Uploaded to VFC Website

~ November 2012 ~

This Document has been provided to you courtesy of Veterans-For-Change!

Feel free to pass to any veteran who might be able to use this information!

For thousands more files like this and hundreds of links to useful information, and hundreds of "Frequently Asked Questions, please go to:

Veterans-For-Change

Veterans-For-Change is a 501(c)(3) Non-Profit Corporation
Tax ID #27-3820181

If Veteran's don't help Veteran's, who will?

We appreciate all donations to continue to provide information and services to Veterans and their families.

https://www.paypal.com/cgi-bin/webscr?cmd=_s-xclick&hosted_button_id=WGT2M5UTB9A78

Note: VFC is not liable for source information in this document, it is merely provided as a courtesy to our members.

Item ID Number	05207 ☐ **Not Scanned**
Author	Harker, Timothy L.
Corporate Author	Environmental Protection Agency, Office of the General
Report/Article Title	United States Environmental Protection Agency (EPA) Before the Administrator, In re: 2,4,5 -T, FIFRA Consolidated Docket No. 295, Respondent's First Pretrial Brief and Second Pretrial Brief
Journal/Book Title	
Year	1974
Month/Day	March 11
Color	☐
Number of Images	82
Descripton Notes	

UNITED STATES OF AMERICA

ENVIRONMENTAL PROTECTION AGENCY

BEFORE THE ADMINISTRATOR

IN RE:

2,4,5-T

FIFRA CONSOLIDATED DOCKET
NO. 295

RESPONDENT'S FIRST PRETRIAL BRIEF

Timothy L. Harker
Attorney for Respondent
Office of the General Counsel
401 M Street, S. W.
Washington, D. C.
(202) 755-0795

Nature of the Proceedings

This case is the culmination of a prolonged effort to test in a public forum the response of the pesticide Registrants herein to serious questions as to the risk to public safety raised by the use of 2,4,5-Trichlorophenoxyacetic Acid (2,4,5-T).

Initial public concern over the use of 2,4,5-T was motivated by reports in the summer and fall of 1969 of an alleged increased incidence of birth defects in South Vietnam, potentially linked to a military defoliation campaign utilizing this phenoxy herbicide. 1/ A broad screening of pesticide and industrial chemicals, thereafter, by the Bionetics Research Laboratory confirmed that 2,4,5-T fed to laboratory mice and rats induced the birth of deformed offspring.

Federal agencies made the initial regulatory response in the spring of 1970 after the Secretary of Health, Education and Welfare speaking on behalf of the Surgeon General informed the Secretary of Agriculture that, " . . . a prudent course of action must be based on the decision that exposure to this herbicide may present an imminent hazard to women of child-bearing age." 2/ On April 15, 1970 the Secretary of Agriculture announced the immediate suspension of the registrations for all

---

1/ Report of the Advisory Committee On 2,4,5-T to the Administrator of the Environmental Protection Agency, May 1971, p. 3.

2/ Ibid, at p. 4.

2,4,5-T products used in lakes, ponds and ditch banks, and for 2,4,5-T liquid formulations used around homes, recreation areas and similar sites involving direct human exposure. [3/] Shortly thereafter USDA cancelled the registrations of all granular 2,4,5-T formulations for use around the home and similar places of potential human exposure and cancelled all registered uses of 2,4,5-T on food crops intended for human consumption. [4/]

Pursuant to the provisions of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) [5/] four registrants challenged the order of cancellation, two requesting a hearing and two moving that the matter be referred to an Advisory Committee of the National Academy of Science. Public hearing was deferred, pending issuance of the Advisory Committee Report, accomplished on May 7, 1971.

The Advisory Committee concluded that based on current patterns of usage of 2,4,5-T and what was known about its fate in the environment, it was unlikely that accumulation could occur so as to constitute a hazard to human health. The majority opinion was, however, accompanied by a warning -- that there was an absence of environmental information about a particularly poisonous contaminant of 2,4,5-T formulations, 2,3,7,8-Tetrachlorodibenzoparadioxin (TCDD or tetra-dioxin), and that this toxicant could pose a problem for human health, although a level of .1 ppm (parts per million) may be acceptable.

3/ USDA-PRD, PR 70-1, 20 Apr. 1970.

4/ USDA-PRD, PR 70-13 1 May 1970.

5/ 7 USC 135 et. seq; amended, 1972, 7 USC 136 et. seq. (Supp. 1973).

A minority report was filed, which reasoned that the Committee in its optimism had neglected to consider fully the consequences of the dearth of data on the fate of TCDD in the food chain and in tissue.

After due consideration of these contrasting opinions the Administrator of the Environmental Protection Agency [6] continued in effect the order of cancellation.[7] In subsequent orders[8] the Administrator elaborated upon the reasons for continuing the cancellation, as follows:

> 1. A contaminant of 2,4,5-T--tetrachlorodibenzoparadioxin (TCDD, or dioxin)--is one of the most teratogenic chemicals known. The registrants have not established that 1 part per million of this contaminant--or even 0.1 ppm--in 2,4,5-T does not pose a danger to the public health and safety.
>
> 2. There is a substantial possibility that even "pure" 2,4,5-T is itself a hazard to man and the environment.
>
> 3. The dose-response curves for 2,4,5-T and dioxin have not been determined, and the possibility of "no effect" levels for these chemicals is only a matter of conjecture at this time.
>
> 4. As with another well-known teratogen, thalidomide, the possibility exists that dioxin may be many times more potent in humans than in test animals.

6/ EPA under the Reorganization Plan No. 3 of 1970 (December 2, 1970, 35 Fed. Reg. 15623) was entrusted with the administration of the FIFRA.

7/ Determination and Order of the Administrator, August 6 1971 (36 Fed. Reg. 14777).

8/ Orders of the Administrator of November 4, 1971 and April 13, 1972 (FIFRA Docket Nos. 42 and 44).

5. The registrants have not established that the dioxin and 2,4,5-T do not accumulate in body tissues. If one or both does accumulate, even small doses could build up to dangerous levels within man and animals, and possibly in the food chain as well.

6. The question of whether there are other sources of dioxin in the environment has not been fully explored. Such other sources, when added to the amount of dioxin from 2,4,5-T, could result in a substantial total body burden for certain segments of the population.

7. The registrants have not established that there is no danger from dioxins other than TCDD, such as the hexa- and heptadioxin isomers, which also can be present in 2,4,5-T, and which are known to be teratogenic.

8. There is evidence that the polychlorophnols in 2,4,5-T may decompose into dioxin when exposed to high temperatures, such as might occur with incineration or even in the cooking of food.

9. Studies of medical records in Vietnam hospitals, and clinics below the district capital level suggest a correlation between the spraying of 2,4,5-T defoliant and the incidence of birth defects.

10. The registrants have not established the need for 2,4,5-T in light of the above-mentioned risks. Benefits from 2,4,5-T should be determined at a public hearing, but tentative studies by this agency have shown little necessity for those uses of 2,4,5-T which are now at issue.

These expressions of doubt as to the safety of and necessity for using 2,4,5-T on human food crops are now among the issues for adjudication in this Consolidated Proceeding.

Registrant Dow Chemical Company then obtained an injunction against further administrative action on 2,4,5-T. [9/] After almost two years of "interlocutory judicial jousting" [10/] the legal impediments to a

---

9/ Unreported; Memorandum and Order; E. D. Ark., June 22, 1972.

10/ Dow Chemical Co. v. Ruckelshaus, 477 F. 2d 1317, 1326 (8 Cir. 1973).

public hearing were removed when the U. S. Court of Appeals overturned the lower court injunction.

At this time significant new information was revealed which altered the course of this controversy. Residues of 2,4,5-T related TCDD were reported in Vietnamese fish and crustaceans, and the development of the refined instrument sensitivity (parts per trillion) necessary for determining whether TCDD is penetrating into the United States environment was disclosed. 11/

In response to the greatly increased analytical sensitivity, Respondent initiated an extensive environmental and human monitoring project for TCDD. The finding of TCDD in Vietnamese fish disclosed a potential threat to public health and to the environment from even the non-food uses of 2,4,5-T (rangeland, rights of way, forestry), and in response, pursuant to section 6(b)(2) of the FIFRA as amended, EPA issued a Notice of Intent to Hold a Hearing to determine whether all remaining registered uses of 2,4,5-T should be cancelled. 12/

The issues therein designated for hearing, in addition to those already set for hearing on the cancelled food uses of 2,4,5-T, are as follows:

11/ Baughman and Meselson. An Analytical Method for Detecting TCDD (Dioxin): Levels of TCDD in Samples from Vietnam; Environ. Health Persp., Exper. Issue No. 5, pp. 27-35, 1973.

12/ 38 Fed. Reg. 19860, July 24, 1973.

A. The health hazards to man and to other animals which may be caused by 2,4,5-T and/or its extremely toxic contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), with emphasis on the following:

1. Is 2,4,5-T or TCDD a teratogen?

2. Does 2,4,5-T or TCDD induce other adverse reproductive effects?

3. Is 2,4,5-T or TCDD a mutagen?

4. Is 2,4,5-T or TCDD a carcinogen?

5. Can exposure to 2,4,5-T or TCDD induce sub-lethal chronic health effects?

6. Can chronic, low-level exposure to 2,4,5-T and/or TCDD cause delayed lethality?

B. The extent of the health risk for man and other animals posed by 2,4,5-T and TCDD, with emphasis on the following conditions:

1. Can additional TCDD be generated in the environment by the thermal stress of 2,4,5-T or its metabolites?

2. Can 2,4,5-T or TCDD persist and bioaccumulate in the environment?

3. What are the avenues of human and animal exposure to 2,4,5-T and TCDD? For example, can aerial drift or water transport of 2,4,5-T or TCDD cause movement of these compounds away from the site of application?

4. Are 2,4,5-T or TCDD residues being stored and accumulated in the human food supply and in human and animal tissue, including humans and wildlife directly exposed to 2,4,5-T?

5. Are other dioxins and similar contaminants, besides TCDD, present in 2,4,5-T and, if so, what risk to health do they constitute?

6. What are other environmental sources of dioxins particularly TCDD, and do these sources enhance the total dioxin body burden and exacerbate the health risks raised by 2,4,5-T and related TCDD?

7. What are the current levels of dioxins in registered 2,4,5-T products and in technical material used to formulate these products?

8. Do the current methods of manufacture of 2,4,5-T provide for consistently low levels of dioxins in the final technical product and what are the quality control measures used to minimize dioxin levels?

C. The necessity for the continuation of the registered uses of 2,4,5-T, with enphasis on the following:

1. What are the pests which each registered use is intended to control and the degree of control achieved by each use?

2. What is the cost, timing, and rate of application of 2,4,5-T for each use?

3. What alternative controls exist for each registered use and what is the cost and effectiveness of each alternative.

4. Do alternative pesticide products cause adverse environmental effects?

5. What are the economic implications of these alternatives, including that of no control?

By motion of Respondent on October 2, 1973 and order of the Chief Administrative Law Judge on November 12, 1973 these hearings on all registered uses of 2,4,5-T have been consolidated into the proceeding herein.

Legal Framework of the Proceeding

From this Consolidated Proceeding a final determination will be derived as to whether the registrations of 2,4,5-T should be cancelled. This decision by the Administrative Law Judge and ultimately by the Administrator is shaped significantly by certain principles.

The registrations at issue must fall unless it can be convincingly demonstrated that these uses of 2,4,5-T do not cause unreasonable adverse effects on the environment. 13/ In reaching the determination as to unreasonable adverse environmental effects, the risk to public health and to wildlife must be balanced against any benefit to the public's welfare from continued use of 2,4,5-T. Constituents of the overall balance are the answers to scientific and technical questions posed as issues for this hearing, supra. It is the burden of Registrants and of the Intervenors in behalf of continued registration to answer these questions and to persuade the Administrative Law Judge and the Administrator by clear and convincing evidence that each contested use of 2,4,5-T does not present an unacceptable risk of adverse environmental effects. 14/

13/ 7 USC 136. The term 'unreasonable adverse effects on the environment' means any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide.

14/ See Neodane Company, Inc.v. Environmental Protection Agency, 470 F. 2d 194 (8 Cir. 1971); In Re Stevens Industries, 37 F.R. 13369 (1972); aff'd EDF v. Environmental Protection Agency, No. 72-1548 (CADC, 1973); EDF v. Ruckelshaus, 439 F. 2d 584 (CADC, 1971); Stearns Electric Paste Company v. EPA, 461 F. 2d 293, 304, 306 (7 Cir., 1972); and Reasons Underlying the Registration Decisions Concerning Products Containing DDT, 2,4,5-T, Aldrin and Dieldrin, Environmental Protection Agency Release, March 18, 1971, at p. 4, where the Administrator stated: "It is clear from the statute, the legislative history, and judicial construction that the burden of establishing the safety and effectiveness of a product remains with the registrant from the time of initial application through continued registration of the product."

That Respondent must go forward with an affirmative exposition of those facts which indicate why the food uses of 2,4,5-T should be cancelled and which address the questions raised as to all 2,4,5-T uses does not obviate Registrants' burden of ultimate persuasion on each issue of this proceeding.

Response to the Hearing Issues

Information available to Respondent will work considerably to resolve the issues in the 2,4,5-T controversy. In its First Pre-Hearing Brief, Respondent sets forth that information which is now developed. Respondent's current data, however, does not thoroughly illuminate certain areas of inquiry. In this regard, it is anticipated that Registrants, in attempting to demonstrate the safety of and social necessity for their pesticide product, will adduce significant new data, derived from thorough research and field monitoring, particularly on the crucial questions involving the toxicity of low-levels of TCDD. The Advisory Committee requested such data in May, 1971. Surely the intervening 2 1/2 years has been sufficient for Registrants to undertake meaningful research on these questions. 15/

15/ The Advisory Committee's recommendations included:

> "That existing deficiencies in information relative to possible accumulation in the soil and possible magnification in the food chain of the dioxin TCDD be rectified by specific research directed to this end, with these questions to be subjected to scientific review within three years of the present date and yearly thereafter until these questions are resolved.
>
> That additional post-registration monitoring for adverse effects of agricultural chemicals be established, to include both surveillance for such effects in man and domestic and wild animals, as well as consideration of the applicability of new methodology that may be evolved for specialized testing, e.g., for carcinogenesis, mutagenesis or teratogenesis." op. cit. Note 1 at p. 67.

Many of the issues presented in the Administrator's 2,4,5-T Orders of November 4, 1971 and April 13, 1972 are subsumed under issues contained in the Statement of Issues of July 19, 1973. Where appropriate herein, Respondent has grouped these related issues. The numerous subsidiary questions are discussed first; ultimate questions are then discussed where Respondent is prepared to adopt a regulatory position.

A. The health hazards to man and to other animals which may be caused by 2,4,5-T and/or its extremely toxic contaminant, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), with emphasis on the following:

Teratogenicity

1. Is 2,4,5-T or TCDD a teratogen?

A contaminant of 2,4,5-T -- tetrachlorodibenzoparadioxin (TCDD, or dioxin) -- is one of the most teratogenic chemicals known. The registrants have not established that 1 part per million of this contaminant -- or even 0.1 ppm -- in 2,4,5-T does not pose a danger to the public health and safety.

There is a substantial possibility that even "pure" 2,4,5-T is itself a hazard to man and the environment.

The dose-response curves for 2,4,5-T and dioxin have not been determined, and the possibility of "no effect" levels for these chemicals is only a matter of conjecture at this time.

As with another well-known teratogen, thalidomide, the possibility exists that dioxin may be many times more potent in humans than in test animals.

Studies of medical records in Vietnam hospitals and clinics below the district capital level suggest a correlation between the spraying of 2,4,5-T defoliant and the incidence of birth defects.

Teratology is concerned with the origin and development of congenital malformations, which are abnormalities in the structural or functional development of the embryo or fetus. Embryotoxicity is a more general term which describes fetal toxicity, growth retardation and teratology. It is clear that 2,4,5-T and TCDD constitute a potential teratogenic and embryotoxic hazard to man.

Ascertaining the effect of 2,4,5-T on the fetus has been complicated by the presence of various amounts of TCDD in the tested 2,4,5-T. However, tests with 2,4,5-T in which the content of TCDD was 1 ppm or less indicate that even so-called "pure" 2,4,5-T is teratogenic. Terata including kidney abnormalities and deformed eyes and tails has been induced by 2,4,5-T in different strains of rats at levels of 100 mg/kg/day. Embryotoxicity has been induced in rats at doses as low as 50 mg/kg. 16/

Fetal deformities, including exencephaly, missing eyelids, delayed head ossification and cleft palate were produced in hamsters tested with 2,4,5-T at doses from 40 to 80 mg/kg, containing less than .1 ppm TCDD 17/ The dosage of 80 mg/kg caused a significant decrease in the percentage of viable fetuses per litter. A dosage of 40 mg/kg with no detectable TCDD caused decreases both in the percentage of viable fetuses and in the average fetal weight. Increasing the amount of TCDD in the 2,4,5-T generally increased the incidence of adverse effects in the hamster.

16/ Op. cit., Note 1.

17/ Collins, T. F. X., and Williams, C. H. Environ. Contam. Toxicol. 6:559-567, 1971.

Courtney and Moore [18] using 2,4,5-T at 100 mg/kg, containing less than .05 ppm TCDD produced cleft palate and kidney malformations in three strains of mice. Roll [19] demonstrated that 2,4,5-T can produce cleft palate in mice at 35 mg/kg. Neubert and Dillman [20] induced cleft palate in mice with 45 mg/kg 2,4,5-T, containing less than .02 ppm TCDD. As little as 15 mg/kg of purified 2,4,5-T and 12 mg/kg of 2,4,5-T butyl ester caused a decrease in fetal weight (fetotoxicity).

TCDD has been demonstrated to be a potent teratogen and embryotoxicant inducing adverse effects in the microgram per kilogram (ug/kg) range in all species tested. Two teratogenic effects have been clearly related to TCDD, cleft palate and kidney abnormalities. [21] Other effects include involution of lymphatic tissues, predominately a drastic reduction in the size of the thymus, the spleen and the lymph nodes. Because this impairment of the lymphatic organs causes a postnatal impairment of a basic defense system and thereby causes a pronounced reduction in postnatal survival the effect may be considered teratogenic, even though they may also occur in young or adult animals treated with TCDD.

Other TCDD effects are embryotoxic, not teratogenic, and are also induced in adult and young animals under the toxic influence of TCDD. These are intestinal hemorrhage, the infiltration of fat into the

---

18/ Courtney, K. D., and Moore, J. A., Toxicol. Appl. Pharmacol., 20:396-403, 1971.

19/ Roll, R., Fd. Cosmet. Toxicol., 9:671-679, 1971.

20/ Neubert, D. and Dillman, I., Naunym-Schmiedeberg's Arch. Pharmacol., 272:243-264, 1972.

21/ Neubert, D., et al., Environ. Health Persp., Exper. Issue No. 5, pp. 67-79, 1973.

liver, subcutaneous edema and delayed ossification.[22] Sparschu, et al.[23] found increased fetal mortality, early and late fetal resorption and intestinal hemorrhage of the fetus of rats at a dietary dose of .125 - .2 ug/kg. In this study no embryotoxic effects were noticed at .03 ug/kg; a dose approximating 600 ppt in the rats' diet during the critical period of pregnancy. Courtney and Moore[24] produced kidney abnormalities in rat fetuses with .5 ug/kg TCDD. They reported cleft palate and kidney abnormalities in three strains of mice after dams were injected with 1 to 3 ug/kg during days 6 - 15 of pregnancy. Neubert[25] reported a clear-cut potentiating teratogenic effect between 2,4,5-T and TCDD.

Available knowledge makes demonstrating the presence of a public risk of 2,4,5-T, TCDD-induced birth defects less difficult than assessing the magnitude of that risk. One gap in the state of the medical art is precise knowledge of the predictive value for man of terata testing in animals. Imprecision is inherent in extrapolating from test animals to

---

22/ Ibid.

23/ Sparschu, et. al., Food Cosmet. Toxicol. 9:405-412, 1971.

24/ Courtney and Moore, Toxicol. Appl. Pharmacol. 20:396-403, 1971.

25/ Op. cit., Note 21.

man, but the application of certain guidelines demonstrates the importance of such testing in predicting risk to man:

1. Society should not knowlingly permit its members to be used as divining rods for discerning hidden destructive forces. Laboratory animals are, therefore, not a convenience but a necessity if public agencies are not to await the noticeable occurence of human birth defects which can be traced directly to a specific source before taking protective measures.

Even a significant increase in human birth defects which might be related to 2,4,5-T, TCDD would likely be inapparent from normal observation of the incidence of birth defects. There is no national registry of teratogenic effects. Nor has any major human teratogen been detected by prospective monitoring of the population at large. The teratogenicity of X-ray, German measles, thalidomide and methyl mercury were recognized not by epidemiological survey but rather by individual medical practitioners who observed small "clusters" of deformities and traced them to the source. 26/ The terata induced in laboratory animals by 2,4,5-T, TCDD, primarily cleft palate and kidney abnormalities, are not so egregious (as contrasted, for example, with the absence of limbs, caused by thalidomide) as to make an increase in the human incidence of such deformities readily noticeable.

26/ Report of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health, Parts I and II, U. S. Department of Health Education and Welfare, December 1969, pp. 661-662.

The fact that public exposure to TCDD would likely come through residues in the food supply, would prohibit even the "cluster" approach to detecting human terata, such as was pursued in the cases of thalidomide and other major teratogens, rendering a very real effect from 2,4,5-T, TCDD all the more hidden from detection by observation of the population. These informational voids compel reliance upon test animals.

2. Physiological variations existing between test animals and man do not necessarily indicate that man will be unresponsive or less responsive to 2,4,5-T and TCDD. They may be such as to render man more susceptible. Variations may exist between man and test animal in the distribution and release of TCDD during vital periods in organogenesis, in the time and degree of association of TCDD with the embryo or fetus, and in the elimination of TCDD from the maternal and fetal receptors. Little is understood about the etiology of birth defects. Even less is known about the long-term behavior of tetra-dioxin in the body of mammals. Nothing is known about the retention, distribution and elimination of TCDD in the human organism. Man may thus respond more readily than test animals to this teratogen.

The thalidomide experience is demonstrative. The lowest observed effective dose for human terata was .5 mg/kg/day. The hamster, dog, rat and mouse exhibited effects at 350, 100, 50 and 30 mg/kg/day, respectively. 27/

27/ Kalter, H., Teratology of the Central Nervous System: Induced and Spontaneous Malformations of Laboratory, Agricultural and Domestic Animals. Chicago, University of Chicago Press, 1968.

Thus, laboratory tests on mammalian species showing that 2,4,5-T and TCDD are teratogenic present real grounds for concern. But these animal tests permit no more refined a practical conclusion, particularly as to TCDD, than that a risk of unknown magnitude exists of causing human birth defects by using 2,4,5,-T so as to contaminate the public food supply. There is no accepted procedure for setting safe levels for man based on no-effect levels for terata produced in the laboratory.

The potential greater sensitivity of man to this teratogen renders highly tenuous any effort to extrapolate "no effect" levels for man. In addition, there is no widely accepted scientific procedure for establishing a safe level for teratogens in the food supply. Further, reliable no-effect levels for tetra-dioxin, in the laboratory species tested, which take into account a proportionality between the number of animals tested and the resultant teratogenic effect, may not have been ascertained. For example, in the case of thalidomide, a teratogen much more potent in man than in the tested animals, laboratory tests may have failed to designate a threshold level even for the test animals. 28/ In this regard, the fact that laboratory testing on TCDD (carried out on very small numbers of animals) demonstrates its teratogenic action at extremely low levels casts even greater doubt on the wisdom of attempting to set an acceptable "safe level" for the millions of people at presumptive risk.

28/ Jusko, William J., Pharmacodynamic Principles in Chemical Teratology: Dose-Effect Relationships. Journ. Pharmac. and Exper. Therap., Vol. 183, No. 3, 1972, pp. 469-480.

Other difficulties make impossible at present predicting an acceptable no effect level for this teratogen. Just as man may be much more susceptible than test animals, some persons in the exposed, at-risk population will be more susceptible to teratogenic effects than others. The genetics of cleft palate, for example, indicate varying susceptibilities to the inheritance of this birth defect.[29/] Further, only a fraction of the women who took thalidomide gave birth to deformed children.[30/] With varying individual susceptibilities, establishing one level for the protection of all women would be speculation.

There is also lacking any clear indication that human exposure to 2,4,5-T, TCDD has not caused significant increases in birth defects. Past surveys of human exposure have not arrived at statistically significant conclusions. However the report to the American Association for the Advancement of Science[31/] does indicate higher stillbirths and malformations in certain areas and during periods of the heaviest 2,4,5-T defoliation campaign in Vietnam. That a spurious effect may have been produced in this survey by incomplete data does not, however,

---

29/ Personal Communication, Matthew Meselson, Harvard University, January 11, 1974.

30/ Op. Cit., Note 26, at p. 659.

31/ Meselson, M. A., A. H. Westing and J. D. Constable, 1970. Background Material Relevant to Presentations at the 1970 Annual Meeting of the AAAS, Herbicide Assessment Commission of the American Association for the Advancement of Science. Revised January 14, 1971.

necessarily indicate that the effect was to exaggerate the incidence of stillbirths and terata. Rather, the importance of this effect may as well have been to disguise a higher level of birth defects. 32/

Available information, then, depicts a hazard of birth defects from 2,4,5-T and related TCDD. The magnitude of the risk cannot be reliably quantified. The extent, therefore, of the hazard to man must depend on the risk of human exposure, particularly to tetra-dioxin. Where the risk of such exposure is direct, Respondent will seek the final cancellation of the related 2,4,5-T use. Where information as to the risk of human exposure is less clear, Registrants must bear the burden of demonstrating that the risk is de minimis or that the particular pesticide use in question has compelling public importance, so as to outweigh even a minor threat of human exposure.

32/ Op. cit., Note 1, at pp. 71-72.

A.2. Does 2,4,5-T or TCDD Induce Other Adverse Reproductive Effects?

Substantial questions have been raised as to whether adverse reproductive effects are induced by 2,4,5-T and TCDD. Moore, et al.[33] have reported adverse postnatal effects on the kidneys of mice whose dams were treated with TCDD. The importance of TCDD in mother's milk is suggested by the fact that the highest incidence of kidney abnormality occurred in those progeny whose mothers had been treated with TCDD during the nursing period.

2,4,5-T administered during pregnancy has been demonstrated to cause increased resportion and decreased fetal and maternal weight.[34] Thomas and Lloyd[35] found that 2,4,5-T behaved similarly to other organochlorines, e.g., dieldrin and DDT, in decreasing the ability of the mouse prostrate gland to accumulate androgen, probably the consequence of reducing the actual uptake of androgen. The research with "toxic fat", infra, p. 24, showed a marked decrease in spermatogenesis linked to TCDD. It is known that decreased sexual drive is among the reported chronic symptoms of persons who have been occupationally exposed to 2,4,5-T, TCDD.[36]

33/ op. cit., Note 18.

34/ Dougherty, W.H., et al., Alst 9 p. 7, 12th Annual Meeting Soc. Toxicol., 1973.

35/ Thomas, J.A. and Lloyd, J.W., Pesticides and the Environment, Intercontinental Medical Book Corp., N.Y. pp. 43-51, 1973.

36/ Bauer, H., Schulz, K.H., Spiegelberg, U., Arch. Gewerbepath, Vol. 18, 538-555, 1961.

The significance of these indicators for human or wildlife reproduction is unclear. While Registrants must attempt to demonstrate the unimportance of such facts, it is unfortunate that there has been a failure to complete necessary multi-generation reproductive studies with 2,4,5-T, TCDD.

A.3. Is 2,4,5-T or TCDD a Mutagen?

As with the various reproductive effects noted, there are indications that TCDD is mutagenic. One in vitro study[37] with bacteria exposed to 2,4,5-T noted no mutagenic effects. However, a practical negative conclusion cannot be reached from this study. Here, also, Registrants' laboratory research and occupational hygiene information should be adduced to speak more clearly to the question of the importance for man of these risks.

Hussain, et al.[38] using three distinct bacterial systems reported TCDD to be mutagenic. Jackson[39] demonstrated a dramatic inhibition of mitosis and the production of cytological abnormalities in the African blood lilly at levels of .2 to 1 ug/l TCDD.

37/ Anderson, K.J., et al., J. Agric. Food Chem. 20:649-656, 1972.

38/ Hussain, S., et al., Ambio., 1(1):32-33, 1972.

39/ Jackson, W.T., J. Cell. Sci. 10:15-25, 1972.

A.4. Is 2,4,5-T or TCDD a Carcinogen?

The carcinogenic potential of 2,4,5-T related TCDD exists. The available information conveys no discernible indication that 2,4,5-T itself, is a carcinogen.

The carcinogenic potential of TCDD is determined from the following work. Buu-Hoi, et al.[40] reported that intraperitoneal doses of TCDD (1 and 10 mg/kg) induced liver lesions in rats. These lesions were characterized by amisokaryosis, frequent binucleation, and focal hyperplas ia of Kuffer cells. They also reported a similarity between TCDD and known heptacarcinogenic compounds in the effects on microsomal hydroxylases and in reducing liver arginase.[41]

Gupta, et al.[42] reported degenerative liver lesions and large multinucleated giant heptatocytes, produced by 10 ug/kg/day TCDD in rats for 13 days. The researchers conclude that the presence of these cells, the increased number of mitotic figures, and the pleomorphism of cord cells point to the need for assessing the possibility that TCDD induces hyperplastic nodules or neoplasms.

40/ Buu-Hoi, N.P., et al., Naturwiss. 59(4):174-175, 1972.

41/ Buu-Hoi, N.P., et al., C.R. Acad. Sci. (Paris) D273(3):708-711, 1971.

42/ Gupta, B.N., Environ. Health Persp. Exper. Issue No. 5., pp. 127-140, 1973.

A.5. Can Exposure to 2,4,5-T or TCDD Induce Sub-lethal Chronic Health Effects?

6. Can Chronic, Low-level Exposure to 2,4,5-T and/or TCDD Cause Delayed Lethality?

Except for the potential reproductive and mutagenic damage previously discussed, available information does not indicate that exposure to low levels of 2,4,5-T, itself, induces chronic effects. The apparent rapid human excretion of 2,4,5-T tends to support a tentative conclusion that chronic ill health would not be expected from long-term low-level exposure.[43/]

The same cannot be said for 2,4,5-T related TCDD or other possible toxic contaminants of 2,4,5-T. The facts on TCDD's chronic health effects are of major evidentiary concern. These facts describe a pernicious, little understood toxicant, capable in minute quantities of inducing a variety of chronic illness and, perhaps, of causing death as a delayed response to exposure. The burden of mitigating this concern must be particularly heavy for Registrants in that the risk is clearly raised by every available research effort and the lifetime feeding studies in mammalian species, necessary to effectively lay to rest these strong signals, have not been conducted.

Of major concern is the effect of TCDD on lymphoid tissue, previously discussed.[44/] Related to such impairment of an organism's basic defense system is the conclusion of Vos, et al.[45/] that TCDD at sublethal doses

43/ Gehring, P.J., et al., Toxicol. App. Pharmacol. 26:352-361, 1973.

44/ supra, p. 13.

45/ Vos, J.G., et al., Envir. Health Persp., Exper. Issue No. 5, pp. 149-162, 1973.

suppresses the cell-mediated immunity in both mice and guinea pigs. The authors suggest that, in the absence of major pathologic effects except in the lymphoid system, the death caused by sub-lethal doses was due to impairment of the organism defense mechanism. Zinkl, et al.[46] observed TCDD related lymphophenia in mice and guinea pigs, a result which is consistent with its noted immuno-suppresive effects.

Allen and Carstens[47] fed monkeys various percentages of "toxic fat", reported to contain 35 ppm of TCDD and other dioxions. There was an inverse relationship between the percent toxic fat in the diets and the number of days the monkeys survived. Monkeys fed 5 or 10% began dying around the third month. At the lowest dose, the total dioxin intake which produced a mean survival time of 445 days was 2.15 mg/l.[48] In all test groups, the TCDD induced a variety of chronic illness one or two months before death, including alopecia and subcutaneous edema, focal neurosis of the liver, gastric ulcers, reduced hematopoiesis and spermatogenesis.

These test data suggest that TCDD poisoning may be cumulative.[49]

Daily doses of 10 ug/kg/TCDD killed 15 of 16 rats, on days 15 through 31.[50] Rats receiving 1 ug/kg for 31 days suffered

46/ Zinkl, et al., Environ. Health Persp., Issue No. 5, pp. 111-123, 1973.

47/ Allen and Carstens, Amer. J. Vet. Res., 28: 1513-1526, 1967.

48/ Flick, et al., Poultry Sci., 52: 1637-1641, 1973.

49/ Baughman and Meselson, Environ. Health Persp., Exper. Issue No. 5, pp. 27-35, 1973.

50/ Gupta, et al., Environ. Health Persp. Issue No. 5, pp. 125-140, 1973.

decreased weight gain which was reversed after cessation of dosing. A no effect level was not found and whether withdrawal after chronic exposure may reverse more serious ill-effects is unclear. Dosing guinea pigs with 1 ug/kg a week killed all animals, on the average within four weeks.[51/]

Fries[52/] added TCDD (C^{-14} labelled) in the diet of rats at 7 and 20 ppb. The rats were placed on the feed for 6 weeks and withdrawn for 4 weeks. After 6 weeks of feeding a plateau in the body residues had apparently not been attained in either sex. Decreased feed consumption and weight gain were observed. The liver/body weight ratio was also increased. This effect was reversed by withdrawal but only as to the lower dose.

Poland and Glover[53/] using the chick embryo conclude that TCDD is approximately 3 orders of magnitude more potent than other known porphyrogenic compounds. Goldstein, et al.[54/] also conclude that TCDD is the most potent porphyrogenic chemical known. A single dose of 150 ug/kg TCDD caused a 1,000 fold increase in the uroporphyrin content of the mice livers within 3 weeks and increased induction of ALA synthetase. Similar effects were induced by weekly doses of 25 ug/kg for one month. In addition to porphyria, extensive liver damage, atrophy of the thymus,

---

51/ ibid. at p. 127.

52/ USDA - Beltsville; unpublished.

53/ Poland, A. and Glover, E., Science, 170, 476-477 (1973).

54/ Goldstein, et al., Fed. Proc., 32 702 (Abstr. 1973)

edema and terminal hemorrhages were observed. The authors suggest effects may be seen at lower levels after longer periods of exposure.

Because the effects of long-term exposure to low levels of TCDD remain undetermined, an acceptable level for man cannot be set. If TCDD exposure causes delayed lethality or, if continuous impingement of TCDD on human organs otherwise causes cumulative effects, or if TCDD concentrates in human tissue, a level of exposure which would be safe for the general population may not exist. Even residues below the current level of detection may be unsafe.

A. The Risk to the Environment (Non-Human)

Of the twenty or so different chemical compounds commonly called 2,4,5-T, each contains impurities or inert ingredients in the technical pesticide product. Among these impurities is such "inert" material as TCDD. The total published wildlife toxicological information for these compounds and their impurities is slightly more than zero.

An abundance of data on other toxicants[55/] has permitted Respondent in its regulatory posture to parse with relative precision. With little environmental data now available, Respondent will adhere to certain guidelines, derived from existing knowledge, in its effort to illuminate the sphere of ecological hazard. Hopefully, Registrants and their intervenors by proffering reliable field and laboratory data on the

55/ See In Re Stevens Industries, 37 F.R. 13369.

degree of environmental risk, will also avoid parsing with a cleaver. Surely Registrants cannot insist that "body counts" are necessary before the trier of fact herein can reasonably conclude that unacceptable risk to the non-human environment exists. Respondents environmental guidelines for this proceeding are as follows:

(1) The "indirect" ecological effects on wildlife from using 2,4,5-T are a subject for discussion in this hearing. Many wild species are dependent for their very survival upon the availability of specific habitats. Some must have even specific plants to exist. For example, "range management," the widespread, indiscriminate removal of sagebrush by 2,4,5-T (or by other means), will eliminate the sage grouse which depends upon sagebrush for 99% of its food.[56/] Similarly, the Montana Fish and Game Commission showed that 2,4,5-T used for total brush control in one area had caused an 86% reduction in mule deer.[57/] The Registrants and appropriate Intervenors must discuss the extent of such range management, and the environmental as well as the economical acceptability of more restricted brush control or strip spraying, by which areas of brush necessary for wildlife habitat are left standing.

(2) There is no reason to assume that the demonstrated low-level toxicity of tetra-dioxin is not exerting its effect in the environment. Rangeland application of 2,4,5-T may amount to 4 pounds acid equivalent per acre, resulting in 120-960 ppm on grasses. The dioxin content of the grasses therefore could reach .96 ppb assuming an initial TCDD level of 1 ppm in the 2,4,5-T. Grass-eating wildlife species with an acute oral LD_{50} of .6 ug/kg (that of the most sensitive

56/ 8th Western States Sage Grouse Workshop Proceedings, Lewiston, Montana, August 7-8, 1973, p. 19.

57/ Personal Communication, State of Montana Department of Fish and Game, Helena, Montana.

non-wildlife species tested so far, the guinea pig) would consume a median lethal dosage by the time of ingesting one-half their body weight in grasses, a feat which would require one to three days for small species. Less TCDD could produce teratogenic effects. Given the extremely rapid environmental scavenging of dead or deformed small species, the detection of such field mortalities would be extremely difficult.

(3) Information discussed, infra, indicates the capacity of TCDD to penetrate, persist, to move and to bio-concentrate in the aquatic and terrestrial environment. Given the incomparable toxicity of this small molecular compound, and given the practical nonexistence of facts about its ecological effects, the Respondent suggests that it cannot make a reliable conclusion that TCDD is not causing serious environmental injury. Demonstrating a socially acceptable risk is the obligation of Registrants.

B. The Extent of the Health Risk For Man and Other Animals Posed by 2,4,5-T and TCDD, with Emphasis on the Following:

1. Can Additional TCDD be Generated in the Environment by the Thermal Stress of 2,4,5-T or its Metabolites?

There is Evidence that the Polychlorophenol in 2,4,5-T May Decompose into Dioxin when Exposed to High Temperatures, Such as Might Occur with Incinceration or Even Cooking of Food.

TCDD can be generated by the thermal stress of 2,4,5-T and some of its metabolites. This raises the potential for the generation of additional dioxin under environmental conditions. The widespread use of 2,4,5-T, coupled with the persistency of TCDD and its extreme toxicity, therefore, raise the possibility that people may be exposed to a latent destructive force -- the accidental or unknown triggering of the thermal release mechanism by which "harmless" amounts of 2,4,5-T, its esters or salts, convert to lethal tetra-dioxin.

Tests[58/] demonstrate the thermal conversion of alkaline salts of 2,4,5-T into TCDD. Sodium 2,4,5-Trichlorophenate held at the melting point produced measureable quantities of TCDD. Baughman and Meselson[59/] report they have repeatedly formed TCDD at the 1000 to 2000 ppm level by heating the sodium salt of 2,4,5-T, a form most likely to persist on wood.

Recent work by Thomas[60/] corroborates the observations of Baughman and Meselson. A summary of these findings is as follows:

1. When the sodium salt fo 2,4,5-T + Cu + NaOH are heated in a closed tube (entire tube heated) at 450°C for 6 hours, ca 10 ppm of TCDD are produced.

2. When the sodium salt of 2,4,5-T and 2,4,5-trichlorophenol are heated in an open tube (only the bottom of the tube is heated) in a sand bath at 350° for 7-1/2 hours, between 250 and 500 ppm of TCDD are produced.

3. When the sodium salt of 2,4,5-T and 2,4,5-trichlorophenol are heated in a closed tube (entire tube heated) at 350° for 7 hours, ca 1500-3000 ppm of TCDD are formed.

58/ Langer, H.G., et al., Environ. Health Persp., No. 5, pp. 259-266 (1973).

59/ Communication with the Office of Pesticide Programs (OPP), U.S. EPA., July 30, 1973.

60/ Private communication with Mr. Carroll Collier, OPP, EPA; Beltsville, Md.

Thus three independent groups have demonstrated this thermal conversion into TCDD.[61/]

Pyrolysis has also been shown to form dioxins from chlorophenates, under presumably anhydrous conditions.[62/] Five chlorophenates, from 2.4 dichlorophenate to pentachlorophenate were tested, each formed a corresponding dioxin.

Crosby[63/] reports the formation of octachlorodioxin from the burning of wood treated with pentachlorophenol.

Buu-Hoi[64/] reported the formation of tetra-dioxin from burning vegetation. No details are available on the procedures followed in burning the foliage or in collecting the samples. Analyses of the mass spectra asserted to be that of TCDD do not appear completely valid.[65/]

Most existing tests on the burning or the heating of 2,4,5-T treated products (vegetation, meat, fat) have not produced detectable tetra-dioxin.[66/] But the level of analytical sensitivity in these experiments was .05 to .1 ppm. Current sensitivity for such analyses is down to about 5 parts per trillion. The generation of TCDD at levels much lower than .05 ppm would be toxicologically significant. In addition, the multitude of environmental conditions under which 2,4,5-T, its salts and esters, can be exposed to thermal stress makes complete laboratory replication impossible and prohibits reliance on only a few negative laboratory tests.

61/ op. cit., Notes 58-60.

62/ op. cit., Note 58.

63 Crosby, et al., Environ. Health Persp., No. 5, pp. 259-266 (1973).

64/ Buu-Hoi, et al., Comptes Rendus Acad. Sci., Paris, 273 Series D, 708 (1971).

65/ op. cit., Note 62.

66/ Watts, R.R. and R. Storher, JAOAC, 56(4)1026 (1973).

B.2 CAN 2,4,5-T or TCDD PERSIST AND BIOACCUMULATE.

THE REGISTRANTS HAVE NOT ESTABLISHED THAT THE DIOXIN AND 2,4,5-T DO NOT ACCUMULATE IN BODY TISSUES. IF ONE OR BOTH DOES ACCUMULATE EVEN SMALL DOSES COULD BUILD UP TO DANGEROUS LEVELS WITHIN MAN AND ANIMALS, AND POSSIBLY IN THE FOOD CHAIN AS WELL.

B.4. ARE 2,4,5-T or TCDD RESIDUES BEING STORED AND ACCUMULATED IN THE HUMAN FOOD SUPPLY AND IN HUMAN AND ANIMAL TISSUE, INCLUDING HUMANS AND WILDLIFE DIRECTLY EXPOSED TO 2,4,5-T

2,4,5-T does not appear to be a persistent compound, but not enough is known about its metabolic products or pathways and about the presence of conjugated including "bound" products, and therefore undetected residues in foods resulting from the use of 2,4,5-T.

Unfortunately, methods for the determination of "bound" residues will only detect those conjugated products to the extent to which they are subject to the technique in use. For example, the method of Chow, et al [67/] can lead to signicantly higher results for "bound" residues of 2,4,5-T in rice straw than the method of Yip and Ney or the current method of the Food and Drug Administration.[68/] There remains however, the possibility of the presence of other conjugated products not so cleaved which would not be detected. Much of this area has not been clarified by the Registrant.

Many species metabolize 2,4,5-T.[69/] Also, 2,4,5,T can be rapidly degraded by soil organisms, usually not persisting into the next growing season. The degradation rate in soil is influenced by climatic conditions and microbial action.[70/] Because definitive soil metabolism studies are unavailable the buildup of persistent metabolites, however, cannot be discounted. Nor can movement of 2,4,5-T metabolites into rotational crops be discounted since current analytical techniques may be unresponsive to residues of bound 2,4,5-T or its metabolites.

67/ Chow, et al, Bull. Env. Cont. Toxic.,6 576 (1971).
68/ Yip and Ney, Weeds 14 167 (1966);and FDA Pesticide Analytical Manual Vol.1.,Sections 222.13c,222.14,222.15,&222.16(b) (1968 rev'd ed.)
69/ Loos. M.A. "Degradation of Herbicides",pp. 1-49, Ed. P.C. Kearney, Marcel Dekker Inc. N.Y. (1969)
70/ Bauer, et al. Weed Sci., 17 567 (1969); Alexander & Aleen, J.Agr. Food Chem. 9 45 (1961)

Storage of 2,4,5-T metabolites in the tissues of certain aquatic organisms may also occur. Exposure of fish to degraded 2,4,-D residues results in tissue accumulation of metabolites.[71] It is reasonable to conclude, based on the similarity of many of the degradation products of 2,4,-D and 2,4,5-T, that acquatic organisms would also store 2,4,5-T metabolites.

Considerable data exists on the persistence of 2,4,5-T in grasses.[72] Rapid decline of 2,4,5-T residue is observed, starting immediately after treatment and reaching "neglible" levels in about 6 months. This decline must be the combined result of dilution, plant metabolism, surface erosion, volatilization and photodegradation. Residues of 2,4,5-T and of the 2,4,5-Trichlorophenol moiety in milk and meat resulting from the use of 2,4,5,-T in pastures and on rangeland have been reviewed.[73] While the author concludes that residues in milk, meat, fat or meat by-products are not likely to be significant if 2,4,5-T is used according to label direction, more recent research shows that "bound" residues of 2,4,5-T in sheep and cattle livers may be measurable (>.05 ppm)even after withdrawal from a diet containing 2,4,5-T.[74] No data are available on the fate of metabolic products from forest or right-of way applications of 2,4,5-T.

Monitoring of human food supply appears to cooroborate these conclusions on the persistency of 2,4,5-T, although nothing is known about potential metabolites of 2,4,5-T in human food or the presence of bound residues which are not subject to detection by existing 2,4,5-T analytical methods.

71/ Schultz, D.P.K. Agr Food Chem.,21, 186 (1973)
72/ op.cit., Note 70; and Bovery,R. Bauer, Bull Env. Cont. Toxic 8 (4) 229 (1972)
73/ Leng. M.L., Down to Earth,28(1)12(1972)
74/ Pesticide Petition, 2,4,5-T, the Dow Chemical Company, No. 1 F 1102.

Since 1969 the Food and Drug Administration (FDA) has monitored for chlorophenoxy acetic acids in the following commodities:

(1) Whole grains for human use, such as wheat, corn, rice, oats, etc.

(2) Animal by-products including slaughtered mammals and fowl.

(3) Milk

(4) Other dairy products.

From 1969-1971, 19 of 1226 samples contained 2,4,5,-T or 2,4,-D derivatives, ranging from a trace to .02 ppm. All but one sample was milk.

Earlier FDA results are summarized reliably in the May 7, 1971 Advisory Committee Report, "From about 10,000 food and feed samples examined from 1964 through 1969 only 25 contained trace amounts of 2,4,5-T (less than 0.1 ppm) and only two contained measurable amounts, 0.19 ppm in a sample of milk in 1965 and 0.29 ppm in a sample of sugar beets in 1966. Furthermore, of the 134 total diet samples involving 1600 food composites (Market Basket Survey) analyzed from 1964 through April 1969, only 3 contained 2,4,5-T. Two were dairy products containing 8 to 13% fat with .008 and 0.19 ppm in the fat. A single meat, fish and poultry composit from Boston consisting of 17 to 23% of fat was found to contain .003 ppm 2,4,5-T on a fat basis."[75/]

75/ op. cit., Note 1

Tetra-dioxin, on the other hand, is clearly both persistent and bioaccumulative. It resists microbial deterioration.[76] Out of 100 microbial strains which degrade most persistent pesticides, only 5 showed any ability to degrade TCDD. Soil studies indicate that tetra-dioxin has a half-life of greater than one year.[77] That no metabolites were found in this research also indicates the absence of microbial degradation. Herbicide test plots sprayed with Agent Orange (2,4,D and 2,4,5-T) have shown measurable amounts of TCDD several years after final treatment.[78]

Model ecosystem studies suggest that TCDD bioconcentrates more than DDT. A two trophic level, model ecosystem with mosquito larvae and brook silverside minnows demonstrated a bioaccumulation factor of TCDD in minnows 540 times that of the TCDD in the water. DDT's accumulation factor by comparison was 306.[79]

A similar acquatic ecosystem showed catfish to accumulate tetra-dioxin in only three days by a factor of 14,000.[80] A direct relationship was observed between concentrations in ambient water and in the tissues of several acquatic species, when tetra-dioxin was introduced into the aquatic system in the form of treated sediment. The following illustrates the observed relationship between TCDD concentration in soil and in the water:

76/ Matsamura.,F. and H. Benezet, Env. Health Persp.No.5;253(1973)
77/ Kearney, P.C.et al., "Chlorodioxins-Origin and Fate," E.Blair,et pp. 105-111, Amer. Chem Soc., Adv. Chem Sin 120,1973.
78/ Private Communication with OPP, Major Mabson, USAF, Wash. D.C.
79/ Op. cit., Note 76
80/ Private Communication,USDA, Isensee

TCDD Concentration in Soil (PPM)	TCDD Concentration in Water (PPT)
0.1	7.13
0.01	0.66
0.001	0.26
0.0001	0.05

When the soil content was .1 ppm TCDD, various acquatic organisms accumulated the following levels of tetra-dioxin:

Organism	TCDD Level (PPM)	Time of Exposure
Algae	.08	28 - 29 days
Duckweek	.03	28 - 29 days
Snails	.12	28 - 29 days
Daphnia	.16	28 - 29 days
Gambusia	.44	3 days
Catfish	.10	3 days

Therefore, rice flood waters and sediment containing 2,4,5-T related TCDD may well transport tetra-dioxin from the ricefields to fish and crayfish, components of the human food supply. For example, a one pound per acre treatment of rice with 2,4,5-T containing .1 ppm TCDD will generate a tetra-dioxin level of approximately 12 ppt in the upper 1/4 inch of soil. A graphical extrapolation of the soil-water data discussed, supra, indicates that this could lead to a water concentration of .01 ppt. A direct correlation between water and fish concentrations would result in a tetra-dioxin level of 140 ppt in fish within 3 days of exposure to rice flood water.

Residue data corroborate these conclusions as to the persistency and bioaccumulation of 2,4,5-T related TCDD.

Analysis of residues in Vietnamese shrimp and crustaceans detected significant levels of tetra-dioxin following defoliation treatments with 2,4,5-T in regions draining into the areas from which the shrimp were collected.[81/] It appears that these residues have not declined appreciably between 1970 and 1973, although the defoliation ceased in 1969.

Wildlife in the vicinity of areas of Agent Orange application at Eglin Air Force Base retained measurable levels of TCDD several years after use of the herbicide was stopped.[82/]

Beef calves fed for 28 days on diets containig 100 and 1800 ppm 2,4,5-T with .5 ppm TCDD, retained substantial amounts of tetra-dioxin in the fat and in the liver.[83/] It therefore appears that at least 25% of the dietary intake of tetra-dioxin may be stored in body tissues. Fries feeding rats 7 and 20 ppb TCDD suggests that 75% of the total retained residues may be stored in the liver.[84/]

Table I infra suggests that the withdrawal of cattle from a diet contaminated with dioxin for as long as one week may have little effect in decreasing TCDD residues. Therefore, current label provisions requiring "feed off" periods on dioxin free food in order to assure the absence of dioxin residues in the meat are not likely to be effective in reducing tetra-dioxin residues if present in any significant amounts.

81/ Baughman and Meselson, op.cit, Note 49
82/ Op. Cit, Note 78
83/ EPA, OPP TCDD Monitoring Project
84/ Private Communication, Fries. G. USDA Beltsville, Md.

Cattle, sheep and goats fed immediately after application of 2,4,5-T to rangeland accumulated residues of tetra-dioxin in their fat from 6 to 41 ppt and in the liver from 1 to 5 ppt.85/ The tetra-dioxin content of the commercial 2,4,5-T used was .04 ppm. Using a factor of fat/TCDD diet of 2.1 (See Table I) one can calculate a value of 10.08 ppt, which could be expected in the fat of a young calf exposed to similar residues.

Monitoring of wildlife collected along rights of way in the U.S. demonstrates, as does the Vietnamese aquatic residue data, that 2,4,5-T related TCDD can enter the food chain from "non-food" uses. Shrews sampled accumulated tetra-dioxin residues up to 397 ppt, averaging 202 ppt.86/

Thus, 2,4,5,-T related tetra-dioxin is persistent and it bioconcentrates. It is quite capable of penetrating into the environment and contaminating the human food supply. While Respondent is in the midst of extensive residue monitoring in order to define this hazard more precisely, it is now the obligation of those who profess the safety of this pesticide to prove their position in the face of these facts.

85/ Op cit Note 83
86/ Ibid

TABLE I - TCDD LEVEL IN BEEF CALF FAT AND LIVER RESULTING FROM CONTROLLED EXPOSURE (28 DAYS) TO DIETS CONTAINING VARIOUS LEVELS OF CONTAMINATED 2,4,5-T

DOW CHEM CO. CALF NO.	TOTAL CALF WEIGHT (kg)	TOTAL AMOUNT OF FORTIFIED DIET FED OVER 28 DAY PERIOD	PPM 2,4,5-T IN FORTIFIED DIET	PPT TCDD IN FORTIFIED DIET	PPT TCDD FOUND IN CALF FAT	PPT TCDD FOUND IN CALF LIVER	TCDD PPT FAT PPT DIET	PPT TCDD EXPECTED IN FAT IF 100% OF TCDD ABSORBED ***	% TCDD UPTAKE FROM DIET
Control	___	0	0	0	N.D.	N.D.	___	___	___
362	242	231	100	50	103	28	2.1	365	28
368	251	255	300	150	300	61	2.0	1171	26
372	213	178	900	450	505	168	1.1	2918	17
378	222	172	1800	900	1120	406	1.2	5440	21
969	215	114	1800**	900	1077	240	1.2	3585	30

*TCDD Content of 2,4,5-T was 0.5 ppm

**Feeding Period followed by 7 day withdrawal from TCDD containing feed.

***Based on a fat content of 13% for a 500# steer (See Morrison, J. B., "Feeds and Feeding", p. 202, Morrison Publishing Co., Ithaca, N.Y., (1954).

B. 3. WHAT ARE THE AVENUES OF HUMAN AND ANIMAL EXPOSURE TO 2,4,5-T AND TCDD? FOR EXAMPLE CAN AERIAL DRIFT OR WATER TRANSPORT OF 2,4,5-T OR TCDD CAUSE MOVEMENT OF THESE COMPOUNDS AWAY FROM THE SITE OF APPLICATION?

Besides the contamination of the sites of 2,4,5-T application with the uptake of pesticide residues by plants and animals in those areas and the resulting bio-concentration, there are indications that 2,4,5-T and related tetra-dioxin will be transported aerially and by water beyond the sites of application.

Aerial application of 2,4,5-T cannot be made without aerial drift. The magnitude of such dispersal depends on the droplet size, wind velocity, humidity, type of formulation used, air temperature and altitude of the aircraft.

Elaborate precautions taken with the aerial use of Tordon 225 (USEPA Reg. No. 464-407) exemplfy this problem of drift on rangeland. Tordon 225, a formulation of 2,4,5-T and picloram used to control mesquite, cannot be aerially applied unless a buffer zone between food crops of up to 1/2 mile is maintained. Aerial applicators are given special training. Similarly the aerial use of 2,4,D - a phenoxy herbicide, on Louisiana rice fields must not be applied closer than 1/2 mile to susceptible crops, and only under the supervision of a state inspector. 87/

87/ Gerlow, A. R., "The Economic Impact of Cancelling the Use of 2,4,5-T in Rice Production", p. 7, ERS-510, USDA, Washington, D. C., 1973.

In addition, drought conditions on the range and the persistency of tetra-dioxin in soil suggest the probability that TCDD contained in topsoil is transported by wind erosion. Thus, in any area of 2,4,5-T application, aerial distribution of 2,4,5-T and TCDD beyond the immediate site of application, uptake from there and further transport, are distinct probabilities. The absence of air monitoring samples of TCDD prevents a determination of whether TCDD persists and is transported long distances in the atmosphere.

Similarly, while Respondent has not yet completed field monitoring, it is probable that water transport of TCDD occurs. Given the demonstrated persistency of TCDD in the soil, gulley and sheet erosion would be expected to carry silt particles from the upper layers of soil into bodies of water for transport. This would be especially true as to poorer quality, over-grazed rangelands, where the ratio of grass tuft to bare ground is low. In poor-condition, short-grass ranges bare spaces of 1 to 4 feet can predominate. 88/ It is probable that 2,4,5-T is also directly applied to rangeland water holes. Livestock and wildlife drinking such water are likely exposed to TCDD via the sediment suspended in such waters or as TCDD which has dissolved in the water.

88/ The Yearbook of Agriculture -- "Grass", p. 525, USDA, Washington, D.C., 1948.

Suspended sediment containing TCDD in rice fields and rights of way would also be transported by run-off from such sites. Once the tetra-dioxin (as sorbed on silt particles) reaches water a new sorption/desorption equilibrium is established, with discrete amounts of tetra-dioxin dissolving directly into the water.

Estimates by Miller, et. al.[89] are that forest applications of 2,4,5-T can be expected to cause residues of about .01 ppt of TCDD in streamwater, if a tetra-dioxin level of .1 ppm exists in the original formulation. Direct application of 2,4,5-T to streamwater would cause most of this residue. Therefore, based on the solubility of tetra-dioxin in water and provided no adsorption occurs on benthic surfaces or suspended solids, all such tetra-dioxin would be expected to remain in solution. Using considerations discussed, supra, for graphically projecting acquatic residue bio-accumulation, tetra-dioxin could be expected to build up to at least 140 ppt in fish from such forest applications.

Contamination of water supplies with tetra-dioxin is further suggested by recent monitoring data on streams in the Western United States.[90] The Canadian River near Whitefield, Oklahoma, and the Arkansas River below Van Buren, Arkansas showed the greatest contamination of 2,4,5-T with levels ranging from .03 ppb - .04 ppb and .01 - .04 ppb, respectively. Other

---

89/ Miller, R., et. al., Envir. Health Persp., No. 5, 177 (1973).

90/ Manigold, D. B. and J. Schulze, Pest. Mon. J., 3(2)2 (1969).

streams with detectable levels were the Brazos River at Richman, Texas (.01 ppb - .06 ppb), the Pecos River near Artesia, N.M. (.05 ppb) and the Green River at Green River, Utah (.07 ppb). Since the analytical methodologies utilized were sensitive only to 2,4,5-T and its esters, TCDD or degraded 2,4,5-T in terms of trichlorophenol moiety metabolites would not be identified. Therefore, the levels of 2,4,5-T detected are indicative of substantially higher inputs of 2,4,5-T followed by microbiol degradation.

In addition, the fact that residues of tetra-dioxin are detected in Vietnamese shrimp caught 30 kilometers from the shore also suggests that this contaminant is quite mobile. 91/

B. 5. ARE OTHER DIOXINS AND SIMILAR CONTAMINANTS BESIDES TCDD PRESENT IN 2,4,5-T AND, IF SO, WHAT RISKS TO HEALTH DO THEY CONSTITUTE?

B. 6. WHAT ARE OTHER ENVIRONMENTAL SOURCES OF DIOXINS PARTICULARLY TCDD, AND DO THESE SOURCES ENHANCE THE TOTAL DIOXIN BODY BURDEN AND EXACERBATE THE HEALTH RISKS RAISED BY 2,4,5-T AND RELATED TCDD?

What are the current levels of dioxins in registered 2,4,5-T products and in technical material used to formulate these products?

The absence of other chlorodioxins, chlorodibenzofurans and chlorinated hydroxy diphenyl ethers has not been carefully established for any currently registered technical 2,4,5-T products. In 1972, Firestone 92/

91/ Personal Communication, Matthew Meselson, Harvard University. These shrimp as juveniles may have ingested the TCDD while in estuaries near the shore.

92/ Firestone, D. et. al., JOAOC, 55(1)85 (1972).

conducted a survey of dioxins in trichlorophenol samples collected in 1970 using a gc/ms (gas chromatograph, mass spectrometry) method. Other dioxins including 2,7 dichloro, 1,3,6,8-tetrachloro and a pentachloro-dioxin were found. Chlorofurans and chloroethers were also found. A hexachlorodiophenyl ether was found in one sample and trichloro-tetrachloro- and pentachloro furans were found in some of the other samples. No information is available on the presence or absence of 2,3,7 trichloro dibenzo-p-dioxin although bioassays by the method of Poland [93/] suggest that this compound may have a potent biological activity in the same order of magnitude as TCDD. The recent findings of additional, unknown "neutral" contaminants in production grade 2,4,5-T [94/] clearly demonstrates how little is known about various impurities in 2,4,5-T. Similar impurities in the "neutral" fraction of 2,4,5-T have also been noted in our own laboratories. [95/]

In any event, all chemicals made by manufacturing processes having the capability of forming impurities with the degree of toxicity of TCDD should be supported with quality control procedures capable of detecting and quantifying such materials. Furthermore, once the Registrants have identified all of the impurities, these should be toxicologically evaluated. The so-called "pre-dioxins", hydroxy

---

93/ Poland, A. and E. Glover, Science 179,476 (1972).

94/ Huston, B., J. Agr. Food Chem., 30(3) 724 (1972).

95/ Op. cit., Note 60.

chlorodiphenyl ethers [96/] should also be evaluated in terms of their possible presence in 2,4,5-T formulations. If present, these materials are potential sources for 2,4,5-T related dioxin formation under environmental conditions.

Table II gives a list of registered pesticide products in addition to 2,4,5-T which are expected to be potential sources of dioxins. Of these, five utilize 2,4,5-trichlorophenol as a manufacturing intermediate, and therefore can be expected to add to the overall environmental burden of dioxin. Since some of these compounds have established tolerances on food or feeds, any dioxins residues entering the food supply from these sources would be directly additive to any similar residues resulting from the use of 2,4,5-T. [97/]

A special and unique situation is encountered with the currently registered use of ronnel [O,O-dimethyl O-(2,4,5-trichlorophenyl) phosphorothioate]. When used as a supplement to cattle food [98/] this compound is a potential source of TCDD in beef and dairy cattle. At the currently registered dosage of .002 lbs. active ronnel (in food) per 100 lbs of body weight per day for 7 consecutive days, a 500 lb. beef containing 13.7% fat could accumulate up to 5 parts per trillion TCDD in its body fat. This is based on a retention factor of 25% (see

---

96/ Nilsson, C. and L. Renberg, "Further Studies on Impurities in Chlorophenol." Unpublished manuscript.

97/ EPA Compensium of Registered Uses; Section III-R-1. 2.

98/ ibid.

Table II), and a TCDD content of .05 ppm in the ronnel. Another potential source of TCDD could be from the photochemical reductive dechlorination of higher dicxins, especially hexachloro, heptachloro and octachloro dioxin found in pentachlorophenol.[99/]

Also, the additive toxic effect of other chlorodioxins, including the octa, hexa, hepta, penta, tri and di isomers, all of which can be found in one or more of the products listed in Table II, cannot be discounted. For example, 2,3,7 trichloro-dioxin demonstrates a high degree of biological activity in the enzyme screening process of Poland.[100/] To date all compounds showing high activity with the Poland enzyme assay have also been found to be patent acnegens and/or are highly embryotoxic. Formation of 2,3,7-trichloro dioxin from TCDD by reductive dechlorination caused by photochemical effects is a distinct possibility. If these residues accumulate as readily as TCDD, their biological effect would, indeed, be additive in nature.

99/ Plimmer, J. et. al., Science 173 748 (1971).

100/ Op. cit., Note 93.

TABLE II

2,4,5-trichlorophenol and salts

2,4,6-trichlorophenol

2,3,4,6-tetrachlorophenol and salts

Pentachlorophenol (and sodium salt)

2,4-dichlorophenyl benzenesulfonate

p-chlorophenyl 2,4,5-trichlorophenyl sulfone (Tetradifon)

2,4-dichlorophenoxy acetic acid (2,4-D) and its derivatives

2,(2,4,5-trichloraphenoxy)propionic acid and derivatives (2,4-DP)

O-2,4-dichlorophenyl O,O-diethyl phosphorothioate (VC-13)

O-2,4-dichlorophenyl p-nitrophenyl ether (TOK)

2-(2,4,5-trichlorophenoxy)ethyl 2,2-dichloropropionate (Erbon)

O,O-dimethyl O-(2,4,5-trichlorophenyl) phosphorothioate (ronnel)

3,6-dichloro-o-anisic acid (Dicamba)

3,5,6-trichloro-o-anisic acid (Tricamba)

Tris!(2,4-dichlorophenoxy)ethyl phosphite

Hexachlorophene

O-(4-bromo-2,5-dichlorophenyl) O,O-dimethyl phosphorothioate (Bromophos)

B-7 WHAT ARE THE CURRENT LEVELS OF DIOXINS IN REGISTERED 2,4,5-T PRODUCTS AND IN TECHNICAL MATERIAL USED TO FORMULATE THESE PRODUCTS

B-8 DO THE CURRENT METHODS OF MANUFATURE OF 2,4,5-T provide FOR CONSISTENTLY LOW LEVELS OF DIOXINS IN THE FINAL TECHNICAL PRODUCT AND WHAT ARE THE QUALITY CONTROL MEASURES USED TO MINIMIZE DIOXIN LEVELS?

Transvaal, Inc., states that the TCDD content of its 2,4,5-T acid, from which their products are derived, is less than 2 ppm and averages less than 1 ppm.[101] Registrant Thompson-Hayward Chemical states that their product contains less than 0.1 ppm TCDD.[102] Dow Chemical Co. has repeatedly stated that technical 2,4,5-T produced since 1970 in their plant contains less than 0.1 ppm.[103] C.H. Boehringer Sohn, Ingleheim, Germany, states that since 1970, the TCDD content of their technical 2,4,5-T has been held at less than 0.1 ppm.[104]

Recent analyses by EPA of technical products from the three U.S. manufacturers are shown in Table III. The representativeness of these levels and the tetra-dioxin levels in formulated products remains to be demonstrated by Registrants.

101/ Letter from Dr. A.E. Sidwell, Transvaal, Inc, 3/30/73.
102/ Letter from Mr. Edwin Upton, Thompson Hayward Chemical Co., 3/29/73
103/ Personal Communication, OPP, EPA
104/ Letter from Mr. Donald Yoder, BASF Wyandotte Corp, May 14, 1973

TABLE III - RECENT ANALYSES* OF TECHNICAL 2,4,5-T PRODUCTS MANUFACTURED IN THE UNITED STATES

Company	EPA Reg. No.	Description	Date of Collection and Lot Size	I.D. #	TCDD Level (PPM)
Dow	464-205	Dow 2,4,5-T Propylene glycol butyl ether ester 69.2%	7/13/73 Lot #675233 1 gal. can	102526	< .1
Dow	464-205	Dow 2,4,5-T Propylene glycol butyl ether ester 69.2%	7/13/73 Lot #675293 1 gal. can	102527	< .1
Dow	464-205	Dow 2,4,5-T Propylene glycol butyl ether ester 69.2%	7/13/73 Lot #675423 55 gal. drum	102530	< .1
Transvaal	11687-30	2,4,5-T Acid, 100%	7/13/73 Bin #90 (3500#)	104593	< .1
Transvaal	11687-30	2,4,5-T Acid, 100%	9/21/73 Bin #121 (3500#)	104593	< .1
Transvaal	11687-30	2,4,5-T Acid, 100%	9/21/73 Bin #100-16 (3500#)	104593	< .1
Transvaal	11687-30	2,4,5-T Acid, 100%	9/21/73 Bin #70 (3500#)	104593	< .1
Transvaal.	11687-30	2,4,5-T Acid, 100%	9/21/73 Bin #100-10 (3500#)	104593	< .1
Transvaal	11687-30	2,4,5-T Acid, 100%	9/21/73 Bin #119 (3500#)	104593	< .1
Thompson Hayward	148-924	2,4,5-T Isooctyl Ester Tech, 97%	7/12/73 From 10,000 gal. bulk tank	102206	< .1

*Analyses conducted at EPA/OPP/TSD Laboratory, Beltsville, Maryland.

C. THE REGISTRANTS HAVE NOT ESTABLISHED THE NEED FOR 2,4,5-T in LIGHT OF THE ABOVE - MENTIONED RISKS.

THE NECESSITY FOR THE CONTINUATION OF THE REGISTERED USES OF 2,4,5-T.

1. What are the pests which each registered use is intended to control and the degree of control achieved by each use?

2. What is the cost, timing and rate of application of 2,4,5-T for each use?

3. What alternative controls exist for each registered use and what is the cost and effectiveness of each alternative?

The registered uses of 2,4,5-T are intended to control a multitude of weed and plant pests.[105/] Over 1.8 million acres of rice are harvested annually in the United States. 100,000 of these acres are treated with 2,4,5-T, virtually all within the States of Arkansas and Mississippi. In Arkansas, 10 percent of the crop (44,000 acres) is treated with 2,4,5-T, while in Mississippi, 85 percent (44,000 of 51,000 acres) receives treatment.

For rice weeds the herbicide is applied in one foliar application of .75 to 1.25 lb/acre at a cost of approximately $4 to $5 acre, for the control of arrowhead, coffeebean, curly indigo, gooseweed, ducksalad, Mexican weed, redstem, smartweed, spikerush and umbrellaplant.

However, the major agricultural use of 2,4,5-T is for the control of brush on rangeland. There is some use for brush control on pastures but it is much less extensive. Texas, Oklahoma and New Mexico are the primary users of 2,4,5-T for rangeland control. Within these 3 states

---

105/ See Table IV for General Estimates of the Rate, Timing and Costs of Application of 2,4,5-T

approximately 1.4 of 177 million acres of rangeland receives 2,4,5-T treatment each year. Because treatment lasts for several years, about 8.4 million acres of range are currently benefiting in varying degrees from chemical brush control.

2,4,5-T is used on pastures and rangland to control woody species; blackjack oak, mesquite, post oak, sand shinnery oak and yucca. One foliar application of 1/2 to 2 lbs/acre, depending on the rate of regrowth is made every 5-6 years at a cost of approximately 4-6 dollars per acre. In heavily infested areas a second application may be necessary the following year. The application is made during the period of rapid growth or while leaves are expanding.

The USDA has estimated that 430,000 acres of forest land are treated annually with 2,4,5-T, exclusive of its use by the United States Forest Service. It is used for site preparation, conifer release, and pine release, to control alder, bigleaf maple, blackjack oak, California black oak, Ceanothus, chinquapin, gum, Oregon white oak, sumac, vine maple, white oak, and wild cherry and other species. Application rates for each major forestry use are:

Site Preparation - One foliar application at a rate of 2-4 lbs acre after leaves of undesirable hardwoods have fully expanded, but before planting of seedlings.

Conifer release - one foliar application 2-4 years after seedlings have been planted (depending on rate of regrowth of undesirable hardwoods). Application should be made prior to budbreak of the conifers to prevent injury at a rate of 2-4 lbs. acre.

Pine Release - one foliar application 2-4 years after seedlings have been planted (depending on rate of regrowth of undesirable hardwoods) after spring growth of pines has hardened, at a rate of 2-4 lbs acre.

Specific data on the remaining registered uses (Rights of ways, Roadways, Fencerows and wasteland) is unavailable, although an estimated 2.2 million acres of rights of way is treated annually. It is used to control ailanthus, alder, ash brambles, basswood, ceanothus, chinquapin, elm, ground cherry, gum, hickory, horsenettle, maple mesquite, poison ivy, locust, oak, persimmon, sassafras, shinnery oak, sumac, Virginia creeper, wild cherry, and other species. 2,4,5-T for these uses is applied as follows.

(a) one foliar application every 5-6 years (depending on rate of regrowth) to brush 6-8 ft tall during the period of most active growth, at a rate of 2-12 lbs acre depending on species to be controlled and density of population
(b) one basal bark treatment anytime of the year gives satisfactory control to susceptible species less than 6 inches in diameter at breast height, at a rate of 12-16 lbs acre/100 gals of solution.
(c) frilling can be employed during anytime of the year on any size tree at a rate of 8-16 lbs. acre/100 gals solution.
(d) injections can be made during anytime of the year on any size tree at a rate of 4 lbs acre 10-20 gals of solution with satisfactory results.
(e) stump treatment are utilized on freshly cut trees more than 2 inches in diameter at the base, at a rate of 12-16 lbs acre/100 gals of solution.

There are available generally effective alternatives for the great majority of these 2,4,5-T uses. 2,4,5-TP, "silvex", appears to be the most broadly effective substitute for all registered uses. Table IV contains a list of registered alternatives to 2,4,5-T.

Silvex, MCPA, and 2,4-D all provide varying degrees of control for the rice weeds that are controlled by 2,4,5-T. The following chart lists these weeds and the herbicide(s) providing the best control:[106/]

Arrowhead	- all provide a similar degree of control
Dayflower	- "
Smartweed	- "
Coffeebean	- 2,4,5-T; Silvex; 2,4-D
Curly indigo	- 2,4,5-T; Silvex
Ducksalad	- 2,4-D
Gooseweed	- 2,4,5-T; Silvex
Mexicanweed	- 2,4,5-T; Silvex
Redstem	- Silvex; 2,4-D
Spikerush	- Silvex; 2,4-D
Umbrellaplant	- 2,4-D

For every weed listed, that is controlled by 2,4,5-T, there is at least one alternative that is either equal to or superior to the control achieved with 2,4,5-T. In most cases there are 2 or more.

The major concern over the use of these alternative herbicides is the phytotoxic hazard to nearby susceptible crops as a result of drift and volatility. All four phenoxy herbicides (including 2,4,5-T) will adversely effect highly susceptible crops, such as cotton and soybeans, if allowed to drift onto them during application. However, they do differ as to the degree of injury. Injury to cotton caused by these four herbicides, in order of greatest to least injury, is 2,4-D; MCPA; Silvex; and 2,4,5-T. For soybeans the order is Silvex; 2,4,5-T; 2,4-D; and MCPA.

It would appear that the most satisfactory alternative to 2,4,5-T (regarding drift hazard) would be Silvex when applied adjacent to cotton. In areas where soybeans are grown both 2,4-D and MCPA would produce even less damage than 2,4,5-T.

106/ USDA Handbook 289 and 292, and State Herbicide Recommendations.

An important point in considering drift is that most injury problems are the direct result of misapplication, and if care is not taken in applying these herbicides, as indicated on the registered labels, even 2,4,5-T is a hazard to nearby susceptible crops.

Concerning volatility, all 3 of the alternative herbicides can be formulated as the salt. Since the hazard from the use of a salt formulation is negligible, their application near susceptible crops poses no greater volatility problem than that of 2,4,5-T.

C.4. Do Alternative Pesticide Products Cause Adverse Environmental Effects?

With the possible exception of one herbicide and on the basis of available information, Respondent believes the registered alternatives are environmentally acceptable. 2,4,5-TP (Silvex), apparently the most broadly substitutable herbicide for 2,4,5-T uses, is suspected of containing tetradioxin. It is anticipated that this question will be resolved, particularly by reliable facts from Silvex registrants, before the close of this proceeding. Should 2,4,5-TP prove to be free of dioxins and of other inordinately toxic, persistent contaminants, it too, would be considered environmentally acceptable.

C.5 What Are the Economic Implications of These Alternatives, Including that of No Control?

Should silvex prove to be a safe alternative, the economic impact of cancelling all registered 2,4,5-T uses would not be significant. Respondent is in the process of developing specific cost-effectiveness information on the remaining substitutes and on the economic impact, if any, of cancelling the remaining registrations of 2,4,5-T.

Table IV

Registered Alternative Herbicides for 2,4,5-T

Rice - 2,4,5; 2,4,5-TP, (Silvex); MCPA: Propanil; Molinate.

Pasture and Rangeland

foliar -2,4,D; 2,4,-D + 2,4,5-T; 2,4-D + Dicamba; 2,4-TP, (Silvex); MCPA; Ammonium sulfamate.

basal bark - 2,4-D + 2,4,5-T; 2,4-D + 2,4-DP; 2,4-D + Dicamba; Dicamba; Bromacil.

Frill - 2,4-D; 2,4-D + 2,4,5-T; 2,4-D + 2,4-DP; 2,4-D + Picloram; Ammonium sulfamate; Dicamba.

stump - 2,4-D; 2,4-D + 2,4,5-T; 2,4-D + 2,4-DP; 2,4-D + 2,4,5-TP; 2,4,5-TP; Ammonium sulfamate.

Rights-of-Way
Reforestation (site preparation)
Roadways, Fencerows,
Wasteland (foliar) - 2,4-D; 2,4-D + 2,4,5-T; 2,4-D + Picloram; 2,4-D + Dicamba; 2,4-D + 2,4-DP; 2,4,5-TP; Karbutilate; Amitrole; Ammonium sulfamate; Maleic hydrazide (growth retardant); Cacodylic acid; MSMA.

Rights-of-Way
Roadways, Fencerows, - See herbicides listed in Pasture and Rangeland.
Wasteland (basal bark,
frill, injection, and
stump)

Reforestation (conifer - 2,4-D; 2,4-D + 2,4,5-T; 2,4,5-TP.
and pine release)

SUMMARY OF RESPONDENT'S POSITION

The use of 2,4,5-T on rice, in accordance with label directions and widely recognized and accepted practice, causes unreasonable adverse effects on the environment and must be cancelled.

The rice use constitutes a direct application (the only remaining one) of 2,4,5-T and 2,4,5-T related tetra-dioxin to human food. By its potential contamination of rice and its associated contamination of water and aquatic species, also a part of the human food supply, this use creates a direct route for the ingestion by man of tetra-dioxin, a teratogenic and immcomparably poisonous compound.

Testing on tetra-dioxin demonstrates the extreme potency of minute quantities, a fact which cannot be obfuscated by specious comparisons between the "small" amounts of this toxicant available for environmental contamination and greater amounts of other infinitely less toxic and non-teratogenic contaminants. Besides the gross qualitative and quantitative differences in toxicity, tetra-dioxin has demonstrated persistency and a propensity for biomagnification.

It has not been demonstrated that the risk to man from this compound is insignificant. Any such assertion is speculative, founded not on reliable research, but on the mere hope that man is less not more sensitive than the mammalian species tested in the laboratory.

In theory, perhaps, Registrants, in fulfilling their burden of ultimate persuasion, cannot "prove a negative", that the use of 2,4,5-T presents absolutely no risk. In fact existing information compels the conclusion that a direct food use of 2,4,5-T presents a clear hazard to public health. Nothing derived from scientific research, field experimentation or experienced observation of widespread human exposure to 2,4,5-T demonstrates, to the contrary, that this risk is of insignificant proportions. Respondent's best scientific judgment, compatible with the conclusion in 1970 of the Surgeon General and the Secretary of Health, Education, and Welfare, is that while the magnitude of this hazard cannot be quantified, it constitutes a direct risk to man. It is untenable that society should unknowingly and involuntarily be subjected to this hazard in light of an absence of substantial benefit from the use of 2,4,5-T on rice and the availability of substitutes for this use. Such risk is, indeed, socially unacceptable.

For the moment, Respondent reserves its judgment on the remaining registered uses of 2,4,5-T. Whether the health hazard raised by the food uses of 2,4,5-T is also presented by the other uses, depends principally upon the risk of human exposure to tetra-dioxin from these uses. In this regard a so-called "non-food" use, on rangeland and pasture, raises serious questions of safety because of its rather obvious link to human ingestion of tetra-dioxin. Respondent believes, the relationship must be established somewhat more firmly.

In addition, while data do not clearly demonstrate its mobility, the patterns of 2,4,5-T application (all uses), TCDD's apparent persistence in soil and its vapor pressure (similar to that of DDT) all suggest that tetra-dioxin, like DDT, can be expected to penetrate readily in the environment, ferreting out human food sources unrelated to and beyond the areas of 2,4,5-T use. Whether widespread environmental distribution is occurring from these "non-food" uses and the ecological and human health impact of such broadcasting of tetra-dioxin are not yet obvious. Clearly the potential for risk exists.

Respondent anticipates that it will develop more information on these remaining substantial questions of safety. Further, those who would favor the continued distribution of this extraordinary toxicant must illuminate their optimistic conclusions of safety with convincing evidence. Respondent would prefer that a decision, herein, rest on thorough scientific information, reasoned inference and reliable prediction, rather than on the sheer force of law. But the hazard to public safety is clearly raised. The Congress has seen fit to protect the public health in such cases by compelling cancellation of these pesticides, unless Registrants can convincingly demonstrate the acceptability of the public risk. There is no overwhelming social benefit from 2,4,5-T. Registrants can, therefore, meet their burden only by reliable negative long-term toxicity testing on tetra-dioxin,

by thorough environmental monitoring for TCDD and by adequate human survey of the chronic effects of exposure.

Conclusion

Respondent's evidence will prove that the risk to public health from the use of 2,4,5-T on rice is unequivocally greater than any social value derived from such use. This pesticide use causes unreasonable adverse effects on the environment and should be cancelled.

Respectfully submitted,

Timothy L. Harker
Office of the General Counsel
Counsel for Respondent
Office of Hazardous Materials Control
Environmental Protection Agency

ENVIRONMENTAL PROTECTION AGENCY

BEFORE THE CHIEF ADMINISTRATIVE LAW JUDGE

IN RE THE DOW CHEMICAL COMPANY, et al., ("2,4,5-T") Registrants	))) I.F. & R. Consolidated) Docket No. 295))

RESPONDENT'S INITIAL SUBMISSION OF PROPOSED EXHIBITS- 2,4,5-T

1. Environmental Health Perspectives; Experimental Issue No. 5, Department of Health, Education and Welfare; U. S. Public Health Service; National Institute of Health; September, 1973. - All reports of research therein.
2. Buu-Hoi, et. al., Comptes Rendus Acad. Sci., Paris, 273, Series D, 708 (1971).
3. Johnson, J., "The Public Health Implication of the Use of Phenoxy Herbicides and Picloram"; Bioscience, 21 (17), 899 (1971).
4. Watts, R. R. and R. Storherr, "Negative Finding of 2,3,7,8 - Tetrachlorodibenzo-p-dioxin in Cooked Fat Containing Actual and Fortified Residues of Ronnel and/or 2,4,5-Trichlorophenol," JAOAC, 56 (4) 1026 (1973).
5. Chow, et. al., Methodology and Analysis for Residues of MCP and 2,4,5-T in Wheat. Bull, Env. Cont. Tox., 6 576 (1971).

6. Bauer, J., Bovey, R. and J. Smith, Herbicide Concentrations in Live Oak Treated with Mixtures of Picloram and 2,4,5-T, Weed Sci, 17, 567 (1969).

7. Alexander, M. and M. Aleem, Effect of Chemical Structure on Microbial Decomposition of Aromatic Herbicides, Food Chem., 9, 45 (1961).

8. Schultz, O. P., Dynamics of a Salt of (2,4-Dichlorophenoxy) Acetic Acid in Fish Water, and Hydrosol, J. Agr. Food Chem., 21 (2) 186 (1973).

9. Bovey, R. and J. Bauer., Persistence of 2,4,5-T in Grasslands of Texas, Bull. Env. Cont. Tox., 8 (4) 229 (1972).

10. Manigold, D. B. and J. Schulze, Pesticides in Water. Pest. Mon. J., 3 (2) 23 (1969).

11. Firestone, D., et. al., Determination of Polychlorodibenzo-p-dioxins and Related Compounds in Commercial Chlorophenols JAOAC, 55 (1) 85 (1972).

12. Poland, A. and E. Glover, 2,3,7,8 - Tetrachlorodibenzo-p-dioxin: A Potent Inducer of Aminolevuliner Acid Synthetase. Science 179,476 (1972).

13. Huston, B., Identification of Three Neutral Contaminants in Production Grade 2,4-D., J. Food Chem., 30 (3) 724 (1972)

14. Nilsson, C. and L. Renberg, "Further Studies on Impurities in Chlorophenol", unpublished manuscript.

15. Plimmer, J. et. al., Photodecompositon of Chlorinated Dibenzo-p-Dioxins, Science 173, Science 173 748 (1971)

16. Emerson, G. L., et al., Teratogenic Studies on Trichlorophenoxyacetic Acid in the Rat and Rabbit, Fd, Cosmet, Toxicol., 9:395-404, 1971.

17. Courtney, K. D., and Moore, J. A. - Teratology Studies with 2,4,5-Trichlorophenoxyacetic Acid and 2,3,7,8 - Tetrachlorophenoxyacetic Acid and 2,3,7,8 - Tetrachlorodibenzo-p-dioxin, Toxicol. Appl. Pharmacol., 20:396-403, 1971.

18. Roll, R., Investigations Concerning the Teratogenic Effect of 2,4,5-T in Mice, Fd. Cosmet. Toxicol., 9:671-679, 1971

19. Neubert, D., and Dillman, I., Embryotoxic Effects in Mice Treated with 2,4,5-T and TCDD, Naunym-Schmiedeberg's Arch. Pharmacol., 272:243-264, 1972.

20. Thomas, J. A., and Lloyd, J. W. Organochloride Pesticides and Sex Accessory Organs of Reproduction," Pesticides and the Environment, Intercontinental Medical Book Corp., N.Y. pp. 43-51, 1973.

21. Flick, et al., Toxicity of Chick Ederma Factors in the Chick, Chick Embryo and Monkey, Poultry Sci., 52:1637-1641, 1973.

22. Allen and Carstens, Light and Electron Microscopic Observations in Macaca Mulatta Monkeys Fed Toxic Fat, Amer. J. Vet. Res., 28:1513-1526, 1967.

23. Buu-Hoi, N. P., et al., Cancerominetic Properties of TCDD, ("Dioxin"), C. R. Acad. Sci (Paris) D273 (3):708-711, 1971.

24. Buu-Hoi, N. P., et al., Organs as Targets of Dioxin Intoxication. Naturwiss. 59 (4):174-175, 1972.

25. Jackson, W. T., Cytological Effects of 2,4,5-T and of Dioxin Contaminants in 2,4,5-T Formulations, J. Cell Sci. 10:15-25, 1972.

26. Hussain, S., et al., Mutagenic Effects of TCDD on Bacterial Systems, Ambio., 1(1):32-33, 1972.

27. Sparschu, et al., Study of the teratogenicity of TCDD in the Rat. Food Cosmet. Toxicol. 9:405-412 (1971).

28. Goldstein, J. A.m et al., Hepatic Porphyria Induced by TCDD in the Mouse. Res. Comm. Path. Pharm. 6(3) 919 (1973).

ENVIRONMENTAL PROTECTION AGENCY

BEFORE THE CHIEF ADMINISTRATIVE LAW JUDGE

IN RE	)	
	)	
THE DOW CHEMICAL COMPANY, et al., ("2,4,5-T")	)	I.F. & R. Consolidated Docket No. 295
	)	
Registrants	)	

OPPOSITION TO FIELD HEARING

Respondent opposes the convening of field hearings in this proceeding, for the following reasons:

1. The issues for adjudication can be resolved only by adducing scientific and technical evidence generally beyond the purview of "lay"witnesses. Consequently, convening field hearings, traditionally scheduled in order to permit the convenient testimony of such persons, would not serve a valuable purpose.

2. In those relatively few instances where non-expert testimony may be relevant, convenience is better served by requiring such individuals to appear in Washington, D. C., than by requiring all parties to travel to a "field location".

Respectfully submitted,

Timothy L. Harker
Counsel for Respondent

UNITED STATES OF AMERICA

ENVIRONMENTAL PROTECTION AGENCY

BEFORE THE ADMINISTRATOR

IN RE:

2,4,5,-T) FIFRA CONSOLIDATED DOCKET NO. 295

RESPONDENT'S SECOND PRETRIAL BRIEF

Timothy L. Harker
Attorney for Respondent
Office of the General Counsel
401 M Street, S. W.
Washington, D. C.
(202) 755-0796

Point I

The Scientific Data to Which Dow Chemical Company Subscribes in its First Prehearing Memorandum, If Accurate, Does Not Sustain Registrant's Burden of Ultimate Persuasion.

Registrant, Dow Chemical Company, in its First Prehearing Memorandum has failed to reckon adequately with numerous important issues in this proceeding. Confronting its burden of proof on substantial questions of public health and safety, Registrant would seek to persuade with demonstrably incomplete scientific information and unreasonable inference.

Particularly as to the hazards birth defects, chronic illness and delayed lethality from long-term exposure to minute quantities of tetra-dioxin (TCDD), associated with the use of 2,4,5-T, Registrant has engaged merely in a recitation of insufficient data and conclusory optimism. Despite the fact that more than 2 1/2 years has elapsed since the 2,4,5-T Advisory Committee expressed concern over the deficiency of information on the environmental presence and risks to health from tetra-dioxin, Registrant has neglected to undertake reliable life-time toxicity testing on, thorough environmental monitoring for and adequate, statistically reliable human survey of the effects of chronic exposure to TCDD.

Such a failing legal stance must not be lent undue credence from the construction of a false issue by Dow Chemical Company and the U. S. Department of Agriculture (USDA) -- the assertion that in meeting their burden of proof the proponents of registration are asked to but cannot

"prove a negative"; i.e. that there is no risk from the use of 2,4,5-T. */ As Respondent stated in its First Pretrial Brief, nothing derived from scientific and field research with 2,4,5-T or from reliable observation of widespread human exposure to 2,4,5-T demonstrates that the threat to public health from 2,4,5-T, TCDD contamination of the food supply is anything less than significant.

Reliable, thorough research which demonstrates such risks to be deminimis is legally necessary in order to permit a reasoned inference to the contrary. This the proponents of 2,4,5-T have failed to undertake or to adduce.

A.

Dow Chemical has not presented statistically significant, reasonably reliable survey of human exposure to 2,4,5-T, TCDD which would tend to support its conclusion that 2,4,5-T, TCDD do not adversely affect fetal development and the well-being of human offspring. **/

*/ Indeed, the statutory obligation of Registrants is to demonstrate by clear and convincing evidence that continued use of 2,4,5-T does not constitute an unacceptable risk of adverse environmental affects. Respondent's Brief, page 8, Note 8. This is logically as well as legally inconsistent with the rhetorical straw man of Dow Chemical and USDA -- that Respondent would have them "prove a negative".

**/ Dow does discuss a survey of 126 employees, exposed allegedly to inhalation of 2,4,5-T, TCDD for 60 to 960 days. (Dow Brief, p. 100). Not only is the route of ingestion inapposite to the health concern over the use of 2,4,5-T -- oral ingestion through the food supply -- but the sample size is far too small, the amount and length of exposure unclear to permit statistically reliable conclusions. Of course the study did not even attempt to answer the questions of teratology in women and chronic illness from life-time exposure. However, Respondent would be interested in investigating the records of this health survey and, perhaps, of utilizing some of these employees to determine the extent of TCDD residue in their fat. Perhaps Dow Chemical would be willing to cooperate in such an effort.

B.

Dow Chemical would opine that human offspring are not jeopardized despite the demonstrated teratogenicity of 2,4,5-T, TCDD in laboratory animals, at very low levels, and the potential greater sensitivity of man to teratogenic effects than of tested laboratory species, and in the face of the demonstrated exceptional toxic potency and biological activity of tetra-dioxin. As Respondent verified in its First Pretrial Brief (p. 15), little is known about the nature of teratogenic effects and even less is understood about the nature and source of TCDD's toxic influence. Registrants and USDA have deposited no additional information in these lacunae in medical knowledge. Reasonable prudence focused on what is not known, in the light of what is known about the destructive influence of tetra-dioxin on normal birth, compels the conclusion that 2,4,5-T containing TCDD must not be permitted to contaminate the human food supply.

C.

Dow Chemical, in addition, concludes that the general public faces no danger of chronic ill-health from tetra-dioxin. Yet, the Registrants and USDA have produced no monitoring data which would demonstrate that TCDD is not contaminating the American food supply or the American public. The Registrants and USDA have ignored or overlooked the disturbing presence of tetra-dioxin in the Vietnamese food supply and have failed, even, to discuss in reasoned and specific fashion the significance for man of known or potential TCDD residue in certain foods. */

*/ See pp. 35-36 and Table I of Respondent's First Pretrial Brief.

It is known that 2,4,5-T related TCDD is environmentally persistent and bioaccumulative, that it has entered food supplies in as well as away from areas of 2,4,5-T uses, that it is extremely poisonous in minute quantities and that its toxic consequences can be incremental and delayed as well as acute. In light of what is known, what is not known and what Registrants have neglected to investigate leaves no rational cause for optimism over the use of 2,4,5-T on or near human food.

Point II

That Scientific Information to Which Registrant Subscribes to Sustain its Burden of Proof is at Times Inadequately Discussed Or Combined With Casual Assumptions in Order to Support Otherwise Unfounded Conclusions.

In addition to the major omissions discussed, supra, the detailed shortcomings in Dow Chemical's scientific analysis, discussed in part, infra, demonstrate that the evidence as developed in Registrant's First Prehearing Memorandum, assuming it to be competent, is wholly inadequate to persuade by clear and convincing evidence that the use of 2,4,5-T on or related to food does not cause unreasonable adverse effects on man.

A. Teratology

Without discussion of the etiology of birth defects or of the relationship between birth defects in laboratory animals and in man, Registrant concludes that TCDD is not a potent teratogen, although concession is made that "TCDD has embryotoxic tendencies." (Dow Brief, pp. 31, 52, emphasis added.)

Dow's observation apparently rests on two grounds. The first is the contention that TCDD does not cause deformities over a wide range of dose levels. Although it does clearly induce birth defects at extremely low dosages, over the broad range of doses tested, Dow argues, TCDD "tends to cause death of the embryo or fetus." (Dow Brief, pp. 5 and 31.) The second ground consists of Dow's argument that TCDD does not produce birth defects as serious as those induced by some other teratogens. (Dow Brief, p. 5.)

Assuming arguendo that its conclusion is technically proper, Registrant misses the practical point for man. Death of the human embryo or fetus must be considered the ultimate malformation. TCDD is, indeed, a very potent toxin. Respondent is, therefore, concerned with the total adverse fetal or embryonic effect of this persistent poison. This concern is well founded, as TCDD, clearly a teratogen at minute levels, also exerts in extremely small doses (albeit, perhaps, across a broader range of doses) general toxic effects (including death) on the fetus which can occur during the entire development in utero and which can as well retard postnatal development. The total toxic effect on embryonic and fetal development and postnatal growth can be exacerbated by the potential for the excretion of low levels of TCDD in mother's milk. */ Thus the toxic effect of tetra-dioxin on the development, survival and growth of mammalian offspring is not necessarily limited to a specific period of gestation.

*/ Respondent's First Pretrial Brief, p. 19.

Registrant's argument as to the dose range of TCDD's teratogenic effects is, therefore, as incomplete as it is unnecessary quibbling.

Of the second ground for Dow's conclusion, its argument that TCDD is not a potent teratogen because to date it has primarily caused cleft palate in the species tested, Registrant has again introduced an inadequate analysis. It has failed to suggest why the teratogenic expression of TCDD in man is necessarily similar to its expression in some lab species (cleft palate). Certainly there is no reason to assume a parallel manifestation of defects. Rather, absent more reliable information on human exposure one can as well assume varying expressions, more or less serious in man.

But of far more importance to demonstrating the failings of Dow's analysis is its conclusion that cleft palate is not a major deformity. One may conclude that cleft palate is far less serious to a given individual than deformed or missing limbs. However, a proper judgment as to the relative public importance of cleft palate and other birth defects would require an assessment of the comparative frequency with which they occur. Dow Chemical has not proffered such analysis.

As a matter of public regulatory policy, Dow's medical distinction between major and minor teratogens is irrelevant. 2,4,5-T related TCDD in food presents a serious risk of birth defects and other toxic effects in the human embryo and fetus. That the most common and obvious consequence of that risk may be cleft palate rather than some other, more horrible defect should be a matter of no legal significance whatsoever.

Registrant also finds "that 2,4,5-T as now manufactured (< 0.1 ppm TCDD) does not present a teratogenic hazard to women when used in accordance with presently registered uses." (Dow Brief, p. 53.) Certain shortcomings, additional to those discussed, supra, render the statement conclusory.

Dow has not demonstrated that reasonably reliable "no effect" levels have been ascertained even in the species tested, which take into account a proportionality between the number of animals tested and the resultant embryotoxic effect, and which utilized sufficiently large samples.

In addition, Registrant's discussion of the gamut of 2,4,5-T toxicity testing (including but not limited to teratology) consistently and improperly resorts to extrapolating a "no-effect" level for TCDD based on laboratory testing with 2,4,5-T in which the TCDD content was known. (For one example, see p. 8.) Dow Chemical takes for granted that sample sizes and the distribution of toxic responses were sufficient even to permit reasonably safe extrapolation to man. (Dow Brief, pp. 8 and 28.) Such assumption must be clearly proven as a prerequisite to Dow's further assumption that a laboratory "no-effect" level is a reliable predictor of a safe level for man.

Furthermore, the use of 2,4,5-T testing as a source of toxicological predictions for TCDD simplistically fails to account for potential effects of the 2,4,5-T itself on the storage of TCDD, and on the quality and degree of TCDD association with the embryo and fetus (or body organs), and on the excretion of TCDD. The extrapolation also fails to give a "real world"

picture because it fails to account for the bioaccumulative impact of TCDD in the environment. Such conclusions are unreliable.

Registrant also obfuscates the importance for regulatory policy of the thalidomide experience. Dow Chemical concludes that had the ratios between the teratogenic dose and the maternal toxic dose of thalidomide been considered, and "all of the available data utilized", the dose level at which thalidomide caused teratogenic effects in humans could have been predicted. (Dow Brief, p. 30.) The argument of "prediction aside" (especially in view of the fact that Dow fails to mention in what manner "all of the available" thalidomide data should have been "utilized"), Registrant's conclusion as stated in no way indicates that man is not potentially more sensitive than laboratory species to embryotoxic (including teratogenic) effects, as the thalidomide case indicates.

Dow Chemical also apparently seeks to exonerate 2,4,5-T of teratogenic implications by spurious analogy to certain environmental circumstances, such as fasting and stress, which may, arguably, produce adverse effects on embryonic or fetal development. (Dow Brief, p. 48.) The fact is that of the 50 pesticide chemicals evaluated in the original Bionetics Laboratory research, only a few induced teratogenic effects. */ (Of course, this does not mean that others are not also teratogenic.)

*/ Report of the Secretary's Commission on Pesticides and their Relationships to Environmental Health, U. S. Department of Health, Education and Welfare. December, 1969. pp. 665-669.

B. Chronic Toxicity and Delayed Lethality

With no lifetime feeding studies in mammalian species from which to derive reasonably safe negative toxicological conclusions and with no reliable environmental or human residue monitoring information on TCDD, Dow Chemical opines:

> Exposure to 2,4,5-T as presently used, and to TCDD resulting from its presence in 2,4,5-T at <0.1 ppm as now produced, causes no chronic sublethal health effects in man or other animals. (Dow Brief, p. 100.)

> Present uses of 2,4,5-T as currently manufactured will not cause delayed lethality in man or other animals because exposure to both 2,4,5-T or TCDD is many times less than that which could cause such an effect. (Dow Brief, p. 114.)

No thorough research effort even suggests that tetra-dioxin will not readily accumulate and be stored in the liver and adipose tissue or other human organs after long-term, low-level exposure through the food supply. Nor is there adequate toxicology testing from which to conclude with even reasonable safety that serious health effects are not caused by chronic exposure to minute quantities of TCDD.

It is known that TCDD can bioaccumulate and can be stored in animal organs and tissue. It is known that TCDD is extremely toxic, both acutely and incrementally. Current data suggests that it may well exert delayed lethal effects. Chronic exposure of the general population to TCDD at any level cannot be permitted.

C. Persistence and Bioconcentration

Registrant contends that a "steady-state" level of TCDD will be attained in man in approximately 90 days. (Dow Brief, p. 178). Dow Chemical then concludes that TCDD does not accumulate in body tissue. (Dow Brief, summary at p. 32 and p. 161.) The manner in which these conclusions are derived from the analysis (Dow Brief, p./ 161-165, 177-178) is totally unclear. The statements appear conclusory and unfounded.

Accepting arguendo the 90 day "steady state" conclusion would of course indicate clear bioaccumulation from exposure, thus refuting Dow's ultimate conclusion as to no accumulation of TCDD. Existing data strongly suggest the presence of TCDD in the food supply, (Respondent's First Pretrial Brief, pp. 35-36) and therefore the potential for such accumulation.

But Dow's steady-state analysis is a mere projection without even minimally supporting analysis or theoretical reasons as to why such a projection is reliable. The one research effort cited (without clear analysis by Dow) to support the conclusory statement (Dow Brief, p. 177), utilized a single, near lethal dose of TCDD. Such extrapolation to the repetitive dose, low-level exposure of the real world is arguably sufficient for limited purposes with an ordinary compound, but is to risky with TCDD because of its exceptional potency and potential for delayed lethality.

The conclusion of a 90 day steady-state should be based on, at least, chronic feeding studies over a considerable portion of the lifetime of the tested species. The cited research takes no account of and Dow fails even to discuss the demonstrated toxic influence of TCDD on the

liver and kidneys which could diminish over the span of long term exposure man's capacity to excrete or to detoxify TCDD -- a vital assumption in Dow's convenient "steady-state" speculation. Similarly, the newborn and the ill, may have less efficient kidneys than those by which Dow predicts a steady state. Nor does Dow discuss the potential significant variation in the detoxification and excretion of TCDD when administered in high single doses versus when administered in continuous, small doses. Also lacking is discussion of the toxicological importance of very small amounts of TCDD which bind to the liver to remain beyond the "steady-state" projection, i.e., why is the accumulation of TCDD as projected by Dow, assuming it ceases at 90 days, not of great significance to man's health? Similarly, the cited study clearly indicates that TCDD has a half-life in the male rat of 17 days. This fact, in itself contradicts Dow's contention and suggest that TCDD can accumulate in mammalian species because it is not readily excreted.

Also Dow Chemical overlooks the serious potential for harm caused by the continuous assault of low levels of TCDD, even if, as Registrant assumes, bioaccumulation does not occur. Existing information suggests that tetra-dioxin is cumulative and/or delayed in its toxic influence. (Respondent's First Pretrial Brief, p. 23. Dow Brief, p. 114.) There is no long-term, reliable research to the contrary.

Finally, several additional facts undermine various bases of Dow's "steady-state", "no-accumulation" conclusion:

1. Existing residue data (Respondent's Brief, pp. 35-36) indicate the contamination of food by TCDD. Dow in its analysis expressed the erroneous view that TCDD was not in food. (Dow Brief, p.161).

2. TCDD is apparently not metabolized by mammalian systems,*/ contrary to Registrant's opinion. (Dow Brief, p. 35.)

3. The authors of the research paper cited by Dow to buttress its "steady state" contention emphasize that the TCDD recovered within 48 hours of administration is probably unabsorbed TCDD, contrary to Dow's opinion that absorbed TCDD is eliminated via the feces. (Dow Brief, p. 35.)

4. The clearance rate of TCDD from body fat would be expected to be considerably different than from the liver, contrary to Dow's opinion that clearance of TCDD would be the same for all tissues. (Dow Brief, pp. 124, 178.) Respondent's cattle feeding study data indicate this variation in clearance. (Respondent's Brief, Table I.) Clearance from different organs in different species would be expected to differ.

C. General Observations of Registrant's Inadequate Analysis and Unfounded Conclusions.

Indicative of Dow Chemical Company's incomplete scientific analysis is a number of errors and self-serving or misleading definitions. Some of these are discussed.

Dow defines "Teratogenic" as, "causing a toxic effect on the embryo which seriously interferes with normal development or survival of the offspring." (Dow Brief, p. 54. Emphasis added.) The use of the modifier

*/ Vinopal, J. H. and Caseida, J. E. Arch. Environ. Contamination and Toxicol. 1: 122-132 (1973).

"seriously" is a scientifically unacceptable, subjective judgment supported by little, if any, research. As with Dow's subjective judgment that TCDD is not a "potent teratogen" because it induces inter alia, cleft palate, this subjective stance is also of misleading convenience, and may be used in partial support of such false statements as, "TCDD has teratogenic tendencies." (Dow Brief, p. 52. Emphasis added.)

Dow concludes that 2,4,5-T at currently registered "environmental use levels" of TCDD poses no threat to public health. (Dow Brief, p. 47 for example.) Registrant neglects even to define "environmental use levels" of TCDD. Apparently, Dow intends thereby to mean less than .01 ppm in the technical material.

Besides the fact that Dow has not even adequately discussed what levels of TCDD may be dangerous for man, it has also failed to adduce refined residue monitoring data on the extent to which TCDD has penetrated the U. S. environment and the food supply. Dow's use of the word "environmental" to define levels of TCDD, thus, has absolutely no bearing on reality. Conclusions derived therefrom as to the absence of a public health risk should be disregarded.

Dow resorts to definitional looseness in concluding that residues of TCDD in human food would be of such "ultra low level as to provide an adequate margin of safety" for the public. (Dow Brief, p. 103.) Since reliable no-effect levels in a variety of laboratory species have not been established for the great majority of TCDD's known toxic effects (e.g. embryotoxicity, fetotoxicity, teratogenicity, chloracne, skin lesions, gastrointestinal hemorrhages, immunosuppression, liver function impact,

including induction of microsomal enzmes and the increase of uroporphyrin, and induction of ALA synthetase) Dow's opinion as to the safety of "ultra low" levels of tetra-dioxin is clearly unfounded, even if it had adduced the environmental monitoring data necessary to define the phrase "ultra low."

Dow reports that the research of Courtney and Moore demonstrates a "low incidence" of TCDD induced cleft palate. (Dow Brief, p. 84.) Yet the data from that terata testing (as reported in Dow Brief, p. 85) reflect a significant number of affected litters.

Registrant makes a number of conclusions as to the persistence and and bioaccumulation of tetra-dioxin that are incomplete or inaccurate.

Dow's conclusion that TCDD has to date not been found in the U. S. environment is now inoperative (Respondent's First Pretrial Brief, pp. 35-36). But of more importance is Dow's rationale for this conclusion -- "(t)his (the alleged absence of TCDD residues) is in accord with theoretical knowledge of the behavior of these compounds . . . " (Dow Brief, p.150). Registrant's "theoretical knowledge" is equally erroneous. Laboratory data suggest that TCDD is both unusually persistent, resisting normal environmental degradation, and has bioaccumulative potential. (Respondent's Brief, pp. 33-34.) Respondent's initially reported monitoring data (ibid. p. 35-36) tends to confirm its "theoretical" conclusions that TCDD is persistent and bioconcentrates.

Dow's conclusions as to TCDD's persistence and bioaccumulation also relate to its opinion that TCDD readily degrades in soil, that it will readily photodegrade in the environment, and that environmental dilution of the available TCDD would dissipate its toxic impact.

Dow's conclusions as to soil and microbial degradation of TCDD are incomplete. (Dow Brief pp. 150 and 159, Respondent's Brief, p. 33.) Its opinion as to photodegradation is misleading. Under environmental conditions of 2,4,5-T uses TCDD can as well be protected by screening. The reliance on dilution to dissipate the effect of any persistent widely used poison is unsound. This is even more so in regard to an extremely potent, persistent compound such as TCDD.

Registrant's report of no TCDD residues in the U.S. environment is due not only to its faulty "theoretical knowledge", but also to the fact that it relies upon a number of monitoring studies which utilized analytical methods of insufficient sensitivity to ascertain levels of TCDD which could well be of importance to human health. (Dow Brief, pp. 124, 140-141, 179.)

Finally, Dow adduces significant new information on the extent of environmental distribution of several dioxins, in addition to TCDD, from 2,4,5-T. Apparently, also present in 2,4,5-T are the contaminants penta-dioxin, hexa-dioxin, and octa-dioxin, each in quantities of less than .1 ppm in the technical material. (p. 194.) Particularly as to hexa-dioxin, there must be concern for public health. Respondent will present additional toxicology information on this risk.

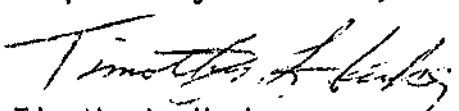
Registrant's conclusion as to the toxicity of this contaminant in 2,4,5-T as well as the risk to man from TCDD and hexa-dioxin in other pesticides (Dow Brief, p. 187) is again mere speculation, resting on Dow's major defense -- that these toxicants are present in "extremely small" quantities (Dow Brief, p. 193). Based on Dow's own reports (id. p. 187) it is difficult to conclude that these levels are "extremely small."

Furthermore, it is Dow's opinion that cumulative toxic effect cannot be expected from TCDD and hexa-dioxin in 2,4,5-T and in other pesticides. From the total absence of reasoned discussion and underlying fact, Dow's conclusion that the "uses of such products are sufficiently remote in time and space so that the cumulative impact is negligible . . . " (Dow Brief, p. 193) can be considered unfounded rhetoric.

Registrant, Dow Chemical Company, must persuade the trier of fact on this and numerous other issues by reliable environmental monitoring, adequate negative toxicity testing and sound inference. Dow Chemical

in its First Prehearing Memorandum has failed to develop and to explicate such convincing proof.

Respectfully submitted,



Timothy L. Harker
Counsel for Respondent
Office of Hazardous Materials Control

Environmental Protection Agency
Office of General Counsel
401 M Street, S. W.
Washington, D. C. 20460

CERTIFICATE OF SERVICE

I hereby certify that I have this 11th day of March, 1974, served by mail one copy of the Respondent's Second Pretrial Brief (FIFRA Consolidated Docket No. 295) upon every other party to the 2,4,5-T proceeding and have served by hand delivery one copy of said Brief on the Administrative Law Judge and 5 copies on the Office of Hearing Clerk of EPA.

Timothy L. Harker

Dated: March 11, 1974.