AO 88 (Rev. 1/94) Subpoena in a Civil Case

Issued by the
UNITED STATES DISTRICT COURT

EASTERN DISTRICT OF MISSOURI

WILLIAM R. GAFFEY
V.
PETER MONTAGUE and
ENVIRONMENTAL RESEARCH FOUNDATION, INC.

SUBPOENA IN A CIVIL CASE

CASE NUMBER:[1] 91-1938-6-CES

TO: Clayton F. Callis
#2 Holiday Lane
St. Louis, MO 63131

☐ YOU ARE COMMANDED to appear in the United States District Court at the place, date, and time specified below to testify in the above case.

PLACE OF TESTIMONY	COURTROOM
	DATE AND TIME

☒ YOU ARE COMMANDED to appear at the place, date, and time specified below to testify at the taking of a deposition in the above case.

PLACE OF DEPOSITION	DATE AND TIME
Leritz, Plunkert & Bruning, One City Centre, Suite 2001 St. Louis, MO 63101	November 2, 1994 9:30 a.m.

☒ YOU ARE COMMANDED to produce and permit inspection and copying of the following documents or objects at the place, date, and time specified below (list documents or objects):

See Attachment "A"

PLACE	DATE AND TIME
Leritz, Plunkert & Bruning, One City Centre, Suite 2001, St. Louis, MO 63101	November 2, 1994 9:30 a.m.

☐ YOU ARE COMMANDED to permit inspection of the following premises at the date and time specified below.

PREMISES	DATE AND TIME

Any organization not a party to this suit that is subpoenaed for the taking of a deposition shall designate one or more officers, directors, or managing agents, or other persons who consent to testify on its behalf, and may set forth, for each person designated, the matters on which the person will testify. Federal Rules of Civil Procedure, 30(b)(6).

ISSUING OFFICER SIGNATURE AND TITLE (INDICATE IF ATTORNEY FOR PLAINTIFF OR DEFENDANT)	DATE
Attorney for Environmental Research Foundation, Inc.	10/4/94

ISSUING OFFICER'S NAME, ADDRESS AND PHONE NUMBER
Edward M. Roth, One City Centre, Suite 2001
St. Louis, MO 63101 (314) 231-9600

(See Rule 45, Federal Rules of Civil Procedure, Parts C & D on Reverse)

[1] If action is pending in district other than district of issuance, state district under case number.

AO 88 (Rev. 1/94) Subpoena in a Civil Case

PROOF OF SERVICE

DATE	PLACE

SERVED

SERVED ON (PRINT NAME)	MANNER OF SERVICE

SERVED BY (PRINT NAME)	TITLE

DECLARATION OF SERVER

I declare under penalty of perjury under the laws of the United States of America that the foregoing information contained in the Proof of Service is true and correct.

Executed on _____
DATE

SIGNATURE OF SERVER

ADDRESS OF SERVER

Rule 45, Federal Rules of Civil Procedure, Parts C & D:

(c) PROTECTION OF PERSONS SUBJECT TO SUBPOENAS.

(1) A party or an attorney responsible for the issuance and service of a subpoena shall take reasonable steps to avoid imposing undue burden or expense on a person subject to that subpoena. The court on behalf of which the subpoena was issued shall enforce this duty and impose upon the party or attorney in breach of this duty an appropriate sanction which may include, but is not limited to, lost earnings and reasonable attorney's fee.

(2) (A) A person commanded to produce and permit inspection and copying of designated books, papers, documents or tangible things, or inspection of premises need not appear in person at the place of production or inspection unless commanded to appear for deposition, hearing or trial.

(B) Subject to paragraph (d)(2) of this rule, a person commanded to produce and permit inspection and copying may, within 14 days after service of subpoena or before the time specified for compliance if such time is less than 14 days after service, serve upon the party or attorney designated in the subpoena written objection to inspection or copying of any or all of the designated materials or of the premises. If objection is made, the party serving the subpoena shall not be entitled to inspect and copy materials or inspect the premises except pursuant to an order of the court by which the subpoena was issued. If objection has been made, the party serving the subpoena may, upon notice to the person commanded to produce, move at any time for an order to compel the production. Such an order to compel production shall protect any person who is not a party or an officer of a party from significant expense resulting from the inspection and copying commanded.

(3) (A) On timely motion, the court by which a subpoena was issued shall quash or modify the subpoena if it

(i) fails to allow reasonable time for compliance;

(ii) requires a person who is not a party or an officer of a party to travel to a place more than 100 miles from the place where that person resides, is employed or regularly transacts business in person, except that, subject to the provisions of clause (c)(3)(B)(iii) of this rule, such a person may in order to attend trial be commanded to travel from any such place within the state in which the trial is held, or

(iii) requires disclosure of privileged or other protected matter and no exception or waiver applies, or

(iv) subjects a person to undue burden.

(B) If a subpoena

(i) requires disclosure of a trade secret or other confidential research, development, or commercial information, or

(ii) requires disclosure of an unretained expert's opinion or information not describing specific events or occurrences in dispute and resulting from the expert's study made not at the request of any party, or

(iii) requires a person who is not a party or an officer of a party to incur substantial expense to travel more than 100 miles to attend trial, the court may, to protect a person subject to or affected by the subpoena, quash or modify the subpoena, or, if the party in whose behalf the subpoena is issued shows a substantial need for the testimony or material that cannot be otherwise met without undue hardship and assures that the person to whom the subpoena is addressed will be reasonably compensated, the court may order appearance or production only upon specified conditions.

(d) DUTIES IN RESPONDING TO SUBPOENA.

(1) A person responding to a subpoena to produce documents shall produce them as they are kept in the usual course of business or shall organize and label them to correspond with the categories in the demand.

(2) When information subject to a subpoena is withheld on a claim that it is privileged or subject to protection as trial preparation materials, the claim shall be made expressly and shall be supported by a description of the nature of the documents, communications, or things not produced that is sufficient to enable the demanding party to contest the claim.

ATTACHMENT A

At the time and place set by the attached subpoena for your deposition to be taken, produce the following records for inspection and copying to the extent that you or your attorney have them in your possession, custody or control.

1. All documents constituting (a) minutes of meetings, (b) reports by or to or (c) communications from, to or among members or staff of the committee sometimes referred to as the "Nitro Health Study Task Force" which discuss or refer to any activiety contemplated or undertaken by the Task Force.

2. All documents discussing or referring to the creation, composition, organization, resources, mission, or purpose at any time of the committee sometimes referred to as the "Nitro Health Study Task Force."

3. All documents constituting or referring to press releases, "backgrounders," position papers, or public relations documents disseminated by any Person, including without limitation Monsanto Company or any chemical or paper industry trade or lobbying organization, to any Person, including without limitation any news organization, labor organization, medical association, governmental agency or governmental representative, or private public health agency, which discuss or refer to the Zack/Suskind or Zack/Gaffey studies or to the mortality experience at any time of any portion of the population of workers at Monsanto Company's Nitro, West Virginia plant exposed or potentially exposed to dioxin or other substances found in association therewith.

4. All documents constituting or referring to news or other media reports or accounts (including print and broadcast news media and scientific or public-health media) of the Zack/Gaffey study.

5. All documents constituting, discussing or referring to the presentation of the report of the Zack/Gaffey study at the 1981 International Dioxin Symposium, including documents actually presented at that conference.

6. All documents constituting, discussing or referring to public presentations, speeches or statements, or statements to the press by William R. Gaffey concerning (a) the mortality experience at any time of workers at Monsanto Company's Nitro, West Virginia plant exposed or potentially exposed to dioxin or other substances found in association therewith, including, without limitation, the presentation made by William R. Gaffey before the American Medical Association, Council on Scientific Affairs' Advisory Panel on Toxic Substances, 17 November 1983 and (b) other matters within the field of occupational or public health.

7. All documents discussing or referring to allegations of fraud, dishonesty, incompetence, or scientific inadequacy or irregularity in any of the Nitro worker studies or their authors, including, without limitation, all communications relating or referring to Dr. Cate Jenkins' allegations or comments regarding any of the Nitro Worker Studies performed by or for Monsanto Company.

8. All documents constituting, relating or referring to critiques, criticisms, reviews, or investigations of William R. Gaffey in connection with any of the Nitro worker studies.

9. All documents constituting, discussing or referring to Marcie Strauss's "Verbatim & Critique," including, without limitation, documents and communications used in its preparation and dissemination.

10. All attachments and materials that accompanied Marcie Strauss June 4, 1987 letter to Dr. Marilyn Fingerhut, a copy of which is appended as EXHIBIT "C" hereto.

11. All documents, including records of communications, which refer to this lawsuit, including, without limitation, any communications between William R. Gaffey and George Roush or any other Person.

12. All scholarly papers (reports, summaries, surveys, etc.) authored or co-authored by William R. Gaffey, whether ultimately published or unpublished.

13. All documents (including audio or video recordings, press reports, personal communications, etc.) discussing or referring in any way to William R. Gaffey's character or integrity.

14. William R. Gaffey's Monsanto Company personnel file and/or any documents known to have been placed in it at any time that are no longer in that file, including, without limitation, documents which discuss or refer to the reasons or purposes for which he was originally hired and subsequently employed by Monsanto Company and his job responsibilities at any time.

15. All documents relating or referring to the designation of William R. Gaffey as an expert witness in any litigation relating to dioxin, including in connection with the cases consolidated with and including Adkins et. al v. Monsanto Company.

16. All documents which discuss, refer to or record the payment of money to William R. Gaffey since his retirement from Monsanto Company.

17. All documents constituting or referring to payments, directly or indirectly, by Monsanto Company, to the law firms of Coburn & Croft or Lewis, Rice & Fingersh or otherwise for the benefit of plaintiff William R. Gaffey in connection with this lawsuit, including without limitation agreements under which Monsanto, directly or indirectly, has paid legal fees to either Coburn & Croft or Lewis, Rice & Fingersh, reimbursed William R. Gaffey for such legal fees, or otherwise compensated or made payment to Gaffey or his attorneys for matters relating to this lawsuit, from the inception of the lawsuit to the present.

18. All documents marked for identification at the depositions in the cases consolidated with the including Adkins et. al v. Monsanto Company of Ferdinand C. Meyer; Monte C. Throdahl, Clayton F. Callis and William R. Gaffey, as indicated in part by the pages appended hereto and identified, collectively, as Exhibit "D".

19. Except to the extent already produced pursuant to the foregoing requests, all affidavits or transcripts (including, if available, notary certification page) of testimony (whether given at trial or deposition) by Judith Zack, Mary Gaffey, William Gaffey, Jan Yung, Raymond Suskind, George Roush, Clayton Callis, Monte Throdahl, Dan Bishop, and Ferdinand C. Meyer, together with copies of any

exhibits identified or discussed by or presented to such witnesses during testimony or in such affidavit.

20. All communications between William R. Gaffey and any Person discussing or referring to any of the Nitro studies.

21. All communications between Judith Zack and any Person relating or referring to any of the Nitro studies.

22. All reports of conclusions and analyses of the Zack/Gaffey study, including, without limitation, prior drafts of the study report finally published.

23. All proposals, contracts, study plans, rationales, protocols, progress reports, for the Zack/Suskind study or any antecedent study however denominated considered in its completion, whether completed or not, including any and all amendments, corrections, or other alterations to any of the foregoing, as well as all documents which refer to any of the foregoing.

24. All proposals, contracts, study plans, rationales, protocols, progress reports, for the Zack/Gaffey study or any antecedent study, however denominated, relied on or considered in the completion of the Zack/Gaffey study (whether such antecedent study was completed or not), including any and all amendments, corrections, or other alterations to any of the foregoing, as well as all documents which refer to any of the foregoing.

25. Except to the extent already produced in response to the foregoing requests numbered 22 through 24, all documents constituting or referring in any way to any and all epidemiologic studies, investigations, tests, etc., however denominated and whether actually completed,

partially completed, proposed, or hypothesized, that did or would examine in whole or in part the mortality experience at any time of the population of workers at Monsanto Company's Nitro, West Virginia plant exposed or potentially exposed to dioxin or other substances found in association therewith, together with any control groups ("worker mortality studies"), including by way of example but without limitation (i) The Zack/Gaffey study, (ii) The Zack/Suskind study (iii) The study described in the published report of the Zack/Suskind Study as "an analysis of the chloracne cases and exposures not associated with this accident but rather with the normal TCP/2,4,5-T production processes"; (iv) The study performed by the National Institute for Occupational Safety & Health combining a Nitro worker population with populations from other plants and companies (including the "Dioxin Registry Report" for the Nitro plant); (v) the workers' union study conducted by or through Mt. Sinai Hospital.

26. Except to the extent already produced in response to the foregoing requests numbered 22 through 25 above, for each such study responsive to the foregoing requests, all records constituting or referring to: (a) any and all proposals, study plans, rationales, contracts, classification criteria, protocols, drafts and progress reports ("study documents"), including for each such study document actual or suggested amendments or corrections thereto or critiques thereof; (b) any and all records generated as part of the effort to hypothesize, propose, justify, design, or perform each study; and (c) any and all records generated by, between, among, directed to, or received by each study participant or subject that discuss or refer to any such study in any manner, including all records of Monsanto Company's "Nitro Health Study Task Force."

27. All documents referring to the table and handwritten notes titled, "Table 9 Observed and Expected Number of Deaths during 1955-1977 by Cause and 2,4,5-T Exposure Category Showing Proportional Mortality Ratios (PMRs) (Not Including Deaths from TCP Incident)", a copy of which is appended as EXHIBIT "E" hereto.

28. All communications discussing, describing or referring to whether or not a follow up to the Zack/Suskind study should consist of an "analysis of the chloracne cases and exposures not associated with this 1949 accident but with the normal TCP/2,4,5-T production processes" as proposed in the Zack/Suskind study.

29. All communications discussing, describing or referring to the participation of William R. Gaffey in any of the Nitro Worker studies, including without limitation the participation of William R. Gaffey in any of the Nitro Worker studies during the period he was employed by Stanford Research Institute or other academic institution.

30. All communications discussing, describing, or referring to the actual or proposed participation of Raymond Suskind in what became know as the Zack/Gaffey study, including, without limitation, documents which refer to any decision to omit Raymond Suskind as a co-author of what became the Zack/Gaffey study.

31. All communications referring to any follow-up study (actual or contemplated) to the Zack/Suskind study concerning the mortality experience at any time of the population of workers at Monsanto Company's Nitro, West Virginia plant exposed or potentially exposed to dioxin or other substances found in association therewith, together with any control groups, including any communications to which Raymond Suskind, George Roush, Marcie Straus, Dan

Bishop, Ferdinand C. Meyer, Monte C. Therodahl, Clayton F. Callis or Richard Mahoney, members of the "Nitro Health Study Task Force," or representatives of the National Institute for Occupational Safety and Health, the Environmental Protection Agency, the United States Department of Justice, or any other agency of government (Federal, state or local) were participants or recipients.

32. All minutes of meetings of the Monsanto Company Board of Directors, Corporate Management Committee, Corporate Administrative Committee, any committee, task force, or other group created by or reporting to the Monsanto Company Board of Directors or any committee or subdivision thereof or any management-level group, which discuss or refer in any way to (a) any mortality study responsive to requests 1 through 4 above, (b) 2,4,5,-T, (c) trichlorophenol, (d) dioxin, (e) Agent Orange, (f) defendants in this action, (g) Rachel's Hazardous Waste News, including without limitation #171, (h) William R. Gaffey, or (i) Judith Zack, together with any reports or documents reviewed or considered by any of the foregoing committee's or groups or any of their members in preparation for, during or as a result of such topics being discussed, presented to or considered by any such committee or group.

33. All documents constituting or referring to communications between Dr. Raymond Suskind (or any person acting on behalf of Monsanto) and any Person concerning the position of the American Medical Association (or of any body affiliated therewith) on the hazards of dioxin.

34. All records that refer to studies responsive to requests numbered 22 through 24 above, including records of communications with the press or public officials or employees of public agencies, peer reviews, records of litigation, post-study records, and any and all records reviewing, criticizing, or otherwise discussing or referring

to the possibility of fraud, scientific irregularity or invalidity, inaccuracy, or incompetence in the conduct of each such study.

35. Except to the extent produced in response to any other request made herein, all documents constituting or referring to reviews, critiques or investigations of the Nitro Workers studies performed by Persons other than Monsanto employees, including without limitation, peer reviews and any investigations by the U.S. Environmental Protection Agency or other governmental agencies into matters relating to the Nitro worker studies, whether civil or criminal, actual or contemplated.

36. Except to the extent produced in response to any other request made herein, all documents constituting, discussing, or referring in any way to sampling and analyses of acnegens, dioxin, or other materials associated therewith at or near the Nitro plant, including but not limited to such efforts by Monsanto, the U.S. E.P.A., or any other entity, including (a) all sample plans, maps and other sampling site identification records, sample decoding information, protocols, sample handling and destruction records, laboratory communications, and analytical results; and (b) all affidavits or transcripts of testimony at trial or deposition, including all exhibits discussed or identified thereby, of all people who have testified in any case or proceeding about contamination of the Nitro plant premises with acnegens, dioxin, or other materials associated therewith.

37. Except to the extent produced in response to any other request made herein, all documents constituting, relating or referring to internal (Monsanto or Kettering) reviews, critiques or investigations of the Nitro worker studies, including, without limitation, investigations performed by Monsanto or any Person on behalf of Monsanto

into whether any or all of the Nitro worker studies were the product of fraud, dishonesty, incompetence or scientifically irregularity.

38. All documents discussing or referring in any way to any demand for retraction from Peter Montague of statements claimed to be defamatory.

39. All documents constituting or referring to any demand of retraction (actual or contemplated) of allegations of fraud or scientific inadequacy attributed to the Nitro worker studies or their authors, together with any such retraction actually made by any Person.

40. All documents which refer to the taking of any legal or public-relations action, actual or contemplated, against any person, other than defendants Peter Montague and Environmental Research Foundation, who published criticisms of the Nitro worker studies.

II.

DEFINITIONS AND INSTRUCTIONS

Please interpret each of the preceding discovery requests in accordance with the following special definitions and instructions, as supplemented by the Federal Rules of Civil Procedure, the Federal Rules of Evidence, and jurisprudence thereunder;

A. "Produce" means to produce any and all originals and any and all non-identical copies of the same document described in its or their most complete form, including, without limitation, any and all surviving portions thereof, and including any and all annexes, appendices, tabs, exhibits, indexes, cover sheets, transmittal letters, or other documents found attached to or

in the same file with the same document or documents, including without limitation, whenever available, the file identification and identification of the system of records in which each document and any and all copies are found. Wherever you are asked to produce affidavits or trial or deposition transcripts, also produce any and all exhibits thereto.

B. The words "document" or "record" shall have the same interpretation as "documents or other things" within the meaning of Fed. R. Civ. P. 34, and shall also include all drafts, alterations, modifications, changes or amendments thereof.

C. The term "person" or "persons" includes not only natural persons, but also all forms or organizations including without limitation unincorporated associations partnerships, corporations, joint ventures, proprietorships, firms, syndicates, and all subsidiaries, affiliates, divisions, departments, branches or other units thereof.

D. The term "communication" refers to any written or oral transmission of information, belief or opinion, including any correspondence, letters, telegraphs, telexes, notes, memoranda, reports, circulars, press releases, discussions or conversations.

E. The connectives "and" and "or" shall be construed either disjunctively or conjunctively or both as necessary to bring within the scope of the discovery request all records that might otherwise be construed to be outside of its scope.

F. Where words or terms are not defined, they shall be given their common and accustomed meaning within the context stated.

G. The words "dioxin or "dioxins" mean any or all of the congeners, homologues, or isomers of the mono- through poly- chlorinated classes of dibenzo-p-dioxins or dibenzofurans.

H. For purposes of this discovery request, the words "dioxin" or "dioxins" shall also include 2,4,5-T and trichlorothenol or any waste byproducts thereof.

I. The phrase "Zack/Gaffey study" shall encompass the final published report of the purported study exhibited hereto as EXHIBIT "A", as well as other study designs or results contemplated, performed, or generated as a follow-up mortality study to the Zack/Suskind study.

J. The phrase "Zack/Suskind study" shall encompass the final published report of the purported study exhibited hereto as EXHIBIT "B", as well as other study designs or results contemplated, performed, or generated in connection with that study as finally published, irrespective of whether such designs or results were incorporated in the study as finally published.

K. The phrase "Nitro worker studies" shall encompass not only the Zack/Gaffey study, and the Zack/Suskind study but also any or all other epidemiologic studies, investigations, tests, etc., however denominated and whether actually completed, partially completed, proposed, or hypothesized, that did or would examine in whole or in part the mortality experience at any time of the population of workers at Monsanto Company's Nitro, West Virginia plant exposed or potentially exposed to dioxin or other substances found in association therewith, together with any control groupsepidemiologic studies.

L. The term "Monsanto Company" shall encompass Monsanto Company together with all subsidiaries and divisions thereof.

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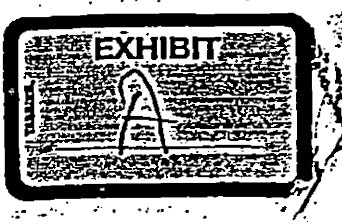

Allan M. [illegible], PhD.
EISA

PREFACE

Increasing international concern is being expressed regarding the contamination of the environment with polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans because certain of these chemicals have been shown to be highly toxic to animals and are ubiquitous in the environment. They are known to be distributed as contaminants of commercial products and as by-products from combustion processes.

A considerable volume of information has accumulated on these chemicals in the past two decades, particularly for the most toxic of them, 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). However, this body of knowledge has not succeeded in resolving genuine judgmental differences among experts in the field as to the degree of hazard to human health and the environment. In light of the widespread public concern, it is clearly imperative to come to grips with the continuing scientific controversy, to review the data, assess the issues, to see where areas of agreement exist, and where further research is needed to resolve remaining areas of disagreement.

This volume represents an effort to contribute to these goals. The volume contains the Proceedings from an International Symposium on Chlorinated Dioxins and Related Compounds which was held October 25 to 29, 1981, in Arlington, Virginia. The objectives of the meeting were to bring together scientists from a wide range of disciplines, all of whom were directly concerned with one aspect or another of the dioxin problem, to review the existing information, evaluate controversial data, present new data, identify areas of agreement, and indicate directions for future research. The 56 papers and panel reports that comprise this volume testify to the success of the Symposium.

The meeting was divided into nine sections:

Definition of the Problem
Analytical Chemistry
Environmental Chemistry
Animal Toxicology

A MORTALITY STUDY OF WORKERS EMPLOYED AT THE MONSANTO COMPANY PLANT IN NITRO, WEST VIRGINIA

Judith A. Zack and William R. Gaffey

Monsanto Company
St. Louis, Missouri USA

BACKGROUND

The compound 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is a highly toxic impurity that is formed in trace quantities during the production of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T). Exposure to TCDD can cause chloracne, a skin disorder characterized by comedones, cysts, and abscesses.[1] Outbreaks of chloracne have been reported among workers associated with the production of 2,4,5-T and 2,4,5-T based products. Such incidents resulting from both accidents and routine occupational exposures have been reported from several countries.[2]

The first reported industrial accident involving exposure to TCDD occurred in 1949 at the Monsanto Company plant in Nitro, West Virginia. A total of 122 employees developed symptoms of chloracne following a trichlorophenol (TCP) process accident. An undetermined number of other employees developed symptoms of chloracne resulting from exposure to the regular operations concerned with 2,4,5-T production over the period 1948-1969.

Between 1949 and 1953, Ashe and Suskind[3,4] examined thirty-eight Nitro plant employees with chloracne. Twelve of these had developed symptoms of chloracne directly following the 1949 TCP accident; twenty-six other chloracne cases had resulted from exposure to the regular 2,4,5-T production operations. In addition to chloracne, other signs and symptoms were observed in this group. These included severe aches in the lower extremities, fatigue, nervousness and irritability, loss or decrease of libido, dyspnia, and vertigo. These findings are consistent with those that have been reported in other industrial incidents.[5]

To examine the chronic health effects of exposure to TCDD, a mortality study of the Nitro plant employees who had developed symptoms of chloracne following the 1949 TCP accident was conducte The study cohort was comprised of 121 of the 122 chloracne cases; one female who was living as of the endpoint of the study was exc from analysis. At the time of the incident, it was assumed that t symptoms were caused by exposure to unknown products of decompositi From today's vantage point, these symptoms suggest exposure to TCD The 121-member study cohort, with a presumptive high-peak exposure to TCDD, was followed for mortality through 1978. The entire coho was traced: thirty-two deaths were observed and eighty-nine person were confirmed as living. Analysis indicated no excess in total mortality or in deaths from malignant neoplasms.

The study presented here examines the mortality of Nitro plan workers who were assigned to an area of TCP or 2,4,5-T production, with potential for exposure to TCDD. The mortality of these worke is examined in the context of the mortality experience of the tota Nitro plant worker population.

The Monsanto Nitro plant began operations in 1922, when the Rubber Service Laboratories purchased the plant as war surplus and began production of chemicals and additives for the growing rubber industry. In 1929, Monsanto Company purchased the Nitro plant fro the Rubber Service Laboratories and entered the rubber chemicals business. Over the years, the Nitro plant has diversified to where it now produces agricultural chemicals, paper chemicals, plasticiz fine chemicals, and intermediates, in addition to rubber chemicals. The plant is situated in the Kanawha River Valley, an area contain one of the largest concentrations of chemical production facilitie in the United States.

Of the many chemicals used over the years at the Nitro plant, one has an established association with the occurrence of cancer in man. Para-aminobiphenyl (PAB), used from 1941 through 1952 for use as a rubber antioxidant and dye intermediate, was shown in 1954 by Walpole et al.[7] to induce bladder cancer in dogs. In 1955, Melick et al.[8] confirmed the carcinogenicity of para-aminobiphenyl to man with the reporting of bladder tumors among workers exposed to this chemical at two Monsanto plants. Para-aminobiphenyl was produced a one plant and then transferred by tank car to the Nitro plant where additional processing was carried out. The minimum duration of exposure reported to have produced a bladder tumor is 133 days; the latent period has ranged from 15 to 35 years.[9] An intensive screen ing program was instituted at Monsanto Company about 1955 to exami on a continuing basis, all workers exposed to this chemical. Seven deaths from bladder cancer have occurred among Nitro plant employee enrolled in this program. These seven deaths are included in the present study.

Other chemicals with known health effects produced at the Nitro plant include methylparathion and carbon disulfide. The acute effects of exposure to each of these chemicals have been described[9,10] while the chronic effects are less well understood. Besides p-aminobiphenyl several other rubber chemicals are of potential health concern. For all of these, there is insufficient evidence to evaluate their carcinogenicity to man. Tetramethyl thiuram disulfide is considered an animal carcinogen[11] and there is some evidence, although not sufficient, that N-methyl-N,4-dinitrosaniline is also an animal carcinogen.[12] For several other rubber chemicals, there is insufficient evidence to evaluate the carcinogenicity to animals. However, these chemicals have the potential for forming nitrosamines, certain of which are known animal carcinogens.[13] Zinc dimethyl dithiocarbamate, tetramethyl thiuram disulfide and tetramethyl thiuram monosulfide have the potential to form N-nitrosodimethylamine. N-Nitrosomorpholine has been found in product samples of 2-(morpholinothio) benzothiazole and 4,4'-dithiodimorpholine (Frisone, G.J., The General Tire and Rubber Company, unpublished data).

Although several of the chemical compounds produced or used at the Nitro plant over the years have been associated with adverse health effects, no attempt has been made to relate chemical exposure to mortality with the exception of decedents exposed to the TCP or 2,4,5-T operations and potentially exposed to TCDD. As a result, the only specific hypothesis that can be tested is whether a relationship exists between potential TCDD exposure and proportional mortality, especially for malignant neoplasms. The mortality for this group is examined in addition to that of the total Nitro plant worker population.

POPULATION AND METHODS

A study cohort was developed from the Nitro plant consisting of employees active on or after January 1, 1955 with one or more years of employment on the hourly roll prior to December 31, 1977. Salaried personnel who had never worked on the hourly roll were excluded from study because many of these employees had no appreciable exposure to the plant environment and, for the most part, their exposure cannot be determined from plant records. Females and non-white males were also excluded because of their small numbers.

The cohort was assembled using government earnings reports, independent of the plant work history records. Annual earnings reports were available on a computer file from 1951 through 1977. Names and social security numbers were identified from this source. Work history records were used to supplement the earnings records. Information on race, sex, date of birth, date of hire, date of separation, and, if deceased, 2,4,5-T exposure was abstracted from these records. Ascertainment of 2,4,5-T exposure was confined to decedents only because it was too tedious to do for the entire cohort. The

information from the work history records was used to determine which names identified from the annual earnings records met the cohort entrance criteria. Employees identified from the earnings records who terminated prior to 1955 were not included in this study because work history records for all such employees were not retained prior to this date.

Exposure to 2,4,5-T was determined by assignment to a 2,4,5-T operation based on the work history records. 2,4,5-T exposure was determined for all but one decedent. Employees holding a job having plant-wide responsibilities with the potential for exposure to 2,4,5-T were, for the purposes of this study, considered to be non-exposed.

The vital status of each member of the study cohort was determined using standard follow-up techniques and ascertained as of December 31, 1977. Death certificates were coded by an independent nosologist for the underlying cause of death, according to the rules of the Eighth Revision of the International Classification of Diseases, Adapted.[14]

Data for the total Nitro plant study population were analyzed by the modified life-table method using the U.S. population as the standard. With this method of analysis, the age-, race-, time-, and cause-specific mortality rates for the U.S. general population are applied to the person-years lived classified by age, race, and time. A standardized mortality ratio (SMR) was calculated for 23 selected cause of death categories. Cause-specific SMR's for 15 selected cancer sites were calculated for subgroups of the total Nitro plant study population defined by date of death, age at death, and year of hire. The statistical significance of the deviation in a SMR from 100 was tested using the formula:

$$\text{standard error of SMR} = \frac{100\ \sqrt{\text{no. observed deaths}}}{\text{no. expected deaths}}$$

If the observed SMR differed from 100 by 1.96 standard errors, it was regarded as significant at the 5% level. A SMR was tested for significance only when the observed number of deaths was five or greater.

Data for those deceased were also analyzed according to 2,4,5-T exposure using the proportional mortality method. In this case, the expected number of deaths is calculated on the basis of proportions of deaths observed in the U.S. general population. A proportional mortality ratio (PMR) was calculated for 23 selected cause-of-death categories. PMR's were calculated separately for those exposed to 2,4,5-T and for those not exposed. The statistical significance of the deviation of a PMR from 100 was tested by calculating the 95%

confidence interval for the PMR for a given cause k according to the formula:

$$\text{confidence interval for } PMR_k = \frac{N(\text{confidence limits for \% of observed deaths})}{exp_k}$$

where N = number of observed deaths for all causes

Both the standardized and proportional mortality analyses were conducted using the computer program developed by Monson.[13] The observed mortality was compared to that of the United States white male population for the time period of study.

RESULTS

A total of 884 men were identified for study and traced for deaths through 1977. The entire cohort was successfully traced. Death certificates were obtained for all deaths. Seven hundred twenty-one (82%) were verified as living and 163 (18%) were confirmed dead by death certificates.

Tables 1-3 characterize the total Nitro plant study population by age at hire, year of hire, and length of employment. The distribution of the study population by age at hire indicates that the workers were fairly young at first hire (Table 1). Seventy-two percent of the study cohort were hired by age 30. None were hired at age 50 or above.

Table 2 shows the distribution of the study population by year of hire. The majority of workers (75.3%) were hired during the period 1940-1959, while smaller percentages of workers were hired prior to 1940 (10.8%) and after 1960 (13.9%).

An examination of the study population by length of employment indicates a fairly even distribution over the intervals less than 10 years, 10-19 years, 20-29 years, and greater than 30 years (Table 3).

Observed and expected deaths occurring during 1955-1977 among the total Nitro plant study population are shown by cause in Table 4. The SMR for all causes of death was 103 with 163 deaths observed and 158.10 expected. There were 35 deaths from malignant neoplasms with 30.92 expected, yielding a SMR of 113. Singificantly elevated SMR's were seen for the categories of malignant neoplasms of the genitourinary organs and of the bladder. The SMR for bladder cancer was 989 with 9 deaths observed and 0.91 expected. This excess in bladder cancer deaths is reflected in the elevated SMR for malignant nioplasms of the genitourinary organs. A significantly elevated SMR is also seen for arteriosclerotic heart disease. There were 79 deaths from this cause with 59.40 expected (SMR = 133). The SMR for

Table 1. Distribution of Total Nitro Plant Study Population by Age at Hire

Age at Hire	Number	Percent
<20	122	13.8
20–29	518	58.6
30–39	191	21.6
40–49	53	6.0
50+	0	0.0
Total	884	100.0

Table 2. Distribution of Total Nitro Plant Study Population by Year of Hire

Year of Hire	Number	Percent
Prior to 1930	21	2.4
1930–1939	74	8.4
1940–1949	361	40.8
1950–1959	305	34.5
1960–1976	123	13.9
Total	884	100.0

Table 3. Distribution of Total Nitro Plant Study Population by Length of Employment

Length of Employment (yrs.)	Number	Percent
<10	225	25.5
10–19	213	24.1
20–29	204	23.1
30+	242	27.4
Total	884	100.1

Table 4. Observed and Expected Number of Deaths During 1955-1977 by Cause Showing Standardized Mortality Ratios (SHR'S) for Total Nitro Plant Study Population

Cause of Death	ICDA Codes 8th Rev.	Observed	Expected	SHR
All causes of death		163	158.10	103
All malignant neoplasms	140-209	35	30.92	113
Buccal cavity and pharynx	140-149	0	1.03	0
Digestive organs and peritoneum	150-159	4	8.65	46
Stomach	151	1	1.63	61
Liver	155-156	0	0.60	0
All other digestive organs	---	3	6.42	47
Respiratory system	160-163	14	10.51	133
Lung	162-163	14	9.91	141
All other respiratory organs	---	0	0.60	0
Skin	172-173	0	0.58	0
Genitourinary organs	185-189	12	3.75	320*
Bladder	188	9	0.91	989*
All other genitourinary organs	---	3	2.84	106
Lymphatic and hematopoietic tissue	200-209	1	3.15	32
Other sites	---	4	3.25	123
Diseases of the nervous system and sense organs	320-389	0	1.28	0
Diseases of the circulatory system	390-458	92	82.59	111
Arteriosclerotic heart disease, including CHD	410-413	79	59.40	133*
All other diseases of the circulatory system	---	13	23.19	56*
Diseases of the respiratory system	460-519	6	9.13	66
Diseases of the digestive system	520-577	5	8.03	62
All other diseases	---	5	10.46	48*
External causes of death	800-998	20	15.69	127

Number at risk: 884
Person-years at risk: 13968.7
*p < .05

other circulatory diseases was significantly low at 56. A signific deficit was also seen for the category of all other diseases where SMR was 48 with 5 deaths observed and 10.46 expected.

Trends for malignant neoplasm deaths with calendar time are sh in Table 5. SMR's which increased consistently over the period 195 1977 are seen for the categories of all malignant neoplasms and mal nant neoplasms of the respiratory system. The SMR for all malignan neoplasms rose from 32 to 131. The SMR for malignant neoplasms of respiratory system rose from 0 to 172 reflecting a SMR for lung can which increased from 0 to 181. Although based on very small number the SMR for malignant neoplasms of the digestive organs and peritoni consistently decreased over time from 99 to 24. The SMR for malign neoplasms of the genitourinary organs peaked during the period 1950-1969. This is reflected in the SMR for bladder cancer which increas from 0 in 1955-1959 to a peak of 1471 in 1960-1969 and decreased to 833 in 1970-1977.

The analysis of observed and expected deaths from malignant neo plasms by age at death revealed little in terms of consistent trends with age (Table 6). For most of the cause-of-death categories, the SMR peaked at age 45-64 rather than continuing to rise with increasi age. Bladder cancer is one category where the SMR remained high at age 65 and over.

The distribution of deaths from malignant neoplasms by year of hire is shown in Table 7. No deaths from malignant neoplasms were observed among workers hired after 1960. The SMR for all malignant neoplasms was similar for those hired prior to 1945 and for those hired in the period 1945-1959. The greatest difference in SMR's between those hired prior to 1945 and those hired from 1945-1959 occurs with bladder cancer. The SMR for bladder cancer is highest for those hired prior to 1945 with a SMR of 1111.

A subset of deaths identified from the total Nitro plant study population was studied separately. Table 8 characterizes the decedents according to 2,4,5-T exposure. Of the 163 decedents, 58 (35.6%) were considered to be exposed to 2,4,5-T based on their work history records, while 104 (63.8%) were considered to be non-exposed. The exposure of one decedent was unkown.

The results of the proportional mortality analysis by 2,4,5-T exposure classification are presented in Table 9. The proportion of cancer deaths among 2,4,5-T workers is lower than in the non-exposed group (PMR: 82 vs. 122). The PMR for lung cancer deaths is slightly higher in the exposed group (PMR: 159 vs. 117). The proportion of deaths due to bladder cancer is higher among the decedents not exposed to 2,4,5-T. There were 7 deaths from bladder cancer among these workers with 0.65 expected (PMR = 1077). The PMR for bladder cancer among decedents exposed to 2,4,5-T was 909 with 2 deaths observed and

Table 5. Observed and Expected Deaths from Malignant Neoplasms During 1955-1977 by Calendar Time Showing Standardized Mortality Ratios (SMR'S) for Total Nitro Plant Study Population

Cause of Death	Calendar Time: 1955-1959 Observed	Expected	SMR	1960-1969 Observed	Expected	SMR	1970-1977 Observed	Expected	SMR
All malignant neoplasms	1	3.13	32	13	11.81	110	21	15.98	131
Buccal cavity and pharynx	0	0.11	0	0	0.41	0	0	0.50	0
Digestive organs and peritoneum	1	1.01	99	2	3.48	57	1	4.16	24
Stomach	0	0.25	0	0	0.70	0	1	0.69	145
Liver	0	0.09	0	0	0.28	0	0	0.23	0
All other digestive organs	1	0.67	149	2	2.50	80	0	3.24	0
Respiratory system	0	0.87	0	4	3.83	104	10	5.81	172
Lung	0	0.80	0	4	3.59	111	10	5.52	181
All other respiratory organs	0	0.07	0	0	0.24	0	0	0.29	0
Skin	0	0.07	0	0	0.23	0	0	0.28	0
Genitourinary organs	0	0.33	0	5	1.37	365	7	2.05	341
Bladder	0	0.09	0	5	0.34	1471*	4	0.48	833
All other genitourinary organs	0	0.24	0	0	1.03	0	3	1.57	191
Lymphatic and hematopoietic tissue	0	0.40	0	0	1.24	0	1	1.50	67
Other sites	0	0.34	0	2	1.25	160	2	1.68	119

*p < .05

Table 6. Observed and Expected Deaths from Malignant Neoplasms During 1955-1977 by Age at Death Showing Standardized Mortality Ratios (SMR'S) for Total Nitro Plant Study Population

	Age at Death								
	<45			45-64			65+		
Cause of Death	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
All malignant neoplasms	2	2.39	84	21	16.85	125	12	11.69	103
Buccal cavity and pharynx	0	0.06	0	0	0.67	0	0	0.31	0
Digestive organs and peritoneum	0	0.51	0	4	4.58	87	0	3.57	0
Stomach	0	0.10	0	1	0.85	118	0	0.68	0
Liver	0	0.03	0	0	0.32	0	0	0.24	0
All other digestive organs	0	0.38	0	3	3.41	88	0	2.65	0
Respiratory system	0	0.54	0	11	6.36	173	3	3.61	83
Lung	0	0.51	0	11	5.99	184	3	3.42	88
All other respiratory organs	0	0.03	0	0	0.37	0	0	0.19	0
Skin	0	0.13	0	0	0.31	0	0	0.14	0
Genitourinary organs	1	0.20	500	3	1.43	210	8	2.12	377*
Bladder	1	0.02	5000	2	0.39	513	6	0.50	1200*
All other genitourinary organs	0	0.18	0	1	1.04	96	2	1.62	123
Lymphatic and hematopoietic tissue	0	0.55	0	1	1.60	63	0	1.00	0
Other sites	1	0.40	250	2	1.90	105	1	0.94	106

*$p < .05$

Table 7. Observed and Expected Deaths from Malignant Neoplasms During 1955-1977 by Year of Hire Showing Standardized Mortality Ratios (SMR'S) for Total Nitro Plant Study Population

Cause of Death	Observed	Expected	SMR	Observed	Expected	SMR	Observed	Expected	SMR
All malignant neoplasms	25	21.30	117	10	8.63	116	0	0.99	0
Buccal cavity and pharynx	0	0.70	0	0	0.31	0	0	0.03	0
Digestive organs and peritoneum	2	6.27	32	2	2.19	91	0	0.19	0
Stomach	0	1.21	0	1	0.39	256	0	0.03	0
Liver	0	0.45	0	0	0.14	0	0	0.01	0
All other digestive organs	2	4.61	43	1	1.66	60	0	0.15	0
Respiratory system	10	7.14	140	4	3.09	129	0	0.27	0
Lung	10	6.73	149	4	2.93	137	0	0.26	0
All other respiratory organs	0	0.41	0	0	0.16	0	0	0.01	0
Skin	0	0.31	0	0	0.22	0	0	0.05	0
Genitourinary organs	9	2.90	310*	3	0.76	395	0	0.09	0
Bladder	8	0.72	1111*	1	0.18	556	0	0.01	0
All other genitourinary organs	1	2.18	46	2	0.58	345	0	0.08	0
Lymphatic and hematopoietic tissue	1	1.95	51	0	1.00	0	0	0.20	0
Other sites	3	2.03	148	1	1.06	94	0	0.16	0

*p < .05

Table 8. 2,4,5-T Exposure Classification for Decendents During 1955-1977 Among Total Nitro Plant Study Population

2,4,5-T Exposure Classification	Number of Deaths	Percent
Exposed	58	35.6
Non-exposed	104	63.8
Unknown	1	0.6
Total	163	100.0

Table 9. Observed and Expected Number of Deaths During 1955-1977 by Cause and 2,4,5-T Exposure Category Showing Proportional Mortality Ratios (PMR'S)

Cause of Death	2,4,5-T Exposure Category: Exposed Observed	Exposed Expected	Exposed PMR	Non-exposed Observed	Non-exposed Expected	Non-exposed PMR
All malignant neoplasms	9	10.94	82	25	20.43	122
Buccal cavity and pharynx	0	0.38	0	0	0.64	0
Digestive organs and peritoneum	0	2.80	0	3	5.74	52
Stomach	0	0.52	0	0	1.06	0
Liver	0	0.19	0	0	0.39	0
All other digestive organs	0	2.09	0	3	4.29	70
Respiratory system	6	3.78	159	8	6.81	117
Lung	6	3.57	168	8	6.42	125
All other respiratory organs	0	0.21	0	0	0.39	0
Skin	0	0.29	0	0	0.55	0
Genitourinary organs	2	0.96	208	10	2.70	370*
Bladder	2	0.22	909	7	0.65	1077*
All other genitourinary organs	0	0.74	0	3	2.05	146
Lymphatic and hematopoietic tissue	0	1.35	0	1	2.07	48
Other sites	1	1.38	72	3	2.12	142
Diseases of the nervous system and sense organs	0	0.61	0	0	0.83	0
Diseases of the circulatory system	31	26.48	117	61	55.34	110
Arteriosclerotic heart disease, including CHD	27	19.72	137	52	39.68	131*
All other diseases of the circulatory system	4	6.76	59	9	15.66	57
Diseases of the respiratory system	2	2.67	75	4	6.49	62
Diseases of the digestive system	1	3.70	27	4	4.93	81
All other diseases	3	4.31	70	2	6.70	30
External causes of death	12	9.29	129	8	9.28	86
Total number of deaths:	58	58.00		104	104.00	

*$p < .05$

..22 expected. PMR's for both exposure groups are quite similar for diseases of circulatory and respiratory system. Slight differences appear in the PMR's between the two groups for diseases of the digestive system and all other diseases. However, the PMR's for both groups are quite low. The PMR for external causes of death is slightly higher in the exposed group (PMR: 129 vs. 86).

A listing of the cancer deaths among the 2,4,5-T exposed is given in Table 10. Table 11 listed the cancer deaths among the non-exposed group.

DISCUSSION

The observation made many years ago of an apparent excess in bladder cancer among Nitro plant workers was confirmed and quantified in the mortality analysis of the total Nitro plant population presented here. The SMR for bladder cancer was 989 and was the only statistically significant SMR among those for malignant neoplasms. The excess in mortality is not seen until 1960. The SMR peaked in the 1960's and declined somewhat in the 1970's. The excess also appeared to be clustered in those decedents aged 65 years and older at death and in those hired prior to 1945. This would suggest that we should see a further decline in the SMR for bladder cancer over time.

Although not statistically significant, the SMR for lung cancer appears to be elevated. The SMR increased with calendar time and was highest in those hired prior to 1945. The elevation appears to be clustered in those aged 45-64 years of age at death (SMR = 184) and does not show a gradient with age. Further analyses to evaluate trends in lung cancer deaths as they relate to occupation cannot be carried out due to limitations in the data collected in this study.

The SMR for diseases of the circulatory system was elevated at 111. This is most likely a reflection of the higher mortality from heart disease which has been observed for Charleston, West Virginia and Kanawha County, West Virginia (unpublished data, Neas LM, 1979 and Enterline PE, 1979). For the total Nitro plant study population, there was a statistically significant excess in deaths from arteriosclerotic heart disease and a deficit in deaths from other circulatory diseases. This variation in the distribution of deaths from that of the U.S. may be due to risk factor or medical care differences in the plant population and the local area. These may include differences in smoking habits, the availability and use of medical services and the specificity of diagnoses.

The proportional mortality analysis of decedents by 2,4,5-T exposure classification indicated no unusual patterns of mortality in the 2,4,5-T exposed. The proportional mortality ratio (PMR for malignant neoplasms was low (PMR = 82) in the exposed group. Lung cancer was the only site among the malignant neoplasms which was somewhat higher in the exposed group.

Table 10. Deaths Due to Malignant Neoplasms Among Nitro Plant Workers Exposed to 2,4,5-T

Year of Birth	Year of Hire	Year of 1st Exposure	Year of Term.	Year of Death	Smoking History*	Cause of Death as Given on Death Certificate
1917	1946	1951	1972	1972	Cigarettes	Carcinoma left lung with metastases (162.1)
1911	1948	1955	1972	1972	Cigarettes	Metastatic carcinoma of the lung (162.1)
1916	1946	1959	1968	1968	Cigarettes	Bronchiogenic carcinoma of right upper lobe (162.1)
1901	1944	1956	1963	1973	Cigarettes	Carcinoma lung with metastases (162.1)
1911	1941	1948	1971	1975	Cigarettes	Bronchiogenic carcinoma with cerebral metastases (162.1)
1922	1945	1948	1972	1973	Non-smoker	Bronchiogenic carcinoma with metastases (162.1)
1923	1946	1950	1972	1972	Cigarettes	Generalized liposarcoma (171.9)
1902	1922	1948	1966	1966	Non-smoker	Metastatic carcinoma urinary bladder (188.0)**
1910	1944	1948	1968	1968	Non-smoker	Carcinoma of the urinary bladder (188.0)**

* Obtained by interview with former coworkers of decedents.
** Included on the Nitro plant PAB roster.

Table 11. Deaths Due to Malignant Neoplasms Among Nitro Plant Workers Not Exposed to 2,4,5-T

Year of Birth	Year of Hire	Year of Termin.	Year of Death	Smoking History*	Cause of Death as Given on Death Certificate
1911	1945	1966	1968	Cigarettes	Carcinoma of colon (153.8)
1904	1935	1957	1957	Cigarettes	Carcinoma of liver (157.9)
1899	1929	1959	1960	Pipe	Intraperitoneal carcinoma (158.9)
1905	1944	1970	1972	Cigarettes	Carcinoma of lung (162.1)
1909	1943	1962	1962	Cigarettes	Carcinoma of left lung (162.1)
1910	1927	1966	1970	Cigarettes	Pulmonary carcinoma (162.1)
1912	1944	1965	1965	Cigarettes	Carcinoma of apex of right lung (162.1)
1915	1937	1977	1977	Cigarettes	Carcinoma of lung (162.1)
1915	1939	1969	1970	Cigarettes	Carcinoma of lungs (162.1)
1894	1944	1960	1964	Non-smoker	Carcinoma of lung (162.1)
1912	1937	1973	1974	Cigarettes	Carcinoma of lung (162.1)
1919	1946	1963	1964	Cigarettes	Carcinoma of urinary bladder (188.0)**
1901	1933	1962	1977	Cigarettes	Carcinoma of bladder (188.0)**
1897	1941	1962	1965	Cigarettes	Carcinoma of urinary bladder (188.0)**
1898	1933	1962	1965	Smoked years ago	Carcinoma of urinary bladder (188.0)**
1905	1943	1971	1975	Cigarettes	Carcinoma of bladder (188.0)
1898	1943	1963	1970	Cigarettes	Bladder tumor (188.0)**
1888	1944	1956	1970	Unknown	Carcinoma of bladder (188.0)
1905	1933	1969	1977	Cigars	Prostatic carcinoma (185.0)
1906	1946	1968	1977	Cigarettes	Carcinoma of prostate (185.0)
1925	1945	1973	1974	Smoked years ago	Carcinoma of prostate (185.0)
1919	1943	1972	1973	Cigarettes	Hodgkin's Disease (201.0)
1901	1941	1964	1965	Cigars	Osteosarcoma arising from left arm (170.4)
1901	1943	1966	1977	Cigarettes	Carcinoma of liver & pancreas (197.8)
1922	1944	1964	1964	Cigarettes	Adenocarcinoma (199.0)

* Obtained by interview with former coworkers of decedents.

** Included on the Nitro plant PAR roster.

The PMR analysis is limited in that an assessment of the tot force of mortality cannot be made. The cause-specific PMR's only approximate what an SMR analysis would have produced.[16] The PMR analysis presented here estimates the cause-specific risks associ with 2,4,5-T exposure and potential TCDD exposure.

It is interesting to compare the results of this study of Mi plant workers potentially exposed to TCDD with the results of the study of Nitro workers involved in the 1949 TCP accident. The wo involved in that incident had presumed TCDD exposure as evidenced chloracne. The results of the two studies are similar in that ne shows an excess in deaths from any site among malignant neoplasms

A recent study of Ott et al.[17] found no excess in total mort. or in deaths from malignant neoplasms among workers exposed to 2, These workers were probably exposed to very low levels of TCDD si: no cases of chloracne were observed. Other studies of workers wh developed chloracne resulting from TCDD exposure have been conduc: and have been reviewed.[6] At the present time, data from these va: studies do not constitute corroborative evidence of a cancer risk man for any particular cancer site.

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The Mortality Experience of Workers Exposed to Tetrachlorodibenzodioxin in a Trichlorophenol Process Accident

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A standardized mortality analysis was conducted on workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident at the Monsanto Company plant in Nitro, West Virginia. One hundred and twenty-one workers who developed chloracne resulting from this accident on March 8, 1949, were selected for study. Follow-up of this group was 100% complete. The standardized mortality ratio for all causes of death was shown to be 0.69, with 32 deaths observed and 46.41 expected. For the categories of malignant neoplasms and circulatory diseases, the standardized mortality ratios were 1.00 and 0.68, respectively. Because of the small size of the cohort and the relatively small number of deaths observed, the results of this study cannot be considered conclusive. However, it is important that no apparent excess in total mortality or in deaths from malignant neoplasms or diseases of the circulatory system was observed in a group of workers with a high peak exposure to tetrachlorodibenzodioxin who were followed over a period of nearly 30 years. The results of this study will be incorporated with those of a larger study which will include plant workers exposed in the course of 2,4,5-trichlorophenoxyacetic acid production during the period 1948 to 1969.

A wide variety of acute and sub-acute health effects has been reported in workers involved in the manufacture of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) from 2,4,5-trichlorophenol (TCP). The most consistent clinical finding is chloracne, a skin disease characterized by comedones, cysts, pustules, and abscesses. Hepatic dysfunction, peripheral neuritis, disorders of fat metabolism, and porphyria cutanea tarda are other frequently reported findings in these workers.[1] Chloracne has been shown to be essentially due to 2,3,7,8-tetrachlorodibenzodioxin (TCDD),[2] a byproduct in the synthesis of 2,4,5-T. The subject of this paper is the chronic health effects of exposure to TCDD, as reflected in the mortality experience of a cohort of Monsanto Company workers who developed symptoms of chloracne following a trichlorophenol process accident at the Nitro, West Virginia, plant in 1949.

Production of trichlorophenol began in the fall of 1948 at the Nitro plant. In this process, the reactants 1,2,4,5-tetrachlorobenzene, sodium hydroxide, and methanol were all added to the autoclave. Heat was applied and, when the pressure reached the desired point, the autoclave was vented. On March 8, 1949, about six months after production start-up, a violent reaction and decomposition occurred when temperature and pressure within the autoclave became excessive. The relief valve opened and the fumes and tarry residues from the decomposed contents of the autoclave were discharged into the atmosphere and into the interior of the building.

Employees who worked in the area of TCP production or were involved in the clean-up began to develop symptoms immediately following exposure to the material which was discharged from the autoclave. Symptoms included eye and respiratory tract irritation, headache, dizziness and nausea, and a severe irritant reaction of the exposed skin. After these initial symptoms subsided, the chloracne and other symptoms became evident. Ashe and Suskind[3-6] examined a total of 12 more severely affected workers on three occasions during the period of 1949 to 1953. Another 26 persons with chloracne, apparently not related to the accident, were also examined in 1953. The

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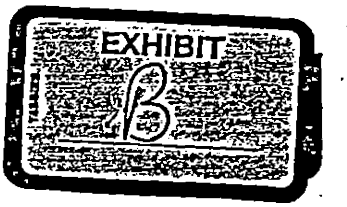

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clinical symptoms, in order of relative frequency,[4] included acneform lesions; severe pains in muscles of upper and lower extremities, shoulders and thorax on exertion; fatigue; nervousness and irritability; decrease in libido; dyspnea; vertigo and intolerance to cold. On examination, all of the cases had chloracne. Several were severely hyperpigmented, especially on the face. Of the six workers examined in 1949 and 1950, four had liver enlargement and one had sensory loss in one foot. Liver impairment as indicated by hepatomegaly, tenderness and soreness in the right upper quadrant and epigastrium and a delayed prothrombin time, was observed.[1,5,6]

In 1953, four of the six workers examined in 1949 and 1950 were re-examined and six additional workers involved in the accident were also examined. The findings in this later examination indicated a general regression of both the cutaneous and noncutaneous symptoms which had been present earlier. All of the workers showed a marked improvement in their skin lesions — there were residua of the acne and a few active lesions. In a few cases, workers continued to complain of aches and pains of the lower extremities and back, nervousness, excessive fatigue, and dyspnea. No clinical explanation for these complaints could be made based on the results of the physical examination.[4]

The findings of the examinations by Ashe and Suskind are consistent with those which have been reported in other industrial episodes which occurred subsequently.[1] The acute health effects of TCDD exposure are described in the literature,[7] but little is known of the chronic effects.

Several reports describe the occurrence of cancer and other deaths in workers exposed to TCDD which suggests an association between exposure and the subsequent development of a variety of neoplasms.[8-11] These reports, however, are generally of small groups of workers with relatively short periods of follow-up and are considered to be preliminary in nature. In a 25-year follow-up study, 17 deaths were observed among a cohort of 75 German workers who had been involved in a 1953 TCP process accident.[8] Of the 17 deaths observed (11-25 expected depending on the choice of a control population), six were from cancer (four or fewer expected), five from cardiovascular disease (as expected), two from suicide (fewer than one expected), one from liver cirrhosis, one from a urogenital tract disease, and two from external causes. Of the six cancer deaths, three were from stomach cancer in the age group 60-69, a number significantly higher than expected. Two other cancer deaths were from oat-cell carcinoma of the lung and one was from adenocarcinoma of the colon.

A similar accident occurred in the Netherlands in 1963 in a factory producing 2,4,5-T.[9] Eight deaths have been observed among 93 exposed workers. Five or six of these deaths were from cardiovascular disease. The proportion of deaths due to myocardial infarction was noted to be high.

Jirasek et al[9,10] and Pazderova[11] followed 55 of the 78 Czechoslovakian workers who were affected by chloracne resulting from occupational exposure to 2,4,5-T and pentachlorophenol. In this study, five deaths were observed. These included two deaths from bronchiogenic carcinoma (less than one expected), one from cardiovascular disease, one from liver cirrhosis, and one from an accidental industrial intoxication.

In 1976, a TCP process accident in Meda, Italy, resulted in the contamination of a large and densely populated area.[8] A preliminary mortality study has been conducted in two of the 11 towns affected. The overall mortality rate did not differ from that expected, but increases in deaths from liver cirrhosis and leukemia were suggested.

The chronic toxicity of TCDD exposure to animals has been more extensively studied. TCDD toxicity has been thoroughly reviewed.[7] Chronic toxicity to TCDD is manifested by liver necrosis, thymic atrophy, and depletion of the lymphoid organs. Two studies indicate that chronic administration of low levels of TCDD to rats is associated with an increased incidence of neoplasia. In one study, the oral administration of TCDD produced an increase in hepatocellular carcinomas and squamous cell carcinomas of the lung, hard palate/nasal turbinates, or tongue.[12] In another study, TCDD fed to rats produced tumors in 38% of the test animals.[13] Neoplastic nodules and cholangiocarcinomas of the liver were observed.

The study reported here will examine the mortality experience of a cohort of 121 employees involved in the 1949 trichlorophenol process accident, with special emphasis on cardiovascular disease and on neoplasms, particularly of the stomach, liver, lung, and skin.

Population and Methods

In this study, the development of chloracne, a hallmark of TCDD exposure, was used to identify employees for study. The study population consists of all persons with chloracne which could be attributed to the 1949 TCP process accident. One hundred and twenty-two employees who developed chloracne following this incident were identified from plant safety records dating to the time of the accident, and from workmen's compensation and plant medical records. One hundred and twenty-one white males were included in this study — one female who was living as of the endpoint of the study was not included in this mortality analysis. It is assumed that all of the skin disorders recorded in the plant records represent true cases of chloracne and not other types of occupational or nonoccupational dermatitis. An analysis of the chloracne cases and exposures not associated with this accident but rather with the normal TCP/2,4,5-T production processes will be the subject of a future paper.

The data were analyzed by the modified life-table method using the updated Monson program.[14] In this method of analysis, the age-, race-, time- and cause-specific mortality rates for a standard population (in this case, the population of the United States) are applied to the person-years lived classified by age, race, and time. A standardized mortality ratio was calculated as the ratio of the observed deaths to the expected deaths for 22 selected causes of death. The statistical significance of differences between observed and expected numbers was based on the Poisson distribution and statistical significance was determined at the 5% level of significance.

For the purpose of analysis, each member of the study cohort was assumed to have entered the study on March 8, 1949, the date of the accident. The vital status of each member was determined using standard follow-up techniques and ascertained as of December 31, 1978. For each person found to be deceased, a death certificate was ob-

Table 1. — Observed and Expected Deaths Among 121 Males Exposed to Tetrachlorodibenzodioxin in a Trichlorophenol Process Accident.

Cause	ICD No. (Eighth Revision)	Observed	Expected	SMR
All causes of death		32	46.41	0.69*
All malignant neoplasms	140-209	9	9.04	1.00
Buccal cavity and pharynx	140-149	0	0.30	†
Digestive organs and peritoneum	150-159	0	2.59	†
Stomach	151	0	0.50	†
Liver	155-156	0	0.18	†
All other digestive organs	—	0	1.91	†
Respiratory system	160-163	5	3.02	1.66
Lung	162.163	5	2.85	1.75
All other respiratory organs	—	0	0.17	†
Skin	172,173	1	0.15	†
Genitourinary organs	185-189	0	1.16	†
Lymphatic and hematopoietic tissue	200-209	3	0.88	†
Other sites	—	0	0.94	†
Diseases of the nervous system and sense organs	320-389	0	0.36	†
Diseases of the circulatory system	390-458	17	25.01	0.68
Arteriosclerotic heart disease, including coronary heart disease	410-413	13	17.74	0.73
All other disease of the circulatory system	—	4	7.27	†
Diseases of the respiratory system	460-519	1	2.78	†
Diseases of the digestive system	520-577	0	2.26	†
All other diseases	—	2	3.18	†
External causes of death	800-998	3	3.78	†

*$p < 0.05$
†Less than 5 observed deaths

tained. The underlying cause of death was coded to the 8th Revision of the International Classification of Diseases, Adapted[15] by an experienced nosologist.

Results

All of the 121 members of the study cohort were traced. Eighty-nine were verified living and 32 were verified deceased by death certificate.

The results of the standardized mortality analysis of the 121-member study cohort are shown in Table 1. The standardized mortality ratio for all deaths is shown to be 0.69, with 32 observed deaths and 46.41 expected. This is the only statistically significant difference shown in this table. There were nine deaths from malignant neoplasms with 9.04 expected. There were no deaths from stomach or liver cancer. There were five lung cancer deaths versus 3.02 expected and one skin cancer death with 0.15 expected. The malignant tumor was a fibrous histiocytoma presumably of dermal origin, which is rare. There were three deaths from neoplasms of lymphatic and hematopoietic tissue with 0.88 expected.

There were 17 observed deaths from circulatory diseases with 25.01 expected. The standardized mortality ratio for circulatory diseases was low at 0.68.

Case summaries for the cancer deaths are given in Table 2.

Discussion

Because the study cohort was small and only 32 deaths were observed, the results cannot be considered conclusive. Nevertheless, the analysis of the mortality experience of these workers indicated no apparent excess of total mortality or of deaths due to malignant neoplasms or circulatory diseases.

The TCDD-exposed workers in the present study represent the largest group ever investigated after long-term follow-up. The criteria for inclusion (presence of the workers at the 1949 accident and the subsequent occurrence of chloracne) limit the group to those with a significant exposure at that time. The latency period of 29 years

Table 2. — Cancer Deaths Among a Cohort of 121 Males Exposed to Tetrachlorodibenzodioxin in a Trichlorophenol Process Accident.

Year of Birth	Year of Hire	Year of Death	Death Certificate Statement of Cause of Death	Smoking History*
1909	1943	1962	Lung cancer (162.1)	Cigarettes
1910	1927	1970	Pulmonary carcinoma (162.1)	Cigarettes
1911	1939	1964	Bronchiogenic carcinoma (162.1)	Cigarettes
1922	1945	1973	Bronchiogenic carcinoma (162.1)	Nonsmoker
1915	1939	1970	Lung cancer (162.1)	Cigarettes
1920	1946	1978	Malignant fibrous histiocytoma of soft tissue origin (173.9)	Cigarettes
1919	1943	1973	Hodgkin's disease (201.0)	Cigarettes
1907	1943	1971	Lymphatic leukemia (204.9)	Pipe
1910	1939	1978	Acute myelogenous leukemia (205.0)	Cigarettes

*Smoking history was obtained by interviews with former co-workers of the decedents

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is longer than that of any pr· us study, and the follow-up is complete. Therefore, alt.ough the cohort is small, it represents the best opportunity so far to study the long-term effects of TCDD on mortality. By augmenting these data with the results of comparable mortality studies, the long-term effects of TCDD may be more definitely evaluated.

The authors wish to thank Mrs. Janet Yung, Mr. Randy Picolet, and Mrs. Phyllis Korte for their assistance with the data collection.

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Human Health Effects of 2,4,5-T and Its Toxic Contaminants

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• A clinical epidemiologic study was conducted to determine the long-term health effects of workplace exposure to the process of manufacturing the herbicide (2,4,5-trichlorophenoxy)acetic acid including contaminants such as 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. The population consisted of two cohorts: 204 clearly exposed and 163 not exposed. Among the exposed, clinical evidence of chloracne persisted in 55.7%. None of the not exposed experienced chloracne development. An association was found between the persistence of chloracne and the presence and severity of actinic elastosis of the skin. There is an association between exposure and the history of gastrointestinal tract ulcer. Pulmonary function values among those who were exposed and who currently smoked were lower than those who were not exposed and who currently smoked. The data assembled in the study indicate no evidence of increased risk for cardiovascular disease, hepatic disease, renal damage, or central or peripheral nervous system problems.

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THE HERBICIDE (2,4,5-trichlorophenoxy)acetic acid (2,4,5-T), first marketed in 1948, was used widely until 1970 in large-scale farming, family gardens, forest management, and weed control along roadsides and railroad rights-of-way.

The medical and scientific community was alerted to health problems arising from exposure to the manufacturing process of 2,4,5-T following a process accident (runaway reaction) that occurred in a plant in Nitro, WVa, on March 8, 1949.[1] The accident involved a kettle in which the intermediate trichlorophenol was being synthesized. Those employees involved in the cleanup of the building and the repair of equipment experienced acute symptoms characterized by skin, eye, and respiratory tract irritation, headache, dizziness, and nausea. These symptoms subsided within one to two weeks and were followed by an acneform eruption, severe muscle pain affecting the extremities, thorax, and shoulders, fatigue, nervousness and irritability, dyspnea, complaint of decreased libido, and intolerance to cold.[1] An examination of the workers in 1949 revealed a severe and generalized acneform eruption (chloracne), hepatic enlargement, peripheral neuritis, delayed prothrombin time, and increased total serum lipid levels. By 1953, those symptoms and findings referrable to the nervous system and liver had subsided. The chloracne, although much improved, persisted.[1]

In 1957, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) was identified as a toxic and acnegenic contaminant of trichlorophenol synthesis.[2] The subacute effects of this agent, which have been repeatedly observed in humans, include chloracne,[3-5] the most consistent clinical marker, liver function impairment,[1,5-8] peripheral neuropathy,[1,5-8] nervousness and irritability,[1] personality changes,[1,5] porphyria cutanea tarda,[1,5] and hypertrichosis and hyperpigmentation.[1,5] Elevation of levels of blood cholesterol,[1,5,8] triglycerides,[1] gamma-glutamyl transpeptidase (GGTP),[1] and alkaline phosphatase have been reported.

Toxicologic studies of TCDD in animals have revealed hepatotoxic effects,[9-11] teratogenic effects,[12,13] suppression of cell-mediated immunity in mice and guinea pigs,[14] and the induction of hepatic carcinoma in rats.[15]

Some of the clinical reports have been concerned with the association of cardiovascular disease[5] and an increased risk for cancer in populations exposed to TCDD.[16-18] Several comprehensive reviews on this entire subject have been published.[19-21]

A mortality analysis of workers exposed to the runaway reaction materials was conducted. As of 1979, the Standardized Mortality Ratio (SMR) for all causes of death was 0.69, with 32 deaths observed and 46.41 expected. For the categories of cancer and circulatory diseases, the SMRs were 1.00 and 0.68, respectively.[22]

A CLINICAL STUDY

In June 1979, a clinical examination program was conducted that included the active and retired employees of the Nitro, WVa, plant, who were exposed to the 2,4,5-T process between 1948 to 1969. The objective of the examination program was

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to determine possible increased risks, on a long-term basis, for adverse cutaneous, pulmonary, cardiovascular, gastrointestinal (GI), hepatic, renal, neurological, behavioral, and reproductive effects; effects on lipid metabolism and the possibility of increased risks for cancer. The population included those exposed to the process accident as well as those exposed to normal manufacturing processes and included chemical operators and service employees, such as pipefitters and mechanics. The control group consisted of current or former employees of the same plant who, according to interview work history and personal work records, were never associated with the 2,4,5-T process or its materials.

Subjects of the Study

The total number of subjects examined was 436. There were 419 white males, five black males, one male of Hispanic descent, one male of American Indian descent, and ten white females. One subject among the 419 was exposed to the runaway reaction residue in 1949 as a child. The seven nonwhite males, ten white females, and the white male exposed as a child were excluded from this analysis. There were also 51 subjects whose possible exposure was limited, poorly documented, and did not include work in the 2,4,5-T production process. They are not included in this analysis. The remaining 367 subjects were designated by exposure as follows: (1) exposure without qualification: 204 subjects who were involved in any aspect of the production of 2,4,5-T, including maintenance from 1948 to 1969; and (2) no exposure: 163 subjects currently or formerly employed at the same plant but never associated with any aspect of 2,4,5-T production or maintenance of the production facility.

All living employees, active, retired, or terminated, as determined from company records, were asked to participate. To constitute cohorts of the target sample size, all those who volunteered participation in the study were examined; thus, it was not possible to randomize the selection of participants. Of the living exposed personnel, approximately 61% voluntarily participated in the study, as did approximately 46% of the living not exposed personnel. The only mortality data available for analysis at the time of this study were for personnel who were exposed to the runaway reaction materials.[4]

Clinical Examination

The interviews and clinical examination with informed consent were conducted during the week July 11 to 18, 1979, in Winfield, WVa.

The routine laboratory analysis of blood and urine was completed by Metpath. Blood plasma lipid fraction examination was carried out by the Lipid Research Division (a National Institutes of Health Center) of the University of Cincinnati Medical Center using methods of the National Lipid Research Project,[5] including determination of plasma cholesterol, plasma triglyceride, plasma high-density lipoprotein (HDL) cholesterol, and estimated plasma low-density lipoprotein (LDL) cholesterol values. Pulmonary function tests, ECG, chest roentgenogram, and nerve conduction velocity measurements, performed by the method described in Goodgold and Eberstein,[6] were done at the time of the physical examination. The nerve conduction velocity measurements were obtained for most subjects from the peroneal nerve for motor and the sural nerve for sensory function.

Clinical laboratory analyses included blood calcium, phosphorus, blood urea nitrogen, creatinine, blood urea nitrogen/creatinine ratio, uric acid, glucose, total protein, albumin, globulin, albumin/globulin ratio, total bilirubin, direct bilirubin, SGOT, SGPT, alkaline phosphatase, iron, total lipids, sodium, potassium, chloride, GGTP, complete blood cell count and differential cell count, thyroxine radioimmunoassay, and thyroxine-binding globulins. Urinalysis included routine examination as well as determination of coproporphyrin and uroporphyrin values. (Values were determined from a single void sample; hence, the measurements cannot be regarded as valid.)

Analysis of Data

Data from questionnaires and the subject's medical history were coded by assigning numerical values to the responses given. The subject's medical history and findings were coded using the Systematized Nomenclature of Medicine[7] System. Laboratory data were entered as received. Data were keypunched and verified. The computer data were compared with the original files for accuracy. The Statistical Analysis System[8] computer package was used for data analysis. As the analysis progressed, editing continued to ensure the greatest possible accuracy. Multiple linear regression analysis[9] was used to compare the exposed group with the not exposed group and to compare the three chloracne subgroups with respect to plasma lipid levels, pulmonary function values, clinical laboratory values, and nerve conduction measurements after adjustment for covariables. The covariables were age in the analysis of clinical laboratory values and nerve conduction measurements, age and smoking status (never, former, and current) in the analyses of pulmonary function values and age, and smoking status and alcohol status (never used, formerly used, and currently used) in the analyses of plasma lipid values. Fisher's exact test[10] and the χ^2 test for independence in contingency tables were used to compare the two exposure groups and the three chloracne categories with respect to frequency of abnormal findings on physical examination, pulmonary function test, and lipid analyses. Fisher's exact test was also used to compare the two exposure groups with respect to reproductive findings. Mantel-Haenszel analysis[11] was used to compare the exposed group with the not exposed group with respect to frequency of abnormal findings on physical examination after adjustment for age group (<50 and ≥50 years) and with respect to frequency of abnormal findings on pulmonary function test or abnormal plasma lipid levels after adjustment for smoking status. Logistic regression analysis[12] was used to detect associations of exposure with abnormal findings on pulmonary function test after adjustment for pack years smoked. Log linear models[13] were used to detect associations between the three chloracne groups and abnormal plasma lipid levels after adjustment for smoking status.

RESULTS

Demographic Information

Demographic data of the 367 white males were examined to determine potentially confounding variables. The mean ages of the exposed and not exposed groups were 56.7 ± 0.7 ($\bar{X} \pm SE$) years and 46.2 ± 1.0 years, respectively ($P < .0001$). The two groups were found to be significantly different with respect to employment status and highest educational level achieved ($P \leq .0001$). In the exposed and not exposed groups, 34.8% and 13.5% were retirees and 9.8% and 0.6% were terminated (left voluntarily or laid off), respectively. Among the exposed and not exposed groups, 9.4% and 1.2% reached no further than the eighth grade, respectively; 72.4% and 56.8% had some high school education, respectively. Among the not exposed, 42.0% attended college, some to completion, while among the exposed, only 18.2% attended college.

Alcohol and Smoking

History of alcohol consumption was not found to be significantly different in the two groups. When smoking status (current, former, or never) was used as the criterion, no differences were found. Among current smokers, the exposed group had smoked significantly longer than the not exposed by 19 pack-years ($.0001 < P < .001$). Among former smokers, the exposed

roup had smoked longer than the not xposed group by seven pack-years ($.05 < P < .10$). This reflected the ten-year age difference between the exposed and the not exposed group.

History of Medical Problems

The comparison of the exposed and not exposed cohorts for self-reported history of illness is given in Table 1. Chloracne was reported only in the exposed group: 86.3% in the exposed v 0.0% in the not exposed. The data about the history of chloracne were determined on the basis of statements from subjects that an acnelike eruption called "weed bumps" appeared after an assignment to a 2,4,5-T production area. Records of the medical department of the company and the state Workmen's Compensation Bureau stating that the person had chloracne confirmed many of these histories. In the not exposed group, a history of acne vulgaris was reported more frequently than in the exposed group. This information was based on the story of adolescent acne before employment at this plant. A history of upper GI tract ulcer was reported almost four times more frequently in the exposed group. When the medical history of the exposed and not exposed was compared for two age groups younger than 50 years v 50 years or older, a history of coronary artery disease and of hypertension were related to age, not exposure. Among the not exposed, angina was significantly related to age; in the history of upper GI tract ulcer, however, exposure, not age, appeared to be a factor.

Closer examination of onset of ulcer in relation to exposure revealed six subjects whose symptoms occurred before exposure. There were also four subjects whose symptoms occurred while they were receiving corticosteroid therapy or high doses of aspirin or that were attributed to chronic alcoholism. If these ten subjects were omitted from the analysis, there remained statistically significant differences between the exposed and not exposed groups (16.6% v 5.5%; $P \leq .01$ on age adjustment).

The complaint of loss of libido occurred more frequently in the exposed group than the not exposed group. When age was considered, the largest number of complaints of loss of libido or impotence were reported by the older age group (Table 2).

Table 1.—History of Medical Problems v Exposure Status and by Age

History	Exposed, % (n=204)*	Not Exposed, % (n=163)	Age <50 yr, % Exposed (n=61)	Age <50 yr, % Not Exposed (n=100)	Age ≥50 yr, % Exposed (n=183)*	Age ≥50 yr, % Not Exposed (n=63)
Chloracne†‖	86.3	0.0	76.3	0.0	89.5	0.0
Acne vulgaris‡¶	9.9	29.8	17.7	42.0	7.2	9.6
Skin cancer	3.9	2.5	0.0	1.0	5.3	4.8
Hypertension§#	34.6	24.6	21.6	16.0	38.8	36.1
Angina#	7.4	6.1	5.9	1.0	7.9	14.3
Coronary artery disease§¶	10.8	6.1	2.0	0.0	13.8	16.9
Upper gastrointestinal tract ulcer‖	20.7	5.5	13.7	5.0	23.0	6.4
Cancer of all sites** (except skin)	3.9	1.2	0.0	0.0	3.9	3.2

*One of the 204 subjects did not complete the interview/physical examination program but had a documented workmen's compensation claim for chloracne.

†$P < .0001$; P value for Mantel-Haenszel comparison of exposed v not exposed across age strata.

‡$.01 < P < .05$; in exposed, young v old, by Fisher's exact test

§$.001 < P < .01$; P value for Mantel-Haenszel comparison of exposed v not exposed across age strata.

‖$.05 < P < .10$; in exposed, young v old, by Fisher's exact test.

¶$P < .0001$; in not exposed, young v old, by Fisher's exact test.

#$.001 < P < .01$; in not exposed, young v old, by Fisher's exact test.

**In the exposed group, bladder cancer, two; colon cancer, three; prostate cancer, one; in the not exposed group, bladder cancer, one; melanoma, one.

Table 2.—Complaints of Nervousness and Sexual Problems to Examining Physician or Interviewer

Complaint	Exposed, % (n=203)	Not Exposed, % (n=163)	Age <50 yr, % Exposed (n=61)	Age <50 yr, % Not Exposed (n=100)	Age ≥50 yr, % Exposed (n=182)	Age ≥50 yr, % Not Exposed (n=63)
"Nervousness"/anxiety/depression*	16.3	11.7	7.8	15.0	19.0	6.4
Decreased libido†‖	16.6	15.3	19.6	6.0	40.8	31.7
Impotence, not otherwise specified‡‖	27.6	11.7	7.8	2.0	34.2	27.0

*$.05 < P < .10$; in exposed, young v old, by Fisher's exact test.

†$.001 < P < .01$; for Mantel-Haenszel comparison of exposed to not exposed across age strata.

‡$P < .0001$; in not exposed, young v old, by Fisher's exact test.

§$.001 < P < .01$; in exposed, young v old, by Fisher's exact test.

‖$.0001 < P < .001$; in exposed, young v old, by Fisher's exact test.

As noted in Table 1, the reported history of skin cancer, hypertension, angina, coronary artery disease, and cancer of all sites (except skin) was not found to be significantly associated with exposure. The sample size obtained was sufficient (at significance level of .05, power of .80 [probability of detecting a true difference]) to detect a fourfold increase in skin cancer, a twofold increase in hypertension, a threefold increase in angina and coronary artery disease, and a sixfold increase in cancer of all sites (except skin) for exposed over what was observed in the not exposed. As noted in Table 2, the complaint of nervousness/depression/anxiety and the complaint of impotence were not related to exposure. The sample size was sufficient to detect a twofold increase in complaint of nervousness/depression/anxiety for exposed over not exposed. Although the sample size was sufficient to detect crude differences between the two groups with respect to complaint of impotence, the difference disappeared when age was considered.

The exposed population was categorized into three subgroups, ie, those who never had chloracne develop (n=28), those who had a history of chloracne only (n=69), and those whose chloracne persisted (n=107). When the histories of medical problems were examined in relation to chloracne status, hypertension and coronary artery disease were found to be age related, not chloracne related. Histories of skin cancer and angina were not statistically significant when related to chloracne or to age within the chloracne groups. While it would seem (Table 3) that skin cancer

Table 3.—History of Medical Problems v Chloracne Status in Exposed Only and by Age

History*	Chloracne Status, %								
				Age <50 yr			Age ≥50 yr		
	History Only (n=68)	Current (n=107)	No History (n=28)	History Only (n=16)	Current (n=23)	No History (n=12)	History Only (n=62)	Current (n=84)	No History (n=16)
Acne vulgaris	8.8	6.5	25.0	18.8	8.7	33.3	5.8	6.0	18.8
Skin cancer	5.9	2.8	3.6	0.0	0.0	0.0	7.7	3.6	6.3
Hypertension†	35.3	36.3	17.9	6.3	34.8	16.7	44.2	39.3	18.8
Anoma	5.9	10.3	0.0	0.0	13.0	0.0	7.7	9.5	0.0
Coronary artery disease‡	8.8	14.0	3.6	6.3	0.0	0.0	9.6	17.9	6.3
Upper gastrointestinal tract ulcer	16.2	25.2	14.3	6.3	21.7	8.3	19.2	26.2	18.8
Cancer of all sites (except skin)	4.4	2.8	0.0	0.0	0.0	0.0	5.8	3.6	0.0

*All comparisons of the three chloracne categories, both for the total group and for the two age groups, were found to be not significant by χ^2 test for independence in contingency tables.
†.01<P<.05 for history only, young v old by χ^2 test for independence in contingency tables.
‡.05<P<.10 for current, young v old by χ^2 test for independence in contingency tables.

is related to age in the three chloracne groups, the number of persons in the age group younger than 50 years was too small to achieve statistical significance. There was no association between the history of upper GI tract ulcer and chloracne status (Table 3).

While the number of subjects reporting a history of cancer (other than skin) was small, all of them were found in the group aged 50 years or older, and the percentage in the exposed group was not significantly different from that in the not exposed group (Table 1). The three bladder cancers were reported by persons exposed to p-aminobiphenyl, a rubber additive that was also made in the plant.

Physical Examination Results

There seemed to be no difference in blood pressure findings between the exposed and not exposed group. The criteria for determining normal for combined systolic/diastolic values were less than 140/90 mm Hg for subjects aged 59 years or younger and less than 160/95 mm Hg for subjects aged 60 years or older. For diastolic alone, less than 80 mm Hg was considered normal. Diastolic values of 80 to 89 mm Hg for ages 59 years and younger and 80 to 94 mm Hg for ages 60 years and older were considered borderline. Diastolic values of 90 mm Hg or greater for ages 59 years and younger and diastolic values of 95 mm Hg or greater for ages 60 years and older were considered high.

The significant clinical examination findings as related to exposure status and age are found in Table 4. Of those who were clearly exposed,

Table 4.—Significant Clinical Findings v Exposure Status and by Age

Finding	Exposed, % (n=203)	Not Exposed, % (n=163)	Age <50 yr, %		Age ≥50 yr, %	
			Exposed (n=51)	Not Exposed (n=100)	Exposed (n=152)	Not Exposed (n=63)
Chloracne*	52.7	0.0	45.1	0.0	55.3	0.0
Acne vulgaris†‡	2.0	11.7	7.8	18.0	0.0	1.6
Actinic elastosis‡¶	59.1	30.1	37.3	18.0	66.4	49.2
Basal cell epithelioma§	6.9	4.3	2.0	0.0	8.6	11.1
Peyronie's disease#	1.5	0.0	0.0	0.0	2.0	0.0
Hirsutism	6.4	1.8	3.9	1.0	5.9	3.2

*P<.0001; P value for Mantel-Haenszel comparison of exposed v not exposed across age strata.
†.05<P<.10; P value for Mantel-Haenszel comparison of exposed v not exposed across age strata.
‡.0001<P<.01; in exposed, young v old, by Fisher's exact test.
§.001<P<.01; in not exposed, young v old, by Fisher's exact test.
‖.0001<P<.001; P value for Mantel-Haenszel comparison of exposed v not exposed across age strata.
¶.0001<P<.001; in exposed, young v old, by Fisher's exact test.
#P<.0001; in not exposed, young v old, by Fisher's exact test.

52.7% still had chloracne, 62.6% were mild cases, 33.9% were regarded as moderate, and 3.8% were severe.

The diagnoses of chloracne and acne vulgaris were made by qualified dermatologists. The criteria for diagnosis of chloracne include the initial appearance of comedones, milia, or epidermal cysts on the malar, temple, and periorbital areas that may subsequently involve other areas of the face, the neck, forearms and arms, and scalp and genitalia. The scrotum and penis are commonly affected in persons whose clothing becomes heavily contaminated by the acnegenic material. Lesions may become secondarily infected, especially on the trunk, forearms, and genitalia. By contrast, acne vulgaris that usually starts in adolescence is seen as inflamed papules, pustules, and comedones, on the perinasal area, cheeks, chin, neck, and back. It rarely, if ever, starts on the malar or periorbital areas. The skin of the affected sites in acne vulgaris is usually very oily or greasy. In the case of chloracne, the skin surface is usually dry. Persons with acne vulgaris, exposed to chloracnegens, may experience the development of chloracne. The lesions of acne vulgaris may increase in severity and lesions may develop in sites not usually or previously affected by acne vulgaris.

Among the exposed, 59.1% were found to have actinic elastosis in contrast to 30.1% among the not exposed. There was a significant difference in the occurrence of actinic elastosis between the exposed and not exposed in both age groups even though age is a factor in this clinical finding. Three cases of Peyronie's disease were observed among the 204 exposed. All of them had chloracne at some time and they were all older than 50 years. Peyronie's disease is characterized by induration and scarring of the corpus cavernosum of the penis, producing distortion on erec-

Table 5.—Significant Clinical Findings v Chloracne Status in Exposed Only and by Age

Finding	History Only, % (n=68)	Current, % (n=107)	No History, % (n=28)	Age <50 yr, % History Only (n=16)	Current (n=23)	No History (n=12)	Age ≥50 yr, % History Only (n=52)	Current (n=84)	No History (n=16)
Acne vulgaris*	1.5	0.0	10.7	6.3	0.0	25.0	0.0	0.0	0.0
Actinic elastosis*†‡	47.1	74.8	28.6	31.3	56.3	8.3	51.9	79.8	43.8
Basal cell epithelioma	5.9	6.4	3.6	6.3	0.0	0.0	5.8	10.7	6.3
Peyronie's disease	2.9	0.9	0.0	0.0	0.0	0.0	3.8	1.2	0.0
Hirsutism†	0.0	10.3	0.0	0.0	8.7	0.0	0.0	10.7	0.0

*.01<P<.05; for overall differences between the three chloracne categories in age 49 years or younger, by χ^2 test for independence in contingency tables.
†.0001<P<.01; for overall differences between the three chloracne categories in age 50 years or older, by χ^2 test for independence in contingency tables.
‡.01<P<.05; in current chloracne, young v old, by Fisher's exact test.
§.05<P<.10; in no history of chloracne, young v old, by Fisher's exact test.

Table 6.—Exposure v Plasma Lipids

Plasma Lipids	Exposed n	Exposed $\bar{X} \pm SE$	Exposed % Out of Range*	Not Exposed n	Not Exposed $\bar{X} \pm SE$	Not Exposed % Out of Range*	P Value
Cholesterol	200	211.15 ± 2.53	7.5	163	204.07 ± 2.97	10.4	NS
Triglyceride	200	149.88 ± 7.44	14.5	163	159.63 ± 7.73	19.0	NS
Low-density lipoprotein cholesterol	196	136.74 ± 2.40	7.7	159	127.08 ± 2.60	8.3	NS
High-density lipoprotein cholesterol	200	46.83 ± 0.91	9.5	163	44.22 ± 0.77	10.4	NS

*Reference ranges for plasma cholesterol, triglyceride, and low-density lipoprotein cholesterol were defined as less than the age-specific 90th percentile as determined by the National Lipid Research Project. Reference ranges for high-density lipoprotein cholesterol were defined as above the age-specific tenth percentile as determined by the National Lipid Research Project.

tion.

As noted in Table 4, there was no association of findings of basal cell epithelioma and hirsutism with exposure. The sample size was sufficient to detect a threefold increase in basal cell epithelioma and a fourfold increase in hirsutism for exposed over what was observed in the not exposed.

Table 5 identifies the clinical findings in the exposed population in relation to chloracne status. In these groups, actinic elastosis was found preponderantly in the subjects with persistent chloracne (74.8%), but it also occurred significantly in those with a history of chloracne only (47.1%). Of the exposed with persistent acne, 10.3% were found to have malar hirsutism: nine of these 11 cases occurred in the group older than 50 years.

Actinic elastosis is a problem found in persons of light coloration exposed over many years to sunlight (eg, farmers' skin and sailors' skin). It is characterized by swelling and fragmentation of the elastic tissue elements of the dermis. There was an association of actinic elastosis with chloracne. It seems that the percentage of persons with severe actinic elastosis was related to presence of chloracne and that it is more severe when found with chloracne.

Plasma Lipids

Plasma cholesterol, triglyceride, LDL cholesterol and HDL cholesterol were classified by age-specific percentiles as determined by the National Lipid Research Project data.[11] Plasma cholesterol, triglyceride, and LDL cholesterol values were classified as out of range if they fell above the 90th percentile; HDL cholesterol values were classified as out of range if they fell below the tenth percentile. The frequency of out-of-range lipid findings was compared for exposed and not exposed groups (Table 6). No significant differences were noted. The sample size was sufficient to detect a twofold increase in the frequency of out-of-range cholesterol, triglyceride, LDL cholesterol, or HDL cholesterol values for exposed over what was observed in the not exposed. After adjusting for smoking status, no significant differences were found. The mean lipid values were also compared for the exposed and not exposed groups (Table 6), and no significant differences were found.

When the lipid levels of the exposed group only were examined in relation to chloracne status, there was a significantly greater number of subjects with low HDL cholesterol levels in those with persistent chloracne than in those with a history only of chloracne or those who never had chloracne (Table 7). There was a greater number of persons with high LDL cholesterol levels among those who had a history only of chloracne than those who had chloracne currently or never. The mean lipid levels for these three chloracne groups were also compared (Table 7), and no significant differences were found.

After adjusting for age, height/weight, smoking status, and alcohol status, no significant differences were found between the two exposure groups with respect to mean lipid values. The interaction of smoking status and alcohol status was also added to the model, and no differences were found between the two exposure groups.

To detect differences between the chloracne groups with respect to mean lipid values, the same adjustments described previously were performed. No significant differences were found.

Log linear models were used to detect associations between frequency of out-of-range lipid values and chloracne status in the exposed group only, adjusting for smoking status. Findings are as follows: (1) Out-of-range cholesterol or triglyceride values were not associated with chloracne status. (2) Out-of-range HDL cholesterol values were associated

Table 7.—Chloracne Status in Exposed Only v Plasma Lipids

Plasma Lipid	History Only n	History Only X ± SE	History Only % Out of Range*	Current n	Current X ± SE	Current % Out of Range*	No History n	No History X ± SE	No History % Out of Range*
Cholesterol	87	215.16 ± 4.87	11.9	106	210.23 ± 3.17	4.8	28	204.96 ± 7.13	7.1
Triglyceride	87	144.00 ± 14.66	7.5	106	163.84 ± 9.39	19.1	28	149.11 ± 18.36	14.3
Low-density lipoprotein cholesterol†	66	142.84 ± 4.69	15.2	103	134.48 ± 2.66	2.9	27	130.96 ± 7.06	7.4
High-density lipoprotein cholesterol‡	87	46.84 ± 1.17	3.0	106	44.93 ± 1.31	14.3	28	47.76 ± 3.31	7.1

*Reference ranges for plasma cholesterol, triglyceride, and low-density lipoprotein cholesterol were defined as less than the age-specific 90th percentile as determined by the National Lipid Research Project. Reference ranges for high-density lipoprotein cholesterol were defined as above the age-specific tenth percentile as determined by the National Lipid Research Project.

†$P<.016$; for comparing frequency of out-of-range levels in the three chloracne groups

‡$P<.05$; for comparing frequency of out-of-range levels in the three chloracne groups.

with chloracne status ($.01<P<.05$), and the degree of association did not vary significantly by smoking status. (3) Out-of-range LDL cholesterol values were associated with chloracne status ($.01<P<.05$), and the degree of association did not differ significantly by smoking status.

Pulmonary Function Examination

Both forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) were considered abnormal if the observed value was less than 80% of the predicted value of Morris. A FEV_1/FVC percentage less than 70% was considered to be abnormal. The forced midexpiratory flow rate (FEF_{25-75}) was considered abnormal if the observed value was less than 70% of the predicted value of Morris.

Consistent differences in abnormal pulmonary function values (FEV_1, FVC, FEV_1/FVC, and FEF_{25-75}) were found when the exposed and not exposed groups were compared (Table 8). Among current smokers, there was a significant difference in frequency of abnormal pulmonary function values between the exposed and not exposed groups, but there were no differences among persons who have formerly smoked or among persons who have never smoked (Table 8).

Logistic regression was performed to evaluate the relationship between frequency of abnormal pulmonary function values and exposure after adjusting for pack years smoked. Odds ratios are given for these parameters in Table 8. Exposure significantly increased the odds for abnormal pulmonary function values even after adjustment for pack years smoked.

The means of the percent-predicted values were compared between the two exposure groups after adjusting for the effect of smoking (Table 9). No difference was found between the two exposure groups with respect to FEF_{25-75} percent predicted. Percent-predicted values for FEV_1/FVC and FVC were significantly lower in the exposed group. Furthermore, there was a significant interaction between smoking status and exposure with respect to FEV_1 percent-predicted values. When adjusted group means for each smoking status exposure combination (Table 9) were examined to determine the nature of the relationship, no significant differences were found between exposed and not exposed workers who never smoked or who formerly smoked. Among current smokers, however, there was a significant difference between exposed and not exposed workers with respect to FEV_1 percent-predicted values.

Clinical Laboratory Findings

With regard to clinical laboratory determinations other than plasma lipids, no significant differences were detected between exposed and not exposed groups. There have been reports of abnormal levels of alkaline phosphatase, SGOT, SGPT, and GGTP in other populations exposed to TCDD for short or long periods; however, no differences were found in these cohorts ten to 30 years after the last date of exposure.

ECG and Roentgenographic Findings

No differences were observed in the ECG findings when the exposed and not exposed groups were compared. When the chest x-ray film findings in the exposed group were compared with those in the not exposed group and separated by age, the arteriosclerotic changes and pleural thickening differences between the groups seemed to be age related, not exposure related.

Neurological Findings and Nerve Conduction Velocity Measurements

When exposed and not exposed groups were compared for frequency of abnormal findings on neurological examination, no differences were found.

Nerve conduction velocity measurements require controlled atmospheric conditions and uniform conditions of testing. Ambient and body temperatures were recorded. With the technology employed, it was at best a screening procedure.

All subjects reporting diabetes or reporting a high weekly alcohol intake (≥35 oz. of alcohol per week) were eliminated from the data analysis. After these deletions, there were 278 with complete sural and 294 with complete peroneal examinations remaining. The data from the nerve conduction velocity studies were corrected for body temperature according to the deJesus[11] method. The age-adjusted values are presented in Table 10. No significant differences were found when the two exposure groups were compared or when the three chloracne groups were compared.

Reproductive Effects

Information on reproductive factors and birth defects was elicited from the male participants. Neither physician nor hospital records were available to confirm the information.

A comparison between the exposed and not exposed groups for pregnancies, live births, infant deaths, mis-

Table 8.—Exposure v Pulmonary Function Findings by Smoking Status

Pulmonary Function Parameter	Smoking Status	Exposed		Not Exposed			Results of Logistic Regression on Pack-Years Smoked	
		n	% Abnormal	n	% Abnormal	P Value	Odds Ratio	P Value
FEV_1*	Never	39	6.1	40	5.0	NS	...	...
	Former	89	11.2	77	5.2	NS	...	...
	Present	74	27.0	45	4.4	.0025	...	...
	Total†	203†	15.8	162	4.9	.0013	2.81	.0159
FVC*	Never	39	5.1	40	12.5	NS	...	...
	Former	89	15.7	77	6.5	NS	...	...
	Present	74	26.7	45	2.2	.0006	...	...
	Total†	203†	17.2	162	6.8	.0038	2.26	.0319
FEV_1/FVC %	Never	39	5.1	40	2.5	NS	...	...
	Former	89	12.4	77	5.2	NS	...	...
	Present	74	25.7	45	6.7	.0143	...	...
	Total†	203†	15.8	162	4.9	.0013	2.97	.0099
FEF_{25-75}*	Never	39	7.7	40	7.5	NS	...	...
	Former	89	19.1	77	13.0	NS	...	...
	Present	74	36.5	45	11.1	.0035	...	...
	Total†	203†	23.2	162	11.1	.0038	1.89	0617

*FEV_1 indicates forced expiratory volume in 1 s; FVC, forced vital capacity; FEF_{25-75}, forced midexpiratory flow rate.
†Unknown smoking status, two subjects, one whose pulmonary function test result was normal and is included in the total.

Table 9.—Exposure Group Means of Percent-Predicted Pulmonary Function Parameters Adjusted for Smoking Status

Pulmonary Function Parameter	Smoking Status	Exposed $\bar{X} \pm SE$	Not Exposed $\bar{X} \pm SE$	P
FEV_1*	Never	107.12 ± 3.06	105.93 ± 3.03	NS
	Former	101.43 ± 2.03	104.96 ± 2.18	NS
	Present	89.63 ± 2.22	102.33 ± 2.86	0.0006
	Total	99.39 ± 1.43	104.42 ± 1.57	0.0184
FVC*	...	92.73 ± 1.17	97.80 ± 1.28	0.0064
FEV_1/FVC %	...	76.49 ± 0.83	79.83 ± 0.88	0.0002
FEF_{25-75}*	...	101.00 ± 4.02	109.16 ± 4.39	NS

*FEV_1 indicates forced expiratory volume in 1 s; FVC, forced vital capacity; FEF_{25-75}, forced midexpiratory flow rate.

Table 10.—Mean Nerve Conduction Velocity* for the Exposure Groups and for the Chloracne Subgroups

Category	Nerve Tested		
	Ulnar	Peroneal	Sural
Exposed† $\bar{X} \pm SE$ (n)	56.90 ± 2.36 (9)	41.77 ± 0.47 (160)	42.06 ± 0.49 (160)
Not Exposed $\bar{X} \pm SE$ (n)	61.91 ± 3.36 (9)	42.62 ± 0.62 (134)	41.49 ± 0.64 (128)
Chloracne, history only† $\bar{X} \pm SE$ (n)	56.92 ± 6.02 (3)	40.68 ± 0.77 (60)	41.14 ± 0.90 (51)
Chloracne, current $\bar{X} \pm SE$ (n)	67.86 ± 4.11 (5)	41.38 ± 0.69 (96)	41.37 ± 0.78 (74)
Chloracne, never $\bar{X} \pm SE$ (n)	52.10 ± 0.00 (1)	40.81 ± 1.12 (24)	41.23 ± 1.30 (26)

*Adjusted for age.
†P equals not significant for comparison of exposed with not exposed with respect to ulnar, peroneal, and sural, and also for comparison of the three chloracne categories with respect to ulnar, peroneal, and sural.

carriages, birth defects, and stillbirths is listed in Table 11. There were no significant differences in these parameters between the exposed and not exposed cohort. No data were available on age of wives of workers.

Other Work Exposures of the Study Population

Other than 2,4,5-T and its intermediates and/or contaminants, all of the workers in the study were exposed to multiple chemicals and industrial processes under varying working conditions, at the same plant and/or other plants, between the late 1930s and 1979.

Rubber processing chemicals identified by the subjects as other exposures included diphenylguanidine, the benzothiazolesulfenamides, derivatives of *m*-cresol, *p*-phenylenediamine derivatives, and 4,4-dithiodimorpholine. Additional chemicals named were ethyl parathion and methyl parathion, phthalic anhydride, *o*- and *p*-dichlorobenzene, *o*- and *p*-nitrophenol, toluene and mercaptobenzothiazole derivatives of tetramethylthiuramdisulfide, and trimethylquinoline components.

Seventy-nine subjects, or 21.5% of the 367, reported in-plant exposure to *p*-aminobiphenyl, a known bladder carcinogen, during the course of their employment. These subjects are periodically examined in a clinical surveillance program established by the medical department of the company. Subjects reported the exposure and the monitoring program during the interview and to the examining physician. The data relating this exposure to 2,4,5-T are described in Table 12.

COMMENT

In any interpretation of the medical significance of data elicited from this study, it is essential to consider the characteristics of the cohorts as well as the strengths and weaknesses of the design of the study. With all industrial populations at risk in the

Table 11.—Exposure v Reproductive Findings

Reproductive History	Exposed* (n=1804)	Not Exposed† (n=1645)	Probability
Pregnancies	655	479	...
Miscarriages	69	61	...
rate per 1,000 pregnancies	105.34	118.86	NS
Live births	575	373	...
Stillbirths	11	6	...
rate per 1,000 fetuses to term	18.77	13.73	NS
Dead in 4 weeks	17	6	...
rate per 1,000 live births	29.68	16.09	NS
Children with birth defects	18	11	...
rate per 1,000 live births	31.30	29.49	NS

*In the exposed, reported birth defects include spina bifida, unspecified cardiac anomalies, pyloric stenosis, undescended testicle, congenital hydrocele, obstructive defects of urinary tract, club foot, congenital short leg, anomalies of sternum, Down's syndrome, hernia, and angioma.

†In the not exposed, reported birth defects include spina bifida, congenital anomalies of eye, polycystic kidney disease, genital web, obstructive defects of urinary tract, club foot, absence of fingers, congenital dislocation of hips, cystic hygroma, Down's syndrome, and hernia.

‡The differences in number (169 v 204 for exposed and 165 v 163 for not exposed) were due to men who were childless or men who did not respond (two nonresponders in the not exposed, three in the exposed).

Table 12.—History of Exposure to *p*-Aminobiphenyl (pAb) and (2,4,5-Trichlorophenoxy)acetic Acid (2,4,5-T) v History of Bladder Neoplasms

History*	No Exposure to Either 2,4,5-T or pAb		2,4,5-T Exposure		pAb Exposure		pAb and 2,4,5-T Exposure	
	No.	%	No.	%	No.	%	No.	%
Bladder tumor†	0	0.0	0	0.0	1	12.5	7	9.9
Bladder cancer†	0	0.0	0	0.0	1	12.5	2	2.8

*History as determined from interview and report to examining physicians.

†Figures are mutually exclusive.

United States, particularly for long-term follow-up, randomization and participation requirements for pristine epidemiological protocols are rarely satisfied. In this study it was not possible to match the exposed and not exposed groups demographically on basis of age, employment status, and education level. Although the two groups were defined on the basis of definite exposure to 2,4,5-T process and no evidence of exposure to 2,4,5-T anywhere in the plant, no information was available about levels of 2,3,7,8-TCDD in the work environment or in the trichlorophenol that was produced or in the final product, 2,4,5-T. Since 2,4,5-T was used ubiquitously as a weed killer in many gardens and farms, the possibility of exposure to some TCDD between 1948 and 1969 exists for both groups. There is current analytical information demonstrating that dioxins including 2,3,7,8-TCDD may also be present in the community environment in fly ash and flue gases[23,24] from incineration of domestic garbage and industrial chemical wastes.[25]

The degree to which each subject may have been exposed to 2,4,5-T, the contaminant TCDD, and other chemicals varied markedly. Subjects reported exposure to the 2,4,5-T process for as little as one month to as long as 20 years, and exposure was often intermittent over a period of years. It was difficult to accurately designate the duration of exposure for many of these persons. The data do not provide characterization of incidence or dose-response relationship.

Data obtained from interviews and clinical examinations conducted by different physicians have inherent biases. Nevertheless, the available populations provide useful information on the prevalence of biologic effects in the population exposed, as compared with those who were not exposed to the 2,4,5-T production.

A comparison of manifestation of effects to TCDD toxicity in humans as observed in this population with those observations made in experimental animals must also consider the acute, subacute, and chronic effects in humans already reported.[1,2,8]

The subacute effects of TCDD toxicity in the group of exposed persons as described in the reports cited in the references were characterized by cutaneous, hepatic, and peripheral nerve damage. In other populations, where hepatic changes were observed as a clinical subacute effect, elevated levels of SGOT, SGPT, and GGTP were reported.[8,26] Doses of 1.0 μg/kg/day in rats will induce altered liver function, elevation of alkaline phosphatase, lymphoid depletion of the thymus, and increased excretion of urinary porphyrins and Δ-aminolevulinic acid.[8] The effects on the thymus have not been noted in humans, although there have been some reports of elevation of alkaline phosphatase and ΔALA levels in long-term exposure.[27] Elevation of alkaline phosphatase levels was not observed in those who were examined in 1949, 1950, or 1953[1] or in this study population ten to 30 years after exposure.

Tetrachlorodibenzo-*p*-dioxin was found to induce cancer of the liver, lung, palate, and nasal turbinates in rats.[28] An excess of cancer of all sites was not observed in the mortality analysis of the group exposed to the runaway reaction materials,[3] nor was an increased prevalence of cancer of all sites observed in this study population. Cancer of the liver was not observed in this study population, nor was an excess of cirrhosis noted.

High doses of TCDD (30 ppm), administered orally or subcutaneously, in pregnant mice and rats may increase the incidence of cleft palate in mice and cystic kidney in rats.[29] No teratogenic effects were observed in rabbits receiving 10 to 40 mg/kg of 2,4,5-T containing 0.5 ppm of TCDD or in rats receiving 1 to 24 mg/kg of 2,4,5-T with the same TCDD content.[30] It has been demonstrated that hyperplasia and ulceration of the gastric mucosa occur in monkeys after lethal doses are administered.[31] In this study population, a statistically significant increase in the history of upper GI tract ulcer was found when the exposed were compared with the not exposed.

Birth defects as reported by participants in this study showed no differences statistically between the exposed and not exposed groups. In rhesus monkeys receiving 500 parts per trillion of TCDD, early abortions and inability to conceive were observed.[32,33] These effects have not been

observed in this study population.

This study indicates that the pilosebaceous effects of exposure to the 2,4,5-T process were persistent in 53% of those exposed. The effects of the kind of care received by the various subjects may be a factor in persistence. Since biopsies of the size required to identify and measure TCDD were not available, the presence of TCDD or its metabolites as a factor in persistence could not be ascertained. There was an association of actinic elastosis with the occurrence and persistence of chloracne. This can be interpreted as increased susceptibility to UV radiation damage.

There was an association of history of upper GI tract ulcer with exposure. It was not possible to ascertain a designation of ulcer by site without GI roentgenography or endoscopic information. Among the exposed group, ten subjects reported surgical treatment of the ulcer, while none of the not exposed group reported surgical treatment of ulcer. These data are suggestive of association with exposure; no definite conclusion can be drawn because of the qualified nature of the data. The association of upper GI tract ulcer with exposure warrants additional study with an appropriately designed protocol.

Among those whose chloracne persisted, there was a higher frequency of low HDL cholesterol values. Among those with only a history of chloracne, there was a higher frequency of high LDL cholesterol levels. There were no differences found between the two exposure groups with regard to plasma lipid and lipoprotein values.

There was an association of altered pulmonary function values, especially FEV, in those who were exposed and who currently smoke. This suggests the influence of the number of pack years smoked as well as exposure.

There was no evidence in this study that exposure to the 2,4,5-T process is associated with an increased prevalence of cardiovascular disease, hepatic disease, renal damage, CNS or peripheral nerve problems, reproductive problems, or birth defects.

This study was supported in part by grants from the National Institute of Environmental Health Sciences (ES-00159) and the Monsanto Company and funds of the Institute of Environmental Health. Invaluable assistance in carrying out the examination was provided by many persons: Ida Blanche Suskind; Pam Winner; Carol Warren; Charlotte Osborne, RN; Lee Rafalow, PhD; Owen E. Delia; A. B. Smith, MD; George W. Hambrick, Jr, MD; Charles L. Heaton, MD; Wayne E. Bauman, MD; and Daniel F. Richfield, MD.

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Monsanto

LAW DEPARTMENT

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

March 16, 1990

Ms. Carol Van Strum
7493 E. Five Rivers Road
Tidewater, Oregon 97390

Re: Mortality Studies of Nitro Plant Population

Dear Ms. Van Strum:

Please find enclosed copies of the two mortality studies referenced during our telephone call today. I have also enclosed for your review, copies of the trial record regarding Dr. Roush and Dr. Suskind which relate to those studies. I have also included in this packet a chart which was prepared during the trial to illustrate for the jury the statistical manipulation which was being undertaken by the plaintiffs' lawyer to artificially create the impression that there was an excess in cancer mortality at the Nitro Plant when as explained by both Dr. Roush and Dr. Suskind; the actual study data would lead to the opposite conclusion.

If you have any further questions regarding this litigation or the matters addressed in this correspondence, please feel free to give me a call at (314) 694-2821.

Sincerely,

David F. Snively

DFS/dlr

Enclosures

CC: Dan Bishop w/o enclosures

EXHIBIT

CAROL VAN STRUM
Science Writer
7493 East Five Rivers Road
Tidewater, Oregon 97390
Telephone: (503) 528-7151 Telefax: (via voiceline)

April 2, 1990

David Snively
Law Department
Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167

Re: Information request

Dear Mr. Snively:

Thank you for the materials you sent from the Kemner case record. They are very informative, and I appreciate the trouble you took to copy them for me.

Would it be possible for you to copy page 2 of the Monsanto Offer of Proof for me? It was missing from the copy of the Offer that I received.

I also have a question about one document that puzzles me. The attached copy of Table 9 was stapled into the copy of the 1983 Zack and Gaffey study that you sent me, in front of page 586 (Table 9) of the study. There is no exhibit number on this page; is it part of some other document in the record of the Kemner case? I would be most grateful if you could send me a copy of the document it is from.

Thank you again for your courtesy and help.

Sincerely,

Carol Van Strum

CVS:cvs

attachment

Table 9 Observed and Expected Number Deaths During 1955-1977 by Cause and 2,4,5-T Exposure Category Showing Proportional Mortality Ratios (PMRs) (Not Including Deaths from TCP Incident)

Cause of Death	Exposed			Non-Exposed		
	Observed	Expected	PMR	Observed	Expected	PMR
All causes of death	58	58.00	100	89	89.00	100
All malignant neoplasms	9	10.94	82	21	17.19	122
Buccal cavity and pharynx	0	0.38	0	0	0.64	0
Digestive organs and peritoneum	0	2.80	0	3	5.74	52
Stomach	0	0.52	0	0	1.06	0
Liver	0	0.19	0	0	0.39	0
All other digestive organs	0	2.09	0	3	4.29	70
Respiratory system	6	3.78	159	4	5.58	72
Lung	6	3.57	168	4	5.26	76
All other respiratory organs	0	0.21	0	0	0.39	0
Skin	0	0.29	0	0	0.35	0
Genitourinary organs	2	0.96	208	10	2.70	370*
Bladder	2	0.22	909	7	0.65	1077*
All other genitourinary organs	0	0.74	0	3	2.05	146
Lymphatic and hematopoietic tissue	0	1.35	0	1	2.07	48
Other sites	1	1.38	72	3	2.12	142
Diseases of the nervous system and sense organs	0	0.61	0	0	0.83	0
Diseases of the circulatory system	31	26.48	117	452	47.37	110
Arteriosclerotic heart disease, including CHD	27	19.72	137	43	33.63	128
All other diseases of the circulatory system	4	6.76	59	9	15.66	57
Diseases of the respiratory system	2	2.67	75	4	6.49	62
Diseases of the digestive system	1	3.70	27	2	4.06	49
All other diseases	3	4.31	70	2	6.70	30
External causes of death	12	9.29	129	8	9.28	86

My analysis showed 65 deaths.

* P<.05

Monsanto

LAW DEPARTMENT

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

April 11, 1990

Carol Van Strum
Science Writer
7493 East Five Rivers Road
Tidewater, OR 97390

Re: Information Request

Dear Ms. Van Strum:

Thank you for your correspondence of April 2, 1990. Please find enclosed a copy of the missing page from Dr. Suskind's offer of proof. The other material which you referenced in your letter was inadvertently included with materials previously forwarded to your office. It is not a portion of a document in the court record of the Kemner case.

To bring you current with the status of that case, I note that the Kemner appeal was argued last week by the parties. Monsanto remains confident that the verdict will be reversed when the decision is issued by the Illinois Appellate Court.

Sincerely,

David F. Snively

A:DFS-046.ch

report health effects he found in Monsanto's workers when asked by the West Virginia Compensation Commission, and of publishing studies intended to downplay the actual human health effects of dioxin. As a result of the extreme and unfair limitations placed upon his testimony and this Court's subsequent ban on his further testimony, Dr. Suskind never had the opportunity to respond to these charges, and to demonstrate that his recollection was totally accurate.

The importance of Dr. Suskind's testimony to plaintiffs' punitive damage case is illustrated by the manner and length (18 days) of cross-examination of Dr. Suskind after a reasonably concise direct exam (2-1/2 days), and the extensive use of Dr. Suskind's testimony in the cross examination of Dr. James Webster, Monsanto's chief examining expert. Plaintiffs' counsel spent days cross-examining Dr. James Webster, Monsanto's final medical expert, with the unclarified, and at times unduly and erroneously restricted, testimony of Dr. Suskind.

In addition, misinformation offered by plaintiffs' counsel which was corrected and clarified by Dr. Suskind during his direct examination (which clarification was left unchallenged by plaintiffs' counsel despite 18 days of cross examination) relating to the number of workers reported by Dr. Suskind in his 184 health study as having cancer was used, nevertheless, in it's incorrect and unclarified state to cross examine Dr. Webster. (Tr. 6/8/87). This Offer of Proof demonstrates that Dr. Suskind's redirect examination is critical to Monsanto's

Monsanto

ENVIRONMENT, SAFETY & HEALTH

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

May 4, 1987

Marilyn Fingerhut, Ph.D.
National Institute for Occupational
Safety and Health
Robert A. Taft Laboratories
4676 Columbia Parkway
Cincinnati, Ohio 45226-1998

Dear Marilyn:

I am enclosing the computer tape you requested in your memo dated April 10, 1987. I am sorry for the delay, but I was on vacation the week you sent me the letter, and your request required much programming, data manipulation and editing on my part. Please disregard any data tape sent to you prior to this one. I used the chronology sent to you on Nov. 12, 1985 to determine who was exposed, and I corrected some social security numbers and conflicting values for birth and hire dates. I did not use the chronology sent to you Feb. 8, 1983 because it does not accurately reflect the exposures. The files are identified in the following way:

COE5577: These are employees who were active between 1955 and 1977, and whose work histories indicate that they worked in either a 2,4,5-T or NaTCP department. The start and end dates of these departments are listed in the chronology sent to you on Nov. 12, 1985.

B55: These are employees who were terminated prior to 1955 and were potentially exposed to 2,4,5-T. See part Ic of my memo sent to you on Nov. 7, 1986 for information on how these employees were identified.

TCP: These are employees who were in the TCP accident study. I have included a female who contacted chloracne as a result of the accident, but wasn't included in the study.

SUS: These are employees who were in the Suskind/Hertzberg morbidity study and were exposed according to either the Monsanto or University of Cincinnati exposure criteria. These criteria were described in part 5 of my memo dated Nov. 7, 1986. Please be aware that Dr. Suskind used only the University of Cincinnati's "Exposed" and "Non-exposed" categories in his study.

In addition to the usual header record variables that you are very familiar with, I have added the additional variables you requested: a Monsanto and UC exposure variable for those in the Suskind study, a data source variable for those in the B455 file who were identified as potentially exposed from a source other than their personnel record, and a variable to indicate whether there was a a work record in our computer file. I have also added a date of termination derived from 941 forms to those in the B455 group who did not have a personnel file.

Since I combined so many different files using various computer programs, I made many diligent attempts to check that I was including everybody I was supposed to. I even compared my final cohort to the names on the three lists I sent to you on Nov. 7, 1986. Unfortunately, I discovered that there were twenty-six names on my current file that weren't on those lists. All the names were from the Suskind study and had a Monsanto exposure code of either 1 or 2. (See attached list). I could not figure out why these omissions occurred, but I can assure you that this current file includes all the exposed Suskind cohort members.

The record format for the header and work records on this tape is in the attachment and the tape specifications are: non-labelled, 9 track, EBCDIC characters, density=6250 BPI, LRECL=97, BLKSIZE=6208, RECFM=FB and #RECS=6382. If you have any questions, please feel free to call.

Sincerely,

Marcie E. Strauss

Marcie E. Strauss
Epidemiologist

IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON, WEST VIRGINIA

JAMES M. ADKINS, Administrator of the Estate of Ralph E. Adkins, Deceased, et al, Plaintiffs, vs. MONSANTO COMPANY, a Delaware Corporation, Defendant.	No. 81-2098

Deposition of
CLAYTON F. CALLIS
taken on behalf of the
Plaintiffs.

* * * * * * * * * * * * * * * *

Reporter: M. Joy Springer

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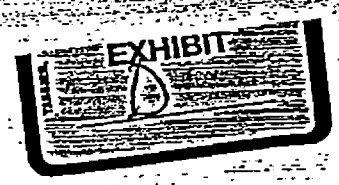

IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON, WEST VIRGINIA

JAMES M. ADKINS, Administrator of the Estate of Ralph E. Adkins, Deceased, et al,

Plaintiffs,

vs.) No. 81-2098

MONSANTO COMPANY, a Delaware Corporation,

Defendant.

APPEARANCES:

Messrs. Calwell, McCormick & Peyton,
by W. Stuart Calwell, Jr., Esq. For Plaintiffs,

Messrs. Bowles, McDavid, Graff & Love,
by Charles M. Love III, Esq.
and
P. Michael Pleska, Esq. For Defendant,

Thomas M. Bistline, Esq. Monsanto Company Counsel.

IT IS STIPULATED AND AGREED by and between counsel for the plaintiffs and counsel for the defendant that the deposition of CLAYTON F. CALLIS may be taken pursuant to Rule 26(a) of the Federal Rules of Civil Procedure, on behalf of the plaintiffs, on July 1, 1983, at the Radisson Hotel, Room 215, 9th &

Convention Plaza, St. Louis, Missouri, before M. JOY SPRINGER,a Notary Public within and for the County of Madison, State of Illinois; that the issuance of notice and dedimus is waived, and that this deposition may be taken with the same force and effect as if all Federal rules and statutory requirements had been complied with.

IT IS FURTHER STIPULATED AND AGREED that any and all objections to all or any part of this deposition except objections as to form of the questions asked or answers given, are hereby reserved and may be raised on the trial of this cause; and that the signature of the deponent is not waived.

* * * * * * * * * * *

CLAYTON F. CALLIS

produced, sworn and examined on behalf of the plaintiffs, deposes and says as follows:

EXAMINATION

BY MR. CALWELL:

(Whereupon the reporter marked Plaintiffs' Deposition Exhibit #170 (Monsanto

#236180 and #236181) consisting of 2 pages; Exhibit #171 (Monsanto #8322238, #8322244 and #8322245) consisting of 3 pages; Exhibit #172 (Monsanto #8322554 and #8322555) consisting of 2 pages; Exhibit #173 (Monsanto #8322905) consisting of 1 page; Exhibit #174 (Monsanto #8331219) consisting of 1 page; Exhibit #175 (Monsanto #8326231) consisting of 1 page; Exhibit #176 (Monsanto #233610 through #233612) consisting of 3 pages; Exhibit #177 (Monsanto #233618 and #233619) consisting of 2 pages; Exhibit #178 (Monsanto #231686 through 231688) consisting of 3 pages; Exhibit #179 (Monsanto #8321639 and #8321640) consisting of 2 pages; Exhibit #180 (Monsanto #8323058 through #8323060) consisting of 3 pages; Exhibit #181 (Monsanto #232571 through #232574) consisting of 4 pages; Exhibit #182 (Monsanto #8323145 and #8323146) consisting of 2 pages; Exhibit #183 (Monsanto #8323173 through #8323176)consisting of 4 pages; Exhibit #184 (Monsanto #233695) consisting of 1 page; Exhibit #185 (Monsanto #8323203 through #8323205) consisting of 3

pages; Exhibit #186 (Monsanto #8331253 through #8331271) consisting of 17 pages; Exhibit #187 (Monsanto #8323177 and #8323178) consisting of 2 pages; Exhibit #188 (Monsanto #8323234 and #8323235) consisting of 2 pages; Exhibit #189 (Monsanto #235616 and #235623) consisting of 2 pages; Exhibit #190 (Monsanto #8323245 through #8323248) consisting of 4 pages; Exhibit #191 (Monsanto #231738 and #231739)consisting of 2 pages; Exhibit #192 (Monsanto #8321904 and #8321905) consisting of 2 pages; Exhibit #193 (Monsanto #231753 through #231756) consisting of 4 pages; Exhibit #194 (Monsanto #8323313 through #8323315) consisting of 3 pages; Exhibit #195 (Monsanto #8323318 through #8323320) consisting of 3 pages; Exhibit #196 (Monsanto #8331273 and #8331274) consisting of 2 pages; Exhibit #197 (Monsanto #8323334 through #8323336) consisting of 3 pages; Exhibit #198 (Monsanto #8323340 through #8323342) consisting of 3 pages; Exhibit #199 (Monsanto #8323354 through #8323356) consisting of 3 pages; Exhibit #200 (Monsanto #8323370 through #8323372)

consisting of 3 pages; Exhibit #201 (Monsanto #236245 and 236246)consisting of 2 pages; Exhibit #202 (Monsanto #8323392 through #8323394) consisting of 3 pages; Exhibit #203 (Monsanto #236249, #236250, #236251 and #236252) consisting of 4 pages; Exhibit #204 (Monsanto #8331279 and #8331280) 2 pages; Exhibit #205 (Monsanto #8304380 through #8304385) consisting of 6 pages; Exhibit #206 (Monsanto #230057 through #230061, and #8319596) consisting of 6 pages; Exhibit #207, consisting of 1 page; and Exhibit #208 (Monsanto #8323373 and #8323374, and #8323376) consisting of 3 pages.

Q (By Mr. Calwell) What is your name?

A Clayton F. Callis.

Q How old a man are you, Dr. Callis?

A 59.

Q Why do they call you doctor?

A I have a Ph. D.

Q What in?

A Inorganic Chemistry.

Q Where did you get that Degree?

A University of Illinois, Urbana-Champaign.

Q When did you do that?

IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON, WEST VIRGINIA

JAMES M. ADKINS, Administrator of the Estate of Ralph E. Adkins, Deceased, et al,	)	
Plaintiffs,	)	
vs.	)	No. 81-2098
MONSANTO COMPANY, a Delaware Corporation,	)	
Defendant.	)	

Deposition of
MONTE C. THRONDAHL
taken on behalf of the
Plaintiffs.

* * * * * * * * * * * * * * * * * *

Reporter: M. Joy Springer

JAMES MAY REPORTING SERVICE
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EDWARDSVILLE, ILLINOIS 62025

IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON, WEST VIRGINIA

JAMES M. ADKINS, Administrator of the Estate of Ralph E. Adkins, Deceased, et al,

Plaintiffs,

vs. No. 81-2098

MONSANTO COMPANY, a Delaware Corporation,

Defendant.

APPEARANCES:

Messrs. Calwell, McCormick & Peyton,
by W. Stuart Calwell, Jr., Esq. For Plaintiffs,

Messrs. Bowles, McDavid, Graff & Love,
by P. Michael Pleska, Esq.
and
John Woods, Esq. For Defendant,

Thomas M. Bistline, Esq. Monsanto Company Counsel.

IT IS STIPULATED AND AGREED by and between counsel for the plaintiffs and counsel for the defendant that the deposition of MONTE C. THRODAHL may be taken pursuant to Rule 26(a) of the Federal Rules of Civil Procedure, on July 19, 1983, at the Radisson Hotel, Room 215, 9th Street and Convention Plaza, St. Louis,

Missouri, before M. JOY SPRINGER, a Notary Public within and for the County of Madison, State of Illinois; that the issuance of notice and dedimus is waived, and that this deposition may be taken with the same force and effect as if all Federal rules and statutory requirements had been complied with.

IT IS FURTHER STIPULATED AND AGREED that any and all objections to all or any part of this deposition, except objections as to form of the questions asked or answers given, are hereby reserved and may be raised on the trial of this cause; and that the signature of the deponent is not waived.

* * * * * * * *

MONTE C. THRODAHL

produced, sworn and examined on behalf of the plaintiffs, deposes and says as follows:

EXAMINATION

BY MR. CALWELL:

(Whereupon the reporter marked Plaintiffs Deposition Exhibit #366 (Monsanto #8322918, #8326238, #8323145, #8323146;

#8323203 through #8323205, #8323234, #8323235, #8323245 through #8323248, #236205 through #236208, #236212 through #236215, #8323313 through #8323315, #8323318 through #8323320, #8323334 through #8323336, #8323340 through #8323342, #8323370 through #8323372, #8323392 through #8323394, #236245, #236246, #236249 through #236252, #8323748 through #8323751, #8323831, #8323832, #235806 through #235808, #8323866 through #8323869, #8323876 through #8323879, #8324039, #8324040, #8324170, #8324171) consisting of 66 pages; Exhibit # 367 (Monsanto #8323075 through #8323079) consisting of 5 pages; Exhibit #368 (Monsanto #8326149 through #8326160, #8326129 through #8326142) consisting of 26 pages; Exhibit #369 (Monsanto #232571 through #232574) consisting of 4 pages; Exhibit #370 (Monsanto #233610 through #233612) consisting of 3 pages; Exhibit #371 (Monsanto #8305445, #8305446, #8305443, #8305444, #8305441, #8305442, #8305439, #8305440, #8306026, #8306025, #8306023, #8306024, #8306022, #8306021, #8306020, #8306019, #8306018, #8306017) consisting of 18 pages; Exhibit #372 (Mon-

santo #8306242, #8306243) consisting of 2 pages; Exhibit #373 (Monsanto #8321750, #8321751), consisting of 2 pages; Exhibit #374 (Monsanto #236191 through #236193) for the purposes of identification.)

Q (By Mr. Calwell) Would you state your name, please.

A Monte C. Throdahl.

Q What is your address, Mr. Throdahl?

A 36 Briarcliff, St. Louis, 63124.

Q And you're obviously employed by Monsanto Company, is that right?

A Right.

Q And are you a Senior Vice President?

A That's right.

Q I'd like to talk to you first about your academic background. Where did you go to school?

A How far back?

Q College.

A Iowa State University from '37 through '41 -- that's 1937, not 18 -- Chemical Engineering.

Q Did you have any post-graduate courses?

A Yeah. I had the Advanced Management Program at Harvard Business School in 1960.

Q O.K. Now, upon graduation from Iowa

IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON, WEST VIRGINIA

JAMES M. ADKINS, Administrator of the Estate of Ralph E. Adkins, Deceased, et al,	)	
Plaintiffs,	)	
vs.	)	No. 81-2098
MONSANTO COMPANY, a Delaware Corporation,	)	
Defendant.	)	

Deposition of
FERDINAND C. MEYER
taken on behalf of
the plaintiffs.

* * * * * * * * * * *

Reporter: M. Joy Springer

JAMES MAY REPORTING SERVICE
CERTIFIED SHORTHAND REPORTERS
R.R. 2 - BOX 65
EDWARDSVILLE, ILLINOIS 62025

IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON, WEST VIRGINIA

JAMES M. ADKINS, Administrator of the Estate of Ralph E. Adkins, Deceased, et al,

Plaintiffs,

vs. No. 81-2098

MONSANTO COMPANY, a Delaware Corporation,

Defendant.

APPEARANCES:

Messrs. Calwell, McCormick & Peyton, by W. Stuart Calwell, Jr., Esq., For the Plaintiffs;

Messrs. Bowles, McDavid, Graff & Love, by Charles M. Love, III, Esq., For the Defendant.

IT IS STIPULATED AND AGREED by and between counsel for the plaintiffs and counsel for the defendant that the deposition of FERDINAND C. MEYER may be taken pursuant to Rule 26(a) of the Federal Rules of Civil Procedure, on behalf of the plaintiffs, on July 6, 1983, at the Radisson Hotel, Room 215, 9th Street and Convention Plaza, St. Louis, Missouri, before M. JOY SPRINGER a Notary Public within and for the County of Madison, State

of Illinois; that the issuance of notice and dedimus is waived, and that this deposition may be taken with the same force and effect as if all Federal rules and statutory requirements had been complied with.

IT IS FURTHER STIPULATED AND AGREED that any and all objections to all or any part of this deposition except objections as to form of the questions asked or answers given, are hereby reserved and may be raised on the trial of this cause; and that the signature of the deponent is not waived.

* * * * * * * * * * *

FERDINAND C. MEYER,

produced, sworn and examined on behalf of the plaintiffs, deposes and says as follows:

EXAMINATION

BY MR. CALWELL:

(Whereupon the reporter marked the following exhibits for the purposes of identification: Plaintiff's Deposition Exhibit #252 (Monsanto's I.D. #8323313 through 8323315, inclusive), consisting of

three pages; Plaintiff's Deposition Exhibit #253 (Monsanto's I.D. #8323245 through 8323248, inclusive), consisting of four pages; Plaintiff's Deposition Exhibit #254 (Monsanto's I.D. #231728 through 231737, inclusive), consisting of ten pages; Plaintiff's Deposition Exhibit #255 (Monsanto's I.D. #8323234 and 8323235), consisting of two pages; Plaintiff's Deposition Exhibit #256 (Monsanto's I.D. #8323217 through 8323219, inclusive), consisting of three pages; Plaintiff's Deposition Exhibit #257 (Monsanto's I.D. #8323177 and 8323178), consisting of two pages; Plaintiff's Deposition Exhibit #258 (Monsanto's I.D. #233695), consisting of one page; Plaintiff's Deposition Exhibit #259 (Monsanto's I.D. #8323203 through 8323205, inclusive), consisting of three pages; Plaintiff's Deposition Exhibit #260 (Monsanto's I.D. #8323173, 8323174, 8323176 and 8323175), consisting of four pages; Plaintiff's Deposition Exhibit #261 (Monsanto's I.D. #8323145 and 8323146), consisting of two pages; Plaintiff's Deposition #262 (Monsanto's I.D. #8323065 through 8323070, inclusive), consisting of six pages; Plaintiff's Deposition Exhibit #263

(Monsanto's I.D. #8323037 and 8323038), consisting of two pages; Plaintiff's Deposition Exhibit #264 (Monsanto's I.D. #231686 through 321688, inclusive), consisting of three pages; Plaintiff's Deposition Exhibit #265 (Monsanto's I.D. #8323147 through 8323149, inclusive), consisting of three pages; Plaintiff's Deposition Exhibit #266 (Monsanto's I.D. #8330067 and 8330068), consisting of two pages; Plaintiff's Deposition Exhibit #267 (Monsanto's I.D. #8331208 8331209), consisting of two pages; Plaintiff's Deposition Exhibit #268 (Monsanto's I.D. #8331208 and 8331209), consisting of two pages; Plaintiff's Deposition Exhibit #269 (Monsanto's I.D. #8322384), consisting of one page; Plaintiff's Deposition Exhibit #270 (Monsanto's I.D. #8330036), consisting of one page; Plaintiff's Deposition Exhibit #271 (Monsanto's I.D. #236066 through 236069, inclusive), consisting of four pages; Plaintiff's Deposition Exhibit #272 (Monsanto's I.D. #236065), consisting of one page; Plaintiff's Deposition Exhibit #273 (Monsanto's I.D. #8325873, 8325874 and 8325872), consisting of three pages; Plaintiff's Deposition Exhibit #274 (Monsanto's I.D. #236180 and 236181), consisting of two pages;

Plaintiff's Deposition Exhibit #275 (Monsanto's I.D. #8326129 through 8326142, inclusive, and #8326149 through 8326160, inclusive), consisting of twenty-six pages; Plaintiff's Deposition Exhibit #276 (Monsanto's I.D. #8331279 and 8331280), consisting of two pages; Plaintiff's Deposition Exhibit #277 (Monsanto's I.D. #235680), consisting of one page; Plaintiff's Deposition Exhibit #278 (Monsanto's I.D. #236249 through 236252, inclusive), consisting of four pages; Plaintiff's Deposition Exhibit #279 (Monsanto's I.D. #8323392 through 8323394, inclusive), consisting of three pages;*Plaintiff's Deposition Exhibit #281 (Monsanto's I.D. #8323340 through 8323342, inclusive), consisting of three pages; Plaintiff's Deposition Exhibit #282 (Monsanto's I.D. #83331273 and 8331274), consisting of two pages; Plaintiff's Deposition Exhibit #283 (Monsanto's I.D. #8330781), consisting of one page; Plaintiff's Deposition Exhibit #284 (Monsanto's I.D. #8300999), consisting of one page; Plaintiff's Deposition Exhibit #285 (Monsanto's I.D. #8300998), consisting of one page; Plaintiff's Deposition Exhibit #286 (Monsanto's I.D. #8325604), consisting of one

*Plaintiff's Deposition Exhibit #280 (Monsanto's I.D. #8323370 through 8323372, inclusive), con-

page; Plaintiff's Deposition Exhibit #287 (Monsanto's I.D. #8331712), consisting of one page; and finally, Plaintiff's Deposition Exhibit #288 (Monsanto's I.D. #8331272), consisting of one page.

Q Would you state your name, please?

A Ferdinand C. Meyer.

Q And where do you live?

A I live at #18 Roclare Lane in Town and Country, Missouri, 63131.

Q And are you employed?

A No. I retired about three and a half years ago, February of 1980.

Q Retired from Monsanto?

A Yes.

Q When you were employed by Monsanto, what was your last job with them?

A I was Director of Special Projects in the Department of Medicine and Environmental Health.

Q In St. Louis?

A Yes.

Q Where did you attend college?

A Shurtleff College in Alton, Illinois.

Q And what degree did you receive?

A A.B.

Monsanto

LAW DEPARTMENT

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

March 16, 1990

Ms. Carol Van Strum
7493 E. Five Rivers Road
Tidewater, Oregon 97390

Re: Mortality Studies of Nitro Plant Population

Dear Ms. Van Strum:

Please find enclosed copies of the two mortality studies referenced during our telephone call today. I have also enclosed for your review, copies of the trial record regarding Dr. Roush and Dr. Suskind which relate to those studies. I have also included in this packet a chart which was prepared during the trial to illustrate for the jury the statistical manipulation which was being undertaken by the plaintiffs' lawyer to artificially create the impression that there was an excess in cancer mortality at the Nitro Plant when as explained by both Dr. Roush and Dr. Suskind; the actual study data would lead to the opposite conclusion.

If you have any further questions regarding this litigation or the matters addressed in this correspondence, please feel free to give me a call at (314) 694-2821.

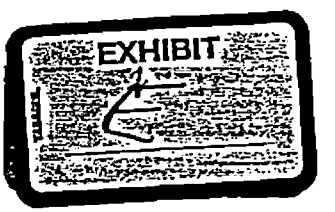
Sincerely,

David F. Snively

DFS/dlr

Enclosures

CC: Dan Bishop w/o enclosures



CAROL VAN STRUM
Science Writer
7493 East Five Rivers Road
Tidewater, Oregon 97390
Telephone: (503) 528-7151 Telefax: (via voiceline)

April 2, 1990

David Snively
Law Department
Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167

Re: Information request

Dear Mr. Snively:

Thank you for the materials you sent from the Kemner case record. They are very informative, and I appreciate the trouble you took to copy them for me.

Would it be possible for you to copy page 2 of the Monsanto Offer of Proof for me? It was missing from the copy of the Offer that I received.

I also have a question about one document that puzzles me. The attached copy of Table 9 was stapled into the copy of the 1983 Zack and Gaffey study that you sent me, in front of page 586 (Table 9) of the study. There is no exhibit number on this page; is it part of some other document in the record of the Kemner case? I would be most grateful if you could send me a copy of the document it is from.

Thank you again for your courtesy and help.

Sincerely,

Carol Van Strum

CVS:cvs

attachment

Table 9 Observed and Expected Number Deaths During 1955-1977 by Cause and 2,4,5-T Exposure Category Showing Proportional Mortality Ratios (PMRs)
(Not Including Deaths from TCP Incident)

Cause of Death	Exposed			Non-Exposed		
	Observed	Expected	PMR	Observed	Expected	PMR
All causes of death	58	58.00	100	89	89.00	100
All malignant neoplasms	9	10.94	82	21	17.19	122
Buccal cavity and pharynx	0	0.38	0	0	0.64	0
Digestive organs and peritoneum	0	2.80	0	3	5.74	52
Stomach	0	0.52	0	0	1.06	0
Liver	0	0.19	0	0	0.39	0
All other digestive organs	0	2.09	0	3	4.29	70
Respiratory system	6	3.78	159	4	5.58	72
Lung	6	3.57	168	4	5.26	76
All other respiratory organs	0	0.21	0	0	0.39	0
Skin	0	0.29	0	0	0.35	0
Genitourinary organs	2	0.96	208	10	2.70	370*
Bladder	2	0.22	909	7	0.65	1077*
All other genitourinary organs	0	0.74	0	3	2.05	146
Lymphatic and hematopoietic tissue	0	1.35	0	1	2.07	48
Other sites	1	1.38	72	3	2.12	142
Diseases of the nervous system and sense organs	0	0.61	0	0	0.83	0
Diseases of the circulatory system	31	26.48	117	52	47.37	110
Arteriosclerotic heart disease, including CHD	27	19.72	137	43	33.63	128
All other diseases of the circulatory system	4	6.76	59	9	15.66	57
Diseases of the respiratory system	2	2.67	75	4	6.49	62
Diseases of the digestive system	1	3.70	27	2	4.06	49
All other diseases	3	4.31	70	2	6.70	30
External causes of death	12	9.29	129	8	9.28	86

My analysis showed 65 deaths.

* P<.05

Monsanto

LAW DEPARTMENT

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63167
Phone: (314) 694-1000

April 11, 1990

Carol Van Strum
Science Writer
7493 East Five Rivers Road
Tidewater, OR 97390

Re: Information Request

Dear Ms. Van Strum:

Thank you for your correspondence of April 2, 1990. Please find enclosed a copy of the missing page from Dr. Suskind's offer of proof. The other material which you referenced in your letter was inadvertently included with materials previously forwarded to your office. It is not a portion of a document in the court record of the Kemner case.

To bring you current with the status of that case, I note that the Kemner appeal was argued last week by the parties. Monsanto remains confident that the verdict will be reversed when the decision is issued by the Illinois Appellate Court.

Sincerely,

David F. Snively

A:DFS-046.ch

report health effects he found in Monsanto's workers when asked by the West Virginia Compensation Commission, and of publishing studies intended to downplay the actual human health effects of dioxin. As a result of the extreme and unfair limitations placed upon his testimony and this Court's subsequent ban on his further testimony, Dr. Suskind never had the opportunity to respond to these charges, and to demonstrate that his recollection was totally accurate.

The importance of Dr. Suskind's testimony to plaintiffs' punitive damage case is illustrated by the manner and length (18 days) of cross-examination of Dr. Suskind after a reasonably concise direct exam (2-1/2 days), and the extensive use of Dr. Suskind's testimony in the cross examination of Dr. James Webster, Monsanto's chief examining expert. Plaintiffs' counsel spent days cross-examining Dr. James Webster, Monsanto's final medical expert, with the unclarified, and at times unduly and erroneously restricted, testimony of Dr. Suskind.

In addition, misinformation offered by plaintiffs' counsel which was corrected and clarified by Dr. Suskind during his direct examination (which clarification was left unchallenged by plaintiffs' counsel despite 18 days of cross examination) relating to the number of workers reported by Dr. Suskind in his 184 health study as having cancer was used, nevertheless, in it's incorrect and unclarified state to cross examine Dr. Webster. (Tr. 6/8/87). This Offer of Proof demonstrates that Dr. Suskind's redirect examination is critical to Monsanto's