Chlorinated Dibenzodioxins and Dibenzofurans*

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The problems and universal concern about chlorinated dibenzodioxin and dibenzofuran compounds were brought to the forefront by the scientific community during the National Institute of Environmental Health Sciences' (NIEHS) Conference on this subject which was held at Research Triangle Park, North Carolina, April 2 and 3, 1973. This idea for this literature collection emanated from that scientific gathering and resulted in this annotated bibliography of 242 references. These references are categorized by year and arranged alphabetically by author. The number of references per year are: 56/1973; 67/1972; 66/1971; 24/1970; 29/1969–1934. Sources searched are summarized in Table 1. Due to the time available to complete this collection, some errors and omissions were inevitable; we apologize for these and hope those using this literature survey will supply us with past, present, and future topical reprints or citation information. We plan to maintain and up-date this file continually.

Most of the nomenclature or terms searched are listed in Table 2. Each particular author, journal, secondary abstracting service, and news copy unfortunately utilizes separate and distinct terminology when reporting on the chlorinated dibenzodioxins and dibenzofurans. As can be seen from Table 2, it is vitally important, therefore, to become thoroughly familiar with the sources being utilized before mounting a massive effort to collate all that is written or reported about a particular compound, series, or class of compounds, or subject. The magnitude of the search effort for this report is self-evident when noting all the necessary terms used.

The original papers were annotated whenever possible; some were gleaned from abstract journals. We did not alter author's remarks or conclusions; the facts are presented in these annotations as they appeared in the literature. As many salient points as possible, due to space limitations, were taken from each paper or report. Many papers and reports were referred to, after the fact, by more recent authors as having dealt intimately with the chlorinated dibenzodioxins and dibenzofurans; these were not included in this bibliography unless the dioxins or furans were mentioned specifically: most of the

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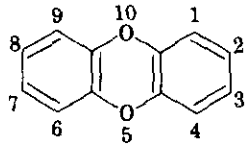
articles were consulted and read however to determine if these compounds were present. For example, numerous articles reporting on the adverse effects of 2,4,5-T were screened but not included because direct mention of TCDD and other dioxin derivatives was missing.

Table 1. Sources and time periods searched.

Source	Period
Multidisciplinary Information Resources	
Bibliography of Agriculture	Vol. 21 (1957) to Vol. 37(1) (1973)
Biological Abstracts	Vol. 31 (1957) to Vol. 55(8) (1973)
Biological and Agricultural Index	Vol. 19 (1964) to Vol. 24 (1970)
Bioresearch Index	Vol. 1 (1965) to Vol. 9(4) (1973)
Chemical Abstracts	Vol. 1 (1907) to Vol. 78(20) (1973)
Chemical-Biological Activities	1965 to 1971
Food Chemical News	Vol. 13 (42) 1972 to Vol. 15(9) (1973)
Health Aspects of Pesticides Abstract Bulletin	Vol. 1 (1966) to Vol. 6(4) (1973)
Health Effects of Environmental Pollutants	Vol. 1 (1972) to Vol. 2(3) (1973)
Index Medicus	Vol. 60 (1956) to Vol. 14(5) (1973)
Pesticide Chemical News	Vol. 1 (1–24) (1973)
Science Citation Index	Vol. 1 (1961) to Vol. 6 (1965); 1966 to 1972
Teratology Lookout	Vol. 3 (1972)
Toxicology Bibliography	Vol. 1 (1968) to Vol. 6(1) (1973)
Specialized Information Centers and Libraries	
Environmental Mutagen Information Center (EMIC)	
Environmental Information System Office (EISO)	
Oak Ridge National Laboratory (ORNL)	
Toxicology Information Response Center (TIRC)	
On-Line Computer Data Bases	
MEDLine	
TOXLine	
Journals	
Ambio	Vol. 1 (1972) to Vol. 2 (1973)
Archives of Environmental Health	Vol. 7 (1963) to Vol. 26(2) (1973)
Bulletin of Environmental Contamination and Toxicology	Vol. 1 (1966) to Vol. 7 (1973)
Clinical Toxicology	Vol. 1(1) (1971) to Vol. 6(1) (1973)
Environment	Vol. 12 (1970) to Vol. 15(3) (1973)
Environmental Health Perspectives	No. 1 (1972) to No. 5 (1973)
Federation Proceedings	Vol. 16(1) (1957) to Vol. 32(4) (1973)
Food and Cosmetic Toxicology	Vol. 1 (1969) to Vol. 10(6) (1972)
Journal of Agriculture and Food Chemistry	Vol. 1 (1953) to Vol. 21(2) (1973)
Journal of the Association of Official Analytical Chemists	Vol. 40 (1957) to Vol. 56 (1973)
Journal of Chromatography	Vol. 1 (1958) to Vol. 73 (1973)
Mutation Research	Vol. 1 (1964) to Vol. 10(6) (1972)
Residue Reviews	Vol. 1 (1962) to Vol. 41 (1972)
Science	Vol. 157 (1967) to Vol. 179 (1972)
Teratology	Vol. 1 (1968) to Vol. 6(2) (1972)
Toxicology and Applied Pharmacology	Vol. 1 (1959) to Vol. 24(3) (1973)

Table 2. Terms searched.

Nomenclature	*Chemical Abstracts* registry number
	
Dibenzo-*p*-dioxin (diphenylene dioxide) (phendioxin)	262-12-4
2,3-Dichloro-	29446-15-9
2,7-Dichloro-	33857-26-0
2,3,7-Trichloro-	33857-28-2
1,2,3,4-Tetrachloro-	30746-58-8
1,3,6,8-Tetrachloro-	33423-92-6
2,3,6,7-Tetrachloro-	
2,3,7,8-Tetrachloro	1746-01-6
Pentachloro-	36088-22-9
Hexachloro-	34465-46-8
1,2,3,7,8,9-Hexachloro	19408-74-3
Heptachloro-	
1,2,3,4,6,7,8,9-Octachloro-	3268-87-9
Benzo-	
Biphenyl-	
Chlorinated	
Chlorinated dibenzodioxin(s)	
Chlorinated dibenzo-*p*-dioxin(s)	
Dibenzo-	
Dibenzo	
Chlorodibenzo dioxin(s)	
Chlorodibenzo-*p*-dioxin(s)	
Dibenzodioxin(s)	
Dibenzo-*p*-dioxins	
Dibenzo-*p*-dioxins, tetrachloro-	
Dibenzo-*p*-dioxin, other chloro-	
Dioxin	
Halogenated dibenzo dioxin(s)	
Halogenated dibenzo-*p*-dioxin(s)	
OCDD	
Polychlorinated dibenzodioxin	
Polychlorodibenzodioxin	
TCDD	
Dibenzofuran (biphenylene oxide)	132-64-9
3-Chloro-	25074-67-3
2,4-Dichloro-	24478-74-8
1,2,4-Trichloro-	24478-73-7
Tetrachloro-	23076-57-6
1,2,3,4-Tetrachloro-	24478-72-6
Pentachloro-	32076-58-7
Benzo-	
Bipheyl-	
Chlorinated	
Chlorinated dibenzofuran(s)	
Chlorodibenzo-	
Di benzo	
Dibenzo-	
Dibenzofuran	
Furan	
Halogenated dibenzofuran(s)	
Polychlorinated dibenzofurans	

1973

ANONYMOUS. Herbicides better for birds than bacteria. *Food Cosmet. Toxicol.* **11**(1): 149–150 (1973).

Teratogenic effects of the 2,4,5-T contaminant, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (dioxin), are well known and the effect of this compound on liver enzymes resembles that of certain carcinogens. Dioxin has also been associated with mutagenic properties through its possible intercalation with DNA; the observed effects resemble those of acridine.

ANONYMOUS. TCDD residue disappears. *Down To Earth* **28**(4): 18 (Spring 1973).

TCDD was not detected (<1 ppm) in 3-ft soil core samples in a sandy area where a total of 947 lb of 2,4,5-T per acre was applied over a 3-yr period. No TCDD residues were found (<0.05 ppm) in bald eagle tissue gathered from 15 states.

ANONYMOUS. 2,4,5-T comes to public attention again. *Pest. Chem. News* **1**(19): 6–8 April 11, 1973).

EPA was asked to suspend the remaining uses of 2,4,5-T until the extent, if any, of TCDD-contaminated food chains is determined. TCDD was labeled a cumulative poison and one of the most potent agents of birth defects in animals ever discovered.

ANONYMOUS. Health hazard of dioxins still uncertain. *Chem. Eng. News* **51**(16): 12 (April 16, 1973).

A selected summary report of the National Institute of Environmental Health Sciences meeting on chlorinated dibenzodioxins and dibenzofurans held at Research Triangle Park in North Carolina on April 2–3, 1973. The conference as a whole, however, seemed to raise as many questions as it answered. From the data discussed there is no doubt that these contaminants are highly toxic and teratogenic, but there is still some doubt as to how much of an actual hazard they represent to human health.

ANONYMOUS. New look may be taken at trichlorophenol compounds. *Pest. Chem. News* 1(21): 9–10 April 25, 1973).

Work showing "surprisingly high" levels of dioxin (ppt) in fish caught in Vietnam has placed doubt on earlier government consideration about dioxin residues. It had been previously thought that the dioxin content of 2,4,5-T was so low that there was little opportunity of residues appearing. In addition to 2,4,5-T and silver, any compound using trichlorophenol intermediates "may be suspect".

ANONYMOUS. Correction. *Pest. Chem. News* 1(22): 2 (May 2, 1973).

The National Academy of Science's Advisory Committee on 2,4,5-T recommended that the registration of 2,4,5-T be restored with the following exceptions: (a) a permissible residue of not more than 0.1 ppm 2,4,5-T on edible parts of food products and in water for human consumption and (b) a limit of 0.5 ppm of contamination with TCDD, except that in all formulations to be used around the home and recreational areas, TCDD contamination should be limited to 0.1 ppm.

ANONYMOUS. Recall program, another look at trichlorophenols urged on EPA. *Pest Chem. News* 1(23): 3–5 (May 9, 1973).

The General Accounting Office urged the Environmental Protection Agency (EPA) to implement full-scale recall procedures for suspended pesticides and raised questions on the dioxin content of trichlorophenol herbicides. GAO stated that "because silvex, ronnel, erbon, and hexachlorophene can contain the same level of dioxin as 2,4,5-T and because a safe level of dioxin has not been determined, we believe EPA should establish a standard for dioxin content and prohibit the use of all pesticides containing dioxin in excess of the established standard."

BAUGHMAN, R. W., and MESELSON, M. S. An analytical method for detecting TCDD (dioxin): levels of TCDD in samples from Vietnam. *Environ. Health Perspect.* (No. 5): 27 (1973).

An analytic procedure involving extensive clean-up and mass spectroscopy detects approximately one picogram of TCDD. The method separates TCDD from DDE, PCB's, and other chlorinated hydrocarbon residues.

BOWES, G. W., SIMONEIT, B. R., BURLINGAME, A. L., DE LAPPE, B. W., PEAKALL, D. B., and RISEBROUGH, R. W. The search for chlorinated dibenzofurans and chlorinated dibenzodioxins in wildlife populations showing elevated levels of embryonic death. *Environ. Health Perspect.* (No. 5): 191 (1973).

Embryonic deaths have been recorded in the laboratory among birds treated with PCB. These deaths have been attributed to chlorinated dibenzofuran contaminants. Also, birth defects in wild populations of birds and sea lions are believed caused by chlorinated dibenzodioxins. High-resolution mass spectrometry was used to examine prepared from aborted sea lions and dead embryos of the herring gull and osprey.

CROSBY, D. G., MOILANEN, K. W., and WONG, A. S. Environmental generation and degradation of dibenzodioxins and dibenzofurans. *Environ. Health Perspect.* (No. 5): 259 (1973).

Both the chlorinated dibenzodioxins and dibenzofurans are unstable to light in the presence of organic substrates. Even if generated under environmental conditions, light provides a mechanism for rapid destruction.

CRUMMETT, W. B., and STEHL, R. H. Determination of chlorinated dibenzodioxins and dibenzofurans in various materials. *Environ. Health Perspect.* (No. 5): 15 (1973).

Chlorinated dibenzo-*p*-dioxins and chlorinated dibenzofurans can be determined in chlorinated phenols, chlorinated phenoxy herbicides, ronnel, fat, and conbustion products by such analytical techniques as gas chromatography, liquid chromatography, thin-layer chromatography, and gas chromatography–mass spectrometry.

DOUGHERTY, W. H.; COULSTON, F.; GOLBERG, L. Non-teratogenicity of 2,4,5-trichlorophenoxyacetic acid in monkeys (*Macaca mulatta*). Twelfth Annual Meeting, Society of Toxicology, New York, NY (March 18–22, 1973), Abstract 9, p. 7.

Technical grade 2,4,5-T which contained less than 0.05 ppm 2,3,7,8-tetrachlorodibenzo-*p*-dioxin was administered orally to forty pregnant Rhesus monkeys daily from day 22 through day 38 of gestation. Dose levels used in the experiment were 0.05, 1.0, and 10.0 mg/kg. Hematology, clinical chemistry, and urinalysis data were recorded for all females before and at various times following treatment until parturition; no toxicity was observed. Examination of live born infants revealed no terata.

ENVIRONMENTAL PROTECTION AGENCY, PUBLICATIONS AND INFORMATION SECTION. Toxicology and pharmacology of 2,4,5-T

(includes dioxins). Bibliography Number 73–04 (February 1973).

A bibliographic listing of 62 references pertaining to 2,4,5-T and dioxins.

ENVIRONMENTAL PROTECTION AGENCY, PUBLICATIONS AND INFORMATION SECTION. Chemistry and residues of 2,4,5-T (includes dioxins). Bibliography Number 73–05 (February 1973).

A bibliographic collection of 58 references on 2,4,5-T containing a limited number of citations on dioxins.

ENVIRONMENTAL PROTECTION AGENCY AND INSTITUTE OF RURAL ENVIRONMENTAL HEALTH. Environmental chemicals: human and animal health. Fort Collins, CO (July 23–27, 1973).

The Institute of Rural Environmental Health, Colorado State University, and the Office of Pesticide Programs, U. S. Environmental Protection Agency, conducted a one-week course on environmental problems, contaminants, toxicants, and chemicals (including dioxins); and human and animal health problems; and poisoning.

FIRESTONE, D. Etiology of chick edema disease. *Environ. Health Perspect.* (No. 5): 59 (1973).

Early work indicated that chick edema factors (CEF) were chlorinated aromatic compounds; later, the compounds were shown to belong to a family of chlorodibenzo-p-dioxins. Further investigation showed that (a) chlorophenols were precursors of the chlorodioxins and (b) chlorodioxins and related compounds are commonly present as minor components in commercial chlorophenols. Characteristic chick edema disease symptoms include excessive fluid in the heart sac and abdominal cavity followed by high mortality starting in the third week.

FOWLER, B., LUCIER, G., BROWN, H., and MCDANIEL, O. Ultrastructural changes in rat liver cells following a single injection of TCDD. *Environ. Health Perspect.* (No. 5): 141 (1973).

Ultrastructure changes in rat liver microsomes and mitochondria were examined at various intervals from 1 to 30 days following a single TCDD injection of 0, 5, or 25 ug/kg. No histologic difference was noted between groups. Observed changes included: proliferation of smooth endoplasmic reticulum (SER), mild increase in rough endoplasmic reticulum (RER), moderate swelling of mitochondria; at 7 days, large aggregates of SER, massive amounts of RER, and small numbers of moderately swollen mitochondria were seen from the 25 mg/kg dosed rats.

GREIG, J. B. Biochemical toxicity of TCDD in rat liver. *Environ. Health Perspect.* (No. 5): 211 (1973).

The persistent toxic effect of 2,3,7,8-tetrachlorodibenzodioxin in rats is evidenced by death as long as 15 weeks after a single oral dose. Alterations, however, in liver constitution (microsomes and cytochrome P–450) and drug metabolism (zoxazolamine and hexobarbital) occurred within 24 hr after dosing.

GUPTA, B., VOS, J., MOORE, J., ZINKL, J., and BULLOCK, B. C. Pathologic effects of TCDD in laboratory animals. *Environ. Health Perspect.* (No. 5): 125 (1973).

Gross and microscopic examinations were performed on rats, guinea pigs, and mice treated with TCDD. A spectrum of dose ranges and schedules were used. Lymphoid organs (thymus, spleen, and lymph nodes) were affected consistently. Thymus atrophy (dose related decrease in weight) was found to be a sensitive index of TCDD exposure. The most severe hepatic effects were seen in rats that received a lethal dose of TCDD. The magnitude of the degenerative and necrotic liver changes were diminished in guinea pigs and mice.

HARRIS, M., MOORE, J., and VOS, J. General biological effects of TCDD in laboratory animals. *Environ. Health Perspect.* (No. 5): 101 (1973).

Albino rats were grouped and treated with single oral doses of 0, 5, 25, 50, or 100 μg/kg TCDD in an acetone–corn oil mixture. Animals that eventually died continued to lose weight until death while survivors exhibited a depressed weight gain. Ruffled hair coat, hunched posture, inactivity, and jaundice were the overt signs seen in the high dose group. Daily oral administration of 10 μg/kg caused death in 15/16 rats with a mean time of 21.8 days. Death resulted in 9/10 female guinea pigs after receiving an oral dose of 3 μg/kg; the mean survival time was 18.1 days. A single oral dose of 1, 10, or 50 μg/kg to adult mice had no effect on appearance or body weight.

HUTZINGER, O., SAFE, S., WENTZELL, B. R., and ZITKO, V. Photochemical degradation of di- and octachlorodibenzofurans. *Environ. Health Perspect.* (No. 5): 267 (1973).

Irradiation of 2,8-dichlorodibenzofuran (low chlorine content) and octachlorodibenzofuran (high chlorine content) in hexane and methanol caused

decomposition to compounds which are formed by reductive dechlorination as well as polar substances.

HWANG, S. W. Effect of TCDD on biliary excretion of indocyanine green. *Environ. Health Perspect* (No. 5): 227 (1973).

Bile flow and biliary excretion of indocyanine green (ICG) in male rats 1, 7, and 16 days after receiving a single oral dose of 5 or 25 μg/kg TCDD. Bile flow rate increased at day 1 through day 16. During a 20-min. collection period, both the concentration and total ICG excreted in bile decreased. ICG disappearance rate decreased with time. These effects were dose related. In contrast, the 5 μg/kg dosed rats accumulated more ICG in liver.

JENSEN, S., and RENBERG, L. Various chlorinated dimers present in several technical chlorophenols used as fungicides. *Environ. Health Perspect.* (No. 5): 37 (1973).

The presence of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in 2,4,5-trichlorophenoxy acid esters originates from 2,4,5-trichlorophenol during the manufacturing process. Dimerization occurs when the phenol is produced by the action of alkali on tetrachlorobenzene. All products originating from alkali-treated chlorinated benzenes logically may contain chlorinated dibenzo-*p*-dioxins. Dimers in pentachlorophenol and in 2,4,6-tri- and 2,3,4,6-tetrachlorophenols from direct chlorination of phenol were presented.

JOHNSON, R. L., GEHRING, P. J., and KOCIBA, R.J. Chlorinated dibenzodioxins and pentachlorophenol. *Environ. Health Perspect.* (No. 5): 171 (1973).

Pentachlorophenol enjoys widespread use as a wood preservative. Commercial grades have been found to contain up to 2500 ppm chlorinated dibenzo-*p*-dioxins. The predominant dioxin is octachlorodibenzo-*p*-dioxin, one of the least toxic members. Evaluating pentachlorophenol toxicity in animals revealed that some untoward effects (chloracne, chick edema disease, and histopathologic alterations) were caused by chlorinated dibenzo-*p*-dioxin content. Purified pentachlorophenol did not produce these effects. A new procedure was capable of producing pentachlorophenol containing lowered concentrations of chlorinated dibenzo-*p*-dioxin and devoid of dioxin-like toxic effects.

KEARNEY, P. C., WOOLSON, E. A. ISENSEE, A. R., and HELLING, C. S. Tetrachlorodibenzodioxin in the environment: sources, fate, and decontamination. *Environ. Health Perspect.* (No. 5): 273 (1973).

TCDD does not leach in soils, does not reside in the economic portion of plants growing in contaminated soil, degrades to about 50% after 1 yr in soils, and does not result from microbial or chemical condensation of 2,4,5-trichlorophenol in soil.

KENDE, A. S., and WADE, J. J., Synthesis of new steric and electronic analogs of 2, 3,7,8-tetrachlorodibenzo-*p*-dioxin. *Environ. Health Perspect.* (No. 5): 49 (1973).

Structural-activity relationships for a series of TCDD analogs were accomplished emphasizing chemical studies in an attempt to distinguish steric from electronic requirements for toxicity. Catechol condensation was used to explore the scope and limitations of polyhalobenzene electrophiles.

KING, M. E., and SHEFNER, A. M., Carcinogenesis bioassay of chlorinated dibenzodioxins and related chemicals. *Environ. Health Perspect.* (No. 5): 163 (1973).

Chlorinated dibenzodioxins were dissolved in acetone and applied to the backs of mice three times a week to assess the activity of dioxins as complete carcinogens and/or promoting agents. Octachlorodioxin caused skin tumor formation in only one female mouse. No other dioxin produced papillomas.

LANGER, H. G. Formation of dibenzodioxins and other condensation products from chlorinated phenols and derivatives. *Environ. Health Perspect.* (No. 5): 3 (1973).

Chlorodioxins are formed in a two-step condensation reaction from ortho-substituted halophenoxy radicals or anions. Reaction of chlorine with pentachlorophenol at elevated temperature proceeds by radicals; anionic condensation products result from strongly exothermic reactions of alkali metal salts of chlorinated phenols above 300° C. Reaction product distribution depends on the total number of halogen substituents, the crystal lattice arrangement of the molecule, steric effects, and an electronic effect. Dioxin formation was the major condensation product only for sodium pentachlorophenate.

LUCIER, G. W., MCDANIEL, O. S., FOWLER, B. A., FAEDER, E., HOOK, G., and SONAWANE, B. R. Studies on TCDD-induced changes in rat liver microsomal and mitochondrial enzymes. *Environ. Health Perspect.* (No. 5): 199 (1973).

A single oral dose of 5 or 25 μg/kg was administered to male rats and time-course measurements were made on some hepatic microsomal and mitochondrial enzymes. Cytochrome P–450 and b–5 contents were increased, hydroxylation of aniline

was induced, microsomal protein contents were increased, aminopyrine demethylation rates were decreased, and most strikingly UDP glucuronyltransferase was increased about 8-fold.

MARTIN, R. L., PORTER, M. L., POMERANTZ, I. H. Studies on the formation potential and presence of chlorinated dibenzofurans in chlorinated biphenyls. NIEHS conference, April 2–3, 1973.

Chlorinated dibenzofurans may arise by photochemical alteration of chlorinated biphenyls under appropriate conditions; this did not occur with pentachlorobiphenyl or 2,2'-dichlorobiphenyl.

MATSUMURA, F., and BENEZET, H. J. Studies on the bioaccumulation and microbial degradation of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. *Environ. Health Perspect.* (No. 5): 253 (1973).

Most organisms capable of degrading other chlorinated hydrocarbons showed no ability to metabolize TCDD; a few exhibited a limited degree of TCDD-metabolizing activity. TCDD leached from sand to organic soil much less than did DDT. With pesticide-coated sand in aquaria containing various organisms, TCDD had the lowest biologic accumulation and affinity.

MESELSON, S. Vietnam dioxin contamination. Center for Short-Lived Phenomena, Event 51–73, No. 1611, Smithsonian Institute, Cambridge, Mass. (April 19, 1973).

Various fish and shellfish collected in 1970 from the Dong Nai and Saigon Rivers and along the Can Guo Coast contained dioxin; catfish had the highest concentration.

MESELSON, S. Vietnam dioxin contamination. Center for Short-Lived Phenomena, Event 51–73, No. 1627, Smithsonian Institute, Cambridge, Mass. (8 May 1973).

Samples of fish and crustaceans caught in Vietnam in September 1970 were analyzed for dioxin content by using mass spectrometry. Dioxin concentrations ranged from 18 to 814 ppt; Dong Nai river carp averaged 540 ppt dioxin.

MILLER, R. A., NORRIS, L. A., and HAWKES, C. L. Acute and chronic toxicity of 2,3,-7,8-tetrachlorodibenzo-*p*-dioxin (dioxin) in aquatic organisms. *Environ. Health Perspect.* (No. 5): 177 (1973).

Guppies and coho salmon fingerlings were exposed to dioxin concentrations ranging from 0.056 ppt to more than 0.2 ppb for 24, 48, and 96 hrs. The initial concentration was found to be more important in causing death than duration of exposure. The coho salmon fingerlings threshold response level for all exposure periods was between 0.056 and 0.56 ppt dioxin. Mosquito larvae, oligochaete worms, and pulminator snails were maintained in water initially dosed with 0.2 ppb dioxin. These aquatic organisms were less sensitive than fish.

MOORE, J.; GUPTA, B.; VOS, J.; ZINKL, J. Postnatal effects of maternal exposure to TCDD. *Environ. Health Perspect.* (No. 5): 81 (1973).

Maternal exposure of C5731/6 mice to TCDD caused dose-related variations in fetal kidney maturation and development. Thymuses were reduced in size; cystic kidneys developed. Mean body weights and thymus and spleen weights (absolute and relative) were reduced in litters whose mothers received 10 μg/kg TCDD; the 3 μg/kg dose group exhibited no weight deviations. Kidney effects were seen at both dose levels.

NEUBERT, D., ZENS, P., and ROTHENWALLNER, A. Survey of the teratogenic effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in mammalian species. *Environ. Health Perspect.* (No. 5): 67 (1973).

The frequency of cleft palate induction was used as a criterion of the teratogenic effects of TCDD. Dose-response relationships and potentiating effects of TCDD with other agents were presented.

NIEHS Conference on Chlorinated Dibenzodioxins and Dibenzofurans. National Institute of Environmental Health Sciences, Research Triangle Park, N.C. (April 2–3, 1973).

The two-way conference reviewed critically and summarized the world literature and research activities on the chlorinated derivatives of dibenzodioxin and dibenzofuran. Approximately 35 papers were presented on all aspects ranging from chemical nature to ultimate biologic effects. More than 110 scientists were in attendance. The proceedings are given in full in *Environmental Health Perspectives*, Experimental No. 5, (1973). (this issue).

NORBACK, D. H., and ENGBLOM, J. F. Chlorinated dibenzo-*p*-dioxin distribution within rat tissues and subfractions of the liver. *Fed. Proc.* 32(3): 236 (1973) Abstract 138.

Radioactivity from orally intubated ^{36}Cl-labeled octachlorodibenzo-*p*-dioxin in rats was confined to the liver, adipose tissue, and skin after 7 weeks on a control diet; concentrations were about 20% that in tissues of rats after 21 days.

NORBACK, D. H., ENGBLOM, J. F., and ALLEN, J. R. Chlorinated dibenzo-*p*-dioxin distribution within rat tissues and subfractions of the liver. *Environ. Health Perspect.* (No. 5): 233 (1973).

Male rats received daily for 21 days 100 μg ^{36}Cl-labeled octachlorodibenzo-*p*-dioxin by gastric intubation. Feces contained 95% of the total dose and urine 4%. Significant levels were found in the kidneys, heart, and serum. The liver contained the highest concentration per unit weight; adipose tissue had 1/3 that of the liver. Microsomes (rough and smooth fractions) had 95% of the liver radioactivity. Urine radioactivity resided in the lipid fraction.

NOVICK, S. Dioxin. *Environment* **15**(4): 23–24 (May 1973).

A news item reports the detection of dioxin in fish and shellfish used for food in Vietnam.

PLIMMER, J. R., RUTH, J. M., and WOOLSON, E. A. Mass spectrometric identification of the hepta- and octa-chlorinated dibenzo-*p*-dioxins and dibenzofurans in technical pentachlorophenol. *J. Agr. Food Chem.* **21**(1): 90–93 (1973).

The presence of contaminant dioxins and dibenzofurans in some samples of technical pentachlorophenol were confirmed by using mass spectrometry. Three samples collected in 1970 contained hexachlorodibenzo-*p*-dioxin (0.5 to 37 ppmw) and heptachlorodibenzo-*p*-dioxin (90 to 135 ppmw). It was reemphasized that high-resolution spectra do not provide chlorine orientation information.

PLIMMER, J. R. Technical pentachlorophenols—origin and analysis of base-insoluble contaminants. *Environ. Health Perspect.* (No. 5): 41 (1973).

Fats used as feed additives from hides preserved with technical pentachlorophenol have been implicated as a source of chick edema factor. Polychlorinated dibenzodioxins and dibenzofurans have been identified in the neutral fractions of pentachlorophenol by gas chromatography, mass spectrometry, and a combination of these two.

POHLAND, A. E., YANG, G. C., and BROWN, N. Analytical and confirmative techniques for dibenzo-*p*-dioxins based upon their cation radicals. *Environ. Health Perspect.* (No. 5): 9 (1973).

Chlorinated dibenzo-*p*-dioxins form cation radicals when dissolved in strong acids such as trifluoromethane sulfonic acid, in the presence of ultraviolet light, or an oxidizing agent like potassium nitrate. These cation radicals are quantified by using electron spin resonance and visible spectroscopic techniques. A general bathochromic shift was observed with increasing chlorine content. These shifts were dependent upon the position of the chlorine atoms.

POLAND, A. P., and GLOVER, E. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin: A potent inducer of δ-aminolevulinic acid synthetase. *Science* **179**(4072): 476–677 (Feb. 2, 1973).

As little as 4.66×10^{-12} mole (1.5 ng) of TCDD per egg induced hepatic-aminolvulinic acid synthetase (ALAS) activity in the chick embryo. Enzyme induction was dose-related and prolonged in time: 70% of the maximum induced activity was present 5 days after a single 150 ng dose. TCDD was linked to an outbreak of porphyria cutanea tarda where 2,4,5-T was synthesized and manufactured. At least three of the 2,3,7, and 8 positions on the ring must be occupied to induce ALAS.

POLAND, A. P., and GLOVER, E. Studies on the mechanism of action of the halogenated dibenzo-*p*-dioxins. *Environ. Health Perspect.* (No. 5): 245 (1973).

Aminolevulinic acid synthetase (ALAS) was stimulated by TCDD in the chick embryo liver; 4.66×10^{-12} mole/egg (1.5 ng) caused doubling of ALAS activity and 1.55×10^{-9} mole/egg (0.5 μg) caused a 35-fold stimulation of enzyme activity. A single dose of TCDD stimulates hepatic aryl hydrocarbon hydroxylase (AHH) and cytochrome P–450 for 35 days and more in the rat. AHH activity was induced in chick embryo liver. It is suggested that the chemically inert parent compound is not the toxic moiety, but that a highly reactive intermediate causes cell damage.

SCHWETZ, B. A., NORRIS, J. M., SPARSCHU, G. L., ROWE, V. K., GEHRING, P. J., EMERSON, J. L.; GERBIG, C. G. Chlorodibenzo-*p*-dioxin toxicology. *Environ. Health Perspect.* (No. 5): 87 (1973).

2,7-Dichlorodibenzo-(DCDD), 2,3,7,8-tetrachlorodibenzo-(TCDD), hexachlorodibenzo-(HCDD), and octachlorodibenzo-*p*-dioxin-(OCDD) were evaluated toxicology. TCDD and HCDD were acnegenic, embryo toxic (TCDD markedly so), teratogenic, and positive for chick edema factor (CEF). DCDD and OCDD were negative for acnegenicity, teratogenicity, and CEF; OCDD was embryotoxic, while DCDD was not. The lethal dose range for DCDD, TCDD, HCDD, and OCDD was g/kg, μg/kg, mg/kg, and g/kg, respectively.

SHAPLEY, D. Herbicides: AAAS study finds dioxin in Vietnamese fish. *Science* **180** (4083): 285–286 (April 20, 1973).

Fish and shellfish from areas of South Vietnam that were heavily sprayed during the U. S. defoliation campaign contained significant quantities of dioxin. This is a news report on the data R. Baughman and M. Meselson presented to the NIEHS Conference on chlorinated dibenzodioxins and dibenzodifurans.

SHAPLEY, D. Herbicides: Agent Orange stockpile may go to the South Americans. *Science* 180(4081): 43–45 (April 6, 1973).

The U. S. Air Force has a surplus stockpile of 2,338,900 gal of Agent Orange (50% 2,4,5-T and 50% 2,4-D); some of these mixtures contain as much as 28 times the maximum acceptable safety limit of dioxin. Presently, dioxin concentrations permissible for new herbicides are 0.1 ppm and 0.5 ppm for stocks already manufactured.

VOS, J. G., MOORE, J. A., and ZINKL, J. Effect of TCDD on the immune system of laboratory animals. *Environ. Health Perspect.* (No. 5): 149 (1973).

TCDD at sublethal dose levels caused atrophy of the thymus, suppressed the cell-mediated immunity in both guinea pigs and mice, but did not affect the humoral immunity in guinea pigs.

WALDBOTT, G. L. *Effects of Environmental Pollutants.* C. V. Mosby Co., St. Louis, Mo., 1973.

Dioxin compounds are listed with other environmental pollutants as examples of airborne pollutants. These substances are contaminants of the popular weed killer, 2,4,5-T. Dioxins caused death and gastrointestinal hemorrhage in rat fetuses when mothers were treated with doses of 0.125 to 8 μg. The mutagenic effects are due to its intercalation with DNA. Dibenzofurans were implicated as being responsible for some of the toxic effects attributed to PCBs.

WEBBER, T. J. N., and BOX, D. G. The examination of tetrachlorvinphos and its formulations for the presence of tetrachlorodibenzo-*p*-dioxins by a gas-liquid chromatographic method. *Analyst* 98: 181–189 (1973).

A gas–liquid chromatographic analytical method was developed for use in detecting tetrachlorodibenzo-*p*-dioxin impurities in samples of the insecticide tetrachlorvinphos and its formulations. Tetrachlorvinphos is the Z- or *trans*-styrene isomer of 2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate. Sequential use of silica gel and aluminum oxide column chromatography followed by concentrated sulfuric acid treatment of the resultant eluate made it possible to detect TCDD levels down to a limit of 0.025 ppm with electron-capture detection. Tetrachlorodibenzo-*p*-dioxins were not detected in any of the 21 tetrachlorvinphos samples or any of its formulations selected for analysis either before or after accelerated storage at 55°C for 2 weeks.

WEISSBERG, J., and ZINKL, J. Effects of TCDD upon hemostasis and hematologic function in the rat. *Environ. Health Perspect.* (No. 5): 119 (1973).

Daily oral doses of 10 μg/kg TCDD to female rats for 10 and 14 days caused nonspecific alterations of hematopoietic function, thrombocytopenia, thrombocytoasthenia, and derangements in blood coagulation. Platelet aggregation, bleeding time, and platelet factor III activity were normal, but clot retraction was abnormal.

WILSON, J. G. Teratological potential of 2,4,5–T. *Down to Earth* 28(4): 14–17 (Spring 1973).

A chronology of the hazards of 2,4,5-T is presented. The report issued by the President's Science Advisory Committee appointed to study the 2,4,5-T question served as the basis for this review. The dioxin contaminant of 2,4,5-T, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, is discussed briefly as a toxicogen.

WOODS, J. S. Studies of the effects of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin on mammalian hepatic δ-aminolevulinic acid synthetase. *Environ. Health Perspect.* (No. 5): 221 (1973).

No differences in hepatic δ-aminolevulinic acid synthetase activity were seen in control rats and those receiving orally 5, 25, or 100 μg/kg TCDD for up to 30 days. Mice and guinea pigs were also nonreactive. Thus, TCDD is not porphyrogenic in mammals, even at several times the LD_{50} dose levels.

ZINKL, J., MOORE, J. A., VOS, J. G., and GUPTA, B. N. Hematologic and clinical chemical effects of 2,3,7,8-tetrachlorodibenzodioxin in laboratory animals. *Environ. Health Perspect.* (No. 5): 111 (1973).

TCDD-induced changes observed in female rats after 10 days treatment with 10 μg/kg and 17 days at 1 μg/kg were increases in serum glutamic oxaloacetic transaminase. After 13 days treatment with 10 μg/kg serum glutamic pyruvate transaminase was increased. Platelet depression was observed after 10 days at all dose levels.

ZITKO, V., WILDISH, D. J.; HUTZINGER, O., and CHOI, P. M. K. Acute and chronic oral

toxicity of chlorinated dibenzofurans to salmonid fishes. *Environ. Health Perspect.* (No. 5) : 187 (1973).

Dry fish food was fed to juvenile Atlantic salmon contaminated with a mixture of 2.7 μg/g di-, 5,7 tri-, 2.8 tetra-, and 9.1 octachlorodibenzofuran. Median mortality was 12 ± 30 days. Only octachlorodibenzofuran was found in tissues of dead fish (0.03 μg/g in muscle and 0.2 μg/g in the gut). Fish surviving 140 days feeding contained corresponding values of 0.01 and 0.02 μg/g.

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ABELSON, P. H. Pollution by organic chemicals. *Our Chemical Environment*, J. C. Giddings and M. D. Monroe, Eds., Canfield Press, San Francisco, 1972, Chap. 28, pp. 183–184.

The most toxic chlorine-containing compound known is 2,3,7,8-tetrachlorodibenzodioxine ($C_{12}H_4O_2Cl_4$), often called dioxin. The acute oral LD_{50} dose in male guinea pigs is about 10^{-6} g/kg. In spite of its toxicity, the behavior of dioxin in the food chain has not been worked out.

ANONYMOUS. TCDD residues disappear. *Agr. Res.* **21**(4) : 6 (1972).

The 2,4,5-T contaminant, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), can be formed during synthesis of some chlorinated phenols if high temperatures are used.

ANONYMOUS. Research heightens concern over PCB's. *Chem. Eng. News* **50**(10) : 27–28 (1972).

Certain polychlorinated biphenyls may contain traces of tetrachlorodibenzofuran. A contaminant found in PCB's, not conclusively identified, has the same mass spectrum as tetrachloro-*p*-dibenzofuran.

ANONYMOUS. Dioxin with a bang! *Food Cosmet. Toxicol.* **10**(1) : 110–111 (1972).

During a manufacturing plant explosion, dioxin was formed by the interaction of sodium 2,4,5-trichlorophenate molecules under the influence of the exothermic decomposition of sodium 2-hydroxyethoxide.

ANONYMOUS. . . . But 2,4,5–T is in the dock again. *Food Cosmet. Toxicol.* **10**(5) : 722 (1972).

Negative teratogenic results have been reported for rats and rabbits treated with 2,4,5-T samples with very minute levels of dioxin impurity. Teratogenic effects have been detected, however, in three mouse strains treated with 2,4,5-T containing as little as 0.05 or 0.5 ppm dioxin.

ANONYMOUS. 2,4,5–T and dioxins accused of teratogenicity. *Food Chem. News* **13** (43) : 24–27 (Jan. 17, 1972).

Responding to challenges on 2,4,5-T cancellation, EPA concentrated its replies on lack of proof that 2,4,5-T and contaminants are not teratogens. The dose-response curves for 2,4,5-T and dioxin (TCDD) have not been determined, and the possibility of no effect levels is only a matter of conjecture.

ANONYMOUS. FDA annual report shows increase in enforcement. *Food Chem. News* **13**(47) : 20 (Feb. 14, 1972).

In the herbicide section of its 1971 annual report, FDA said the toxicity of 2,4,5-T is chiefly due to dioxins.

ANONYMOUS. Senate settlement expected on pesticides bill. *Food Chem. News* **14** (27) : 53–54 (Sept. 25, 1972).

A wide range of teratogenic dioxins can be produced both in the manufacture of 2,4,5-T and during pyrolysis (incomplete combustion).

BOER, F. P., NEUMAN, M. A., and ANILINE, O. 2,8-Dichlorodibenzo-*p*-dioxin. *Acta Crystallogr.* **B28**(9) : 2878–2880 (1972).

Crystals of 2,8-dichlorodibenzo-*p*-dioxin are orthorhombic; molecules are slightly nonplanar with an unusual packing arrangement.

BOER, F. P., and NORTH, P. P. Crystal and molecular structure of 2,7-dichlorodibenzo-*p*-dioxin. *Acta Crystallogr.* **B28**(5) : 1613–1616 (1972).

Three-dimensional single-crystal x-ray diffraction data revealed the crystal and molecular structure of 2,7-dichlorodibenzo-*p*-dioxin. The C–Cl bond distance is 1.742 A, the C–0 distances are 1.380 and 1.382, and the 6 C–C distances range between 1.370 and 1.397. The C–O–C angle in the heterocyclic ring is 116.3°.

BOER, F. P., VAN REMOORTERE, F. P., and MUELDER, W. W. Preparation and structure of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and 2,7-dichlorodibenzo-*p*-dioxin. *J. Amer. Chem. Soc.* **94**(3) : 1006–1007 (1972).

The preparation, isolation, and isometric structures of 2,3,7,8-tetrachloro and 2,7-dichlorodibenzo-*p*-dioxin are described.

BOER, F. P., VAN REMOORTERE, F. P., NORTH, P. P., and NEUMAN, M. A. Crystal and molecular structure of 2,3,7,8-tetrach-

lorodibenzo-*p*-dioxin. *Acta Crystallogr.* B28(4): 1023–1029 (1972).

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin was studied by using three-dimensional single-crystal x-ray diffraction. The four unique C–Cl distances range from 1.726 to 1.730 A, the 4 C–O distances from 1.377 to 1.379, and the 12 C–C bonds are all between 1.374 and 1.388. The C–O–C angles are 115.6° and 115.8°.

BRENNER, K. S., MULLER, K., and SATTEL, P. Detection and determination of 2,3,7,8-tetrachloro dibenzo-*p*-dioxin in chloro-substituted phenoxyalkane acids. *J. Chromatogr.* 64: 39–48 (1972).

Dioxin separation from the herbicide phenoxyalkane acids was accomplished by extractive distillation of the potassium salts with *n*-hexane in the Bleidner apparatus. Quantitative determination of the hexane extracts for dioxin was done by gas chromatography. Sensitivity was about 0.1 ppm.

BROOKS, G. T. Pesticides in Britain. In: Environmental Toxicology of Pesticides, F. Matsumura, G. M. Boush, and T. Misato, Eds., Academic Press, New York, 1972, pp. 61–114.

The reported teratogenic effects of 2,4,5-T in mammals and the isolation of the highly toxic contaminant tetrachlorodibenzo-*p*-dioxin are cautionary, but 2,4,5-T has been used in Europe for nearly 15 years without evidence of ill effects. More studies are needed in comparative detoxication between mammals, birds, fishes, and insects.

BROWNRIGG, J. T., EASTWOOD, D., and HORNIG, A. W. Identification of polychlorinated biphenyls in the presence of DDT-type compounds. Office of Research and Monitoring, U.S. Environmental Protection Agency, Washington, DC (Oct. 1972), EPA–R2–72–004.

Low temperature (77°K) luminescence techniques could in principle be applied to a wide variety of compounds including the highly toxic chlorinated dibenzofurans and dibenzo-*p*-dioxins.

BUU-HOI, N. P., CHANH, P-H., SESQUE, G., AZUM-GELADE, M. C., and SAINT-RUF, G. Enzymatic functions as targets of the toxicity of "dioxin" (2,3,7,8-tetrachlorodibenzo-*p*-dioxin). *Naturwiss.* 59(4): 173–174 (1972).

Following a single I.P dose of 10 mg/kg dioxin to rats, deep pertubations in several enzymatic systems were observed, i.e., a decrease in cholinesterase or an increase in serum glutamic oxaloacetic acid transaminase. Effects in homeostasis indicate the liver is one of the main targets for dioxin intoxication.

BUU-HOI, N. P., CHANH, P-H., SESQUE, G., AZUM-GELADE, M.C.; Saint-Ruf, G. Organs as targets of "dioxin" (2,3,7,8-tetrachlorodibenzo-*p*-dioxin). *Naturwiss.* 59(4): 174–175 (1972).

Organ damage was found along with weight loss and hematologic effects following IP injection of 1 and 10 mg/kg dioxin to rats. Ten days after treatment, damage was observed to the liver, thymus, heart. Less damage was observed in the lungs and blood cells.

BUU-HOI, N. P., SAINT-RUF, G., and MANGANE, M. Fragmentation of dibenzo-*p*-dioxin and its derivatives under electron impact. *J. Heterocycl. Chem.* 9(3): 691–693 (1972).

Mass spectra were reported and discussed on five chloro derivatives of dibenzo-*p*-dioxin: 2,7-dichloro-, 1,6-dichloro-, 1,3,6-trichloro-, 2,3,7,8-tetrachloro-, and 1,2,3,4,6,7,8,9-octachlorodibenzo-*p*-dioxin.

CHEN, J. T. Infrared studies of chlorinated dibenzo-*p*-dioxins and structurally related compounds. Division of Pesticide Chemistry, 164th National Meeting of the American Chemical Society, New York, Aug. 27–Sept. 1, 1972, Abstract No. 12.

Data are reported on the reference infrared spectra of 24 chlorinated dibenzo-*p*-dioxins and the observed characteristic frequencies are tabulated.

COURTNEY, K. D. The teratogenic evaluation of the herbicide 2,4,5-T and dioxin. Item 4.0785, Page 1–632. Part 4. Pesticides, Environmental Protection Research Catalog, Research Information Division, U.S. EPA, Washington, D.C., Jan. 1972.

Phenoxyacetic acid herbicides and dioxins are being evaluated for teratogenic and perinatal toxic effects.

CROSBY, D. G., MOILANEN, K. W., NAKAGAWA, M., and WONG, A. S. Photonucleophilic reactions of pesticides. *Environmental Toxicology of Pesticides*, F. Matsumura, G. M. Bousch, and T. Misato, Eds., Academic Press, New York, 1972, pp. 423–433.

Photonucleophilic displacement of chloride by chlorophenoxide ion in *o*-chlorophenols introduced

the possibility of the photochemical generation of chlorinated dibenzo-*p*-dioxins. Sunlight wavelengths exposure to sodium pentachlorophenate yielded 1,2,3,4,6,7,8,9-octachlorodibenzo-*p*-dioxin; no 2,3,7,8-TCDD resulted from irradiated 2,4,5,-T or 2,4,5-trichlorophenol.

CUNNINGHAM, H. M., and WILLIAMS, D. T. Effect of tetrachlorodibenzo-*p*-dioxin on growth rate and the synthesis of lipids and proteins in rats. *Bull. Environ. Contam. Toxicol.* 7(1) : 45–51 (1972).

Protein concentration in the rat liver was slightly reduced 3 days after dioxin treatment. This decrease was accompanied by a significant increase in ^{14}C-leucine incorporation into liver proteins. The lowest single dose of dioxin that caused an increase in rat liver weight was 0.1 μg/kg

CURLEY, A., BURSE, V. W., and JENNINGS, R. Metabolite or contaminant of Aroclor 1254® found in rat urine. Division of Pesticide Chemistry, 163rd National Meeting of the American Chemical Society, Boston, April 9–14, 1972, Abstract No. 5.

Mass spectra of urine collected from rats on dietary levels of 100 or 500 ppm Aroclor 1254 for intervals up to eight months indicated the presence of a molecular ion at m/e 304 and the characteristic isotopic cluster of 4 chlorine atoms. Others have shown the presence of tetra and pentadibenzofurans (mass numbers 304 and 338) as contaminants in the foreign products.

ENVIRONMENTAL PROTECTION AGENCY, PUBLICATIONS AND INFORMATION SECTION. Chemistry and residues of 2,4,5-T (includes dioxins). Bibliography Number 72–59 (1972).

A reference list of 43 references is given.

ENVIRONMENTAL PROTECTION AGENCY, PUBLICATIONS AND INFORMATION SECTION. Toxicology and pharmacology of 2,4,5-T (includes dioxins). Bibliography Number 72–58 (1972).

A list of 75 references is given.

EPSTEIN, S. S. Environmental pathology. A review. *Amer. J. Pathol.* 66(2) : 352–373 (1972).

Toxicity testing must not be confined to the test agent *per se*, but should be extended to its chemical and metabolic derivatives, its pyrolytic and degradation products and its contaminants and reaction products, especially when various derivatives or degradation products are of toxicologic or environmental consequence. Dioxin pyrolytic products in phenoxy herbicides are illustrative.

FIRESTONE, D., RESS, J., BROWN, N. L., BARRON, R. P., and DAMICO, J. N. Determination of polychlorodibenzo-*p*-dioxins and related compounds in commercial chlorophenols. *J. Assoc. Offic. Anal. Chem.* 55(1) : 85–92 (1972).

Twenty-one commercial chlorophenols were dissolved separately in aqueous alkali, extracted with petroleum ether, fractionated on an alumina column, and examined by electron capture gas chromatography and combined gas chromatography–mass spectrometry. The 2,3,7,8-tetrachlorodioxin was found in 3 of 6 samples of 2,4,5-trichlorophenol but not in any of the 11 samples of tetra- and pentachlorophenol. Hexachlorodioxin, present in all 8 pentachlorophenols tested, ranged from 0.17 to 39 ppm. Hexa-, hepta-, and octachlorodioxins and chlorofurans were present in most of the tetra- and pentachlorophenols.

FISHBEIN, L. Human directed aspects of PCBs. In: *Polychlorinated Biphenyls and the Environment*, Report No. ITF–PCB–72–1, (COM–72–10419), Interdepartmental Task Force on PCBs, Washington, D.C., May, 1972, pp. 122–151.

Work reported previously in the literature was summarized. Emphasis was placed on the tetra- and pentachlorodibenzofuran impurities in commercial PCB products; the tri- and tetrachlorodibenzofuran single oral liver necrotic dose (0.5 to 1.0 mg/kg) in rabbits; and the 2,3,7,8-tetrachlorodibenzo-*p*-dioxin contaminant in 2,4,5–T and 2,4,5-trichlorophenol caused lethal liver necrosis and chloracne in rabbits at a dose range of 0.05 to 0.1 mg/kg.

FISHBEIN, L. Chromatographic and biological aspects of polychlorinated biphenyls. *J. Chromatog.* 68(1) : 345–426 (1972).

Chromatographic methods of analysis for chlorinated dibenzofurans were reviewed as part of a more extensive review of polychlorinated biphenyls.

FISHBEIN, L., and FLAMM, W. G. Potential environmental chemical hazards. Part II. Feed additives and pesticides. *Sci. Total Environ.* 1: 31–64 (1972).

The action of alkali on 1,2,4,5-tetrachlorobenzone, a by-product from lindane synthesis, produces 2,4,5-trichlorophenol which, when interacted with sodium monochloracetate, yields 2,4,5-T. The chloracnegen, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, is an impurity produced in the manufacture of 2,4,5-T: 1,2,4,5-tetra-

chlorobenzene under the influence of high pressure and temperature, methanol, and sodium hydroxide, is converted to sodium trichlorophenate which reacts with another molecule of sodium trichlorophenate which reacts with another molecule of sodium trichlorophenate with high temperatures to form TCDD; or two molecules of trichlorophenol combine to form TCDD.

GOLDMANN, P. J. Severe acute chlorine acne caused by trichlorophenol decomposition products: A contribution to the perna problem. *Arbeitsmed. Sozialmed. Arbeitshyg.* 7(1): 12–18 (1972) (Ger.).

Occupational and case histories are reported describing 2,3,6,7-tetrachlorodibenzodioxin as the causative agent in 42 cases of serious skin changes, 14 cases of internal organ damage, and 7 cases of nervous system disturbances.

GREIG, J. B. Effect of 2,3,7,8-tetrachlorodibenzo-1,4-dioxin on drug metabolism in the rat. *Biochem. Pharmacol.* 21(23): 3196–3198 (1972).

Rats given a single oral 200 μg/kg dose of dioxin exhibited a decreased duration of zoxazolamine (100 mg/kg IP) induced paralysis by 54%. After 200 μg/kg oral dioxin, sleeping time induced by hexabarbital, 150 mg/kg (male rats) or 75 mg/kg (female rats), was prolonged—more than double at 3 days. These results indicate that dioxin has simultaneous stimulatory and inhibitory effects on different pathways of oxidative drug metabolism in the rat liver.

HAMMOND, A. L. Chemical pollution: polychlorinated biphenyls. *Science* 175 (4018): 155–156 (Jan. 14, 1972).

Some commercial PCB mixtures, especially those manufactured in Europe or Japan, may contain trace amounts of dibenzofurans or other toxic impurities. These may be the cause of some toxic effects of the PCBs.

HUSSAIN, S., EHRENBERG, L., LOFROTH, G., and GEJVALL, T. Mutagenic effects of TCDD on bacterial systems. *Ambio* 1(1): 32–33 (1972).

Results from three distinct bacterial assay systems showed TCDD to be mutagenic: (1) reversion to streptomycin independency in *E. coli* SD-4, (2) reversion to histidine prototrophy in *Salmonella typhimurium* strains, and (3) prophage induction in *E. coli* K-39. The results indicated that an acridine-like behavior of DNA intercalation may have caused these genetic effects.

HUSTON, B. L. Identification of three neutral contaminants in production grade 2,4-D. *J. Agr. Food Chem.* 20(3): 724–727 (1972).

Three chemical impurities of 2,4-D are profiled. These contaminants interfere with the gas–liquid chromatographic analysis of 2,4-D for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin.

JACKSON, W. T. Regulation of mitosis. III. Cytological effects of 2,4,5-trichlorophenoxyacetic acid and of dioxin contaminants in 2,4,5-T formulations. *J. Cell Sci.* 10: 15–25 (1972).

Inhibition of mitosis and development of cytological abnormalities observed in dividing endosperm cells of the African blood lily were believed caused by 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, a contaminant of 2,4,5-T, rather than the herbicide itself. In contrast to 2,4,5-T, which has no effect, dramatic inhibition of mitosis was observed in cells subjected to 0.2 to 1.0 μg/l dioxin, 0.2 μg/l dioxin plus $10^{-4}M$ 2,4,5-T, or $10^{-4}M$ 2,4,5-T containing dioxin as a contaminant. These preparations also induced formation of dicentric bridges and chromatin fusion with formation of multinuclei or a single large nucleus.

JENSEN, S. The PCB story. *Ambio* 1(4):123–131 (1972).

The work of Vos et. al. is reported. Tetra- and pentachlorodibenzofuran impurities in commercial PCBs may have been formed from a phenolic contaminant in PCB in similar manner as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin is formed from 2,4,5-T.

JENSEN, S., and RENBERG, L. Contaminants in pentachlorophenol: chlorinated dioxins and predioxins (chlorinated hydroxydiphenylethers). *Ambio* 1(2): 62–65 (1972).

Octachlorodioxin and 2-hydroxynonachlorodiphenyl ether (labeled predoxin) were identified in technical pentachlorophenate using ion exchange, diazomethane treatment, gas chromatography–mass spectrometry, and thinlayer chromatography. Predioxins have not been discovered or detected previously because: (1) clean-up procedures remove the substance, e.g., alumina column chromatography or concentrated sulfuric acid treatment of extract, (2) predoxin spontaneously forms dioxin in a gas chromatograph.

KEARNEY, P. C., WOOLSON, E. A., and ELLINGTON, C. P. Persistence and metabolism of chlorodioxins in soils. *Environ. Sci. Technol.* 6(12): 1017–1019 (1972).

Persistence of 1, 10, or 100 ppm 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) was determined by electron-capture gas chromatography in soils after 20,

40, 80, 160, and 350 days. After 1 yr, 56–63% TCDD was recovered. Neither 2,7-dichlorodibenzo-*p*-dioxin (DCDD) nor TCDD was detected in soils receiving 10, 100, or 1000 ppm 2,4-D or 2,4,5-T after 70 days. TCDD is degraded slowly in soils. TCDD and DCDD are not biosynthesized by microbial condensation reactions.

KHERA, K. S., and MCKINLEY, W. P. Pre- and postnatal studies on 2,4,5-trichlorophenoxyacetic acid, 2,4-dichlorophenoxyacetic acid and their derivatives in rats. *Toxicol. Appl. Pharmacol.* 22: 14–28 (1972).

2,4,5-T (containing less than 0.5 mg/kg 2,3,7,8-tetrachlorodibenzo-*p*-dioxin) induced fetopathy and skeletal anomalies in progeny from females treated with a single daily oral dose of 100 to 150 mg/kg on gestation days 6 to 15. Number of conceptions and numbers of viable and dead fetuses per litter gave no indication that *in utero* treatment of offspring with up to 100 mg/kg 2,4,5-T had impaired fertility.

KIMBROUGH, R. D. Toxicity of of chlorinated hydrocarbons and related compounds. A review including chlorinated dibenzodioxins and chlorinated dibenzofurans. *Arch. Environ. Health* 25(2): 125–131 (1972).

Trace amounts of chlorinated dibenzofurans and dibenzodioxins were identified as contaminants in many chlorinated technical compounds, e.g., 2,4,5-trichlorophenol, 2,4,5-trichorophenoxyacetic acid (2,4,5-T), and European chlorinated biphenyls (Phenoclor DP6 and Clophen A60). Toxic fat containing chick edema factor also contained chlorinated dibenzodioxins.

KINS, N., and BARANDY, J. Short method for the detection of chick edema factor in fats, oils, and fatty acids by electron capture gas chromatography. *J. Amer. Oil Chem. Soc.* 49(2): 115–117 (1972).

A modification of the official electron capture-gas chromatographic AOAC assay for chick edema factor, e.g., hexa-, hepta-, and octachlorodibenzo-*p*-dioxins, was presented to shorten the assay time and eliminate problems in the alumina column fractionation. In place of the alumina fractionation following 2,2,4-trimethylpentane extraction, a second sulfuric acid treatment and a caustic wash were done before the final sulfuric acid wash.

KRAYBILL, H. F. Chemical and physical properties of PCBs. In: Polychlorinated Biphenyls and the Environment, Report No. ITF-PCB-72-1, (COM-72-10419), Interdepartmental Task Force on PCBs, Washington, D.C. (May 1972). pp. 22–40.

Tetrachlorodibenzofuran (mass number 304) and pentachlorodibenzofuran (mass number 338) were identified from a fractionated PCB sample.

MAIER-BODE, H. Contribution to 2,4,5-T question. *Anz. Schaedlingskd. Pflanzenschutz* 45(1): 2–6 (1972) (Ger.).

The teratogenic effect of 2,4,5-T in an earlier U.S. experiment is attributable to the content (30 ppm) of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in the test sample.

MARTIN, H. (Ed.). Pesticide Manual. Basic Information on the Chemicals used as Active Components of Pesticides, 3rd. ed. British Crop Protection Council, Worcester, England (1972).

A contaminant of 2,4,5-T (2,3,7,8-tetrachlorodibenzo-*p*-dioxin) caused serious acne in man and produced fetal death in hamsters at 9.1 μg/kg. Modern methods of synthesis now limit the dioxin concentration in 2,4,5-T to less than 0.5 ppm.

MATSUMURA, F. Biological effects of toxic pesticidal contaminants and terminal residues. In: Environmental Toxicology of Pesticides, F. Matsumura, G. M. Boush, and T. Misato, Eds., Academic Press, New York, 1972, pp. 525–548.

Chlorinated dibenzo-*p*-dioxins have been classified as terminal residues-chemicals which accumulate in biologic material in the environment as a result of pesticide introduction. The presence of terminal residues in the environment is due to stable pesticides, conversion products, and chemical impurities (dioxins) that remain in the environment longer than the principal pesticides. The importance of such terminal residues in relation to the final magnitude of environmental hazardousness needs further definition.

NEUBERT, D., and DILLMANN, I. Embryotoxic effects in mice treated with 2,4,5-trichlorophenoxyacetic acid and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Naunyn-*Schmiedeberg's Arch. Pharmacol.* 272: 243–264 (1972).

Oral doses of 1 μg/kg 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDBD) in NMRI mice on days 6 to 15 of gestation produced cleft palate; embryo mortality was significant for doses of 4.5 μg/kg or more. Cleft palate without pronounced embryo lethality was produced in mice with high single doses (20–50 μg/kg) TCDBD given between days 7 and 13 of pregnancy. A maximum teratogenic effect was

observed on day 11 of gestation, but another peak in cleft palate frequency occurred when TCDBD was given on day 8 of pregnancy.

NEUMAN, M. A., NORTH, P. P., and BOER, F. P. Crystal and molecular structure of octachlorodibenzo-*p*-dioxin. *Acta Crystallogr.* B28(8): 2313–2317 (1972).

Three-dimensional single-crystal x-ray diffraction was used to elucidate the crystal and molecular structure of octachlorodibenzo-*p*-dioxin. The four unique C–Cl distances ranged from 1.714 to 1.718A, the two C–O distances were 1.373 and 1.374, and the six C–C bonds ranged between 1.382 and 1.396. The C–O–C angle was 115.8°.

NORBACK, D. H., and ALLEN, J. R. Chlorinated aromatic hydrocarbon induced modifications of the hepatic endoplasmic reticulum: concentric membrane arrays. Environ. Health Perspect. 1: 137–143 (1972).

Separate groups of rats were fed diets containing 1% highly chlorinated triphenyls (PCTs, Aroclor 5460), 0.02% polychlorinated biphenyls (PCBs, Arochlor 1254), and 0.002% chlorinated diphenyl-*p*-dioxin. The dioxin and PCT groups ate readily and attained 80% of control weight in 3 weeks. Liver hypertrophy varied from moderate enlargement (dioxin group) to an increase in relative liver weight of 8/100 body weight for the PCB and PCT groups.

POHLAND, A. E., and YANG, G. C. Preparation and characterization of chlorinated dibenzo-*p*-dioxins. *J. Agr. Food Chem.* 20(6): 1093–1099 (1972).

A series of 13 chlorinated dibenzo-*p*-dioxins (nine of these were new and previously unreported) was prepared containing from 1 to 8 chlorine atoms to provide pure standards of the various chlorinated derivatives for use in methods development and toxicology studies. Synthesis, utility, yield, purity, and physical and chemical properties were presented and discussed. Stability, color reactions, and infrared, ultraviolet, nuclear magnetic resonance, and phosphorescence spectra were also reported. Phosphorescence and triplet state lifetime wavelengths were dependent on the number of chlorine atoms and their positions on the dibenzo-*p*-dioxin nucleus.

RAPPE, C., and NILSSON, C.-A. An artifact in the gas chromatographic determination of impurities in pentachlorophenol. *J. Chromatogr.* 67: 247–253 (1972).

The main impurity of commercial samples of pentachlorophenol was 3,4,5,6-tetrachloro-2-(2,3,4,5,-pentachlorophenoxy)phenol; this compound underwent ring closure during gas chromatography to 1,2,3,4,6,7,8,9-octachlorodibenzo-*p*-dioxin.

SAINT-RUF, G. Formation of "dioxin" in the pyrolysis of sodium α-(2,4,5-trichlorophenoxy)-propionate. *Naturwiss.* 59 (12): 648 (1972).

A residue of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin resulted from the pyrolysis (500°C for 5 hr) of sodium-α-(2,4,5-trichlorophenoxy)-propionate, a compound used in the synthesis of Sylvex. The dioxin impurity yield was much less than that observed during 2,4,5-T synthesis.

TASK FORCE. Polychlorinated biphenyls and the environment. Report No. ITF–PCB–72–1, (COM–72–10419), Interdepartmental Task Force on PCBs, Washington, DC (May, 1972).

This report emanated from a six-month review on the polychlorinated biphenyls by five Federal agencies. The main emphasis was PCBs; however, numerous statements and discussions centered on chlorinated dibenzodioxins and dibenzofurans. For example, fractionated samples of some PCBs of foreign manufacture contained as contaminants tetra- and pentachlorodibenzofurans. The task force recommended: (1) toxicological evaluation of a select number of representative, purified PCB isomers as well as purified trace contaminants such as the chlorinated dibenzofurans; (2) definitive mammalian elaboration of the kinetics, absorption, distribution, metabolism, and excretion of the technical PCBs as well as a number of key isomers and the chlorinated dibenzofurans; and (3) elaboration of the subcellular and intracellular actions of the technical PCBs as well as a number of representative isomers and chlorinated dibenzofurans.

VASILIU, G., and BACIU, I. Acetylation of some 2,7-dihalodibenzo-*p*-dioxins. *Rev. Chim.* (Bucharest) 23(9): 523–525 (1972) (Rom.).

Reaction of 2,7-dichlorodibenzo-*p*-dioxin with chloroacetic acid in the presence of aluminum chloride and carbon disulfide gave the corresponding 3-monoacetyl derivative. Confirmation was by infrared spectra.

VOS, J. G. Toxicology of PCB's for mammals and for birds. *Environ. Health Perspect.* 1: 105–117 (1972).

Polychlorinated dibenzofurans or other toxic impurities in crude PCB preparations caused difficulty in interpreting toxicity studies.

VOS, J. G. Toxicology of polychlorinated biphenyls (PCB's) and impurities. *Tijdschr. Diergeneesk.* 97(22): 1378–1385 (1972) (Neth).

The most toxic impurities in polychlorinated biphenyls were found to be chlorinated benzofurans.

VOS, J. G., and NOTENBOOM-RAM, E. Comparative toxicity study of 2,4,5,2′,4′,5′,-hexachlorobiphenyl and a polychlorinated biphenyl mixture in rabbits. *Toxicol. Appl. Pharmacol.* 23: 563–578 (1972).

The major acnegenic action of crude PCB mixtures originates from chlorinated dibenzofurans. The probable contribution of chlorinated dibenzofuran and pure PCB to the toxicity of technical PCB preparations in rabbits is discussed: chloracne (–furan ++, PCB +), edema formation (++, –), liver damage (++, +), and hepatic porphyria (–, ++).

WARMBRUNN, K. Considerations regarding the ban or limitation on the use of some pesticides imposed July 23, 1971. *Gesunde Pflanz.* 24(1): 6–8 (1972) (Ger).

The dioxin content of 2,4,5-T produced in Germany is approximately 1 ppm, a level at which malformation hazards are practically eliminated.

WILLIAMS, C. S. The current status of phenoxy herbicides. *Down to Earth* 27(4): 20–24 (Spring 1972).

A chronology of events from April 13, 1966 to December 6, 1971 pertaining to phenoxy herbicides is presented, with particular attention devoted to TCDD.

WILLIAMS, D. T., and BLANCHFIELD, B. J. Screening method for the detection of chlorodibenzo-*p*-dioxins in the presence of chlorobiphenyls, chloronaphthalenes, and chlorodibenzofurans. *J. Assoc. Offic. Anal. Chem.* 55(1): 93–95 (1972).

The chlorodibenzo-*p*-dioxins were chlorinated to octachlorodibenzo-*p*-dioxin and identified by electron capture–gas-liquid chromatography. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin was determined at the 1 ppm level in corn oil. This method should be considered as a screen for dioxins, since it does not distinguish among the large number of isomers.

WILLIAMS, D. T., CUNNINGHAM, H. M., and BLANCHFIELD, B. J. Distribution and excretion studies of octachlorodibenzo-*p*-dioxin in the rat. *Bull. Environ. Contam. Toxicol.* 7(1). 57–62 (1972).

Absorption, distribution, and excretion of octachlorodibenzo-*p*-dioxin in the rat were examined. The AOAC method was used to analyze organs and tissues for dioxin content. The only gross pathology observed was congestion of the liver. Octachlorodibenzo-*p*-dioxin was absorbed by the rat mainly in the liver with small amounts in the adipose tissue and bile.

WILLIAMS, D. T., and BLANCHFIELD, B. J. Improved screening method for chlorodibenzo-*p*-dioxins. *J. Assoc. Offic. Anal. Chem.* 55(6): 1358–1359 (1972).

Conversion of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin to octachlorodibenzo-*p*-dioxin allowed detection by electron capture–gas-liquid chromatography of as low as 0.05 ppm in corn oil. The author's previous method was modified to include different chlorination conditions and a later alumina column cleanup.

WILSON, J. G. Teratological potential of 2,4,5-T. Proceedings Twenty-Fifth Annual Meeting Southern Weed Science Society, Dallas, TX, Jan. 18–20, 1972.

A chronology of the hazards of 2,4,5-T was presented. The report issued by the President's Science Advisory Committee appointed to study the 2,4,5-T question served as the basis for this review. The dioxin contaminant of 2,4,5-T, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, was discussed briefly as a toxicogen.

WOOLSON, E. A., THOMAS, R. F., and ENSOR, P. D. J. Survey of polychlorodibenzo-*p*-dioxin content in selected pesticides. *J. Agr. Food. Chem.* 20(2): 351–354 (1972).

Electron capture–gas chromatography was used to examine 129 samples of 17 different pesticides derived from chlorophenols for polychlorinated dibenzo-*p*-dioxins. Clean-up entailed concentrated sulfuric acid extraction of impurities from hexane and mild nitration of the chlorophenol extracts. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) was detected in the samples analyzed: 76% contained less than 0.1 μg/g, 7% between 0.1 to 1.0 μg/g, and 9% had greater than 10 μg/g. The 20 tri-, tetra-, and pentachlorophenols examined contained no TCDD. Phenoxy herbicides from current production had less than 0.5 μg/g TCDD.

YANG, G. C., and POHLAND, A. E. Electron spin resonance studies of cation radicals in trifluoromethane sulfonic acid. *J. Phys. Chem.* 76(10): 1504–1505 (1972).

Electron spin resonance spectra were obtained for chlorinated dibenzo-*p*-dioxins in trifluoromethane sulfonic acid (MSA); no oxidizing agents were used to produce the spectra in sulfuric acid. An oxidizing agent or ultraviolet light was needed for octachlorodibenzo-*p*-dioxin to yield a spectum in MSA; no spectrum was shown in sulfuric acid.

ZITKO, V. Absence of chlorinated dibenzodi-

oxins and dibenzofurans from aquatic animals. *Bull. Environ. Contam. Toxicol.* 7(2/3): 105–110 (1972).

Chlorinated dibenzodioxin and dibenzofuran residues were not detected in any of the aquatic samples analyzed.

ZITKO, V., HUTZINGER, O., and CHOI, P. M. K. Contamination of the Bay of Fundy–Gulf of Maine area with polychlorinated biphenyls, polychlorinated terphenyls, chlorinated dibenzodioxins, and dibenzofurans. *Environ. Health Perspect.* **1**: 47–50 (1972).

No residues of chlorinated dibenzodioxins and dibenzofurans were found in the samples analyzed: muscle and liver of white shark, eggs of double-crested cormorants and herring gulls, commercial herring oil, and ground fish herring meal. Detection limits ranged from 0.01 μg/g octachlorodibenzofuran wet tissue to 0.04 μg/TCDD/g wet tissue.

1971

ANONYMOUS. A close look at TCDD. *Agr. Res.* 20(4): 8–10 (1971).

The toxicological properties of tetrachlorodibenzo-*p*-dioxin were investigated following the discovery that the mutagenic and teratogenic potential of 2,4,5-T may be due to this contaminant.

ANONYMOUS. Herbicides: More research on 2,4,5-T. *Chem. Eng. News* 49(20): 11 (1971).

The President's Science Advisory Committee's report on 2,4,5-T and its dioxin impurity is reviewed. The panel made a number of recommendations, including one asking for a mechanism that would temporarily restrict the use of certain registered pesticides on the basis of information that implicates the chemical as a possible health hazard, pending the collection of more conclusive information.

ANONYMOUS. Herbicides: Secret 2,4,5-T report. *Chem. Eng. News* 49(29): 15 (1971).

An advisory committee's report submitted to the Environmental Protection Agency concerning 2,4,5-T and its dioxin contaminant was criticized by a dissenting advisory committee member and the Committee for Environmental Information. Specifically stated was that a level at which TCDD is not teratogenic has not been established and that the report did not consider the consequences of the fate of TCDD in food chains and animal tissue.

ANONYMOUS. A taste of honey (flavoured with 2,4,5,-T). *Food Cosmet. Toxicol.* **9**: 152 (1971).

This is a commentary on the teratogenic evaluation of 2,4,5-T by K. D. Courtney, et al.; a note added in proof indicate the 2,4,5-T contained 30 ppm dioxin. Thus, conclusions from the paper labeling 2,4,5-T teratogenic must be considered tentative.

ANONYMOUS. The PCB story unfolds. *Food Cosmet. Toxicol.* 9(4): 568–571 (1971).

Lesions resembling those produced by chick edema factor were traced to a PCB contaminant, chlorinated dibenzofurans which is present in some commercial PCBs.

ANONYMOUS. Working with 2,4,5-T. *Food Cosmet. Toxicol.* **9**: 908–909 (1971).

Chloracne, characterized by inclusion cysts, comedones, and pustules, was found in 13 workers, and was correlated in severity with the presence of scarring, hyperpigmentation, hirsutism, and complaints of eye irritation. A. P. Poland et al. commented that chloracne was not correlated with occupations within plants manufacturing 2,4,5-T, duration of employment, or coproporphyrin excretion.

ANONYMOUS. Tetrachlorodibenzodioxin—intimations of carcinogenicity? *Food Cosmet. Toxicol.* **9**: 909 (1971).

Although such effects as described by Buu-Hoi, et al. of the carcinomimetic activity of TCDD exist, the relationship is by no means exclusive. For example, stimulation of hydroxylating enzymes can be induced by many compounds, including BHT, which has been shown not to be carcinogenic in long-term feeding studies.

ANONYMOUS. PSAC hiccoughs over 2,4,5-T. *Nature* 231(5300): 210–211 (1971).

The President's Science Advisory Committee (PSAC) report on 2,4,5-T is questioned: justification by the PSAC concerning permissable levels of dioxin in 2,4,5-T was not based on scientific review; also, the need for establishing a dose–response curve for the teratogenicity of 2,4,5-T should have been cited.

ANONYMOUS. 2,4,5-T report attacked. *Nature* 232(5308): 218 (1971).

The response of the Committee for Environmental Information (CEI) to the scientific advisory committee's recommendation that 2,4,5-T be restored was one of strong opposition. With respect to dioxins, the CEI indicated that dioxins may accumulate in the soil and that present analytical techniques were not sensitive enough to detect them. Furthermore, lack of concrete proof that the use of 2,4,5-T was correlated with the occurrence of birth defects in Vietnam did not mean that no correlation existed.

BAUGHMAN, R. W., and MESELSON, M. An improved analysis for 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDBD). Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971, Abstract No. 89.

Current analytical methods for the detection of potentially hazardous levels of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin are inadequate. A combined gas chromatography–mass spectroscopy method was utilized with modifications in extraction concentration and detection.

BEVENUE, A., and KAWANO, Y. Pesticides, pesticide residues, tolerances, and the law (U.S.A.). *Residue Rev.* **35**: 103–149 (1971).

Politics and science surround the 2,4,5-T and hence dioxin controversy. Contents include: Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended through 1969; the DDT episode; the 2,4,5-T episode; Federal Food, Drug, and Cosmetic Act (FDCA); and food imports and international pesticide control. Mention is made of the USDA's investigation of possible excessive contamination of 17 polychlorophenolic pesticides by tetrachlorodibenzo-*p*-dioxin.

BOER, F. P., NEUMAN, M. A., VAN REMOORTERE, F. P., NORTH, P. P., and RINN, H. W. X-ray diffraction studies of chlorinated dibenzo-*p*-dioxins. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 82.

The crystal structures of four chlorinated dibenzo-*p*-dioxin compounds (2,7-dichloro; 2,8-dichloro; 2,3,7,8-tetrachloro; and octachloro) were determined by x-ray diffraction. The structures were elucidated in order to provide absolute standards for isomeric structure assignment.

BUU-HOI, N. P., HIEN, D. P., SAINT-RUF, G., and SERVOIN-SIDOINE, J. Canceromimetic properties of tetrachloro-2,3,7,8 dibenzo-*p*-dioxin ("dioxin"). *C. R. Acad. Sci.* (Paris) **D272**(10): 1447–1450 (1971) (Fr).

Tetrachloro-2,3,7,8-dibenzo-*p*-dioxin in rats caused induction of zoxazolamine hydroxylase, marked reduction in phenobarbital sedative effect, and a decrease in hepatic arginase. Dioxin therefore, has a pronounced inhibitory effect on the enzymatic systems as do the carcinogens benzo [a]-pyrene and *p*-dimethylaminoazobenzene.

BUU-HOI, N. P., SAINT-RUF, G., BIGOT, P., and MANGANE, M. Preparation, properties and identification of "dioxin" in pyrolysates of defoliants containing 2,-4,5-trichlorophenoxyacetic acid, their esters, and contaminated plants. *C. R. Acad. Sci.* (Paris) **D273**(7): 708–711 (1971) (Fr).

Synthesis and physico-chemical properties of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and its less toxic isomer 1,3,6,8-tetrachlorodibenzo-*p*-dioxin are described. Caution was urged about the burning of wooded areas treated with 2,4,5-T or its butyl ester because of possible dioxin formation.

CAMPBELL, A. D., and FIRESTONE, D. Chick edema factor—toxic dioxins. In: International Symposium on Identification and Measurement of Environmental Pollutants, June 14–17, 1971, Ottawa, Ontario, Canada, B. Wesley, Ed., National Research Council, Canada, 1971, pp. 195–198.

The formation, occurrence, toxicity, tissue distribution in the chick, and analytical methods for the detection of polychlorodibenzo-*p*-dioxins are described. Dioxins were implicated in chick edema disease. Dioxins belong to one of the most toxic classes of chlorinated compounds known, being almost 1000 times as toxic as most pesticides.

COLLINS, T. F. X., WILLIAMS, C. H., and GRAY, G. C. Teratogenic studies with 2,-4,5-T and 2,4-D in the hamster. *Bull. Environ. Contam. Toxicol.* **6**(6): 559–567 (1971).

2,4,5-T commercial samples given on days 6 to 10 of organogenesis were feticidal and teratogenic in the golden Syrian hamster. The incidence of the observed effects increased with an increasing content of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Dioxin impurity caused edema and hemorrhages in newborn animals.

COMMITTEE FOR ENVIRONMENTAL INFORMATION. Critique of the report of the advisory committee on 2,4,5-T. *Environment* **13**(7): 24, 29 (1971).

Criticism by the Committee for Environmental Information levied against the Advisory Committee's report on 2,4,5-T centered on the following areas: no effect levels; environmental accumulation, transmission and degradation; human hazards from

dioxins; 2,4,5-T teratogenicity; and the benefits vs. risks of 2,4,5-T usage.

COURTNEY, C. D., and MOORE, J. A. Teratology studies with 2,4,5-trichlorophenoxyacetic acid and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. *Toxicol. Appl. Pharmacol.* 20(3): 396–403 (1971).

2,4,5-T and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) were teratogenic in three strains of mice; combinations of these compounds did not potentiate observed results. Both produced cleft palates and kidney malformations. Studies with rats gave negative results with 2,4,5-T; TCDD induced kidney anomalies.

CROSBY, D. G., WONG, A. S., PLIMMER, J. R., and WOOLSON, E. A. Photodecomposition of chlorinated dibenzo-*p*-dioxins. *Science* 173(3998): 748–749 (1971).

2,4,5-T and 2,3,7,8-tetrachlorodibenzo-*p*–dioxin homologs photodecompose rapidly in an alcohol solution exposed to artificial light and natural sunlight. The decomposition rate was correlated with the degree of chlorination. Negligible photodecomposition was observed in aqueous suspensions and on wet or dry soil.

DAVRING, L., and SUNNER, M. Cytogenetic effects of 2,4,5-trichlorophenoxyacetic acid on oogenesis and early embryogenesis in *Drosophila melanogaster*. *Hereditas* 68(1): 115–122 (1971).

2,4,5-T with dioxin contaminants less than 0.1 ppm was evaluated in a wild-type *Drosophila* population, Canton-S 109. Adult flies were exposed to 250 ppm 2,4,5-T in their food within or later than 24 hr of eclosion. Results indicated that this 2,4,5-T formulation effected early oogenesis and caused chromosome disturbances which could result in sterility.

ELVIDGE, D. A. The gas-chromatographic determination of 2,3,7,8-tetrachloro-*p*-dioxin in 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), 2,4,5-T ethyl-hexyl ester, formulations of 2,4,5-T esters and 2,4,5-trichlorophenol. *Analyst* 96(1147): 721–727 (1971).

A gas chromatographic method is described for the detection of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin impurities in herbicides. Dioxin recoveries ranged from 89 to 98%; limit of detection was 0.05 ppm.

EMERSON, J. L., THOMPSON, D. J., STREBING, R. J., GERBIG, C. G., and ROBINSON, V. G. Teratogenic studies of 2,4,5-trichlorophenoxyacetic acid in the rat and rabbit. *Food Cosmet. Toxicol.* 9(3): 395–404 (1971).

Treatment of rabbits and rats with 2,4,5-T containing 0.5 ppm 2,3,7,8-tetrachlorodibenzo-*p*-dioxin did not cause any teratogenic or embryotoxic effects. Rats received 1, 3, 6, 12, or 24 mg 2,4,5-T/kg on days 6 to 15 of pregnancy. Rabbits received 0, 10, 20, or 40 mg 2,4,5-T/kg on days 6 to 18 of pregnancy.

FIRESTONE, D. Determination of polychlorodibenzo-*p*-dioxins (dioxins) in chlorophenols and lipids. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 80.

High resolution mass spectrometry was reported to offer a sensitive method for detecting specific dioxins after adequate sample cleanup, e.g., chromatography and gas chromatography.

FIRESTONE, D. FLICK, D. F., RESS, J., and HIGGINBOTHAM, G. R. Distribution of chick edema factors in chick tissues. *J. Assoc. Offic. Anal. Chem.* 54(6): 1293–1298 (1971).

Chickens fed toxic animal fat containing 9.9 ppm chlorinated dibenzo-*p*-dioxins excreted over 90% the ingested hexa-, hepta-, and octachlorodioxins. Decreased chlorination resulted in greater body retention. Residues were found in many tissues but was most prominent in the liver.

HANSEN, W. H., QUAIFE, M. L., HABERMANN, R. T., and FITZHUGH, O. G. Chronic toxicity of 2,4-dichlorophenoxyacetic acid in rats and dogs. *Toxicol. Appl. Pharmacol.* 20: 122–129 (1971).

2,4-D preparations, having undetectable levels of 2,7-dichlorodibenzo-*p*-dioxin or 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, were tested for chronic toxicity in rats and dogs. No significant effect on growth, survival, organ weight, or hematologic values were noted.

HAYS, H., and RISEBROUGH, R. W. The early warning of the terms. *Natural History* 80(9): 39–46 (Nov. 1971).

Possible health implications to humans and wildlife from environmental pollution with chlorinated dibenzofurans are reviewed.

HELLING, C. S. Pesticide mobility in soils. II. Applications of soil thin-layer chromatography. *Soil Sci. Soc. Amer. Proc.* 35(5): 737–743 (1971).

Relative mobility by thin-layer chromatography and diffusion in moist and air-dry soils were used to test pesticide movements. The two chlorinated dibenzo-*p*-dioxins were immobile.

HOLDEN, C. Critics weigh EPA herbicide report, find it wanting. *Science* 173(3994): 312 (1971).

The EPA's Advisory Committee on 2,4,5-T recommended that the ban on 2,4,5-T be lifted with certain qualifications, i.e., no more than 0.1 ppm 2,4,5-T in drinking water and formulations containing no more than 0.1 ppm dioxin. The Committee for Environmental Information voiced five major objections.

ISENSEE, A. R., and JONES, G. E. 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(6): 1210–1214 (1971).

Measured uptake of ^{14}C-labeled 2,7-dichloro- and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin from nutrient solution, soil, and foliage by oats and soybeans indicated that accumulation of TCDD in plants via the soil is unlikely.

JOHNSON, J. E. The public health implications of widespread use of the phenoxy herbicides and picloram. *Bioscience* 21 (17): 899–905 (Sept. 1, 1971).

A review presenting the myriad historical aspects of the dioxin–2,4,5-T(and other herbicides) picture. The potential adverse health effects from phenoxy herbicides were documented. One conclusion reported was that impurities—particularly the chlorodibenzo-*p*-dioxins—can be an important factor, but these can be controlled by proper manufacturing techniques.

JOHNSON, J. E. Safety in the development of herbicides. *Proc. Ann. Calif. Weed Conf.* 23: 43–67 (1971).

Experiments using 2,4,5-T alone and in combination with dioxin allowed the conclusion that commercially produced 2,4,5-T containing less than 1 ppm dioxin does not present a hazard to health.

JOHNSON, J. E. Safety in the development of herbicides. *Down to Earth* 27(1): 1–7 (1971).

After the discovery of highly toxic dioxin residues in the herbicides 2,4,5-T, precautionary control measures were instituted to insure greater quality control in pesticide production. Pregnant rats were treated orally with 2,4,5-T at doses of up to 100 mg/kg/day. No symptoms of teratology were produced in the offspring. Dioxin was toxic to embryos at 0 125 μg/kg/day, whereas 0.03 μg/kg/day was below the "no-effect" level. Some aspects of production and costs are discussed.

KEARNEY, P. C., and WOOLSON, E. A. Persistence and metabolism of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in soils. Division Pesticide Chemistry, 161st National Meeting of the American Chemical Society, Los Angeles, March 28–April 2, 1971; Abstract No. 21.

TCDD applied 1, 10, and 100 ppm to two soils held at 30°C remained relatively unchanged (80–85% of original samples were recovered) after 20, 40, 80, and 160 days. Incubation of 10, 100, and 1000 ppm, 2,4-dichlorophenol, and 2,4,5-trichlorophenol in soils for 70 days produced no detectable di- or trichlorodioxins.

KEARNEY, P. C., ISENSEE, A., HELLING, C. S. WOOLSON, E. A., and PLIMMER, J. R. Environmental significance of chlorodioxins. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 90.

Studies on TCDD under controlled environmental conditions revealed that TCDD was persistent and immobile in soil, not readily absorbed by plants, subject to photodecomposition, and slowly degraded to polar metabolites. Other studies revealed that the environmental contamination is small and not detectable in biological samples.

KHERA, K. S., and RUDDICK, J. A. Perinatal effects of dibenzodioxins in Wistar rats. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C. Sept. 12–17, 1971; Abstract No. 87.

Oral administration of 16 to 0.125 μg/kg 2,3,7,8-tetrachlorodibenzo-*p*-dioxin to pregnant rats on days 6–15 of gestation caused a reduction in viable litter size and a high incidence of resorptions. No effect was observed at the 0.125 level. Histological examination of fetuses revealed brain and intestinal hemorrhages and edema of subcutaneous tissue.

KHERA, K. S., HUSTON, B. L., and MCKINNEY, W. P. Pre- and postnatal studies on 2, 4,5-T, 2,4-D, and derivatives in Wistar rats. *Toxicol. Appl. Pharmacol.* 19:369–370 (1971).

Results from teratogenic studies with rats treated with 2,4,5-T, 2,4-D, and several derivatives were

either negative or inconclusive. The 2,3,7,8-tetrachlorodibenzbo-*p*-dioxin levels in these preparations were not known in all cases, but most were suspected to be less than 0.5 ppm.

LANGER, H. G., BRADY, T. P., DALTON, L. A. SHANNON, T. W., and BRIGGS, P. R. Thermal chemistry of chlorinated phenols. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 83.

At the decomposition temperatures of chlorinated phenols and derivatives, the following conditions are ideal for dioxin formation: (a) high concentration of the phenol, (b) high degree of chlorination of the phenol, and (c) presence of base.

LOEFROTH, G. Environmental poisons, man and the physician. *Laekartidningen* 68 (18): 2113–2133 (1971) (Swed.).

Possible adverse health effects from environmental poisons demands caution. Tetrachlorobenzo-*p*-dioxin was mentioned for its adverse effects of fetal development.

MILNES, M. H. Formation of 2,3,7,8-tetrachlorodibenzodioxin by thermal decomposition of sodium 2,4,5-trichlorophennate. *Nature* (London) 232(5310): 395–396 (1971).

Hydrolysis of 1,2,4,5-tetrachlorobenzene in methyl alcohol with sodium hydroxide at high pressures or in ethylene glycol at 1 atm formed sodium monochlorophenate. This allowed exothermic decomposition of 2,4,5-trichlorophenate sodium to 2,3,7,8-tetrachlorodibenzodioxin.

MUELDER, W. W., and SHADOFF, L. The preparation of uniformly labeled ^{14}C-2,7-dichlorodibenzo-*p*-dioxin and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 78.

2,7-Dichlorodizenzo-*p*-dioxin was prepared from isotopic potassium 2,4-dichlorophenate uniformly labeled with ^{14}C. Chlorination of the dioxin in a chloroform solution containing $FeCl_3$ and I_2 gave a mixture of tri-, tetra-, and pentachlorosubstitution products. Purification by digestion in boiling chloroform, fractional sublimation, and recrystallization from anisole yielded a product containing 92% 2,3,7,8-tetrachlorodibenzo-*p*-dioxin.

PIPER, W. N., and ROSE, J. Q. The excretion and tissue distribution of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in the rat. Division Pesticide Chemistry, 162nd National Meeting of the Amercian Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 88.

TCDD was administered to male rats in a single oral dose of 50 μg/kg. The primary excretion route was via the feces and the highest tissue concentration was in the liver.

PLIMMER, J. R., CROSBY, D. G., WONG, A. S., and KLINGEBIEL, U. I. Photochemistry of dibenzo-*p*-dioxins. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 85.

Ring closure and photochemical reaction of *o*-chlorophenols yield dioxin. Dibenzo-*p*-dioxins were decomposed in solution by light or sunlight. Absorption of dioxin on soil reduced its rate of photodecomposition.

PLIMMER, J. R., and KLINGEBIEL, U. I. Riboflavin photosensitized oxidation of 2,4-dichlorophenol: assessment of possible chlorinated dioxin formation. *Science* 174(4007): 407–408 (1971).

Chlorophenols in aqueous solution were exposed to the action of light in wavelengths greater than 280 nm. Products were characterized by gas chromatography and mass spectrometry. Possible chlorinated dibenzo-*p*-dioxins from ring closure of a 2-phenoxyphenol derivative were not detected in the photolysis products. Under environmental conditions, dioxins are unlikely products of lower chlorinated phenols or phenoxy-alkanoic acids.

POHLAND, A. E., YANG, G. C., and HANSEN, E. A. The preparation and characterization of chlorinated dibenzo-*p*-dioxins. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 77.

Twelve chlorinated dibenzo-*p*-dioxin standard compounds containing from one to eight chlorine atoms were prepared as standards to develop analytical techniques and to use in toxicity studies. The wavelength associated with the observed phosphorescence and the triplet state lifetime were dependent upon the number of chlorine atoms and their positions on the dibenzo-*p*-dioxin nucleus.

POLAND, A. P., SMITH, D., METTER, G., and POSSICK, P. A health survey of workers

in a 2,4-D and 2,4,5-T plant. *Arch. Environ. Health* 22:316–327 (1971).

A study and review of employee health in a plant producing 2,4,5-T and 2,4-D. Chloracne was found in 13/73 male workers and was believed caused by chlorinated dioxins. The plant has begun several programs to reduce dioxin levels in 2,4,5-trichlorophenol; the contaminant concentration has dropped from 10 to 25 ppm to 1 ppm.

PORTER, M. L., and BURKE, J. A. Separation of three chlorodibenzo-*p*-dioxins from some polychlorinated biphenyls by chromatography on an aluminum oxide colum.

Chlorodioxins (2,3-di-, 2,3,7-tri-, and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin) were separated from polychlorinated biphenyls by column chromatography on aluminum oxide. Recoveries of both dioxins and the polychlorinated biphenyls were approximately 100%.

RISEBROUGH, R. W. Determination of polychlorinated biphenyls in environmental samples. In International Symposium on Identification and Measurement of Environmental Pollutants, Ottawa, Ontario, Canada, June 14–17, 1971, B. Westley, Ed., National Research Council, Canada, 1971, pp. 147–153.

Even though it is not known whether dibenzofurans can be formed from environmental residues of polychloronated biphenyls (PCB), they should be considered as a part of the PCB problem. Dibenzofurans have been found in commercial PCB mixtures sampled from France, Germany, and the United States in concentrations ranging from 5 to 20 ppm. The European samples had higher levels than the U.S. sample.

ROLL, R. Teratogenic effect of 2,4,5-T [2,4, 5-trichlorophenoxyacetic acid] in mice. *Food Cosmet. Toxicol.* 9(5): 671–676 (1971) (Ger).

2,4,5-T having a 2,3,7,8-tetrachlorodibenzo-*p*-dioxin content of less than 0.1 ppm caused embryotoxic effects and a significant increase in the incidence of cleft palate in mice. Concentrations used in the study ranged from 35 to 130 mg/kg 2,4,5-T/dioxin which were given orally on days 6–15 of pregnancy. The teratogenic "no-effect" level of 2,4,5-T/dioxin was found to be 20 mg/kg.

ROWE, V. K., NORRIS, J. M., SPARSCHU, G. L., SCHWETZ, B. A., and GEHRING, P. J. Toxicology of chlorinated dibenzo-*p*-dioxins. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Division, Washington, D.C., Sept. 12–17, 1971, Abstract No. 86.

The toxicology of several chlorinated dibenzo-*p*-dioxins were investigated in rats, guinea pigs, and rabbits. The compounds studied were 2,7,-dichlorodibenzo-*p*-dioxin (DCDPD); 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDPD); hexachlorodibenzo-*p*-dioxin (HCDPD), and octachlorodibenzo-*p*-dioxin (OCDPD). TCDPD was found to be the most toxic of the compounds investigated. DCDPD and OCDPD were the least toxic. For instance, little if any fetotoxic effects were observed with these two compounds; doses of 2 to 4 g/kg were not lethal to rats. On the other hand, TCDPD and HCDPD induced chloracne, fetotoxicity, and teratogenic effects.

SCHWETZ, B. A., SPARSCHU, G. L., and GEHRING, P. J. The effect of 2,4-dichlorophenoxyacetic acid (2,4-D) and esters of 2,4,D on rat embryonal, foetal and neonatal growth and development. *Food Cosmet. Toxicol.* 9:801–817 (1971).

The teratogenicity of 2,4-D was investigated in the rat. Formation of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) in the manufacture of 2,4-D is not theoretically possible. The 2,4-D sample used was analyzed for the TCDD contaminant with a method having a 0.2 ppm sensitivity and none was found. Doses of 12.5, 25, 50, 75, and 87.5 mg/kg 2,4-D were administered orally on days 6–15 of gestation. High dose levels caused signs of embryotoxicity and fetotoxicity.

SOMERS, E., and SMITH, D. M. Source and occurrence of environmental contaminants. *Food Cosmet. Toxicol.* 9(2): 185–193 (1971).

The sources, occurrences, and some of the toxicological effects of polychlorinated biphenyls and chlorodioxins were discussed. Chlorophenols exposed to high temperatures may form chlorinated derivatives of dibenzo-*p*-dioxin. Inadequate methodolgy prevents analysis for these contaminants in foods.

SPARSCHU, G. L., DUNN, F. L., LISOWE, R. W., and ROWE, V. K. Study on the effects of high levels of 2,4,5-trichlorophenoxyacetic acid on foetal development in the rat. *Food Cosmet Toxicol.* 9(4): 527–530 (1971).

Commercial-grade 2,4,5-T containing 0.5 ppm 2,3,7,8-tetrachlorodibenzo-*p*-dioxin did not induce a teratogenic response when administered orally to rats on days 6 to 15 of gestation at a dosage level of 50 mg/kg/ day.

SPARSCHU, G. L., DUNN, F. L., and ROWE, V. K. Study of the teratogenicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in the rat. *Teratology* 4: 247 (Abstract) (1971).

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin was administered orally to pregnant rats during days 6 to 15 of gestation in doses of 0, 0.03, 0.125, 0.5, 2.0, and 8.0 g/kg/day [sic]. No effect was observed on the fetus or mother at the 0.03 dose level. However, at the 0.125 level and above, fetal mortality, early and late resorptions, and fetal intestinal hemorrhage occurred. The effects became more pronounced with the increase in dose. Maternal toxicity was noted beginning at the 0.5 level which also increased with the dose.

SPARSCHU, G. L., DUNN, F. L., and ROWE, V. K. Study of the teratogenicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in the rat. *Food Cosmet. Toxicol.* 9(3): 405–412 (1971).

Investigations of the teratogenicity of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in rats revealed that this compound is capable of inducing a high degree of adverse effects in the fetus and mother. Doses of 0, 0.03, 0.125, 0.5, 2.0, and 8.0 μg kg/day were given orally to pregnant rats during days 6 to 15 of gestation. Effects such as fetal mortality, intestinal hemorrhage, and early and late resorptions began appearing at the 0.125 level and increased with dose. It is suggested that the teratogenic effects of 2,4,5-T observed in other studies may have been due to this contaminant (30 ppm).

STEHL, R. H., PAPENFUSS, R. R., BREDWEG, R. A., and ROBERTS, R. W. The stability of pentachlorophenol and chlorinated dioxins to sunlight, heat, and combustion. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971; Abstract No. 92.

Degradation of pentachlorophenol in the environment could theoretically lead to the formation of chlorinated dibenzo-*p*-dioxins. Several simulated environmental conditions were checked for possible dioxin formation. Pentachlorophenol–treated wood and paper indicated no increase in dioxins when burned; likewise photolysis of sodium pentachlorophenol yielded only a trace of the compound. 2,7-Di- and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin were rapidly decomposed under artificial sunlight, whereas octachlorodibenzo-*p*-dioxin was not.

STEHL, R. H., WILKE, E., PAPENFUSS, R. R., and MATALON, R. Determination of nonphenolic impurities in chlorinated phenols and related compounds. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Division, Washington, D.C., Sept. 12–17, Abstract No. 81.

Analytical techniques for the detection of neutral impurities (chlorinated dibenzo-*p*-dioxins) in chlorinated phenols, were ion-exchange chromatography for removal of the matrix, liquid-liquid chromatography for separation of the various neutral components, followed by gas chromatographic examination of the separated components using electron capture detection.

STORHERR, R. W., WATTS, R. R., GARDNER, A. M., and OSGOOD, T. Steam distillation technique for the analysis of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in technical 2,4,5-T. *J. Assoc. Offic. Anal. Chem.* 54(1): 218–219 (1971).

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin was separated from 2,4,5-T by steam distillation and analyzed by microcoulometric gas–liquid chromatography.

THOMPSON, D. J., EMERSON, J. L., and SPARSCHU, G. L. Study of the effects of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) on rat and rabbit fetal development. *Teratology* 4:243 (Abstract) (1971).

2,4,5-T was investigated for its effects on fetal development in the rat and rabbit. Doses ranging from 1 to 50 mg/kg were administered during days 6 to 15 of gestation. No clinical or gross pathology was observed. Detailed examination of the visceral and skeleton revealed no teratogenic effects. However, rats receiving 100 mg/kg during day 6 to 10 of gestation did produce maternal toxicity and death, early fetal resorptions, fetal toxicity, but no malformations.

CURRIER, W. F., GRAHAM, C., GRATKOWSKI, H., and NORRIS, L. A., U.S. Forestry Service. Report on background information for the phenoxy herbicides 2,4-D—2,4,5-T—2,4,5-TP. U.S. Forestry Service Report, pp. 1–165 (1971).

A through review is given on the phenoxy herbicides, 2,4-D (2,4-dichlorophenoxyacetic acid), 2,4,5-T (2,4,5-trichlorophenoxyacetic acid), and 2,4,5-TP [2-(2,4,5-trichlorophenoxy)propionic acid], and their potential contaminant, e.g., dioxin.

VINOPAL, J. H., YAMAMOTO, I., and CASIDA, J. E. Preparation of tritium-labeled 2,3,-7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and structure-activity investigations of

TCDD and other related dibenzo-*p*-dioxins. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971, Abstract No. 79.

Preparation of tritium-labeled 2,3,7,8-tetrachlorodibenzo-*p*-dioxin was investigated. One approach used was the tritiation of 2,4-dichlorophenol or 2,4,5-trichlorophenol, lithiummetalation and subsequent aqueous hydrolysis of a chlorinated dibenzo-*p*-dioxin, and the catalytic reduction of a chlorinated dibenzo-*p*-dioxin.

WESTING, A. H. Herbicides as agents of chemical warfare: Their impact in relation to the Geneva Protocol of 1925. *Environ. Affairs* **1**(3): 578–586 (1971).

The use of herbicides as chemical warfare agents is reviewed with respect to the Geneva Protocol of 1925. The total impact of these agents on the environment and man is not usually known or considered before widespread use. For example, 47 million lb of 2,4,5-T was used in Indochina over an 8-yr period before it was discovered that about 1000 lb dioxin was also being applied as an unsuspected contaminant.

WILLIAMS, D. T., and BLANCHFIELD, B. J. Thin layer chromatographic separation of two chlorodibenzo-*p*-dioxins from some polychlorinated biphenyls and organochlorine pesticides. *J. Assoc. Offic. Anal. Chem.* **54**(6): 1429–1431 (1971).

Thin-layer chromatography was used for the isolation of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin and octachlorodibenzo-*p*-dioxin from polychlorinated biphenyls and organochlorine pesticides. After isolation, these dioxins were analyzed by the electron capture-gas chromatography.

WILSON, J. G., BOUTWELL, R. K., DAVIS, D. E., DOST, F. N., HAYES, W. J., KALTER, H., LOOMIS, T. A., SCHULERT, A., STERLING, T. D., and BOWEN, D. L. Report of the Advisory Committee on 2,4,5-T to the Administrator of the Environmental Protection Agency. (Submitted May 7, 1971).

The 2,4,5-T Scientific Advisory Committee's report to the U.S. Environmental protection Agency was stimulated after experimental results and environmental indicators pointed to a potential health threat to humans. This nine-member committee was selected from a list of names supplied by the National Academy of Science. The Committee recommended by an 8 to 1 vote to restore registration of 2,4,5-T with certain conditions; those applicable to TCDD were: (1) a limit of 0.5 ppm TCDD on existing 2,4,5-T inventories and 0.1 ppm on future 2,4,5-T production, and (2) conduct specific research on TCDD for potential soil accumulation and food drain magnification.

WILLIAMS, C. S. The status of 2,4–D, 2,4,5-T, Silvex and MCPA herbicides. *Down to Earth* **26**(4): 12–15 (1971).

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) is the causative agent in experiments reporting terotogenic effects from 2,4,5-T. TCDD was found in 2,4,5-T formulations but not in 2,4-D samples. The precursor for 2,4,5-T is 2,4,5-trichlorophenol which is prepared from 1,2,4,5-tetrachlorobenzene; the high temperature and alkaline conditions necessary to produce this compound also favor dioxin formation. Since 2,4-D is formed by direct chlorination of 2,4-dichlorophenol and not by alkaline hydrolysis of 1,2,4-trichlorobenzene, no dioxin impurities are theoretically possible.

WOOLSON, E. A., REICHEL, W. L., and YOUNG, A. L. Dioxin residues in lakeland sand and eagle samples. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971. Abstract No. 91.

Between 1962 and 1969 a lakeland region in Florida was treated with 912 lb 2,4,5-T per acre. To assess the ecological importance of chlorinated dioxins in the environment, samples of soil to a depth of 3 ft, and tissues from eagles were analyzed for dioxins by electron capture-gas chromatography. No dioxins were detected at a minimum detection limit of 50 ppb for the eagle tissue samples and 5 ppb for the soil samples. Small residues of about 20 ppb 2,4,5-T were found in soil samples.

YANG, G. C., and POHLAND, A. E. Cation radicals from chlorinated dibenzo-*p*-dioxins. Division Pesticide Chemistry, 162nd National Meeting of the American Chemical Society, Washington, D.C., Sept. 12–17, 1971. Abstract No. 84.

Characteristic blue coloration and electron spin resonance (ESR) spectra of cation radicals were obtained following dissolution of chlorinated dibenzo-*p*-dioxins in trifluoromethanesulfonic acid. The mono- and dichlorodibenzo-*p*-dioxins showed well resolved ESR by hyperfine lines; the tetrachloro analogs exhibited single broad ESR lines.

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ABELSON, P. H. Pollution by organic chemicals. *Science* 170(3957): 496 (30 Oct. 1970).

When manufacture of 2,4,5-T is controlled carefully, dioxin contamination is less than 1 ppm. Dioxin was identified in 1962 as the culprit of damage and death in 1957 of uncounted numbers of chicks. Dioxin produces neurological disturbances and is teratogenic. The acute LD_{50} for male guinea pigs is 0.000001 g/kg.

ANONYMOUS. HEW, USDA hold firm; 2,4,5-T ruling postponed. *Chem. Eng. News* 48(7): 11–12 (1970).

Because early studies indicated that most of the adverse toxicological effects of 2,4,5-T were due to high dioxin contamination (27 ppm) of test samples, the USDA did not feel obligated to cancel registration of currently manufactured 2,4,5-T containing about 1 ppm dioxin. Preliminary tests have shown that 2,4,5-T containing 1 ppm dioxin is not teratogenic. However, problems may still exist, since excessive heat exposure of the tri- or pentachlorophenols, used as intermediates in 2,4,5-T production, liberates dioxins.

ANONYMOUS. Government steps up pressure on pesticides; recent joint action restricting use of 2,4,5-T herbicide portends changes in pesticide regulations and testing. *Chem. Eng. News* 48(18): 60–61 (1970).

Evidence from Congressional hearings catalyzed the government's eventual suspension and cancellation of consumer and food crop usage of 2,4,5-T and curtailment of its use in Vietnam. HEW and the USDA issued a joint statement declaring that both 2,4,5-T and its dioxin contaminant may cause birth defects. The pesticide industry reacted adversely to these actions and statements.

ANONYMOUS. Pesticide policies scored at Ag meeting. *Chem. Eng. News* 48(42): 7 (1971).

The politics and pressures brought about by the 2,4,5-T/dioxin controversy between government and industry were reviewed. The Chairman of the Secretary's Pesticide Advisory Committee (SPAC) castigated both the federal government and the pesticides industry for failure to avoid the panicky crises which brought about an "era of chemical McCarthyism."

ANONYMOUS. The strange case of the government vs. 2,4,5-T. II. *Farm Chem.* 133(3): 26 (1970).

A review of the government involvement in the 2,4,5-T controversy which began after preliminary research reports indicated 2,4,5-T was teratogenic. These government studies were instituted in an attempt to determine whether 2,4,5-T or its dioxin contaminant was the causative agent of these effects.

ANONYMOUS. The 2,4,5-T identification parade. *Food Cosmet. Toxicol.* 8: 596–597 (1970).

Inconsistent test data on the teratogenicity of 2,4,5-T were thought resultant of the level of its chief contaminant, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. Levels of 27 ppm have been found in some 2,4,5-T samples.

ANONYMOUS. Defoliants, deformities: What risk? *Med. World News* 11(9): 15–17 (1970).

Fertilized chicken eggs were injected with 2.5 pg (2.5×10^{-12}g) (50 ppt) of 2,3,6,7-tetrachlorodibenzo-*p*-dioxin. The dioxin caused leg deformities, cleft palates, and beak defects in 11 of 15 survivors from 25 eggs. Unhatched birds showed tissue edema, necrotic livers, and deformities similar to hatched birds.

ANONYMOUS. Another herbicide on the blacklist. *Nature* 226(5243): 309–311 (1970).

A commentary was presented to clarify the controversy of whether 2,4,5-T or 2,3,7,8-tetrachlorodibenzo-*p*-dioxin was the causative teratogenic and mutagenic agent. Hearings with government and industrial representatives were held before the Subcommittee on Energy, Natural Resources and the Environment of the Senate Committee on Commerce.

ANONYMOUS. The tangled tale of 2,4,5-T. PANS 16(3): 421–422 (1970).

Use of 2,4,5-T has been restricted where foodstuffs for human consumption might be contaminated. The possibility exists that dioxin (2,3,7,8-tetrachlorodibenzo-*p*-dioxin) may be the contaminant in 2,4,5-T formulations or that there may be a synergistic effect between 2,4,5-T and dioxin. Hypothetically, if dioxin contaminated the 2,4,5-T reported in food in the U.S. to the extent of 1 ppm, it would take 100 years for a normal person to accumulate a dose 600 times less than that which produced toxic effects during the pregnancy of a rat.

COURTNEY, K. D., GAYLOR, D. W., HOGAN, M. D., FALK, H. L., BATES, R. R., MITCHELL, I. Teratogenic evaluation of 2,4,5-T. *Science* 168(3933): 864–866 (May 15, 1970).

2,4,5-T samples were evaluated in rats and mice for teratogenicity. Results indicated that 2,4,5-T s.c. or orally administered was teratogenic and fetotoxic

to the mouse and orally to the rat. Cleft palate and cystic kidneys were among the effects observed. A note added in proof indicated that the 2,4,5-T samples contained 30 ppm 2,3,7,8-tetrachlorodibenzo-*p*-dioxin.

DARSOW, G., and SCHNELL, H. Chlorodibenzo-*p*-dioxins. Ger. Patent 1,930,259, Appl. 13 June 1969, Granted 17 Dec. 1970, 10 pp (1970).

Chlorodibenzo-*p*-dioxins were prepared from tetra- or hexachlorobenzene. The compounds were useful for flameproofing polymers, e.g. polyesters.

DAY, B. E. 2,4,5-T and government decisions. *Proc. West. Soc. Weed Sci.* **23**: 4–6 (1970).

Unpublished material which influenced the 2,4,5-T ban was held as questionable and suspect since preparations tested contained 27 ppm dioxin. It was stated that 2,4,5-T containing 1 ppm dioxin is not teratogenic; therefore, the alarm about the adverse effects of 2,4,5-T was unjustified.

EMERSON, J. L., THOMPSON, D. J., GERBIG, C. G., ROBINSON, V. B. Teratogenic study of 2,4,5-trichlorophenoxyacetic acid in the rat. *Toxicol. Appl. Pharmacol.* **17**: 317 (1970).

The teratogenicity of 2,4,5-T containing 1 ppm of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin was evaluated in rats. No teratogenic effects from 1,3,6,12, or 24 mg/kg/day 2,4,5-T or other pathological signs were observed. These results do not substantiate the adverse effects observed with 2,4,5-T containing 27 ppm dioxin.

EPSTEIN, S. S. A family likeness. *Environment* **12**(6): 16–25 (July/August, 1970).

The human and environmental implications of the widespread chemical exposure problem have been accentuated by the increased use of herbicides during the past ten years. For example, although recently dioxin impurities in 2,4,5-T have been reduced, dioxin is still present; even minute concentrations are potential hazards. The analysis, formation, and teratogenic and other toxicological consequencies of dioxins were reviewed.

EPSTEIN, S. S. Testimony on teratogenic effects of 2,4,5-T formulations. U.S. Senate Hearing before the Subcommittee of Energy, Natural Resources and the Environment of the Committee on Commerce (April 15, 1970).

Polychlorophenol contaminants and their dioxin pyrolytic products in phenoxy herbicides are of toxicologic and environmental consequence. Some dioxins are highly toxic and teratogenic at the microgram per kilogram level; most dioxins are, however, toxicologically uncharacterized.

GALSTON, A. W. Herbicide usage. *Science* **168** (3939): 1607 (1970).

The phenoxyacetic acid herbicides should not be used until all questions regarding the teratogenicity of 2,4,5-T have been resolved. A tetrachlorodibenzodioxin impurity found in some commercial preparations of 2,4,5-T was the teratogenic agent in 2,4,5-T samples tested for teratogenicity by the Bionetics Research Laboratories. The possibility that phenoxyacetic acids may be degraded in plants and soil or by fire or bright sunlight into dioxin-like teratogens should be studied. Extensive research should be accomplished on all aspects of the biomedical and environmental consequences of dioxins.

Hearings Before the Subcommittee on Energy, Natural Resources and the Environment of the Committee on Commerce, U. S. Senate, Serial 91–60, Governmental Printing Office, Washington, D.C. (1970).

An impurity in 2,4,5-trichlorophenol was found to be 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, a compound with a high mammalian toxicity and teratogenic effect.

HORWITZ, W. (Ed.). Official Methods of Analysis, 11th Ed. Association of Official Analytical Chemists, Washington, D.C., 1970, p. 468 (28.109).

The official first action gas chromatographic method for chick edema factor is presented in Section 28 on oils and fats. Fat, oil, fatty acid, or lipid is treated with H_2SO_4, and extracted with petroleum ether. The extract is purified on an Al_2O_3 column, further treated with H_2SO_4, and examined by electron capture-GLC. Peaks with retention times relative to aldrin (R_a) between 8 and 45 indicate presence of chick edema factors (hexa-, hepta-, and octachlorodibenzo-*p*-dioxins).

KEARNEY, P. C. Paper presented before a joint (United Kingdom, Canada, and United States) meeting on Pesticides, Washington, D.C., (November 5, 1970).

The Agricultural Research Service, USDA, began a program to assess the significance of chlorinated dioxin impurities in currently registered pesticides. Theoretically, any pesticide with a chlorinated phenoxy nucleus or which is derived from a chlorinated phenol precursor could contain chlorinated dioxin contaminants.

RESS, J., HIGGINBOTHAM, G. R., and FIRESTONE, D. Methodology for chlorinated aromatics in fats, oils, and fatty acids. *J. Assoc. Offic. Anal. Chem.* 53(3): 628–634 (1970).

Following review of the current status of chemical and biological methods for chlorophenols and chlorinated dibenzo-*p*-dioxins in fats, oils, and fatty acids, the modified electron capture-gas liquid chromatography method for the detection of chick edema factors was recommended for adoption as official first action to replace all existing gas-liquid chromatography methods.

ROBSON, J. M. Testing drugs for teratogenicity and their effects on fertility: The present position. *Brit. Med Bull.* 26(3): 212–216 (1970).

The problems of interpreting test results involving teratogenic compounds were outlined using data gathered on the teratogenicity of 2,4,5-T and its dioxin contaminant.

SPARSCHU, G. L., DUNN, F. L., and ROWE, V. K. Teratogenic study of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in the rat. *Toxicol. Appl. Pharmacol.* 17(1): 317–318 (1970).

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin was studied to determine whether this 2,4,5-T impurity could account for fetal abnormalities in test animals. Rats received 0, 0.03, 0.125, 0.5, 2.0, and 8.0 μg/kg body weight /day on days 6 to 15 of gestation. At the 0.5 level, the number of fetuses was reduced, and the number of resorptions and fetal deaths was increased.

VOS, J. G., and KOEMAN, J. H. Comparative toxicologic study with polychlorinated biphenyls in chickens with special reference to porphyria, edema formation, liver necrosis, and tissue residues. *Toxicol. Appl. Pharmacol.* 17: 656–668 (1970).

Briefly stated were the concerns and evidence pertaining to dioxins, particularly to the chick edema factor and whether PCBs and/or the dioxins were the culprit(s).

VOS, J. G., KOEMAN, J. H., VAN DER MAAS, H. L., TEN NOEVER DE BRAUW, M. C., and DE VOS, R. H. Identification and toxicological evaluation of chlorinated dibenzofuran and chlorinated naphthalene in two commercial polychlorinated biphenyls. *Food Cosmet. Toxicol.* 8(6): 625–633 (1970).

Three commercial polychlorinated biphenyl compounds (Phenoclor DP6, Clophen, and Aroclor 1260) were analyzed for impurities. In two of these (Phenoclor DP6 and Clophen A60) pentachlorodibenzofuran and tetrachlorodibenzofuran were among the polar compounds found.

1969

CANTRELL, J. S., WEBB, N. C., and MABIS, A. J. Identification and crystal structure of a hydropericardium-producing factor: 1,2,3,7,8,9-hexachloro-dibenzo-*p*-dioxin *Chem. Abstr. Acta. Crystrallogr.* B25(1): 150–156 (1969); 70: 51805u (0000).

Chemical identity of hexachlorodibenzo-*p*-dioxin, one of the toxic substances capable of producing the chick edema disease, was established by x-ray crystallography of a sample of edema-inducing lipid material.

RIED, W., and ENG, J. T. S. Reactions with diazocarbonyl compounds. *Ann. Chem.* 727: 219–221 (1969) (Ger.); *Chem. Abstr.* 72: 12458e (0000).

o-Quinone diazides added benzene with nitrogen elimination to yield chloro substituted dibenzofurans: 1,2,3,4-tetrachloro-, 1,2,3,-trichloro-, and 1,3-dichloro-.

1968

HIGGINBOTHAM, G. R., HUANG, A., FIRESTONE, D., VERRETT, J., RESS, J., and CAMPBELL, A. D. Chemical and toxicological evaluations of isolated and synthetic chloro derivatives of dibenzo-*p*-dioxin. *Nature* 220(5168): 702–703 (1968); *Chem. Abstr.* 70:18509c (0000).

Commercial chlorophenols including 2,4-dichlorophenol, 2,4,5,-trichlorophenol, and 2,3,4,6-tetrachlorophenol, were pyrolyzed to chlorinated dibenzo-*p*-dioxins. These were examined by electron capture-gas liquid chromatography and tested bibliogically by the chick embryo assay. 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin was prepared by direct chlorination of dibenzo-*p*-dioxin. These dioxins proved to be chick edema factors (hydropericardium factors) and toxic.

1967

ANONYMOUS. Search for chick edema factor. *Chem. Eng. News* 45(5): 10 (Jan. 30, 1967).

Chicks afflicted with edema, or hydropericardium, suffer an accumulation of fluid in the heart sac and gross kidney and liver damage; as little as 5 μg can kill a chick. X-Ray crystallographers have determined the molecular structure of one of the toxic compounds known as the chick edema factor. Single-crystal structural analysis showed that the structure is 1,2,3,7,8,9-hexachlorodibenzo-*p*-dioxin. Two crystals, each about 0.2×0.1×0.1 mm and weighing about 3μg were recrystalized from a benzene – hexane solution. The final data showed that the 1,2,3,7,8,9-hexachlorodibenzo-*p*-dioxin molecules are nearly planar, and are packed in the 044 crystallographic planes, with an interplanar separation of about 3.3 Å. No unusual bond lengths or angles were apparent.

1965

COX, J. M., WRIGHT, B. A., and WRIGHT, W. W. Thermal degradation of poly(phenylene oxides). *J. Appl. Polymer Sci.* **9**(2): 513–522 (1965).

The thermal degradation in vacuum of various phenylene oxide polymers and copolymers was studied by a weight-loss method. Thermal stability decreased with increasing substitution in the aromatic nuclei. This may be due to the presence of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, formed as an alternate reaction product. Chloro derivatives were more stable than the corresponding bromo derivatives, except for the tetra-substituted phenylene oxides.

KULKA, M., Perhalodibenzo-*p*-dioxins. Can. Patent 702,144, Appl. May 3, 1961; Granted Jan. 19, 1965, 13 pp. (1965)

Octahalodibenzo-*p*-dioxins, useful as chemical intermediates, biocides, and flame retardants, were prepared by using a pentahalophenol in the presence of a catalytic amount of halogen or a halogenated cyclohexadienone at 200–400°C. An 83% yield was attained for octachlorodibenzo-*p*-dioxin.

1962

JONES, E. L., and KRIZEK, H. A technique for testing acnegenic potency in rabbits, applied to the potent acnegen 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. *J. Invest. Dermatol.* **39**: 511–518 (1962).

Hyperkeratinization of the inner surface of the rabbit ear was induced by topical application of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin in acetone. The weight of keratin served as a criterion of acnegenic activity.

KULKA, M., Octahalodibenzo-*p*-dioxins. Belg. Patent 616,197, Appl. May 2, 1961; Granted July 31, 1962, 9 pp. (1962)

Octahalodibenzo-*p*-dioxins were prepared by heating pentahalophenols in the presence of catalytic amounts of halogen or halocyclohexadiene. For example, 40 g pentachlorophenol and 2 g 2,3,4,4,5,6-hexachloro-2,5-cyclohexadienone in 120 ml 1,2,4-trichlorobenzene was refluxed at 213°C to give 30 g of octachlorodibenzo-*p*-dioxin.

1961

BAUER, H., SCHULZ, K. H., and SPEIGELBERG, U. Occupational intoxications in manufacturing chlorophenol compounds. *Arch. Gewerbepath. Gewerbehyg.* **18**: 538–555 (1961).

Thirty-one workers in an industry manufacturing 2,4,5-trichlorophenol by sodium hydroxide saponification of 1,2,4,5-tetrachlorobenzene exhibited acne and symptoms of psychopathologic disturbances. Solutions of 0.01 to 0.05% of 2,3,6,7-tetrachlorodibenzo-*p*-dioxin painted on rabbit ears produced acne; oral administration of 0.05–0.1 mg/kg caused serious liver damage.

KULKA, M. Octahalodibenzo-*p*-dioxins. *Can. J. Chem.* **39**: 1973–1976 (1961).

Nearly 100% conversion from pentahalophenols to 1,2,3,4,6,7,8,9-octahalo-dibenzo-*p*-dioxins was accomplished by using reaction initiators such as halogens or halogen-generating compounds.

1960

DENIVELLE, L., FORT, R., and VAN HAI, P. Octachloro- and octabromodibenzo-*p*-dioxins and decachloro- and decabromodiphenyl ether. *Bull. Soc. Chim. France* **1960**. 1538–1543 (1960).

Pentachlorophenol was pyrolyzed at 300°C extracted with carbon tetrachloride and aqueous alkali, recrystalized from phenyl nitrite, and yielded "perchlorophenylene oxide" (melting point of 326°C). Steric considerations dictated ring fusion in the 1,2-position leaving octachlorodibenzo-*p*-dioxin the only acceptable structure for perchlorophenylene oxide. Sodium 2,4-dichlorophenate gave dichlorodibenzo-*p*-dioxin.

KAUPP, J., and KLUG, H. Perchlorodiphenylene dioxide. Ger. Patent 1,092,480, Appl. June 27, 1956, Granted Nov. 10, 1960 (1960).

Octachlorodibenzo-*p*-dioxin was prepared by heating pentachlorophenol and 2,3,4,4,5,6-hexachloro-2,5-cyclohexadien-1-one; the yield was 84%.

1959

TOMITA, M., UEDA, S., and NARISADA, M. Dibenzo-*p*-dioxin derivatives. XXVII. Synthesis of polyhalodibenzo-*p*-dioxin. *Yakugaka Zasshi* **79**: 186–192 (1959).

Pentachlorophenol was heated at 300°C for 12 hr. Recrystallization of the product from benzene, yielded octachlorodibenzo-*p*-dioxin needles.

1958

SANDERMANN, W., CASTEN, R., KRASTING, W., and PIEPER, J. Studies on wood-protection chemistry. IX. Investigations concerning oily blue stain protection agents. *Holzforsch. Holsverwert.* **10**(4): 57–66 (1958).

Compounds formed by heat treatment of pentachlorophenol such as octachlorodiphenylene oxide were inactive for preventing blue stain. Tetrachlorodiphenylene oxide was especially toxic to man and beast.

1957

GILMAN, H., and DIETRICH, J. J. Halogen derivatives of dibenzo-*p*-dioxin. *J. Amer. Chem. Soc.* **79**: 1439–1441 (1957).

Dibenzo-*p*-dioxin was synthesized and reacted with chlorine gas to form 2-chlorodibenzo-*p*-dioxin; a similar run coupled with ultraviolet light gave 2,7-dichlorodibenzo-*p*-dioxin.

KIMMIG, J., and SCHULZ, K. H. Chlorinatedaromatic cyclic ethers as a cause of the so-called chloracne. *Naturwiss.* **44**: 337–338 (1957) (Ger.).

Trichlordibenzo furan, tetrachlorodibenzofuran, and 2,3,6,7-tetrachlorodibenzodioxin were especially effective acne-inducing agents on rabbit ears. 2,3,6,7-Tetrachlorodibenzodioxin proved most toxic; the characteristic changes were achieved with concentrations of 0.01 to 0.002%. Higher concentrations caused liver necrosis and death. Single oral administration of 0.05 to 0.1 mg/kg body weight caused death in 1–2 weeks. Autopsy revealed necrosis and fatty degeneration of the liver. Pure 2,4,5-trichlorophenol and pentachlorophenol did not cause chloracne.

KIMMIG, J., and SCHULZ, K. H. Occupational acne (so-called chloracne) due to chlorinated aromatic cyclic ethers. *Dermatologia* **115** (4): 540–546 (1957) (Ger.).

The agent causing occupational chloracne in 31 employees of chlorophenol producing factories was found to be 2,3,6,7-tetrachlorodibenzodioxin. The toxic action in animals was due to the alkaline hydrolysis product of 1,2,4,5-tetrachlorobenzene. Tetrachlorodibenzo-*p*-dioxin and tri- and tetrachlorodibenzofuran were active skin irritants. 2,3,6,7-Tetrachlorodibenzodioxin formation from sodium trichlorophenolacetate was established as was isolation from the by-products.

SANDERMANN, H. S., CASTEN, R., and STOCKMANN, H. Pyrolysis of pentachlorophenol. *Chem. Ber.* **90**: 690–692 (1957).

Octachlorodiphenylene dioxide was formed after pentachlorophenol was heated at 300°C for 24 hr, distilled at 320°C, and crystallized from benzene or extracted with benzene and fractional crystallization. 2,3,7,8-Tetrachlorodiphenylene dioxide was active against insects and wood-destroying fungi; octachlorodiphenylene dioxide was inactive.

SCHULZ, K. H. Clinical and experimental studies on the etiology of chloracne. *Arch. Klin. Exp. Derm.* **206**: 589–596 (1957).

The acnegenic properties occurring as a refractive dermatologic condition in factory workers involved in the production of chlorinated aromatic compounds were ascribed to TCDD, an unwanted side product in the sythesis of 2,4,5-T.

1955

OITA, K., JOHNSON, R. G., and GILMAN, H. The chlorination of dibenzofuran and some of its derivatives. *J. Org. Chem.* **20**: 657–667 (1955).

Step-by-step reaction procedures were presented for the chemical synthesis of chlorinated dibenzofurans, i.e., 2-chloro-, 2,8-dichloro-, 3-chloro-, and a chlorodibenzofuran.

1954

CERNIANI, A., PASSERINI, R., and RIGHI, G. Ultraviolet spectra of some dibenzofurans. *Boll. Sci. Fac. Chim. Ind.* **12**: 75–79 (1954).

2-Chloro- and 3-chloro-dibenzofurans were characterized by ultraviolet spectrometry. These derivatives had little effect on spectra of the parent compound.

1953

JULIA, M., and BAILLARGE, M. Growth factors in plants. III. (1-Carboxymethyl-2-naphthoxy) acetic acid and (2-carboxymethyl-4-chlorophenoxy) acetic acid. *Bull. Soc. Chim. France.* 640–643 (1953).

In the preparation of 2,4-dichlorophenol, a portion of the mixture was insoluble in benzene–water; the substance was extracted with boiling ligroine and recrystallized to yield 2,7-dichlorodibenzo-*p*-dioxin.

1952

SHIBATA, I. S., NATORI, S., and SUMI, Y. Antibacterial effects of lichen substances and their related compounds. *J. Pharm. Soc. Japan* 72: 1333–1336 (1952).

The chlorinated dibenzofurans synthesized and tested for antibacterial activity included: 2-chloro-, 3-chloro-, 2,8-dichloro-, and 3,8-dichloro-. The chlorine atom, when in the 8-position of the dibenzofuran ring, increased its antibacterial effect.

1951

TOMITA, M., and WATANABE, W. Antibacterial activity of some organic compounds in vitro. II. Antibacterial activity of dibenzo-*p*-dioxin, phenoxathiin, and 1,4-benzodioxan derivatives on *Mycobacterium tuberculosis, Staphylococcus aureus,* and *Escherichia coli. J. Pharm. Soc. Japan* 71: 1204–1206 (1951).

2,7-dichlorodibenzo-*p*-dioxin was tested for antibacterial activity and found to be inactive.

1941

HIGASI, K. The molecular structures of diphenylene dioxide and phenoxathliin as revealed by dipole-moment data. *Sci. Papers Inst. Phys. Chem. Research* 38: 331–340 (1941).

2,6-Dichlorodiphenylene dioxide exhibited a dipole moment of 0.62 Debyes. This indicated a folded molecule and no optical isomers.

HIGASI, K., and UYEO, S. Polarity and molecular structure of diphenylene dioxide. *J. Chem. Soc. Japan* 62: 396–399 (1941).

2,6-Dichlorodiphenylene dioxide was found to have a small but finite dipole movement. This molecule and the parent probably fold along the line joining the two oxygen atoms.

UEO, S. 2,6-Dichlorodiphenylene dioxide. *Bull. Chem. Soc. Japan* 16: 177–179 (1941).

Synthesis of 2,6-dichlorodiphenylene dioxide, a light yellow compound with a melting point of 207°C and a dipole moment of 0.62 was described. The dipole movement of 2,6-dichlorodiphenylene dioxide was somewhat less than the dipole moment of diphenylene dioxide which was 0.64.

1939

British Thompson-Houston Co. Ltd. Electric insulation. Brit. Pat. 506,560 (May 31, 1939).

Direct chlorination of diphenylene oxide in the presence of a catalyst produced solid, waxlike products of high dielectric constants; i.e., mixture of chlorinated diphenylene oxide and pentachlorobiphenyl.

CLARK, F. M. Chlorinated diphenylene oxide composition for treating paper in capacitors, U.S. Patent 2,198,473 (April 23, 1939).

Chlorinated diphenylene oxide containing 1 to 4 atoms of chlorine per molecule imparts a constant electrical capacity when used to impregnate paper in capacitors.

1936

BELL, F. Pyrolysis of chlorophenols. *J. Chem. Soc.* 1936: 1244.

o-Chlorophenol was pyrolyzed at 180–340°C; diphenylene oxide and 3,6-dichlorodiphenyl oxide were isolated from the distillate.

1934

GILMAN, H., BROWN, G. E., BYWATER, W. G., and KIRKPATRICK, W. H. Dibenzofuran. III. Nuclear substitutions. *J. Amer. Chem. Soc.* 56: 2473–2477 (1934).

2-Chloro- and 2,8-dichlorodibenzofuran were synthesized. Dibenzofuran and chlorine in carbon tetrachloride gave 38% of the 2,8-dichloro derivative which had a melting point of 185°C. Dibenzofuran in alcohol at 60°C gave the 2-chloro derivative which had a melting point of 102.5°C.