexa-chlorodibenzodioxin mixture (the specific isomer composition is unknown) has been found to induce chloracne in the rabbit ear bioassay as indicated by the formation of comedones (Schwetz et al., 1973). In teratology studies, this hexachlorodibenzodioxin mixture was found to cause maternal toxicity in rats at a dose of 100 ug/kg/day; doses of 10 or 100 ug/kg/day of hexachlorodibenzo-p-dioxins were highly lethal to fetuses during late gestation. The weight and length of surviving fetuses were also significantly decreased. A significant increase in fetal abnormalities was observed in offspring from rats that received the 100 ug/kg/day dose. Subcutaneous edema of the fetuses was observed at a 1 or 10 ug/kg/day dose, whereas the 0.1 ug/kg/day dose did not yield any fetal anomalies. Schwetz et al. (1973) also produced chick edema in birds treated with 10 and 100 ug/kg/day of hexachlorodibenzo-p-dioxin.

There are two heptachlorinated dibenzodioxin isomers possible, both of which have been found in pentachlorophenol. Of these two, the 1,2,3,4,6,7,8- isomer would be expected to be the more toxic. Specific toxicity studies on this isomer are incomplete. In a guinea pig toxicity study, animals survived a single oral dose of 180 ug/kg with little or no toxicity observed (McConnell et al., 1978). Further studies are currently in progress at the National Institutes of Environmental Health Sciences (NIEHS) in which guinea pigs are receiving doses of 200, 400, or 600 ug/kg.

The toxicity of octachlorodibenzo-p-dioxin is not known. Oral doses of 1 g/kg did not cause death in five female rats or in four male mice that received 4 g/kg (Schwetz et al., 1973). In a teratology study with octachlorodibenzodioxin, no signs of maternal toxicity were observed in rats that received either 100 or 500 mg/kg/day of OCDD. No increase in fetal absorptions or fetal anomalies was observed at the 500 mg/kg dose. The incidence of subcutaneous edema was significantly increased. In a chick edema bioassay, edema was not observed in chicks that were maintained on a diet containing 0.5% OCDD for 21 days (Schwetz et al., 1973).

Table 3.3 summarizes relative dibenzo-p-dioxin/dibenzofuran toxicity where data are available. Comparative toxicologic data show that the pattern of toxicity caused by dioxin isomers is the same as that produced by TCDD (McConnell et al., 1978). Experiments with carbon 14-labelled TCDD indicated that dioxins pass the placental barrier and are secreted in milk (Moore et al., 1976). It has been shown that TCDD causes immunosuppression (Vos and Moore, 1974); increased susceptibility to bacteria (Thigpen et al., 1975); and fetal death or birth defects (Courtney and Moore, 1971).

3.2.2 Dibenzofurans

Relatively little work has been directed toward the specific indentification of dibenzofuran isomers present in pentachlorophenol. Preliminary work reported by Stehl and Crummett (1977) records the presence of the 2,3,6,7- and 2,4,6,7-tetrachlorodibenzofurans and the 2,3,4,6,7-, 1,2,4,7,8- and 2,3,4,7,8-pentachlorodibenzofurans as well as the 1,2,3,6,7,8-hexachlorodibenzofuran. Quantification of the levels of these isomers in pentachlorophenol was not done due to interferences with other chemicals (chlorinated diphenyl oxides). Of the isomers reported, the 2,3,4,7,8

TABLE 3.3

TOXICOLOGY DATA SUMMARY

	DIBENZODIOXINS											DIBENZOFURANS		
	Tetra Chloro	Hexachloro-							Heptachloro-		Octa Chloro-	Tetra Chloro	Penta Chloro	Hexa-Chloro
	2,3,7,8	Mixture of Hexa Isomers	1,2,3, 6,7,8	1,2,3, 7,8,9	1,2,4, 6,7,9	1,2,4, 6,8,9	1,2,3, 6,7,9	1,2,3, 6,8,9	1,2,3,4, 6,7,8	1,2,3,4, 6,7,9	1,2,3,4, 5,6,7,8	2,3,7,8	2,3,4, 7,8	1,2,3 6,7,8
LD_{50} (single dose) µg/kg														
Guinea Pig	2		70-100	60-100					>180			>5<10	>3<10	
Mice	114/283		1250	>1440							>1,000,000	>6000		
Rat	22										>4,000,000	>1000		
Monkey (Rhesus)	<70											1000		
AHH Induction in Chick Embyro Relative to TCDD	1		0.25	0.25	0.002		0.15		0.15	0.002	0.002	0.7	0.7	
Teratogenic Dose µg/kg	1 (mice)	100 (rat)												
Fetotoxic Dose µg/kg														
Mice	1													
Rat	0.5	>.10									500 mg/Kg			
3-Generation Study - Rat µg/Kg	0.01 NE 0.001													
Reproduction - Primates	500 ppt toxic													
90-Day Study - Rat µg/Kg	0.01 NE 0.001													
2-Year Study	In Progress	In Progress												
Chloracne	Yes	Yes												
Chick Edema Bioassay (21-day)	1µg/Kg/day	10µg/Kg/day									0.5% in Diet - NE	1µg/Kg/ day		
Increased Disease Susceptibility	1µg/Kg 1/wk x 4 wks													

NE= no effect

Data taken from references in section 3.2.4

and 1,2,3,6,7,8 would be of prime toxicologic interest. Toxicity studies with the 2,3,4,7,8-pentachlorodibenzofuran have been performed in guinea pigs (Moore, 1977). A single oral dose caused death in 6/6 animals that received 30 or 10 ug/kg. All animals survived a 30-day observation period subsequent to receiving 3 or 1 ug/kg. Toxicity was observed at the 3 ug/kg dose while only an increase in liver size was seen at the 1 ug/kg dose. The pattern of the toxic response is similar to that reported in studies using the 2,3,7,8-tetrachlorodibenzofuran (Moore et al., 1975).

3.2.3 Chlorinated Dibenzo-p-dioxin/Dibenzofuran Toxicity/Contamination Associated with Exposures to PCP

The dibenzofurans and dibenzo-p-dioxins present in pentachlorophenol have been responsible for animal health problems. The chick edema disease problem of the 1950's and 1960's was in part traceable to pentachlorophenol contaminants (Firestone,1973).

Recent studies at the National Institute of Environmental Health Sciences have identified the presence of hexa-, hepta-, and octachlorinated dibenzo-p-dioxins in tissues from a dairy herd in Michigan. The results of dioxin analyses of tissue samples taken from the herd are summarized as follows:

Tissue	Number of Samples	Number of Samples in which Detected Octadioxin	Heptadioxin	Hexadioxin
Liver	15	15	15	9
Fat	7	7	6	1
Range (ppb)		0.23-47.0	0.03-12.0	0.01-1.3

A possible source of these tissue contaminants was PCP-treated wood used in the construction of a new barn in which the cows were housed and fed (Moore, 1977).

Although the presence of toxic chlorinated dioxins in tissues of food animals is a matter for serious public health concern, there is insufficient evidence to conclude that contaminants from PCP-treated wood were the cause of illness in the Michigan cows. Van Gelder (1977) concluded that although the contaminants were more toxic than the PCP itself, they were not present in sufficient amounts to cause illness. Controlled dosing experiments, recently completed, may help answer questions raised by the Michigan field studies concerning the pharmacokinetics and toxicity of PCP and its contaminats in cattle (Moore, 1978). Results of these experiments are expected in late 1978.

3.2.4 References

Courtney, K. D. and J.A. Moore (1971). Teratology studies with 2,4,5-trichlorophenozyacetic acid and 2,3,4,8-tetrachlorodibenzo-p-dioxin. Toxicology and Applied Pharmacology 20: 396-403

Firestone, D. (1973). Etology of chick edema disease. Environmental Health Perspectives, Experimental Issue Number 5:59-66.

McConnell, E. E., J.A. Moore, J.K. Haseman, and M.W. Harris (1976). The Comparative toxicity of chlorinated dibenzo-p-dioxin isomers in mice and guinea pigs. Toxicology & Applied Pharmacology 37: 145, abstract (Manuscript in preparation).

Moore, J. A. (1977). Memorandum to Director, NIEHS (March 21,1977), subject: Studies on Possible Pentachlorophenol/ Dibenzodioxin Intoxication Progress Report #2.

Moore, J.A. (1978). NIEHS. Personal communication. August 1978.

Moore, J. A., B.N. Gupta and J.G. Vox (1975). Toxicity of 2,3,7,8-tetrachlorodibenzofuran - - preliminary results. National Conference on Polychlorinated Biphenyls, (November 19-21, 1975), Chicago, Illinois, Conference Proceedings, EPA-560/6-75-004.

Moore, J. A. , M.W. Harris and P.W. Albro (1976). Tissue distribution of carbon 14 tetrachlorodibenzo-p-dioxin in pregnant and neonatal rats. Toxicology & Applied Pharmacology 37 :146, abstract (Manuscript in preparation).

Poland, A. and E. Glover (1973). Chlorinated dibenzo-p-dioxin: Potent inducers of -aminolevulinic acid synthetase and aryl hydrocarbon hydroxylase. II. A study of the structure--activity relationship. Molecular Pharmacology 9, 736-747.

Schwetz, B. A., J.M. Norris, G.L. Sparschu, V.K. Rowe P.J. Gehring, J.L. Emerson, and C.G. Gerbig (1973). Toxicology of chlorinated dibenzo-p-dioxins. Environmental Health Perspectives, Experimental Issue Number 5: 87-100.

Stehl, R. and W.Crummett (1977). Letter to Dr. Thomas Bath, EPA.

Thigpen, J. E., R.E. Faith, E.E. McConnell, and J.A. Moore (1975). Increased susceptibility to bacterial infection as a sequela of exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Infection and Immunity 12 (6): 1319-1324.

Van Gelder, G. A. (1977). Prepared statement on the toxicity of pentachlorophenol and chlorodioxins in cattle and laboratory animals and results of field investigations of dairy farms in Michigan. Statement presented at administrative hearing, Michigan Department of Agriculture, Lansing, Michigan July 18-22, 1977).

Vogel, S. H. (1977). Presentation to PCP Ad Hoc Working Group (March 3, 1978).

Vos, J. G. and J.A. Moore (1974). Suppression of cellular immunity in rats and mice by maternal treatment with 2,3,7,8-tetrachlorodibenzo-p-dioxin. International Archives of Allergy and Applied Immunology 47:777-794.

3.3 Human Poisoning Involving PCP

The EPA Pesticide Episode Review System Report (PERS) No. 60 describes poisoning espisodes involving pentachlorophenol which occurred from 1966 to September 1, 1976. A total of 64 alleged episodes were located, 47 of which involved humans. Of these, 42 involved adults, four involved children, and one did not specify the age group. Three of the episodes involving children occurred at home and one at a job site. Eleven episodes involving adults (over 17 years old) occurred in the home and 28 at various job sites. Four of the human-related episodes involved combinations of pentachlorophonel and active ingredients other than chlorophenols and petroleum distillates.

Twenty-nine episodes involving humans (one a child less than 6 years old) were associated with occupational activities. Eight of these occurred at lumber-treating establishments.

Six episodes occurred during construction activities. Four of these involved individuals who were painting or otherwise applying the chemical to structures, and two involved carpenters who were working with treated lumber.

Five episodes occurred during occupationally-related agricultural activities. One of these involved a child who was splashed with the chemical while watching a man apply it to a post. The remaining four episodes involved adults.

Two episodes involved commercial pest control operators engaged in application of the chemical. In one episode, a man sprayed PCP in the crawl space beneath a house. He developed symptoms of weakness, headache, double vision, tachycardia, nausea and hyperpyrexia. He recovered after a short period of hospitalization. In the other episode, an individual working for a pest control company accidentally splashed the chemical into his eyes. This was diagnosed as mild chemical conjunctivitis.

In another job-related incident, an employee at a greenhouse worked for several weeks around benches which were treated with the chemical; he subsequently developed headaches and chronic coughing.

In one incident the affected person was working inside a school building while pentachlorophenol and bromacil were being applied nearby. A quantity of the mixture was drawn into the building through an air intake duct and blew directly into the face of a teacher. The only symptoms reported were shortness of breath and weakness.

Six episode reports concerning incidents associated with occupationally-related operations did not specify the type of job the affected individual was engaged in at the time of the accident. Five of these were minor reactions to the chemical; however, the remaining episode resulted in the death of the victim. In this episode the individual ingested the pesticide which was in an unmarked bottle. The man mistakenly thought the bottle contained water; he died enroute to the hospital.

In addition to those episodes which occurred during job-related activities, 14 others took place in the home. Of these, 11 involved adults and three involved children.

Of the three episodes involving children, one occurred when a child spilled the chemical on himself, resulting in a mild dermatitis; one involved a 5-year old who took a small amount of the chemical into his mouth without swallowing and recovered, the only symptoms to develop were nausea and vomiting; and one in which the report did not specify the circumstances of the episode.

All of the episodes affecting adults in the home were the result of application of products containing pentachlorophenol to the home. Five of these involved reactions of persons other than the applicator to the chemical after it was applied. Commonly reported in this type of involvement was a protracted period of illness which increased in severity over time. Three episodes were reported in which individuals who applied the material were affected. One of these was a minor reaction; however, those remaining were quite severe and persisted for an extended period. One involved an individual who applied the chemical to the exterior of an addition to his home. The man developed a severe cough persisting from at least August through November 1974. This was allegedly in response to an initial period of chemical application, with more severe symptoms occurring after a second period of application. The man was hospitalized for an extended period. In the other incident the subject had a number of manifestations compatible with poisoning by penta-chlorophenol or other polychlorinated phenols shortly after exposure to the product. These included excess perspiration, nausea without vomiting, abdominal pain, dry mouth, listlessness, and generalized dermatitis. Shortly afterwards she also developed generalized pruritus and several peripheral nerve manifestations, particularly numbness and pain in the left first dorsal segment,

generalized paraesthesia and Herpes Zoster of the tenth right dorsal segment.

Two additional episodes involved individuals who were opening cans of the chemical and were sprayed by the material in the process. Symptom development was not reported in either case. The final episode report was submitted with no reference to circumstances of exposure or the effects therefrom.

Four reports did not specify the episode location. One of these did not contain information about the circumstances of exposure, one involved a can which exploded in a man's face while he was opening it, one was an attempted suicide, and one involved a 68 year old man who accidentally swallowed a mouthful of 2.5 percent pentachlorophenol and recovered after hospital treatment.

Table 3.4 presents data showing the degree of medical attention required in the 47 episodes of alleged human poisoning from pentachlorophenol along with the circumstances surrounding the episodes.

A study (Sato et al., 1978) conducted in Hawaii from 1967 to 1973 examined the clinical findings in workers exposed to PCP. The concluding statement reads as follows:

> "The information gathered in this study suggests that despite high chronic exposures to PCP, individuals in the wood treatment group of workers had not undergone any serious health effects from this exposure. The only evidence of tangible health effects, part of which could have been caused by exposures to chemicals other than PCP, were the low-grade infections or inflammations of the skin and subcutaneous tissue, of the protective membrane of the eye, and of the mucous membrane of the upper respiratory tract. No long-time (sic) effects could be elicited in the exposed group."

3.3.1 References

Sato, N.M., H.W. Klemmer, L. Wong, E.L. Reichert, R.J. Korsak, and N.N. Rashad (1978). Clinical findings in workers exposed to pentachlorophenol. Draft report USEPA, Washington, D.C.

TABLE 3.4
Distribution of Human Episodes Resulting from Exposure to Pentachlorophenol by Medical Attention and Circumstances (PERS 1966 to September 1, 1976)*+

Medical Attention	Circumstances	Total Number of Episodes
Hospitalization followed by death	-Ingestion	1
	-Chronic Exposure	1
	-Unspecified	1
Hospitalization followed by recovery	-Treated wood at home	2
	-Attempted suicide	1
	-Ingestion	1
	-Exposed during nearby application	1
	-Contacted chemical during application	1
	-Spill	1
	-Reaction to treated home	1
	-Unspecified	1
Medical attention at a doctor's office or emergency room	-Contacted chemical during application	9
	-Exposed to treated object	4
	-Container exposed	1
	-Reaction to treated home	1
	-Ingestion	1
	-Exposed during nearby application	1
	-Contacted contaminated object	1
	-Unspecified	8
Effects not requiring medical attention	-Opening container	2
	-Reaction to treated home	2
	-Contacted chemical during application	2
	-Working with treated wood	1
	-Unspecified	2
	TOTAL	47

*A cause-effect relationship has not been confirmed between the pesticide and reported reactions for all of these episodes.

+From the EPA Pesticide Episode Review System Report No. 60

3.4 Human Poisonings Involving Exposure to Chlorinated Dibenzo-p-dioxins

Over the last 30 years a number of cases of human poisoning have occurred as a result of industrial exposure to the chlorinated dibenzo-p-dioxins. Although less well documented, it is also possible that human poisoning has occurred as a result of industrial and non-industrial exposure to the chlorinated dibenzofurans. The references on the next two pages list reports on cases of human poisoning from industrial exposure to the chlorinated dibenzo-p-dioxins. Most of these are exposures to TCDD. Some of these reports (Baader and Bauer, 1951; Jirasek et al., 1973; Jirasek et al., 1974; Pazderova et al., 1974) represent dioxin poisoning in factory workers involved in the manufacture of pentachlorophenol; these would represent exposures to chlorinated dibenzo-p-dioxins other than TCDD.

Chloracne was the predominant sign of toxicity reported in these workers. However, a number of other symptoms have been reported. These include emphysema, myocardial degeneration, toxic nephritis, hypertension, peripheral edema, anorexia, gastritis, weight loss, bursitis, peripheral neuropathy, paraesthesia, headaches, vertigo, coordination disturbances, fatigue, loss of libido, easy fatigability, emotional instability, pancreatic necrosis, polyneuritis, encephalomyelitis, hyperpigmentation, hirsutism, eye irritation, oiliness of the skin, hyperlipidemia and hypercholesterolemia.

A report recently issued from a January meeting of an NIEHS/IARC ad hoc Working Group summarizes available epidemiological and laboratory research on chlorinated dibenzo-p-dioxins and dibenzofurans (NIEHS/IARC, 1978). The report includes exposure incidents and discusses several aspects of toxicity including chloracne, hepatoxicity, embryotoxicity and teratogenicity.

3.4.1 References

Baader, E.W. and H.J. Bauer (1951). Industrial intoxication due to pentachlorophenol. Industr. Med. Surg. 20: 286-290.

Bauer, H., K.H. Schultz, and U. Spiegelberg (1961). Beruflich vergiftungen bei der herstellung von chlorphenol-verbindunge. Arch. f. Gewerbepath. und Gewerbehyg. 18: 538-555.

Bleiberg, J., M. Wallen, R. Brodkin, and I.L. Applebaum (1964). Industrially acquired porphyria. Arch. Dermatol. 89: 793-798.

Dugois, P. and L. Colomb (1957). Remarques sur l'acne chlorique. J. Med. Lyon 38: 899-903.

Goldman, P. J. (1973). Schwerste akute chloracne, eine Massenintoxikation durch 2,3,6,7-tetrachlorodibenzo-dioxin. Der Hautarzt 24: 149-152.

Jirasek, L., J. Kalensky, and K. Kubec (1973). Acne chlorina and porphyria cutanea tarda during the manufacture of herbicides. Cs Derm. 48: 306-317.

Jirasek, L., J. Kalensky, K. Kubec, J. Pazderova, and E. Lukas (1974). Acne chlorina, porphyria cutanea tarda and other manifestations of general intoxication during the manufacture of herbicides. Cs Derm. 49: 145-157.

Kimmig, J. and K.H. Schultz (1957). Occupational acne (so-called chloracne) due to chlorinated aromatic cyclic ethers. Dermatologica 115: 540-546.

May, G. (1973). Chloracne from the accidential production of tetrachlorodibenzodioxin. Brit. J. Ind. Med. 30: 276-283.

NIEHS/IARC. (1978). Long term hazards of polychlorinated dibenzodioxins and polychlorinated dibenzofurans. Joint NIEHS/IARC Working Group. International Agency for Research on Cancer. Lyon, France 1978.

Oliver, R. M. (1975). Toxic effects of 2,3,7,8-tetrachlorodibenzo 1,4 dioxin in laboratory workers. Brit. J. Ind. Med. 32: 49-53.

Pazderova, J., E. Lukas, M. Nemcova, M. Spacilova, L. Jirasek, J. Kalensky, J. John, A. Jirasek, and J. Pickova (1974). Chronic intoxication by chlorinated hydrocarbons produced during the manufacture of sodium 2, 4, 5-trichlorophenoxyacetate. Prac. Lek. 26: 332-339.

Poland, A. P., D. Smith, G. Metter, and P. Possick (1971). A health survey of workers in a 2, 4-D and 2, 4, 5-T plant. Arch. Environ. Health 22: 316-327.

Schultz, K. H. (1957). Untersuchungen zur atiologie der Chloracne. Arch. Klin. exp. Derm. 206: 589-596.

Schultz, K. H. (1968). Clinical picture and etiology of chloracne. Arbeitsmed. - Socialmed. - Arbeitshyg. 3: 25-29.

Taylor, J. S. (1974). Chloracne - A continuing problem. Cutis 13: 585-591.

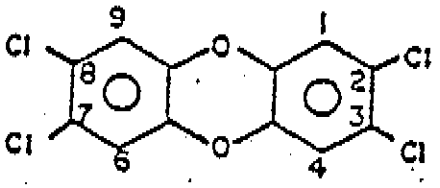
4. Mechanistic Relationships in the Toxicity of Compounds Structurally Related to the Chlorinated Dibenzo-p-dioxins

The chlorinated dibenzo-p-dioxins appear as trace contaminants in the commercial synthesis of certain chlorinated phenol products. Clinical-epidemiologic investigations of industrial and environmental accidents involving these compounds and laboratory investigations have established the extraordinary toxic potency of certain chlorinated dibenzo-p-dioxins and the potential human health hazards they pose. Less well appreciated is the similar spectrum of toxic effects produced by certain chlorinated dibenzofurans, chlorinated azoxy- and azobenzenes, polychlorinated biphenyls and polybrominated biphenyls. We wish to draw attention to these compounds as a group: 1) their similar toxic spectrum, 2) their isosterism in chemical structure, and 3) their similar biochemical actions.

The prototype dibenzo-p-dioxin, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), produces a number of well defined toxic actions in laboratory animals and human beings. 1) Lethality - While the cause is unknown there is an order of species sensitivity--guinea pigs and chickens are very sensitive, rats and mice much less so. 2) Chloracne and Hyperkeratosis - Reported in humans, rabbits and hairless mice. 3) Involution of Lymphoid Tissue - Particularly thymus, also in spleen and lymph nodes. In young animals this is reported to be accompanied by suppression of the immune response. Thymic involution has been seen in guinea pigs, rats and mice. 4) Teratogenicity, Embryo Toxicity and Fetal Wastage - Has been demonstrated in rats and mice. 5) Edematous Syndrome-Young chickens (and occasionally in mice). 6) Liver Toxicity - Seen in rats, rabbits and mice. Liver necrosis is greatest in rats and rabbits; distinct histologic damage is seen in mice. Little or no damage is seen in guinea pigs. 7) Disturbance in porphyria metabolism - Induction of - aminolevulinic acid (ALA) synthetase in chicken embryos. Porphyria in mice and chickens and presumably the causative agent of porphyria cutanea tarda seen in factory workers.

The administration of TCDD and certain other chlorinated dibenzo-p-dioxins to chicken embryos, rats and mice induces a number of hepatic enzyme activities, the most well studied of these being aryl hydrocarbon hydroxylases (AHH) (Poland and Glover, 1973, 1974) and δ -aminolevulinic acid (ALA) synthetase (Poland and Glover, 1973). The capacity of halogenated dibenzo-p-dioxin isomers to induce

hepatic ALA synthetase and AHH activities (in the chicken embryo) was found to have a well-defined structure activity relationship: 1) halogens in at least three and preferably four of the lateral ring positions (positions 2, 3, 7, and 8); 2) the order of potency for substitution was Br> Cl> F> NO_2; and 3) at least one unsubstituted ring position -- octachlorodibenzo-p-dioxin is very weak or inactive.



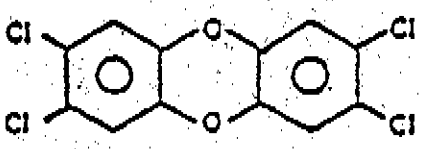
This structure activity relationship for the induction of AHH or ALA also corresponds to the structure activity relationship for the lethality of these compounds in experimental animals.

Recently, a binding protein has been identified in the cytosol fraction of mouse liver which binds TCDD reversibly with a high affinity (Poland and Glover, 1976a). The binding affinity of other chlorinated dibenzo-p-dioxin and halogenated aromatic compounds for this protein corresponds to their biological potency to induce AHH; this and other evidence suggest that this cytosolic binding species is the receptor for the induction of AHH activity.

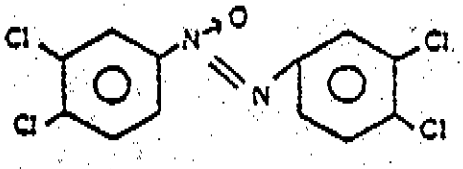
Recently it has been shown that certain chlorinated biphenyls show symptoms of toxicity similar to the chlorinated dibenzo-p-dioxins when administered to chickens and to rats. Thus, 3,4,5,3',4',5' -hexachlorobipnenyl causes marked involution of the thymus, loss of subcutaneous and visceral adipose tissues, liver necrosis and hydropericardium when administered to chickens (McKinney et al., 1976). Quite similar symptoms are seen in chickens administered either 2,3,7,8-tetrachloro-dibenzofuran or 2,3,7,8-tetrachlorodibenzo-p-dioxin. The compound 2,3,4,3',4'-pentachlorobiphenyl has an LD_{50} of about 12 mg/kg in the rat with death occurring in about 11 days (Yamamoto et al., 1976). A marked decrease in body weight, disappearance of fat from adipose tissues and liver necrosis were the primary symptoms of toxicity in these animals. These symptoms are very similar to those seen upon administration of 2,3,7,8-tetrachlorodibenzo-p-dioxin, 2,3,7,8-tetrachlorodibenzofuran and other chlorinated dibenzo-p-dioxins and dibenzofurans to rats.

The major symptom of toxicity in man exposed to the halogenated dibenzo-p-dioxins is chloracne. The outbreak of chloracne in workers exposed to 3,4,3',4'-tetrachloroazoxybenzene and 3,4,3 .4'-tetrachloroazobenzene has recently been reported (Poland and Glover, 1976b). These compounds, like 2,3,7,8-tetrachlorodibenzo-p-dioxin and 2,3,7,8-tetrachlorodibenzofuran, are potent inducers of arylhydrocarbon hydroxylase. They also have a high affinity for a receptor for 2,3,7,8-tetrachlorodibenzo-p-dioxin recently described in rat liver by Poland and Glover (1976a).

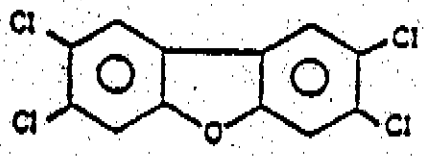
Although the data is not extensive at this time, there appears to be a strong correlation between toxic symptoms produced by a number of halogenated aromatic compounds. The prototype compounds are shown below:



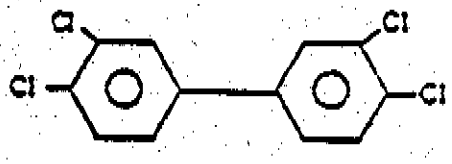
2,3,7,8-tetrachlorodibenzo-p-dioxin



3,4,3',4'-tetrachloroazoxybenzene



2,3,7,8-tetrachlorodibenzofuran



3,4,3',4'-tetrachlorobiphenyl

In examining these prototype compounds planarity is important. In the biphenyl series, substitution at the 2,2',6, or 6' position leads to nonplanarity and inactivity. The general structure necessary for these toxic effects appears to be a rectangle of about 10Å by 3Å with halogens in three or preferably four of the corners of the rectangle.

The current data suggest we should not view chlorinated dioxins, chlorinated dibenzofurans, PCBs or PBBs, and chlorinated azoxybenzenes separately, but rather as a class. This permits anticipation of other potentially hazardous compounds which might be isostereomers.

4.1 References

McKinney, J.D., K. Chae, B.N. Gupta, J.A. Moore, and J.A. Goldstein, (1976). Toxicology assessment of hexachlorobiphenyl isomers and 2,3,7,8-tetrachlorodibenzofuran in chicks. Toxicol. Appl. Pharmacol. 36: 65-80.

Poland , A. and E. Glover (1973). Chlorinated dibenzo-p-dioxins: Potent inducers of δ -aminolevulinic acid synthetase and aryl hydrocarbon hydroxylase. Mol. Pharmacol. 9: 736-747.

Poland, A. and E. Glover (1974). Comparison of 2,3,7,8-tetrachlorodibenzo-p-dioxin, a potent inducer of aryl hydrocarbon hydroxylase, with 3-methylcholanthrene. Mol. Pharmacol. 10: 349-359.

Poland, A. and E. Glover (1976a). Stereospecific, high affinity binding of 2,3,7,8-tetrachlorodibenzo-p-dioxin by hepatic cytosol. J. Biol. Chem. 251: 4936-4946.

Poland, A. and E. Glover (1976b). 3,4,3',4'-tetrachloroazoxybenzene and azobenzene: Potent inducers of aryl hydrocarbon hydroxylase. Science 194(4265): 627-630.

Yamamoto, H., H. Yoshimura, A. Fujita, and T. Yamamoto (1976). Metabolic and toxicological evaluation of 2,3,4,3',4'-pentachlorobiphenyl in rats and mice. Chem. Pharm. Bull. 24: 2168-2174.

5. Appendix A

SCIENCE ADVISORY BOARD
ENVIRONMENTAL HEALTH ADVISORY COMMITTEE
Ad Hoc Study Group on Pentachlorophenol Contaminants

Chairman:

Dr. Sheldon D. Murphy, Professor of Toxicology, Department of Pharmacology, University of Texas Medical School at Houston, P.O. Box 20708, Houston, Texas 77025

Members:

Dr. Donald G. Crosby, Professor and Toxicologist, Department of Environmental Toxicology, University of California, Davis, California 95616

Dr. David Firestone, Division of Chemistry and Physics, HFF-147, Food and Drug Administration, 200 C Street, S.W., Washington, D.C. 20204

Dr. Virgil H. Freed, Department of Agricultural Chemistry, Oregon State University, Corvallis, Oregon 97331

Ms. Dorothy B. Hood, Consultant, Toxicology, Haskell Laboratory for Toxicology and Industrial Medicine, E.I. du Pont de Nemours and Company, Wilmington, Delaware 19898

Dr. John Moore, National Institute of Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, North Carolina 27709

Dr. Robert A. Neal, Director, Center in Toxicology, Department of Biochemistry, Vanderbilt Medical School, Nashville, Tennessee 37323

Dr. Alan Poland, Assistant Professor, McArdle Laboratory for Cancer Research, University of Wisconsin, Madison, Wisconsin 53706

SAB Staff Officers:

Mr. Ernst Linde, Scientist Administrator, Science Advisory Board, A-101, U.S. Environmental Protection Agency, Washington, D.C. 20460 Phone: (703) 557-7720

Mr. A. Robert Flaak, Science Advisory Board, A-101, U.S. Environmental Protection Agency, Washington, D.C. 20460

6. APPENDIX B

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 12, 1977

OFFICE OF THE ADMINISTRATOR

SUBJECT: Charge to ad hoc Study Group on Pentachlorophenol Contaminants

FROM: Chairman, Environmental Health Advisory Committee

TO: Study Group Members

A recent inquiry from EPA has been referred to the Environmental Health Advisory Committee (EHAC). The request (attached) asks for opinion as to the implications regarding hazard to human health of the observed presence of various chlorinated dibenzodioxin isomers in pentachlorophenol (PCP).

The Environmental Health Advisory Committee feels that this inquiry provides a timely opportunity to review, rather more broadly than the original inquiry implied, the toxicology and analytical methodology pertinent to both the chlorinated dibenzofurans and the dibenzodioxin isomers.

Accordingly, we ask the study group to review and report in summary form on the available information (with particular emphasis on recent work) on the chemistry and toxicology of the dibenzodioxins and dibenzofurans.

To the extent possible, it would also be desirable to comment on the potential hazard to humans which can be attributed to registered uses of PCP and the extent that this hazard may be mitigated by use of the commercial process which results in lower levels of the contaminants of interest. It would be most helpful if you can complete your work by March 25 so that the Committee will have an opportunity to study your report before acting to advise the Agency at its April 19 meeting.

Norton Nelson

cc: Ernst Linde

7. APPENDIX C

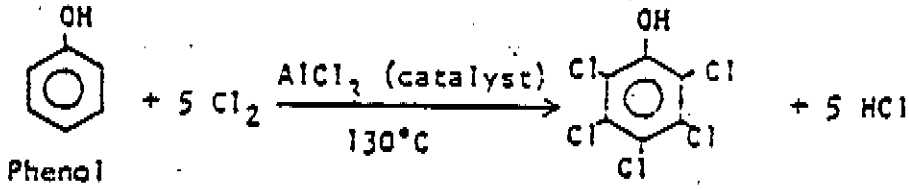
7. Appendix C

7.1 Chemistry of Pentachlorophenol and its Contaminants

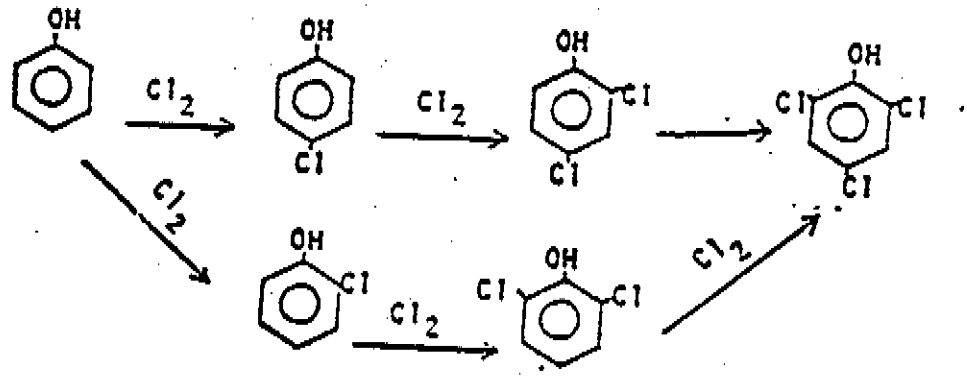
7.1.1 Commercial Synthesis of PCP and Formation of By-Products

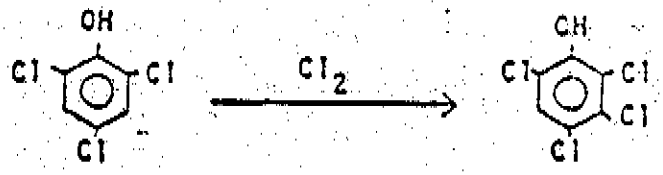
Chlorinated phenols, including PCP, are excellent bactericides and fungicides and have been widely used for these purposes since the 1930s. Two commerical processes are available for the manufacture of PCP. One process involves the alkaline hydrolysis of hexachlorobenzene, and the other process involves direct chlorination of phenol or a mixture of chlorophenols (Doedens, 1964; Sittig, 1969).

Pentachlorophenol is produced in the United States solely by the chlorination of phenol (American Wood Preservers Institute, 1977). The overall reaction follows:



The chlorination is carried out at substantially atmospheric pressure using two reactors. The temperature of the phenol in the primary reactor at the start is in the range of 65-130°C (generally 105°C) and is held in this range until the melting point of the product reaches 95°C. About three to four atoms of chlorine are added at this point:





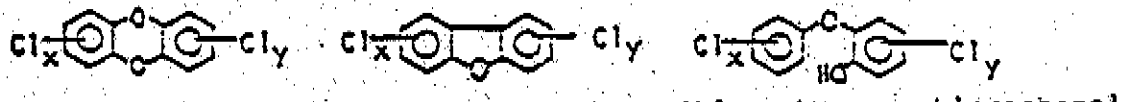
The temperature is progressively increased to maintain a temperature of about 10°C above the product melting point, until the reaction is completed in 5-15 hours. The reaction mixture, containing about 80% PCP is a liquid so that no solvent is required, but catalyst concentration is critical. Generally, 0.0075 mol of anhydrous aluminum chloride is used per mol of phenol.

The off-gas from the primary reactor (largely HCl initially and chlorine near the end) is sent to a second reactor (scrubber-reactor system) containing excess phenol. The reactor is held at such a temperature that the chlorine is almost completely reacted to yield lower chlorinated phenols, which may be separated and purified or returned to the primary PCP reactor. The residual gas is substantially pure HCl.

In the chlorination of phenol to form PCP, there is a progressive increase in temperature to keep the reaction mixture fluid. The higher temperature not only favors the primary synthetic reaction but also, to some extent favors formation of the various contaminants found in PCP.

The composition of technical PCP from different sources varies somewhat. The PCP content is in the range of 85-90%. Several percent of other chlorophenols are also present, as well as a number of impurities including chlorophenoxy chlorophenols, chlorodibenzo-p-dioxins, chlorodioxins (1500-3000 ppm), chlorofurans (200-600 ppm) and chlorodiphenyl ethers. The structure of these various impurities is shown below.

The presence of hydroxydiphenyl ethers in tetra- and pentachlorophenol has been discussed by Swedish chemists (Jensen and Renberg, 1972; Nilsson and Renberg, 1974; Rappe and Nilsson, 1972).

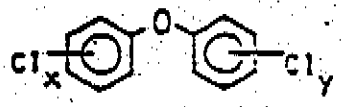


Chlorodioxin

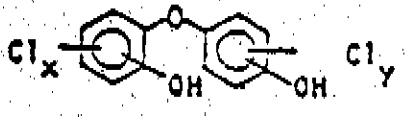
Chlorofuran

Chlorophenoxy chlorophenol (predioxin)

chlorophenoxy chlorophenol (isopredioxin)



chlorodiphenyl ether



chlorodihydroxydiphenyl ether

7.1.2 Composition of Commercial PCP

Results of analysis of a commercial PCP (Dowicide 7, Sample 9522 A), produced by Dow Chemical Company in June 1970 (Dow Chemical Co., 1971), and a purified grade of PCP prepared by distillation of Dowicide-7 are shown in Table 7.1.

The results of recent analyses of a number of domestic (Dow) PCP samples for chlorodioxins and chlorofurans by Swiss workers (Buser and Bosshardt, 1976) are shown in Table 7.2.

The results of analyses of hexa- and octachlorodioxin in various domestic PCPs (Crummett, 1975) are presented in Table 7.3.

TABLE 7.1

Comparison of composition of commercial grade and purified grade Pentachlorophenol (PCP)

Component	Analytical Results	
	Commercial[a] (Dowicide 7)	Purified[b] (Dowicide EC-7)
Pentachlorophenol	88.4%	89.8%
Tetrachlorophenol	4.4%	10.1%
Trichlorophenol	0.1%	0.1%
Chlorinated phenoxyphenols	6.2%	----
Octachlorodioxins	2500 ppm	15.0 ppm
Heptachlorodioxins	125 ppm	6.5 ppm
Hexachlorodioxins	4 ppm	1.0 ppm
Octachlorodibenzofurans	80 ppm	1.0 ppm
Heptachlorodibenzofurans	80 ppm	1.8 ppm
Hexachlorodibenzofurans	30 ppm	1.0 ppm

[a] Sample 9522 A
[b] Technical grade PCP reduced by distillation

Table 7.2

Chlorodioxins and Chlorofurans in Dow PCP Products
(Buser and Bosshardt, 1976)

Samples	PCDD[a] ppm			PCDF[b] ppm				
	Hexa-	Hepta-	Octa-	Tetra-	Penta-	Hexa-	Hepta-	Octa-
PCP(EC-7)	0.15	1.1	5.5	0.45	0.03	0.3	0.5	0.2
PCP(EC-7)	0.03	0.6	8.0	<0.02	<0.03	<0.03	<0.1	<0.1
PCP[c]	9.5	125	160	<0.02	0.05	15	95	105
PCP[c]	9.1	180	280	0.05	0.25	36	320	210
PCP-Na[c]	3.4	40	115	<0.02	0.05	11	50	24
PCP	10.0	130	210	0.20	0.20	13	70	55
PCP	5.4	130	370	0.07	0.20	9	60	65

(a) PCDD = Polychlordibenzo-p-dioxin

(b) PCDF = Polychlorodibenzofuran

(c) Dow product, supplied by Fluka, a laboratory chemical supplier.

Table 7.3

Hexa- and Octachlorodioxins in Domestic PCPs
(Crummett, 1975)

Sample	Mfgr	Hexachlorodioxin[a]	Octachlorodioxin[b]
1	Vulcan	10ppm	1700ppm
2		N.D.	N.D.
3	"	15	2500
4	"	16	3600
5	Reichhold	20	700
6	"	17	600
7	"	23	900
8	"	N.D.	N.D.
9	Monsanto	15	1400
10	"	12	1100
11	"	15	1900
12	Dow	N.D.	2
13	"	N.D.	2
14	"	N.D.	N.D.
15	"	16	1500
16	"	16	1800
17	"	21	3400

(a) Detection limit 0.3 ppm, except for sample 8 which is 2 ppm; N.D. = not detected.

(b) Dection limit 1 ppm, except for sample 8 which is 6 ppm; N.D. = not detected.

A composite lot of PCP (Lot MB-306) was recently prepared from samples from each of the three domestic producers of technical PCP. This sample, analyzed by Monsanto (Vogel et al., 1976), gave the following results (see also Table 7.4 below, which gives results of GC-MS analysis of a sample of Monsanto PCP):

	Hexa-	Hepta-	Octa-
PCDD, ppm	11	199	1170
PCDF, ppm	19	81	137

Since the structure-biological activity relationships of the individual hexa- and heptachlorodioxin isomers vary considerably (Poland et al., 1976; McConnell et al., 1978), it is also necessry to determine the levels of individual isomers in PCP samples. However, little information is available on the levels of individual chlorodioxin or chlorofuran isomers in PCP. Estimates of the relative amounts of hexa- and heptachlorodioxin isomers in PCP (Dowicide 7) and a sodium pentachlorophenate (PCP-Na) sample examined by Buser (1975, 1976) are given in Table 7.5. The levels of individual dioxins were estimated from chromatogram or mass fragmentogram peak heights and the total recorded concentration of hexa- and heptachlorodioxins.

Table 7.4

GC-MS Analyses of Monsanto PCP
(Goldstein et al., 1977)

HxCDD	8 ppm
HCDD	520 ppm
OCDD	1380 ppm
PCDF	40 ppm
HCDF	90 ppm
HpCDF	400 ppm
OCDF	260 ppm

The Dow Chemical Co. has been engaged in research directed towards fractionation and identification of contaminants present in various grades of PCP (Stehl and Crummett, 1977). Results of examination of three Dow products for hexachlorodioxin isomers are shown in Table 7.6.

Table 7.5

Chlorodioxins in a Commercial PCP and PCP-Na Sample (Buser, 1975, 1976)

Chlorodioxin	ppm Chlorodioxin in PCP-Dowicide 7	PCP-Na
1,2,3,6,7,9-Cl_6D	1	0.5
1,2,3,6,8,9-Cl_6D	3	1.6
1,2,3,6,7,8-Cl_6D	5	1.2
1,2,3,7,8,9-Cl_6D	0	0.1
1,2,3,4,6,7,9-Cl_7D	63	16
1,2,3,4,6,7,8-Cl_7D	171	22
1,2,3,4,6,7,8,9-Cl_8D	250	110

Table 7.6

Hexachlorodioxin (HxCDD) Isomers in Three Dow Products as Determined by Gas-Liquid Chromatography (GLC) (Stehl and Crummett, 1977)

GLC Peak	HxCDD Isomer	Relative Isomer %, HxCDD Concentration Dowicide G	Dowicide 7	Dow Std 82-A
A	1,2,4,6,7,9- (or 1,2,4,6,8,9-)	35	25	--
B	1,2,3,6,8,9- (or 1,2,3,6,7,9-)	43	50	29
C	1,2,3,6,7,8-	20	25	71
D	1,2,3,7,8,9-	2	Trace	--

Ratios of 25-50-25 (Dowicide 7) for the A-B-C isomers compare with Buser's values of 10-35-55.

Table 7.7

Chlorodibenzofurans in Dow PCP Products

Tetra	Penta	Hexa
2,3,6,7-	2,3,4,6,7-	1,2,3,6,7,8-
2,4,6,7-	1,2,4,7,8-	
	2,3,4,7,8-	

A list of chlorodibenzofurans tentatively identified by Dow chemists in Dowicide or EC-7 is shown in Table 7.7.

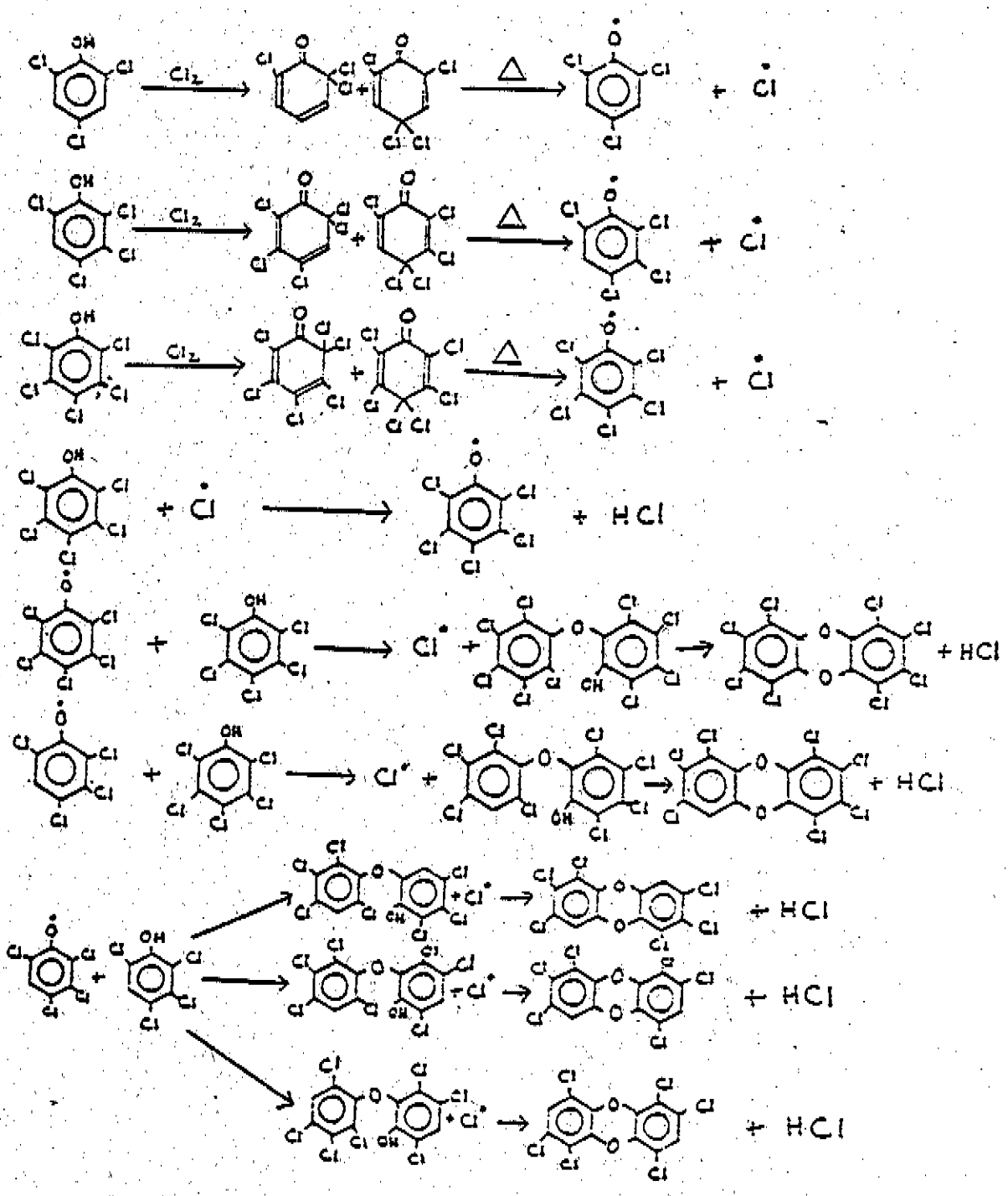
7.1.3 Formation of Chlorodioxins and Chlorofurans during Commercial Synthesis of PCP

Chlorodioxins may be prepared in condensation reactions from ortho-substituted chlorophenoxy radicals (Kulka, 1961) or anions (Pohland and Yang, 1972). According to S.L. Vogel, Monsanto Industrial Chemicals Co. (Vogel, 1977), dioxin formation occurs during commercial synthesis of PCP via a series of reactions involving phenoxy radicals. Phenoxy radicals are produced from decomposition of polychlorocyclohexadienone produced by over-chlorination of tri-, tetra-, or pentachlorophenol. The phenoxy radical (an electrophile) attacks electronegative sites (ortho or para positions) on a polychlorophenol molecule to form phenoxyphenols which undergo further reaction to form chlorodioxins.

The decomposition of tri-, tetra-, or pentachlorophenol can also be catalyzed by chlorine (the chlorine radical is the initiator). The tetrachlorophenol present in commercial reaction mixtures (very little trichlorophenol is present) serves as a substrate for chlorine radicals, limiting the chain reaction with PCP molecules which accelerates PCP decomposition. The chlorination is normally stopped when 3-7% tetrachlorophenol remains. Further chlorination results in increased decomposition (Table 7.8).

TABLE 7.8

Reactions in Chlorination of Trichlorophenol



Rearrangement via a spirocyclic anion (Smiles rearrangement) can yield additional isomers (Gray et al., 1975). Highly alkaline conditions are required for efficient operation of the Smiles rearrangement since the reaction involves rapid equilibration of the anion forms of a phenoxyphenol through a spirocyclic intermediate. This is illustrated by the formation of 1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin from 2,3,4,6-tetrachlorophenol.

In the manufacture of pentachlorophenol a considerable amount of HCl is present, so the Smiles rearrangement is unlikely. Dioxin congeners formed by normal and spirocyclic rearrangement vs. the levels of individual dioxin found in PCP (Vogel, 1977) are shown in Table 7.9. The hexachlorodioxins found agree with those predicted to form without the Smiles rearrangement.

TABLE 7.9

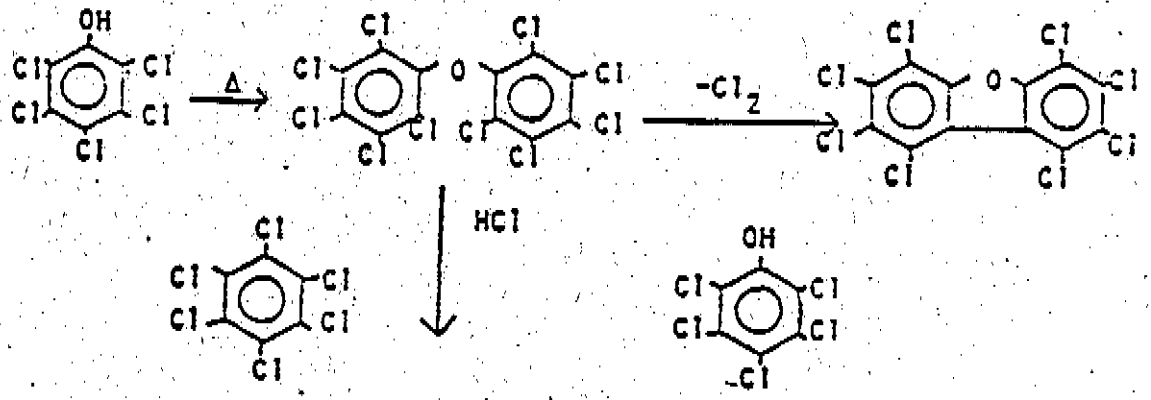
Dioxin Congeners in Commercial PCP

Possible Dioxin Congeners in PCP			
No Smiles Rearrangement	With Smiles Rearrangement	Relative % Isomers Found	PCP in ppm[a]
1,3,6,8 (100%)	1,3,6,8 (25%) 1,3,7,9 (75%)	None	N.D.
1,2,4,7,9 (75%) 1,2,3,7,9 (25%)	1,2,4,7,9 (31.25%) 1,2,3,7,9 (25%) 1,2,4,6,8 (43.75%)	None	N.D.
1,2,3,6,8,9 (50%) 1,2,3,6,7,8 (25%) 1,2,4,6,7,9 (25%)	1,2,3,6,7,9 (31.25%) 1,2,3,6,8,9 (18.75%) 1,2,4,6,7,9 (12.5%) 1,2,4,6,8,9 (12.5%) 1,2,3,7,8,9 (18.75%) 1,2,3,6,7,8 (6.25%)	40-50 20-40 Trace 20-40	ca 15
1,2,3,4,6,7,9 (75%)	1,2,3,4,6,7,9 (75%)	ca 60	ca 200
1,2,3,4,6,7,8 (25%)	1,2,3,4,6,7,8 (25%)	ca 40	
1,2,3,4,6,7,8,9(100%)	1,2,3,4,6,7,8,9(100%)	100	ca 1000

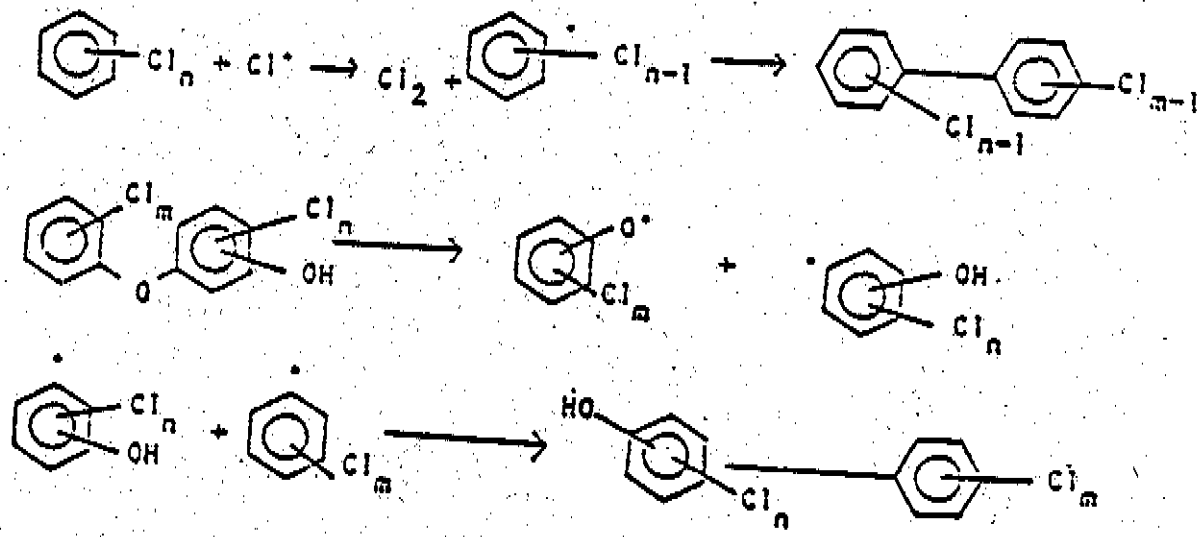
(a) PCP producers composite sample.

Little information is available on the formation of dibenzofurans during PCP production. Formation of dibenzofurans can be explained by the production of polychlorodiphenyl ether intermediates (Kulka, 1961; Plimmer, 1973; Arsenault, 1976) which can lose chlorine to yield dibenzofuran.

Cleavage of the polychlorodiphenyl ether in the presence of HCl yields PCP and hexachlorobenzene.



Various free radical reactions might also yield a number of biphenyl compounds.



Mass spectral data obtained from analysis of contaminants in PCPs (Firestone et al., 1972) suggested that polychlorohydroxybiphenyls were present in these products.

7.1.4 Chemical and Physical Properties of PCP, Chlorodioxins and Chlorofurans

7.1.4.1 Pentachlorophenol

The chemical and physical properties of compounds play an important role in their behavior, persistence in the environment, and biological effects. Properties of PCP are given in Table 7.10. PCP is volatile in steam and soluble in most organic solvents, although of limited solubility in CCl_4 and in paraffinic petroleum oils (British Crop Protection Council, 1971). Also see Bevenue and Beckman (1967) for data on solubility in various solvents.

Differential thermal analysis of PCP (Langer et al., 1973) revealed a solid state transition at 75°C, followed by melting below 200°C and vaporization above 300°C. Prolonged heating in bulk above 200°C resulted in formation of octachlorodioxin in a tar residue. Heating the PCP in a sealed capillary at 250°C for ten hours resulted in formation of about 50% polychlorophenoxyphenol and a small amount of octachlorodioxin. Sodium pentachlorophenate exhibited a strongly exothermic reaction at about 360°C; upon cooling, essentially pure octachlorodioxin crystallized.

TABLE 7.10

Physical Properties of Pentachlorophenol (PCP)

Molecular Weight	266.35
Melting Point	191°C
Boiling Point	310°C (decomposes)
Density	1.987
Vapor Pressure	1.6×10^{-4} mm Hg (25°)
	1.2×10^{-1} mm Hg (100°C)
	40 mm Hg (211°C)
Solubility H_2O	20 ppm at 30°C
Solubility of sodium salt, H_2O	33g/100g
Partition Coefficient	$1 \times 10^{5.01}$
Molar Refraction	53.5

7.1.4.2 Chlorodioxins

Properties of various chlorodioxin congeners are given in Table 7.11. The solubilities of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), hexachlorodibenzo-p-dioxin (HxCDD, a sample of mixed isomers), and octachlorodibenzo-p-dioxin (OCDD) in several solvents (Stehl and Crummett, 1977) are shown in Table 7.12.

The visible absorption spectra and electron spin resonance spectra and g factors of a number of chlorodioxin cation radicals have been reported (Pohland et al., 1973). The crystal structures of several chlorodioxins have been determined by x-ray diffraction studies. The compounds studied included 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin (Cantrell et al., 1969), and 2,7-dichloro-2,3,7,8,-tetrachloro- and octachlorodibenzo-p-dioxins (Boer et al., 1973). The x-ray diffraction data indicate that the C-Cl distances shorten with increasing chlorine substitution on the rings. This effect could result from a reduction in effective electronegativity difference between Cl and C as more electron density is drawn from the aromatic ring, which should, in turn, result in increased covalency of the C-Cl bonds and give shorter distances (Boer et al., 1973).

Infrared spectra and characteristic frequencies of a number of chlorodioxins as well as 2,8-dichloro- and octachlorofuran have been reported by Chen (1973).

7.1.4.3 Chlorofurans

Little information is available to date on the physical and chemical properties of chlorofurans. It is presumed that in the immediate future increased emphasis will be placed on identification of specific chlorofuran isomers occurring in commerical PCP and synthesis of these compounds for chemical and toxicological study. Some properties of several chlorofurans (Gray et al., 1976; Page, 1976) are given in Table 7.13.

7.1.4.4 Chlorodiphenyl Ethers and Chlorophenoxy Phenols

Data on the physical and chemical properties of chlorophenoxy phenols are limited. Lundstrom and Hutzinger (1976) prepared several chlorodiphenyl ethers and also cited a number of these compounds prepared by other workers via various routes. The melting points of some of the chlorodiphenyl ethers are given in Table 7.14.

TABLE 7.11

Physical Properties of Various Chlorodioxins

Chlorodioxin	Mol. Wt.	M.P. C	"P" Value[a]	Estimated Vapor (b) Pressure	Molar Refraction	UV Max (CHCl) nm
2,7,-Cl_2	253.08	--	0.76	6.0×10^{-6}	--	302
2,3,7-Cl_3	287.53	162	0.86	3.6×10^{-6}	--	305
2,3,7,8,-Cl_4	321.87	306	0.51	1.7×10^{-6}	71.4	310
1,2,4,7,8-Cl_5	356.42	206	--	--	72.6	307
1,2,3,7,8-Cl_5	356.42	241	--	--		308
1,2,4,6,7,9-Cl_6	390.86	240	0.94[d]	6.6×10^{-7}	--	310
1,2,3,6,8,9-Cl_6	390.86	--		--	81.1	--
1,2,3,6,7,8-Cl_6	390.86	285	--	--		316
1,2,3,7,8,9-Cl_6	390.86	243	--	--		317
1,2,3,4,6,7,9-Cl_7	425.31	--	0.90	3.0×10^{-7}	85.9	--
1,2,3,4,6,7,8-Cl_7	425.31	--	0.90	--		--
1,2,3,4,6,7,8,9-Cl_8	459.75	331	0.90	1.8×10^{-7}	90.7	318

(a) Beroza, M. and M.C. Bowman, "p" value determined for dioxin between hexane and acetonitrile, J. Assoc. Offic. Anal. Chem. 48:358-370 (1965).

(b) Vapor pressure estimated from data of Woolson (Woolson et al., 1973).

(c) Estimated by summing atomic refractions.

(d) "p" value determined for mixture of hexachlorodioxin isomers.

TABLE 7.12

Solubility of Several Chlorodioxins in Various Solvents[a]

	Solubility in mg per liter		
Solvent	TCDD	HxCDD[b]	OCDD
acetone	90	--	5
anisole	--	2600	1700
benzene	470	1600	1000
chloroform	550	--	560
methanol	10	--	--
toluene	--	1800	1500
o-xylene	--	--	3600
water	0.0002	--	--

-- indicates no data

(a) Firestone observed that 1,2,3,6,7,8-HxCDD is considerably less soluble in organic solvents than other HxCDD isomers. The solubility of the 1,2,3,6,7,8-isomer in isooctane is about 20 mg/l.

(b) Dow standard 82-A, a mixture of 71% 1,2,3,6,7,8-HxCDD and 29% 1,2,3,6,7,9-HxCDD and 1,2,3,6,8,9-HxCDD.

TABLE 7.13

Properties of Chlorinated Dibenzofurans

	Molecular Weight	Melting Point °C	Vapor Pressure[a] (Estimated) 25°C	Molar Refraction[b]	UV max ($CHCl_3$) nm
Dichloro	269.1			60.2	
2,4			7.3×10^{-6}		
3,7			7.0×10^{-6}		
2,8		105[c]	6.8×10^{-6}		
Trichloro	243.5			65.0	
2,4,6		116-117[d]	4.0×10^{-6}		
2,3,8		189-191[d]	3.7×10^{-6}		256,302,313
2,4,7					
2,4,8					
Tetrachloro	278.1			69.8	
1,4,6,8			2.5×10^{-6}		
2,4,6,8		198-200[d]	2.5×10^{-6}		
2,3,6,8		202-203[d]	2.2×10^{-6}		257,294,310,323
2,4,6,7			2.1×10^{-6}		
1,2,7,8			2.0×10^{-6}		
2,3,7,8		227-228[d]	2.0×10^{-6}		
2,3,6,7			1.9×10^{-6}		259,309,316
3,4,6,7			1.8×10^{-6}		
Pentachloro	312.6			74.6	
1,3,4,7,8			1.3×10^{-6}		
1,2,4,7,8		234-235[d]	1.3×10^{-6}		263,272,297,320
1,2,3,6,7			1.1×10^{-6}		256,266,297
2,3,4,7,8			1.1×10^{-6}		
Heptachloro	381.6			84.2	
			4.4×10^{-7}		
			3.6×10^{-7}		
			3.0×10^{-7}		
Octachloro	416.1		1.9×10^{-7}	89.0	

(a) From data supplied by Dr. David Firestone--private communication.
(b) Calculated from Table of Atomic Refraction.
(c) H. Gilman, et al., J. Am. Chem. Soc., 56:2473, 1934.
(d) A.P. Gray, et al., J. Org. Chem., 41(14):2428, 1976.

Table 7.14

Melting Points of Chlorodiphenyl Ethers

Diphenyl ether	M.P. °C
2,4,4'-	51-52
2,2',4,4'-	70
2,3',4,4'-	oil
3,3',4,4'-	oil
2,3,4,5,6-	132-133
2,2',4,4'5-	oil
2,3',4',5'-	65-67
2,2',4,4',5	oil
2,3',4,4',6-	36
2,2',3,4,5,6,6'-	147-148
Deca-	224-225

7.1.4.5 Gas Liquid Chromatography (GLC) Behavior of Chlorodioxin and Chlorophenol Congeners

The GLC behavior of various chlorodioxins and chlorofurans on nonpolar (OV-101) and Polar (Silar 10-C) columns is recorded in Tables 7.15 and 7.16. Retention times depend on the number and location of chlorine atoms in the ring system. Order of elution and retention times of chlorodioxins on glass capillary columns is reported by Buser (1975, 1976).

7.1.5 Reactions

7.1.5.1 Pentachlorophenol

PCP is relatively stable and will not decompose when heated up to its boiling point; however, it is rapidly and extensively degraded by ultraviolet irradiation in the laboratory and by sunlight (when PCP is in solution) and is decomposed by strong oxidizing agents (Bevenue and Beckman, 1967).

Similar to any phenol, the phenolic hydroxyl of PCP takes part in nucleophilic reactions, e.g., it forms esters with organic and inorganic acid and ethers with alkylating agents such as methyl iodide or diazomethane. Electron withdrawal by the ring-chlorines causes PCP to be unusually acidic (pK_A 5.26), roughly comparable to propionic acid (pK_A 4.9), and causes it to be a relatively weak nucleophile while stabilizing its salts (sodium pentachlorophenate is a stable item of commerce). While the high degree of chlorination makes the aromatic ring sufficiently electropositive to form stable charge-transfer complexes with electron donors, the ring chlorines are as resistant to nucleophilic displacement under normal conditions as are those of the chlorinated aromatic hydrocarbons.

TABLE 7.15

Chlorinated Dibenzofurans
GLC Retention Times Relative to
2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)

Congener	RRT(1) OV-101(2)	RRT(1) Silar 10C(3)
2,4,-Cl_2	0.24	0.38
3,7-Cl_2	0.25	0.40
2,8-Cl_2	0.26	0.47
2,4,6-Cl_3	0.44	0.73
2,3,8-Cl_3	0.47	0.83
2,4,7-Cl_3	--	0.64
2,4,8-Cl_3	--	0.64
1,4,6,8-Cl_4	0.70	--
2,4,6,8-Cl_4	0.70	--
2,3,6,8-Cl_4	0.80	--
2,4,6,7-Cl_4	0.82	1.26
1,2,7,8-Cl_4	0.89	1.04
2,3,7,8-Cl_4	0.89	1.50
2,3,6,7-Cl_4	0.93	1.56
3,4,5,7-Cl_4	0.95	1.78
1,3,4,7,8-Cl_5	1.35	1.27
1,2,4,7,8-Cl_5	1.35	1.27
1,2,3,6,7-Cl_5	1.52	1.66
2,3,4,7,8-Cl_5	1.63	--
Cl_7	--	3.95
Cl_7	--	4.78
Cl_7	--	5.87
Cl_8	8.8	8.75

(1) RRT = retention time relative to TCDD.
(2) Data of D.W. Phillipson, FDA; 2 m x 0.2 cm i.d. column packed with 3% OV-101; column temperature, 200°C.
(3) Data of D.W. Phillipson, FDA; 2 m x 0.4 cm i.d. column packed with 3% Silar 10C; column temperature, 200°C.

TABLE 7.16

Chlorinated Dibenzo-p-dioxins,
GLC Retention Times Relative to
2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD)

Congener	RRT(1) OV-101(2)	RRT(1) Silar 10C(3)	EC Response(4) (Silar 10C Column)
2,7,-Cl_2D	--	0.30	0.90
1,2,4-Cl_3D	0.49	0.52	0.38
2,3,7-Cl_3D	0.55	0.54	0.40
1,3,6,8-Cl_4D	0.76	0.62	0.32
1,3,7,8-Cl_4D	0.88	0.78	0.41
2,3,7,8-Cl_4D	1.00	1.00	0.40
1,2,3,4-Cl_4D	0.97	1.01	0.25
1,2,3,8-Cl_4D	0.99	1.04	--
1,2,4,7,8-Cl_5D	1.57	1.56	0.41
1,2,3,4,7-Cl_5D	1.70	1.76	0.41
1,2,3,7,8-Cl_5D	1.80	1.82	0.33
1,2,4,6,7,9-Cl_6D	2.48	2.62	0.28
1,2,3,6,7,9-Cl_6D	2.78	2.92	0.36
1,2,3,4,7,8-Cl_6D	3.05	3.11	0.40
1,2,3,6,7,8-Cl_6D	3.10	3.23	0.37
1,2,3,7,8,9-Cl_6D	3.24	3.56	0.42
1,2,3,4,6,7,9-Cl_7D	4.75	5.41	0.60
1,2,3,4,6,7,8-Cl_7D	5.32	6.20	0.70
Cl_8D	9.1	10.3	0.84

(1) RRT = retention time relative to 2,3,7,8-Cl_4D.
(2) Data of D. Firestone, FDA; glass coil, 2m x 0.4 cm i.d., packed with 2% OV-101 on 80-100 mesh Chromosorb WHP; column temperature 210°C.
(3) Data of D. Firestone; glass coil, 2m x 0.4 cm i.d., packed with 1.2% Silar 10C on 80-100 mesh Chromosorb WHP; column temperature 200°C.
(4) EC Response = nanograms to give 1/2 full scale deflection (127 mm) at 16 x attenuation. Hewlett-Packard Model 5713A gas chromatograph.

Chlorination of PCP (or overchlorination of phenol during PCP manufacture) can give rise to a series of interconvertible nonaromatic cyclic ketones including hexachloro-2,5-cyclohexadien-1-one, hexachloro-3-cyclohexen-1-one, heptachloro-3-cyclohexen-1-one, and octachloro-3-cyclohexen-1-one. Reduction of these compounds under mild conditions or treatment with base provides chlorophenols; for example, PCP is formed from heptachloro-3-cyclohexen-1-one by boiling with aqueous acetone or from hexachloro-2,5-cyclohexadien-1-one by reduction with aqueous sulfur dioxide or potassium iodine. Heat (as in a gas chromatograph) also generates phenols (Svec and Kubelka, 1975).

Pentachlorophenol, being a weak acid, reacts with strong bases to give the corresponding water-soluble salts at a pH of 5.0; the solubility of the sodium salt is about 79 ppm; at pH 8.0, the solubility is greater than 4000 ppm. PCP is readily converted to the ether derivative, which is useful for analysis by gas chromatography. PCP is a powerful uncoupler of oxidative phosphorylation in various tissues and apparently reacts with bovine serum albumin (anion-anion reaction) to form a stable complex from which the PCP can be liberated with strong base. PCP forms colored electron acceptor complexes as do other phenol derivatives (Hutzinger, 1969); these complexes are useful for chromogenic detection and mass spectrometric identification.

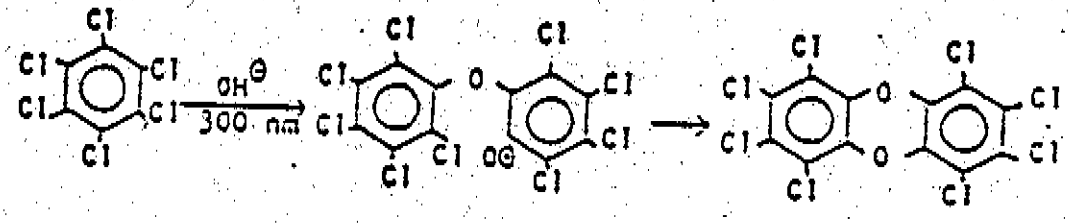
Treatment of PCP with powerful oxidizing agents produces pentachlorophenoxyl radicals which combine reversibly to form "dimers." For example, in the presence of fuming nitric acid or nitronium fluoroborate, PCP provides 2,3,4,5,6-pentachloro-4-pentachlorophenoxy-2,5-cyclohexa-dienone (Chang, 1962). The radicals or their dimers can be oxidized further to 2,3,5,6-tetrachlorobenzoquinone (chloranil). Chemical oxidation of PCP under anhydrous conditions was found to result in production of the radical dimer 2,3,4,5,6-pentachloro-2-pentachlorphenoxy-3,5-cyclo-hexadienone (Denivelle and Fort, 1954).

Pyrolysis of alkali metal salts of PCP (300°C) results in condensation of two molecules to form OCDD, 1,2,3,4,6,7,8,9-octachlorodibenzo-p-dioxin (Sandermann et al., 1957). The reaction proceeds through an intermediate phenoxyphenol, now called a "predioxin," which is readily detectable in technical PCP. Nonvolatile, polymeric phenylene ethers are formed concurrently by reaction of the chlorophenol at positions other than ortho. Small amounts of initiators such as chlorine or hexachloro-2,5-cyclo-hexadien-1-one allow OCDD formation to take place at comparatively low temperatures (200°C) in high yield from PCP rather than its salts (Kulka, 1961); and pyrolysis of the chlorinated cyclohexenes themselves smoothly provides OCDD (73% yield from hexachloro-2,5-cyclohexadien-1-one at 270 - 280°C), probably through a pentachlorophenoxy-pentachlorocyclohexadiene such as 2,3,4,5,6-4-pentachloro-phenoxy-2,5-cyclohexadienone.

Results of combusting wood and paper treated with PCP or PCP-Na indicate that octachlorodioxin was not formed during combustion with PCP. However, ppm levels of octachlorodioxin are formed during combustion of paper treated with PCP-Na (Stehl and Lamparski, 1977; Ahling and Johansson, 1977).

The absorption of light energy rather than heat allows PCP to undergo a number of reactions under very mild conditions; maximum light absorption lies in the ultraviolet region (245 and 318 nm). In either water or organic solvents, PCP undergoes photochemical reduction to isomeric tri- and tetrachlorophenols (Crosby and Hamadmad, 1971). Nucleophiles, such as bromide ion, can displace chloride from the PCP ring (Crosby and Wong, 1976), and in water the predominant reaction is replacement of an ortho-, meta-, or para-chlorine by hydroxyl to provide tetrachlorocatechol, tetrachlororesorcinol, and tetrachlorohydroquinone, respectively. The pentachlorophenoxide anion can also displace chloride in sufficiently concentrated solution with eventual cyclization to OCDD in water at ambient temperatures (Crosby and Wong, 1976).

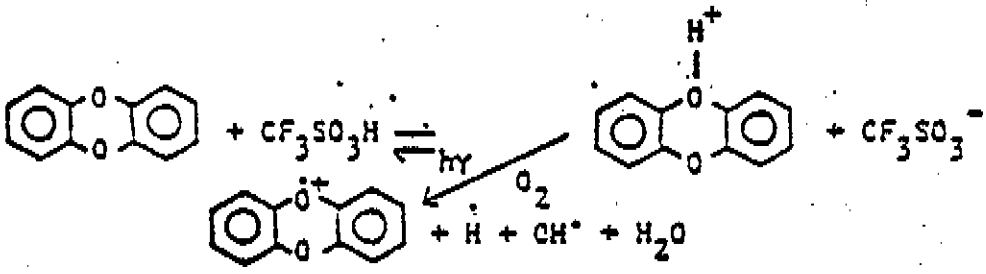
Photoreactions of PCP in organic solvents result primarily in reductive dechlorination (Zabik et al., 1976). The sodium salt of PCP in aqueous solutions yields a variety of colored products when irradiated with sunlight including phenoxybenzoquinones, chloranilic acid (2,5-dichloro-3,6-dihydroxybenzoquinone), and 2,4,5,6-tetrachlororesorcinol (Munakata and Kuwahara, 1969). Plimmer et al. (1973) showed that alkaline aqueous solutions of PCP, irradiated with light in the 300-350 nm region, yielded octachlorodibenzo-p-dioxin. Although a free radical mechanism was proposed to account for the observed products of unsensitized photolysis of PCP-Na (Munakata and Kuwahara, 1969), Crosby and Wong (1976) demonstrated that octachlorodibenzo-p-dioxin is generated photochemically from PCP in dilute aqueous sodium hydroxide by a cyclization process analogous to its generation from PCP by heat (Sandermann et al., 1957). This mechanism involves photonucleophilic displacement of chloride ions from PCP by pentachlorophenoxide ion.



7.1.5.2 Chlorinated Dibenzodioxins

OCDD and related cyclic ethers appear to be rather stable chemically, perhaps due to their planar and electropositive rings. For example, OCDD distills (sublimes) unchanged at 350°C and can be recovered quantitatively from hot sulfuric acid (Sandermann et al., 1957). However, these polychlorinated ethers share with PCP the facile photochemical reduction upon ultraviolet irradiation. For example, in the presence of an organic solvent as hydrogen donor, 2,3,7,8-tetrachlorodibenzo-p-dioxin is rapidly dechlorinated via tri- and dichloro-dioxins (Crosby et al., 1971); di-and octachloro-dibenzo-furans are dechlorinated more slowly, and the rate of OCDD photoreduction is still slower although transient hepta- and hexachlorodioxins are detectable.

These compounds are relatively stable and only slowly biodegradable. When dissolved in concentrated sulfuric acid or trifluoromethanesulfonic acid with oxidizing agents such as H_2O_2 or KNO_3 or with ultraviolet irradiation, blue to blue-green colored species are obtained, due to formation of cation radicals (Pohland et al., 1973; Yang and Pohland, 1973).



TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin) is quite stable to 700°C (50% decomposition at this temperature after 21 second exposure), whereas decomposition is complete at 800°C after 21 second exposure (Stehl et al., 1973).

TCDD is stable in refluxing aqueous alkali solution (50 ml of 32% aqueous KOH solution plus 20 ml ethanol) whereas other higher chlorinated dioxins decompose at varying rates (first-order reaction), presumably due to hydrolysis (nucleophilic displacement of halogen by hydroxyl groups) (Firestone, 1977). Estimated half-lives (t 1/2) of several dioxin congeners in refluxing KOH solution are shown in Table 7.17.

Table 7.17

Estimated Half-Lives (t 1/2) of
Several Chlorodioxins in Refluxing KOH Solution [a]

Congener	t 1/2
1,2,3,5,7,8- and 1,2,3,7,8,9-HxCDD	7 hrs
1,2,4,6,7,9- and 1,2,3,4,7,8-HxCDD	2 hrs
1,2,3,4,6,7,8- HCDD	23 min
1,2,3,4,6,7,9-HCDD	16 min
1,2,3,4,6,7,8,9-OCDD	4.5 min

(a) 10-40 ng chlorodioxin refluxed gently with 50 ml of 32% aqueous KOH solution and 20 ml ethnol.

Crosby et al. (1971, 1973) found that TCDD is rapidly photodecomposed (by reductive dechlorination) in alcohols whereas octachlorodioxin is much more stable. In either sunlight or simulated sunlight, 2,7-dichloro-, 2,3,7-trichloro- and 2,3,7,8-tetrachlorodibenzo-p-dioxins (5 mg/l in methanol) were entirely decomposed in a few hours.

Kim et al. (1975) irradiated various chlorodioxin congeners in isooctane as well as in methanol. The photolysis rates of the chlorodioxins in methanol solvent were similar to those reported by Crosby et al. (1973).

While photochemical dechlorination is by far the most rapid known reaction of these compounds, three conditions are required: the dioxin or dibenzofuran must be accompanied by an organic, hydrogen-donating solvent (such as a pesticide or formulating agent), UV light in the wavelength region of 290-320 nm must be present, and the light must penetrate the solvent (Crosby and Wong, 1977). The rate of photoreduction is inversely proportional to the degree of chlorination, and, therefore, dechlorinated products do not accumulate. Unlike PCP and 2,8-dichlorodibenzofuran, pure OCDD and TCDD do not appear to be photolyzed in water at appreciable rates due, perhaps, to their very low solubility.

It has been reported that a hydrogen-donating solvent is not required for photolysis to occur. There are indications that a cellulose substrate will permit photolysis.*

*See Testimony of Robert D. Arsenault, Koppers Company, Inc., April 3, 1978, in "Testimony of Interested Parties," section 8.2.3 of this report.

It seems probable that the observed hexa- and heptachlorodioxins are formed thermally from o-phenoxyphenols (predioxins), detectable in technical PCP and originating in the small proportions of tri- and tetrachlorophenol present (Jensen and Renburg, 1973). (In environmental samples, these dioxins can arise by similar ring closure by photoreduction.) Other phenoxyphenols ("isopredioxins") are also detectable and may account for the observed dibenzofurans; dibenzofurans can also be formed photochemically by rearrangement and subsequent dehydration of o-phenoxyphenols (Crosby et at., 1973). The original pyrolytic conversion of a PCP salt to OCDD was accompanied by a large proportion of hexachlorobenzene (Sandermann et al., 1957), suggested to arise from decomposition of decachlorodiphenyl (Kulka, 1961), but this reaction has not been confirmed.

7.1.6 Methods of Analysis

7.1.6.1 Pentachlorophenol

The review of PCP by Bevenue and Beckman (1967) discusses a variety of colorimetric and chromatographic methods of analysis, including gas chromatography. Colorimetric methods suffer from lack of sensitivity and from spectral interferences. Gas chromatographic methods usually involve preparation of the methyl ether derivative with diazomethane. Argauer (1968) prepared the chloroacetate for detection of chlorophenols including PCP by electron-capture gas chromatography (EC-GLC). Rudling (1970) described a method for determining PCP in tissues and water by acetylation of extracted PCP and analysis by EC-GLC. The identity of PCP in sample extracts was confirmed by combined gas chromatography-mass spectrometry (GC-MS). Farrington and Munday (1976) described the preparation of chlorophenyl 2,4-dinitrophenyl ether for EC-GLC determination of trace amounts of PCP and other chlorophenols.

Barthel et al. (1969) described a method for determination of PCP in blood, urine, tissue and on clothing in which the extracted, underivatized PCP was injected on a GLC column containing 3% diethylene glycol succinate (DEGS) plus 2% syrupy phosphoric acid.

Fountaine et al. (1975) reported a procedure for determining PCP in water by ultraviolet ratio spectrophotometry. Fritz and Willis (1973) described the chromatographic separation of PCP and other phenols using an acrylic resin, and Renberg (1974) reported an ion exchange technique for determination of PCP in fish and water.

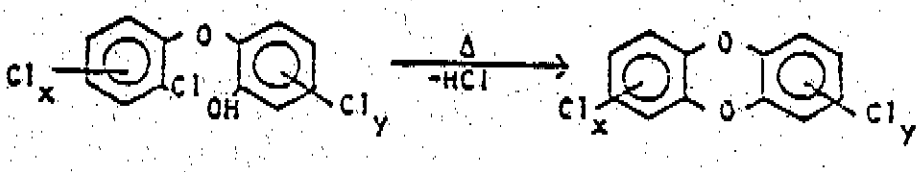
Yip (1971) reported a modified method for PCP and chlorophenoxy acid herbicides in total diet samples involving extraction of the sample with acetonitrile or chloroform, methylation, Florisil chromatography to separate PCP from the other herbicides, and EC-GLC analysis. Modifications, based on Yip's method, are currently used by FDA for total diet analyses. However, the method suffers from low and erratic recoveries, particularly for high-fat samples at the limits of detection (ca 0.01-0.02 ppm). In some instances diethyl ether or diethyl ether-petroleum ether (1:1) have been used as extracting solvents in an effort to improve recoveries of PCP.

7.1.6.2 Chlorodioxins, Chlorofurans and Other Contaminants in PCP

PCP contains a number of hexa-, hepta- and octachlorodioxins as well as other contaminants (Firestone et al., 1972; Woolson et al., 1972; Buser, 1975). Until recently, EC-GLC had been used mainly for chlorodioxin analysis. But because of the presence of other components, mass spectrometry has come into use for specific detection and confirmation of chlorodioxins as well as chlorofurans.

Villanueva et al. (1975) compared four methods (Firestone et al., 1972; Jensen and Renberg, 1973; Crummett and Stehl, 1973; Rappe and Nilsson, 1972) for analyzing for chlorodioxins in PCP. The Crummett and Jensen method, which involved extraction of non-acidic material in PCP with etherhexane (1:1), gave the best recoveries, although the Crummett method, employing ion exchange to remove the acidic components, was simpler than the Jensen method.

Crummett and Stehl (1973) employed GC-MS for determination of hexa- and octachlorodioxin in PCP. Buser (1975) developed a specific method for analysis of chlorodioxins and chlorofurans in PCP and other chlorophenols. Phenolic compounds were extracted with alkali and the neutral material chromatographed on a basic alumina micro-column to eliminate polychlorinated benzenes and polychlorodiphenyl ethers. The fraction containing chlorodioxins and chlorofurans was then subjected to mass fragmentographic (GC-MS) analysis at selected m/e values. It is important to remove ortho-phenoxyphenol isomers from the extract since they can undergo ring closure by elimination of HCl upon injection in the gas chromatograph, resulting in formation of a chlorodioxin (Jensen and Renberg, 1973).



Recoveries were determined with hexachlorodioxin; the values ranged from 85% at the 0.2 ug level (0.05 ppm) to over 95% at the 10 ug level (2.5 ppm).

Buser and Bosshardt (1976) employed the GC-MS procedure to examine a number of commercial PCP and PCP-Na samples. Chlorodioxins and chlorofurans were detected by mass fragmentography and their presence confirmed by complete mass spectral analysis. Hexachlorodioxins were recovered from PCP and PCP-Na samples with 80-95% efficiency (0.1-30 ppm), and octachlorodioxins with 95% efficiency (10-30 ppm).

Buser (1976) prepared glass capillary columns with OV-101, OV-17 and Silar 10C stationary phases for high resolution gas chromatography of chlorodioxins and chlorofurans. The best separations of hexachlorodioxin isomers were obtained with the OV-17 glass capillary column. Sample introduction was effected by a isothermal splitless injection technique, using n-tetradecane as the solvent for column temperatures in the range of 205-225^{o}C. The use of high resolution glass capillary columns permits the detection and quantization of individual isomers.

Pfeiffer (1976) investigated the use of liquid chromatography for determination of chlorodioxins in PCP. The technique was found to be useful for paid examination of non-phenolic impurities in PCP. Samples could be analyzed in four hours with detection limits of 0.2 ppm for hexa-chlorodioxin and 0.1 ppm for octachlorodioxin.

Vogel et al. (1976) evaluated three methods for analyzing for chlorodioxins in PCP. In method (A) (Blaser et al., 1976) phenolics are removed by ion-exchange chromatography, and hexa- and octachlorodioxin are determined by GC-MS. In method (B), proposed by J.P Mieure and O. Hicks, Monsanto Industrial Chemical Co., phenolics are removed by chromatography on slightly deactivated basic alumina, and chlorobenzenes, chlorobiphenyls and chlorodiphenyl ethers are removed by activated (super 1) basic alumina. Quantization of chlorodioxins and chlorofurans is accomplished by GC-MS. In method (C), also proposed by Mieure and Hicks, chlorodioxins and chlorofurans are isolated by chromatography on activated basic alumina and examined by GC-MS (or GLC). Good agreement was obtained between the three methods. Method (B) was considered the most sensitive when MS detection was used; methods (A) and (C), however, required less time for analysis.

Hass (1977) reported a procedure for analysis of chlorodioxins in beef liver and fat samples involving solvent extraction, H_2SO_4 cleanup, chromatography on basic alumina and mass spectral analysis using either electron impact (EI) mass spectrometry or negative chemical ionization (NCI) mass spectrometry (Hunt et al., 1975) in the selected ion monitoring mode. Limits of detection of hexa-, hepta-, and octachlorodioxin in liver (17-25 g sample) were 0.2-0.5 ng/g (EI) and 0.005-0.1 ng/g (NCI); in fat (3-5 g sample) the respective detection limits were approximately 2 ng/g (EI) and 0.01 ng/g (NCI).

Firestone (1976) reported detection of 0.1 to 28 ppb of total chlorodioxins (hexa-, hepta-, and octachlorodioxin) in commercial gelatin. Samples after extraction and cleanup on alumina and Florisil columns were examined by EC-GLC. The presence of hexa-, hepta-, and octachlorodioxin and penta-, hexa-, and heptachlorofuran in one of the samples (imported from Mexico) was confirmed by GLC-MS. Photodechlorination was used to confirm the presence of octachlorodioxin in some of the samples.

The possible number of positional isomers of chlorodioxins and chlorofurans are shown in Table 7.18. Aryl hydrocarbon hydroxylase activity (AHH) for dibenzo-p-dioxins and dibenzofurans are shown in Tables 7.19 and 7.20 respectively.

TABLE 7.18

Chlorinated Dibenzodioxins and Dibenzofurans
Isomers and Sources

Possible Number of Positional Isomers

Cl Substitution	No. of Isomers	
	Dioxin	Furan
Mono-	2	4
Di-	10	16
Tri-	14	28
Tetra-	22	38
Penta-	14	28
Hexa-	10	16
Hepta-	2	4
Octa-	1	1
	75	135

7.2 Environmental Contamination and Exposure

7.2.1 Environmental Behavior of PCP and its Contaminants

7.2.1.1 Atmospheric Behavior

Most compounds have a measurable vapor pressure at ambient temperatures. It is this characteristic of the chemical that gives an indication of the propensity for the substance to escape into the air. Vapor pressure alone is not the determining factor in the rate of escape or volatilization since other factors such as absorption, heat flux, air movement, i.e., the thickness of diffusion layer, and a number of other factors are of equal importance (Hartley, 1969; Haque and Freed, 1974; Plimmer, 1973). It is the rate of escape or volatilization that is of interest in considering aerial contamination and transport rather than vapor pressure, per se. The rate of volatilization may be determined experimentally, but, where constraints make this impractical the rate of volatilization may be calculated using the vapor pressure data by the following equation:

$$Q = \bar{\beta} P \sqrt{\frac{M}{2\pi RT}}$$

This equation gives an estimate of the rate of volatilization in terms of $g/cm^2/sec$ when the material is vaporizing from its own surface. However, when adsorbed on a solid surface or within a matrix, the rate of volatilization is reduced by a factor of 10-100 by adsorption forces. Where dealing with compounds such as pentachlorophenol and its contaminants, a conservative factor would be about 20 fold. In view of the apparent strength of adsorption of these materials, this factor is more likely to overestimate rate of volatilization than underestimate.

Turning to the consideration of pentachlorophenol, we observe that it has a vapor pressure of 1.6×10^{-4} mm Hg at $25^{\circ}C$, and this would yield a vapor density of 2.3×10^{-9} g/cm^2 when evaporating from its own surface. Following adsorption on a solid surface, the calculated rate of evaporation would be 1.7×10^{-10} $g/cm^2/sec$.

TABLE 7.19

Dibenzo-p-dioxins (D):
Approximate Activity of Congeners in Chick Embryo Assay
for Induction of Aryl Hydrocarbon Hydroxylase(1)

Compound	Source(2)	Approx. Activity Relative to TCDD(3)
1-Cl_1D	A	Inactive
2-Cl_1D	A	"
1,3-Cl_2D	B	"
1,6-Cl_2D	B	"
1,9-Cl_2D	B	"
2,3-Cl_2D	B,D	"
2,7-Cl_2D	A,E	"
2,8-Cl_2D	A	"
1,2,3-Cl_3D	B	"
1,2,4-Cl_3D	A	"
2,3,7-Cl_3D	A,B,C	0.001
1,2,3,4-Cl_4D	A,B	Inactive
1,2,6,7-Cl_4D	B	0.002
1,3,6,8-Cl_4D	A	Inactive
1,3,7,8-Cl_4D	B	0.1
2,3,7,8-Cl_4D (TCDD)	A.B.C.D.E	1.0
1,2,3,4,7-Cl_5D(4)	A	0.1
1,2,3,7,8-Cl_5D	C	0.3
1,2,4,7,8-Cl_5D	C	--
1,2,4,6,7,9-Cl_6D	A,C	0.002
1,2,4,6,8,9-CL_6D	B	--
1,2,3,6,7,9-Cl_6D	C	0.15
1,2,3,4,7,8-Cl_6D	A,C,D	0.3
1,2,3,6,7,8-Cl_6D	C	0.25
1,2,3,7,8,9-Cl_6D	C	0.25
1,2,3,4,6,7,9-Cl_7D	C	0.002
1,2,3,4,6,7,8-Cl_7D	C	0.15
1,2,3,4,6,7,8,9-Cl_8D	A,E	0.002
2,3-Cl_2(UL-^{14}C)D_3	B	Inactive
2,3,7,8-Cl_4(1,6-^{3}H)D	B	1.0

(1) Activity data provided by A. Poland; see also Environmental Health Perspectives (1973) 5:245-251; J. Org. Chem. (1974), 931-937; and J. Biol. Chem. (1976) 251:4936-4946.
(2) (A) A.E. Pohland (See J. Ag. Food Chem. (1972) 20:1093-1099); (B) A.S. Kende (See paper ORGN 130, manuscript in preparation, 167th Nat. Mtg. ACS, L.A., Cal., April 4, 1974); (C) A. Gray (See Tetrahedron Letters (1975) No. 33: 2373-2376 and J. Org. Chem. (1976) 41: 2435-2437; (D) J.D. McKinney; and (E) Dow Chemical Co.
(3) 2,3,7,8-TCDD is assigned a relative activity of 1.0.
(4) Contains 5% of 1,2,3,4,7,8-Cl_6D impurity.

TABLE 7.20

Dibenzofurans (F):

Approximate Activity in Chick Embryo Assay for Induction of Aryl Hydrocarbon Hydroxylase.[1]

Compound	Source[2]	Approx. Activity Relative to TCDD[3]
2,4-Cl_2F	D	Inactive
2,8-Cl_2F	A,B	"
3,7-Cl_2F	B	"
2,3,4-Cl_3F	B	0.001
2,3,6-Cl_3F	B	0.001
2,3,7-Cl_3F	B,C	----
2,3,8-Cl_3F	B,C	0.001
2,3,9-Cl_3F	C	----
2,4,6-Cl_3F	C	----
2,4,8-Cl_3F	B	0.001
1,4,6,8-Cl_4F	F	----
1,2,7,8-Cl_4F	C	----
1,3,6,7-Cl_4F	B	Inactive
1,3,7,8-Cl_4F	B	0.02
2,3,6,7-Cl_4F	B	0.01
2,3,6,8-Cl_4F	B,C	0.005
2,3,7,8-Cl_4F	B,C	0.7
2,4,6,7-Cl_4F	B	0.01
2,4,6,8-Cl_4F	B,C	Inactive
3,4,6,7-Cl_4F	B	0.01
1,2.3,6,7-Cl_5F	B	0.2
1,2,3,7,8-Cl_5F	B	0.2
1,2,4,7,8-Cl_5F	C	----
1,3,4,7,8-Cl_5F	C,D	0.005
2,3,4,6,7-Cl_5F	B	0.1
2,3,4,7,8-Cl_5F	B	0.7
2,3,4,6,7,8-Cl_6F	B,E	0.2
2,3,4,7,8,9-Cl_6F	B	0.3
1,2,3,4,6,7,8-Cl_7F	B	0.2
1,2,3,4,6,7,8,9-Cl_8F	A,B	0.002

[1] Activity data provided by A. Poland; see also J. Biol. Chem. (1976) 251, 4936-4946.

[2] (A) A. E. Pohland: (B) A. S. Kende (See paper ORGN 130. manuscript in preparation. 167th National Meeting, American Chemical Society, L. A., Cal., April 4. 1974); (C) A. P. Gray (See J. Org. Chem. (1976) 41, 2428-2434); (D) I. H. Pomerantz; and (E) J. D. McKinney (in preparation); (F) S.W. Page (See paper ORGN 63, manuscript in preparation. 172 nd National Meeting, ACS, San Francisco, Cal, Aug. 30-Sept 3, 1976.)

[3] 2,3,7,8-TCDD is assigned a relative activity of 1.0.

Table 7.21 presents the estimated vapor density and rate of evaporation of chlorodioxins. The low vapor pressure of the chlorodioxins coupled with the strong adsorption to surfaces, as indicated by the high molar refraction and the data of Kearney et al. (1972, 1973), lend credibility to the values.

Table 7.21

Estimated Vapor Density[a] and Rate of Evaporation[b] (Q) of Chlorodioxins

Compound	Vapor Density (g/cm^3)	Q ($g/cm^2/sec$)
2,7-di	8.2×10^{-11}	6.1×10^{-12}
2,3,7,8-tetra	2.9×10^{-11}	2.0×10^{-12}
penta	1.7×10^{-11}	1.1×10^{-12}
hexa	1.4×10^{-11}	8.4×10^{-13}
hepta	6.9×10^{-12}	4.0×10^{-13}
octa	4.5×10^{-12}	2.5×10^{-13}

(a) Above own surface, (b) from adsorbing surface.

According to Table 7.21, the rate of volatilization of the chlorodioxins is very low. This low rate of evaporation compared to pentachlorophenol could very rapidly explain the findings of Levin et al. (1976).

Table 7.22 presents similar data for the chlorinated dibenzofurans. The data here indicate a slightly greater vapor density and evaporative loss for the chloro-dibenzofurans. This would be expected of compounds of slightly lower molecular weight, higher vapor pressure, and lower molar refraction.

TABLE 7.22

Estimated Vapor Density[a] and Rate of Evaporation[b] (Q) of Chlorinated Dibenzofurans

Compound	Vapor Density ($g.cm^3$)	Q ($g/cm^2/sec$)
2,4-di	8.2×10^{-11}	6.8×10^{-12}
2,4,6-tri	5.2×10^{-11}	4.0×10^{-12}
2,3,7,8-tetra	3.0×10^{-11}	2.1×10^{-12}
1,4,6,8-tetra	3.7×10^{-11}	2.7×10^{-12}
2,3,4,7,8-penta	1.9×10^{-11}	1.3×10^{-12}
1,3,4,7,8-penta	2.2×10^{-11}	1.5×10^{-12}
octa	4.3×10^{-12}	2.5×10^{-13}

(a) Above own surface, (b) from adsorbing surface.

Although PCP has a relatively high vapor pressure (1.6×10^{-4} torr at 25°C and 3.1×10^{-3} torr at 50°C, the temperature of a sunlit surface), there is evidence that it may be slow to volatilize. However, its volatilization from wood into an enclosed airspace is measurable, and the atmosphere in a wood-treatment plant has been shown to contain as much as 1.7 ug/m^3 of PCP (Wyllie et al., 1975). PCP has been detected in rainfall (Bevenue et al., 1972), but the possibility remains that of this may have been due to its presence on airborne particles rather than as atmospheric vapor. Laboratory experiments indicate that PCP vapor is stable to sunlight.

No evidence exists concerning the presence of dioxins or dibenzofurans in air. The solubility and vapor pressure of TCDD and OCDD are roughly similar to those of DDT, and DDT is known to volatilize readily from soil and rapidly from water. Neutral PCP impurities might logically be expected to behave similarly, but their vapor should be stable to light.

7.2.1.2 Behavior in Soil

Three processes are of significance in soil. These are adsorption, leaching and breakdown (Hamaker, 1975; Haque and Freed, 1974). Adsorption occurs predominantly on the organic matter (Hartley, 1969) and clay of soil, though the coarser mineral particles also adsorb. Laboratory measurements that have been shown to correlate well with adsorption include molar refraction, latent heat of solution, and partition coefficient. Based on this, one would expect that pentachlorophenol and its various contaminants would all be relatively strongly adsorbed by soil.

A number of studies have been performed on the soil behavior of pentachlorophenol. PCP is adsorbed to a moderate degree under acidic conditions (as neutral molecules) but moves quite readily in ionized form (under neutral or alkaline conditions) (Kuwatsuka, 1972). Adsorption is greatest in a soil in the pH range of 4.6-5.1, with very little adsorption above pH 6.8 (Choi and Amoine, 1974). Microbial degradation is relatively rapid, especially in wet soil where a variety of tetra-, tri-, and dichlorophenols are formed; meta-chlorines are the most stable (Ide et al., 1972). In aerated soil, oxidation and methylation to pentachloroaonisole and 2,3,5,6-tetrachlorol,4-dimethoxybenzene represent major routes of degradation. Similarly, Kearney et al. (1973) and others indicate a strong adsorption of 2,3,7,8-tetrachloro-dibenzodioxin and octachlorodioxin (Arsenault, 1976).

Neither pentachlorophenol (Bevenue and Beckmen, 1967; Arsenault, 1976; Kearney et al., 1973) nor the dioxins have been found to leach readily in soil, largely because of the strong adsorption.

The breakdown of pentachlorophenol and chlorodioxins in soil have been incompletely studied. In the case of pentachlorophenol, it is known that the breakdown is fairly rapid (5 to 8 weeks in a moist soil at rates up to 20 lbs/acre). Kearney et al. (1972, 1973) report a half-life of approximately one year for 2,3,7,8-tetrachlorodibenzo-p-dioxin in soil; the number of species of microorganisms attacking the chemical appears limited (Matsumura and Benezet, 1973).

The fate of PCP and its impurities in or on treated wood is not known, but practical experiments indicate that PCP remains fungicidally effective for years (Arsenault, 1976). PCP conceivably could generate OCDD in sunlight, but the usual presence of hydrocarbon solvents would tend to promote eventual dioxin photolysis on the wood surface. The burning of PCP-treated wood or sawdust generates OCDD which subsequently volatilizes, but the proportion is small in comparison to that already present in the wood (Crosby et al., 1973; Stehl et al., 1973; Jensen and Renberg, 1973). (There is a report, presently discounted, that TCDD forms similarly from organic matter containing trichlorophenol derivatives (Buu-Hoi et al., 1971), but attempts to repeat the observation have failed.)

7.2.1.3 Behavior in Aquatic Systems

7.2.1.3.1 Physical Behavior

The transport and persistence of PCP and sodium PCP in aquatic systems has been extensively studied, particularly where these chemicals had been used as a molluscicide (Strufe, 1968). Here it has been found that the material is rapidly adsorbed on suspended particulates. Where there is a heavy load of sediment in the water, the concentration of PCP or sodium PCP is rapidly reduced in the aqueous phase and the material settles to the bottom with these particles. PCP, both as a free phenol and as a sodium salt, has been found to undergo quite rapid degradation in water, both from sunlight and anaerobic processes in the bottom mud.

Little information is available on behavior and fate of the chlorodioxins and the chlorodibenzofurans in aquatic systems, but it would seem correct to infer that with their greater propensity for adsorption they would even more rapidly and tightly bind to sediment than PCP. Since the biological activity of pentachlorophenol has been shown to be markedly reduced by the adsorption (Strufe, 1968), it would be presumed that the same would hold true for the dioxins and dibenzofurans.

7.2.1.3.2 Breakdown in Aquatic Systems

In dilute aqueous solutions exposed to sunlight, PCP or its salts undergo the replacement of ring chlorines by hydroxyl groups described above. The resulting tetrachlorohydroquinone and tetrachlorocatechol are readily oxidized by air to quinones which in turn are dechlorinated. If the original PCP solution is sufficiently concentrated (as in the

case of a rice-paddy), the tetrachlorodiphenols can react with the quinones to give a variety of nontoxic minor products. However, under most circumstances, the quinone solution is rapidly degraded to dichloromaleic acid which itself is converted to small fragments within a few days (Wong, 1977).

Considering the similarity between the vapor pressures and solubilities of TCDD or OCDD and DDT, one might expect more rapid volatilization of dioxins from water than from soil. As mentioned, dioxins in water appear stable to light due, perhaps, to their insolubility. In view of their high degree of adsorption to particulate matter, the amount in solution would be expected to be low (Matsumura and Benezet, 1973; Isensee and Jones, 1975).

7.2.2 Occupational Use and Exposure

Pentachlorophenol, both as a free phenol and as a sodium salt, has been used as a wood preservative, an herbicide, a fungicide, and a molluscicide. Use as a wood preservative in recent years has consumed many times more pentachlorophenol than all of the other uses. In fact, the use of pentachlorophenol or sodium pentachlorophenate as an herbicide or a fungicide has markedly declined in recent years as other chemicals have replaced them.

In the United States pentachlorophenol, in an appropriate solvent, has been the principal form used in wood preservation. There are limited uses of the sodium pentachlorophenate for prevention of the development of "blue mold." However, in some countries, e.g., Indonesia, sodium pentachlorophenate is the principal form in which this preservative is used.

There are two principal methods by which pentachlorophenol may be applied for wood preservation (Arsenault, 1976), pressure treatment or direct application of a solution of pentachlorophenol by painting, dipping or spraying. For the most part the last three methods are employed by the individual while the pressure treatment is used by commercial treatment plants. Another commercial treatment is the thermal process (hot and cold bath/submersion) which is used to introduce PCP into wood (Ochrymowych, 1978).

In the pressure treatment with pentachlorohenol, the phenol, in appropriate solvent, is applied to the pole or lumber in a pressure retort at somewhat elevated temperatures. The pressure treatment may be preceeded by a vacuum to increase penetration, and it may be followed by a flash vacuum to reduce surface deposits. Occupational exposure of humans, in this case, may occur during preparation of the treatment solution or when the retort is opened following treatment and the system is still hot. Relatively lower levels of exposure would be expected in handling the treated wood. The greatest exposure comes to the worker in the immediate area of the treatment operation, whether by dip, spray, or pressure treatment. In most of these instances unless there is direct contact with the treatment mixture or treated materials, the principal route of exposure appears to be respiratory. This is in contrast to the experience in Indonesia where the worker handles the freshly dipped lumber or in herbicide treatment where there may be direct dermal exposure.

7.2.3 Environmental Transport and Exposure

Pentachlorophenol has been found in a number of different environmental samples (Kutz et al., 1976), e.g., house dust, air, water, and in the urine (Bevenue et al., 1972) of presumably non-exposed humans. This would appear to indicate a rather high environmental mobility for pentachlorophenol. However, it must be remembered that pentachlorophenol may be generated in chlorination of water and that there is a residual background found upon analyses of soil that gives analytical results similar to PCP. However, based on the properties of pentachlorophenol, namely that of vapor pressure and rate of volatilization, measurable quantities would be expected to escape into the air either from the chemical's own surface or from poorly adsorbing surfaces to which it had been applied. But based on pentachlorophenol's propensity for adsorption, one would expect that a substantial amount of this vaporized material would be found adsorbed to particulates in air. Another route of transport to air would be the erosion of contaminated dust particles.

On the other hand, the chlorodioxins and chlorodibenzofurans that occur in pentachlorophenol, having much lower rates of volatilization, would not be expected to be found as frequently in air samples. Again, because of the propensity for adsorption and the low water solubility (about 3 ppt for OCDD; Arsenault, 1976) one would not expect to find a great deal of these materials in water. As indicated earlier, the relative vapor pressures and rate of evaporation of pentachlorophenol, chlorodioxins and dibenzofurans would perhaps account for the findings of the Swedish workers (Levin et al., 1976). Here it appeared that the ratio of chlorodioxins and chlorodibenzofurans to pentachlorophenol in wood increased appreciably over the ratio found in the original treatment solution. It seems that a reasonable explanation would be the probable greater loss of pentachlorophenol through vaporization from the sawdust in contrast to the other two types of chemicals.

Though pentachlorophenol and its contaminants are probably transported by air and water (probably in the adsorbed state), their biological activity is probably much reduced by adsorption, thus attenuating the effect of exposure. It has been found, for example, that pentachlorophenol adsorbed on sediment found in water had low activity so far as control of snails is concerned (Strufe, 1968). It is likely that the adsorptions of the chlorodioxins and chlorodibenzofurans also result in a reduction of their biological availability.

Breakdown is another factor in reducing the concentration and biological effects on these chemicals in transport.

7.2.4 Food and Feed

PCP is a powerful herbicide, and its intentional use around food crops would be expected to be negligible. However, PCP is used as a desiccant on seed alfalfa and seed clover, and sodium PCP is used in dilute aqueous solution as a postharvest fungicidal dip. These are considered as non-food uses, and no tolerance has been established, although feeding treated forage or threshings to livestock is not permitted in the United States.

Measurement of total diet residues (FDA Market Basket Survey) has shown occasional PCP contamination (for example, nine of 30 composite samples showed 0.01-0.02 ppm of PCP in 1972-3; two dairy products, one legume vegetable, and six of sugar) (Johnson and Manske, 1976). OCDD and HCDD have not been reported in food, although Firestone (1976) reported the presence of dioxins in commercial and "edible" packages of gelatin. The presence of dioxins (chick edema factors) in food grade oleic acid and oleic acid derivatives, e.g., glyceryl monooleate and a food emulsifier, prompted FDA to issue a food additive regulation in 1960 (Firestone, 1973). Chlorinated anisoles, originating in henhouse litter, have been detected in chicken meat (0.02-0.08 ppm) and have caused a musty taste (Curtis et al., 1972). PCP was reported to occur at low ppb levels in fish caught in open water not expected to contain appreciable levels of PCP (Zitko et al., 1974).

7.2.5 Biological Uptake and Concentration

Higher plants do not absorb appreciable amounts of PCP or TCDD from soil (Miller and Aboul-Ela, 1969; Isensee and Jones, 1971), and administration of these compounds directly to leaves resulted in retention rather than translocation. Algae, however, rapidly absorbed and concentrated TCDD about 10,000 fold from water (Isensee and Jones, 1975), although they metabolized rather than concentrated PCP (Lu and Metcalf, 1975).

Rodents excreted PCP partly unchanged, partly as glucosonide conjugate, and partly as tetrachlorohydroquinone and its conjugates (Jakobson and Yllner, 1971; Ahlborg et al., 1974). Tetrachlorohydroquinone also was detected in the urine of human workers occupationally

exposed to PCP (Ahlborg et al., 1974). However, the rhesus monkey excreted PCP more slowly, and apparently only as free PCP, with a half-life of about 40 hours in the male and 90 hours in the female (Braun and Sauerhoff, 1976). There appear to be no data on organ accumulation of PCP during chronic exposure, but recovery of PCP and its conjugates from urine and feces certainly is not quantitative; for example, about 11% of a 10 mg/kg dose of PCP was still retained by the monkey after 360 hours (1% in liver, 7% in intestines, and 3% in other organs) (Braun and Sauerhoff, 1976).

Animals in a model aquatic ecosystem concentrated PCP as much as 300-fold during 48 hours of continuous exposure (Lu and Metcalf, 1975), although up to 74% of the applied dose was metabolized in that period. Fish accumulated the most PCP after 120 hours of exposure to 0.1 ppm of PCP. Fish had concentrated it 1000-fold, primarily in the gallbladder; return to clean water caused an initially rapid clearance, mostly in conjugated form. Eventually up to 30% of the original PCP body burden was retained (Kobayashi and Akitake, 1975).

Surprisingly, no data were available on the bioconcentration of dioxins or dibenzofurans in higher animals during chronic exposure. After a single oral dose of 50 ug/kg, the rat cleared TCDD with a half-life of 17 $\pm$ 6 days (Piper et al., 1973). Retention was primarily in the liver and secondarily in the fat; the liver still contained 47% of the initial dose after three days and 11% after 21 days. Body burden of TCDD was only determined to 21 days, at which time it still represented 40% of initial dose; there is no indication of what terminal residue eventually might exist, if any. No metabolism of dioxins was evident.

Bioconcentration of TCDD in aquatic model ecosystems was reported by Matsumura and Benezet (1973) and Isensee and Jones (1975). Bioconcentration was proportional to the amount of TCDD in the water; the bioconcentration factor of approximately 10^4 in the species included and was rather independent of the aqueous concentration. Attempts to detect TCDD and other dioxins in samples from terminal predators in the environment (gull eggs, eagle fat, and sea-lion blubber) were unsuccessful, although the analytical sensitivity was limited to the ppb range (Woolson et al., 1973; Bowes et al., 1973).

While the potential exists for limited bioconcentration of PCP from food and the environment, its rather effective metabolism by higher and lower animals suggests that the effect may not be pronounced. On the other hand, TCDD shows a bioconcentration potential (10^4) roughly similar to that of the more inert chlorinated hydrocarbons (10^5).

7.2.6 Sources of Exposure

Table 7.23 lists major registered uses of PCP. From these, it is possible to determine a variety of potential sources of occupational exposure (Table 7.24), but in only a few instances (primarily in wood treatment industries) has the exposure of workers been analyzed (Klemmer, 1972; Ahlborg et al., 1974; and Wyllie et al., 1975, are typical).

The widespread use of PCP in these applications likewise provides increasing opportunities for incidental exposure of the public to PCP and its impurities in the home, business, and outdoor environment. Table 7.25 lists a few of the more obvious possibilities. Such instances as the detection of ppb levels of PCP in rainfall over a remote island (Bevenue et al., 1972), in freshwater and marine fish caught in areas remote from direct PCP discharge (Zitko et al., 1974), and in the urine of random samples of human populations not exposed occupationally suggests a continual low-level background of environmental PCP which requires further investigation.

Table 7.23

Major Registered Uses of PCP

Herbicide and desiccant for forage seed crops
Insecticide for beehives, seed flats, greenhouse use.
Microbiostat for commercial and industrial water cooling
Postharvest wash for fruit
Microbiocide for burlap, canvas, cotton, rope, and twine
Microbiocide for leather
Microbiocide and insecticide for wood treatment
Preservative for oil- and water-based paint
Slime control for pulp and paper
Microbiocide for petroleum drilling mud and flood water
Fumigant for shipping-van interiors
Preservative for hardboard and particle board
Herbicide for non-food vegetation control

Table 7.24

Some Potential Sources of Occupational Exposure to PCP and PCP Impurities

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

Table 7.25

Some Potential Sources of Incidental Exposure to PCP and PCP Impurities

Smoke from sawmills and burning scrap lumber
Sawdust (fuel, floor covering, particle board, etc.)
Vapor from treated lumber and plywood
Home treatment of lumber for termite control
Burlap, canvas, and rope
Leather products
Paper products
Contact with paint and painted surfaces
Uses of utility and structural poles and railroad ties
Ornamental wood-chips
Dairy products, sugar products, and fish

7.3 References

Ahling, B. and L. Johansson (1977). Combustion experiments using pentachlorophenol on a pilot scale and full-scale. Chemosphere 6 (7) : 425.

Ahlborg, V.G., J.E. Lindgren, and M. Mercier (1974). Metabolism of pentachlorphenol. Arch. Toxicol. 32: 271.

American Wood Preservers Institute (1977) Pentachlorophenol--A Wood Preservative. Memorandum for the Office of Pesticide Programs, EPA, McLean, Virginia, p. 40.

Argauer, R.J. (1968). Rapid procedure for the chloroacetylation of microgram quantities of phenols and detection by electron-capture gas chromatography. Anal. Chem. 40: 122.

Arsenault, R.D. (1976). Pentachlorophenols and contained chlorinated dibenzodioxins in the environment. Proc. Am. Wood Preserv. Assoc. 72: 1.

Barthel, W.F., et al. (1969). Determination of pentachlorophenol in blood, urine, tissue, and clothing. J. Assoc. Offic. Anal. Chem. 52: 294.

Bevenue, A., J.N. Ogata, and J.W. Hyline (1972). Organochlorine pesticides in rainwater, Oahu, Hawaii, 1971-1972. B. Env. Cont. Tox. 8: 238.

Bevenue, A., and H. Beckman (1967). Pentachlorophenol: A discussion of its properties and its occurrence as residue in human and animal tissues, Residue Reviews 19: 984.

Blaser, W.W., et al. (1976). Determination of chlorinated dibenzo-p-dioxins in pentachlorophenol by gas chromatography-mass spectrometry. Anal. Chem. 48: 984.

Boer, F.P., et al. (1973). X-ray diffraction studies of chlorinated dibenzo-p-dioxins, In: Chlorodioxins--Origin and Fate. Adv. Chem. Series 120: 14.

Bowes, G.W., et al. (1973). The search for chlorinated dibenzofurans and chlorinated dibenzodioxins in wildlife populations showing elevated levels of embryonic death. Env. Health Perspect. 5:191.

Braun, W.J., and M.W. Sauerhoff (1976). The pharmacokinetic profile of pentachlorophenol in monkeys. Tox. Appl Pharm. 38:525.

British Crop Protection Council (1971). Pesticide Manual, 2nd edition. H. Martin (ed.), Worcester, England P. 359.

Britton, E.C., and F.N. Alquist (1940). Pentachlorophenol. U.S. Patent 2,176,417 (October 17, 1940), Chem. Abstr. 34: 1038.

Buser, H.-R (1975a). Analysis of polychlorinated dibenzo-p-dioxins and dibenzofurans in chlorinated phenols by mass fragmentography. J. Chromatog. 107:295.

Buser, H.-R (1975b). Polychlorinated dibenzo-p-dioxins. separation and identification of isomers by gas chromatography-mass spectrometry. J. Chromatog. 114:95.

Buser, H.-R. (1976). Higher resolution gas chromatography of polychlorinated dibenzo-p-dioxins and dibenzofurans. Anal. Chem. 48:1553.

Buser, H.-R. and H.P. Booshardt (1976). Determination of polychlorinated dibenzo-p-dioxins and dibenzofurans in commercial PCP's by combined gas chromatography-mass spectrometry. J. of the ADAC, 59(3):562-569.

Buu-Hoi, N.P., et al. (1971). Preparation, properties, and identification of "dioxin" (2,3,7,8-tetrachlorodibenzodioxin) in the pyrolyzate of defoliants based on 2,4,5-trichlorophenoxy acetic acid and its esters and contaminated vegetation. Compt. Rend. Acad. Sci. Paris 273D:708.

Cantrell, J.S., N.C. Webb, and A.J. Mabis (1969). The identification and crystal structure of a hydropericardium-producing factor: 1,2,3,7,8,9- hexachlorodibenzo-p-dioxin, Acta Crystallogr. B25:150-156.

Chang, W.-H. (1962). Tetrachloro-o-benzoquinone by direct oxidation of pentachlorophenol. J. Org. Chem. 27: 2921.

Choi, J. and S. Aqmine (1974). Adsorption of pentachlorophenol by soils. Soil Sci. Plant Nutr. Tokyo 20: 135.

Crosby, D.G., K.W. Moilanen, and A.S. Wong (1973). Environmental generation and degradation of dibenzodioxins and dibenzofurans. Environ. Health Perspec. 5:259.

Crosby, D.G., et al. (1971). Photodecomposition of chlorinated dibenzo-p-dioxins. Science 173: 748.

Crosby, D.G., and N. Hamadmad (1971). The photoreduction of pentachlorobenzenes. J. Agr. Food Chem. 19:1171.

Crosby, D.G., and A.S. Wong (1976). Photochemical generation of chlorinated dioxins. Chemosphere 5:327.

Crosby, D.G., and A.S. Wong (1977). Environmental degradation of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Science 195:1337.

Crummett, W. and R.H. Stehl (1973). Determination of chlorinated dibenzo-p-dioxins and dibenzofurans in various materials. Environ. Health Perspect. 5:15.

Crummett, W.B. (1975). Memo of 7/28/75 to R. Ross, EPA Office of Pesticide Programs.

Curtis, R.F., et al. (1972) 2,3,4,6-tetrachloroanisole association with musty taint in chickens and microbiological formation. Nature 235:223.

Denivelle, L. and R. Fort (1954) Hexachloro-cyclohexadiene-1,5-one-3 from pentachlorophenyl pseudohypochlorite, Compt. Rend. Acad. Sci. Paris 238:124.

Doedens, J.D. (1964). Chlorophenols. In: Kirk-Othmer Encyclopedia of Chemical Technology, 2nd edition (A. Standen, ed.) Interscience Publishers, J. Wiley & Sons, New York, pp. 336.

Dow Chemical Company (1971). Private communication.

Dow Chemical Company (1973). Private communication.

Farrington, D.S. and J.W. Munday (1976). Determination of trace amounts of chlorophenols by gas-liquid chromatography. Analyst 101:639.

Firestone, D. (1977). Report on oils and fats. J. Assoc. Offic. Anal. Chem. 60:354.

Firestone, D. (1973). Ethology of chick edema disease. Environ. Health Perspect. 5:59.

Firestone, D. (1976). Determination of polychlorodibenzo-p-dioxins and polychlorodibenzofurans in commercial gelatins by gas-liquid chromatography. J. Agric. Food Chem. 25:1274.

Firestone, D., et al. (1972). Determination of polychlorodibenzo-p-dioxins and related compounds in commercial chlorophenols. J. Assoc. Offic. Anal. Chem. 55:85.

Firestone, D., M. Clower, A.P. Borsetti, R.H. Teske, and P.E. Long (1978). Polychlorodibenzo-p-dioxin and PCP residues in milk and blood of cows fed commercial PCP. Submitted to J. Agric. Food Chem.

Fountaine, J.E., P.B. Willis (1973). Chromatographic separation of phenols using an acrylic resin. J. Chromatog. 79:107.

Fountaine, J.E., P.B. Joshipura, and P.N. Keliher (1975). Determination of pentachlorophenol by ultraviolet ratio spectrophotometry. Anal. Chem. 47:157.

Fritz, J.S. and R.B. Willis (1973). Chromatographic separation of phenols using an acrylic resin. J. Chromatog. 79:107.

Gab, S., et al. (1975). Photomineralization of certain aromatic xenobiotica. Chemosphere 4:251.

Goldstein, J.A., M. Friesen, R.E. Linder, P. Hickman, J.R. Hass, and H. Bergman (1977). Effects of PCP on hepatic drug-metabolizing enzymes and porphyria related to contamination with chlorinated dibenzo-p-dioxins and dibenzofurans. Biochem. Pharmacol. 26: 1549.

Gray, A.P., S.P. Cepa, and J.S. Cantrell (1975). Intervention of the Smiles rearrangement in synthesis of dibenzo-p-dioxins 1,2,3,6,7,8- and 1,2,3,7,8,9-hexachlorodibenzo-p-dioxin (HCDD). Tetrahedron Letters 33:2873.

Gray, A.P., V.M. Dipinto, and I.J. Solomon (1976). Synthesis of specific polychlorinated dibenzofurans. J. Org. Chem. 41:2428.

Hamaker, J.W. (1975). In: Environmental Dynamics of Pesticides, (R. Haque and V.H. Freed, eds.). Plenum Press, New York.

Haque, R., and V.H. Freed (1974). Residue Reviews 52:89.

Hartley, F.S. (1969). In: Adv. Chem. Series 86:115.

Hass, J.R. (1977). Private communication.

Helling, C.S., et al. (1973). J. Env. Qual. 2:171.

Hunt, D.F., T.M. Harvey, and J.W. Russell (1975). Oxygen as a reagent gas for the analysis of 2,3,7,8-tetrachlorodibenzo-p-dioxin by negative ion chemical ionization mass spectrometry. J. Chem. Soc. Chem. Comm. 151.

Hutzinger, et al. (1973). Photochemical degradation of di- and octachlorodibenzofuran. Environ. Health Perspect. 5:267.

Ide, A., et al. (1972). Decomposition of pentachlorophenol in a paddy soil. Agric. Biol. Chem. 36:1937.

Isensee, A.R., and G.E. Jones (1975). Distribution of 2,3,7,8-tetrachlorodibenzo-p-dixon (TCDD) in aquatic model ecosystem. Environ Sci. Technol. 9:669.

Isensee, A.R., and G.E. Jones (1971). Absorption and translocation of root and foliage applied 2,4-dichlorophenol, 2,7-dichlorodibenzo-p-dioxin, and 2,3,7,8-tetrachlorodibenzo-p-dioxin. J Agr. Food Chem. 19:1210.

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

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

Jensen, S. and L. Renberg (1973). Chlorinated dimers present in several technical chlorophenols used as fungicides. Environ. Health Perspect. 5:37.

Kearney, P.C., et al. (1973). In: Chlorodioxins--Origin and Fate (E.H. Blair, ed.). ACS Series 120.

Kearney, P.C., et al. (1973). Environ. Health Perspect. 5:273.

Kearney, P.C. et al. (1972). Environ. Sci. Technol. 6:1017.

Kende, A.S., et al. (1974). Regiospecific synthesis and NMR spectroscopy of toxic polyhalodibenzo-p-dioxins and dibenzofurans. Paper presented, 167th Ann. Mtg. Am. Chem. Soc. March 31, 1974 (Abstract ORGN 130).

Kim, P., et al. (1975). Photochemical dechlorination of chlorinated dibenzo-p-dioxins. Paper presented, 1st Chemical Congress of North America, November 30-December 5, 1975, Mexico City.

Kobayashi, K. and H. Akitake (1975). Studies on the metabolism of chlorophenols in fish-I. Absorption and excretion of PCP by goldfish. Bull. Jap. Soc. Sci. Fish. 41(1):87-92.

Kulka, M. (1961). Octahalogenodibenzo-p-dioxins. Can. J. Chem. 39:1973.

Kutz, F. et al. (1976). In: Air Pollution by Pesticides and Agricultural Processes (R. Lee, ed.). Chapter 4, CRC Press.

Kuwatsuka, S. (1972). Degradation of several herbicides in soils under different conditions. In: Environmental Toxicology of Pesticides (F. Matsumara, G.M. Boush, and T. Misato, eds.). Academic Press, New York, p. 385.

Langer, H.G., et al. (1973). Thermal chemistry in chlorinated phenols, In: Chlorodioxins--Origin and Fate. ACS Series 120, Washington, D.C. p. 26.

Leo, et al. (1971). Chemical Reviews 71:525.

Levin, J. et al. (1976). Scan. J. Work Env. Health 2:71.

Lu, P.-Y and R.L. Metcalf (1975). Environmental fate and biodegradability of benzene derivatives as studied in a model aquatic ecosystem. Environ. Health Perspect. 10:269.

Melnikov (1971). Residue Reviews 36.

Matsumura, F. and H.J. Benezet (1973). Studies on the bioaccumulation and microbial degradation of 2,3,7,8-tetrachlorodibenzo-p-dioxin. Environ. Health Perspect. 5:253.

McConnell, E.E., J.A. Moore, J. Haseman and M. Harris (1978). The comparative toxicity of chlorinated dibenzo-p-dioxins isomers in mice and guinea pigs. Toxicol. Appl. Pharmacol. In press.

Miller, C.S. and M.M. Aboul-Ela (1969). Fate of pentachlorophenol in cotton. J. agr. Food Chem. 17:1244.

Munakata, K. and M. Kuwahara (1969). Photochemical degradation products of PCP. Residue Reviews, 25:13-23.

Nilsson, C.-A. and L. Renberg (1974). Further studies on impurities in chlorophenols. J Chromatogr. 89:325.

Ochrymowych, J., Western Electric (1978). Personal communication.

Page, S.W. (1976). Synthesis of chlorinated dibenzofurans, Paper presented at the 172nd Am. Chem. Soc. Mtg. San Francisco, California, August 30- September 3, 1976 (Abstract ORGN 63).

Pfeiffer, C.D. (1976). Determination of chlorinated dibenzo-p-dioxins in pentachlorophenol by liquid chromatography. J. Chromatog. Sci. 14:386.

Pierce, R.H. (1978). Fate and impact of PCP in a freshwater ecosystem. U.S. EPA, 600/3-78-063, pp 1-62.

Piper, W.N., J.Q. Rose, and P.J. Gehring (1973). Excretion and tissue distribution of 2,3,7,8-tetrachlorodibenzo-p-dioxin in the rat. Env. Health Perspect. 5:241.

Plimmer, J.R., et al. (1973). Photochemistry of dibenzo-p-dioxins. In: Chlorodioxins: Origin and Fate. ASC Services 120, pp. 44-54.

Plimmer, J.R., and U.I. Klingebiel (1971). Riboflavin photosensitized oxidation of 2,4-dichlorophenol: assessment of possible chlorinated dioxin formation. Science 174:407.

Plimmer, J.R. (1973). Technical pentachlorophenol: origin and analysis of base-insoluble contaminants. Environ. Health Perspect. 5:41.

Pohland, A.E. and G.C. Yang (1972). J. Agric. Food Chem. 20:1093.

Pohland, A.E., G.C. Yang, and N. Brown (1973). Analytical and confirmative techniques for dibenzo-p-dioxins based upon their cation radicals. Environ. Health Perspect. 5:9.

Poland, A. and E. Glover (1976). Stereospecific high affinity binding of 2,3,7,8-tetrachlorodibenzo-p-dioxins by hepatic cytosol. J. Biol. Chem. 251:4936.

Rappe, C., and C. A. Nilsson (1972). An artifact in the gas chromatographic determination of impurities in pentachlorophenol. J. Chromatogr. 67:247.

Renberg, L. (1974). Ion exchange technique for the determination of chlorinated phenols and phenoxy acids in organic tissue. Soil & Water Anal. Chem. 46:459.

Rudling, L. (1970). Determination of pentachlorophenol in organic tissues and water. Water Research 4:533.

Sandermann, W., H. Stockmann, and R. Casten (1957). Pyrolysis of pentachlorophenol. Chem. Ber. 90: 690.

Sittig, M. (1969). Organic Chemical Process Encyclopedia. 2nd edition. Noyes Development Corp., Park Ridge, New Jersey, pp. 506.

Stehl, R.H., et al. (1973). The stability of pentachlorophenol and chlorinated dioxins to sunlight, heat, and combustion. In: Chlorodioxins--Origin and Fate. ACS Series 120, pp. 119-125.

Stehl, R.H., and W.B. Crummett (1977). Letter of 2/15/77 to T.D. Bath.

Stehl, R.H., and L.L. Lamparski (1977). Combustion of several 2,4,5-trichlorophenoxy compounds: formation of 2,3,7,8-tetrachloro-dibenzo-p-dioxin. Science 197:1008.

Strufe, R. (1968). Residue Reviews 24:79.

Sundstrom, G., and O. Hutzinger (1976). The synthesis of chlorinated diphenyl ethers. Chemosphere 5:305.

Svec, P. and V. Kubelka (1975). Anomalous behavior of polychloro alicyclic ketones in gas chromatography and gas chromatography-mass spectrometry. J. Anal. Chem. 277:113.

Villanueva, E.C., et al. (1975). A comparison of analytical methods for chlorodibenzo-p-dioxins in pentachlorophenol. J. Agric. Food Chem. 23:1089.

Vogel, S.H., et al. (1976). Determination of chlorinated dibenzo-p-dioxins in pentachlorophenol. Analytical Methods Review, Report of December 1976.

Vogel, S.H. (1977). Communication of 3/7/77 to T. Atkeson (edited slides and comments used in discussion with Science Advisory Board, 3/3/77).

Woolson, E.A., et al. (1973). Dioxin residues in Lakeland sand and bald eagle samples. Adv. Chem. Series 120: 112.

Woolson, E.A., R.F. Thomas, and P.D.J. Ensor (1972) Survey of polychlorodibenzo-p-dioxin content in selected pesticides. J. Agr. Food Chem. 20:351.

Wong, A.S. (1977). The environmental degradation of pentachlorophenol. Ph.D. Thesis, University of Calfornia (Davis).

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

Yang, G.C., and A.E. Pohland (1973). Cation radicals of chlorinated dibenzo-p-dioxins. In: Chlorodioxins--Origin and Fate. ACS Series 120, pp. 33.

Zabik, M.J., R.A. Leavitt, and G.C.C. Su (1976). Photochemistry of bioactive compounds. A review of pesticides photochemistry. In: Annual Review of Entomology 21:61.

Zitko, V., O. Hutzinger, and P.M.K. Choi (1974). Determination of pentachlorophenol and chlorobiphenyls in biological samples. B. Env. Cont. Tox. 12:649.

8. APPENDIX D

8.1 Agenda of Environmental Health Advisory Committee Meeting of April 3-4, 1978.

FINAL

U.S. ENVIRONMENTAL PROTECTION AGENCY
SCIENCE ADVISORY BOARD
ENVIRONMENTAL HEALTH ADVISORY COMMITTEE

Conference Room A (Room 1112)
Crystal Mall Building No. 2
Arlington, Virginia

April 3-4, 1978

AGENDA

Monday, April 3, 1978

9:00 a.m. 1. Introductions and Opening Remarks — Dr. Whittenberger

2. Draft Report of Study Group on Pentachlorophenol Contaminants (Draft dated March 1978)

- Introductory Remarks — Dr. Murphy

9:30 a.m. 3. Statements by Members of the Public

- Mr. Dennis Lindsay, Chairman, PCP Committee
  American Wood Preservers Institute
- Mr. Robert Arsenault, Director, New Product Development
  Koppers Company
- Mr. Dennis Lindsay, Technical Services
  Vulcan Materials Company
- Dr. Gary A. van Gelder, Veterinary Toxicologist,
  College of Veterinary Medicine
  University of Missouri, Columbia, Missouri
- Mr. Fred Shelton, Vice President, Science and Technology
  Reichhold Chemicals
- Dr. Robert L. Johnson, Senior Research Analyst
  Dow Chemical Company

11:00 a.m. ***BREAK***

ENVIRONMENTAL HEALTH ADVISORY COMMITTEE

April 3-4, 1978

AGENDA
(Continued)

April 3, 1978

11:15 a.m.	4.	Comments and Discussion by Members of Committee and Study Group	Dr. Whittenberger
12:30 p.m.		***LUNCH***	
1:30 p.m.	5.	Comments and Discussion (Cont'd) and Development of Committee Recommendations	Dr. Whittenberger
3:00 p.m.	6.	Informational Items	
		- Publication of "Noise - A Health Problem"	Mr. Marrazzo
		- Status of Benzene Assessment Reports	Dr. Saz
3:30 p.m.	7.	Concluding Remarks	Dr. Whittenberger

RECESS

Agenda Notes:

Dr. James L. Whittenberger, Professor of Physiology, James Stevens Simmons Professor of Public Health, School of Public Health, Harvard University, Boston, Massachusetts

Dr. Sheldon D. Murphy, Professor of Toxicology, Department of Pharmacology, University of Texas Medical School at Houston, Houston, Texas

Mr. Rudy Marrazzo, Science Advisor, Office of Noise Abatement and Control, U.S. Environmental Protection Agency, Washington, D. C.

Dr. Arthur K. Saz, Criteria Development and Special Studies Division, Office of Research and Development, U.S. Environmental Protection Agency, Washington, D. C.

8.2 Testimony of Interested Parties

8.2.1 SAB Meeting - April 3, 1978

Statement as AWPI Committee Chairman

My name is Dennis Lindsay. I am employed by Vulcan Materials Company, a pentachlorophenol producer. The remarks I wish to make now are on the behalf of the American Wood Preservers' Institute, also known as AWPI. Approximately three years ago the wood preserving industry organized an Environmental Programs Task Group within the AWPI, a pre-existing trade association. The purpose and goal of the task group was and still is to make possible the survival of the wood preserving industry during this time of extensive governmental regulation. We monitor the governmental regulatory agencies and comment when appropriate upon proposed regulation. We frequently offer our assistance in helping the agencies understand what it is they are attempting to regulate. Our task group chairman appoints subcommitties and assigns to them various responsibilities.

I am Chairman of EPTG subcommittee #6, on pentachlorophenol which was formed about two years ago with the primary purpose being to defend penta during the anticipated RPAR process and eventually get it reregistered under FIFRA.

Our subcommittee appeared before your study group on penta contaminants at a meeting they held 13 months ago today. We made comments and supplied information which I trust was somewhat useful to them. Your study group has worked diligently as evidenced by their draft report. It is by far the most

comprehensive document to date and does an excellent job of explaining the many facets of this complex problem.

Our subcommittee has also been very active during these past 13 months, both as a group and as individual companies. I wish to point out some of our activities and inform you of certain facts.

First of all I wish to call to your attention the fact that we, as penta producers, are one less in number than we were a year ago. In the fall of 1970, when the U.S. Department of Agriculture first expressed concern about the presence of chloro-dioxins in some "economic poisons", that now missing producer was the greatest among us. Their production and sales of penta exceeded that of any other producer.

Thirteen months ago, I reported to your study committee that we had been negotiating with the Pacific Bio-Medical Research Center at the University of Hawaii concerning the retrieval and statistical analysis of data generated in a long term project known as the Community Studies on Pesticides. This study deals with chronic occupational exposure to technical penta. We did fund that project. We had hoped for an earlier report; however, it is due within the next two or three months. We will make it available to your study group and would hope that they at least consider the report before writing their final draft and recommendations.

This committee has also made possible the generation of other data relevant to the charge of your study group. Most of the work done during the past year by Dr. Gary Van Gelder, University of Missouri, concerning Michigan dairy herds was funded

by this committee. It was largely Dr. Van Gelder's work which led the hearing officer, Dr. Gilbert H. Wise, D.V.M. to conclude:

> "The evidence, while not removing all possibility of hazard, does not support a finding of any measurable magnitude of risk or likelihood of harm to the human food chain from exposure of food animals to CDD in technical penta." (Page 16 of hearing officer's report).

I have attached a copy of Dr. Wise's full report and findings for your information. The underlining and notations are my own.

Next, I would like to call your attention to the current draft report. Under III, Section 2, "Toxicology of Chlorinated Dioxins and Dibenzofurans"; page 5, the last sentence states,

> "Controlled dosing experiments, recently initiated, may help answer questions raised by the Michigan field studies concerning the pharmacokinetics and toxicity of PCP and its contaminants in cattle."

It is hoped that that report, when completed, would also be considered by your study group prior to their reaching a conclusion and recommendation.

In addition, we are aware of a study by Dr. Firestone in which he fed technical penta to lactating cows. Any information relevant to this problem should be considered prior to a final report by this committee.

Our committee is currently considering the funding of a 180-day calf feeding study using varying doses of different kinds of pentachlorophenol which would be done by Dr. Van Gelder.

We are presently waiting upon the results of the Firestone and Moore studies to help us decide what questions remain unanswered.

At the request of AWPI, the American Wood Preservers' Association, AWPA, the standards writing organization for our industry, has appointed a special committee to establish standards for treating wood intended for use in housing food producing animals. My point is to show you that we are attempting to act responsibly in dealing with these problems.

SAB Meeting - April 3, 1978

Statement as VMC Representative

Gentlemen, I am changing hats now. The remarks I will make from here on are as a representative of Vulcan Materials Company.

I would first like to direct your attention to the draft report, I, page 4. The last sentence of the top paragraph reads as follows:

> "Of course, the production of this more purified product entails increased production costs, and some representatives of industry felt this would result in a product which may be more difficult to handle."

That statement is not strong enough. I am convinced that this would result in a product which is more difficult to handle. I know of three separate cases where it was attempted to use Dowicide EC-7 in conventional bulk handling systems. All were considered failures in the eyes of the customer, and one resulted in considerable damage to the equipment.

Dow has apparently acknowledged this fact, since they recently announced that they will now produce penta only in the block form. That action has caused a large number of smaller consumers of penta who have been Dow customers to come to the other producers for a source. They (the smaller consumers) cannot afford to purchase the block dissolving equipment. Vulcan introduced bulk handling of penta ten years ago, and we believe it to be unequaled in convenience, flexibility and

reducing exposure to plant personnel. Blocks may be a useful manner of handling penta, but blocks or bulk handling simply will not serve the purpose of everyone in the industry.

Thirteen months ago our greatest concern with penta was that of its contaminants. Today we hear concern expressed over fetotoxicity, teratogenicity and even mutagenicity. In the face of these concerns, it is difficult for a producer to justify the capital expenditure in purification facilities for a product with an environmentally doubtful future. One producer has ceased production; and while environmental considerations were not the underlying reasons, you can be sure that the uncertain future for this product helped tip the scale in their decision-making process.

I would like to propose what I believe is a common sense solution to this problem. It is not a new idea. Others have proposed it before, but in my opinion, it has merit.

After studying the draft report of your study group, I conclude that sufficient scientific evidence upon which to base a decision is lacking. Further, since technical penta has been used for 40 years with only minor and controllable incidents, I believe that this study group should direct their attention to outlining the testing which would enable them to make a decision. Such testing might be accomplished on a cooperative basis by the chemical producers. In this way the wood treaters would be spared the cost of different handling equipment until such time as it was necessary, if at all.

Forest Products Division, Koppers Company, Inc.
Pittsburgh, PA 15219, Telephone 412-~~XXX-XXXX~~ 227-2460

8.2.3

Robert D. Arsenault
Manager
Product Development

KOPPERS
Architectural and
Construction Materials

April 13, 1978

Mr. Ernst Linde
Scientist Administrator
Science Advisory Board, A-101
Environmental Protection Agency
Washington, D. C. 20460

Dear Mr. Linde:

Attached is the written statement of essentially what I said at the SAB Meeting.

Sincerely yours,

Robert D. Arsenault

Robert D. Arsenault

RDA/mz

enclosures

Testimony to the EPA Science Advisory Board
Environmental Health Advisory Committee on Pentachlorophenol
April 3, 1978

My name is Robert D. Arsenault. I am Manager of Product Development, Forest Products Group, Koppers Company, Inc. I was formerly associated with Monsanto Company, Paper & Wood Chemicals Group, as Market Manager for pentachlorophenol and as such I had considerable working knowledge of pentachlorophenol chemistry and use in wood preservation. Koppers Company uses considerable quantities of PCP in its wood treating facilities and in formulating blended products for millwork, sapstain control and other uses. In addition, Koppers sells PCP as a broker, formerly for Monsanto and now for Reichhold and Vulcan.

I appreciate the opportunity to speak to the Environmental Health Advisory Committee today. I will restrict my comments to the draft report of the Study Group on PCP Contaminants. I will first make some general comments followed by specific comments.

On the whole I feel that the study group has done an excellent job in reviewing the current knowledge on PCP contaminants. Their conclusions concerning the potential hazards are especially noteworthy, but these conclusions are inconsistent with the bottom line conclusion.

For example, on page 1-5 the statement reads, "there is really very little data on the environmental persistence and transport of the dioxin and dibenzofuran contaminents of pentachlorophenol". On page 1-6 the paper reads, "The toxicological information necessary to make the evaluation of relative hazard of purified versus standard commercial PCP is also deficient. Pentachlorophenol itself is a toxic chemical in its own right." On page 1-7 the paper reads, "This finding of low, but detectable, levels of chlorinated dioxins in tissues of these animals is a matter of public health concern, however, the biological significance of this finding is not presently known." And, "There is insufficient information concerning the identity and dosage of dioxins involved to allow these observations in man to be useful in a quantitative assessment of the relative hazard of purified PCP versus commercial products containing dioxin contaminants. There are no data that permit an estimate of the relative susceptibility of humans to systemic effects of the dioxins and related contaminants of PCP." "As yet, there is no quantitative information which permits a comparison of the toxicity of dioxin to humans versus other animals."

All these statements reinforce our consistent opinion that there are no known significant hazards related to the current levels of impurities in PCP, and there are no data to set any target level judged to be "safe". Yet, these conclusions were the result of a review of all known data on hazards. No such review was made of the costs associated with gaining these unstated "benefits" from removing the impurities; yet, the statement is made on page I-4, "Of course, the production of this more purified product entails increased production costs and some representatives of industry felt this would result in a product which may be more difficult to handle". A thorough study of the "costs" would have shown that not only are they huge, but the costs would include an increase in exposure to PCP due to the product being more dusty. Also, the costs would include disposal problems with dioxin still bottoms and difficulty in using the purer grade in some industry solvents such as Koppers Cellon process.

Despite all the above mentioned lack of information, the Study Group wrote conclusion 10 which simply states that since technology is available to clean up PCP, "it would seem prudent" to do so. This statement seems to us to be unjustified, though it is politically expedient.

On pages II-7 and V-3-35 acknowledgement is made that some of the PCP in the environment may come from generation of PCP by chlorination of water or creation by natural processes. However, the implication is that PCP in the environment, found in urine of non-exposed humans, and in tissue comes from exposure to treated wood in the environment.

One of the problems that has arisen is that pentachlorophenol in the environment seems to be ubiquitous. It is found in samples taken from the environment, from animals, and from humans. For example, the March 1st issue of Pesticide & Toxic Chemicals News reports that the "Environmental Protection Agency's national human monitoring program has found in the 400 samples of human urine analyzed that nearly 85% of the samples show 'quantifiable amounts of pentachlorophenol', a constituent of many wood preservatives and a contact herbicide". Also, the June 30, 1976 issue of Pesticide Chemical News contained an article that stated, "hexachlorobenzene residues have been found in 75% of mother's milk samples and 95% of human adipose tissue samples collected in the U.S. by the EPA". Attached is a copy of the entire text of this article. It also states that HCB contamination of meat is increasing and breast fed infants, in a worst case situation, could be exposed to HCB levels approaching those demonstrating adverse effects in laboratory animals.

Tying these two findings together in order to show that PCP and HCB are interrelated one would only have to prove that pentachlorophenol is a metabolite of hexachlorobenzene, or vice-versa. Since pentachlorophenol is used in small quantities as a wood preservative compared to hexachlorobenzene production in the chemical industry, one would have to agree that pentachlorophenol could be a metabolite of hexachlorobenzene in humans, if shown in laboratory animals. In fact, it was shown in monkeys that hexachlorobenzene metabolized to pentachlorophenol. I am attaching a copy of a paper by Yang, et al entitled, "Chromatographic Methods for the Analysis of Hexachlorobenzene and Possible Metabolites in Monkey Fecal Samples".

Another paper by Engst, et al, "The Metabolism of Hexachlorobenzene in Rats", confirmed earlier findings by Mahendale in 1975 that pentachlorophenol was a metabolite of hexachlorobenzene in animals. I am also attaching a copy of a paper by Rourke, et al entitled, "Identification of Hexachlorobenzene as a Contaminant in Laboratory Plastic Wash Bottles", which references three papers by Yang, et al on the metabolism of hexachlorobenzene in Rhesus monkeys. I have given you a copy of the paper by Renner entitled, "2,4,5-trichlorophenol, A New Urinary Metabolite of Hexachlorobenzene".

Now how does the hexachlorobenzene get in the environment? To answer that question I am enclosing a copy of a paper written for the Hazardous Waste Management Division of EPA entitled, "Sources, Characteristics, and Treatment and Disposal of Industrial Waste Containing Hexachlorobenzene". According to the paper there are 23,665 tons per year of hexachlorobenzene containing waste materials from chlorinated solvent production alone plus 2,650 tons of hexachlorobenzene from chlorinated solvents which were presumably removed from the chlorinated solvents before the sale of the solvents. It is also known that many of the chlorinated solvents used for dry cleaning contained traces of hexachlorobenzene and this could be another reason why humans are exposed to hexachlorobenzene everywhere.

Another paper which was sent to us from the Office of Toxic Substances entitled, "Hexachlorobenzene, A Man Made Pollutant", is attached for your information.

It is apparent also that this is not a one-way proposition. Pentachlorophenol could conceivably degrade to hexachlorobenzene under certain conditions. Dr. Donald Crosby in his paper to the EPA Science Advisory Board, "Reactions and Environmental Fate of Pentachlorophenol and its

Impurities", stated, "the original pyrolytic conversion of a PCP salt to OCDD was accompanied by a large portion of hexachlorobenzene, suggested to arise from decomposition of decachlorodiphenyl, but this has not been confirmed". Hexachlorobenzene also appears to be a byproduct of UV light degradation of pentachlorophenol on the surface of wood. It is my impression that hexachlorobenzene contamination of the environment is caused from the hexachlorobenzene impurities in chlorinated chemicals as well as the over 26 million tons per year of HCB containing waste which are dumped.

Also attached are two articles which appeared in J. Environ. Sci. Health in 1976, both covering another source of penta in the environment. The use of lindane as an insecticide on lettuce and endives resulted in the lindane to convert to trichlorophenol, tetrachlorophenol, pentachlorophenol, and conjugates of tetra and pentachlorophenols. Non-polar compounds including hexachlorobenzene were also formed. In the top soil was also some penta. While the article calls these breakdown products metabolites from the crop, I think it more likely that they are UV light breakdown products.

The other article covers the metabolism of lindane in rats. Pentachlorophenol is shown to be one of the metabolites. Other metabolites include 2,3,4,6-tetrachlorophenol, 2,3,5,6-tetrachlorophenol, and 2,4,6-trichlorophenol. Minor metabolites were gamma 2,3,4,5,6-pentachlorocyclohexene and its metabolite, tetrachlorocyclohexanol.

This work also shows other chemicals which have penta as a metabolite. They are pentachlorobenzene and 2,3,4,5,6-pentachlorocyclohexene-(2)-ol-(1) and gamma 2,3,4,5,6 pentachlorocyclohexene.

It is beginning to look like there are many ways for penta to end up in the food chain, both as metabolites and as breakdown products of other commonly used pesticides, including hexachlorobenzene and lindane.

We at Koppers feel so strongly about this issue of pentachlorophenol being a universal contaminant "caused by use in wood preservation" that I asked R. S. Detrick of Koppers to present a paper which appeared in the Forest Products Journal in 1977. Attached is a copy of the paper. It refers to many of the items which I have already discussed, but in summary it shows that pentachlorophenol in the ppb level can be caused from other factors than pentachlorophenol exposure.

There is another area of concern which I feel must be dealt with in the Report. Photolysis of PCP can create OCDD and hexachlorobenzene in

the environment. Since both of these contaminants are already present in technical PCP, we question why take them out if they are only going to form again from sunlight. However, they also rapidly break down in the same sunlight.

The paper on page II-8 states that PCP photodegrades in water and various solvents. This is covered again briefly on pages V-3-17, V-3-19, V-3-20, V-3-22, and V-3-32. However, on page V-3-22 the Report states that organic, hydrogen-donating solvent must be present for photolysis of dioxins or dibenzofuran to occur. This is not true. We have demonstrated repeatedly that photolysis and rapid degradation occurs when dioxins are present on cellulose substrate without solvent. We have extensive information to EPA with a letter to Mr. Edwin Johnson dated June 1, 1977 on the degradation of PCP and OCDD by sunlight and artificial UV light. None of these data are referenced in this report.

I am attaching a copy of that June 1st letter and also a copy of a letter written to Dr. Donald Islib as part of the Michigan Hearing Record. These documents show that both technical PCP and EC-7 PCP reach the same maximum of OCDD level in micrograms per unit surface area after one day irradiation by UV light. This maximum was then depleted as the OCDD photodegraded and there is no difference in the rate of buildup or the rate of breakdown between commercial PCP and EC-7 PCP. The OCDD concentration on the surface reached 3060 ppm on the basis of initial PCP concentration regardless whether the initial PCP started with commercial PCP (1600 ppm OCDD) or EC-7 PCP (60 ppm OCDD).

Hexachlorobenzene also is a degradation byproduct of photolysis of PCP. However, HCB is also a contaminant of PCP. In fact, we found a sample of EC-7 PCP contained approximately four times the HCB level (170 ppm) as Monsanto's PCP (45 ppm). In wipe tests of wood utility poles exposed to sunlight for less than one week, poles treated with EC-7 PCP in oil had approximately ten times the level of HCB on the surface of the poles as expected based on the amount of PCP present. When compared to poles treated with commercial PCP in oil after three years exposure in Ohio (different oil), the EC-7 treated poles had about four times the level of HCB on the surface as the commercial PCP treated poles. While these levels are not judged to be an environmental hazard (levels of 0.001 to 0.02 ug/in.^{2} HCB), they do indicate that there is no benefit from the environmental standpoint of reducing the contaminants in PCP.

We are continuing our work on photolysis of PCP, OCDD, and HCB using wood as a substrate. As more information is generated, we are finding that UV light degradation eliminates these products from the environment.

Therefore, although the grade of PCP makes no difference in quantitative amount of impurities formed, in reality the impurities are not a hazard, whether in the PCP initially or formed from UV light.

June 1, 1977

Mr. Edwin L. Johnson
Deputy Assistant Administrator
for Pesticide Programs
Environmental Protection Agency
Washington, D. C. 20460

Dear Mr. Johnson:

In the past we have submitted information to you on the environmental fate of pentachlorophenol (PCP) including information on degradation of PCP in soil and the degradation of octachlorodibenzo-p-dioxin (OCDD) in soil. This was a part of the package which was submitted by Ron Dreer to the Science Advisory Board Ad Hoc Panel studying the dioxin question.

We understand that the Science Advisory Board will shortly be completing their report and recommendations. One part of the Draft copy of the report, written by Dr. Crosby, referred to pentachlorophenoxide-ion undergoing cyclization to OCDD in water, and also photodegradation of OCDD by ultraviolet (UV) light in the presence of a hydrogen donor such as alcohol. Dr. Crosby wrote that, "the rate of photo-reduction is inversely proportional to the degree of chlorination", indicating that the lower chlorinated dioxins degrade faster than the higher chlorinated dioxins. He further wrote that, "PCP could conceivably generate OCDD in sunlight, but the usual presence of hydrocarbon solvents would tend to promote eventual dioxin photolysis on the wood surface".

As part of our continuing program of environmental and health studies with wood preservatives, we have been investigating the photochemistry of pentachlorophenol and the contained dioxins. Thus far, this work supports the statements made by Dr. Crosby, and the results emphasize that dioxins that may be generated from PCP irradiation on the surface of the wood are themselves degraded. A hydrogen donor solvent, however, is not necessary. Cellulosic material can act as the hydrogen donor.

From an environmental point of view the surface of the treated wood is important because it constitutes an avenue of exposure to man and the environment. In order to simulate the surface of the wood without having interactions such as bleeding, variability, and analytical difficulty, we have done most of our work with filter paper impregnated with a solution of PCP or OCDD.

We have conducted several experiments exposing technical PCP, purified PCP, Dowicide EC-7 PCP, and OCDD on filter paper and technical PCP and Dowicide EC-7 PCP on wood, with and without oil present, in artificial UV light and in sunlight. Our experiments are continuing, but we have preliminary results that we feel are meaningful even though we have not yet completed these studies.

Working with filter paper, our studies show that when PCP is exposed to UV light, photodegradation occurs and OCDD is one of the products formed. Continued exposure to UV light degrades the OCDD. These chemical reactions occur whether the PCP being exposed to UV light is of the EC-7 grade or the technical grade. What surprised us in our studies, however, was that regardless of the original OCDD content of the PCP, the ultimate level to which the OCDD builds up is about the same.

The EC-7 sample we used contained 13 ppm of OCDD. The commercial PCP sample contained 1,466 ppm of OCDD. When 15 mg of EC-7 grade PCP was irradiated for two days, the dioxin level on the filter paper rose from the initial 0.2 ug to 58 ug of OCDD. When 15 mg of commercial PCP was irradiated, the dioxin level rose from the initial 22 ug to 64 ug. The EC-7 grade PCP generated 58 ug in the same time that commercial PCP generated 42 ug, and both grades of PCP developed approximately the same level of OCDD. Once a critical level of OCDD was reached, the OCDD photodegraded to lower levels.

After seven days only 3% of the original PCP remained and the OCDD level had dropped about 33% from the peak value. After ten days the OCDD level had dropped to about 50% of the peak value.

In our tests, a large part of the PCP was lost due to volatilization rather than photolysis. Working without UV light, but keeping all other conditions constant, 52% of a 7.5 mg sample volatilized in three days' exposure. Similar studies have not been conducted as yet on OCDD. However, inasmuch as OCDD has a vapor pressure less than 1/800 that of PCP, it is

assumed that significant loss by volatilization does not occur. We would expect higher chlorinated dioxins to degrade on the surface by UV light rather than vaporize into the environment.

Our work with PCP treated wood poles has not reached the point today that we can prove conclusively that dioxins are formed from the PCP on the surface of wood that is exposed to sunlight. We believe, however, that such is the case. The work does indicate that there is a breakdown of dioxins that are originally present or which may be formed on the surface of the wood.

Wipe tests conducted on three commercial PCP/Cellon treated poles which were in place for three years in California, show lower PCP and OCDD concentrations on the sunny south side of the pole than on the north shaded side. The PCP content on the south side of these poles averaged 0.34 ug/sq. in. and on the north side averaged 2.08 ug/sq. in. The corresponding OCDD levels were 0.010 ug/sq. in. on the south side and 0.024 ug/sq. in. on the north side. The lower OCDD content on the south side of the pole as compared to the north side reflects the effect of UV light on OCDD. We interpret the higher ratio of OCDD to PCP on the south side of the pole as compared to the north side of the pole to reflect both the effect of UV light on the degradation of PCP and vaporization of PCP.

We have found somewhat the same relationship when PCP/oil treated poles were tested. These also had been in service three years. On the south side of these poles the PCP level was 0.7 ug/sq. in. and on the north side the PCP level was 3.1 ug/sq. in. The OCDD levels respectively were 0.013 and 0.032 ug/sq. in. These data substantiate that even though dioxins might form from PCP in wood exposed to the sun, they also are eventually destroyed by the sun.

We have indications that these same phenomena occur on poles treated with EC-7/oil solution. The wood inside these poles was extracted and analyzed to confirm that the poles were, in fact, treated with EC-7. The PCP contained the average of 22.5 ppm of OCDD. The wood contained an average of 1.15% PCP. However, on the surface of the poles, wipe tests showed from 0.001 to 0.008 ug/sq. in. of OCDD on poles which were two weeks to two months old. We have found substantially the same levels of OCDD (.001 to .008 ug/sq. in.) on the surface of

Cellon poles treated with the technical grade of PCP after 15 weeks' exposure to the sun in Pennsylvania. Whether these numbers reflect results from bleeding, PCP loss or sunlight generation is unconfirmed.

We feel that these results support the conclusions drawn from the laboratory tests that (1) EC-7 grade PCP on a cellulose substrate exposed to UV light photodegrades to OCDD, reaching the same OCDD concentration level as technical grade PCP exposed under the same conditions, and (2) after reaching some critical level, the OCDD concentration decreases due to photodegradation.

It is important to note that we have not found any tetrachlorodibenzo-p-dioxin formed, due to photolysis of PCP or OCDD, either in the laboratory or field studies. Much of the work reported here are the preliminary results in a continuing study.

We will keep you informed as new information is generated. We will appreciate the opportunity to visit with you to discuss the results of our work in more detail.

Sincerely yours,

Robert D. Arsenault

RDA/mz

bcc: R. E. Spatz
D. L. Davies
D. G. Hallahan

KOPPERS

July 20, 1977

Mr. Donald R. Islib
Chief Deputy Director
Michigan Dept. of Agriculture
Louis Cass Bldg.
P. O. Box 30017
Lansing, Michigan 48909

Subject: Effect of UV Light on
Pentachlorophenol (PCP)

Dear Mr. Islib:

At the Public Hearing on Proposed Regulation No. 637 on May 26, 1977, our Mr. R. D. Arsenault mentioned that studies by Koppers Company had shown that pentachlorophenol deposited on cellulosic filter paper and exposed to UV light was decomposed and one of the products of decomposition was octachlorodibenzodioxin (OCDD) which in turn was also decomposed by the UV light. At the continuation of the hearing on July 12, the validity of the Koppers data was questioned on the basis that the artificial light used by Koppers was substantially different from sunlight. The purpose of this letter is to provide you with additional information and comments on these subjects.

Even though pentachlorophenol is toxic in its own right, much of the discussion of risks before the hearing board has focused on the chlorodibenzodioxins that are impurities in commercial grades of pentachlorophenol. Octachlorodibenzodioxin (OCDD) is the most prevalent chlorodibenzodioxin in commercial grades of pentachlorophenol and its analysis is subject to fewer uncertainties. Therefore, much of the following discussion will focus on octachlorodibenzodioxin (OCDD). Tetrachlorodibenzodioxin (TCDD) was not detected as a degradation product of either OCDD or pentachlorophenol. Hexa- and heptachlorodibenzodioxins were detected, but not quantified.

Octa- and tetrachlorodibenzodioxins (OCDD and TCDD) deposited on filter paper are readily degraded by UV light from both sunlight and artificial light sources. Experimental data are summarized in the attached tables I and II. These tables include long and short wavelength intensities of the artificial light source and Pittsburgh sunlight and are shown to be similar. The calculated velocity constants, assuming first order reactions, are shown in Table III. The experimental procedure by which these data were obtained is also attached.

Pentachlorophenol (PCP) (both commercial grade and Dow EC-7 grade) deposited on filter paper is readily degraded by UV light. Experiments were confined to artificial light, because this light source was considered to be a reasonable facsimile of sunlight, it is uniform from hour to hour while sunlight is not, and the degradation of pentachlorophenol by sunlight had already been demonstrated by other investigators.

The attached paper entitled "Weathering and Stabilization of Polyolefins" by J. A. Melchore (I&EC Product Research & Development, Vol.1, No. 4 pp 232-235 (1962) describes the artificial light source used in our work. The wavelengths of light in sunlight and the artificial light are shown in Figure 1. Both sources emit light at wavelengths below 350 mu which is the wavelength below which pentachlorophenol (PCP) absorbes UV light. Pentachlorophenol (PCP) absorbes UV light strongly at wavelengths below about 310 mu. Presumably, these are the wavelengths that provide the energy for the observed degradation of PCP.

Experimental data for the UV degradation of pentachlorophenol (PCP) obtained in recent weeks are summarized in Table IV and V, for commercial grade and EC-7 grade PCP, respectively. Starting at 7500 µg PCP, about the same concentration on the filter paper that would be used for the treatment of wood, more than 90% of the PCP had degraded in seven days. In both cases, OCDD was produced as a degradation product at a peak value of 23 µg OCDD regardless of the initial concentration of OCDD in the PCP. The same data are shown in Tables VI and VII, in which the OCDD on the UV exposed paper is expressed in parts per million (ppm) of the initial quantity of PCP that was applied to the paper. On this basis, the OCDD concentration reached 3060 ppm in both cases.

In assessing the risks of exposure of either humans or animals to treated wood, chemicals on the surface of the wood should be the principal concern, not the chemicals embedded in the internal structure of the wood. From this point of view, the foregoing experiments on filter paper strongly suggest that exposure of either humans or animals to either commercial grade or EC-7 grade of Pentachlorophenol would not be significantly different.

Yours truly,

R. S. Detrick

R. S. Detrick, Manager
Environmental Health and Safety Section

RSD:mjt

Attachments

bcc: Mr. R. D. Arsenault
Mr. D. L. Davies

EFFECT OF UV LIGHT ON PENTACHLOROPHENOL (PCP) AND SELECTED CHLORODIBENZODIOXINS

1. Experimental Procedure

Standards of OCDD and 1,2,3,4-TCDD were obtained from Analabs, and the 2,3,7,8-TCDD from D. Firestone of the FDA. All dioxins were used without further purification. All stock solutions were prepared in reagent grade benzene, and stored in aluminum foil covered bottles in the dark. All work concerning the TCDD was done on the 1,2,3,4-TCDD isomer unless noted.

Dioxins to be irradiated by UV were applied in benzene solutions via a 2 cc pipet onto a 2-inch by 5-inch strip of Whatman No. 42 ashless filter paper. The weight of a strip of filter paper was 0.72 gram, and the concentrations of the OCDD were calculated to be in the same ratio as they exist on a typical penta-treated pole.

The UV degradation rates of OCDD and TCDD in various sample systems were determined in both sunlight and artifically produced UV light. The description and operation of the artificial UV exposure system is discussed by Melchore.[3] The UV radiation was measured at the surface of the samples by an Ultra-Violet Products UV Meter at both short and long wavelengths. The average intensities for the unit were 1.02 milli-watts/cm^2 for the short wavelength (254 nm peak), and 0.63 mwatts/cm^2 for the long wavelength (365 nm peak) detector.

The dioxins were recovered from the filter paper by cutting the paper into small strips and placing them in a small bottle along with a 25 cc aliquot of benzene. The samples were shaken on a wrist action shaker for 30 minutes, and the benzene solution was analyzed by a gas chromatographic technique.

Gas chromatographic analyses (GC) were carried out on a Hewlett-Packard instrument (Model 5701A) using a 3' x 1/4" glass column packed with 10% OV-101 on 60/80-mesh Chrom Q, a silane-treated diatomaceous earth support. Programmed temperature gas chromatography was used for the analysis of all samples containing OCDD. Samples containing only TCDD were analyzed isothermally at 250°C. The temperature program consisted of holding at 250°C for 8 minutes, raising the temperature to 280°C at 8°C/min. and holding at that temperature for an additional 8 minutes. Under these conditions the TCDD eluted at 4.4 minutes and the OCDD at 17.0 minutes. A Ni63 electron capture detector was used because of its sensitivity to halogenated compounds. The carrier gas was a 90/10 mixture of argon/methane, and its flow rate was 40 cc per minute. Samples were analyzed quantitatively for either TCDD or OCDD by using band area measurements (the height x width at half-height method) and absolute standards.

3. "Weathering and Stabilization of Polyolefins," Melchore, J.A., I&EC Product Research and Development, Vol. 1 No. 4, pp 232-235, December, 1962.

2. Clean-up Procedures

a. Monsanto Method No. 70-20

This method provided by Monsanto is designed to remove from the sample phenolic compounds which might interfere with the analysis of the various chlorodioxins. In this method, the sample, which has been dissolved in benzene, is extracted three times with 20-cc portions of 5% NaOH, and backwashed twice with 20-cc portions of distilled water containing about 0.2 gram NaCl. The benzene solution is then passed through clean cotton in the tip of the separatory funnel. This benzene solution is either analyzed directly or further purified by the alumina column described below.

b. Alumina "Mini" Columns

The "mini" columns were prepared from 5 mm I.D. glass tubing which was drawn to a fine tip. A small plug of glass wool was inserted, and the column filled with Alcoa F-20 alumina heated for 16 hours at 400°C. The height of the alumina was approximately 200 mm. A 5-cc aliquot of the sample solution was placed on the column. Since some of the sample solution was absorbed on the column, additional benzene was added until exactly 5 cc was eluted from the column. This was done by placing the tip of the column into a 5-cc volumetric flask and filling it to the mark as the benzene solution eluted from the column.

3. Recovery of OCDD and TCDD from Filter Paper Strips

Standard solutions of OCDD and TCDD, were applied to the filter paper strips and recovered as previously described. The recovery was determined for various periods of time. These included: (a) immediately after the benzene had evaporated, (b) after 18 hours in the dark, and (c) after 67 hours in the dark. The results show that the recovery of OCDD was at least 95% with or without oil; the recovery of TCDD averaged 92% with or without oil.

4. Recovery of OCDD from Alumina "Mini" Columns

Since the alumina "mini" columns were used to clean up the wood extracts, the recovery of the OCDD was determined to insure that no OCDD was being adsorbed by the columns. A 5-cc aliquot of an OCDD standard, treated as previously described, gave 100% recovery.

5. Degradation Rates of OCDD and TCDD by Artificial UV Light

Standards of OCDD, 1,2,3,4-TCDD, and 2,3,7,8-TCDD were applied to filter paper strips and exposed to artificial UV light for varying periods of time. The data which is shown in Table I can be summarized as follows: a) the degradation of TCDD is faster than OCDD, b) the degradation of OCDD is faster in systems containing oil (P-9 or Nujol) than in systems not containing oil, c) the degradation of OCDD is faster in systems containing Nujol than systems containing P-9 oil, and d) the degradation of 2,3,7,8-TCDD is faster than that of 1,2,3,4-TCDD. The UV degradation of both OCDD and TCDD on cellulose appears to occur at a faster rate than in solution.[1]

1. "Photo Decomposition of Chlorinated Dibenzo-p-Dioxins," Plimmer, J. R., and Woolson, E. A., Science, August 1971.

6. Degradation Rates of OCDD and TCDD by Sunlight

Standards of OCDD, with an without oil, and TCDD were applied to filter paper strips and exposed to sunlight for varying periods of time. The 8-hour and 16-hour exposure tests were run over a period of 2 to 3 days, and were stored in a dark cupboard overnight. The UV intensity during exposure was measured quite frequently because of the extreme variation that was observed. The intensity data was integrated over the exposure time to measure total exposure. The degradation data which can be seen in Table IV showed the same trends observed for the samples exposed to artificial UV light, except that the rates in sunlight were slower than those observed in the artificial light. The first order velocity constants were calculated for all samples to further substantiate the observations noted above and can be seen in Table III.

Table 1

Degradation of OCDD and TCDD by Artificial UV Light

Dioxin	Oil	Exposure (hrs.)	Exposure Intensity (mwatts/cm^2) Long Wavelength	Short Wavelength	% Remaining
OCDD	None	1	0.63	1.02	94
		2	1.26	2.04	88
		4	2.52	4.08	85
		6	3.78	6.12	77
		16	10.1	16.3	60
		67	42.1	68.3	33
TCDD	None	1	0.63	1.02	86
		2	1.26	2.04	81
		4	2.52	4.08	69
		6	3.78	6.12	58
		16	10.1	16.3	20
TCDD[1/]	None	4	2.52	4.08	38
		8	5.04	8.16	28
		16	10.1	16.3	6
OCDD	Nujol	6	3.78	6.12	2
		16	10.1	16.3	< 0.5
	P-9	67	42.1	68.3	8

1/ This TCDD is the 2,3,7,8 isomer.

Table II

Degradation of OCDD and TCDD by Natural Sunlight

Dioxin	Oil	Exposure (hrs.)	Exposure Intensity ($mwatts/cm^2$) Long Wavelength	Short Wavelength	% Remaining
OCDD	None	5.5	2.26	4.19	89
		8	3.86	6.78	91
		16	6.88	12.1	83
OCDD	P-9	5	2.26	4.19	47
		8.8	3.86	6.78	47
		16	6.88	12.1	34
OCDD	Nujol	5	2.26	4.19	48
		8.8	3.86	6.78	42
		16	6.88	12.1	18
TCDD	None	5.5	2.26	4.19	82
		8.8	3.86	6.78	77
		16	6.88	12.1	57

Table III

Velocity Constants for the Decomposition of OCDD and TCDD

Dioxin	UV Source	Oil	Velocity Constant, $Hrs.^{-1}$
OCDD	Artificial	-	.002*
2,3,7,8-TCDD	Artificial	-	.140*
OCDD	Artificial	None	.039
1,2,3,4-TCDD	Artificial	None	.100
2,3,7,8-TCDD	Artificial	None	.215
OCDD	Sunlight	None	.012
OCDD	Sunlight	P-9	.081
OCDD	Sunlight	Nujol	.108
1,2,3,4-TCDD	Sunlight	None	.035

*These reaction velocity constants were calculated by the Mathematics Group from data presented in the paper "Photo Decomposition of Chlorinated Dibenzo-p-Dioxins," Plimmer, J. R. and Woolson, E. A., which appeared in the August 1971 issue of Science. Rate studies were done in methanol solutions.

Table IV

Effect of UV Light on
Commercial Pentachlorophenol (PCP)
on Filter Paper

(7.5 mg PCP)

Exposure Time Days	OCDD Found µg	PCP Remaining µg
0	12	7500
1	23	2540
2	23	1800
3	19	1350
7	15	450
14	7.8	150

Table V

Effect of UV Light on
EC-7 Pentachlorophenol (PCP)
on Filter Paper
(7.5 mg PCP)

Exposure Time Days	OCDD Found µg	PCP Remaining µg
0	0.45	7500
1	23	2100
2	23	1420
3	21	1350
7	18	600
14	8.5	180

Table VI

Effect of UV Light on

Commercial Pentachlorophenol (PCP)

on Filter Paper

OCDD Relative to Initial PCP

Exposure Time Days	OCDD as ppm of starting PCP
0	1600
1	3060
2	3060
3	2530
7	2000
14	1040

Table VII

Effect of UV Light on

EC-7 Pentachlorophenol (PCP)

on Filter Paper

OCDD Relative to Initial PCP

Exposure Time Days	OCDD as ppm of starting PCP
0	60
1	3060
2	3060
3	2800
7	2400
14	1130

8.2.4

March 24, 1978

TO: Environmental Health Advisory Committee
Science Advisory Board
U.S. EPA
Washington, D.C. 20460

FROM: G. A. Van Gelder
Veterinary Toxicologist
College of Veterinary Medicine
University of Missouri
Columbia, Missouri 65201
Telephone 314-882-7011

RE: Draft Report on Pentachlorophenol

Introduction:

During the past year I have served as a consultant to FDA, the American Wood Preserver's Institute, Reichhold Chemical Company and Vulcan Materials Company in matters relating to pentachlorophenol and animal health. My reports have been made a matter of public record.

THIS STATEMENT WAS PREPARED AT MY OWN INITIATIVE AND EXPENSE. IT REPRESENTS MY PERSONAL OPINIONS IN THIS MATTER AND NOT NECESSARILY THOSE OF ANY OTHER INDIVIDUAL OR ORGANIZATION.

In the interest of your and my time this statement will be brief. In summarizing complex issues there is a risk of being imcomplete or misunderstood. If any of the committee have questions please feel free to call or write. A copy of a letter I wrote earlier is attached as an appendix. This discusses in more detail some of the animal health aspects.

Background:

1) I have visited most of the farms, including those in Michigan, in which pentachlorophenol related health problems were alleged.
2) I have conducted limited studies with pentachlorophenol and related concentrated contaminants.
3) I have reviewed the available chronic rodent studies with pentachlorophenol including inhouse reports submitted as part of the Michigan hearings.
4) I set through and heard all testimony at all the Michigan Pentachlorophenol Hearings except for the one day Dow Hearing on the proposed rule.
5) I reviewed all material available under freedom of information in the files of the Michigan Department of Agriculture related to the alleged pentachlorophenol related herd health problems.

6) I have studied in detail the medical and diagnostic records related to the herds in question.

Opinions and Conclusions:

1) The statement on page III-2-4 which in part states ". . . dioxins in tissues from a dairy herd in Michigan in which there were undiagnosed health problems of chronic duration.", is not an accurate statement of the facts in this case. Serious communication and decision making process related problems existed within the diverse group of people handling this herd. In fact, a number of diagnoses were made. The problem was one of poor communication. To the best of my knowledge not a single person involved in that case had all of the information in front of him. Investigator A was not aware of what investigator B had found previously. The regulatory people acted without a careful review and understanding of the situations on the several farms. Politics played a larger role than science. The problems existing on the Lemunyon farm based on information in the Michigan Department of Agriculture files included:

   a) fatty cow syndrome related to feeding of high energy ration in excess of milk production.
   b) a random culturing of cows showed a 50% incidence of infectious mastitis, including bacteria that are more resistent to usual treatment.
   c) infectious diseases in the calves of a type that are associated with severe early calf losses.
   d) a serious ventilation problem in the barn.
   e) at times a lack of adequate bedding that contributed to the mastitis problem.

A complete serious study of the multiple herd health findings in the Lemunyon herd does not support the statement of "undiagnosed health problems." Some of the problems went unmanaged, others received partial attention.

The second part of the statement that needs amplification is ". . . problems of chronic duration." The problems were persistent in that mastitis, calf losses and cow losses continued over a two year period. However, this does not mean that individual cows were sick for extended periods. In fact, a careful review of the history shows that cows became ill during the 21 day post-calving period, loss body condition and in many cases died. This is generally recognized as part of the fatty cow syndrome.

Continuing calf losses due to infectious diarrhea and respiratory diseases in calves maintained in a totally unventilated, unheated calf room are not unexpected.

It is my opinion that the allegation of undiagnosed health problems should be deleted from the draft report. There is no need to perpetuate this unfounded statement any further than has already been done.

The problems in the Lemunyon herd do not provide acceptable scientific data on which decisions related to potential adverse health effects of pentachlorophenol can be based. In my opinion, the Lemunyon herd represents a pentachlorophenol and dioxin chemical residue problem and not a toxicologic problem.

2) As an example of the decision making process occurring at the time, it is pointed out that one of the herds included in the pentachlorophenol related quarantine had blood penta levels reported as 2 parts per billion. This is consistent with the fact they were not being housed in a penta treated facility.

3) Two toxicologists have estimated the daily penta exposure in the Lemunyon cattle. One estimate was 0.12 mg/kg and my estimate was 0.3 mg/kg. Both levels are less than the no significant effect levels in long term rodent feeding studies with technical or purified pentachlorophenol.

No one has shown by experimental studies or by calculations that there is any reason to believe that the levels of exposure occurring in the cattle could account for death or even illness.

4) In my opinion, the principle source of dioxin exposure for the Lemunyon cattle was the sludge residue on the 2x6's used to construct the sides of the feedbunk. I have been in numerous penta treated pole barns and wood eating is something you just do not see with cattle. It did not occur even in the herd that was not being fed an adequate diet.

The sludge was present as dry residue on the wood that could be scrapped off with a knife. The residue was pretty much gone from both sides of the feedbunk by February 1977.

5) The data in the table at the bottom of page III-2-4 means next to nothing to a toxicologist. What the toxicologist wants to know is:

a) what were the levels?
b) what were the recoveries for the method and,
c) what was the repeatability?

If the levels of HxCDD were 10-60 ppt then it should be so stated. Few readers of this report are likely to have access to the actual data unless it is included.

6) Page III-2-5 refers to my work on this problem. The pertinent findings were:

a) injections of extracts of the surface residue did not affect the health of mice at doses estimated to be equivalent to the cattle consumming all of the material in 1-2 days.
b) Extracts of the residue did not cause skin lesions when injected subcutaneously in albino rabbits.
c) Guinea pigs fed finely ground wood obtained from the Lemunyon barn were unaffected during the 64 day exposure to wood, solvent, penta and whatever else was in the wood. Exposure was at a level comparable to the cattle eating the barn in 180 days.

7) I am incompletely quoted on page III-2-5 where the statement ". . . Van Gelder concluded . . . that the PCP contaminants in the treated wood were less toxic than PCP itself." Certainly, HxCDD is more toxic than penta. But when one is exposed to technical penta, for each gram of material there is much more penta present than HxCDD. My position has been and continues to be that if one eats technical pentachlorophenol the level of penta exposure will kill you several times over before the HxCDD exposure gets to a significant level.

8) Regulations and standards are needed relative to where treated wood should and should not be used and also specifications should be developed on the type of treatment and surface characteristics that are acceptable for various end uses.

9) I am unconvinced that low non-phenolic pentachlorophenol solves any significant actual real world problems. I follow the arguement on a theoretical basis; but on a realistic basis the hazard to people and animals is greater for pentachlorophenol than for the contaminants when considered from the viewpoint of relative exposures.

10) One must keep in mind that reported laboratory studies with technical pentachlorophenol do shed light on the relative toxicity of the contaminants. Statements like "minimal focal hepatocellular degeneration" in rats fed 30 mg/kg technical pentachlorophenol for 90 days is hardly alarming.

11) Considerations of chloroacne in industrial workers is a mixed bag. Most of these people are also exposed to other chemicals, some including TCDD. A process of producing low non-phenolic penta from technical penta does not eliminate the industrial exposure. Workers are still needed to operate, clean and maintain the technical penta manufacturing equipment. In addition, individuals involved in the distillation of technical penta to produce the low non-phenolic product are also potentially exposed. Arguements based on industrial considerations must include full consideration of the entire process.

12) The overall hazard of accumulating concentrated penta related contaminants in barrels, tanks or flasks for later off-line incineration or other form of disposal needs to be weighed against the low magnitude of problems generated by technical pentachlorophenol manufacture and usage over the past 40 years. One judgement error in handling a barrel of contaminants could have great environmental and/or health impact.

UNIVERSITY OF MISSOURI-COLUMBIA

College of Veterinary Medicine

Veterinary Anatomy—Physiology

Veterinary Science
Columbia, Missouri 65201
Telephone (314) 882-7011

December 13, 1977

Dr. B. A. Schwetz
Research Manager
Toxicology Research Laboratory
Health & Environmental Research
1803 Building
Dow Chemical U.S.A.
Midland, Michigan 48640

Dear Bern:

Thank you for your letter of December 8. I certainly agree that communications are needed in this entire matter. Unfortunately, your letter catches me at a rather busy time. Consequently I will not be able to generate a detailed assessment of the Michigan PCP-Dioxin situation with cross references to testimony and laboratory reports. A complete description of my appraisal and analyses of the Michigan dairy herd health situation would require a minimum of 50 pages.

1) Statistical Analysis:

As I stated in our October 13 meeting, I quite agree that Dunnett is an appropriate test for comparing treatment means against a common control group. (Dunnett, J. Am. Stat. Assoc. 50: 1096-1121, 1955). My point is that Dunnett should also be used on the data from the first study. See Steel and Torrie (1960) pages 101-112 for a discussion of the various multiple comparison tests and their relative sensitivity. I disagree that the Dunnetts t would have detected more differences than a blanket application of student t tests. If you make 78 comparisons at the 5% level, 4 of them by chance alone will appear significant. Dunnetts is a more conservative test. Dunnetts will discover more "real" differences in your data, that is differences due to treatment as compared to differences due to treatment and chance.

My concern is not that you would declare EC-7 similar to 95/5 on the basis of your analyses, but rather that by using the multiple "t" tests on the Dow-7, 95/5 data you would be led into declaring differences which may be due to chance. Whether or not you or your management makes those decisions is your business. I hardly think decisions costing millions of dollars based on less than appropriate available statistical procedures is an academic matter. I do not know if the results would change if you used Dunnett on the original data. You will have to run the analysis to find out. Check me to see if I am wrong, but if you use the multiple t test on the EC-7, 83 day data, I believe you would find

that 1 mg/kg has a statistically significant effect on absolute liver weight. In other words, multiple t finds differences that Dunnetts more conservative test which takes into consideration the number of treatment levels keeps the investigator from declaring significantly different.

My other points regarding the 83 and 2 year studies not addressed in your summary are included here. There are 2 biological changes occurring in the Dow-7 groups that do not fit the overall response pattern. The first is the depression in RBC (and coupled PCV, Hb) at 30 mg/kg. This effect at the high dose (1/4 - 1/5 the acute LD_{50}) has been found by others and not found by others. Since it is a relatively small change and occurs at such a high dose it can be described as interesting but not very exciting.

The other effect was the change in albumin levels with Dow-7. My question was why you did not follow that up in the EC-7 studies? Since the EC-7 studies do not include this measure one cannot say much about it.

The other responses fit a common pattern although there are differences in dose-response. But my point is that before one can completely compare the results one would like to see the data analyzed with a uniformly applied method.

2) Communication:

It is my opinion that had MDA personnel been communicating with each other and with the MSU faculty a lot of the present situation would have been avoided. For example, it was very clear from my first visit to Michigan in February, 1977, that the MDA-MSU people were not communicating in a 2-way manner. One person would say the problem was XYZ and another would later say it was ABC. Consequently, my first report recommended "I think all those involved should reconsider the evidence upon which they are making various decisions. My concern is that we not chase after something which may turn out to be present but only as a secondary or tertiary factor and not related to the cause of the problem. Those parties involved are encouraged to go back and review the information upon which they are making decisions to ensure that each decision is being made on cold, hard facts and not on isolated comments or observations." My report also pointed out "there also seems to be a number of different ideas amoung the people who have been involved in the problems associated with this farm (Lemunyon). I am not sure who is responsible to try and pull all these people together with all the information that each one has and present some kind of debate or discussion as to what the problem(s) really is(are). Further"as a start it would seem appropriate for someone to obtain or prepare a detailed history as to when the death losses occurred, how long the cows were in the barn before dying, when did deaths occur relative to calving and what diagnostic services were actually conducted on each of the animals that died."

3) Regarding the Herd Health Problems in Michigan:

You need to decide whether you are going to be in or out on this matter. In the past, Dow has maintained the posture of "non-involvement". If now you want to get involved then please do your homework. Read all the transcripts, study the laboratory reports, go to the farms, look at the cattle, look at the management, get a herd history, look at the entire picture.

Furthermore, separate out the conditions on the various farms, each one was different in one aspect or another. I did not intend to leave the impression that the only problem on the Lemunyon farm was Fat Cow disease. He had other problems as well. Certainly all of these disease problems can interact. The diagnosis of fatty cow was not mine, it was made by Dr. Coy in a letter to Lemunyon on August 24, 1976, and by Phase III team in a report on October 27, 1976, and by Dr. Davis in a visit to the farm in May 1976, at which time he necropsied a cow that had just died. The other piece of information to consider is the herd history. The problem as defined by MDA occurred during the early post partum period which is all part of the fatty cow syndrome. Your summary table on body weight changes is confused because you did not separate acute from chronic effects in the fatty cow syndrome. Reread the paper by Morrow, p. 1626 - "When recovery from the fat cow syndrome does occur there is frequently a delay in the onset of post partum estrus and conception due to retained fetal membranes and metritis, and a marked loss in weight in severely affected cows".

By way of explanation one needs to sort some things out in this complex situation. First, one rarely finds only one problem present in a herd health situation with dairy cattle. One often finds a number of problems including mastitis, metritis, some foot/joint problems especially with cattle on concrete 24 hours/day and compounded by deficient bedding, some calf problems and some nutritional problems. If I left the impression that the only problem was fatty cow than I was too brief in my comments since my findings in this matter from the very beginning have identified a number of problems.

One must also sort out the clinical workups and necropsies done on animals submitted live versus those done on animals dying on the farm. The diagnosis of fatty cow was based on animals necropsied at the farm. The clinical workup reported by Dr. Ellis et al was on chronically ill, live cows submitted to the University

I also seriously question the purported observation of "general debilitation" in the Michigan dairy cattle. I observed the cattle on the Lemunyon farm as well as four other involved farms. Even in Lemunyon's case one could not say there was a general debilitation. The herd I saw in February was in average condition. There were some thin

cows as well as some very fat cows. They were bright, alert, active. The alleged chloracne simply was not present. The few skin lesions I observed on the dorsal neck were typical of skin rubbing lesions seen in cattle that have an opportunity to rub the top board on the manger. In the case of Lemunyon, this was a 2x6 with tongue down. The tongue was worn smooth. To conclude that chloracne was present without substanting histopathology is unwarranted in my opinion. Consequently, since I have personally observed the cattle, looking specifically for significant skin lesions and not finding them I must conclude that they did not exist. I do not know who actually made such a diagnosis. The discussions I attended alluded to open abscesses or bleeding skin ulcers on the legs. Again, I did not see these when I examined the cattle.

What I did see were some hemotomas on the legs which often result from cattle getting banged around against free stalls and other corners or protrusions. On occasion these become infected, abscess and ulcerate. You might be interested in noting that some Michigan farmers were blaming the hemotomas on PBB's as they stood and talked to you while leaning on a sharp ended pipe jutting out in the main alley way!

The herd in the worst shape was the Dale Hice herd in which he had been quarantined for unsanitary conditions because of a deep accumulation of manure and several dead cows being found in the barn by the milk inspector. Hardly a usual situation. He was quite frankly, by his own admission, not providing adequate care for the cows. Consequently, he lost his milk market, then ran out of feed, was broke and could not buy feed, and his cattle, as per the Michigan Veterinary Diagnostic Laboratory report of February 28, 1977, suffered from malnutrition secondary to poor quality feed; suppurative mastitis. I saw the Hice herd in March, they were uniformly thin, but alert and active. They were receiving a minimal amount of hay as their total diet. Anyone wanting more information on the management and operation of this farm can obtain access to other reports in MDA files under the Michigan sunshine law. I have read them and as a result concur with the opinion of Dr. Davis, MDA that the problems on the Hice farm were caused by factors other than PCP or dioxins. If cattle are being fed a grossly inadequate diet one does not need to look under rocks to determine the cause for loss of body flesh.

The diagnoses of mastitis and calf viruses were made by MDA or MSU veterinarians. The remarkable conclusion is that the mastitis was claimed to be caused by bacteria which were allegedly cleared up by antibiotics but cell counts persisted. This conclusion was reached in the light of 1) there is nothing concrete in the record that any cows were cultered after treatment to see if in fact the infection was eliminated. This in the light of a 50% infection rate that included not only strep, but also staph. A background staph problem is more difficult to eliminate than the strep and furthermore, a background staph problem may become more severe when the strep infection is cleared up.

A great deal was being made about immune suppression based on this mastitis situation. One must seriously question such an implication based on the above workup. The other factors not accounted for in the workup as testified to included lack of evidence that milking equipment was, in fact, checked to make sure it was in proper working condition, the stage of lactation was not considered in the evaluation of cell counts and other stress factors such as bedding were either ignored or not considered.

Other information on the Lemunyon herd was obtained which showed that cow death losses were occurring primarily in the period of 21 days post partum. This fits the fatty cow syndrome. This coupled with the feeding pattern and radical changes in diet, to advice given Mr. Lemunyon to feed dry cows separately from lactating cows plus the NDA diagnosis of fatty cow syndrome cannot be ignored.

If one reads the paper of Morrow one finds that marked loss of weight is seen in severely affected cattle. What one needs to differentiate is pre-partum condition from post partum condition. Consequently, the initial recommendation to NDA was to get a good herd history. This was never done by NDA to the best of my knowledge. Others have done more in this area.

A similar restraint is warranted in the interpretation of clinical pathology data. Are the samples from acutely ill cows? Chronic cows? Cows with systemic infections? These are important factors because fatty cow syndrome is not a simple pathologic condition.

Regarding your comment about white blood cell counts the following is offered. Cows have WBC counts ranging from 7-10,000 with aged dairy cows having counts as low as 5,000. Cattle normally have (approximate) 25-30% neutrophils, 60-65% lymphocytes, 5% monocytes and 2-5% eosinophils.

If you look at the blood picture for the 13 Lemunyon cows obtained by MSU in March, 1977 you will find two cows with elevated WBC counts both of which have greatly increased neutrophil counts which indicates an active infectious process. The remaining cows have WBC counts within published normal ranges. Furthermore, if one looks closely at the chlorodioxin immune suppression data one gets a picture of immune suppression coupled with a decrease in absolute lymphocyte counts. If you carefully analyze the Lemunyon blood data you will find that absolute lymphocyte counts are within normal ranges with the exception of the two cows with a left shift indicating an active infection.

The above comments hold for the blood picture on the other farms as I remember them. It has been some time since I carefully studied those. Consequently, I do not know what data your summary table is referring to when it makes the summary statement of "WBC count markedly increased".

Dr. Coy mentioned an eosinophelia in six cows. I would guess you were as surprised as I was when he did not follow that up with a diagnostic check for internal parasites. You may recall the response from Dr. Wise the hearing officer.

As an aside we also found a marked eosinophelia in the Hice cattle we necropsied. The intestinal parasitic lesions fit the usual pattern. I would suggest a bottom line along this avenue. Both Dow toxicologists and myself have estimated the PCP dose for Lemunyon's cows to be 0.12-0.3 mg/kg per day. Your group analyzed the lumber and as I interpret the results the dioxin levels found indicate a typical technical PCP. Based on all your studies on PCP and on all the literature do you really think there is any perceptible risk to the health of a cow with 10 ppt HxCDD or 1.4 ppb HxCDD in liver in light of the published work on larger TCDD liver residues in rats at levels claimed to be no effect? I appreciate the fact one can always say "We do not know because we have not tested it", but as a toxicologist one often uses his total data base in making interpretations subject to experimental verification.

I feel much more confident about accepting the MDA diagnosis of fatty cow, mastitis and viral infections and questioning the totally unsubstantiated diagnosis of chloracne than I would be by accepting the chloracne diagnoses and rejecting the other diagnoses made by MDA. At least I know MDA veterinarians have seen the other conditions on numerous occasions. I doubt if they ever saw chloracne or ever heard of it before. Add staph to your list of causes of infectious mastitis. It is an important consideration in view of the way the situation was handled.

Also, differentiate between the acute phase of fatty cow and the chronic sequalea. Cows may take one entire lactation to recover. If appropriate management changes are not made then the syndrome can be more severe in the second and third lactations.

Dr. Davis's primary reservation with the fatty cow diagnosis as the primary factor was because he had not seen such large death losses previously. Yet MSU has published on such a high mortality. More recent studies out of Tennessee support the finding of high morbidity and high mortality with this disease.

I am a little bit confused by your reference to the gross and histopath data on the various PCP studies as being the primary concern. In the production grade study of November 1971, on page 10 of the report it is stated "Gross examination at necropsy revealed no compound related changes. Minimal focal hepatocellular degeneration and necrosis were observed upon microscopic examination of livers from rats maintained on diets containing the top dosage level of sample 9822A; these changes were not observed in rats maintained on a diet containing 95/5 which provided a similar dosage of PCP." In view of the apparent minimal nature of the changes at a daily dose equivalent to 1/4 - 1/5 the acute LD_{50} one can also come to the conclusion that there is not much of a hazard associated with low level (fractions of mg's) exposure to technical PCP.

I quite agree with the findings of Dr. Wise that sensible use restrictions and use guidelines will do more to reduce the hazard associated with PCP. Alone that line has Dow come up with a recommendation on the use of EC-7 to treat feed bunks?

I quite agree with your statement "also because the dioxin content of PCP could be reduced, we have consistently recommended that the nonphenolic content of PCP be reduced, etc.". If I was a corporate manager and had just invested a million dollars in a thermal oxidizer(incinerator) and saw an opportunity to get dual use by cleaning up 2,4,5-T and PCP at the same time, I would do it also. It is a neat marketing manuver. Unfortunately, the toxicologic picture is less clear because of the difference in opinion on the actual hazard associated with technical penta. Is Dow aware of any problems encountered in livestock related to the non-phenolic content in Dowicide-7? Or did that product have a clean use record for 30 years except for the obvious occasional misuse?

Sincerely yours,

Gary A. Van Gelder, D.V.M., Ph.D.
Professor and Chairman

GAVG:nc

cc: Dennis Lindsay

8.2.5

REICHHOLD CHEMICALS, INC.

Creative Chemistry . . . Your Partner in Progress

World Headquarters • RCI BUILDING, WHITE PLAINS, N. Y. 10603

April 18, 1978

Address Reply To
REICHHOLD CHEMICALS, INC
P.O. Box 1482
Tacoma, Washington 98401
Telephone 206-572-5800
Teletype 910-449-2355

Dr. Sheldon D. Murphy
Professor of Toxicology
Department of Pharmacology
University of Texas Medical School at Houston
P.O. Box 20708
Houston, Texas 77025

Dear Dr. Murphy:

SCIENCE ADVISORY BOARD
ENVIRONMENTAL HEALTH ADVISORY COMMITTEE
Ad Hoc Study Group on Pentachlorophenol Contaminants
Draft Report -- Public Hearing April 3, 1978

The purpose of this communication is to amplify Reichhold's testimony presented to the Committee April 3, 1978.

On page 4 of our testimony, I made reference to the Committee's draft report, page I-10, paragraph 10, where it is concluded that technology is now available which could markedly reduce the levels of chlorodioxin and dibenzofuran contaminants in pentachlorophenol (PCP). I pointed out that consideration must be given to the question of trade-off of occupational hazards. It is assumed that the process referred to in the draft report is the facility designed to produce low-dioxin content pentachlorophenol at Dow Chemicals' Midland, Michigan complex. It has been known for some time, to those skilled in the art, that the dibenzo-p-dioxin and dibenzofuran contaminants can be separated from pentachlorophenol and tetrachlorophenol by various methods. The problem arises in how to safely handle and safely dispose of the concentrated residual waste streams created by removing these contaminants. We have been informed by Dow that they destroy these contaminants by diluting them with large quantities of other liquid wastes and then incinerating this large quantity of highly contaminated material.

Reichhold has considered a number of possible ways of handling and disposing of the waste streams, which would result from removing and concentrating these contaminants, and have discarded each because of potentially insurmountable problems. Some of the disposal methods which we have considered include:

1. Collecting and shipping to a suitable disposal site. No disposal site is known which is licensed to accept these wastes. In addition, permits to transport these hazardous wastes would have to be obtained from various governmental agencies. Also, transportation requirements would have to be set out.

2. Incineration. It has been suggested in the report that technology to dispose of these waste streams exists -- presumably this means by incineration. Construction of a suitable incinerator designed to handle this highly toxic chlorinated material, as the principal material to be incinerated, is a very expensive and difficult proposition. Experts advise us that these highly chlorinated refractory materials require temperatures in the order of 1200°C to assure complete conversion to HCl, CO_2 and H_2O. Because of the presence of HCl and other corrosive by-products, the materials of construction are critical and expensive. Operating costs to achieve and hold the necessary temperatures are high.

   To the best of our knowledge, there is no licensed incinerator in operation that will accept these materials for incineration. Therefore, we must conclude that the technology is not available to satisfactorily dispose of these waste streams with the confidence that the chlorinated materials will be completely destroyed. We are aware of work performed by various departments of government which have addressed this problem. Reichhold strongly suggests that before the assumption is made that technology is available to safely dispose of the hazardous waste streams created by removing and concentrating the contaminants in PCP, that the Technology Assessment Pollution Control Advisory Committee of the Science Advisory Board be requested to review this entire question. The secretary of this Committee is Lloyd Taylor.

We have applied substantial resources to the investigation of the chlorination of phenol without the formation of chlorodioxins and have, as a result of this study, substantially reduced the chlorodioxin and dibenzofuran content. This reduction yields a technical grade PCP with a total dioxin content in the range of 1200 ppm.

The ideal solution would be to produce pentachlorophenol without co-producing any toxic contaminants. The technology to do this is not known. We believe that the years of experience with technical grade pentachlorophenol has indicated that it is far better to widely distribute a less than no effect concentration of the contaminants than to have them separated and exist in one highly concentrated stream at several widely dispersed manufacturing sites. These highly concentrated streams would be subject to possible catastrophic error in handling which would result in a major hazard to the immediate surroundings. The handling and disposing of these highly toxic waste materials is subject to all of the hazards of transportation -- broken pipelines, leaking drums, derailed rail cars, etc.

If they are ultimately conveyed safely to an incinerator, then the safe operation of the incinerator is of paramount importance. The incinerator must be constantly monitored or the contaminants will merely be made airborne and dispersed over a substantial area in more than toxic effect concentrations. An improperly operated incinerator could contaminate large areas of land and create an incident of the magnitude comparable to that which occurred at

Seveso, Italy. We feel that the question of safe disposal of the highly contaminated waste streams created by removing the impurities from technical grade PCP must be thoroughly addressed by experts before industry is forced to create a dangerous waste for which there is currently no acceptable means of disposal.

We would appreciate your communicating this addendum of our testimony to the Committee members for consideration.

Again, thank you for the opportunity to appear before your Committee. We deeply appreciate the many hours of concentrated effort that the members applied in bringing the facts to light regarding pentachlorophenol.

Very truly yours,

REICHHOLD CHEMICALS, INC.

F. J. Shelton
Vice President
Science & Technology Worldwide

FJS:cm

TESTIMONY ON PENTACHLOROPHENOL TO THE
SCIENCE ADVISORY BOARD ENVIRONMENTAL HEALTH
ADVISORY COMMITTEE

April 3, 1978

My name is Frederic J. Shelton. I am Vice President, Science & Technology Worldwide, for Reichhold Chemicals, Inc. Reichhold is one of the three major manufacturers of pentachlorophenol in the United States, and as such has a direct interest in all phases of regulatory activity concerning PCP. Other manufacturers include Vulcan Materials Company and Dow Chemical Company. Reichhold is appearing here today in response to a letter dated March 14, 1978, advising of a two-day meeting of the Environmental Health Advisory Committee of the Science Advisory Board. Since the principal purpose of this meeting was to consider and discuss the draft report of the committee's study group on pentachlorophenol contaminants, Reichhold requested time during the meeting of the Environmental Health Advisory Committee to present comments on the draft report. Reichhold thanks the Environmental Health Advisory Committee for this opportunity.

As background, Reichhold has manufactured commercial grade pentachlorophenol (PCP) since 1955, and since the beginning of production has been deeply concerned about the health and safety aspects of PCP, both in regard to the general public, to the environment, and to its employees. PCP, and the contaminants which are present as the result of manufacture, have been a subject of study at Reichhold since manufacturing was commenced. Through the years, Reichhold has sponsored and participated in several scientific investigations into the chemical makeup of commercial grade PCP and has conducted a number of toxicological studies designed

to assess the safety of commercial grade PCP. As a result of the work which Reichhold has conducted, the company is not aware of any studies or reports which support the premise that commercial grade PCP containing trace quantities of contaminants, including chlorodibenzo-p-dioxins (CDD's) and chlorodibenzofurans (CDF's), present any significant hazard to man and the environment when properly used. The results of these studies and investigations have been presented to the Federal EPA as well as to various state regulatory bodies.

Reichhold conducts physical examinations on each of its production employees on an annual basis, and more often if the man requests. No unusual physical conditions have ever been reported for these men. Reichhold field personnel have had more than twenty years of contact with its PCP users and are unaware of any human or animal health problems attributable to properly used PCP. PCP finds commercal use in the wood treating and preservation industries because of its toxic properties. It must be handled and treated with respect because of its innate toxicity. The handling and treatment afforded PCP and PCP containing products, because of the toxicity of PCP itself, is sufficient to protect the users, and others who come into contact with PCP treated wood, from any hazards due to the chlorodioxins contained in the product.

In the early 1950's, PCP was used and recommended for a broad spectrum of pesticide uses. In most of these uses, PCP was applied from a solution prepared by dissolving the PCP in a petroleum distillate. If a water solution was required, the alkali salt of PCP was prepared by reacting the PCP with aqueous sodium or potassium hydroxide. Early uses of PCP included all phases of wood preservation and protection, both against microorganisms and insect attack. The preservation of water based paints and adhesives, and the preservations of textiles and cordage, as well as weed control, were also significant uses of PCP. In addition, PCP was used in red mite control in

poultry houses. Reichhold felt that many of these historical uses of PCP presented the possibility of excess user exposure to the irritational and toxicological properties of PCP itself. Although Reichhold has had a large number of registrations covering a wide variety of PCP uses, it currently maintains a registration for the use of PCP for manufacturing purposes (wood preservation) only. Reichhold's PCP is sold to commercial wood treaters and is used in the industrial treatment of wood by a variety of processes. We believe that commercial grade PCP, as manufactured by Reichhold and others, does not pose undue hazard to man, livestock and the environment, when properly used.

We would like to now comment specifically on several portions of the draft report of the Ad Hoc Study Group on pentachlorophenol contaminants, dated March 1978. On page I-8, under Item 3, Conclusions, paragraph 1, Reichhold confirms that it has not detected any TCDD (2,3,7,8-tetrachlorodibenzo-para-dioxin) in any samples of PCP which it has analyzed. On page I-9, paragraph 5, the conclusion is drawn that exposure to man and animals to CCD's migrating from PCP treated wood should be prevented. Reichhold supports this conclusion and suggests that consideration be given to promulgating appropriate rules and regulations to prevent contact of human foodstuffs or animal feeds directly with PCP treated wood. In addition, we think it would be desirable to restrict the use of uncoated PCP treated wood from certain portions of decorative fencing, porches and other recreational structures where direct human contact could be anticipated.

Reichhold agrees with the conclusion drawn in paragraph 7 that the most probable opportunity for excess human exposure to PCP is in the PCP production and utilization industries. Reichhold would like to emphasize the point that any proposed significant changes in manufacturing or application of PCP must consider the effect

that these changes would have on the workers involved.

A number of alternative methods for producing various grades of PCP have been proposed. Some of these processes present the possibility of increased worker exposure to PCP and/or PCP contaminants because of the characteristics of the final PCP produced. Reichhold has examined its process for the production of PCP, as well as the handling characteristics of its finished product, and feels that presently it cannot suggest a reasonable alternate to its PCP product. Reichhold urges that before any action is taken, that all aspects of the production and utilization of any new PCP product be thoroughly examined. We feel that particular emphasis should be placed upon the physical characteristics of the final PCP product, as well as the creation and disposal of any waste or by-products caused by its production.

On page I-10, paragraph 9, Reichhold certainly agrees that certain uses of PCP be objectively examined and that regulation be considered to reduce those applications of PCP treated wood which may come in contact with humans or animals, or food products. However, as we have repeatedly stated, we believe that there is an absolute need for PCP treated wood for use in and around farm buildings and structures where degradation by microbial attack from soil and other materials is critical.

Paragraph 10, on the same page, states that certain technology has been disclosed which is designed to reduce the levels of CDD's and CDF's in PCP through distillation of technical PCP. However, we do not totally agree with the statement, "It would seem prudent.....to control the contaminants to the extent possible by best manufacturing practice." We would like to emphasize that consideration must be given to the question of trade-off of occupational hazards. Reichhold feels that there are significant occupational hazards associated with the use and handling of the PCP

products which it has seen on the market which are claimed to have reduced levels of CDD's and CDF's. Reichhold, furthermore, is very concerned about the concentration of CDD's and CDF's in waste streams generated by the distillation process used for the cleanup of the technical PCP. The economic impact evaluation would have to take into consideration the distillation process and cleanup of PCP as well as the incineration of the waste stream generated. It would also have to take into account the automation of the process which would then minimize exposure to the waste stream. The commercial process used by Reichhold to produce PCP does not produce a concentrated waste stream containing CDD's and CDF's. We urge the Science Advisory Board Environmental Health Advisory Committee to very seriously consider this possible route of exposure to concentrated CDD's and CDF's streams produced in a PCP distillation process when considering possible hazard trade-offs.

Continuing, on page II-3, a chart is given exemplifying the composition of a purified grade of PCP, labeled Dowcide EC-7. It is noted that only certain chlorinated CDD's are listed, namely the octachloro, the heptachloro and hexachloro dibenzo-para-dioxins. However, on referring to Section V-3, page 52, Appendix No. 4, it is indicated that the possible number of CDD's are listed as being 75 in number. The hexa, hepta and octa CDD's would account for approximately 13 of the possible 75. This would appear to leave 61 additional CDD's which could be present since it has been established that no 2,3,7,8-tetrachlorodibenzo-para-dioxin has been detected in any domestic grade of PCP commercially available today. Since the purpose of this Ad Hoc Study Group is to examine and report on all of the CDD contaminants in PCP, we feel that comment is needed relative to the presence or absence of one or more of these other possible CDD's. We feel that the study should be thorough and complete before any regulatory action is taken. It would be extremely disruptive to the industry

if considerable sums of money and technical development were expended to reduce certain CDD's only to learn at some later date that certain remaining CDD's were present at levels which were then determined to be environmentally undesirable. It is Reichhold's position that prior to any regulatory action mandating a reduction in chlorodioxins, that consideration should be given to all of the chlorodioxins which might be present.

On page III-1, the report states that octochlorodibenzo-para-dioxin, or OCDD, has shown little toxicity. Reichhold would like to point out that the commercial technical grade of PCP which it manufactures, as well as material manufactured by other companies, contains as the major CDD contaminant, OCDD. Typically, the amount of OCDD present is on the order of five to seven times greater than the amount of hepta and hexa CDD's.

On page III-3, one reference was cited which detailed an experiment producing chloracne in rabbit ears. This test indicated that commercial samples of PCP have produced chloracne in the rabbit ear bioassay tests wherein purified PCP did not produce chloracne. Reichhold conducted similar tests at IBR-US Laboratories, in Miamisville, Ohio. The results of these tests indicated that no significant differences could be discerned in the results obtained using either commercial, analytical or purified commercial grades of PCP. The results obtained from one material were comparable to results obtained with another. This information was submitted to the Science Advisory Board Ad Hoc Group, and the results of this tests have not been included in this report.

On page III-9, paragraph 4, reference is made to work done by Kimbrough in 1972. Reichhold has reviewed all referenced articles authored by Renate Kimbrough, dated 1972 and has not seen any report implicating technical grade PCP in

causing teratogenic effects in women. We suggest that this reference be verified.

On page III-12, Conclusion 4, Reichhold agrees that all commercial grades, technical and purified, of PCP contain quantifiable amounts of CDD's; however, we are not convinced, nor are we aware of any studies which conclusively demonstrate that the concentrations of CDD's present in technical PCP are sufficient to ~~be biologically active~~ cause adverse health effects. While it might be proven academically that by isolating certain chlorodioxins and conducting laboratory biological studies with them, effects might be noted, Reichhold feels that these results are not applicable to the real world situation wherein man or animals do not come in contact with sufficient quantities of these materials to produce harm. Reichhold's opinion is ~~does not feel that the total picture involving possible harm to man or the environment from the proper use of technical grade PCP to treat and preserve wood is conclusive and~~ that regulatory action totally banning PCP, or requiring PCP to have certain levels of CDD's is not indicated.

On page III-2-4, reference is made to a study done at the National Institute of Environmental Health Sciences which consisted of analyzing tissues taken from a dairy herd in Michigan for CDD's. The impression given by the information provided on page III-2-4, would lead one to conclude that significant quantities of CDD's were discovered in the animal tissues and that they could be linked to the undiagnosed health problem in this dairy herd in Michigan. We would like to point out that the level of CDD's reported in these tissues ranged as follows:

Hexa CDD	.01 ppb to 1.3 ppb
Hepta CDD	.03 ppb to 12 ppb
Octa CDD	.23 ppb to 47 ppb

Investigation by a team of highly qualified toxicologists, dairy herd specialists, and wood treatment specialists, of the entire Michigan dairy herd incident

allegedly connected with PCP exposure, has resulted in a number of papers being published which define and describe the herd health problems in these Michigan dairy herds. As a result of this work, it was concluded that these dairy herd problems were not related to exposure to PCP or CDD contaminants. All of these data and reports have been previously submitted to the National Institute of Environmental Health Sciences, Environmental Protection Agency, as well as to the Food and Drug Administration, and to the Ad Hoc Study Group on pentachlorophenol contaminants.

In addition, the Michigan Department of Agriculture conducted a hearing on the application of Reichhold for reinstatement of its state PCP registration which was summarily suspended during the dairy herd incident. Dr. Gilbert H. Wise, DVM, the hearing officer appointed by the Department concluded, after the week-long hearing, that the cancelled registrations should be reinstated. Dr. Wise, in an 18-page decision, found in part as follows:

> "No evidence was developed showing that wood preservative formulations containing penta have presented demonstrable risk to the food chain through exposure of food animals to CDD (chlorodioxins) in penta.
>
> "The evidence, while not removing all possibility of hazard, does not support a finding of any measurable magnitude of risk or liklihood of harm to the human food chain from exposure of food animals to CDD in technical penta."

On page IV-5, a hypothesis has been put forth which suggests that chlorinated dioxoins, chlorinated dibenzofurans, polychlorinated biphenyls, polybrominated biphenyls, and chlorinated azoxy benzenes should be considered as a class from the

toxicological standpoint. Reichhold disagrees with this premise because it has been repeatly demonstrated that specific members of a class of compounds may have vastly different biological activities. One needs only to review the work done in the drug industry to realize that it is dependent upon these variations in activity, relative to structure, to produce drugs which minimize pain and suffering. We think it would be extremely risky and unsupportable to regulate various individual readily identifiable chemical compounds as a class rather than as individuals.

There are numerous reports that PCP has been found in many parts of the environment, including in man and animals. It has generally been assumed that this PCP has been coming from the wide-spread commercial use of PCP as a wood preservative or pesticide. It should be noted that it has been reported that PCP may be formed as a metabolite ~~from~~ in animals and microorganisms. Furthermore, it is reported that PCP may be formed in the environment from other chemicals such as hexachlorobenzene and LINDANE and from the chlorination of drinking water.

The source of CDD's in the environment is not exclusively from PCP. Other chemicals such as hexachlorophene and polychlorinated biphenyls also contribute CDD's. Other widely used pesticides such as 2,4,5-T are recognized as containing CDD's.

PCP has a number of registered uses for which there are reasonable alternatives. Reichhold would urge consideration of these registered uses of PCP and that an effort be made to determine where proven alternative materials are available. Perhaps this concern over a wide-spread use of PCP can be more easily regulated by restricting the registered uses of PCP to those for which there is no reasonable alternative, such as for wood preservation.

On the whole, Reichhold applauds the work which has gone into the pre-

paration of this draft report. We feel that much effort has been made to factually evaluate and report on the data and literature which is available; however, we would appreciate consideration of the points which we have raised today.

Again, thank you for this opportunity to appear here today.

8.2.6 Testimony of Dr. Robert L. Johnson

The Dow Chemical Company's position with respect to the non-phenolic impurities in PCP has been and continues to be:

1. that pentachlorophenol containing such impurities above certain levels manifests enhanced toxicological responses as demonstrated by laboratory test animal experiments.

2. that these non-phenolic impurities should be minimized by the manufacture and use of a PCP containing the least amount of these impurities technically possible.

3. that it would not be possible to assess adequately the hazard of the many individual non-phenolic impurities in PCP. Therefore, it was logical and prudent to reduce these impurities to the lowest possible level for commercial PCP and, thereby minimize the risk to the producer, the users, and the environment.

4. that readily identified adaptable technology is available to separate the non-phenolic impurities from PCP and that disposal of such impurities can be dealt with at the producing site where acknowledged risk can be minimized.

5. that a pentachlorophenol can be manufactured in commercial quantities that mimics chemically pure PCP in both acute and subchronic toxicological studies. With the urging of the EPA and at reasonable expense to Dow, such a commercial facility has been constructed and is being operated.

The ad hoc committee draft report represents a significant and worthwhile effort to compile all the available information pertinent to the presence of non-phenolic impurities in technical PCP. The report is thorough in pointing out that:

1. Suitable analytical methods for the specific dioxin and furan isomers present in technical PCP are lacking.

2. There are very little data on the environmental persistence and transport of the dioxin and furan contaminants of PCP.

3. The comparative chronic toxicological information on purified versus standard commercial PCP is limited. (Sub-chronic studies have revealed toxicological differences between these two grades of PCP, especially in the liver.)

4. There are virtually no data on the chronic toxicity of the non-phenolic contaminants of PCP.

5. The biological significance of the finding of low, but detectable, levels of chlorinated dioxins in tissues of farm animals is not presently known.

6. There is insufficient information on occupational exposure of man to these PCP contaminants by manufacturers or users to allow quantitative assessment of the relative hazard of purified PCP versus commercial products containing dioxin contaminants.

These information deficiencies are used in the draft report to explain why an ultimatum to the wood treating industry to manufacture and use only purified grades of pentachlorophenol cannot be issued.

On the other hand, the draft report, without exception, describes the constant concern associated with the presence of the non-phenolic impurities in PCP. For example:

1. The toxicity of the polychlorinated dibenzodioxins and dibenzofurans is recognized.

2. The recent reports of induction of neoplasms by TCDD raise the specter that the polychlorinated dibenzodioxin contaminants in PCP may also have this potential.

3. The finding of low but detectable levels of chlorinated dioxins in tissues of farm animals is a matter of public health concern.

4. Reports of occupational exposure to chlorinated dibenzodioxins, which resulted in adverse health effects in man, were mentioned.

All these references and comments clearly indicate the relevency of conclusion, No. 10, which reads in part,

> *"Technology is now available which could markedly reduce the levels of dibenzodioxin and dibenzofuran contaminants (in PCP). It would seem prudent, therefore, to control the contaminants to the extent possible by best manufacturing practice".*

The PCP producers were initially urged by federal regulatory agencies to reduce the non-phenolic impurities content in 1971, and again advised to proceed in that direction in 1973. It is now 1978; specific timing as to when all commercial PCP should be of a purified grade, or the specific reasons as to why a purified PCP grade is no longer necessary, is urgently needed. The original charge to the ad hoc committee was to comment, to the extent possible, on the potential hazard to humans which can be attributed to registered uses of PCP and the extent that this hazard may be mitigated by the use of the commercial process which results in lower levels of the contaminants of interest. We urge that this charge be completely satisfied as soon as possible in a less ambiguous manner and without encumbrances of economic constraints which have created ambiguity in the present conclusions.

8.3 COMMENTS OF INTERESTED PARTIES

MAY 8 1978

8.3.1

SUBJECT: Comments on EPA Science Advisory Board Environmental Health Advisory Committee Meeting: Pentachlorophenol Contaminants (April 3, 1978)

TO : Ernst Linde, Executive Secretary, Science Advisory Board (RD-673)

FROM : Paul E. des Rosiers, Senior Staff Engineer, Industrial and Extractive Division (RD-681)

I believe it is important that the Science Advisory Board (SAB) be made aware of certain facts in order that all aspects of the pentachlorophenol (PCP) contaminants issue are addressed correctly.

As you know, I was present during the session held on Monday, April 3, 1978, during which time current producers of PCP, namely, Dow Chemical Company, Reichhold Chemicals, and Vulcan Materials Company presented their respective statements to the SAB Environmental Health Advisory Committee. I am considered an Agency expert on the treatment and control of organochlorine chemicals, have in-depth experience with military defoliants dating back to 1967, and as a result, am thoroughly familiar with disposal/detoxification methods for Herbicide Orange and its teratogenic artifact, tetrachlorodibenzo-p-dioxin (TCDD).

In this respect, I was a member of the EPA Herbicide Orange Disposition Advisory Panel to the U. S. Air Force/Defense Supply Agency, provided technical consultation to the State of Missouri Department of Health concerning the Verona, MO TCDD episode, and was interviewed by the British Broadcasting Corporation regarding the Seveso Icmesa plant TCDD incident in Italy.

In retrospect, I was particularly impressed at the meeting by the perception of Dr. Van Gelder, a veterinarian, who in his testimony, alluded to the fact that disposal of concentrated quantities of PCP contaminants might prove to be more of a problem than maintaining the status quo.

At this time, I wish to delineate some pertinent historical facts relating to significant dioxin-type incidents:

(1) 2.3 million gallons (24 million lbs) of Herbicide Orange with approximately 2 mg/kg TCDD (about 49 lbs) could not be disposed of by incineration either in Illinois (Monsanto's Sauget facility) or in Texas (Rollins contract facility), or by land assimilation

in Utah or in Oregon.

(2) Chemical detoxification of Herbicide Orange was proposed to the U. S. Air Force by the Velsicol Chemical Corporation, which entailed deesterification via alkaline hydrolysis/solvent extraction/UV-photochemical decomposition/reformulation; however, Velsicol withdrew its proposal. Agent Chemical Incorporated was selected by the Air Force to demonstrate at pilot scale, an activated coconut charcoal method for "stoichiometric" selective removal of TCDD from Herbicide Orange; however, disposal of spent charcoal cartridges containing high concentrations of TCDD presented a significantly greater environmental risk, and the project was officially curtailed.

(3) The M/T Vulcanus incinerator ship was employed to combust Herbicide Orange at sea some 200 miles southwest of Johnston Island in the South Pacific. Incineration of the defoliant was accomplished at 1250-1450°C with a dwell/retention time of 1.3 second, at a cost exceeding $3 million.* Subsequent to the successful incineration, the M/T Vulcanus has been unable to obtain recertification because of contamination of the ship's storage tanks/deck with miniscule amounts of TCDD (ppt).

(4) There also exists today in Verona, MO, approximately 4600 gallons of highly contaminated (300-350 ppm TCDD) chlorinated still bottoms from previous hexachlorophene manufacture. Systex Agribusiness, the present owners of the industrial site, and the State of Missouri have been unable to secure an environmentally acceptable method for the ultimate disposition of the waste residue.

(5) Presently, for every 5000 lbs/hr of PCP manufactured, approximately 10 percent or 500 lbs/hr of still bottom residues are produced, which may contain, at varying concentrations: octa-, hepta-, hexa- chlorodibenzodioxins and chlorodibenzofurans, tetrachlorophenol, trichlorophenol, chlorophenoxyphenols, hydroxydiphenyl ethers, hexachlorobenzene, chlorinated biphenyls, chlorinated polymers, etc. This residue production would be equivalent to roughly a 2000 tons/year quantity requiring disposal.

* Specifications for the first at-sea incineration of Shell Chemical Company organochlorine waste residues by the M/T Vulcanus were based on Mississippi State University Prof. B. J. Stojanovic's muffle furnace data obtained with analytical grade TCDD. He found TCDD completely combusted between 980-1000°C.

From the foregoing, it becomes obvious that public awareness and anxiety play important roles as to how, when, where, and by which method a "dioxin" contaminated material/waste is to be treated.

Should the SAB Environmental Health Advisory Committee recommend that technical grade PCP be purified to reduce contaminant levels to less than 0.1 percent, then EPA is faced with a predicament - the question of trade-off of occupational hazards.

There is no doubt that it is technically feasible, although at a higher cost, to produce commercially purified grade PCP that can meet reasonable regulatory constraints relative to chlorinated dioxins and dibenzofurans. Furthermore, I have doubt concerning Dow's contention that it possesses incineration capability to "destroy" the waste residues therefrom. Nevertheless, the Dow case is unique - the Midland, MI facility represents probably the largest integrated petrochemical complex in the U. S. and large volumes of waste residues are admixed with relatively small volumes of PCP wastes, the latter essentially losing its identity through volumetric dilution before incineration commences.

Such is not the case with Reichhold and Vulcan, however. Special incinerators would have to be designed, parts ordered, constructed, and subsequently evaluated prior to application for an operating permit. Such a permit request would undoubtedly require a public hearing because "dioxins" are present in the wastes. Based on my experience, I can assure you that the resulting permit requirements will be severely restrictive (e.g., exhaustive monitoring, operational constraints, etc.) and quite possibly could eliminate land-based incineration as a technology option. (Since both Reichhold and Vulcan would solicit strong guarantees from EPA that, once equipment was on order, they would indeed be allowed to proceed with full-scale construction and be able to operate the incineration units without undue harassment from environmental groups. Naturally, EPA would be in no position, legally or otherwise, to honor such requests.)

In my opinion, there are but four alternatives available for consideration by the SAB regarding this matter:

(1) At-sea incineration aboard a vessel similar to the M/T Vulcanus.
(2) Privately owned/contractor operated incineration facility (e.g., Marquardt's high efficiency SUE incineration unit.)
(3) In-process change/process modification (i.e., catalyst substitution) to minimize dioxin/dibenzofuran byproduct production - to include analysis of feedstock (phenol) quality.
(4) Encouragement of accelerated R&D into incorporation of PCP waste residues as feedstocks to cement kilns.

All options could be explored should the SAB desire.

8.3.2

UNIVERSITY OF MISSOURI-COLUMBIA

College of Veterinary Medicine

Veterinary Anatomy—Physiology

Columbia, Missouri 6520
Telephone (314) 882-701

April 24, 1978

Mr. Ernst Linde
Executive Secretary
Environmental Health Advisory Committee
Science Advisory Board A-101
Washington, D.C. 20460

Dear Mr. Linde:

Enclosed are 20 copies of a report containing my additional comments on the draft report on pentachlorophenol contaminants.

Please distribute these to the proper persons.

Sincerely yours,

G. A. Van Gelder

Gary A. Van Gelder, D.V.M., Ph.D.
Veterinary Toxicologist

GAVG:nc

April 15, 1978
Part II (part I dated 3/24/78)

TO: Mr. Ernst Linde

FROM: Dr. Gary Van Gelder

RE: Comments on Draft Report on Pentachlorophenol

The following additional comments are made relative to the draft report.

1) The charge to the committee was to assess the hazard to humans due to contaminants in pentachlorophenol. Other than industrial chloracne resulting in all probability from exposures to mixtures of various chemicals the document fails to document any significant human health hazard that has resulted from 40 years of use and exposure. This statement is made with the acknowledged exception of reported instances of gross negligence or intentional ingestion resulting in illness and death.

   The report fails to clearly elucidate the point that the present methods of producing low non-phenolic content PCP will still possess the presently alleged chloracne hazard since the starting reactions are similar for both processes. The report implies that obtaining concentrates of the contaminants is less hazardous than working with very diluted concentrations. The above implication is made in the report without any evidence that there was any attempt to assess the risk involved. Additionally, comments made at the hearing clearly demonstrated the lack of unanimous agreement among waste disposal specialists on the reliability of incineration. Critical issues are:

   a) frequency of stack monitoring
   b) levels of detection
   c) location of stack relative to wind direction and population
   d) presence of fail/safe devices

   Without such information and risk assessment data, how can a responsible decision be made to move from technology A to technology B, especially when technology A has not been shown to be associated with any significant, isolatable problem? Risk assessment involves more than simply saying since process B exists we should use it.

2) Page 1-7 of the report refers to dioxins being found in milk from Michigan cattle but no data are presented. The report later refers to dioxins in liver and fat. This point needs clarification.

3) Page III-14, Table II - The data are summarized in such a way as to ignore dose. An important part of risk assessment is consideration of dose and evaluation of dose-response patterns.

In one sense the draft report begins to pull together the available information. The next steps are evaluation and interpretation. In my opinion, the last steps remain as uncompleted tasks for the committee.

4) Page III-9 - states "technical grade PCP has been implicated in causing teratogenic effects in women - Kimbrough, 1972." The report by Kimbrough does not make this statement. Stillbirths with PCB's are reported.

5) Page III-9 - The Larsen study cited is inadequate to address the question of placental transfer. Based on information presented it is likely that placenta/fetal PCP levels are comparable to maternal blood levels.

6) Statistical methods used to evaluate the various 90-720 day studies are not consistent. See my letter to Dr. Schwetz of Dow Chemical which was attached to my comments dated March 24.

7) While I appreciate the comments of several members of the committee that their concern is not animal health, I need to point out that there are people in the public sector who, based on their understanding of comments made by members of this committee believe that low level exposures to technical PCP kills cows. I am satisfied with the progress being made to resolve that misconception.

8) The remaining issue is one of safety/hazard evaluation. It is amazing that an EPA sponsored committee was not provided or did not review the results of studies sponsored by EPA to evaluate the human health effects of PCP. Why this body of information has been ignored is unexplainable.

One cannot prove safety for any product or process, what one does is evaluate toxicity and assess risk (hazard). Consequently, studies done where technical PCP was fed to animals provide information on the toxicity of the PCP related contaminants.

Furthermore, evaluation of worker related health problems or the lack of problems are also important items to consider in risk assessment.

9) My principle concern in this entire matter has been based on a broad view of the entire situation. First, PCP is an economic poison. Fortunately, it's toxicologic characteristics are such that it does not present a large hazard. But PCP residues have been found in food products of animal origin. To the extent that those residues can be reduced or eliminated without causing a major economic effect is a worthwhile goal. Additionally, PCP constitutes only 5% of what is put into wood to preserve it. The toxicity and residue characteristics of the other 95% of the material has not been determined. What is found as residues are generally those things that excite an electron capture detector.

These considerations plus my own observations of over use and unnecessary use of PCP treated wood in places that facilitate animal exposure leads me to a broad based recommendation that addresses

the entire problem. Namely, the need to develop sensible use restrictions to reduce animal exposure. The casual rubbing against a post or occasional lick of a post is of no concern to me. The issue is one of feed bunks, bunker silos and use of treated wood in above grade, dry locations. The concern expressed in item 10 below is also a part of my decision information base.

10) I have reason to believe that the level of dioxin formation on the surface of treated wood exposed to light is higher than that felt to occur as expressed in the committee discussion. It is of sufficient concern that Dow has conducted and has expressed their intent to conduct additional studies in this regard.

8.3.3

DOW CHEMICAL U.S.A.

May 9, 1978

P. O. BOX 1847
2040 DOW CENTER
MIDLAND, MICHIGAN 48640

Mr. Ernst Linde
Executive Secretary
Environmental Health Advisory Committee
Science Advisory Board
U. S. Environmental Protection Agency
Washington, D. C. 20460

Dear Mr. Linde:

Attached is the requested description of the general procedures utilized by Dow Chemical U.S.A. to contain and destroy the contaminants resulting from the production of DOWICIDE* EC-7 Antimicrobial grade of pentachlorophenol. We believe this is the kind of additional information that was needed by the Environmental Health Advisory Committee Study Group on Pentachlorophenol Contaminants to assure itself that these impurities can be feasibly handled.

As Dow has repeatedly stated, we contend that disposal of the toxic impurities inherent to commercial pentachlorophenol should be dealt with at the producing site where acknowledged risk would be minimized. The fact that we produce and market a grade of pentachlorophenol with significantly reduced non-phenolic impurity content supports this position.

We have included 10 copies of the requested information. If additional copies are required for distribution, for example, to members of the Environmental Health Advisory Committee, please do not hesitate to let us know.

Very truly yours,

Robert L. Johnson
Designed Products Department
Technical Service & Development
517/636-1524

mbh

attach.

*Trademark of The Dow Chemical Company

DISPOSAL OF PENTACHLOROPHENOL IMPURITIES

Dow Chemical U.S.A.

The product known as DOWICIDE* EC-7 Antimicrobial grade of pentachlorophenol (PCP) differs in chemical assay from the older form of PCP. Numerous publications describe the commercial process utilized in the U.S. to make PCP. As noted in these publications, the process reaction mixture is maintained as a liquid (approximately 10°C above the product melting point); no solvent is used or required. The commercial process utilizes final chlorination and the necessary temperatures to produce a product with a pentachlorophenol content in the range of about 85-90%. These production conditions also result in the formation of the various contaminants found in PCP.

The finished reaction mixture, in the Dow process, is distilled to yield a grade of PCP which meets the imposed specifications for DOWICIDE EC-7. A copy of the DOWICIDE EC-7 technical bulletin, which describes the composition, is attached.

The still bottoms resulting from this additional PCP processing contain the non-phenolic contaminants identified as chlorinated dibenzo-p-dioxins and chlorinated dibenzofurans. Other materials included in the still bottom residue, or tars, are the chlorophenoxyphenols, chlorodiphenyl ethers, and even a percentage of higher phenols such as pentachlorophenol itself.

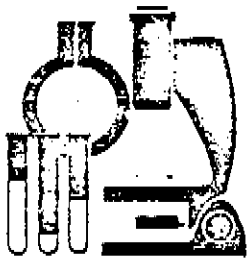
These tars are handled, stored and transported to the Dow tar burner in closed systems. Eye protection, rubber gloves and protective clothing are routinely used by all personnel

*Trademark of The Dow Chemical Company

involved in these operations. A rigorous industrial hygiene and health monitoring program is and has been in effect for these personnel. Anytime that work on contaminated equipment is needed, extreme protective measures are taken including full rubber suits and self-contained breathing apparatus.

Normal operating conditions in the tar burner are maintained to achieve a minimum 1.8-second residence time at temperatures of 900-1000°C. The temperature is continuously monitored with appropriate warning alarms and shut-off devices. Combustion gases go through a three-stage scrubbing system before discharge to the atmosphere. The scrubber water is treated in the waste water treatment plant before recycle and/or discharge to the Tittabawassee River.

5/9/78



technical data

DOWICIDE EC-7 ANTIMICROBIAL

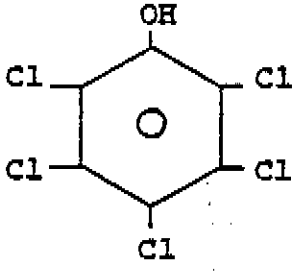
GENERAL

DOWICIDE EC-7 Antimicrobial is Dow's designation for pentachlorophenol, purified grade. This antimicrobial is designed to complement DOWICIDE 7 Antimicrobial in all industrial uses that require the control of bacteria and fungi, particularly in the area of wood preservation.

PHYSICAL PROPERTIES

(These are laboratory or literature data typical of the product and are not to be considered as, or confused with, specifications.)

STRUCTURE



Formula	C_6Cl_5OH
Molecular Weight	266.4
Flash Point, °F	None
Fire Point, °F	None
Specific Gravity, 25/25°C	1.9
Solubility, approx. g/100 g solvent at 25°C	
Acetone	52
Methanol	175
Ethanol (F30)	125
Isopropanol	80
Diacetone Alcohol	145
DOWANOL TPM Glycol Ether	115
Ethylene Glycol	12
Methylene Chloride	7
o-Xylene	18
Turpentine	7

THE DOW CHEMICAL COMPANY
DESIGNED PRODUCTS DEPARTMENT • MIDLAND, MICHIGAN 48640

PRODUCT DESCRIPTION

DOWICIDE EC-7 Antimicrobial has the following composition:

Active ingredients	100%
Pentachlorophenol	88%
2,3,4,6-Tetrachlorophenol	12%
Chlorinated Dioxins	
Octachlorodibenzo-p-dioxin	30 ppm, max.
Hexachlorodibenzo-p-dioxins	1 ppm, max.
Description	Off-white to light yellow prills.

EPA Reg. No. 464-431

PACKAGES

Prilled and pelleted forms of DOWICIDE EC-7 Antimicrobial are sold in multiwall paper bags having a net weight of 50 pounds, in fiber drums having a net weight of 300 pounds, in wire-bound boxes having a net weight of 2500 pounds and in bulk to be transported in tank trucks and rail cars. The block form is sold in units having a net weight of 2000 pounds.

(Typical Laboratory Data)

Test Organism	% DOWICIDE EC-7 for Inhibition
Trichoderma viride, ATCC#8678	0.0025-0.005
Trichoderma sp., Madison P-42	0.001-0.0025
Ceratocystis pilifera, ATCC#15457	0.0005-0.001
Polyporus tulipiferae, ATCC#11245	<0.0001
Rhizopus stolonifer, ATCC#6227a	0.0001-0.00025
Lenzites trabea, Madison 617	0.0001-0.00025
Ceratocystis ips, ATCC#12860	0.001-0.0025
Chaetomium globosum, ATCC#6205	0.0001-0.00025
Aspergillus niger, ATCC#6275	0.001-0.0025
Bacillus cereus var. mycoides, ATCC#11778	0.0005-0.001
Bacillus subtilis, ATCC#8473	0.005-0.01
Escherichia coli, ATCC#11229	0.025-0.05
Pseudomonas aeruginosa, ATCC#15442	0.1-0.25
Enterobacter aerogenes, ATCC#13048	0.05-0.1
Streptomyces griseus, ATCC#10137	0.0005-0.001
Flavobacterium arborescens, ATCC#4358	0.00025-0.0005

Formulators may be required to develop their own efficacy data as well as use and precautionary labeling based on the represented properties and intended uses of their finished formulations, and in accordance with all pertinent laws and regulations.

HEALTH HAZARDS

DOWICIDE EC-7 Antimicrobial is capable of causing conjunctival redness, iritis, and slight corneal injury. Prompt flushing of contaminated eyes will lessen the degree of injury. A single, prolonged skin contact with the product may cause slight redness and swelling. Repeated, prolonged contact may result in a chemical burn. DOWICIDE EC-7 is not absorbed through the skin in acutely toxic amounts. However, the product, in solution, may be absorbed through the skin in acutely toxic amounts depending upon the solvent and the concentration of DOWICIDE EC-7. Dusts may be irritating to the nose and throat.

PRECAUTIONS FOR SAFE HANDLING

Safety goggles should be worn to protect the eyes when DOWICIDE EC-7 Antimicrobial is handled.

Protective clothing should be worn when skin contact with DOWICIDE EC-7 is anticipated. Work clothes should be changed at regular intervals and when gross contamination occurs. Grossly contaminated clothing, shoes or gloves should not be reused until they have been thoroughly cleaned.

Any exposure to obviously dusty atmospheres will require the use of a dust respirator approved by the U.S. Bureau of Mines for use with toxic dusts.

FIRST AID MEASURES

Eye Contact - Contaminated eyes should be flushed with plenty of water for at least 15 minutes. Medical attention should be obtained promptly.

Skin Contact - Contaminated skin should be washed with soap and plenty of water. Any irritation that develops should receive medical attention.

Inhalation - Anyone experiencing any noticeable ill effects from breathing the dusts of the product should be removed to fresh air. Medical attention should be obtained.