DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Centers for Disease Control

Memorandum

EXHIBIT 5

Date April 26, 1985

From Chief, Superfund Implementation Group

Subject Review of EPA, Region V, Evaluation of the Midland, Michigan Soil Data
Midland, Michigan

To Louise A. Fabinski
Public Health Advisor
EPA Region V

The material submitted on the subject site has been reviewed by the Chronic Disease Division, Center for Environmental Health, Centers for Disease Control. I hope that you find their comments useful.

COMMENTS

In followup to previous reviews of the environmental soil sampling results from Midland, Michigan, we were asked to review a draft Risk Assessment evaluation of these data which had been prepared by EPA. The essential conclusion of this Risk Assessment is that, because of a history of occupational exposures to TCDD and the documented potential for exposure to contaminated fish from the Tittabawassee River, exposure should be limited to soil contaminated to 50 parts per trillion (ppt) of lower. This level, approximately 1/20th of the CDC's previous site-specific recommendation, is generally consistent with levels seen in other industrialized areas of the country where the manufacturing of TCDD containing products is known not to have occurred.

We find no major fault with the methodology used in preparing this risk assessment; the methodologies and approaches are similar to previous work done at CDC except that different assumptions have been used in several areas such as: a greater amount of dermal contact with soil, using only upper level confidence limits for the estimates of a virtually safe dose (VSD), the lower average lifetime body weight measure, etc. It is to be expected that, given the level of uncertainity regarding many of these parameters, different risk assessments using slightly different methodologies and/or different sets of assumptions will derive somewhat divergent end-results. (It should be noted that the CDC estimate was reviewed extensively by a peer review panel of outside experts before being formally adopted.) However, even in this situation in which estimates of excess risks were different by more than one order of magnitude, the absolute risks of developing cancer during a putatively exposed individual's lifetime are essentially unchanged when one considers that the "background" of "normal" lifetime risk of cancer in the United States is between 25 and 30 percent. All of the approaches discussed within this document are generally perceived to be conservative approaches in an attempt to develop prudent and responsible recommendations for the protection of the public's health.

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Therefore, we reiterate our previous recommendations concerning access restriction or cleanup/stabalization of onsite, contaminated areas to prevent current, as well as, future exposures. The logistics of implementing these public health protective measures do not appear to be exceedingly difficult. The more severe problem of exposure to contaminated fish from local rivers is best addressed directly and not through compensatory decreases in allowable exposures to contaminated soils.

To this end, we also strongly suggest a concentrated public health education campaign to limit, or preferably eliminate, consumption of the highly contaminated local fish as well as the development of reasonable alternatives thereto.

Georgi A. Jones

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EPA says dioxin levels in local fish to persist

July 17, 1986

By KATHY GRAY
Daily News staff writer

The levels of dioxin in the Tittabawassee River sediments and fish downstream from Dow Chemical Co. will not go down significantly in at least the next several years, according to a report released today by the U.S. Environmental Protection Agency.

Even though Dow has significantly decreased the levels of dioxin in its discharge to the river, the EPA stated in its report that low levels in both river sediments and native fish will persist for at least several years.

River sediments containing toxic contaminants attributable to Dow were found 19.5 miles downstream from Midland, the EPA reported.

The EPA did not include health risk assessments of fish consumption in this study, but will release that data separately at a future date.

The fish data with regards to dioxin didn't show any significant changes in in the levels in carp over time, but the EPA did note that the levels in catfish seem to have decreased since 1978. The 1985 levels in walleye and smallmouth bass (averaging 4.4 and 5.0 parts per trillion respectively) were virtually unchanged from 1983 levels.

Dioxin is an unwanted byproduct of herbicide production and in its most toxic form—2,3,7,8 TCDD—is a known animal carcinogen. Its effects on humans is less certain.

"Because of the distribution of 2,3,7,8 TCDD in Midland area soils and the persistence of 2,3,7,8 TCDD in the environment, bottom feeding fish and other game fish from the Tittabawassee River may not exhibit significantly lower levels of 2,3,7,8 TCDD in the near future," the report stated. "Runoff from the city, the wastewater discharge from Dow Chemical, and atmospheric deposition from Dow Chemical operations will continue to contribute 2,3,7,8-TCDD to the river system."

The EPA said the wastewater treatment system at Dow is comparable if not superior to best available technology, (BAT) but "in-process controls for several organic chemical process are not equivalent to BAT, even when considered with superior end-of-pipe treatment."

The report noted that several volatile organic chemicals, including carbon tetrachloride, methylene chloride and styrene were among those not equivalent to BAT. Residual levels of toxic semi-volatile organic pollutants, such as pentachlorophenol and chlorinated benzenes also were consistently present in samples tested by the EPA.

"This data suggest that scattered or diffuse sources throughout the plant (sewer sludges, contaminated soils, pond sediments) may be contributing residual discharge loadings to the outfall," the report stated.

When Dow's current wastewater permit expires in 1988, the EPA will work with the Michigan Department of Natural Resources to discharge limitations for several volatile and semi-volatile organic pollutants.

The report is one part of the EPA's dioxin initiative in Midland. This particular study examined Dow's wastewater, Tittabawassee River sediments and native fish. Representatives from the EPA will be in Midland July 29 to review the report with interested Midland residents. Appointments are available between 2:30 to 5:30 p.m. and from 7 to 9 p.m. on that date. To make appointments, call John Perrecone at (800) 621-8431 or (800) 572-2515.

The EPA already has released reports on the levels of dioxins in Midland surface soils and the quality of public and private water supplies in the Midland area and Dow's brine operations. Reports still are scheduled to be released based on emissions from Dow's incinerator.

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UNITED STATES
ENVIRONMENTAL PROTECTION AGENCY
REGION V
230 SOUTH DEARBORN ST.
CHICAGO, ILLINOIS 60604

REPLY TO ATTENTION OF:
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July 15, 1986

Enclosed is a copy of a report titled, "Dow Chemical Wastewater Characterization Study, Tittabawassee River Sediments and Native Fish." This report presents the results of USEPA's recent study of dioxins and other toxic pollutants at the Dow Chemical-Midland Plant. The report also presents summaries of prior USEPA and Michigan Department of Natural Resources studies at the Dow Chemical-Midland Plant, including studies of Tittabawassee River native fish and sediments conducted during the period 1978 to 1985. Finally, the report includes an overview of the Clean Water Act requirements for National Pollutant Discharge Elimination System (NPDES) permit conditions for best available technology as they pertain to the Dow Chemical-Midland Plant. The information and data contained in this report are being considered by several program offices at the Michigan Department of Natural Resources and USEPA - Region V for processing of environmental control permits for Dow Chemical.

The major findings are highlighted below:

- The discharge of 2,3,7,8-tetrachlorodibenzo-p-dioxin (2378-TCDD, or dioxin) from Dow Chemical to the Tittabawassee River, and bioaccumulation of 2378-TCDD in caged fish and native fish have been confirmed.

- Dow Chemical began operating an effluent filtration system in November 1985 to remove 2378-TCDD from its discharge to the Tittabawassee River. Since that time the company has achieved a 67% reduction in the discharge of 2378-TCDD. Current discharge levels have consistently been less than 10 parts per quadrillion (ppq), the interim discharge limit established by the Michigan Water Resources Commission and approved by USEPA. The estimated current annual discharge loading of 2378-TCDD from Dow Chemical to the Tittabawassee River is 0.00012 kg (0.00026 lbs). Further reduction of the discharge may result from additional in-plant control measures currently being installed by Dow Chemical.

- Although significant progress has been made in reducing the discharge levels of 2378-TCDD from Dow Chemical, it is not likely that the improvement in 2378-TCDD levels found in native fish from the Tittabawassee River will be as rapid. 2378-TCDD is persistent in the environment. Continued low

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level releases from Dow Chemical, surface runoff from the Midland area, and the current burden of dioxins in river sediments may result in a gradual decline in 2378-TCDD levels in fish over a number of years.

° Although 2378-TCDD was not detected in Tittabawassee River sediments at detection levels ranging from 10 to 30 parts per trillion (ppt), it is most likely present at lower levels. The distribution of the other tetrachlorinated dibenzo-p-dioxins (TCDDs) in Dow Chemical treatment pond sediments, effluent solids, and Tittabawassee River sediments is consistent. Tittabawassee River sediments contaminated by chlorinated dioxins and furans attributable to the Dow Chemical-Midland Plant extend from Midland to the Gratiot Road-Center Road reach of the river, or about 17.1 to 19.5 miles downstream from Midland.

° Dow Chemical's discharges of total suspended solids, ammonia-N, total phosphorus, and toxic organic pollutants have been reduced from levels determined by USEPA in 1981. Discharge levels of total dissolved solids have remained about the same and limited data suggest an increased discharge of toxic metals (chromium). The overall improvement in the discharge levels can be attributed to changes in production operations at Dow Chemical, reduction in the discharge flow rate, and installation of the effluent filter system.

° For the most part, wastewater treatment facilities installed by Dow Chemical are consistent with model wastewater treatment facilities considered by USEPA for development of national effluent limitations guidelines for organic chemicals, pesticides, and related chemical manufacturing processes. Best available technology effluent limitations and best management practices programs will be developed for several volatile and semi-volatile organic pollutants found in Dow Chemical untreated and treated wastewaters. These BAT effluent limitations and control programs will be considered with water quality-based effluent limitations developed by the Michigan Department of Natural Resources as part of the next NPDES permit for the Midland Plant.

This report is one of a series that present results of different aspects of USEPA's studies of dioxins and other toxic pollutants in the Midland, Michigan, area. To date, a report has been distributed regarding levels of dioxins in Midland surface soils and potential public health risks associated with exposure to those levels, and a report was issued regarding the quality of public and private water supplies in the Midland area and the Dow Chemical brine operations. We are planning to issue a report concerning Dow Chemical incinerator emissions testing and ambient air monitoring later this year. At that time an overall review of public health risks will be presented.

USEPA representatives will be available on July 29, 1986, at the Grace A. Dow Memorial Public Library in Midland to review this report with interested members of the public during the afternoon (2:30-5:30 p.m.) and evening (7:00-9:00 p.m.). Appointments may be arranged by calling John Perrecone, Office of Public Affairs at 1-800-621-8431 or 1-800-572-2515 (Illinois). Any questions or comments you may have in the interim should be directed to Gary Amendola at the following address:

U.S. Environmental Protection Agency
Region V
Eastern District Office
25089 Center Ridge Road
Westlake, OH 44145
Phone: (216) 835-5200

Sincerely yours,

Valdas V. Adamkus
Regional Administrator

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DOW CHEMICAL WASTEWATER CHARACTERIZATION STUDY

TITTABAWASSEE RIVER SEDIMENTS AND NATIVE FISH

JULY 1986

GARY A. AMENDOLA
DAVID R. BARNA

U.S. ENVIRONMENTAL PROTECTION AGENCY
REGION V
ENVIRONMENTAL SERVICES DIVISION
EASTERN DISTRICT OFFICE
WESTLAKE, OHIO

II. OBJECTIVES

The primary objectives of this work are to quantify the conventional, nonconventional, toxic organic and toxic inorganic pollutant discharges from the Dow Chemical - Midland Plant and to assess the need for additional wastewater treatment and best management practices necessary to achieve Best Available Treatment Economically Achievable (BAT) as defined by the Clean Water Act. The information and data contained in this report are being used by the Michigan Department of Natural Resources and USEPA-Region V to develop a proposed BAT NPDES permit for Dow Chemical.

Secondary objectives include: (1) characterization of untreated wastewaters and in-plant sludges and sediments; (2) determination of the types and the extent of bioaccumulation of pollutants discharged by Dow Chemical in fish; (3) sub-part per trillion analyses of effluent samples for PCDDs and PCDFs; and (4) development of information about contamination of native fish and sediments in the Tittabawassee River.

III. SCOPE OF WORK

Major field surveys were conducted by Region V and MDNR in 1981 and by Region V in 1984. A multi-phased field program was planned in the spring and summer of 1981 and executed in late summer and early fall of 1981. Field programs included the following: (1) a sediment survey of the Tittabawassee River to determine whether significant toxic pollutant contamination of the sediments has occurred; (2) four 24-hour composite samples of Dow Chemical water intakes and effluent discharges to determine pollutant discharges at the low parts per billion range; (3) one large-volume 24-hour composite sample of Dow Chemical water intakes, certain effluent discharges, and the receiving water to determine discharge rates of PCDDs and PCDFs in the sub-part per trillion range; (4) a static daphnia bioassay and an algal assay to determine whether or not the Dow Chemical main process wastewater effluent exhibits acute toxic effects or stimulatory effects on algal growth; (5) an Ames test of the main process wastewater discharge to determine whether the effluent exhibits mutagenic properties; (6) a fish bioaccumulation study to determine the level and rate of bioaccumulation of pollutants discharged by Dow Chemical; and (7) analyses of native fish from the Grand River for organic compounds.

As part of USEPA's comprehensive study of dioxins and other toxic pollutants, sampling was conducted in 1984 at the major process wastewater sewers at Dow Chemical; at other nonprocess wastewaters, including incinerator wastewaters, ground water collection systems, and landfill dewatering systems; at the treated discharge to the Tittabawassee River; and for Tittabawassee River sediments. Data obtained from USEPA's 1981 and 1984 surveys are compared with Dow Chemical monitoring data and other available data from preliminary dioxin investigations conducted by Region V in 1978.

IV. MAJOR FINDINGS AND CONCLUSIONS

A. Dow Chemical - Midland Plant

1. Untreated Wastewaters and Sewer Sludges

Untreated wastewaters from process and nonprocess operations at the Dow Chemical - Midland Plant contain high levels of numerous chemical compounds. Raw waste loadings of volatile compounds determined during the 1984 USEPA survey [carbon tetrachloride (940 lbs/day); methylene chloride (920 lbs/day); styrene (570 lbs/day); chloromethane (410 lbs/day); toluene (350 lbs/day); benzene (160 lbs/day); and ethylbenzene (122 lbs/day)] were greater than raw waste loadings of semi-volatile compounds [phenol (520 lbs/day); 2,4-dichlorophenol (45 lbs/day); 1,2-dichlorobenzene (20 lbs/day); pentachlorophenol (16 lbs/day); 2,4,6-trichlorophenol (13 lbs/day); and naphthalene (13 lbs/day)]. The high levels of volatile compounds are significant from an air pollution standpoint. Emission of one-sixth of the volatile compounds from the sewerage and wastewater treatment systems would be sufficient to classify the plant as a major source of volatile organic carbon (VOC). The findings of chlorinated benzenes and pentachlorophenol in untreated wastewaters long after termination of production of these compounds suggests continued leaching of the compounds from sewer system sludges and plant soils.

Most of the untreated wastewater loading of PCDDs and PCDFs can be attributed to contributions from various process sewers and the hazardous waste incinerator. The raw waste loading of TCDDs was estimated to be about 6.9×10^{-4} lbs/day (3.1×10^{-4} kg/day) and about 1.3×10^{-2} lbs/day (6.1×10^{-3} kg/day) for TCDFs. Although 2378-TCDD was not detected in untreated wastewaters from the process sewers or the hazardous waste incinerator, other tetra-octa CDDs and CDFs were found in the 1984 USEPA study.

2. Tertiary Pond Sediments

Sediments from the tertiary pond system were found to be contaminated with several organic chemicals. Surface sediments from the primary (pentagonal) and secondary (rectangular) ponds were found to contain larger numbers and higher levels of pollutants than found in tertiary pond sediments. These data suggest the pond system has been at least partially effective in removing settleable pollutants not removed in the biological treatment facility. Chlorinated benzenes were found at relatively high levels in primary and secondary pond sediments (13-67 ppm) compared to tertiary pond sediments (ND-1.5 mg/l). Surface sediments in the ponds were generally found to be more heavily contaminated than bottom pond sediments.

The gradient of PCDDs and PCDFs across the pond system was substantially less than for other pollutants. These data suggest that PCDDs and PCDFs entering the pond system are attached to finer particles that tend to settle over a wider area than other semi-volatile pollutants which may be associated with

heavier particles. 2378-TCDD was detected at 1.7 ppb in primary pond surface sediments, 3.8 ppb in secondary pond surface sediments, and from 0.10 to 0.93 ppb in tertiary pond surface sediments.

B. Dow Chemical - Outfall 031 Discharge

1. Wastewater Characterization

Process changes at the Midland plant and water conservation measures have resulted in a gradual reduction in the average discharge flow from outfall 031 from over 50 MGD in the mid 1970s to less than 20 MGD today. Recent monitoring by USEPA and Dow Chemical suggest that discharges of toxic organic pollutants and certain nonconventional pollutants have been reduced since 1981. The apparent increase in the discharge of toxic metals is attributed to chromium discharges which are higher than measured by USEPA in 1981. A summary of annualized effluent discharge loadings is presented below:

	Estimated Annualized Discharge in Tons		
	1981 USEPA Survey	1984 USEPA Survey	1984-1985 Dow Chemical Monitoring
Total dissolved solids	148,000	150,000	129,000 (net)
Total suspended solids	680	1,040 [180]	420 (net)
Total kjeldahl nitrogen	330	87	--
Ammonia-N	270	27	23 (net)
Total phosphorus	46	14 [5]	11
Toxic organic pollutants	15.5	1.9	4.9
Toxic metal pollutants	5.7	6.9	16.7

Note: [ ] Estimated current annual full-scale discharge loading based upon pilot plant filter data. Effluent phosphorus data from the full-scale filter system installed in November 1985 are not available at this writing.

The estimated annual discharge of phosphorus from outfall 031 is 5 tons/year based upon limited pilot plant studies, about 90% less than loadings determined in 1981.

2. PCDDs and PCDFs

Based upon six months of full-scale operation of the effluent filtration system, Dow Chemical has achieved a 67% reduction in the discharge loading of 2378-TCDD (9.9×10^{-7} kg/day to 3.3×10^{-7} kg/day). The current estimated annual discharge is 1.20×10^{-4} kg/year. TCDD analyses by Dow Chemical indicate that 2378-TCDD comprises less than 3% of the total TCDDs present. The predominant TCDD isomers, both before and after pilot filtration, are 1368-TCDD, 1379-TCDD, and 1237+1238-TCDD. Based upon limited data, the unfiltered outfall 031 discharge appears to contain higher levels of TCDFs than TCDDs and higher levels of other PCDFs than corresponding PCDDs. Pilot plant filter data suggest

the full-s... ...r may be achieving more than 90% removal of TCDDs, 2378-TCDF, and HxCDDs, ... and OCDD. Only data for 2378-TCDD have been reported for the full-sc... ...ter system at this writing.

3. Biomonitoring

Static bioassays (Daphnia magna) conducted by USEPA in 1981 for the outfall 031 discharge indicated the discharge exhibited no acute toxicity to test organisms. The discharge exhibited a stimulatory effect on algal growth and caused no mutagenicity in the Ames test (direct and rat liver enzyme activated test procedures). The 1981 USEPA studies were completed at a time when the average effluent discharge was about 34 MGD. Biomonitoring conducted by Dow Chemical in 1985 as required by NPDES permit MI0000868 yielded the following results for flow-through studies:

	Daphnia Magna	Pimephelas Promelas (fathead minnow)
Acute toxicity		
48-Hour LC_{50}	40% effluent	No toxicity
Chronic toxicity		
MATC (geometric mean)	35.8% effluent	21.7% effluent*

*embryo-larval test

At the time of the Dow Chemical studies, the discharge flow was about 20 MGD. Dow Chemical attributed acute toxicity to daphnia to the salinity of the effluent. The mass discharge of salts was about the same as that encountered during the 1981 USEPA studies. However, the concentration of dissolved solids was about 40% higher due to the reduction in discharge flow. Dow Chemical also reports that for the minnow study (embryo-larval test), there were no observed concentration related effects at hatch and a normal hatch occurred, yet no organisms survived beyond 13 days. No cause for the chronic toxicity observed was suggested by Dow Chemical. Test water for the Dow Chemical bioassays was prefiltered through a 25-micron sock. Since, chemical analyses of the wastewater before and after filtration were not reported, the effects of this procedure are not known.

4. Bioaccumulation Studies

Final results from the 1981 USEPA-MDNR bioaccumulation study confirmed preliminary results with respect to the discharge of 2378-TCDD from outfall 031 and the accumulation of 2378-TCDD and other TCDDs in caged catfish exposed to the plume of outfall 031 in the Tittabawassee River. The preliminary contract laboratory results for PCDFs could not be confirmed. A unique finding is that 1368-TCDD accumulated in caged fish exposed to the outfall/river water mixture at higher levels than 2378-TCDD. After 28 days of exposure, 2378-TCDD reached nearly 40 ppt and 1368-TCDD to about 160 ppt. Penta-CDDs (140 ppt), hexa-CDDs (43 ppt), and TCDFs (454 ppt) were found in these fish by USEPA analysts. There was no indication that an equilibrium level of 2378-TCDD had been reached after

28 days of exposure. The fish exposed to the plume of the discharge accumulated greater numbers and higher levels of other organic chemicals, including polynuclear aromatic compounds, chlorinated phenols, and pesticides, than did fish exposed at control sites.

A recent biouptake study conducted by Dow Chemical did not demonstrate significant uptake of 2378-TCDD or 2378-TCDF in catfish exposed for 28 days to a mixture of 15% effluent and 85% river water. Hexachlorobenzene uptake reached 3.7 ppm (whole fish sample) in the Dow Chemical study. Most other organic chemicals included in the study protocol did not exhibit significant accumulation over the test period. As with other biomonitoring by Dow Chemical, the test water was prefiltered using a 25-micron sock prior to exposing the organisms. The effect of that procedure on the test results is not known.

5. Pollutants of Concern

From a wastewater treatment technology standpoint, the principal toxic pollutants of concern are listed below. The evaluation of appropriate Best Available Technology effluent limitations and Best Management Practices programs will focus primarily on these toxic pollutants.

Volatile Organic Pollutants
- Benzene
- Carbon tetrachloride
- Ethylbenzene
- Methylene chloride
- Toluene
- Styrene

Semi-Volatile Organic Pollutants
- 2,4-Dichlorophenol
- 2,4,5-Trichlorophenol
- 2,4,6-Trichlorophenol
- Pentachlorophenol
- 1,2-Dichlorobenzene
- 1,3-Dichlorobenzene
- 1,4-Dichlorobenzene
- 1,2,4-Trichlorobenzene
- 1,2,4,5-Tetrachlorobenzene
- Hexachlorobenzene
- 2,4-D
- 2,6-D
- 2,4,5-T
- Dinoseb
- Bis(chlorobutyl) ether
- 2,3,7,8-TCDD (PCDDs and PCDFs)

Toxic Metal Pollutants
- Antimony
- Chromium
- Nickel
- Zinc

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

REGION V

EXHIBIT 3

Date: February 28, 1985

To: David Stringham, Deputy Director
Waste Management Division

From: J. Milton Clark, Ph.D.
Toxic Substances, Section

Subject: Evaluation of Data Collected during U.S. EPA's 1984 Field Study of Midland, Michigan

Attached is a draft of my report. A rigorous evaluation of data recently gathered in Midland has been made with emphasis on human health risk. Based upon the risk analysis performed, recommendations have also been developed. This document should further discussion to guide decision making regarding the need for remedial actions, additional monitoring and human health studies in Midland. It has offered to provide one possible analysis of the Midland field study and should not be viewed as representing any position the Agency may ultimately chose.

I recommend that the document be forwarded to the Chlorinated Dioxin Work Group in EPA/HQ and the Centers for Disease Control for internal peer review.

It is hoped that the document will be useful in the effort to develop the interagency evaluation of the available data.

28 FEB 1985

FOR INTERNAL REVIEW ONLY

DRAFT

FOR IN... REVIEW ...

Evaluation of Data Collected during U.S. EPA's 1984 Field Study of the Midland, Michigan Area
Pesticides and Toxic Substances Branch
Region V, U.S. EPA

I. Soil Data

A. Dow Chemical In-Plant Samples

1. 2,3,7,8-TCDD

Analytical results, found in Table 1 (attached), of analyses of 15 surface soil samples (0-1") taken inside the Dow plant grounds revealed 2,3,7,8-TCDD concentrations ranging from 10 parts per trillon (ppt) to 30 parts per billion (ppb). The high value of 30 parts per billion, station/sample #15, found south and east of building 874 and immediately north of the railroad tracks, represents an average of duplicate analysis on the sample. The average soil concentration of the 15 samples was found to be 2.4 ppb, with three of the 15 samples having more than 1 ppb 2,3,7,8-TCDD. The median value was 220 ppt. Sample #5, collected southwest of building 956 and immediately south east of the Dow incinerator, was found to contain 3.50 ppb of 2,3,7,8-TCDD. Sample #7, collected about 1/2 mile northeast of the Dow incinerator at the northwest corner of 11th and J streets contained 4.60 ppb of 2,3,7,8-TCDD.

Samples #11, 12, 13, and 15 were all collected about 1/2 mile northeast of the incinerator. Concentration of 2,3,7,8-TCDD in samples #11, 12, and 13 were reasonably consistent ranging from 220 to 440 ppt; however, sample 15, at 30 ppb 2,3,7,8-TCDD is disporportionately high. Samples #4,7,8, and 9, collected in a line moving northwest from the incinerator to an approximate distance of one mile reveals an inconsistent pattern. Sample #4 was 20 ppt; sample #7, (1/3 mile) 4,600 ppt; sample #8, (3/4 mile) 150 ppt; and sample #9, (1 mile) 10 ppt.

2. Total PCDDs and PCDFs

PCDD and PCDF concentrations were determined in one soil sample, collected west of building 934 (station/sample #4). The concentration of 2,3,7,8-TCDD (0.27 ppb) was found to be 84% of the total TCDDs detected (0.32 ppb). Concentrations of penta CDDs and hexa CDDs were 0.24 ppb and 4.0 ppb, respectively. The ratio of hexa CDDs to 2,3,7,8-TCDD was 14.8. Hepta CDDs were found at a concentration of 75 ppb. Several PCDFs were also detected in this sample. 2,3,7,8-TCDF was present at a concentration of 27 ppt, while total TCDFs amounted to 900 ppt. Hexa CDFs and hepta CDFs were 3.1 and 15.4 ppb respectively.

B. Residential Soil Samples

1. 2,3,7,8-TCDD

Superficial soil samples (0-1") were collected and analyzed from Midland, Michigan; an industrial area in Middleton, Ohio; and four natural areas in Minnesota. This sampling design was to determine if 2,3,7,8-TCDD

contamination was more or less unique to a location, such as Midland, where 2,4,5-Trichlorophenol (2,4,5-TCP) and a variety of 2,4,5-T derivatives had been manufactured. For more information on design and sampling see the September 22, 1983 EPA document, "Soil Screening Survey at Four Midwestern Sites" (1).

Data from this sampling effort is attached and found in Tables 2-5A. Yard composite soil samples from three locations, upwind (west/southwest) of Dow Chemical, see Table 2, were found to contain non-detectable levels of 2,3,7,8-TCDD. Detection limits ranged from 2 to 4 ppt. At two of these locations soils collected near downspouts or under roof drip lines, were found to have low levels of 2,3,7,8-TCDD; 6 and 9 ppt.

Of four locations sampled from the perimeter of the Armco plant in Middleton, Ohio only one soil sample of six collected and analyzed was found to be positive for 2,3,7,8-TCDD and at a level of 4 ppt. (Table 4). In contrast, all nine samples collected along the perimet- of the Dow-Midland plant were found to be positive for 2,3,7,8-TCDD. Concentrations of 2,3,7,8-TCDD ranged from a low of 10 ppt to a high of 2.03 ppb, the average concentration being 327 ppt and the median value, 69 ppt. (See Table 2).

Of seven public use locations sampled in Middleton, Ohio only one was found to contain 2,3,7,8-TCDD at a concentration of 4 ppt. All nine public use areas sampled in Midland were found to have 2,3,7,8-TCDD in soils with values ranging from 3 to 170 ppt. The arithmetic mean was 56 ppt; the median value, 19 ppt. The highest concentrations of 2,3,7,8-TCDD observed were those collected from locations most near the Dow plant or located from east northeast to north northeast of the facility. As prevailing wind direction in Midland, see Figure 1, in "Soil Screening Survey at Four Midwestern Sites," is from the southwest or westerly direction, deposition of 2,3,7,8-TCDD by air is suggested. The highest 2,3,7,8-TCDD concentration of 110 ppt, however, was found at Bullock School, located about 1/2 mile southwest of the Dow facility.

Of the 19 residential superficial soil samples (0-1") analyzed in Midland, 18 were positive for 2,3,7,8-TCDD. Concentrations ranged from non-detectable to 270 parts per trillion. The arithmetic mean of this data was 54 ppt; the median, 22 ppt. Two of seven soil samples from residential areas in Middletown, Ohio were found to be positive for 2,3,7,8-TCDD. These samples, both found at one location, contained 4 and 5 ppt of 2,3,7,8-TCDD. The median value of all the Ohio samples was "non-detectable" (< 3 ppt). An average value of 2.2 ppt was reported by Dow Chemical in soils from 20 industrialized areas in the U.S. (November 5, 1984 report) (2). None of the three natural areas sampled in Minnesota contained detectable levels of 2,3,7,8-TCDD. (See Table 5). The data from our studies of the four natural areas, and Middleton, Ohio, when combined with the results on 20 industrialized areas reported by Dow, reveals higher levels of 2,3,7,8-TCDD in Midland, than in other areas studied. If fish data is included for comparison, discussed later, this finding becomes even more apparent.

Concentrations of 2,3,7,8-TCDD found in soils from yards tended to decrease with distance from Dow Chemical. (See Table 2). For instance, all yard samples, B-3, D-3, and E-3, collected about 3700 yards from the Dow incinerator, were found to have lower concentrations of 2,3,7,8-TCDD than samples, B-1, C-1, and E-1, which were all taken about 2100 yards from the incinerator. This pattern suggests 2,3,7,8-TCDD deposition by air. An air deposition hypothesis is further supported by comparing the 2,3,7,8-TCDD levels observed in soils collected near downspouts or under driplines with those found in yards. Downspout and dripline soil concentrations of 2,3,7,8-TCDD were approximately two to ten times higher than those found in yards.

2. Total PCDDs and PCDFs

Concentrations of PCDDs and PDCFs in surface soil samples are presented in Table 6 (attached). Samples collected upwind of Dow Chemical (#13401 and #13395) contained only low levels of hepta and octa CDDs (≤340 ppt) and no detectable levels of PCDFs. All six public access areas sampled in Midland had measurable concentrations of hexa CDDs, ranging from 63 to 441 ppt and all samples contained PCDFs, three with 2,3,7,8-TCDF and hexa CDFs (sample #s 13375, 13393, and 13394). Of five samples analyzed from Middletown, Ohio only one contained detectable levels of hexa CDDs and only one with detectable levels of PCDFs. No hexa CDFs were found in the soil samples. Surface soil samples from three wilderness areas in Minnesota contained low levels of hepta and octa CDDs (≤200 ppt) and no detectable levels of PCDFs.

3. Computation of 2,3,7,8-TCDD Equivalent Risks

Methods are currently being developed to assess the risk from exposure to chlorinated dioxins and dibenzofurans other than for 2,3,7,8-TCDD. These are discussed in the September 26, 1984 draft EPA document entitled "Health Hazard Assessment for Chlorinated Dioxins and -Dibenzofurans other than 2,3,7,8-TCDD" (3). Of the eight methods cited in the document two, the Swiss enzyme and the EPA methods, appear to have the best scientific foundations as they are based upon enzyme inductive properties and carcinogenic assessments. These methods are shown below. Where isomer specific analyses were unavailable, the toxicity of the 2,3,7,8-substituted homologues is utilized.

Table A: Estimates of Relative Toxicities For PCDDs and PCDFs Expressed as Equivalents of 2,3,7,8-TCDD

Compound	EPA Method (1984)	Swiss Method
2,3,7,8-TCDD	1	1
other TCDDs	0.01	0.01
2,3,7,8-PeCDDs	0.2	0.1
other PeCDDs	0.002	0.1
2,3,7,8-HxCDDs	0.04	0.1
other HxCDDs	0.004	0.1
2,3,7,8-HpCDDs	0	0.01
other HpCDDs	0	0.01
OCDDs	0	-

Table A: Continued

Compound	EPA Method (1984)	Swiss Method
2,3,7,8-TCDFs	0.1	0.1
other TCDFs	0.001	0.1
2,3,7,8-PeCDFs	0.1	0.1
other PeCDFs	0.001	0.1
2,3,7,8-HxCDFs	0.1	0.1
other HxCDFs	0.001	0.1
HpCDFs, OCDF	0	-

PCDD and PDCF data from Midland, converted to 2,3,7,8-TCDD equivalents, is presented in the following section.

Table B: 2,3,7,8-TCDD Equivalents of Other PCDDs and PCDFs Found in Midland Soils

Location:	Bullock School			Virginia Park		
		Method			Method	
PCDDs/PCDFs	Level (ppt)	EPA	Swiss	Level (ppt)	EPA	Swiss
2,3,7,8-TCDD	110	110	110	76	76	76
TCDDs	220	2	2	290	2	2
PeCDDs	120	24	12	110	22	11
HxCDDs	410	16	41	240	10	24
HpCDDs	2,400	0	24	410	0	4
2,3,7,8-TCDF	15	2	2	13	1	1
TCDFs	-	-	-	-	-	-
PeCDFs	110	11	11	40	11	11
HxCDFs	170	17	17	64	17	17
Equivalents (ppt):		182 -	219		139 -	146
	Longview School			Mapelton School		
2,3,7,8-TCDD	78	78	78	15	15	15
TCDDs	170	1	1	40	0	0
PeCDDs	100*	20*	10*	ND	0	0
HxCDDs	340	14	34	63	2	6
HpCDDs	2,300	0	23	380	0	4
2,3,7,8-TCDF	13	1	1	ND	0	0
TCDFs	-	-	-	-		
PeCDFs	ND	0	0	ND	0	0
HxCDFs	260	26	26	ND	0	0
Equivalents (ppt):		139 -	172		17 -	25

* value estimated

Table B: Continued

Location:	Central School (Ball diamond)			County Line Road		
	ppt	EPA	Swiss	ppt	EPA	Swiss
2,3,7,8-TCDD	12	12	12	3	3	3
TCDDs	40	0	0	ND	0	0
PeCDDs	ND	0	0	ND	0	0
HxCDDs	86	3	9	67	3	7
HpCDDs	350	0	4	350	0	3
2,3,7,8-TCDF	ND	0	0	ND	0	0
PeCDFs	ND	0	0	ND	0	0
HxCDFs	ND	0	0	ND	0	0
Equivalents (ppt):		15 -	25		6 -	13

The PCDD and PCDF concentrations expressed as 2,3,7,8-TCDD equivalents range from a low of 6-13 ppt to a high of 182-219 ppt. Relatively small differences exist between the Swiss and EPA methods to derive 2,3,7,8-TCDD equivalents for other PCDDs and PCDFs. Three of the locations sampled; Bullock School, Virginia Park, and Longview School have 2,3,7,8-TCDD equivalents of 7 to 20 times the equivalents found in soils at County Line Road, Central School, and Mapelton School. Consistent ratios of 2,3,7,8-TCDD equivalents to 2,3,7,8-TCDD measured soil levels can be observed. At Bullock School this ratio is 1.83; 1.88 for Virginia Park and 1.99 for Longview School. The average of these ratios is 1.90. The consistency in the ratio suggests a single primary source for the PCDDs and PCDFs observed in these residential, public use soils.

Assuming that a ratio of 1.90 2,3,7,8-TCDD equivalents to 2,3,7,8-TCDD exists for all other locations sampled in Midland, it is possible to derive estimated 2,3,7,8-TCDD equivalents for residential soil samples from measured 2,3,7,8-TCDD soil data. An average yard soil concentration of 2,3,7,8-TCDD can be estimated assuming that concentrations of 2,3,7,8-TCDD in soils near downspouts represent 10% of the area of the yard contaminated at this level and 2,3,7,8-TCDD concentrations in yard composite soil samples away from downspouts, represent 90% of the contaminated soils. These calculations are shown below in Table C.

Table C: Average 2,3,7,8-TCDD Equivalent Levels in Residential Surface Soil Samples in Midland, Michigan

Field Number	Measured 2,3,7,8-TCDD (ppt)	Average 2,3,7,8-TCDD Soil Concentration (ppt)	Estimated 2,3,7,8-TCDD Equivalents in Soils 2 (ppt)
B-1-L[1]	76	84	160
B-1-12	160		
B-3-L	20	45	86
B-3-1	270		

20032
19380

Field Number	Measured 2,3,7,8-TCDD (ppt)	Average 2,3,7,8-TCDD Soil Concentration (ppt)	Estimated 2,3,7,8-TCDD Equivalents in Soils [2] (ppt)
C-1-L	26	28	53
C-1-1	54		
C-3-L	12	35	67
C-3-1	240		
D-3-L	18	19	36
D-3-1	31		
E-1-L	26	28	53
E-1-1	49		
E-3-L	9	10	19
E-3-1	20		

L = Yard composite soil sample, 0-1"
1 = Downspout composite soil sample, 0-1"
[1] Swiss Model
[2] Equivalents using Swiss Model, EPA model yields estimates approximately 20% less

As shown in Table C, superficial soil concentrations of PCDD and PCDFs, expressed as 2,3,7,8-TCDD equivalents, would range from 19 to 160 ppt. If corrected for recoveries of internal standards some values would be slightly higher (10-25%). Five of the seven locations have 2,3,7,8-TCDD equivalents over 50 ppt. The average is 68 ppt; the median, 53 ppt. In contrast, soil samples from Middletown, Ohio would have 2,3,7,8-TCDD equivalents ranging frm 1 to 13 ppt, with an average of 5 ppt and a median of 3 ppt, using the Swiss Model. For two of the sites, B-1 and C-3, concentrations of 2,3,7,8-TCDD in downspout soils make a large contribution to the overall yard average of 2,3,7,8-TCDD.

C. Risk Assessment from Exposure to 2,3,7,8-TCDD and other PCDDs and PCDFs in Midland Residential Soils

1. Background

Both EPA and Centers for Disease Control (CDC) have prepared risk assessments for exposure to 2,3,7,8-TCDD in soils. EPA's first exposure and risk assessments were performed by the Chlorinated Dioxin Work Group in response to the finding of 2,3,7,8-TCDD contamination in Hyde Park, Love Canal, and at the Syntex site. Based upon these assessments, EPA entered into consent decrees and administrative orders to require cleanup and capping of contaminated areas to the detection limit of 2,3,7,8-TCDD (from 1-50 ppt) (4). In September 1982, EPA prepared an exposure and risk assessment for contaminated sites found in Missouri ("Region 7 Exposure/Risk Assessment", Draft, September 28, 1982) (5). The cancer risks from exposure to 2,3,7,8-TCDD in residential soils were determined using the Carcinogen Assessment Group Model. The highest cancer risk

was found to be for young children who could ingest soil by the behavior called pica. In the Region 7 assessment, it was assumed that children would consume 0.5 grams of soil per day for 7 years. Under these conditions a child would have a cancer risk of approximately one chance in a 1000 (10^{-3}), using a upper bound limit of risk of 95%, if exposed to soils having 1 ppb 2,3,7,8-TCDD. Since 1982, as discussed in EPA's Ambient Water Quality Document, February 1984, the extrapolated slope line of 2,3,7,8-TCDD animal cancer data has now been changed from 4.25×10^5 (mg/kg-bw/day) $^{-1}$ to 1.56×10^5 (mg/kg-bw/day) $^{-1}$ (6). Therefore, using this new slope derivation and EPA's exposure assessment of 1982, a level of 1 ppb of 2,3,7,8-TCDD in soils would pose a slightly lower lifetime cancer risk of 0.37×10^{-3}. Inhalation of 2,3,7,8-TCDD contaminated dusts was found to pose much lower risks than from ingestion and dermal absorption of 2,3,7,8-TCDD from soils was considered so unlikely as to not to pose a risk.

In early, 1983 EPA requested CDC to determine if a 1 ppb level of 2,3,7,8-TCDD in soils represented an appropriate level of concern. This action, in part, was prompted by the widespread utilization of 1 ppb detection limits by Region 7 for their analyses of 2,3,7,8-TCDD in soils. In January 1984, CDC published an abbreviated analysis of their risk assessment for exposure to 2,3,7,8-TCDD which concluded that a level 1 ppb of 2,3,7,8-TCDD in residential soils was an appropriate level of concern for human health (7).

A more complete 2,3,7,8-TCDD exposure and risk assessment document was released by CDC in July 1984 ("Health Implications of 2,3,7,8-TCDD contamination of Residential Soil," Kimbrough, et al.) (8). The authors concluded that soil levels greater than 1 ppb, pose a level of concern, however, it was recommended that management decisions should also consider an evaluation of specific circumstances at each contaminated site. CDC's risk assessment considered 2,3,7,8-TCDD via exposure to soils including that from dermal contact and by inhalation, although the dust concentration used in calculations was not provided. Unlike EPA's exposure model, CDC utilizes a 10-12 year soil half-life for 2,3,7,8-TCDD. Air and water contamination of 2,3,7,8-TCDD were believed not to make a significant contribution to TCDD intake in most situations, and therefore was not considered in the model. However, CDC did state that TCDD could eventually end up in the food chain, particularly in fish. Under these conditions CDC stated, "if TCDD enters a food chain, there is an unknown additional source of exposure which must be added to the risk of those individuals exposed to contaminated soil and of a larger, undefined population". CDC also commented that if contaminated soils were near waterways and could contaminate these waterways, acceptable levels of 2,3,7,8-TCDD may need to be lower (than 1 ppb).

The CDC risk assessment is based upon a liner-multistage extrapolation of the Kociba animal cancer data for 2,3,7,8-TCDD as interpreted by Squire (8). CDC's extrapolation differs from EPA in three ways (6). First, the curve fit was performed not on administered dose but on liver concentration at terminal sacrifice. Second, CDC's extrapolation does not adjust

for high early mortality of test animals. Finally, CDC uses a rat-to-man extrapolation on the basis of body weight rather than surface area. These modifications result in a 95% upper-limit potency value estimate, when corrected back to administered dose, yields a slope factor of 3.6×10^{4} $(mg/kg\text{-}bw/day)^{-1}$ which is less potent by a factor of 4.3 than that derived by EPA. In CDC's exposure assumptions a 70 kg individual (male) was used as a model. A potentially higher risk individual, one of lower body weight, such as a 50 kg person (female) is often used when performing risk assessments.

Using CDC's exposure and risk assessment assumptions, exposure to 1 ppb of 2,3,7,8-TCDD in soil over lifetime has an upper 95% probability of causing cancer of 2.3×10^{-5}. Expressed slightly differently, at a concentration of 1 ppb, exposure to 2,3,7,8-TCDD in soils could accumulate to a sufficient dose in just three years to increase an individual's risk of cancer by one chance in a million (8). If no more than 10^{-6} upper probability of causing cancer is desired, using upper 95% confidence limits, then a soil concentration of 44 ppt would be an acceptable level of 2,3,7,8-TCDD. For a 10^{-5} upper 95% probability of cancer a soil level of 440 ppt would be required. If EPA's extrapolation of animal cancer is employed in the CDC model these values decrease to 10 ppt for a 10^{-6} risk and to 102 ppt for a 10^{-5} risk. These values decrease further to approximately 7 ppt and 73 ppt, respectively, if a 50 kg individual is used as a model.

2. Risk From Exposure to Residential Soils

Table D, below, presents the upper 95% lifetime cancer risks from exposure to contaminated soils observed in Midland, Michigan using (1) EPA's 1982 exposure and risk model modified by the new, 1984 cancer extrapolation (2) CDC's exposure and risk model and (3) CDC's exposure and risk model using EPA's 1984 animal extrapolation (4) a 50 kg individual as a model and (5) estimated total PCDDs and PCDFs. (See discussion, page 5).

Table D: Estimation of Cancer Risks from Exposures to Soils in Midland, Michigan using Risk and Exposure Models of EPA and CDC[1]

Location (Field #)	Estimated Average 2,3,7,8-TCDD Equivalents in Soil (ppt)	Cancer Risk Models		
		EPA 1982[2]	CDC	CDC Modified[3]
B-1-L	160	5.9×10^{-5}	3.7×10^{-6}	2.2×10^{-5}
B-3-L	86	3.2×10^{-5}	2.0×10^{-6}	1.2×10^{-5}
C-1-L	53	1.9×10^{-5}	1.2×10^{-6}	7.2×10^{-6}
C-3-L	67	2.5×10^{-5}	1.5×10^{-6}	9.0×10^{-6}
D-3-L	36	1.3×10^{-5}	8.3×10^{-7}	5.0×10^{-6}
E-1-L	53	1.9×10^{-5}	1.2×10^{-6}	7.2×10^{-6}
E-3-L	19	7.0×10^{-6}	4.4×10^{-7}	2.6×10^{-6}
Upwind of Midland (2 samples)	2	7.4×10^{-7}	4.6×10^{-8}	2.8×10^{-7}

Table D: Continued

Location (Field #)	Average 2,3,7,8-TCDD Equivalents in Soil (ppt)	Cancer Risk Models		
		EPA 1982[2]	CDC	CDC Modified[3]
Middletown, Ohio (5 samples)	5	1.8×10^{-6}	1.1×10^{-7}	6.9×10^{-7}
Minnesota Area (3 samples)	<1	$<10^{-7}$	$<10^{-8}$	$<10^{-7}$

[1] Using Swiss Model; EPA model yields equivalents about 20% less
[2] Slope factor of 1.56×10^5 $(mg/kg\text{-}bw/day)^{-1}$ utilized
[3] EPA slope factor of 1.56×10^5 $(mg\text{-}kg\text{-}bw/day)^{-1}$; 50 kg-bw individual. (Modified model is 6.0x CDC's original model)

All three cancer risk models yield roughly equivalent risks. The EPA model yielding the highest risks. For 2,3,7,8-TCDD equivalents greater than 50 ppt all models produce cancer risks exceeding 10^{-6}. Above 75 ppt the CDC modified model and the EPA model indicate cancer risks of 10^{-5} or greater, at the 95% upper confidence limit.

It should be noted that EPA's exposure and risk assessment for 2,3,7,8-TCDD may not adequately consider intake of soil from vegetables or gardens grown in contaminated soils. While 2,3,7,8-TCDD bioaccumulation does not occur, coating of plant material by 2,3,7,8-TCDD contaminated soils has been documented (6). CDC assumes in their exposure and risk assessment a soil ingestion of 100 mg/day, although it is not clear if soil ingestion from garden work or from consumption of foods grown in gardens has been included in this figure. Some authors have estimated soil intake by geophagia to be as great as 3g/day (9). If this value were substituted into CDC's assessment model the risks from 2,3,7,8-TCDD would be dramatically increased. A range of assumptions can also be made to estimate dermal exposure to soils. CDC estimated daily dermal exposure after age 15 as 100 mg/day. According to CDC, 10 grams of soil less than 1 mm thick can be spread over an area of about $15 cm^2$ or about 6 $inches^2$ (8). This is less of a surface area which exists for one side of a hand. For a individual working in a garden, an exposed skin surface area of 30 $inches^2$ and contact with 50g of soil may be more realistic. While such direct exposure would only exist for a portion of the year, for instance 5-6 months, one or more days per week, it could be a very significant route of exposure if human dermal absorption of 2,3,7,8-TCDD exists. In animal studies, Poiger and Schlatter determined that 0.1-6% of dermally applied 2,3,7,8-TCDD in applied soils was absorbed (10). If these soil exposure assumptions, are placed into the CDC model, risks from exposure to 2,3,7,8-TCDD in soils would be increased. Converting PCDDs and PCDFs to 2,3,7,8-TCDD equivalents when isomeric specific analyses are unavailable also increases calculated cancer risk.

Given the uncertainties in the exposure to soils, the cancer potency of 2,3,7,8-TCDD, and supportive human epidemiological studies, a prudent policy would be one eliminating exposure to contaminated soils which have 2,3,7,8-TCDD equivalent concentrations exceeding 75 ppt. In Midland, exposure to PCDDs and PCDFs could be reduced by removing the top 3" of soil from yards where concentrations exceed 75 ppt as 2,3,7,8-TCDD equivalents. In many instances, risks could be reduced to acceptable levels by eliminating exposure to downspout soils. At play areas at schools it would be desirable to limit exposure to soils having 150 ppt or more 2,3,7,8-TCDD equivalents. Play activity in such areas may occur for a number of years, exposure occurring primarily by dermal contact and by inhalation. A higher level of concern for these areas, as compared to contaminated soils at private residences, probably is acceptable as a larger amount of exposure would be expected to occur in pre-school aged children less than 5 years of age playing in private residential yards.

These recommendations have also been made in the context of other routes of exposure to 2,3,7,8-TCDD in Midland, primarily by inhalation of ambient air and fish consumption, discussed in subsequent sections, and suggestive health data from Midland. Rates of connective and soft tissue cancer among Midland women, have been statistically significant for over two decades (11). No other Michigan county and only 13 counties in the nation have had statistically significant rates for two successive decades, 1950-1979, where there have been two or more cases recorded per decade (12). Connective and soft tissue cancers have been associated with exposure to 2,3,7,8-TCDD (6). While exposure to 2,3,7,8-TCDD or other PCDDs and PCDFs is yet to be determined in these cases, animal studies show that females exposed to 2,3,7,8-TCDD are more sensitive than males (6). Birth defects in Midland county have also been elevated compared to other Michigan counties (13). In the early 1970s the rates of oral facial and urogenital defects rose precipitously, then declined (14,15). Such defects are consistent with those observed in animals exposed to 2,3,7,8-TCDD (6,14). EPA's Health Review Division in 1979 conducted preliminary analyses of Midland birth defect data and beleived sufficient evidence existed to warrant a case control study of these birth defects in cooperation with the Michigan Department of Health and CDC, but the study has not been initiated (14). CDC's analysis of Dow Chemical's reproductive study of wives of Midland workers exposed to PCDD's revealed a rate of oral facial clefts twice twice that expected (15,16).

While such health information demonstrating a relationship with exposure to PCDDs/PCDFs and adverse human health effects in Midland is far from conclusive, it may be sufficiently suggestive to warrant reducing further exposure to these substances. For this and the following reasons a clean-up level for 2,3,7,8-TCDD in this instance of less than 1 ppb is justifible in Midland:

(1) Cancer risks equal or exceed 10^{-5} or 10^{-6} for lifetime exposure to soil concentrations of PCDDs and PCDFs of 75 ppt or greater expressed as 2,3,7,8-TCDD equivalents.

(2) Large uncertainties exist in 2,3,7,8-TCDD exposure analyses developed to date, with some not being sufficiently conservative.

(3) Historic exposure to PCDDs and PCDFs in Midland may have occurred for a time period of 40 years or more, given chemical manufacturing history.

(4) Other routes of PCDD and PCDF exposure, by ambient air and fish consumption, still exist in Midland and historic concentrations in these media may have been far greater, having already contributed to high body burdens of PCDDs and PCDFs.

(5) A portion of Midland's population, perhaps a large portion, has had occupational exposure to PCDDs, with some smaller groups possibly experiencing adverse health effects from this exposure.

At the present time insufficient data exists to identify areas in Midland needing remedial actions. Further sampling efforts would be necessary to identify those areas where 2,3,7,8-TCDD concentrations exceed a chosen action level.

II. Ambient Air Data

Data provided by Dow Chemical on 2,3,7,8-TCDD concentrations in ambient air are presented below in Table E (2). A total of 10 measurements were taken: two within the Dow Plant, six at the Dow Plant fence line and two in the city of Midland. All samples were found to be positive for 2,3,7,8-TCDD. The data generated indicate rather large fluctuations in air concentrations of 2,3,7,8-TCDD.

Table E: Ambient Air Concentrations (pg/m^3) of 2,3,7,8-TCDD in Midland, Michigan (March 1983-February 1984) [1,2]

Location	Number of Measurements	Range	Arithmetic Mean
Dow Plant	2	0.019-0.022	0.021
Dow Plant Fence Line	6	0.010-0.21	0.064
City of Midland	2	0.019-0.16	0.090

1. Data supplied by Dow Chemical (Reference #2)
2. Data of EPA unavailable at this time

Risk assessments from inhalation of 2,3,7,8-TCDD have been made by EPA in regards to emissions from municipal waste incinerators. Exposure, bioavailability and other assumptions are discussed in more detail in the document, "Assessment of Emissions from a Recent Municipal Waste Combustor," December 16, 1983 (17). Given these assumptions and incorporating the most recent change in the cancer slope determination for 2,3,7,8-TCDD, the lifetime cancer risks from exposure to various air levels of 2,3,7,8-TCDD, measured in Midland are shown below in Table F. Using a ratio of 1.90 to estimate total risks from PCDDs and PCDFs as done for soils; 2,3,7,8-TCDD equivalent risks for estimated air levels of PCDDs and PCDFs has been derived.

Table F: Lifetime Cancer Risks from Exposure to Ambient Air Levels of 2,3,7,8-TCDD and Estimated PCDDs and PCDFs in Midland

Concentration (pg/m^3)	Cancer Risk 2,3,7,8-TCDD	Cancer Risk PCDDs/PCDFs
0.21 (high value at Dow Plant Fence line)	6.9×10^{-6}	1.3×10^{-5}
0.16 (high value in Midland) Fence line)	5.3×10^{-6}	1.0×10^{-5}
0.09 (average value in Midland	3.0×10^{-6}	5.7×10^{-6}

[1] As upper 95% confidence limit
[2] Estimated from the ratio of PCDD and PCDF to 2,3,7,8-TCDD as 2,3,7,8-TCDD equivalants found in soil

As shown from data presented in the Table F, cancer risks from lifetime exposure to 2,3,7,8-TCDD and from the estimated concentrations of total PCDDs and PCDFs are all in the 10^{-5} to 10^{-6} range. No information is available on historic air levels of PCDDs and PCDFs in Midland, although particulate matter from Dow's rotary kiln incinerator in 1978 operated without supplementary fuel had reported particulate concentrations of 2,3,7,8-TCDD as high as 13,200 ppb and hexa-CDDs of 65,000 ppb (17). With supplementary fuel, the concentration of PCDDs in particulate matter was reduced to low ppb levels, or by a factor of 1000 or more. Historic operations of these and other incinerators, as well as fugitive PCDD emissions from the facility when 2,4,5-T manufacture was occurring, could have given rise to far higher air levels of PCDDs and PCDFs in previous years than those observed currently. If so, exposure to PCDDs and accumulated cancer risks may have reached unacceptable levels for long term residents of Midland. In Dow Chemical's November 5, 1984 report of point sources of 2,3,7,8-TCDD in Midland, historic waste incinerator practices were identified as the principal sources of 2,3,7,8-TCDD soil contamination, as current emission rates from the rotary kiln incinerator and three other smaller incinerator sources could not account for levels of 2,3,7,8-TCDD which have accumulated in soils in Midland or at the plant site (2). Dow reported that incinerator combustion gases were directly vented to the atmosphere until 1968 and high temperature incineration, needed to destroy dioxin was not fully implemented until 1978. Although historic air concentrations of PCDDs and PCDFs are unknown at this time, it should be possible to produce models using records of past disposal practices and incinerator operation in order to produce estimates of previous exposure and associated risks. Adding to the risks calculated for PCDDs and PCDFs are air concentrations of other carcinogens or suspect carcinogens found presently or historically in Midland. The Michigan Department of Natural Resources has accumulated air data in Midland which should be evaluated in order to assess additional risks. In one national survey of air emissions from industrial facilities, using estimated emission data, the Dow facility in Midland was ranked as the number one air source for toxic substances in the State of Michigan (19). As lifetime cancer risks from ambient air exposure to just PCDDs and PCDFs are in the 10^{-6} to 10^{-5} range, more air monitoring of these and other hazardous chemicals is recommended.

III. Cancer Risks from Exposure to Soils and Ambient Air Levels of PCDDs

In CDC's exposure and risk assessment it was assumed that concentrations of 2,3,7,8-TCDD in airborne dusts would equal those found in soils. Furthermore, it was assumed that indoor air levels of 2,3,7,8-TCDD on particulate matter would equal those found in ambient air. This assumption was viewed by some commenters as overly protective.

Assuming that Midland residential soils average 50 ppt of 2,3,7,8-TCDD and total particulate matter averages 70 ug/m^3, the expected maximum concentration of 2,3,7,8-TCDD in air would be 3.5 fg/m^3. Air levels in Midland exceed this value by as great as 50 fold, suggesting that residential soil alone could not be responsible for the observed concentrations of 2,3,7,8-TCDD in ambient air in Midland. A value of 70 ug/m^3 is the primary air standard for total suspended particulates.

It is unclear what particulate matter concentrations were used in CDC's inhalation exposure assessments. Therefore, with the CDC risk models it may not be valid to add cancer risks from measured air concentrations of 2,3,7,8-TCDD and other PCDDs to those risks calculated from soils. If CDC assumed dust levels of 140 ug/m^3, as mentioned in their report, then a soil concentration of 1 ppb, would result in air levels of 2,3,7,8-TCDD approximately equal to those measured in Midland. Therefore, if the CDC soil exposure risk model was derived with these assumptions it is inappropriate to add risks from ambient air exposure to 2,3,7,8-TCDD to those previously found for soils. It is interesting to note that the average soil concentration observed on the Dow plant site was 2.38 ppb and 0.74 ppb along its perimeter. Given the very large area of the Dow plant site, 1500 acres, airborne dust and soils from the site may be a primary contributer to current air levels of 2,3,7,8-TCDD. Modeling should be conducted to determine contributions from existing air sources in Midland to those from plant and residential soils.

Using the EPA model, cancer risks from inhalation could be added. For soils containing 75 ppt 2,3,7,8-TCDD equivalents, lifetime cancer risks would increase from 2.8 x 10^{-5} to 3.8 x 10^{-5} if the cancer risk from lifetime exposure to the peak value of 0.16 pg/m^3 2,3,7,8-TCDD converted to 2,3,7,8-TCDD equivalents for estimated air levels of other PCDDs and PCDFs is included.

IV. Fish Analysis

1. Overview of 2,3,7,8-TCDD Fish Data

Fish from 13 Michigan Rivers were analyzed in 1983 to determine flesh concentrations of 2,3,7,8-TCDD. A total of 74 fish were analyzed. Whole fish carp samples ranged from non-detectable to 190 ppt of 2,3,7,8-TCDD, with the high value found in carp collected from the Tittabawassee River in Midland. This data is found in Table 11 (attached). The average of 2,3,7,8-TCDD found in whole carp in rivers other than the Tittabawassee averaged 3 ppt, or 1.6% of the concentration observed in whole fish from the Tittabawassee River. No fish analyzed exceeded 10 ppt. A statistical t-test of this data reveals that carp from the Tittabawassee river are significantly different from fish from other Michigan rivers at a confidence limit greatly exceeding 0.001. It therefore can be stated with virtual certanty that Tittabawassee River fish are uniquely contaminated and not the result of chance.

Individual carp fillet samples from the Tittabawassee River ranged from 12 to 530 ppt 2,3,7,8-TCDD, with an arithmetic mean of 50 ppt and a median of 25 ppt. A skinless fillet composite of five catfish averaged 75 ppt of 2,3,7,8-TCDD while a composite of skin-on fillets of five smallmouth bass contained 5.1 ppt of 2,3,7,8-TCDD. Five individual skin-on fillets of walleye averaged 3.9 ppt of 2,3,7,8-TCDD.

2. Overview of PCDD and PCDF Fish Data

A composite of five whole carp samples analyzed in 1981, downstream of Midland were found to contain 81 ppt TCDD, 31 ppt penta CDD, 44 ppt hexa CDD, 53 ppt hepta CDD and 14 ppt octa CDD. PCDFs were found to be as follows: 37 ppt TCDF, 73 ppt penta CDF, 145 ppt hexa CDF, 31 ppt hepta CDF, and 4 ppt octa CDF. About 90% of the total TCDD observed was 2,3,7,8-TCDD (18).

3. Exposure and Risk Analysis From Consumption of Tittabawassee River Fish

Although a fish advisory against consumption of fish from the Tittabawassee River has been in place since 1978, there have been reports of individuals consuming fish from the river (20). This is not to be unexpected as many people tend to ignore fish advisories, particularly those in poorer economic groups. For people consuming even small amounts of bottom fish from the Tittabawassee River over their lifetimes, the cancer risks are fairly dramatic. To provide a perspective of such risks, Table G has been developed which gives frequency of fish consumption and associated cancer risks, for different species, and for both 2,3,7,8-TCDD and estimated total PCDDs and PCDFs as 2,3,7,8-TCDD equivalents. PCDDs and PCDFs other than 2,3,7,8-TCDD have been estimated from 1981 composite carp analysis by the ratios of congeners to total TCDD, assuming that 90% of the measured TCDD is 2,3,7,8-TCDD.

Table G: Lifetime Cancer Risks From Consumption of Tittabawassee River Fish in Midland

Frequency of Consumption[1]	Carp		Catfish		Sportfish	
	2,3,7,8-TCDD[2]	Total PCDDs/PCDFs[3]	2,3,7,8 TCDD[4]	Total PCDDs/PCDFs[5]	2,3,7,8 TCDD[6]	Total PCDD/PCDFs[7]
Once per week	7.0×10^{-4}	1.1×10^{-3}	1.1×10^{-3}	1.6×10^{-3}	5.7×10^{-5}	8.6×10^{-5}
Once per month	1.8×10^{-4}	2.6×10^{-4}	2.7×10^{-4}	4.0×10^{-4}	1.4×10^{-5}	2.1×10^{-5}
Once per yr.	1.5×10^{-5}	2.2×10^{-5}	2.2×10^{-5}	3.2×10^{-5}	1.2×10^{-6}	1.8×10^{-6}
Ten times over Lifetime	2.2×10^{-6}	3.2×10^{-6}	3.2×10^{-6}	4.7×10^{-6}	1.7×10^{-7}	2.6×10^{-7}

1 Assumes 1/2 pound fish per meal
2 Average value of 50 ppt
3 Calculated from ratios of PCDDs/PCDFs observed in composite sample of carp analyzed from the Tittabawassee River in 1981. Both Swiss and EPA models yield 2,3,7,8-TCDD equivalents of 22 ppt for PCDDs and PCDFs other than for 2,3,7,8-TCDD

4 75 ppt
5 See footnote #3 above. Both Swiss and EPA models yield 2,3,7,8-TCDD equivalents of approximately 35 ppt for PCDDs and PCDFs other than 2,3,7,8-TCDD.
6 4 ppt
7 See footnote #3 above. PCDDs and PCDFs other than 2,3,7,8-TCDD have equivalents of 2 ppt.

Cancer risks for the infrequent consumer of Tittabawassee River fish, for instance ten times over lifetime, are reasonably small being in the range of 10^{-6}. For more frequent consumers of carp and catfish, even a 1/2 pound meal once per year, cancer risks exceed 10^{-5}. If consumption is more frequent, once a month, risks exceed 10^{-4}. Consumers of only sportfish would have excessive risks, greater than 10^{-5}, for consumption equaling or exceeding 1/2 pound meal monthly. A once a month consumption of 1/2 pound of fish is equal to 7.3 grams of fish daily or slightly higher than EPA's average fish consumption value of 6.5 g/day used in ambient water quality criteria documents. It is likely that a small fraction, of Midland's population would consume bottom fish or sportfish as frequently as once per year or once per month, adding significantly to cancer risks received from exposure to PCDDs and PCDFs in soils and ambient air.

Probably many fishermen of the Tittabawassee River would tend to discard carp being less desirable for eating than catfish or sportfish. Perhaps the most realistic way to generate an average risk is to assume that a consumer would eat equal amounts of carp, catfish, and sportfish. For an individual consuming 1/2 pound of fish per year the cancer risk would be 5.6×10^{-5}; on a monthly basis the risk would be 6.8×10^{-4} for total PCDDs and PCDFs expressed as 2,3,7,8-TCDD equivalents. Other chemicals, such as PBBs and pentachlorophenol, have also been dectected in Tittabawassee fish, so the risk estimates calculated here, may underestimate the cancer risk.

For women consuming a 1/2 pound meal of fish, with an average of 63 ppt 2,3,7,8-TCDD equivalents, intake would be over 2,000 pg/day or about 40 ng/kg-bw/day for a 50 kg woman. Short term sub-human primate studies have demonstrated reproductive effects, including conception failures and miscarriages at dosages as low as 1.8 ng/kg-bw/day (6,8). Clearly woman consuming meals of fish from the Tittabawassee in Midland would have a high risk of adverse reproductive outcomes. If a safety factor of 1000 is utilized for humans, as by CDC, then no consumption by women of any quantity of Tittabawassee River fish would be recommended.

V. Cumulative Risks from Exposure to Soil, Ambient Air, and Fish in Midland and Recommendations for Remedial Actions

Total risks from exposure to PCDDs and PCDFs in all media are presented in Table H. The assessment does not include exposure to other chemicals which may be in ambient air and in fish. Realistic and worst case scenarios have been calculated. All risks represent lifetime exposure and the upper 95% probability of contracting cancers. Using typical (average) concentrations of 2,3,7,8-TCDD equivalents found in residential soil (50 ppt) and in air (0.09 pg/m^3) cancer risks would range from 6.9×10^{-6} to 2.4×10^{-5}, using the CDC modified model and the EPA model, respectively. Using the worst observed soil and air levels measured in Midland, cancer risks would

be in the range of 2.2×10^{-5} to 6.9×10^{-5}. If fish consumption of ten, 1/2 pound meals in a lifetime are added to those risks found from exposure to average levels of PCDDs and PCDFs, then risks increase to 1.5×10^{-5} - 3.3×10^{-5}. For worst case situations, more frequent consumers of Tittabawassee River fish, would have cancer risks in the range of 10^{-4} to 10^{-3}.

Table H: Combined Lifetime Cancer Risks From Exposure to PCDDs and PCDFs in Residential Soils, Ambient Air and Fish in Midland, Michigan

Exposure Scenario	Soil[1]		Air[1]		Fish[1]	
1. Typical (Average)	50 ppt:	6.9×10^{-6} (CDC)[2] 1.8×10^{-5} (EPA)	0.17pg/m^3:	5.7×10^{-6}	10x:	8.2×10^{-6}
2. Worst Observed	160 ppt:	2.2×10^{-5} (CDC)[2] 5.9×10^{-5} (EPA)	0.30pg/m^3:	1.0×10^{-5}	1. Mo: 2. Wk:	6.8×10^{-4} 2.7×10^{-3}

Soil + Air

Typical (Average): Soil + Air = 6.9×10^{-6} (CDC modified)
2.4×10^{-5} (EPA)

Worst Observed: Soil + Air = 2.2×10^{-5} (CDC modified)
6.9×10^{-5} (EPA)

Soil + Air + Fish

Typical (Average): Soil (CDC modified) + Air + Fish (10x in lifetime)= 1.5×10^{-5}

Soil (EPA) + Air + Fish (10x in lifetime)= 3.3×10^{-5}

Worst Observed:

Soil (CDC) modified) + Air + Fish (Once per month)= 7.0×10^{-4}

Soil (CDC modified) + Air + Fish (Once per week)= 2.7×10^{-3}

Soil (EPA) + Air + Fish (Once per month)= 7.5×10^{-4}

Soil (EPA) + Air + Fish (Once per week)= 2.7×10^{-3}

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[1] Using estimated values of some PCDDs and PCDFs expressed as 2,3,7,8-TCDD equivalents.
[2] CDC model as modified

If only 2,3,7,8-TCDD is included in the risk analyses, the calculated risks decrease by about half, still leaving risks higher than acceptable. This is particularly true for the worst-observed case situation of residential soil and air contamination. Where cancer risks have exceeded 10^{-6} or approached 10^{-5}, U.S. EPA has generally required remedial actions. Prior to the 2,3,7,8-TCDD contamination in Missouri, sites were capped or cleaned up where 2,3,7,8-TCDD exceeded detection limits (1-50 ppt) (4). Although the risks in Midland do not warrant emergency action, if only soil and air risks are considered, long term reduction in risk is indicated and would be consistent with previous actions of the Agency. It is also important, as discussed by CDC, that each 2,3,7,8-TCDD site should be evaluated as to its own unique characteristics. While a 1 ppb 2,3,7,8-TCDD action level for clean-up of residential soils and relocation of individuals can be defended, it is more applicable to situations where prior exposure has been of a shorter duration and other exposure routes such as air, fish and occupation do not exist (i.e., Times Beach). In Midland, chlorophenolic manufacture and disposal operations began in the 1930s (2). Historic air and fish concentrations of PCDDs and PCDFs and human exposure and resultant body burdens is unknown. For these reasons and due to the suggestive health data which exists in Midland county it is recommended that lower action levels for 2,3,7,8-TCDD in soils be employed.

Recommendations

1. Consideration should be given to covering or removing soils on the Dow Plant site and around its perimeter exceeding 1 ppb 2,3,7,8TCDD equivalents. This action would reduce the potential for off-site dispersal, help decrease existing air levels in Midland, and reduce worker exposure to contaminated soils.

2. Risk reduction from exposure to private residential soils having 2,3,7,8-TCDD equivalents exceeding 75 ppt or where 2,3,7,8-TCDD exceeds 40 ppt should be considered. Emphasis should be placed on those areas where children principally play (i.e., back yards) or where gardens exist. In many instances, perhaps in the majority of cases, limiting exposure to soils in the vicinity of downspouts may be sufficient to reduce risk to acceptable levels. Additional sampling will be required to identify residences having soil 2,3,7,8-TCDD concentrations of 40 ppt or greater.

3. Limiting exposure to soils in recreational areas of public use sites and at schools having 150 ppt or greater as 2,3,7,8-TCDD equivalents or about 80 ppt 2,3,7,8-TCDD should be considered.

4. Estimates of risks from historic air levels of PCDDs and PCDFs; as well as other toxic substances, should be made using appropriate modeling and air data.

5. Additional ambient air and source monitoring for PCDDs and PCDFs and other hazardous chemicals should be implemented on a regular basis to determine existing risks and to consider remedial actions.

6. Preliminary health studies should be considered for Midland residents at high potential health risk. Ideally, these would be individuals living (1) near the Dow facility for over 20 years and with average or higher than average soil concentrations (2) employees and their families of Dow Chemical exposed to PCDDs as identified in the Townsend reproductive study and (3) consumers of Tittabawassee River fish. The incidence rates of disease, reproductive outcomes, and blood chemistry in these groups should be compared to matched groups outside of Midland. Smith and Thompson have recently identified and interviewed 128 fishermen of the Tittabawassee and have preliminary data regarding fish consumption (20). Standard epidemological approaches to gather and evaluate such information have been developed and should not be difficult to implement in this situation. To assess reproductive outcomes of Dow workers, the Townsend data set, could be re-evaluated and compared with control populations outside of Midland. The Health Review Division of EPA has been reported to have a computer printout of the Townsend study (15). Human milk samples could also be collected for residents of 20 years or more to estimate PCDD and PCDF body burdens. A unique opportunity exists in Midland for assessing human health impacts from long term exposure to PCDDs, particularly from fish consumption. Performing such studies would serve not only in the assessment of public health in Midland but would contribute further to the understanding of health impacts from PCDDs and PCDFs.

Disclaimer

The document in no manner should be viewed as representing U.S. EPA's final position regarding actions in Midland, Michigan.

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References

1. U.S. EPA, Region V "Soil Screening Survey at Four Midwestern Sites", September 22, 1983.

2. Dow Chemical, "Point Sources and Environmental Levels of 2,3,7,8-TCDD on Midland Plant Site of the Dow Chemical Company and in the City of Midland, November 5, 1984.

3. Bellin, J. and D. Barnes, "Health Hazard Assessment for Chlorinated Dioxins and - Dibenzofurans other than 2,3,7,8-TCDD, Draft, U.S. EPA, September 26, 1984.

4. Kurent, E "Enforcement Concerns In the Process and Outcomes of Clean-up Levels for Dioxin in Soil", memorandum to C. Kleveno, U.S. EPA, September 17, 1982.

5. U.S. EPA, "Outline For Region 7 Exposure/Risk Assessment, "Draft #1, September 28, 1982.

6. U.S. EPA, Ambient Water Quality Criteria For 2,3,7,8-TCDD, February 1984.

7. Centers for Disease Control, "Health-Risk Estimates for 2,3,7,8-Tetra chlorodibenzo dioxin in Soil," Morbidity and Mortality Weekly Report, Vol. 33, No. 3, January 27, 1984.

8. Kimbrough, R.D, et al., "Health Implementations of 2,3,7,8-Tetrachloro-dibenzodioxin (TCDD) contamination of Residential Soil", Centers For Disease Control, July 1984.

9. Wedeen, R. P. et al., "Geophagic Lead Nephropathy"; Case Report, Environmental Research, Vol. 17, pg. 409, 1978.

10. Poiger, H. and C. Schlatter, "Influence of Solvents and Absorbance on Dermal and Intestinal Absorption of TCDD", Food Cosmet. Toxicol., Vol. 18, pg. 477, 1981.

11. Michigan Department of Public Health, "Evaluation of Soft and Connective Tissue Cancer Mortality Rates in Midland and other Selected Michigan Counties Compared Nationally and Statewide," May 4, 1983.

12. Riggan, W. et al., U.S. Cancer Mortality Rates and Trends, 1950-1979, Volume II, EPA-600/1-83-015b, September 1983.

13. Harger, J.R.E., "First Cut Analysis of Birth Defect Data", memorandum to D. Isleib, Toxic Substance Control Commission, State of Michigan, October 29, 1980.

14. Poole, C., "Case-control study of Birth Defects in Midland County, Michigan", Health Review Division, U.S. EPA, October 4, 1979.

15. EPA Oversight on Dioxin Contamination, Hearing before the Subcommittee on Natural Resources, Agricultural Research and Environment of the Committee on Science and Technology U.S. House of Representatives, First Session, Number 88, March 23, 1983, U.S. Government Printing Office, 29-9560, Washington, 1984.

16. Townsend, et al., "Survey of Reproductive Events of Wives of Employees Exposed to Chorinated Dioxins", Amer. Jour. of Epidem., Vol. 115, No. 5, pg. 695, 1982.

17. Cook, M. "TCDD Emissions for Municipal Waste Combustors", memorandum, U.S. EPA, December 16, 1983.

18. U.S. EPA, Region V, "A Report on Polychlorinated Dibenzo-p-Dioxins (PCDDs) and Polychlorinated Dibenzofurans (PCDFs): A Summary of Studies conducted in the Great Lakes Area, July 1981.

19. National Clean Air Coalition," Major Industrial Sources of Potential Toxic Air Pollutants", April 16, 1982.

20. Smith, F. and W. Thompson, "Fisherman of the Tittabawassee", Environment, Vol. 26, No. 5, 1984.

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TABLE 1

2378-TCDD
DOW CHEMICAL - MIDLAND PLANT
IN-PLANT SURFACE SOIL SAMPLES

Field Identification	Location	2378-TCDD (DL) (ppb)		% Recovery	% Solids
Station 1	South of 492 Building	0.018	(0.003)	71	92.9
Station 2	South of 1005 Building; Southwest of 703 Building	0.074	(0.005)	52	96.2
Station 3	South of 703 Building	0.42	(0.013)	90	96.1
Station 4	West of 703 Building	0.020	(0.003)	63	95.0
Station 5	Southwest of 956 Building; East of 703 Building	3.50	(0.039)	100	96.4
Station 6	Northwest of 1159 Building; North of Shot Pond	0.13	(0.013)	103	98.5
Station 7	11th and J Streets - Northwest Corner	4.60	(0.083)	101	96.3
Station 8	8th and G Streets - Northwest Corner at Steam Pipeline	0.15	(0.010)	65	99.1
Station 9	Northwest of 1050 Building at F Street	0.010	(0.003)	61	90.2
Station 10	South of 543 Building; West of 14th Street	0.045	(0.005)	80	99.3
Station 11	16th and G Streets - Southwest Corner	0.44	(0.016)	119	99.6
Station 12	16th and G Streets - Northwest Corner	0.46	(0.012)	94	96.0
Station 13	17th and G Streets - Northwest Corner	0.22	(0.007)	51	99.3
Station 14	West of 934 Building	0.27	(0.007)	100	100.0
Station 15	South and East of 874 Building North of RR Tracks	25.0	(0.50)	66	85.5
		[36.0]R	(0.28)		

(1) 2378-TCDD concentrations and detection levels (DL) reported in parts per billion (ppb).
(2) % Recovery - Recovery of internal standard (Cl^{37} 2378-TCDD or ^{13}C 2378-TCDD) expressed as percent.
(3) % Solids - Solids content of sample determined after sample homogenization, expressed as percent. Analytical results not adjusted for moisture content.
(4) [ ]R = Repeat analysis of same sample.

25700
2004s
19396

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TABLE 2

2378-TCDD
SITE #1 - MIDLAND, MICHIGAN AREA
SURFACE SOIL SAMPLES

Sample Number	Field Identification	Location	2378-TCDD (DL) (ppb)	% Recovery	% Solids
Upwind Areas					
13354	UPW-1-L	[redacted]	ND (0.002)	82%	94.9%
13343	UPW-1-1		0.006 (0.002)	76%	98.6%
13401	UPW-2-L		ND (0.004)	90%	94.0%
13395	UPW-4-L		ND (0.004)	84%	98.1%
13342	UPW-4-D		0.009 (0.001)	84%	84.2%
Track Out and Perimeter Samples - Dow Chemical-Midland Plant					
13353	TO-4-G	West - RR at Poseyville Rd.	0.011 (0.003)	52%	99.3%
13360	TO-6-G	North - Austin St. and Jefferson Ave.	0.25 (0.018)*	21%	99.0%
13367	TO-9-G	East - Saginaw Rd near Gate 25	0.014 (0.002)	68%	99.0%
14186	PER-2-L	[redacted]	0.31 (0.014)	84%	82.8%
14177	PER-2-1		0.069 (0.003)	55%	99.0%
14191	PER-5-L		0.21 (0.008)	62%	99.2%
13402	PER-8-L	North - Washington St. and Bay City Road	0.010 (0.005)	104%	99.0%
13389	PER-9-G	East - South Saginaw St.	2.03 (0.042)	72%	95.6%
14181	PER-10-L	[redacted]	0.040 (0.002)	73%	97.1%
Public Use Areas					
13362	P-1-L	Sugnet School	0.019 (0.002)	64%	99.5%
13364	P-2-L	Wallen Park	0.028 (0.002)	64%	89.7%
13374	P-5-L	County Line Road	0.003 (0.001)	104%	99.7%
13392	P-6-L	Mapleton School	0.015 (0.003)	86%	80.2%
13393	P-7-L	Longview School	0.078 (0.003)	88%	98.8%
13340	P-8-L	Parkwood Park	0.17 (0.006)	94%	96.5%
13375	P-9-L	Virginia Park	0.076 (0.003)	58%	89.2%
13391	P-10-L	Central School (ball diamond)	0.012 (0.003)	92%	96.6%
13394	P-11-L	Bullock Schoool	~~0.010~~ 0.110 (0.002)	81%	100.0%
Residential Areas					
13007	A-1-L	[redacted]			
13008	A-1-1				
13101	A-3-L				
13102	A-3-1				

25701
20049
~~19377~~

TABLE 2 (continued)

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2378-TCDD
SITE #1 - MIDLAND, MICHIGAN AREA
SURFACE SOIL SAMPLES

Sample Number	Field Identification	Location	2378-TCDD (DL) (ppb)	% Recovery	% Solids
Residential Areas (continued)					
13328	B-1-L		0.076 (0.007)	100%	93.2%
13305	B-1-1		0.16 (0.006)	63%	97.0%
13306	B-3-L		0.020 (0.001)	71%	97.8%
13325	B-3-1		0.27 (0.013)	74%	87.1%
13103	B-4-L				
13104	B-4-1				
13317	C-1-L		0.026 (0.001)	86%	78.7%
13303	C-1-1		0.054 (0.003)	64%	84.4%
13314	C-3-L		0.012 (0.001)	100%	98.6%
13307	C-3-1		0.24 (0.015)	71%	98.1%
13105	C-4-L				
13106	C-4-1				
13318	D-1-L		ND (0.001)	94%	84.0%
13331	D-1-D		0.024 (0.001)	100%	99.5%
13319	D-2-6		0.028 (0.001)	92%	94.9%
13315	D-3-L		0.018 (0.001)	100%	90.9%
13329	D-3-1		0.031 (0.004)	86%	99.8%
13312	E-1-L		0.026 (0.003)	96%	97.5%
13330	E-1-1		0.049 (0.001)	80%	97.0%
13301	E-3-L		0.009 (0.001)	75%	97.6%
13304	E-3-1		0.020 (0.001)	70%	99.1%
13302	F-1-L		0.031 (0.001)	73%	99.0%
13313	F-1-1		0.013 (0.001)	92%	96.8%
Miscellaneous					
14175	Sludge	Midland Sewage Sludge	0.021 (0.008)*	49%	88.7%

Notes: (1) 2378-TCDD concentrations and detection levels (DL) reported in parts per billion (ppb).
(2) % Recovery - Recovery of internal standard (Cl^{37} 2378-TCDD or ^{13}C 2378-TCDD) expressed as percent.
(3) % Solids - Solids content of sample determined after sample homogenization, expressed as percent. Analytical results not adjusted for moisture content.
(4) Field identification of samples:

Location	Type
UPW - Upwind	L - Yard, lawn, or open area composite
TO - Track Out	1 or D - Downspout or dripline composite
PER - Perimeter	G - Open area grab sample
P - Public Use	
A-K - Residential	

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TABLE 4

2378-TCDD
SITE #3 - MIDDLETOWN, OHIO AREA
SURFACE SOIL SAMPLES

Sample Number	Field Identification	Location	2378-TCDD (DL) (ppb)	% Recovery	% Solids
Upwind Area - Hamilton, Ohio					
13400	UPW-5-L		0.004 (0.002)	98%	79.3%
13377	UPW-5-L		0.003 (0.001)	106%	79.9%
Perimeter - ARMCO, Inc., Middletown Plant					
13366	PER-12-L		ND (0.002)	70%	87.4%
13337	PER-12-1		ND (0.001)	88%	88.4%
13387	PER-13-L		0.004 (0.003)	94%	86.4%
13363	PER-13-D		ND (0.002)	76%	87.4%
13372	PER-14-L		ND (0.002)	106%	84.9%
13376	PER-15-L		ND (0.002)	76%	88.4%
Public Use Areas					
13349	G-1-L		ND (0.001)	94%	77.5%
13386	P-11-L		ND (0.002)	72%	87.5%
13327	P-12-L		0.004 (0.001)	82%	87.5%
13338	P-13-L		ND (0.001)	96%	83.2%
13339	P-14-L		ND (0.001)	96%	82.0%
13390	P-15-L		ND (0.002)	106%	78.8%
13352	P-15-1		ND (0.002)	82%	67.3%
Residential Areas					
13336	G-2-L		0.004 (0.001)	92%	87.7%
13348	G-2-1		0.005 (0.002)	84%	86.7%
13355	H-1-L		ND (0.002)	78%	95.9%
13403	H-1-1		ND (0.002)	70%	94.7%
13361	K-1-L		ND (0.002)	86%	81.3%
13351	K-1-1		ND (0.003)	54%	88.3%
13350	K-2-L		ND (0.002)	86%	86.4%
iscellaneous					
14189	Sludge	Middletown Sewage Sludge	ND (0.031)*	6%	92.3%

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TABLE 4 (continued)

2378-TCDD
SITE #3 - MIDDLETOWN, OHIO AREA
SURFACE SOIL SAMPLES

Notes: (1) 2378-TCDD concentrations and detection levels (DL) reported in parts per billion (ppb).
(2) % Recovery - Recovery of internal standard (Cl^{37} 2378-TCDD or ^{13}C 2378-TCDD) expressed as percent.
(3) % Solids - Solids content of sample determined after sample homogenization, expressed as percent. Analytical results not adjusted for moisture content.
(4) Field identification of samples:

Location		Type	
UPW	- Upwind	L	- Yard, lawn, or open area composite
TO	- Track Out	1 or D	- Downspout or dripline composite
PER	- Perimeter	G	- Open area grab sample
P	- Public Use		
A-K	- Residential		

* Data not valid. Quality assurance objective not achieved.

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TABLE 5

2378-TCDD
SITE #4 - MINNESOTA NATURAL AREAS
SURFACE SOIL SAMPLES

Sample Number	Field Identification	Location	2378-TCDD (DL) (ppb)	% Recovery	% Solids
13373	IWD-1-L	Itasca Wilderness	ND (0.003)	64%	94.7%
13378	BSP-4-L	Bluestem Prairie	ND (0.001)	98%	98.0%
13379	KR-1-L	Kettle River	ND (0.002)	106%	79.5%
13388	PT-1-L	Pembina Trail Preserve	ND (0.002)	80%	53.5%

Notes: (1) 2378-TCDD concentrations and detection levels (DL) reported in parts per billion (ppb).
(2) % Recovery - Recovery of internal standard (Cl^{37} 2378-TCDD or ^{13}C 2378-TCDD) expressed as percent.
(3) % Solids - Solids content of sample determined after sample homogenization, expressed as percent. Analytical results not adjusted for moisture content.
(4) Field identification of samples:

Location		Type	
UPW	- Upwind	L	- Yard, lawn, or open area composite
TO	- Track Out	1 or D	- Downspout or dripline composite
PER	- Perimeter	G	- Open area grab sample
P	- Public Use		
A-K	- Residential		

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TABLE 5-A

2378-TCDD
Control and Blank Samples

Sample Number	Field Identification	2378-TCDD (DL)	% Recovery	% Solids
14196	Control Soil	ND (0.006)*	46%	98.4%
14184	Control Soil	0.013 (0.004)	59%	98.4%
13368	Control Soil	0.006 (0.002)	66%	98.4%
13308	Control Soil	0.032 (0.003)	58%	98.4%
13320	Control Soil	0.012 (0.003)	50%	98.4%
13333	Control Soil	ND (0.010)*	40%	98.4%
13344	Control Soil	ND (0.007)*	34%	98.4%
13344	Control Soil	0.015 (0.005)*	22%	98.4%
13357	Control Soil	ND (0.001)*	23%	98.4%
13380	Control Soil	0.005 (0.003)	66%	98.4%
13396	Control Soil	ND (0.019)*	10%	98.4%
13396	Control Soil	ND (0.007)*	19%	98.4%
13409	Control Soil	ND (0.054)*	22%	98.4%
13385	Control Soil	ND (0.042)*	13%	98.4%
14183	Blank Soil	ND (0.002)	97%	53.7%
14195	Blank Soil	ND (0.003)	81%	53.7%
13309	Blank Soil	ND (0.001)	83%	53.7%
13321	Blank Soil	0.002 (0.001)	80%	53.7%
13332	Blank Soil	ND (0.002)	73%	53.7%
13345	Blank Soil	ND (0.002)	96%	53.7%
13356	Blank Soil	ND (0.001)	100%	53.7%
13369	Blank Soil	ND (0.002)	70%	53.7%
13381	Blank Soil	ND (0.001)	100%	NR
13397	Blank Soil	ND (0.001)	106%	53.7%
13408	Blank Soil	ND (0.001)	84%	53.7%
13414	Can Blank (PER-5)	ND (0.027)	102%	
13415	Can Blank (In-Plant)	ND (0.024)	100%	
13416	Can Blank (Middletown)	ND (0.025)	96%	
13417	Can Blank #6	ND (0.030)	80%	
13384	Blank Soil	ND (0.003)	103%	53.7%

Notes: (1) 2378-TCDD concentrations and detection levels (DL) reported in parts per billion (ppb).
(2) % Recovery - Recovery of internal standard (Cl^{37} 2378-TCDD or ^{13}C 2378-TCDD) expressed as percent.
(3) % Solids - Solids content of sample determined after sample homogenization, expressed as percent. Analytical results not adjusted for moisture content.
(4) NR - Not reported.

* Data not valid. Quality assurance objective not achieved.

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TABLE 6

PCDDs and PCDFs
SITE #1 - MIDLAND, MICHIGAN AREA
SURFACE SOIL SAMPLES

	Upwind		Dow Chemical In-Plant	
Sample No.:	13401	13395	13406	13412
Field ID.:	UPW-2-L	UPW-4-L	Station 5	Station 14
Location:	[redacted]		Incinerator	West of 934 Building
PCDDs (DL)				
2378-TCDD	ND (0.004)	ND (0.004)	3.5 (0.039)	0.27 (0.007)
Total iso TCDDs	ND (0.004)			0.32
Total penta CDDs	ND (0.024)	ND (0.023)		0.24 (0.067)
Total hexa CDDs	ND (0.024)	ND (0.023)		4.0 (0.067)
Total hepta CDDs	0.15 (0.024)	0.17 (0.034)		75.0 (0.9)
OCDD	0.34 (0.026)	0.33 (0.034)		375.0 (1.3)
PCDFs (DL)				
2378-TCDF	ND (0.004)	ND (0.004)	0.45 (0.06)	0.027 (0.007)
Total TCDFs				
Total penta CDFs	ND (0.008)	ND (0.008)		0.90 (0.14)
Total hexa CDFs	ND (0.022)	ND (0.023)		3.1 (0.13)
Total hepta CDFs	ND (0.031)	ND (0.028)		15.4 (0.38)
OCDF	ND (0.051)	ND (0.045)		8.6 (0.48)

Notes: (1) Concentrations of PCDDs, PCDFs, and detection levels (DL) reported in parts per billion (ppb).

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TABLE 6

PCDDs and PCDFs
SITE #1 - MIDLAND, MICHIGAN AREA
SURFACE SOIL SAMPLES

	Public Use Areas					
Sample No.:	13374	13392	13393	13375	13391	13394
Field ID.:	P-5-L	P-6-L	P-7-L	P-9-L	P-10-L	P-11-L
Location:	[redacted]					
<u>DDs (DL)</u>						
78-TCDD	0.003 (0.001)	0.015 (0.003)	0.078 (0.003)	0.076 (0.003)	0.012 (0.003)	0.11 (0.002)
tal iso TCDDs	ND (0.001)	0.040	0.17	0.29	0.040	0.22
tal penta CDDs	ND (0.014)	ND (0.035)	interference	0.10 (0.018)	ND (0.034)	0.12 (0.022)
tal hexa CDDs	0.067 (0.007)	0.063 (0.035)	0.34 (0.02)	0.24 (0.018)	0.086 (0.034)	0.41 (0.022)
tal hepta CDDs	0.35 (0.013)	0.38 (0.028)	2.3 (0.055)	0.41 (0.093)	0.35 (0.031)	2.4 (0.042)
DD	3.1 (0.096)	0.86 (0.027)	7.0 (0.068)	12.0 (1.5)	0.68 (0.031)	7.0 (0.052)
<u>DFs (DL)</u>						
78-TCDF	ND (0.002)	ND (0.005)	0.013 (0.007)	0.013 (0.002)	ND (0.005)	0.015 (0.003)
tal TCDFs	ND (0.002)					
tal penta CDFs	ND (0.01)	ND (0.008)	ND (0.025)	0.040 (0.01)	ND (0.007)	0.11 (0.017)
tal hexa CDFs	ND (0.01)	ND (0.024)	0.26 (0.036)	0.064 (0.01)	ND (0.029)	0.17 (0.037)
tal hepta CDFs	0.065 (0.02)	0.14 (0.043)	0.72 (0.021)	0.50 (0.034)	0.16 (0.062)	0.82 (0.045)
DF	0.044 (0.023)	0.10 (0.071)	0.64 (0.037)	0.37 (0.049)	0.11 (0.070)	0.66 (0.045)

tes: (1) Concentrations of PCDDs, PCDFs, and detection levels (DL) reported in parts per billion (ppb).

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TABLE 8

PCDDs and PCDFs
SITE #3 - MIDDLETOWN, OHIO AREA
SURFACE SOIL SAMPLES

	Upwind		Perimeter		
Sample No.:	13377	13400	13387	13372	13376
Field ID.:	UPW-5-L	UPW-5-L	PER-13-L	PER-14-L	PER-15-L
Location:	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
PCDDs (DL)					
2378-TCDD	0.003 (0.001)	0.004 (0.002)	0.004 (0.003)	ND (0.002)	ND (0.002)
Total iso TCDDs	ND (0.001)	ND (0.002)	ND (0.003)	ND (0.002)	ND (0.002)
Total penta CDDs	ND (0.010)	ND (0.044)	ND (0.020)	ND (0.014)	ND (0.039)
Total hexa CDDs	ND (0.010)	0.072 (0.044)	ND (0.020)	ND (0.009)	ND (0.039)
Total hepta CDDs	0.023 (0.007)	0.20 (0.17)	0.15 (0.014)	0.073 (0.018)	0.12 (0.009)
OCDD	0.20 (0.009)	10.6 (0.23)	0.28 (0.014)	0.17 (0.026)	0.84 (0.071)
PCDFs (DL)					
2378-TCDF	0.002 (0.001)	ND (0.004)	0.006 (0.004)	ND (0.001)	ND (0.005)
Total TCDFs					
Total penta CDFs	ND (0.008)	ND (0.016)	ND (0.010)	ND (0.012)	ND (0.015)
Total hexa CDFs	ND (0.008)	ND (0.036)	ND (0.028)	ND (0.012)	ND (0.015)
Total hepta CDFs	ND (0.018)	ND (0.023)	ND (0.026)	ND (0.017)	0.043 (0.023)
OCDF	ND (0.026)	ND (0.056)	ND (0.046)	ND (0.024)	0.050 (0.026)

Notes: (1) Concentrations of PCDDs, PCDFs, and detection levels (DL) reported in parts per billion (ppb).

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TABLE 9

PCDDs and PCDFs
SITE #4 - MINNESOTA NATURAL AREAS
SURFACE SOIL SAMPLES

Sample No.:	13373	13378	13379
Field ID.:	IWD-1-L	BSP-4-L	KR-1-L
Location:	Itasca Wilderness	Bluestem Prairie	Kettle River
PCDDs (DL)			
2378-TCDD	ND (0.003)	ND (0.001)	ND (0.002)
Total iso TCDDs	ND (0.003)	ND (0.001)	ND (0.002)
Total penta CDDs	ND (0.010)	ND (0.012)	ND (0.004)
Total hexa CDDs	ND (0.005)	ND (0.012)	ND (0.011)
Total hepta CDDs	0.047 (0.009)	0.091 (0.010)	0.025 (0.009)
OCDD	0.13 (0.019)	0.20 (0.012)	0.092 (0.011)
PCDFs (DL)			
2378-TCDF	ND (0.002)	ND (0.002)	ND (0.001)
Total TCDFs	ND (0.002)		
Total penta CDFs	ND (0.010)	ND (0.009)	ND (0.013)
Total hexa CDFs	ND (0.010)	ND (0.009)	ND (0.013)
Total hepta CDFs	ND (0.017)	ND (0.009)	ND (0.009)
OCDF	ND (0.024)	ND (0.010)	ND (0.014)

Notes: (1) Concentrations of PCDDs, PCDFs, and detection levels (DL) reported in parts per billion (ppb).

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TABLE 10

PCDDs and PCDFs
CONTROL AND BLANK SAMPLES

	Blank and Control Samples					
Sample No.:	13380	13381	13414	13415	13416	13417
Field ID.:	Control Soil	Blank Soil	Can Blank	Can Blank	Can Blank	Can Blank
Location:			PER-5	In-Plant Blank	Blank Middletown	Blank #6
CDDs (DL)						
2378-TCDD	0.005 (0.003)	ND (0.001)	ND (0.027)	ND (0.024)	ND (0.025)	ND (0.03)
Total iso TCDDs	ND (0.003)	ND (0.001)	ND (0.027)	ND (0.024)	ND (0.025)	ND (0.03)
Total penta CDDs	0.081 (0.033)	ND (0.015)	ND (0.097)	ND (0.10)	ND (0.098)	ND (0.11)
Total hexa CDDs	0.64 (0.033)	ND (0.015)	ND (0.097)	ND (0.10)	ND (0.098)	ND (0.11)
Total hepta CDDs	NA	0.031 (0.005)	ND (0.17)	ND (0.15)	ND (0.17)	ND (0.19)
OCDD	NA	0.27 (0.007)	0.63 (0.22)	0.74 (0.19)	0.89 (0.23)	0.44 (0.24)
CDFs (DL)						
2378-TCDF	0.017 (0.005)	ND (0.001)	ND (0.039)	ND (0.022)	ND (0.023)	ND (0.027)
Total TCDFs			ND (0.039)	ND (0.022)	ND (0.023)	ND (0.027)
Total penta CDFs	NA	ND (0.011)	ND (0.021)	ND (0.032)	ND (0.14)	ND (0.074)
Total hexa CDFs	NA	ND (0.011)	ND (0.35)	ND (0.14)	ND (0.13)	ND (0.12)
Total hepta CDFs	NA	ND (0.012)	NA	ND (0.15)	ND (0.19)	ND (0.16)
OCDF	NA	ND (0.013)	NA	ND (0.15)	ND (0.19)	ND (0.16)

Notes: (1) Concentrations of PCDDs, PCDFs, and detection levels (DL) reported in parts per billion (ppb).
(2) NA - Not analyzed. Peak broadening in GC/MS system prevented quantitation.

TABLE 11
MICHIGAN DIOXIN STUDY

1983 FISH COLLECTION
RESULTS FOR 2,3,7,8-TCDD

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Sample Identification EPA	MDNR	Species	Fish/ Sample	Sample Type	Length (cm)	Weight (gm)	Lipid Content (%)	2,3,7,8-TCDD ppt (DL)
St. Joseph River at Berrin Springs								
13218	SJR-1W	Carp	5	WHL	35-37.5	460-700	3.6	3.1 (2.5)
Huron River at Flatrock								
13281	HR-2W	Carp	6	WHL	32-38	400-780	5.8	0.6 (0.2)
River Raisin at Monroe								
13282	RR-4W	Carp	3	WHL	59-64.5	3300-5020	8.7	5.7 (0.2)
Clinton River at Mt. Clemens								
13283	CR-6W	Carp	1	WHL	65	4400	6.8	2.4 (0.3)
Kalamazoo River at Allegin								
13284	KR-4W	Carp	5	WHL	35-41	680-1000	2.1	2.8 (0.7)
Pine River at Alma								
13286	PR-1W	Carp	5	WHL	54-59	2000-3580	7.3	8.6 (0.4)
Muskegon River at Rogers Dam								
13287	UMR-1W	Carp	5	WHL	40-43.5	940-1100	---	ND (<0.8)
St. Clair River at Algonac								
13288	SCR-1W	Carp	5	WHL	51-54	1920-2480	11	4.3 (0.3)

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1983 FISH COLLECTION
RESULTS FOR 2,3,7,8-TCDD
(continued)

Sample Identification EPA	MDNR	Species	Fish/ Sample	Sample Type	Length (cm)	Weight (gm)	Lipid Content (%)	2,3,7,8-TCDD ppt (DL)
Ausable River at Mio								
13289	AR-1W	Carp	4	WHL	57-72.5	2680-5370	---	ND (<0.8)
Shiawassee River at Chesaning								
13290	SR-1W	Carp	5	WHL	52-68	2360-4840	---	ND (1.2)
Muskegon Lake at Muskegon								
13420	ML-2A	Carp	8	SF-R	54-66	2040-4420	8.1	5.2 (2.0)
13422	ML-5W	Pike	3	WHL	57-63	1140-1720	5.3	3.9 (1.6)
13421	ML-5A	Pike	2	SF-R	55-76	920-3080	---	ND (2.4)
Grand River at Grand Ledge								
13245	GR-1W	Carp	5	WHL	34.5-39.5	680-1040	5.4	6.0 (0.6)
13219	GR-1	Carp	1	SF-L	30	400	---	ND (2.5)
13220	GR-2	Carp	1	SF-L	31	420	1.9	6.9 (2.5)
13221	GR-3	Carp	1	SF-L	31.5	510	---	ND (2.5)
13222	GR-4	Carp	1	SF-L	31.6	540	---	ND (2.5)
13223	GR-5	Carp	1	SF-L	27	300	---	ND (2.5)
13224	GR-6	Carp	1	SF-L	32	510	---	ND (2.5)
13225	GR-7	Carp	1	SF-L	29	380	---	ND (2.5)
13226	GR-8	Carp	1	SF-L	29	410	---	ND (<0.4)
13227	GR-9	Carp	1	SF-L	40	1010	2.9	3.7 (0.3)
13228	GR-10	Carp	1	SF-L	40	1020	1.9	0.4 (0.2)
13229	GR-11	Carp	1	SF-L	42.5	1140	2.2	7.2 (0.2)
13230	GR-12	Carp	1	SF-L	41	1140	3.7	3.5 (0.2)
13231	GR-13	Carp	1	SF-L	38.5	880	1.6	1.5 (0.5)
13232	GR-14	Carp	1	SF-L	36.5	770	---	ND (1.2)
13233	GR-15	Carp	1	SF-L	37	830	0.6	0.6 (0.3)

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1983 FISH COLLECTION
RESULTS FOR 2,3,7,8-TCDD
(continued)

Sample Identification EPA	MDNR	Species	Fish/ Sample	Sample Type	Length (cm)	Weight (gm)	Lipid Content (%)	2,3,7,8-TCDD ppt (DL)
Grand River at Grand Ledge (con't)								
13234	GR-16	Carp	1	SF-L	36	700	---	ND (0.7)
13236	GR-17	Carp	1	SF-L	53	2190	---	ND (0.5)
13237	GR-18	Carp	1	SF-L	45	1600	8.1	11 (0.9)
13238	GR-19	Carp	1	SF-L	57	2940	1.2	1.8 (0.3)
13239	GR-20	Carp	1	SF-L	55	2900	---	ND (1.8)
13240	GR-21	Carp	1	SF-L	54	2940	---	ND (0.4)
13241	GR-22	Carp	1	SF-L	40	1100	---	ND (2.7)
13242	GR-23	Carp	1	SF-L	45.5	1400	---	ND (1.5)
13243	GR-24	Carp	1	SF-L	46	1540	1.3	1.2 (0.5)
13244	GR-25	Carp	1	SF-L	35	660	1.7	12 (0.3)
13246	GR-5A	Bullhead	5	SF-R	24.5-29	240-340	---	ND (<0.2)
13247	GR-6A	Bass	5	SOF-R	28-36	280-690	---	ND (<0.2)
Tittabawassee River at Midland								
13273	TR-1W	Carp	5	WHL	34-56	500-2860	10%	190 (0.6)
13248	TR-1	Carp	1	SF-L	37	700	4.5	38 (0.4)
13249	TR-2	Carp	1	SF-L	39	840	1.7	18 (0.3)
13250	TR-3	Carp	1	SF-L	37	780	2.7	28 (0.2)
13251	TR-4	Carp	1	SF-L	40	860	5.3	27 (1.5)
13252	TR-5	Carp	1	SF-L	42	860	3.5	16 (0.3)
13253	TR-6	Carp	1	SF-L	37	720	1.2	16 (1.0)
13254	TR-7	Carp	1	SF-L	35	560	1.8	12 (0.6)
13255	TR-8	Carp	1	SF-L	36.5	640	0.9	18 (0.2)
13256	TR-9	Carp	1	SF-L	43	1040	6.6	45 (0.3)
13257	TR-10	Carp	1	SF-L	45	1240	1.2	38 (0.6)
13258	TR-11	Carp	1	SF-L	41	880	3.8	13 (0.3)
13259	TR-12	Carp	1	SF-L	43	1030	4.3	14 (0.6)
13260	TR-13	Carp	1	SF-L	41.5	1060	6.4	26 (0.4)
13261	TR-14	Carp	1	SF-L	43	1070	4.9	22 (0.6)

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1983 FISH COLLECTION
RESULTS FOR 2,3,7,8-TCDD
(continued)

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Sample Identification EPA	MDNR	Species	Fish/ Sample	Sample Type	Length (cm)	Weight (gm)	Lipid Content (%)	2,3,7,8-TCDD ppt (DL)
Tittabawassee River at Midland (con't)								
13262	TR-15	Carp	1	SF-L	41	1000	7.9	46 (0.6)
13263	TR-16	Carp	1	SF-L	39.5	820	3.4	19 (0.7)
13264	TR-17	Carp	1	SF-L	63.5	3300	8.0	34 (1.2)
13265	TR-18	Carp	1	SF-L	64.5	3450	2.3	12 (1.6)
13266	TR-19	Carp	1	SF-L	51.5	1820	4.0	24 (1.6)
13267	TR-20	Carp	1	SF-L	48	1560	3.3	25 (1.4)
13268	TR-21	Carp	1	SF-L	47	1500	4.6	90 (0.3)
13269	TR-22	Carp	1	SF-L	44	1320	11	530 (1.6)
13270	TR-23	Carp	1	SF-L	51.5	1680	3.6	41 (1.3)
13271	TR-24	Carp	1	SF-L	49	1540	3.6	70 (1.4)
13272	TR-25	Carp	1	SF-L	46.5	1380	1.4	17 (1.6)
13274	TR-4A	Ch. Catfish	5	SF-R	45-55	800-1760	7.3	75 (0.4)
13275	TR-6A	Sm. Bass	5	SOF-R	24-38	220-860	1.0	5.1 (0.2)
13276	TR-66A	Walleye	1	SOF-R	56	1580	1.4	5.1 (0.2)
13277	TR-67A	Walleye	1	SOF-R	52	1320	2.0	3.6 (0.4)
13278	TR-68A	Walleye	1	SOF-R	49	1070	1.3	3.9 (0.2)
13279	TR-69A	Walleye	1	SOF-R	39	570	0.6	2.8 (0.3)
13280	TR-70A	Walleye	1	SOF-R	38	500	0.6	4.1 (0.3)

Sample Types

SF-R = Skinless Fillet - Right Side
SF-L = Skinless Fillet - Left Side
SOF-R = Skin on Fillet - Right Side
SOF-L = Skin on Fillet - Left Side
WHL = Whole Fish

DL = Detection Limit

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MICHIGAN DIOXIN STUDY

AVIAN SAMPLES
RESULTS FOR 2,3,7,8-TCDD

Sample Identification EPA	FWS	Species	Sample Description	Lipid Content (%)	2,3,7,8-TCDD ppt (DL)
Saginaw Bay near Bay City					
13291	FWS SBC3-032	Common Tern	Whole Body (1) Adult	3.1	25 (3.1)
13297	FWS SBC2-011,012	Common Tern	Composite (2) Chicks	3.8	23 (3.5)
13292	FWS SBC3-012,013,014	Common Tern	Composite (3) Chicks	3.3	35 (2.4)
13293	FWS SBC3-015,018,019,020	Common Tern	Composite (4) Chicks	4.3	38 (2.2)
13294	FWS SBC3-021,024,025,026,028	Common Tern	Composite (5) Chicks	4.4	34 (2.9)
13295	FWS SBC3-001,006,007,008	Common Tern	Composite (4) Eggs	6.7	40 (1.5)
13296	FWS SBC3-003,004,005	Common Tern	Composite (3) Eggs	7.7	51 (1.6)
13298	FWS SBC2-001,002	Common Tern	Composite (2) Eggs	*	63 (1.5)
13299	FWS SBC2-004	Common Tern	Composite (4) Eggs	7.6	37 (1.2)

* Insufficient sample to analyze for lipid content.

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2378-TCDD
SUMMARY OF RECENT ENVIRONMENTAL MEASUREMENTS
MIDLAND, MICHIGAN AREA

	Number of Measurements	Range		Arithmetic Mean	Arithmetic Standard Deviation	Geometric Mean
Ambient Air* (March 1983-February 1984)						
Total - all measurements	10	0.010-0.21	pg/m^3	0.061	0.069	0.036
Dow Plant	2	0.019-0.022	pg/m^3	0.021		
Dow Plant Fence Line	6	0.010-0.21	pg/m^3	0.064	0.075	0.038
City of Midland	2	0.019-0.16	pg/m^3	0.090		
Tittabawassee River Fish (August-September 1983)						
Carp - whole fish composite (5 fish)	1	190	ppt			
Carp - individual skinless fillets	25	12-530	ppt	50	102	28.6
Catfish - skinless fillet composite (5 fish)	1	75	ppt			
Smallmouth Bass - skin-on fillet composite (5 fish)	1	5.1	ppt			
Walleye - individual skin-on fillets	5	2.8-5.1	ppt	3.9	0.8	3.8
Surface Soils (October-December 1983)						
Dow Plant	15	0.01-25.0	ppb	2.38	6.41	0.24
Dow Plant Perimeter	9	0.01-2.03	ppb	0.74	1.43	0.17
Public Use and Residential Areas	17	0.003-0.17	ppb	0.037	0.042	0.026
Residential Areas*	8	0.009-0.076	ppb	0.025	0.022	0.020
Residential Downspouts*	8	0.013-0.27	ppb	0.104	0.103	0.062

* Data provided by Dow Chemical Company

* Data for four additional sites available 12/15/84.

Dave

RECEIVED 7/27/80

JUL 21 1980

MEMORANDUM

SUBJECT: Epidemiologic Investigation of Birth Defects in Oregon

FROM: Martin P. Halper, Director
Survey and Analysis Division (TS-793)

TO: Edwin Johnson
Deputy Assistant Administrator
for Office of Pesticides Programs

THRU: Marilyn C. Bracken
Deputy Assistant Administrator
for Office of Program Integration and Information
(TS-793)

The Survey and Analysis Division (SAD) recently received the attached proposal from the Center for Disease Control (CDC). The Center is proposing that OPTS support an epidemiologic retrospective matched case control investigation in western Oregon. The object of this endeavor would be to determine whether parental exposure to aerial herbicide application is associated with the birth of infants having central nervous system (CNS) defects.

This proposal was the result of a preliminary assessment of the situation by CDC personnel after they were contacted by Oregon physicians and other concerned citizens in the area. CDC's review of data amassed through their National Birth Defects Monitoring Program indicated that there were increases in rates of certain CNS birth defects between 1970 and 1979. Specifically, 8 cases of anencephaly were observed with 4 expected; 16 cases of hydrocephaly were observed with 10 expected.

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Accordingly, SAD is forwarding a copy of the CDC proposal for review and comments. We would appreciate receiving all comments by July 29 so that we may respond to CDC in a timely fashion.

Attachment

cc: Dave Menotti, OGC
Jim Reisa, OTS

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
CENTER FOR DISEASE CONTROL
ATLANTA, GEORGIA 30333
TELEPHONE: (404) 633-3311

404-452-4036
June 18, 1980

Susan Strassman-Sundy
Survey & Analysis Division
(TS-793)
U.S., E.P.A.
401 M Street, S.W.
Washington, D.C. 20460

Dear Ms. Strassman-Sundy:

As follow-up to our telephone conversation regarding a proposed study of herbicide exposure and birth defects, I am sending the report we prepared for the Oregon Pesticide Analytic Research Center (PARC) and the State Health Department.

We feel the proposed study, if PARC and the Oregon Health Department decide to formally invite CDC to help conduct it, is very much the type of cooperative effort that would be covered by the pending interagency agreement between SAD/EPA and the Chronic Diseases Division, CDC. Our problem as mentioned in our conversation, is that we currently do not have the manpower or the funds to conduct such a large study. Because of our mutual interest in herbicide exposure and health effects, the proposal should be of interest to the E.P.A. If EPA finds the proposal of interest and current funding is available, we should explore our mutual interest as soon as possible in anticipation of the request for assistance from the PARC h- d and the Oregon Health Dept.

Sincerely yours,

Larry Edmonds

Larry Edmonds, M.S.P.H.
Epidemiologist
Birth Defects Branch
Bureau of Epidemiology

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REPORT TO THE PESTICIDE ANALYTIC RESEARCH CENTER (PARC)

THROUGH JAMES GOOGINS, M.D. STATE EPIDEMIOLOGIST

OREGON HEALTH DEPARTMENT

June 10, 1980

Larry D. Edmonds

Birth Defects Branch
Chronic Disease Division
Center for Disease Control
Atlanta, Ga. 30333

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During the Fall of 1979, a group of physicians and other concerned citizens from Lincoln County, Oregon reported their belief that an excessive number of babies in that county were being born with birth defects. They linked these data with herbicide exposure (2,4-D) and called for a ban on the use of 2,4-D until more data are available. Because of these concerns, and the results of the EPA Study of abortions and 2,4,5-T in Alsea, Oregon, the Birth Defects Branch reviewed the data available through the National Birth Defects Monitoring Program. That review indicated that there were increases in the rates of anencephaly in Benton County (8 observed cases, 4 expected), and of hydrocephaly in Lane County (16 observed cases, 10 expected) between 1970 and 1977.

The BDMP findings, along with the concerns of the Lincoln County physicians led us to discuss these data with the Oregon Health Department. John Googin, M.D, State Epidemiologist, invited CDC to meet with the Oregon Pesticide Analysis Research Center (PARC) Board on November 21, 1979. The Board was formed to evaluate possible adverse health effects of chemicals used in agriculture. The PARC Board asked the Birth Defects Branch to review available data and make a recommendation about what kind of epidemiologic study should be done to evaluate the relationship between maternal exposure to herbicide spraying and birth defects.

Study Approach

A retrospective case-control study appeared to be the most appropriate type of study for several reasons. First because birth defects are rare events, it would be difficult otherwise to obtain enough cases for a study with sufficient statistical power. Second, the ban of 2,4,5-T in 1978 eliminated the source of exposure. In addition, a retrospective study would also allow the opportunity to evaluate possible increases in malformation rates from sources other than herbicides. The definition of cases and controls would be relatively straight forward. Cases would be identified as Oregon resident births identified with central nervous system defects and controls as normal Oregon infants matched on maternal race, place and date of birth. All cases would be identified, even those from urban areas, because the preliminary BDMP data found high CNS defect rates in counties predominantly urban as well as those predominantly rural. A reliable, unbiased estimate of exposure would be needed for both cases and controls. Determining this rate poses some difficulty. Because of obvious bias resulting from questioning individuals about spraying exposure and the unavailability of a retrospective biochemical test, we needed some other method of determining exposure. We undertook a pilot study to learn if it was feasible to obtain an unbiased estimate of exposure, and if it was, to learn the rate of exposure. The latter figure is necessary to determine an adequate sample size or to determine the statistical power of any smaller sample size.

Pilot Study

The purpose of the pilot study was to estimate the rate of herbicide exposure in Benton, Polk and Lincoln Counties as a measure of exposure in western Oregon. These three counties are primarily forested and Lincoln and Benton counties are where the initial concerns about birth defects were raised. For the pilot study, a random sample of 72 births was selected from each country using vital records. An equal number of birth certificates (12) were chosen for each year, 1973-1977, and one was randomly selected from each month. The residences of the 72 births were determined, and for those with rural addresses, the owners of tracts of land within two miles of the residence of the case were sought. Identified landowners were contacted and asked to give spray history occurring from 1 month before conception of the case to 3 months after conception.

Results of Pilot

Thirty rural cases were identified. The original approach to identify exposures was not feasible. There were too many owners within 2.0 miles and the owners had no, or few written records, so they had to depend upon recollection of any spraying, when it occurred, or what was sprayed. It was obvious, from this pilot study, that we could not reliably document herbicide usage by questioning individuals or land owners.

Extension of Pilot

The only definition of herbicide exposure that appeared to be workable was for aerial herbicide spraying near a residence that is documented in some official form. With this definition in mind, we plotted all the sample births on county maps. We plotted the 30 rural births as before, and all the remaining births listed with a city address were plotted as residents within the city limits. We also used computer printouts, generated for the pilot study by the Department of Forestry, to identify any forest land that was sprayed between Jan. 1974 and Jan. 1980. Under Oregon law, all land owners (excluding the U.S. Forest Service and the Bureau of Land Management have to file a proposed spraying plan with the State Department of Forestry. The majority of the births plotted were not near U.S. Forest Service land so the state clearinghouse was a good source of information. We assumed the U.S. Forest Service would furnish data if requested.

We next reviewed the spray data to identify any aerial herbicide spraying that occurred within two miles of any sample birth. Using this admittedly crude estimate, we identified 8 births that had aerial herbicide spraying within 2 miles of their residence during the critical period around conception. There were 2 additional babies that had possible spraying within two miles of their residence. The exact location of spraying was unknown, but spraying occurred in the area. Thus, we identified a maximum of 10 "exposed" infants, for a rate of 4.6%. This "exposure" rate should be applicable to the western areas of Oregon where the vast majority of births occur.

It is important to note that this "exposure" rate is only a rough estimate of aerial herbicide spraying within 2 miles of a residence, and not a measure of actual exposure to herbicides. It appears to be impracticable, if not impossible, to determine retrospectively what the true exposure of pregnant women was. We can only evaluate if aerial spraying occurred in the general proximity of infants with CNS defects more often than in a group of normal infants. The misclassification of women into exposed and not exposed categories would have the effect of lowering the power of the study to detect possible teratogenicity.

Sample Size Estimate

The sample size needed to detect an exposure effect depends on the rate of "exposure", the increase in risk among these exposed, and the statistical power desired. Using the estimate of 4.6% overall "exposure" from the pilot, if we want to have at least an 80% chance of finding a 2-fold increase in risk, we would need 435 cases and 435 controls. If the attack rate is 1-1/2 times greater in exposed than in unexposed, we would need 1,533 each of cases and controls.

A statistical power of 80% was the minimum figure we had hoped for. Unfortunately, we can't find enough cases in western Oregon with documented exposure status to achieve this power. Table 1 presents an estimate of the number of cases that could be located, interviewed, and the herbicide exposure documented. This number of cases (264) and an equal number of controls would produce a study with a 62% chance of detecting a 2-fold difference in attack rates, using a 1-tailed test at the 0.05 level of significance. If the attack rate is 1-1/2 times greater in cases than controls, then we have a 27% chance of finding a difference.

Proposed Epidemiologic Study

Hypothesis: The hypothesis to be tested is whether maternal exposure to aerial spraying of herbicide is associated with the birth of infants with central nervous systems (CNS) defects.

Study Design: A retrospective matched case-control study in western Oregon. Indepth personal interviews would be conducted of 264 CNS cases and 264 normal controls to evaluate various maternal and paternal risk factors.

Cost: To conduct this proposed study would cost approximately $192,000 (See attached budget).

Required Time: With adequate staff the study could be completed in 9 to 18 months after approval to conduct the study has been given.

Summary: With completion of the pilot, some judgements can be made about the merits of the proposed epidemiologic study of "herbicide exposure" and birth defects. The measurement of exposure is troublesome. Lacking some better way to identify exposed mothers, we can only investigate the relationship between proximate aerial herbicide spraying and CNS birth defects. Such a study would compare these exposure rates in infants with CNS defects and normal infants.

With the available sample of 264 cases and 264 controls, we would have a 62% chance of detecting a 2-fold relative risk. If there is a 50% increase in the attack rate among the exposed, we would have a 27% chance of detecting this difference. These power figures are not particularly encouranging. In addition, it may well be that these relative risks apply only to women with a specific level or type of exposure. Since the available measure of exposure is so coarse, the relative risks of "exposed" women based on aerial spraying data might be much lower. In that case, the statistical power would be even lower.

It is important that the limits of such an epidemiologic study are identified in the beginning. We feel that if a study is undertaken, the case-control approach is the best approach. If you decide to go ahead with such a study, the Birth Defects Branch would be willing to assist the State Health Department and the PARC Board in planning and implementing the study.

Table I

Estimated number of central nervous system cases in Oregon in the years (1974 to 1979) for which exposure can be documented. (Estimate based on Oregon rate from the Birth Defects Monitoring Program data.)	380
Estimated number of cases in eastern Oregon. (The exposure rate here may be lower than in pilot area.)	50
Estimated number of CNS cases in western Oregon, 1974-1979.	330
Estimated number of cases in western Oregon that we will be able to locate and interview. (Estimate of 20% lost to followup based on Atlanta experience.)	264

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Budget of Proposed Case-Control Study
In Oregon

Personnel - Salary and Benefits			$120
Person Years	Category & grade	Salary & Benefits	
2.0	Health Technician (GS-7) (case finding - 8 persons @ 12 wks)	$31,000	
2.0	Health Technicians (GS-7) interviewing - 8 persons @ 12 wks)	31,000	
1.0	Coder (GS-5)	13,000	
1.0	Public Health Advisor (GS-11)	24,000	
.2	Statistician (GS-13)	7,000	
.50	Epidemiologist (0-5)	14,000	
Travel			35,0
Equipment & Supplies			1,5
Rent and Communications & Utilities			2,0
Printing			1,5
		Subtotal	160,
		Plus CDC overhead @ 20%	32,
		Total	$192,

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BDMP DATA — Oregon, 1970-1978

Defect	Code	County: Lincoln No. Cases	Lincoln Rate	Benton No. Cases	Benton Rate	Polk No. Cases	Lane No. Cases	Lane Rate	Total Lincoln, Benton, Polk, Lane Counties No. Cases	Total Lincoln, Benton, Polk, Lane Counties Rate	All Oregon No. Cases	All Oregon Rate	70-77 U.S. Rate
Anencephaly	45	2	15.3	9	9.9*	--	12	4.6	23	6.2	85	4.9	4.6
Hydrocephaly	65	-	--	4	4.4	--	17	6.6*	21	5.6	39	4.0	4.4
Spina Bifida	56	1	7.7	10	11.0	--	9	3.5	20	5.4	72	4.1	6.2
Total CNS	125	4	30.6	27	29.6*	--	48	18.6	79	21.2	307	17.6	
Cleft Lip	325	-	--	5	5.5	--	23	8.9	28	7.5	102	5.8	5.2
Cleft Palate	329	1	7.7	7	7.7	--	33	12.8*	41	11.0	167	9.6	9.6
T.E. Fistula	375	-	--	1	1.1	--	11	4.3	12	3.2	46	2.6	1.6
Rectal Atresia	393	-	--	4	4.4	--	11	4.3	15	4.0	61	3.5	3.4
Renal Agenesis	450	-	--	1	1.1	--	4	1.5	5	1.3	23	1.3	1.0
Reduction Deformity	483	1	7.7	3	3.3	--	17	6.6*	21	5.6	59	3.4	3.3
Downs	626	1	7.7	3	3.3	--	27	10.4	31	8.3	155	8.9	8.1
Births in BDMP		1,307		9,123		1,051	25,860		37,341		174,659	7,903,544	
Monitored		100%		100%			89%				65%	33%	

70-77 significant increases Benton - anencephaly (observed 8, expected 3.7) p = .05
Total CNS (observed 23, expected 16.68) p = .05

Lane - hydrocephaly (observed 16, expected 9.9) p = .05
cleft lip (observed 23, expected 11.6) p = .01
reduction deformity (observed 16, expected 7.3) p = .01

2006 Rate 10,000

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Look at 'highly exposed' segment proposed . . .

PARC shifts study emphasis

By CLAUDE STEUSLOFF
Capital Press Farm Editor

SALEM, Ore. — The Pesticide Analytical Research Center (PARC) has rejected a "retrospective type of study" of the pesticide problem in coastal counties of Oregon as outlined in a report made by the U.S. Center for Disease Control, Atlanta, Ga.

In a change of direction, PARC members decided to study a proposal to be made by Oregon State University on the effect of the pesticide 2,-4-D "on highly exposed people in Eastern Oregon and the Willamette Valley."

That proposal is due at the next meeting of the group, Jan. 30, at which time they will also consider a report of pesticide studies made by Dr. James Googin of the University of Oregon Health Sciences Center, Portland.

Marla Gillam, Eugene, of the Northwest Coalition for Alternatives to Pesticides, suggested PARC study "the rise and distribution of the use of chemicals in Oregon."

The action came after a morning of technical discussion on pesticides by a group of 15 scientists last Thursday at the Oregon Department of Agriculture, under direction of Bill Kosesan, administrator of the department plant division and chairman of PARC.

Warren Westgarth of the Department of Environmental Quality, made the original motion. He said he did so "after looking at all the data in the CDC report" and with the hope something could be going from the center before the summer applications of pesticides.

Larry Edmunds, epidemiologist with the disease control center at Atlanta, said the pesticide study he outlined would require $100,000 in funding from the state of Oregon. He said the CDC is not a funding group, the U.S. Environmental Protection Agency would not contribute, but the U.S. Forest Service could have some funds. Edmunds estimated total cost of the proposed study at $132,000.

Edmunds said birth defects among children born in Oregon runs lower than the national average but two counties have defects significantly higher than the U.S. average.

A pilot study by the Atlanta CDC was done in Lincoln, Benton and Polk counties on use of 2,4-D in primarily forested areas. Based on the Oregon rate of central nervous system birth defects from the Birth Defects Monitoring Program data, it was estimated 264 cases could be located and interviewed in Western Oregon.

Specifically, the study design rejected by PARC was "A retrospective matched case-control study, in-depth personal interviews would be conducted of 264 central nervous system cases and 264 normal controls to evaluate various maternal and paternal risk factors. With adequate staff, the work could have been completed in nine to 18 months.

The report states that a reliable, unbiased estimate of exposure to 2,4-D would be needed for both cases and controls. Because birth defects are rare events, it would be difficult to obtain enough cases for a study with sufficient statistical power, other than in a retrospective study.

Edmunds said the CDC report is "only an outline of an approach to the problem." During the discussion, he said the proposed further study has some advantages but there may be more disadvantages and there is no need to make a study for the sake of a study.

Mike Newton, professor of forest ecology at OSU, contended throughout his remarks that the CDC pilot study hypothesis blaming 2,4-D in coastal county birth defect problems is erroneous.

He said use of 2,4-D is a national problem and in many farming areas the use is much greater than in the timbered coastal community. He cited widespread roadside weed and brush use of 2,4-D and other herbicides.

Newton questioned whether the incidence of coastal defects is extraordinary and said birth defects in the region may be due to other causes such as high phosphate levels in soils and excessive rates of mercury and copper in water supplies at the coast.

He said a study of residents in urban areas at the coast — well removed from timber — showed that 17 percent of the population had high residues of 2,4-D in their urine.

"A study, if it is positive, would show defects but they would be subject to other variable causes than herbicides. We don't know what causes defects. There is only a 50 percent chance of picking up herbicide effects with a study," said Newton.

He said there is a 10,000-to-1 safety factor in herbicide applications. "Drugs, alcohol, etc., show birth defects in users, such confounding factors are large and will confuse the study." Newton continued.

Gillam said "lots of citizens are angry" about 2,4-D applications and warned that "sooner or later you must look at use of herbicides."

James Witt, agricultural Extension specialist in chemistry, OSU, proposed looking at positive controls for birth defects due to 2,4-D.

Virgil Freed, head of the agricultural chemistry department at OSU, called for a study of possible defects among husbands and wives who have used pesticides on family farms in Morrow and Umatilla counties, for many continuous years.

Dr. Stringham, family physician in Lincoln County, suggested both fathers and mothers should be studies for birth defects.

The Pesticide Analytical Research Center consists of representatives from the state departments of Agriculture, Health Division, Environmental Quality, Forestry and Fish & Game. One member from the public at large is appointed by the governor.

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38. R. T. Sauer, R. R. Yocum, R. F. Doolittle, M. Lewis, C. O. Pabo, *Nature (London)* **298**, 447 (1982).
39. B. von Wilken-Bergmann and B. Müller-Hill, *Proc. Natl. Acad. Sci. U.S.A.* **79**, 2427 (1982).
40. H. Nick *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **79**, 218 (1982); H. Nick *et al.*, *J. Mol. Biol.* **161**, 417 (1982); K. Arndt, H. Nick, F. Boschelli, P. Lu, J. Sadler, *ibid.*, p. 439; R. Kaptein and K. Wuthrich, personal communication.
41. T. A. Steitz, D. H. Ohlendorf, D. B. McKay, W. F. Anderson, B. W. Matthews, *Proc. Natl. Acad. Sci. U.S.A.* **79**, 3097 (1982).
42. D. H. Ohlendorf and B. W. Matthews, unpublished data.
43. I. T. Weber, D. B. McKay, T. A. Steitz, *Nucleic Acids Res.* **10**, 5085 (1982).
44. D. H. Ohlendorf, W. F. Anderson, B. W. Matthews, *J. Mol. Evol.* **19**, 109 (1983).
45. D. H. Ohlendorf, W. F. Anderson, M. Lewis, C. O. Pabo, B. W. Matthews, *J. Mol. Biol.*, in press.
46. J. C. Wang, M. D. Barkley, S. Bourgeois, *Nature (London)* **251**, 247 (1974).
47. T. Maniatis and M. Ptashne, *Proc. Natl. Acad. Sci. U.S.A.* **70**, 1531 (1973).
48. N. C. Seeman, J. M. Rosenberg, A. Rich, *ibid.* **73**, 804 (1979); C. Hélene, *FEBS Lett.* **74**, 10 (1977).
49. P. H. von Hippel, in *Biological Regulation and Development*, R. F. Goldberger, Ed. (Plenum, New York, 1979), p. 279.
50. M. H. Caruthers, *Acc. Chem. Res.* **13**, 155 (1980).
51. O. G. Berg, R. B. Winter, P. H. von Hippel, *Biochemistry* **20**, 6929 (1981); R. B. Winter and P. H. von Hippel, *ibid.*, p. 6948. R. B. Winter, O. G. Berg, P. H. von Hippel, *ibid.*, p. 6961.
52. L. Guarente, J. S. Nye, A. Hochschild, M. Ptashne, *Proc. Natl. Acad. Sci. U.S.A.* **79**, 274 (1982).
53. A. Hochschild, N. Irwin, M. Ptashne, *Cell* **32**, 319 (1983).
54. D. K. Hawley and W. R. McClure, *J. Mol. Biol.* **157**, 493 (1982); *Cell* **32**, 327 (1983).
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Science, Risk, and Public Policy

William D. Ruckelshaus

We are now in a troubled and emotional period for pollution control; many communities are gripped by something approaching panic and the public discussion is dominated by personalities rather than substance. It is not important to assign blame for this. I appreciate that people are worried about public health and about economic survival, and legitimately so, but we must all reject the emotionalism that surrounds the current discourse and rescue ourselves from the paralysis of honest public policy that it breeds.

I believe that part of the solution to our distress lies with the idea that disciplined minds can grapple with ignorance and sometimes win: the idea of science. We will not recover our equilibrium without a concerted effort to more effectively engage the scientific community. Frankly, we are not going to be able to emerge from our current troubles without a much improved level of public confidence. The polls show that scientists have more credibility than lawyers or businessmen or politicians, and I am all three of those. I need the help of scientists.

This is not a naïve plea for science to save us from ourselves. Somehow, our democratic technological society must resolve the dissonance between science and the creation of public policy. Nowhere is this more troublesome than in the formal assessment of risk—the estimation of the association between exposure to a substance and the incidence of some disease, based on scientific data.

Summary. A climate of fear now dominates the discussion of environmental issues. The scientific community can help alleviate this fear by making a greater effort to explain to the public the uncertainties involved in estimates of risk. Current statutory mandates designed to protect public health both demand levels of protection that technology cannot achieve and are uncoordinated across government agencies. A common statutory framework for dealing with environmental risks is needed. In addition, care must be taken to separate the scientific process of assessing risk from the use of such assessments, together with economic and policy considerations, in the management of risks through regulatory action.

Science and the Law at EPA

Here is how the problem emerges at the Environmental Protection Agency. EPA is an instrument of public policy, whose mission is to protect the public health and the environment in the manner laid down by its statutes. That manner is to set standards and enforce them, and our enforcement powers are strong and pervasive. But the standards we set, whether technology- or health-related, must have a sound scientific base.

Science and the law are thus partners at EPA, but uneasy partners. The main reason for the uneasiness lies, I think, in the conflict between the way science really works and the public's thirst for certitude that is written into EPA's laws. Science thrives on uncertainty. The best young scientists flock into fields where great questions have been asked but nothing is known. The greatest triumph of a scientist is the crucial experiment that shatters the certainties of the past and opens up rich new pastures of ignorance.

But EPA's laws often assume, indeed demand, a certainty of protection greater than science can provide with the current state of knowledge. The laws do no more than reflect what the public believes and what it often hears from people with scientific credentials on the 6 o'clock news. The public thinks we know what all the bad pollutants are, precisely what adverse health or environmental effects they cause, how to measure them exactly and control them absolutely. Of course, the public and sometimes the law are wrong, but not all wrong. We do know a great deal about some pollutants and we have controlled them effectively by using the tools of the Clean Air Act and the Clean Water Act. These are the pollutants for which the scientific community can set safe levels and margins of safety for sensitive populations. If this were the case for all pollutants, we could breathe more easily (in both senses of the phrase); but it is not so.

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More than 10 years ago, EPA had the Clean Air Act, the Clean Water Act, a solid waste law, a pesticide law, and laws to control radiation and noise. Yet to come were the myriad of laws to control toxic substances from their manufacture to their disposal—but that they would be passed was obvious even then.

When I departed EPA a decade ago, the struggle over whether the federal government was to have a major role in protecting our health, safety, and environment was ended. The American people had spoken. The laws had been passed; the regulations were being written. The only remaining question was whether the statutory framework we had created made sense or whether, over time, we would adjust it.

Scientific Realities

Ten years ago I thought I knew the answer to that question as well. I believed it would become apparent to all that we could virtually eliminate the risks we call pollution if we wanted to spend enough money. When it also became apparent that enough money for all the pollutants was a lot of money, I came to believe that we would begin examining the risks very carefully and structure a system that would force us to balance our desire to eliminate pollution against the costs of its control. This would entail some adjustment of the laws, but not all that much, and it would happen by about 1976. I was wrong.

This time around as administrator of EPA, I am determined to improve our country's ability to cope with the risk of pollutants over where I left it 10 years ago. It will not be easy, because we must now deal with a class of pollutants for which it is difficult, if not impossible, to establish a safe level. These pollutants interfere with genetic processes and are associated with the diseases we fear most: cancer and reproductive disorders, including birth defects. The scientific consensus is that any exposure, however small, to a genetically active substance embodies some risk of an effect. Since these substances are widespread in the environment, and since we can detect them down to very low levels, we must assume that life now takes place in a minefield of risks from hundreds, perhaps thousands, of substances. We can no longer tell the public that they have an adequate margin of safety.

This worries all of us, and it should. But when we examine the premises on which such estimates of risk are based, we find a confusing picture. In assessing a suspected carcinogen, for example, there are uncertainties at every point where an assumption must be made: in calculating exposure; in extrapolating from high doses where we have seen an effect to the low doses typical of environmental pollution; in what we may expect when humans are subjected to much lower doses of a substance that, when given in high doses, caused tumors in laboratory animals; and finally, in the very mechanisms by which we suppose the disease to work.

One thing we clearly need to do is ensure that our laws reflect these scientific realities. The administrator of EPA should not be forced to represent that a margin of safety exists for a specific substance at a specific level of exposure where none can be scientifically established. This is particularly true where the inability to so represent forces the cessation of all use of a substance without any further evaluation.

Functions of Regulatory Agencies

It is my strong belief that where EPA, OSHA (the Occupational Safety and Health Administration), or any other social regulatory agency is charged with protecting public health, safety, or the environment, we should be given, to the extent possible, a common statutory formula for accomplishing our tasks. This statutory formula may well weigh public health very heavily, as the American people certainly do.

The formula should be as precise as possible and should include a responsibility for assessing the risk and weighing it, not only against the benefits of continued use of the substance under examination, but against the risks associated with substitute substances and the risks associated with the transfer of the substance from one environmental medium to another through pollution control practices. I recognize that legislative change in the current climate is difficult. It is up to those of us who seek change to make the case for its advisability.

But my purpose here is not to plead for statutory change; it is to speak of risk assessment and risk management and the role of science in both. It is important to distinguish these two essential functions, and I rely here on a recent National Academy of Sciences report on the management of risk in the federal government. Scientists assess a risk to find out what the problems are. The process of deciding what to do about the problems is risk management. The second procedure involves a much broader array of disciplines and is aimed toward a decision about control.

In risk management it is assumed that we have assessed the health risks of a suspect chemical. We must then factor in its benefits, the costs of the various methods available for its control, and the statutory framework for decision. The NAS report recommends that these two functions—risk assessment and risk management—be separated as much as possible within a regulatory agency. This is what we now do at EPA and it makes sense.

Risk Assessment

We also need to strengthen our risk assessment capabilities. We need more research on the health effects of the substances we regulate. I intend to do everything in my power to make clear the importance of this scientific analysis at EPA. Given the necessity of acting in the face of enormous scientific uncertainties, it is more important than ever that our scientific analysis be rigorous and the quality of our data be high. We must take great pains not to mislead people about the risks to their health. We can help to avoid confusion be ensuring both the quality of our science and the clarity of our language in explaining hazards.

I intend to allocate some of EPA's increased resources to pursuing these ends. Our 1984 request contains significant increases for risk assessment and associated work. We have requested $31 million in supplemental appropriations for research and development, and I expect that risk assessment will be more strongly supported as a result of this increase as well.

I would also like to revitalize our long-term research program to develop a base for more adequately protecting the public health from toxic pollutants. I will be asking the outside scientific community for advice on how best to focus those research efforts.

In the future, this being an imperfect world, the rigor and thoroughness of our risk analyses will undoubtedly be affected by many factors, including the toxicity of the substances examined, the populations exposed, the pressure of the regulatory timetable, and the resources available. Despite these often conflicting pressures, risk assessment at EPA must be based only on scientific evidence and scientific consensus. Nothing will erode

public confidence faster than the suspicion that policy considerations have been allowed to influence the assessment of risk.

Risk Management

Although there is an objective way to assess risk, there is, of course, no purely objective way to manage it, nor can we ignore the subjective perception of risk in the ultimate management of a particular substance. To do so would be to place too much credence in our objective data and ignore the possibility that occasionally one's intuition is right. No amount of data is a substitute for judgment.

Further, we must search for ways to describe risk in terms that the average citizen can comprehend. Telling a family that lives close to a manufacturing facility that no further controls on the plant's emissions are needed because, according to our linear model, their risk is only 10^{-6}, is not very reassuring. We need to describe the suspect substances as clearly as possible, tell people what the known or suspected health problems are, and help them compare that risk to those with which they are more familiar.

To effectively manage the risk, we must seek new ways to involve the public in the decision-making process. Whether we believe in participatory democracy or not, it is a part of our social regulatory fabric. Rather than praise or lament it, we should seek more imaginative ways to involve the various segments of the public affected by the substance at issue. They need to become involved early, and they need to be informed if their participation is to be meaningful. We will be searching for ways to make our participatory process work better.

For this to happen, scientists must be willing to take a larger role in explaining the risks to the public—including the uncertainties inherent in any risk assessment. Shouldering this burden is the responsibility of all scientists, not just those with a particular policy end in mind. In fact, all scientists should make clear when they are speaking as scientists, ex cathedra, and when they are recommending policy they believe should flow from scientific information. What we need to hear more of from scientists is science. I am going to try to provide avenues at EPA for scientists to become more involved in the public dialog in which scientific problems are described.

Lest anyone misunderstand, I am not suggesting that all the elements of managing risk can be reduced to a neat mathematical formula. Going through a disciplined approach can help to organize our thoughts so that we include all the elements that should be weighed. We will build up a set of precedents that will be useful for later decision-making and will provide more predictable outcomes for any social regulatory programs we adopt.

In a society in which democratic principles dominate, the perceptions of the public must be weighed. Instead of objective and subjective risks, the experts sometimes refer to "real" and "imaginary" risks. There is a certain arrogance in this—an elitism that has ill served us in the past. Rather than decry the ignorance of the public and seek to ignore their concerns, our governmental processes must accommodate the will of the people and recognize its occasional wisdom. As Thomas Jefferson observed, "If we think [the people] not enlightened enough to exercise their control with a wholesome discretion, the remedy is not to take it from them, but to inform their discretion."

Interagency and International Coordination

Up to this point I have been suggesting how risks should be assessed and managed in EPA. Much needs to be done to coordinate the various EPA programs to ensure a consistent approach. I have established a task force with that charter.

I further believe we should make uniform the way in which we manage risk across the federal regulatory agencies. The public interest is not served by two federal agencies taking diametrically opposed positions on the health risks of a toxic substance and then arguing about it in the press. We should be able to coordinate our risk assessment procedures across all federal agencies. The risk management strategies that flow from assessment may indeed differ, depending on each agency's statutory mandate, the judgment of the ultimate decision-maker.

But even at the management stage, there is no reason why the approaches cannot be coordinated to achieve the goal of risk avoidance or minimization with the least societal disruption possible. I have been exploring with the White House and the Office of Management and Budget the possibility of effecting better intragovernmental coordination on the way in which we assess and manage risk.

To push this one step further, I believe it is in our nation's best interest to share our knowledge of risks and our approaches to managing them with the other developed nations of the world. The environmental movement has taught us the interdependence of the world's ecosystems. In coping with the legitimate concerns raised by environmentalists, we must not forget that we cope in a world with interdependent economies. If our approach to the management of risk is not sufficiently in harmony with those of the other developed nations, we could save our health and risk our economy. I do not believe we need to abandon either, but to ensure that it does not happen, we need to work hard to share scientific data and understand how to harmonize our management techniques with those of our sister nations.

In sum, my goal is a government-wide process for assessing and managing environmental risks. Achieving this will take cooperation and goodwill within EPA, among Executive Branch agencies, and between Congress and the Administration, a state of affairs that may partake of the miraculous. Still, it is worth trying, and the effort is worth the wholehearted support of the scientific community. I believe such an effort touches on the maintenance of our current society, in which a democratic polity is grounded in a high-technology industrial civilization. Without a much more successful way of handling the risks associated with the creations of science, I fear we will have set up for ourselves a grim and unnecessary choice between the fruits of advanced technology and the blessings of democracy.

NATIONAL CANCER INSTITUTE

Office of Cancer Communications

Building 31, Room 10A24
Bethesda, Maryland 20892

January 1991

Occupational Risk of Cancer from Pesticides: Farmer Studies

Studies from the United States and other countries have shown that farmers have a higher risk for certain cancers, particularly cancers of the blood and immune systems (leukemia, non-Hodgkin's lymphoma, and multiple myeloma). The reasons for the increased risks are not clear, and scientists are looking at chemical and other occupational exposures common to farming to identify the possible cause or causes.

Farmers are exposed to a variety of potentially harmful substances during their work day, including: pesticides (fungicides, herbicides, insecticides, rodenticides, and others), chemical solvents, fuels and oils, animal viruses, and other microbes. Some of these agents are known or suspected carcinogens.

In the 1980s, National Cancer Institute (NCI) researchers began several studies comparing pesticide use by farmers with cancer to those without the disease (case-control studies). The first of these investigations was a study of Kansas farmers with soft-tissue sarcomas, Hodgkin's disease, and non-Hodgkin's lymphoma (NHL). Published in 1986, this study showed that farmers who used herbicides, especially 2,4-dichlorophenoxyacetic acid (2,4-D), had an excess of NHL as compared to farmers and nonfarmers who did not use these chemicals.

The risk of developing NHL increased with frequency of herbicide use. Farmers who used herbicides on their farms 20 or more days per year had a six times greater risk of developing NHL than nonfarmers. Within the high-

exposure group, farmers who mixed and applied the herbicides themselves had an eight-fold greater risk. Soft-tissue sarcomas and Hodgkin's disease were not linked with use of herbicides.

NCI scientists have now completed case-control studies of NHL among farmers in eastern Nebraska and leukemia among farmers in Iowa and Minnesota. Each study included all cases of these cancers occurring in a specific geographic area. Hospital records and pathology slides from the cases were carefully reviewed by pathologists to verify the cancer diagnoses.

Study subjects, or their next-of-kin, were interviewed for details about the subjects' use of agricultural pesticides and other factors that might be associated with these cancers. Pesticide exposure reported by the cancer patients was compared to exposure reported by randomly selected men without those cancers who lived in the same area.

Non-Hodgkin's Lymphoma

Shelia Hoar Zahm, Sc.D., and collaborators at NCI and the University of Nebraska Medical Center studied 201 men living in 66 counties in eastern Nebraska who developed NHL between 1983 and 1986. The researchers compared the pesticide exposures of these men to exposures of 725 men from the general population who did not have this cancer. Although there was no overall excess of NHL among farmers, farmers who mixed or applied 2,4-D had a 50 percent increased risk of the disease. The risk of NHL also increased with frequency of 2,4-D use. Farmers who used the pesticide for 20 or more days per year had a three-fold higher risk than those not exposed to the chemical.

The longer farmers waited to change into clean work clothes after pesticide application, the higher their risk of NHL. The risk of NHL among farmers who changed out of work clothes immediately after completing the 1

application was similar to that seen among nonfarmers. Farmers who continued to use these work clothes the following day or longer had nearly five times the NHL risk of nonfarmers.

The investigators also looked at the possible effects of pesticides other than 2,4-D, and other factors that might be associated with risk of NHL, such as other agricultural exposures, medical conditions, exposure to radiation, and tobacco use. In other reports, non-2,4-D pesticides, particularly organophosphate insecticides, have also been shown to increase the risk of NHL. The NCI study results suggest that 2,4-D and organophosphate insecticides have independent influences on the risk of cancer. Further evaluation of organophosphate insecticides is necessary to quantify any possible risks associated with their use.

The association of 2,4-D and NHL in Nebraska farmers is consistent with the previous NCI study conducted in Kansas. Pesticide exposures occurring many years in the past are difficult to assess accurately, and tend to cause an underestimation of the cancer risk. Dr. Zahm and her collaborators believe the evidence suggests that the use of 2,4-D in the agricultural setting increases the risk of NHL among persons handling this pesticide frequently.

Leukemia

Linda Morris Brown, M.P.H., and colleagues at NCI, the University of Iowa, and the University of Minnesota studied a total of 578 cases of leukemia diagnosed among men in Iowa and Minnesota between 1981 and 1984 (293 cases in Iowa and 285 cases in Minnesota).[5] To compare the effects of pesticide exposure, 1,245 men without the disease were selected at random from the general population.

The researchers found a slight excess of leukemia, especially chronic lymphocytic leukemia, among farmers. Exposure to specific fungicides,

herbicides (including 2,4-D), or crop insecticides did not increase the risk.

The risk for leukemia was significantly elevated among farmers who used certain pesticides to inhibit insects on animals rather than on crops. The insecticides were: the organophosphates crotoxyphos (11 times greater risk), dichlorvos (2 times), and famphur (2 times); the natural product pyrethrins (4 times); and the chlorinated hydrocarbon methoxychlor (2 times).

Risk of leukemia did not increase consistently with how often any pesticide was used. However, the greatest risk among farmers using chlordane, DDT, dichlorvos, and malathion occurred among those using the chemicals on animals 10 or more days a year. The risk of leukemia was further increased among those farmers who had used insecticides at least 20 years before the study.

The investigators improved the accuracy of the risk estimate from individual pesticides by accounting for the cancer risk from smoking, nonfarming occupational and chemical exposures, family history of cancer, and other factors. Larger studies are still needed to fully evaluate the effects of any single pesticide on leukemia risk. The increased cancer risk from animal insecticides versus crop pesticides may result from closer proximity to animals on a regular basis. Animal insecticides need to be carefully scrutinized in future studies.

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For additional information about cancer, write to the Office of Cancer Communications, National Cancer Institute, Bethesda, MD 20892, or call the Cancer Information Service toll free at 1-800-4-CANCER. Spanish-speaking staff members are also available during daytime hours.

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Cancer Facts

NATIONAL CANCER INSTITUTE

Office of Cancer Communications

Building 31 Room 10A24
Bethesda, Maryland 20892

September 1991

Dogs Exposed to Herbicide Develop More Lymphomas

Dogs whose owners used a common weed killer on their lawns have an increased rate of an immune system cancer (lymphoma) closely related to human non-Hodgkin's lymphoma, according to a National Cancer Institute (NCI) study. The findings are consistent with previous studies showing that humans have an increased risk of non-Hodgkin's lymphoma due to frequent exposure to the herbicide (weed killer) 2,4-dichlorophenoxyacetic acid (2,4-D).[1-3]

Published in the September 4 issue of the Journal of the National Cancer Institute,* the study showed that owners of dogs diagnosed with malignant lymphoma applied the herbicide 2,4-D to their lawns and/or employed professional lawn care companies to treat their lawns about a third more often than owners of dogs that did not have the disease. When the owners alone applied four or more treatments of liquid or granular 2,4-D to the lawn each year, the risk of lymphoma among their dogs doubled.

Dogs and humans are known to have similar reactions to some cancer-causing substances, and dogs may signal cancer risk in people exposed to the same substances.[4-8] "This study supports the idea that exposure to 2,4-D, as used for lawn care, plays a role in causing lymphomas in dogs," said Howard M. Hayes, D.V.M., of NCI's Environmental Epidemiology Branch, the principal

*The study is titled "A case-control study of canine malignant lymphoma: positive association with dog owner's use of 2,4-dichlorophenoxyacetic acid herbicides."

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investigator for the study. "The study also suggests that the potential health hazards of human exposure to 2,4-D at home warrant further study."

Dogs exposed to 2,4-D consistently showed an increased risk of lymphoma compared to dogs not exposed to the herbicide, regardless of the sex or breed of the dog. In general, male dogs are normally at a slightly higher risk than female dogs. Boxer, bull mastiff, and Scottish terrier breeds are also more frequently diagnosed with this disease.

Separate analyses showed no increase in lymphomas due to exposure to other chemicals including: flea- and tick-control products, household insecticides, tobacco smoke, commercial cleaners (on draperies and carpeting), and outdoor insecticides and/or fertilizers.

No list of chemical products was provided to the owners during the written or telephone interviews with the researchers. "We did not want to 'prompt' the owners to identify certain products or chemicals," explained Hayes.

Hayes and his colleagues interviewed the owners of dogs treated for lymphomas (491 dogs), other cancers (479 dogs), or other illnesses (466 dogs) at one of three veterinary teaching hospitals. Information was gathered about the amount of tobacco smoked in the house, the dog's life history, use of chemicals (in the house, on the dog, and on the lawn), and the dog's access to the yard. Dogs with no access to their owners' yards were considered to be unexposed. Dogs with illnesses known or thought to be related to chemical exposures (lower urinary tract cancer, nonspecific skin inflammations, and nerve disorders) were not included in the study.

Other authors of the study are Robert E. Tarone, Ph.D., and Kenneth P. Cantor, Ph.D., from NCI; Carl R. Jessen, D.V.M., from the College of Veterinary Medicine, University of Minnesota, St. Paul, Minn.; Dennis M.

McCurnin, D.V.M., from the College of Veterinary Medicine, Colorado State University, Fort Collins, Colo.; and Ralph C. Richardson, D.V.M., from the School of Veterinary Medicine, Purdue University, West Lafayette, Ind.

References

1. Blair A: Herbicides and non-Hodgkin's lymphoma: New evidence from a study of Saskatchewan farmers. J Natl Cancer Inst 82:544-545, 1990.

2. Hoar SK, Blair A, Holmes FF, et al: Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. J Amer Med Assoc 256:1141-1147, 1986.

3. Zahm SH, Weisenburger DD, Babbitt PA, et al: A case-control study of non-Hodgkin's lymphoma and the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) in eastern Nebraska. Epidemiol 1:349-356, 1990.

4. Hueper WC, Wiley FH, Wolfe HD: Experimental production of bladder tumors in dogs by administration of beta-napthylamine. J Indust Hyg Toxicol 20:46-84, 1938.

5. Glickman LT, Domanski LM, Maguire TG, et al: Mesothelioma in pet dogs associated with exposure of their owners to asbestos. Environ Res 32:305-313, 1983.

6. Hayes HM, Tarone RE, Casey WW, et al: Excess of seminomas observed in Vietnam service U.S. military working dogs. J Natl Cancer Inst 82:1042-1046, 1990.

7. Tarone RE, Hayes HM, Hoover RN, et al: Service in Vietnam and risk of testicular cancer. J Natl Cancer Inst (in press, 1991).

8. Hayes HM, Hoover RN, Tarone RE: Bladder cancer in pet dogs: A sentinel for environmental cancer? Am J Epidemiol 114:229-233, 1981.

Attached is a list of questions and answers about the study.

Questions and Answers

Study of Herbicide Exposure in Dogs with Lymphoma

1. What is lymphoma?

Lymphoma is a general term for cancers of the immune system, the complex network of specialized organs and cells that help defend the body against disease and infection. The two main types of lymphoma found in humans are called Hodgkin's disease and non-Hodgkin's lymphoma. Malignant lymphoma in dogs is considered the canine equivalent of non-Hodgkin's lymphoma in humans.

2. How common is malignant lymphoma in dogs? What causes the disease?

Malignant lymphoma is a common cancer in dogs. About one out of seven dogs diagnosed with cancer at university veterinary teaching facilities in the United States has lymphoma.

The causes of lymphoma in dogs are not fully understood. The disease occurs at all ages but more frequently in older dogs. Slightly more male dogs than female dogs get lymphoma. Boxers, bull mastiffs, and Scottish terriers are more likely to develop this cancer than other breeds of dogs. Although lymphoma in other laboratory and domestic animals has been associated with a certain type of virus (retrovirus), no such association has been observed in dogs.

3. How common is lymphoma in humans? What causes the disease?

In the United States, over 37,000 people will be diagnosed with non-Hodgkin's lymphoma and another 7,400 with Hodgkin's disease in 1991. Between 1973 and 1988, the incidence rate for non-Hodgkin's lymphoma increased over 50 percent; one of the largest increases for any cancer.

As with dogs, scientists cannot yet explain the causes of lymphoma in humans. A number of possible causes are being studied, including immune system damage, exposure to certain chemicals, viruses, heredity, and radiation.

4. Can humans "catch" lymphoma from their pets?

There is no evidence that any form of cancer can be spread from pets to their owners. Although a retrovirus is known to cause lymphoma in cats, humans are not susceptible to this virus.

5. What did this study show?

The study showed that dogs ing in households in which the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) was applied to the lawn, by owners or commercial lawn care companies, developed malignant lymphoma more

frequently than dogs in households where this was not the case. The study was not designed to look at the causes of other cancers.

6. Why is the study important?

The study points out the need to conduct additional studies on the human health implications of 2,4-D exposure in the home environment. Dogs and humans may react similarly when exposed to a cancer-causing substance.

7. What is 2,4-D and what products contain it?

The chemical 2,4-D is used to kill broadleaf weeds (not crab grass) on lawns and in gardens. It is one of the most frequently used herbicides in the United States. Many companies manufacture and use it in lawn and garden weed killers. This herbicide is listed on the label as 2,4-D, 2,4-D acid, or 2,4-dichlorophenoxyacetic acid.

8. Is the risk the same from liquid and granular herbicides?

The researchers found no difference in the risk of lymphoma in dogs between owners who used products containing liquid 2,4-D and owners who used products with granular (dry) 2,4-D.

9. How do dogs come into contact with 2,4-D?

Dogs can be exposed to 2,4-D by walking, rolling, and lying on a treated lawn; licking their fur; and eating treated grass. Researchers do not believe that dogs are harmfully exposed by inhaling the herbicide.

10. What are pesticides and herbicides?

A pesticide is a poison used to destroy "pests." The term includes herbicide (a substance that is destructive to plants), insecticide (an agent that kills insects), rodenticide (a poison for rodents), and fungicide (a compound that destroys molds).

11. Could exposure to other substances have caused the increase in canine lymphoma seen in this study?

In this study, the researchers also looked at use of flea and tick control products, use of household insecticides, cigarette smoking in the home, frequency of commercial cleaning of draperies and carpets, and the use of insecticides and/or fertilizers in the yard. Exposure to these substances was not shown to increase the risk of lymphoma. The possibility exists that exposure to other unstudied substances may have caused the increase in the incidence of lymphoma.

12. Is there evidence that exposure to 2,4-D increases the risk of lymphoma in humans?

Several studies of pesticide use among farmers have led scientists to believe that the use of phenoxyacetic acid herbicides in agriculture, in particular 2,4-D, increases the risk of non-Hodgkin's lymphoma among people handling this herbicide frequently.

13. Has exposure to 2,4-D been linked to other types of cancer in humans?

At this time, there is no evidence linking exposure to 2,4-D to increased risk of other types of cancer in humans. NCI continues to study the potential hazards of exposure in specific populations, including lawn care workers, herbicide applicators, and farmers.

14. What should be done to reduce exposure to 2,4-D?

The herbicide 2,4-D is absorbed by plants and broken down by sunlight within a few days of application. Exposure can be minimized by limiting the amount of time spent in treated areas for several days.

15. Are children at risk if they play on lawns treated with this chemical?

This study showed that dogs whose owners used 2,4-D on the lawn were more likely to develop malignant lymphoma. While dogs and humans exposed to the same cancer-causing agent may develop the same disease, the results of this study cannot prove that using herbicides on the lawn is dangerous to children. Parents who are concerned should limit their children's exposure to treated areas.

16. Is 2,4-D the same chemical as Agent Orange?

Agent Orange, a mix of herbicides used to strip leaves from trees in Vietnam during the war, was a combination of 2,4-D and 2,4,5-T (2,4,5-trichloro-phenoxyacetic acid). The chemical commonly known as "dioxin" (2,3,7,8-tetrachlorodibenzo-p-dioxin) often forms when 2,4,5-T is manufactured and can be found as an impurity in that herbicide.

17. Is further research planned?

NCI is currently conducting several studies of the cancer risk of frequent exposure to 2,4-D including studies of cancer among lawn care workers, cancer in county herbicide applicators, and brain and stomach cancer among farmers. These studies will be completed in two to four years.

NCI and the NCI-funded Children's Cancer Study Group are also conducting a study of the potential causes of childhood leukemia, including exposure

to herbicides like 2,4-D, and other pesticides. The study began in 1989 and is expected to conclude in 1994.

An NCI study of the risk of testicular cancer in men who served in Vietnam, and thus had possible exposure to Agent Orange and other chemicals, will be published in October. A previous NCI study of military guard dogs in Vietnam showed an increased risk of seminomas (testicular cancers).

18. **Where can more information about environmental hazards from exposure to herbicides and other pesticides be obtained?**

Questions about the potential environmental and health hazards of pesticides can be answered by calling the National Pesticide Telecommunications Network (NPTN) at 1-800-858-PEST (1-800-858-7378). NPTN is sponsored by the U.S. Environmental Protection Agency.

19. **Where can a dog be treated for cancer?**

For information on treatment for dogs with cancer, contact any college of veterinary medicine, the local office of the Veterinary Medical Society, or a private veterinarian.

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For additional information about cancer, write to the Office of Cancer Communications, National Cancer Institute, Bethesda, MD 20892, or call the Cancer Information Service toll free at 1-800-4-CANCER. Spanish-speaking staff members are available.

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REPORTS

Case-Control Study of Canine Malignant Lymphoma: Positive Association With Dog Owner's Use of 2,4-Dichlorophenoxyacetic Acid Herbicides

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A hospital-based case-control study of companion dogs examined the risk of developing canine malignant lymphoma associated with the use of chemicals in and about the home. Information from a self-administered owner questionnaire and/or a telephone interview of about 491 cases, 466 nontumor controls, and 479 tumor controls indicated that owners in households with dogs that developed malignant lymphoma applied 2,4-dichlorophenoxyacetic acid (2,4-D) herbicides to their lawn and/or employed commercial lawn care companies to treat their yard significantly more frequently than control owners (odds ratio = 1.3). In addition, the risk of canine malignant lymphoma rose to a twofold excess with four or more yearly owner applications of 2,4-D. The findings in this study are consistent with occupational studies in humans, which have reported modest associations between agricultural exposure to 2,4-D and increased risk of non-Hodgkin's lymphoma, the histology and epidemiology of which are similar to those of canine malignant lymphoma. The present study suggests that human health implications of 2,4-D exposure in the home environment should receive further investigation. [J Natl Cancer Inst 83:1226–1231, 1991]

Non-Hodgkin's lymphoma has had the second fastest increase in cancer incidence rates of all human cancers in the United States over the last 15 years (*1*). The etiology of non-Hodgkin's lymphoma is unclear, although there are several well-established risk factors. Known risk factors include age, male gender (*2*), congenital immunodeficiency states, infection with the human immunodeficiency virus (*3*), other immune-altering conditions [e.g., transplant recipients (*4*)], chemotherapy for Hodgkin's disease (*5*), and being a member of a lymphoma-prone family (*6*).

Evidence continues to accumulate implicating phenoxyacetic acid herbicides, in particular 2,4-dichlorophenoxyacetic acid (2,4-D), with risk of non-Hodgkin's lymphoma in farmers (*7*). A population-based case-control study of non-Hodgkin's lymphoma in Kansas farmers reported a 2.2-fold excess risk for those who frequently mixed or applied herbicides (specifically 2,4-D) that rose to over sixfold among frequent users (*8*). A mortality study of 70 000 Saskatchewan farmers, age 35 years and older, showed a significant positive association between non-Hodgkin's lymphoma and the number of acres sprayed with herbicides, predominantly (i.e., 75%–90% by weight) 2,4-D (*9*). A recent case-control study of non-Hodgkin's lymphoma in Nebraska found a significant threefold excess in farmers who mixed or applied 2,4-D more than 20 days per year (*10*). With the extensive use of phenoxyacetic acid herbicides in the United States since the mid-1960s (*11*) and the frequent use of 2,4-D on public park lands, golf courses, and private lawns (*12*), particularly by commercial lawn care companies (*13*), the potential exposure opportunities to people and farm and companion animals continue to be substantial.

Malignant lymphoma, the canine equivalent of non-Hodgkin's lymphoma, is the most frequently diagnosed hematolymphopoietic cancer in dogs (*14*). Approximately one in seven companion dogs brought to medical attention at U.S. university veterinary teaching facilities and diagnosed with any type of malignancy will have malignant lymphoma. Presently, seven new cases of malignant lymphoma are diagnosed per 1000 canine patient years-at-risk at U.S. university veterinary medical teaching hospitals (Hayes HM: unpublished results).

Although canine malignant lymphoma has been extensively studied, its etiology is obscure. The disease occurs at all ages, but it is more frequently diagnosed as the dog grows older (*15*); as in humans, there is a male excess. Several breeds have been identified at increased risk (*14*), including the boxer (*16*), bull mastiff (*17*), and Scottish terrier (*18*). Unlike malignant lymphoma in other laboratory and domestic animal species, no canine retrovirus has been associated unequivocally with the disease, although virus-like

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particles in affected tissue have been reported (*19-21*). Naturally occurring canine malignant lymphomas are similar to human non-Hodgkin's lymphoma in histologic type, biological behavior, and cell responses to the same chemotherapeutic agents (*22-24*). These malignancies have occurred in companion pets and their owners in the same household (*25,26*).

The pet dog is normally fastidious about its grooming habits. It is common for a dog to clean itself by licking its paws, thereby ingesting any substances it has walked in or that have been applied to its body accidentally or intentionally as therapy or prevention. The companion dog is not generally subjected to direct occupational exposures experienced by its owners, although it may have contact with particulate matter or residues brought into the home on its owner's clothing and shoes (*27*). Thus, environmentally related cancer in the pet dog may be considered primarily the result of local exposures in and around the owner's home.

To investigate canine malignant lymphoma and its relationship to chemical exposures, particularly the herbicide 2,4-, we conducted a case-control study of dogs diagnosed with malignant lymphoma at three university veterinary medical teaching hospitals. We used a questionnaire to obtain information from dog owners on demographics, lifestyle, and household and lawn chemical exposure.

Materials and Methods

Subjects

Dogs with histopathologically confirmed malignant lymphoma, newly diagnosed from January 1984 through February 1988, were identified using computerized medical record abstracts from three veterinary medical teaching hospitals that participate in the Veterinary Medical Data Program (*28*). The collaborating veterinary medical teaching hospitals were the University of Minnesota at St. Paul, Purdue University at West Lafayette, Ind., and Colorado State University at Ft. Collins.

Two comparison groups of hospital-based control animals, matched by age group, but not by sex, were chosen from dogs seen at the same veterinary medical teaching hospital in the same year as the identified case, with one-to-one matching for each control group. Age was reported in range values on the Veterinary Medical Data Program medical record abstract (i.e., 1, 2-3, 4-6, 7-9, 10-14, and 15+ years). The first control group was selected from all other tumor cases diagnosed at the veterinary medical teaching hospital, excluding transitional cell carcinomas of the lower urinary tract because of a potential etiology related to chemical exposures. Twenty percent of these tumor controls had bone cancer, 19% skin tumors (excluding melanoma), 13% oral and/or nasal tumors, 7% mast cell tumors, and 41% other neoplasms. The second control group was selected from dogs seen for any other diagnostic reason, excluding those with conditions possibly related to chemical exposures (e.g., nonspecific dermatitis, neuropathies). Twenty-six percent had degenerative diseases, 18% broken bones or soft tissue trauma, 14% diagnostic examinations or elective surgery, 14% infections, and 28% other conditions.

Written Questionnaire/Telephone Interview

Owners of selected case and control animals were identified by the participating veterinary medical teaching hospital. A standardized questionnaire was sent to the last known address of each owner. The cover letter to the questionnaire noted that the dog in question had been seen at the veterinary medical teaching hospital on a particular date and was selected to be part of a study being conducted by the National Institutes of Health. No mention was made of the animal's diagnosis at that time or of the disease of interest in the study. The questionnaire requested information about demographic characteristics of all people living in their home, basic information about the pet's life history, household use of chemicals (in and about the home) including those directly applied to the pet, and personal use of and/or the employment of commercial companies applying chemicals of whatever kind on the lawn and garden. In addition, owners were asked about opportunities for exposure of their pets to lawn and garden chemicals, including frequency and seasonality of access to the yard. The questionnaire did not provide a list of chemicals which the owner could consult in responding to the various questions regarding home, lawn, and gardening chemicals.

After 2 weeks, owners who did not respond were sent another letter requesting participation. U.S. Postal Service forwarding addresses were used when available. If there was no subsequent response, an attempt was made to conduct a telephone interview using the standardized questionnaire. Trained interviewers were not told the name of the disease or exposures of interest or which households had case subjects.

Data Analysis

The relative risk, as estimated by the maximum likelihood estimate of the odds ratio (OR) (*29*), was used as the measure of association between malignant lymphoma and the variables of interest. Summary ORs and 95% confidence intervals (CIs) were calculated, stratifying to control for potential confounding factors as judged by a change in the effect estimate. The Haldane-Smith-Mantel procedure was used to test for trends in proportions (*30*). Logistic regressions evaluated the effects of several factors simultaneously (*31*).

Results

Malignant lymphoma was diagnosed in 588 canine patients that met eligibility criteria. Questionnaires were returned or telephone interviews were completed by 491 (84%) households with dogs having malignant lymphoma (case households). Of the 583 nontumor control households, 466 (80%) responded; of the 586 tumor control households, 479 (82%) responded. Forty-five percent of the total completed responses came from telephone interviews. Most nonresponses were due to the inability to contact the owner. Only four owners (owners of one case animal and three tumor controls) who were contacted refused to participate.

There were no discernible differences between study groups in demographic variables, although median income was slightly higher for case households versus control households, as was the number of household members supported by that income (Table 1). Slightly fewer case than

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Table 1. Demographics, lifestyle and environmental characteristics of reporting households expressed as a percentage of the eligible study group

Characteristic	Malignant lymphoma (n = 491)	Nontumor control (n = 466)	Tumor control (n = 479)
Median income*	$43 500	$40 500	$39 500
Mean household members supported by income†	2.77	2.67	2.68
Mean No. of years dog lived with owner	9.32	9.05	9.75
Home location			
In rural area	29.5	32.8	32.6
Within 2 miles of factory of plant that emitted gases, fumes, or particles of some kind	12.4	13.5	16.9
Pet's diet			
Commercial dog food	97.6	97.0	97.7
Drinking water from community source	69.2	72.5	70.4
Potential for in-home chemical exposures			
Dog allowed inside home	95.7	95.3	93.3
Home had carpet/area rugs	93.9	93.3	92.5
Carpets or rugs ever commercially cleaned	12.1	12.6	11.1
Drapes present in home	88.8	86.7	87.5
Drapes ever commercially cleaned	45.9	46.3	48.0
Cigarettes smoked in home	47.5	46.4	48.2
Insecticides used in home	37.9	38.0	42.2
Ever applied flea and tick preparations	6.3	7.1	7.6
Potential for exposures outside of home			
Owner had yard used by dog	95.7	94.9	94.8
Chemicals ever used on yard during dog's lifetime	67.2	67.6	64.9
Dog ever in American Kennel Club show or hunting trial	10.6	11.6	10.6
Dog ever commercially groomed	2.2	3.9	2.5

*Percent not answering question was 8.1% of case households, 8.4% of nontumor control households, and 9.8% of tumor control households.

†Percent not answering question was 3.5% of case households, 4.3% of nontumor control households, and 5.2% of tumor control households.

control households were located in rural areas. However, case households were less frequently located within 2 miles of industrial plants or facilities reported as emitting into the atmosphere.

Dogs studied in this investigation usually ate commercial dog food, and most were provided drinking water from a community source. They were usually allowed inside their owner's home, and most of these homes had carpet and/or area rugs and window drapes. Most dogs were allowed access to their owner's yard. Lifestyle experiences and exposures inside and outside the home were quite similar between the two control groups. Because of a lack of discernible differences between tumor and nontumor control households, subsequent analyses utilized pooled controls (Table 1). Using mixed breed dogs as the standard (OR = 1), canine breeds previously identified as having a low risk of malignant lymphoma (*14*) were found to be underrepresented in the case series (OR = 0.3); breeds expected to be at high risk had a twofold excess representation (Table 2). Approximately two thirds of all households surveyed had used lawn chemicals of some type on their yards (OR = 1.1). When all dogs who did not have access to their owner's yard were classified as unexposed, the OR for owner application of 2,4-D and/or the employment of commercial lawn care service was 1.3 (95% CI = 1.04-1.67). No difference in OR was detected for owner application of 2,4-D only (OR = 1.3) and sole use of commercial lawn treatments (OR = 1.3); however, the OR for owner application plus the employment of commercial lawn service was 1.9 (95% CI = 0.88-4.14) (Table 3). Adjustment for age in these analyses did not change the ORs. Liquid 2,4-D was sprayed by fewer owners of case animals than owners of control animals applying 2,4-D, a difference that was not significant.

A positive trend ($P<.02$) was evident for the yearly number of owner applications of 2,4-D. This trend was significant ($P<.05$) for both long-term use (≥5 years' duration prior to diagnosis) and short-term use (<5 years' duration). No significant association was observed between malignant lymphoma risk and duration of owner application of 2,4-D (OR = 1.5 for ≥5 years of use; OR = 1.3 for <5 years of use). We could not distinguish possible latency effects from duration effects, as the questionnaire did not ask for the date on which the owner began 2,4-D use or the employment of professional lawn care services. No discernible trend was observed for yearly number of commercial lawn treatments (Table 3).

Multivariate analyses considered the ever-never variables of flea and tick control exposures (i.e., collars, powder, spray, dip), in-home use of insecticides, cigarette smoking, the presence of carpet and window drapes (and whether they were commercially cleaned), use of yard insecticides and/or fertilizers, dog breed risk group and sex, and application of 2,4-D by owner and/or commercial lawn care service. Separate analyses considered 1) number of applications per year of flea- and tick-control products, 2) number of applications of household insecticides per year, number of cigarette packs smoked per year by household members, and the number of times carpets and drapes were commercially cleaned per year for dogs allowed inside the owner's home, and 3) number of applications per year of yard insecticides and fertilizers for those yards available to the dog. The only factors related to case households in the multivariate analyses were breed risk group and owner application of 2,4-D and/or use of a commercial lawn care service.

When the OR for owner application of 2,4-D and/or commercial lawn treatments was evaluated for each breed risk group, an inverse relationship with breed risk

Table 2. ORs of canine malignant lymphoma by host

Characteristic	No. of cases	No. of controls	OR	95% CI
Breed*				
Mixed breed	128	243	1.0	
Low-risk breeds combined	16	94	0.3	0.17-0.59
Average-risk breeds combined	228	496	0.9	0.66-1.14
High-risk breeds combined	119	112	2.0	1.40-2.83
Sex*				
Female	237	508	1.0	
Male	254	437	1.2	0.97-1.54

*Adjusted for sex in calculating breed risk group ORs and breed risk group in calculating the effect of sex.

Table 3. ORs of canine malignant lymphoma by exposure

Characteristic	No. of cases	No. of controls	OR	95% CI
Owner application of any yard chemical and/or commercial lawn treatment*				
No	161	319	1.0	
Yes	330	626	1.1	0.84-1.37
Owner application of 2,4-D and/or commercial lawn treatment*				
None or dog never allowed in yard	300	641	1.0	
Yes	191	304	1.3	1.04-1.67
Commercial lawn treatment only*	115	189	1.3	0.96-1.70
Owner application of 2,4-D only*	60	99	1.3	0.90-1.90
Owner application of 2,4-D and commercial lawn treatments*	16	16	1.9	0.88-4.14
No. of commercial lawn chemical treatments/y†				
0	300	641	1.0	
1	16	25	1.4	0.70-2.84
2	20	25	1.5	0.75-2.86
3	19	33	1.1	0.60-2.14
≥4	76	122	1.3	0.95-1.87
No. of owner applications of 2,4-D/y†				
0 or dog never allowed in yard	300	641	1.0	
1	20	34	1.3	0.72-2.50
2	28	47	1.3	0.74-2.13
3	11	17	1.3	0.57-3.13
≥4	17	17	2.0	0.92-4.15
			Trend test	$P<.02$

*Adjusted for sex and breed risk group.
†Adjusted for sex and breed risk group; includes 16 cases and 16 control households where the owner applied 2,4-D and also had commercial lawn treatments.

level was found, the OR being highest for low-risk breeds (Table 4). Male dogs, known to be at elevated risk for malignant lymphoma, exhibited the same OR (1.3) as females for owner application of 2,4-D and/or commercial lawn treatment (Table 4).

To test recall, owners were asked if their dog had died; if so, they were asked if it had cancer and the cancer type was requested. Among the owners of case animals who reported never using 2,4-D and/or commercial lawn care services or never allowing their pet access to their yard, slightly more knew that their pet died of malignant lymphoma compared with the case households that applied 2,4-D or employed commercial lawn services (Table 5).

Discussion

We found a modest association (OR = 1.3; 95% CI = 1.04-1.67) between malignant lymphoma in companion dogs and their owners' applying 2,4-D on their lawn and/or using commercial lawn care services, with the risk rising with increasing number of owner applications per year. These findings are consistent with studies suggesting that agricultural 2,4-D use increases the risk of non-Hodgkin's lymphoma among farmers (*8-10*). Also consistent with human studies was the lack of a significant association with duration of 2,4-D application by the owner.

Findings of case-control interview studies may be biased because of differential recall of cases and referents. In the last several years, results from several studies of this design have suggested links between use of phenoxyacetic acid herbicides and development of non-Hodgkin's lymphoma in humans. Some have suggested problems in recalling may explain these associations (*13*). In the current study, recall bias could have occurred if owners of case animals were more likely to remember using such herbicides on their yards and, therefore, exposing their pets. The lack of any association, among cases, of owner's knowledge of their pet's type of cancer at death and opportunity for exposure to 2,4-D strongly argues against such a bias in this study (Table 5).

Any recall bias related to socioeconomic status probably did not affect this study because case and control households were strikingly similar in median income, number of household members supported by such income, use of commercial dog food, home lifestyle (service by municipal water supply, presence of carpet/area rugs and drapes, access inside the home by the dog), or the presence of yards. Bias may also arise from an unwillingness of certain selected subjects to participate. The percentages of responses from case and control household groups, however, were nearly the same. The major limiting factor was the ability to locate owners, not an unwillingness to participate. Only four of 1440 successfully contacted owners refused to participate.

Recall may be hampered by the lapsed time between the time period of interest and the questionnaire/interview date. The response data analyzed in this study were acquired 10-58 months after the selected animals were seen at the veterinary medical teaching hospital; however, control dogs were matched to case dogs by age and year of medical attention. Therefore, the lapsed time between the period of interest (the years the dog lived with its owner until the date of university treat-

Table 4. ORs for exposure to owner-applied 2,4-D and/or commercial lawn treatments for malignant lymphoma by canine breed risk groups and by sex

Characteristic	No. of cases		No. of controls		OR*	95% CI
	Exposed	Unexposed	Exposed	Unexposed		
Risk group						
Mixed breed	45	83	80	163	1.1	0.69-1.78
Low-risk breeds	8	8	29	65	2.0	0.60-6.89
Average-risk breeds	91	137	155	341	1.4	1.03-2.03
High-risk breeds	47	72	40	72	1.2	0.67-2.10
Sex						
Female	88	149	152	356	1.3	0.94-1.87
Male	103	151	152	285	1.3	0.93-1.84

*Adjusted for sex in calculating breed risk group ORs and breed risk group in calculating the effect of sex.

Table 5. Owner's recall of pet's malignancy at death by yard chemical use among malignant lymphoma case households

Yard chemical use	No.	Owner's knowledge of malignant lymphoma, %
Owner applied 2,4-D only	60	61.3
Commercial lawn treatment only	115	60.8
Owner applied 2,4-D and also used commercial lawn care treatments	16	58.8
Owner neither applied 2,4-D nor used a commercial lawn care company or the pet was not allowed in the yard	300	64.8

ment) and the date of the questionnaire or interview was approximately the same for owners of case and control dogs.

It is possible that unmeasured confounders could explain the risk, but we collected data on the most likely concomitant exposures in the household environment. Household insecticides, contact insecticides for flea and tick control, and outdoor insecticides played no discernible role in the association between 2,4-D exposure and development of malignant lymphoma. We controlled for sex and breed association in all analyses; these two factors play a role in the occurrence of the disease, but they did not strongly affect the risk from 2,4-D exposure. Although viruses have been associated with lymphoma development in many animal species (*32*), they have not been linked to lymphoma development in the dog. While viral infection of some type may be an important factor, it is unlikely to be responsible for the significant association between canine malignant lymphoma development and owner use of 2,4-D and/or commercial lawn care services.

The type of 2,4-D applied by the owner, liquid spray or granular, had little influence on risk. The consistency between the ORs for male and female case animals with 2,4-D exposure also argues against inhalation of herbicide spray as a likely route of exposure, because the male dog's sniff-scent marking tendencies might place males at greater risk than females (*33*). Occupational studies of herbicide exposures by agricultural workers generally agree that inhalation is a minor source of human exposure (*34*).

A major weakness of the current study is the lack of precise exposure data for herbicides. Frequency of application was the primary measure of exposure used in this study. The lack of a clear pattern of association with total number of yearly commercial lawn treatments contrasts with the consistent application-response relationship ($P<.02$ for trend) exhibited for owner application of 2,4-D (Table 3). The yearly number of applications of 2,4-D by the owner is more likely to reflect the actual 2,4-D exposure opportunity for pet dogs than the number of lawn treatments by commercial lawn care companies because some commercial treatments during each year may contain only fertilizer and/or insecticides and, thus, not lead to herbicide exposure.

In a laboratory carcinogenicity study, 12 male and 12 female beagles were exposed to 2,4-D in their diet for 2 years (*35*). No malignant tumors were reported in any of the exposed dogs or in the three male or three female control dogs. A related 2-year feeding study of 2,4-D in Osborne-Mendel rats (*35*) resulted in an increased incidence of lymphosarcomas in exposed male rats (10 of 125 exposed male rats developed lymphosarcomas compared with 0 of 25 control rats; Fisher's exact test yields $P = .15$) but no evidence of increased tumors in female rats (1 of 125 exposed female rats compared with 0 of 25 control rats).

Studies involving 18 male and 18 female mice from each of two strains gave no evidence of carcinogenicity for 2,4-D fed for 18 months (*36*). The isopropyl, butyl, and isooctyl esters of 2,4-D were also tested, and no significant increases in tumor incidence were observed (*36*). In companion studies, 2,4-D and its esters were administered by subcutaneous injection in 18-month carcinogenicity experiments. Although the results of the injection studies were not given in the initial report (*36*), a significant increase in reticulum cell sarcomas was reported for the isooctyl ester of 2,4-D in one female mouse strain (*37*). No reticulum cell sarcomas were observed in the 18 male mice of the same strain similarly exposed. Thus, although lymphoreticular tumors have been found in excess in two rodent studies, laboratory animal experiments provide only weak support for a role of 2,4-D in lymphoreticular carcinogenicity.

The current investigation began with an a priori hypothesis that exposure to 2,4-D might be associated with development of malignant lymphoma in the pet dog. Our findings support this proposition, with a modest statistically significant OR of 1.3 for owner application of 2,4-D and/or commercial lawn treatments. Further support derives from the higher risk observed for pets of owners who applied their own 2,4-D in addition to exposure to commercial applications (OR = 1.9; 95% CI = 0.88-4.14) and the increase in risk to a twofold excess with four or more owner applications per year. In view of a suggested link between non-Hodgkin's lymphoma in humans and farm exposures to 2,4-D, and because malignant lymphoma

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in the dog is considered the equivalent of non-Hodgkin's lymphoma in humans, our finding of an association between 2,4-D exposure and development of malignant lymphoma in companion dogs suggests that the human health implications of 2,4-D exposure in the home environment warrant further investigation.

References

(1) National Center for Health Statistics: Cancer Statistics Review 1973-87. DHHS Publ No. (NIH)90-2789. Bethesda, Md: National Center for Health Statistics, 1990

(2) Surveillance, Epidemiology, and End Results: Incidence and Mortality Data, 1973-77. Natl Cancer Inst Monogr 57:1–1082, 1981

(3) Frieter CE: Acquired immunodeficiency syndrome-associated lymphomas. *In* The Lymphomas: Current Concepts in Patho-genesis and Management. J Natl Cancer Inst Monogr 10:45–54, 1990

(4) Hoover R, Fraumeni JF Jr: Risk of cancer in renal-transplant recipients. Lancet 2:55–57, 1973

(5) Tucker MA, Coleman CN, Cox RS, et al: Risk of second cancers after treatment for Hodgkin's disease. N Engl J Med 318:76–81, 1988

(6) Greene MH: Non-Hodgkin's lymphoma and mycosis fungoides. *In* Cancer Epidemiology and Prevention (Schottenfeld D, Fraumeni JF Jr, eds). Philadelphia: Saunders 1982, pp 754–778

(7) Blair A: Herbicides and non-Hodgkin's lymphoma: New evidence from a study of Saskatchewan farmers. J Natl Cancer Inst 82:544–545, 1990

(8) Hoar SK, Blair A, Holmes FF, et al: Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. JAMA 256:1141–1147, 1986

(9) Wigle DT, Semenciw RM, Wilkins K, et al: Mortality study of Canadian male farm operators: Non-Hodgkin's lymphoma mortality and agricultural practices in Saskatchewan. J Natl Cancer Inst 82:575–582, 1990

(10) Zahm SH, Weisenburger DD, Babbitt PA, et al: A case-control study of non-Hodgkin's lymphoma and the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) in eastern Nebraska. Epidemiology 1:349–356, 1990

(11) Eichers TR, Andrilenas PA, Anderson TW: Farmers' Use of Pesticides in 1976. Agricultural Economic Report 418. Economics, Statistics, and Cooperatives Service. Washington, DC: USDA, 1978

(12) International Agency for Research on Cancer: Some fumigants, the herbicides 2,4-D and 2,4,5-T, chlorinated dibenzodioxins and miscellaneous industrial chemicals. IARC Monogr Eval Carcinog Risk Chem Man 15:1–354, 1977

(13) Council for Agricultural Science and Technology: Comments from CAST, Perspectives on the safety of 2,4-D. Ames, Iowa: CAST, December 1987

(14) Priester WA, McKay FW: The occurrence of tumors in domestic animals. Natl Cancer Inst Monogr 54:1–210, 1980

(15) Schneider R: Comparison of age- and sex-specific incidence rate patterns of the leukemia complex in the cat and the dog. JNCI 70:971–977, 1983

(16) Priester WA: Canine lymphoma: Relative risk in the boxer breed. JNCI 39:833–845, 1967

(17) Osgoss DE: A prospective survey of familial canine lymphosarcoma. J Natl Cancer Inst 72:909–912, 1984

(18) Hayes HM: Hospital prevalence of cancer in the Scottish terrier. *In* Scottish Terrier Club of America Handbook (Cooke CM, Hach S, eds). 3rd ed. Lynchburg, Va: Scottish Terrier Club of America, 1986, pp 158–167

(19) Chapman AL, Bopp WJ, Brightwell AS, et al: Preliminary report on virus-like particles in canine leukemia and derived cell cultures. Cancer Res 27:18–25, 1967

(20) Cohen H, Chapman AL, Ebert JW, et al: Cellular transmission of canine lymphoma and leukemia in beagles. J Natl Cancer Inst 45:1013–1023, 1970

(21) Rudolph R: Virus-like structures in canine lymphatic leukosis tumor cells. Berl Munch Tierarztl Wochenschr 84:68–70, 1971

(22) MacEwen EG, Brown NO, Patnaik AK, et al: Cyclic combination chemotherapy of canine lymphosarcoma. J Am Vet Med Assoc 178:1178–1181, 1981

(23) Weller RE, Theilen GH, Madewell BR: Chemotherapeutic responses in dogs with lymphosarcoma and hypercalcemia. J Am Vet Med Assoc 181:891–893, 1982

(24) MacEwen EG: Spontaneous tumors in dogs and cats: Models for the study of cancer biology and treatment. Cancer Metastasis Rev 9:125–136, 1990

(25) Squire RA, Melby EC: Naturally occurring canine and feline lymphomas as biomedical models. *In* Animal Models for Biomedical Research. National Academy of Sciences Report. Publ No. 1594. Washington, DC: NAS, 1968

(26) Holmberg CA, Wilson FD: Lymphoid neoplasia in the canine. *In* The Canine as a Biomedical Research Model. Immunological, Hematological and Oncological Aspects (Shtrinc M, Wilson FD, eds). Washington, DC: Technical Information Center, US Department of Energy, 1980, pp 296–313

(27) Glickman LT, Domanski LM, Maguire TG, et al: Mesothelioma in pet dogs associated with exposure of their owners to asbestos. Environ Res 32:305–313, 1983

(28) Hayes HM, Wilson GP, Moraff H: The veterinary medical data program (VMDP): Past, present, and future. *In* Proceedings of International Symposium on Animal Health and Disease Data Banks, December 4-6, 1978. APHIS Misc Publ No. 1381. Washington, DC: USDA, 1979, pp 127–132

(29) Gart JJ: Point and interval estimation of the common odds ratio in the combination of 2×2 tables with fixed marginals. Biometrika 57:471–475, 1970

(30) Thomas DG, Gart JJ: Stratified trend and homogeneity analyses of proportions and life table data. Comput Biomed Res 16:116–126, 1983

(31) Engelman L: Stepwise logistic regression. *In* BMDP Statistical Software (Dixon WJ, ed). Berkeley: Univ Calif Press, 1983, pp 330–344

(32) Theilen GH, Madewell BR: Leukemia-sarcoma disease complex. *In* Veterinary Cancer Medicine (Theilen GH, Madewell BR, eds). Philadelphia: Lea & Febiger, 1979, pp 204–208

(33) Sprague RH, Anisko JJ: Elimination patterns in the laboratory beagle. Behaviour 47:257–267, 1973

(34) Yeary RA: Urinary excretion of 2,4-D in commercial lawn specialists. Appl Ind Hyg 1:119–121, 1986

(35) Hansen WH, Quaife ML, Haibrmann RT, et al: Chronic toxicity of 2,4-dichlorophenoxyacetic acid in rats and dogs. Toxicol Appl Pharmacol 20:122–129, 1971

(36) Innes JRM, Ulland BM, Valerio MG, et al: Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: A preliminary note. J Natl Cancer Inst 42:1101–1114, 1969

(37) Reuber MD: Carcinogenicity and toxicity of 2,4-dichlorophenoxyacetic acid. Sci Total Environ 31:203–218, 1983

Low-Grade, Latent Prostate Cancer Volume: Predictor of Clinical Cancer Incidence?

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We hypothesize that each cell in low-grade (Gleason grade 1-3) prostate cancer tissue is at risk of transformation into a cell which produces a high-grade (Gleason grade 4-5) clinical cancer after a short period of growth. As a consequence, the volume of low-grade, latent cancer tissue in the prostate glands of men at any age determines their incidence rate for high-grade, clinical cancer a few years later. Autopsy and incidence data for both white men and black men support this conclusion, with a tumor growth period of about 7 years. The transformation rate is similar for black men

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