Uploaded to VFC Website

~ October 2012 ~

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

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

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

Veterans-For-Change

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

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

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

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

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

Item ID Number	02300
Author	
Corporate Author	
Report/Article Title	Report: Request for OMB Approval to Proceed to Phase II of the NIOSH Dioxin Morbidity and Reproductive Study of U.S. Chemical Workers
Journal/Book Title	
Year	1986
Month/Day	
Color	☐
Number of Images	151
Description Notes	Ten attachments include; January 1986 letter from OMB, 1985 Notice of OMB Action, Appeal memorandum from DHHS, Executive Summary of Study Proposal, Protocol for Dioxin morbidity Study, Selected Demographic Characteristics of Worker Sample, February 1987 Exposure Matrix Review, TCDD in Adipose Tissue chart, tables detailing Participation of Workers in In-Home Interviews and other tables of survey response.

Request for OMB Approval to Proceed to Phase II
of the NIOSH Dioxin Morbidity and Reproductive Study
of U.S. Chemical Workers

In a letter of January 7, 1986 (Attachment 1), OMB approved Phase I of the NIOSH Dioxin Morbidity and Reproductive Study of U.S. Chemical Workers. OMB first disapproved the study (Attachment 2) but reconsidered the decision after receiving an appeal from the Department of Health and Human Services (Attachment 3). However, several technical concerns were expressed by OMB in the approval letter of January 7, 1986, and NIOSH was directed to address these concerns following the experience in Phase I, and to obtain OMB approval to proceed to Phase II of the study.

In this document, we present our experience with Phase I of the study and address the concerns expressed in the OMB Letter of January 7, 1986. This report describes our experience as of April 1, 1986. To date, 68 workers (of a maximum sample of 80) have been interviewed and 52 have had medical examinations. Matched referents have been obtained for 44 workers; all have been interviewed and 10 have had medical examinations. (This report will be updated to include progress through May before submission to OMB.)

A. Rationale for approaching OMB prior to the completion of Phase I

We have had excellent participation in Phase I, which is described in detail in this document, and we believe we are able at this time to address the concerns expressed by OMB. We are approaching OMB prior to the completion of Phase I for approval to award the contract for Phase II for two reasons:

1. We arranged contractually for a two-month "downtime" between Phase I and Phase II in order to obtain approval from OMB. During the "downtime," no data will be collected. However, we must pay the contractor about $100,000 for each month of "downtime," and we would like to avoid this nonproductive cost. We can save about $200,000 by obtaining immediate approval from OMB to award the contract for Phase II and notifying the contractor to proceed directly to Phase II at the end of Phase I period of performance.

2. Our contractor (Lovelace Medical Foundation) has informed us that staff trained specifically for this study will be laid off unless we know soon that there will be a Phase II. The loss of staff who are experienced in the standardization procedures of this study could be a critical problem for Phase II. Each technician and physician examiner assigned to the NIOSH Dioxin Morbidity Study has been trained and certified in the examination methods of this study and has gained substantial experience during Phase I.

B. History of the Study

On November 21, 1986, the government awarded a fixed price contract to Lovelace Medical Foundation (LMF), Albuquerque, N.M., and its subcontractor, Research Triangle Institute (RTI), Research Triangle Park, N.C. to conduct Phase I. Demographic and occupational history interviews were initiated by RTI on February 14, 1987, in the homes of the participants, and the first medical examinations were conducted at LMF in Albuquerque, N.M. on March 5, 1987. All examinations will be completed during May, 1987, and the Phase I period of performance ends on June 21, 1987. Our contract with LMF includes an optional "downtime" from June 21 to August 21, 1987 (at a cost of about $100,000 per month) in order for us to obtain permission from OMB to continue to Phase II. The contract prohibits an increase in the negotiated price for Phase II if NIOSH signs the Phase II contract by August 21, 1987. In order to ensure that the experienced Lovelace Medical Foundation staff will remain intact in Phase II, and also to avoid paying $200,000 for the two month "downtime," we would prefer to begin Phase II on June 22, 1987, if we are able to obtain immediate approval from OMB.

C. Description of the Study

NIOSH is currently conducting Phase I of the Dioxin Morbidity and Reproductive Study of U.S. Chemical Workers. This study involves the interview and medical examination of workers who made dioxin-contaminated products and a comparison group of nonexposed persons, as well as a reproductive interview of the wives of the participants (See Attachment 4, Executive Summary and Attachment 5, Protocol). Phase I consists of a weighted random sample that includes 80 of approximately 400 workers employed at a facility in Newark, New Jersey between 1951 and 1969, and a referent group, matched individually to the worker by age ($\pm$ 5 years), gender, race and resident neighborhood. The sample of 80 was drawn using an algorithm to select increased proportions of persons with longer lengths of employment. Attachment 6 describes the demographic and employment characteristics of the sample of 80 workers.

The study was reviewed for technical competence and approved by a NIOSH Peer Review Panel and by the Science Panel of the Agent Orange Working Group. The protocol is enclosed as Attachment 5.

D. Responses to Three Specific Concerns of OMB

The Office of Management and Budget (OMB) notified NIOSH on January 7, 1986 that approval was given for a portion of the study (Phase I). However, OMB expressed concern about three aspects of the study, and requested that NIOSH demonstrate, from experience in Phase I, that these technical concerns of OMB are resolved. NIOSH was asked to share this information with the Science Panel of the Agent Orange Working Group and the Executive Office of the President (See Attachment 1).

We believe that our experience in Phase I resolves the technical concerns of OMB. Below, we present the technical concerns expressed by OMB in the letter of January 7, 1986 and our responses:

1. "HHS will complete the exposure model and develop exposure estimates for the entire sample."

   NIOSH has conducted two peer review meetings on the exposure matrix system for the NIOSH Dioxin Registry. On March 14, 1985 the exposure matrix protocol was reviewed, and on February 20, 1987, a review was held of the application of the model using data obtained from two plants (Attachment 7). The review included the New Jersey plant whose workers are in Phase I; the plant is identified as Site One in the document. Since our Phase I sample of 80 includes short- and long-term workers who were employed from 7 days to 10,000 days and is a weighted random sample of the entire population, the ratings calculated for the Phase I workers should be representative of the remainder of the worker population at the New Jersey plant.

   The exposure matrix protocol (Attachment 7) decribes the systematic procedures devised for estimating the potential exposure to dioxin for the 7000 workers at 14 plants in the NIOSH Dioxin Registry. These estimates will reflect the exposure ranking for each individual, relative to the other members. For each worker in the Registry, a complete work history has been compiled from company records. Through plant site visits, interviews with long-term employees and company officials, and careful examination of plant process descriptions, a set of work tasks has been defined for each worker in the study. These tasks describe the work activities at which each person may have had contact with dioxin-containing materials. Each task has been assigned a dioxin exposure rating which is the product of three factors. The first factor is the dioxin content of the material which was present at the point in the process where the task was performed. This value is multiplied by the amount of time required to perform each task (on a daily basis) and by an exposure weighting factor which reflects the likelihood that contact with the dioxin-containing material actually occurred. Using the work histories, we have identified the tasks performed by each worker in the study and the period of time in his career (in days) for which he performed those tasks. Each worker's total dioxin exposure rating for his entire working history is calculated by multiplying the exposure rating for each task he performed by the number of days he performed that task, and summing these to compile the lifetime exposure rating.

   For the sample of New Jersey workers in Phase I of the Morbidity Study, we have used this system to calculate from their work history records the cumulative dioxin exposure ratings for their working careers. The ratings were calculated using employment records, which contain substantial gaps for some workers. The cumulative ratings

from the company records range from 4 to 7000, a factor of approximately 1750. (We are obtaining detailed work histories and job duties in the interviews of this study, and this information will be utilized to prepare "reported" exposure ratings.) These ratings are ordinal numbers which reflect the exposure of the individuals relative to each other. The interpretation of relative exposures of these workers will be approached in two ways: 1) comparison of exposures in the New Jersey workers with the ratings of workers at the other 13 plants in the NIOSH Dioxin Registry, and 2) comparison with the levels of 2,3,7,8-TCDD measured in the serum of the New Jersey workers during the NIOSH Morbidity Study.

During Phase I, blood was drawn from workers under the age of 65 years and in good health for an analysis of the serum concentration of 2,3,7,8-TCDD. These data will be compared with the exposure ratings. Although we do not yet have results of analyses for the Phase I workers, we do have results of adipose tissue measurements of 2,3,7,8-TCDD in some Missouri workers who will be in Phase II of the NIOSH study. These measurements were obtained in a community survey conducted by the Center for Environmental Health, CDC, and the State of Missouri from adipose tissue of nine workers who made 2,4,5-trichlorophenol and 2,4,5-trichlorophenoxy-acetic acid at a Missouri Chemical plant, which will be included in Phase II of the NIOSH study. Attachment 8 presents this information. The average level of 2,3,7,8-TCDD in the adipose tissue of nine workers employed in the dioxin-contaminated processes ("P") at a Missouri plant is 326 ppt, with a range of 67 to 978 ppt. By contrast, the level in seven persons employed at the same plant but in departments other than the dioxin-contaminated processes ("C") is 12 ppt with a range of 4 to 41 ppt. The figure shows a relationship between the adipose tissue levels of 2,3,7,8-TCDD and the number of days these workers were employed in the production of dioxin-contaminated products. It is of interest to note that the maximum length of employment for the Missouri workers in these processes was less than two years. The New Jersey workers could have worked in dioxin-contaminated processes for 18 years. Therefore, we expect that the distribution of 2,3,7,8-TCDD levels in the Phase I sample will be at least equivalent to the distribution in the Missouri workers.

2. "HHS will evaluate the ability to select and recruit appropriate control cases."

A. Participation in the Home Interview

In this section, we present a description of the current participation rates in home interviews in Phase I as of April 1, 1987. We are very pleased with the level of participation. As of April 1, 73 of the 80 workers had been located and invited to participate in the study (Table 1, Attachment 9). Interviews have been completed for 68

(includes 5 proxies for 2 dead, and 3 incapacitated) and are scheduled for 2 others, giving us an interview rate of 95.9% (70/73). Of the 73 workers (including 5 proxies), only 3 persons refused to be interviewed (3/73, 4.1%).

B. Participation in the Medical Examination

It is during the home interview that the individuals are invited to participate in the medical examination at Lovelace Medical Foundation in Albuquerque, New Mexico. As of April 1, 68 worker interviews had been completed (including proxy interviews for 2 deceased workers and 3 incapacitated workers). Therefore, as of April 1, 66 living workers were invited to the medical examination. The results are presented in Table 2, Attachment 9.

As of April 1, examinations had been scheduled or completed for 52 workers, and 5 workers had agreed to the examination, but were not yet scheduled. The participation rate is 78.8% (52/66) for completed exams as of April 1, and is anticipated to be 86.4% (57/66) when the workers who agreed are scheduled. Nine workers (including proxies for three incapacitated workers) refused the examination. The reasons include physical or mental impairment (5), unavailability due to work or other conflicts (2), and refusals (2) for other reasons.

Table 3, Attachment 9 presents the participation of the referents in both interview and examination. As of April 1, matched referents had been sought and obtained for 44 workers (100%). On average, it required inviting 2.3 appropriately matched individuals to obtain one referent who agreed to participate both in the in-home interview and in the medical examination. As of April 1, 44 referents had been interviewed, 10 referents have been examined, and the other 34 referents have been or are being scheduled for the medical examination.

We feel that the level of participation by workers and by referents in the in-home interviews and medical examinations compares very well with other studies. Four recent studies which included both an interview and an examination are the Vietnam Experience Study (VES), the second National Health and Nutrition Examination Survey (NHANES II), the Northwestern University Study of Pentachlorophenol Workers (NUS), and a Study of T-cell Subsets in Healthy Individuals in Washington, D.C. conducted by the National Cancer Institute (NCI).

The VES, the NHANES, and the NCI studies included a multi-staged process, whereby the individuals were first asked to complete an administered interview and later were recontacted and asked to participate in an examination. In our study, we use a two-stage approach to solicit participation from the workers; however, they have been informed before the interview by a series of lead letters sent to their homes that they will be asked to participate in an interview and

an examination. Potential referents are informed that participation requires involvement in the interview and the examination. Therefore, workers may agree to an interview and refuse the examination, but our referent participation rate in the study reflects a pre-selection to participate in two parts of the study.

In the VES, 85.6% of the study group was interviewed by telephone and 69.3% of a selected subset of those interviewed received medical examinations. These participation rates include the exposed study subjects (Vietnam Veterans) and non-exposed study subjects (Vietnam Era Veterans).

In the NHANES II, which took place between 1976-1980, approximately 90% of the sample was interviewed, and 73.1% of a selected sample agreed to be examined. Unlike our study or the VES study, the NHANES II examination is brief and took place within close proximity of the partipant's home, most often at a center in the home town, rather than at a facility requiring air travel to reach it. On the other hand, the NHANES Study is similar to our study in that it does request individuals who have no vested interest in the objective of the study to donate time to the study.

The Northwestern University Study of pentachlorophenol workers has just recently been completed. The exposed worker group and the referents (unexposed) were drawn from the same chemical plant population. The interview and examinations are conducted on the same day and at the same site, which is located near the plant. Approximately 90% of the study population resides within 100 miles of the study site, necessitating few overnight trips. Preliminary data indicate that the participation rate for this study (interview during examination) was 71.5%. The researchers do not distinguish between the participation of exposed versus unexposed workers.

The NCI conducted a three phase population-based study of T-cell subsets in a random sample of individuals in the Washington, D.C. area. Individuals were selected using random digit dialing and administered a five minute screening interview over the telephone. 79.4% responded to this questionnaire. A selected sample of the respondents were asked to participate in a 25 minute telephone interview. The response rate was 81.5% in the selected sample. A third sample was asked to to donate a small amount of blood at a local center. The overall response rate for the phlebotomy was 66.5%.

In ordinary interview studies, the general level of participation is 80-90%, as demonstrated in NHANES II and VES. Participation in medical examination studies is lower. In the NHANES II study, participation in a brief examination near the participant's home was 73%. The Northwestern University Study included in a one-day exam at site close to most participating workers; the participation rate was

71.5%. In the VES study, the medical examination was comparable in length to our NIOSH examination and conducted at the same facility in New Mexico; participation was 69.3% overall by the veterans. Our study referents differ from this group because they have no vested interest in participating.

Our study is unique because it requires individuals (referents) who are not directly involved with the goal of the study to spend considerable time and energy to travel, in many cases, great distances from their home to participate in the study. Based on the participation rates of other studies, we feel that we are achieving an acceptable overall participation rate in our study among the workers and the referents. Overall participation in interview and examination for the workers is 83.8%. To date every worker has a matched referent who participates in the interview and in the examination.

B. Assessment of the Adequacy of the Referent Population

As described in the protocol (Attachment 5), referents for this study are selected from among individuals living within the census block of the worker who match the worker by age (within 5 years), gender, race, and who were never employed at the study plant. A detailed description of the selection algorithm is included in the protocol.

As of April 1, 1987, we have sought matched referents for 44 workers. We invited 101 individuals who are eligible for participation as referents for the 44 workers in order to obtain the 44 referents who have agreed to participate in both the in-home interview and the two-day medical examination. Therefore, we have obtained matched referents for all of the workers for whom they have been sought. To date, it takes invitations to 2.3 eligible individuals (101/44) to obtain a referent who agrees to participate in the interview and examination.

The referent selection algorithm described in the protocol was designed to obtain an unbiased sample of eligible referents. In the selection process, the interviewer must enumerate households in the census block in which the worker resides, starting at the northeast corner of the census block and proceeding in a specified order. The interviewer ascertains whether each household contains an individual meeting the eligibility criteria until she locates six suitable individuals. Each eligible individual is assigned a sequence number as he/she is identified. The sequence numbers are randomized at the contractor's office, and the interviewer must interview the eligible individuals in the randomized order.

As of April 1, we have received from the contractor copies of interviews of 38 referents. We have reviewed the 38 referent interviews to evaluate the number of contacts required to obtain the eligible referent for each of 38 workers.

# Contacts Necessary	# Referents Obtained	% Referents Obtained
1	16	42
2	5	13
3	7	19
4	2	5
5	3	8
6	5	13
Total	38	100

Forty-two percent of the referents were obtained in the first contact, more than 50% of the participating referents were located after the second contact, and more than 70% after the third contact.

It should be noted that our selection algorithm sets up a random order of contact for the six matched referents identified for each worker. We utilize a system requiring contact of the next (randomly assigned) matched referent following a refusal by a potential referent as a substitute for heavy "refusant conversion" procedures utilized in many studies. Under this system, any of the six possible referents should be an equivalent random match for a worker.

The concern to be addressed regarding the level of participation in any study is whether bias is introduced in the comparison group because the inviduals who don't participate may be different from the participating referents. In order to evaluate whether or not the participating referents (respondents) and the nonrespondents (eligible matches who refuse to participate) are similar, we are administering a brief questionnaire to every eligible individual in our study who refuses the interview and examination. The interview obtains basic demographic data including years of education, total income, and limited information on current and past medical conditions. The questions are worded exactly the same as on the questionnaires administered to participating workers and referents.

As of April 1, 1987, we have received from the contractor completed questionnaires for 38 referents and 18 nonrespondents. To evaluate whether there are meaningful differences in the overall characteristics of participating referents and the nonrespondents, we have examined information on income, education level and

self-perceived health status. The results are presented in Attachment 10, Tables 1,2, and 3. Comparison (chi square) of these three indices indicates that there is no statistically significant difference between the referents and the nonrespondents on these characteristics. Based on this preliminary information, we believe that the referents and nonrespondents are similar in income, education, and in self-perceived health status. Because of our matching criteria, we know that the participating referents and the nonrespondents share the same characteristics of age, gender, race, and resident neighborhood.

Tables 4, 5, and 6 of Attachment 10 indicate that the workers and the referents are also similar in income, education, and self-perceived health status.

3. "HHS will ensure the quality and appropriateness of survey instruments."

We are utilizing the following survey instruments, which form the basis of our interview data collection.

a) Demographic and Occupational History Questionnaire. This is given in the home of the participant by trained interviewers with an average length of field interview experience of approximately 12 years.

b) Medical History Interview. This is given during the medical examination day by a nurse and a physician's assistant who are experienced interviewers.

c) Wives Reproductive Interview. This is given by telephone by experienced interviewers at Research Triangle Institute.

d) Refusant Questionnaire. This is given at the home by the interviewers to individuals who refuse to complete the Demographic and Occupational History Questionnaire.

e) Various instruments specific to the medical, neurobehavioral and psychological tests.

We believe that the instruments are of high quality and are appropriate to obtain the data needed for the study. These questionnaires were designed to obtain demographic information, detailed information on occupational dioxin exposures to 2,3,7,8-TCDD-contaminated material, and information on confounders for hypothesized medical outcomes, medical and reproductive histories, current symptoms, names of medical providers from whom medical records can be obtained to document medical problems, and demographic and health information from persons who refuse the

interview or exam. Other data collection instruments and questionnaires utilized in the various medical and psychological tests are specific to the particular test.

We have taken the following steps to ensure the quality and appropriateness of the instruments:

1. The questions are designed to provide appropriate data for testing of the a priori hypotheses of this study.

2. We utilized the questionnaires of the Air Force Ranch Hand Study, the CDC Veterans Experience Study, N HANES, and others as background in preparing the questionnaires. We focused the instruments on medical outcomes which had been reported in the literature to have an association with dioxin exposure, and we added some medical tests as a service to the participants.

3. Each section of the medical history questionnaire and the questionnaires used in the medical exams was reviewed by an expert in the appropriate field. We specifically asked the experts to determine whether the responses would permit us to test the hypothesis of interest. We also asked each expert to assess whether the instruments adequately addressed potential confounders.

4. Medical records are being obtained to confirm medical conditions reported by participants and which have been previously reported in the literature as health effects related to dioxin exposure.

5. In order to obtain the most accurate information possible on the occupational histories of the workers, the worker is presented with the employment history obtained by NIOSH from company records and asked at the time the demographic and occupational interview to confirm, deny or amplify the information on each job he held while working at the New Jersey facility.

6. The instruments are pretested and are administered by experienced interviewers with extensive survey research.

7. The contractors provide manual and machine edits to check for missing data and illogical responses. NIOSH has independently developed edit programs to provide further checks of the contractor edits.

Responses to Other Concerns of OMB

In addition to the three points enumerated above, the OMB letter of January 7, 1986 points out several other concerns. We list them here with our responses:

1. (Paragraph 2, lines 9 and 12) "...we continue to have reservation regarding the ...practical utility of study results."

We believe that the results of the study will have several practical applications. For example, we will establish the range of dioxin levels in the bodies of workers with known exposure to dioxin-contaminated products. The Missouri workers who have high levels of dioxin in their bodies are extremely worried about their health, and there are thousands of other workers with known dioxin exposures. If Phase II is conducted, our study will have adequate statistical power to address concern about some health outcomes. The results of our study will also be of benefit in extrapolating to the possible health outcomes of community residents with substantially lower body burdens of dioxin, as well as to Vietnam veterans.

Currently, the CDC and the Air Force are conducting studies in which the levels of 2,3,7,8-TCDD are being measured in the serum of veterans. Our study will provide data on serum 2,3,7,8-TCDD levels in workers with a wide range of occupational exposure levels. Interpretation of the levels of serum 2,3,7,8-TCDD in all three studies will bring us closer to understanding whether exposure to dioxin-contaminated products is associated with hypothesized medical outcomes.

There are thousands of citizens and other workers in Missouri, New Jersey and elsewhere who fear that they have been exposed to dioxin and who worry whether they will suffer medical problems because of that exposure. Because there is documented evidence that the Missouri workers had substantially higher than background serum levels of 2,3,7,8-TCDD with less than 2 years of exposure, our study may provide evidence that persons with minor exposures are not at excess risk, if the results show that no adverse health effects are related to body burden of 2,3,7,8-TCDD or length of employment in contaminated production processes.

The State of New Jersey is under a court order to conduct a study of all workers employed at the New Jersey facility. The New Jersey Department of Health informed the judge that the department is collaborating with NIOSH to conduct this study.

2. (Paragraph 3, lines 6 - 9) "This study should be constructed in such a way that if the design is demonstrated as workable, the results could be merged with results of any subsequent data collection."

We believe that our experience with Phase I has demonstrated that the study design is workable. Prior to initiating Phase I, we took great care to develop fully all questionnaires and to establish careful standardization of all medical and psychological test administration. We are very pleased with the performance of the

contractors in the conduct of the interviews and the medical and psychological tests. Consequently, there will be no major changes made in the questionnaires or tests, and the data will be collected in the same manner during Phases I and II. Therefore, all data can be merged.

As we noted above, we hope to obtain a rapid decision from OMB regarding Phase II in order that the contractor can retain the experienced staff members who have conducted Phase I. If we must conduct Phase II with new, inexperienced staff, that would be the one area in which we might experience problems in equivalent data collection.

3. (Paragraph 3, lines 13 - 16) "Future consideration of the remainder of the study will be dependent on the demonstration that the objectives of the full study can be reasonably met, as shown through the experience gained.

We hope that we have demonstrated that our experience of Phase I shows that the full study can be conducted with an excellent participation rate, with appropriate quality survey instruments, and with adequate standardization of test administration.

E. Request for A Rapid Response from OMB

We have two concerns which prompt us to request a rapid approval by OMB permitting us to award the contract for Phase II: 1) We would like to save approximately $200,000 by avoiding two months of "downtime", and 2) We would like to retain the experienced staff of the contractor by informing the contractor as soon as possible that the contract will continue on to Phase II.

ATTACHMENT 1

EXECUTIVE OFFICE OF THE PRESIDENT
OFFICE OF MANAGEMENT AND BUDGET
WASHINGTON, D.C. 20503

JAN 7 1986

Honorable John J. O'Shaughnessy
Assistant Secretary for Management and Budget
Department of Health and Human Services
Washington, D.C. 20201

Dear Mr. O'Shaughnessy:

In your letter of December 11, 1985, you requested that OMB reconsider its disapproval of the information collection entitled "Dioxin Morbidity and Reproductive Study of U.S. Chemical Workers" sponsored by the National Institute for Occupational Safety and Health (NIOSH).

We have carefully reviewed the additional material submitted with your appeal, and have also discussed your proposal with other interested parties within the Executive Office of the President (EOP). As you point out in your letter, and which was not clear to us from your original proposal, the unique aspect of this NIOSH dioxin study is that it has the capacity of producing exposure data that other dioxin studies have not been able to provide. While we agree that this exposure data could contribute significantly to the state of the art, we continue to have reservations regarding the degree to which there will be adequate variation in exposure levels, appropriate selection of the control cases and the practical utility of study results.

Therefore, we will agree to approve a portion of the study during which HHS will: (1) complete the exposure model and develop exposure estimates for the entire sample, (2) evaluate the ability to select and recruit appropriate control cases, and (3) ensure the quality and appropriateness of survey instruments. This study should be constructed in such a way that if the design is demonstrated as workable, the results could be merged with results of any subsequent data collection. The sample for this portion of the study shall not exceed 80 and shall be drawn exclusively from the New Jersey site. The results of this study shall be submitted to OMB and will be shared with other EOP offices and with the Agent Orange Working Group (AOWG) Science Panel. Future consideration of the remainder of the study will be dependent on the demonstration that the objectives of the full study can be reasonably met, as shown through the experience gained. Once the technical concerns are resolved, the practical utility of the study must be demonstrated.

A revised request for OMB approval should be submitted through normal channels, and we promise to review your request expeditiously. If you have any questions regarding this matter, please have your staff contact Fay Iudicello at 395-7316.

Sincerely,

SIGNED

Robert P. Bedell
Deputy Administrator
Office of Information
and Regulatory Affairs

NOTICE OF OFFICE OF MANAGEMENT AND BUDGET ACTION

OCT 24 1985

ATTACHMENT 2

TO: JOSEPH P. COSTA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
526F HUBERT HUMPHREY BUILDING
WASHINGTON, D. C. 20201
Centers for Disease Control

ACTION DATE
10/17/85

ON 07/19/85, YOU REQUESTED APPROVAL OF THE FOLLOWING INFORMATION COLLECTION:
TITLE: DIOC
KIN
AGENCY FORM NOS.:

IN ACCORDANCE WITH THE PAPERWORK REDUCTION ACT, WE HAVE TAKEN THE FOLLOWING ACTION ON THIS INFORMATION COLLECTION:

NOT APPROVED. SEE "REMARKS" BELOW.

EFFECT ON BURDEN:	RESPONSES	REPORTING HOURS
PREVIOUS STATUS	0	0
NEW STATUS	0	0
DIFFERENCE	0	0

REMARKS:

Not approved. conduct of this study is unnecessary in view of the fact that workers proposed for examination are already included in nioshs dioxin registry study of dioxin-exposed chemical workers, and since numerous dioxin exposure in the workplace studies have been conducted , to which the proposed study would add little if any, further intelligence.

OMB NO. XXXX-XXXX

ABSTRACT:
THIS EPIDEMIOLOGICAL STUDY OF WORKERS IN TWO CHEMICAL PLANTS IN NEW JERSEY AND MISSOURI IS DESIGNED TO DETERMINE WHETHER THERE MAY BE A CAUSAL RELATIONSHIP BETWEEN HEALTH PROBLEMS AND EXPOSURE TO TCDD (DIOXIN). THE RESULTS WILL BE USED FOR RECOMMENDATIONS AND INTERVENTION PROGRAMS FOR PERSONS EXPOSED TO TCDD.

ALLOWANCE LETTER: NO FUNCTION: MULTIPLE FUNCTIONS
ON PLAN: YES EXCEED BUDGET: NO 3504(H): N/A
NO. OF FORMS: 1 USE: PUBLIC REQUEST: NEW
RESPONDENTS: 528 RESPONSES: 0 HOURS: 0
AFFECTED PUBLIC: IND/HHLD
SMALL BUSINESS: NO ACTIVITY TYPE:
PURPOSE: RESEARCH
FREQUENCY: OTHER
COLLECTION METHOD: MAIL S/A
RETENTION: COLLECTION AGENT: RQSTNG DPT/AGCY CONFIDENTIALITY: NO
COMPULSORY STATUS: VOLUNTARY
FEDERAL COST: PUBLIC COST:
REVIEWER: FAY S. INDTCFLLO

ACTION	AUTHORIZING OFFICIAL	TITLE: DEPUTY ADMINISTRATOR	DATE
APPROVED BY:	/S/JAMES B. MACRAE FOR	OFFICE OF INFORMATION AND REGULATORY AFFAIRS	10/17/85

ATTACHMENT 3

DEPARTMENT OF HEALTH AND HUMAN SERVICES

NOV 12 1985

Acting Director
Centers for Disease Control

Request to Appeal OMB Decision Not to Approve Dioxin Study

The Acting Assistant Secretary for Health

We request that the Department of Health and Human Services appeal the OMB decision not to approve the Centers for Disease Control (CDC) "Study of Persistent Health Effects among Chemical-Herbicide Workers and Community Residents." In their decision, OMB stated:

> Conduct of this study is unnecessary in view of the fact that workers proposed for examination are already included in NIOSH dioxin registry study of dioxin-exposed chemical workers, and since numerous dioxin exposure in the workplace studies have been conducted, to which the proposed study would add little, if any, further intelligence.

We need considerable additional intelligence. Several Federal organizations are concerned with the possible adverse health effects of dioxin. They include the Centers for Disease Control [National Institute for Occupational Safety and Health (NIOSH) and Center for Environmental Health (CEH)], Occupational Safety and Health Administration (OSHA), Agency for Toxic Substances and Disease Registry (ATSDR), and Environmental Protection Agency (EPA). Within their respective missions, all of these organizations have raised the issue of the health effects of dioxin. NIOSH and OSHA are particularly concerned with the health of workers, CEH is concerned with nonoccupational exposures and exposure of Vietnam veterans to dioxin-contaminated agent orange, and ATSDR and EPA are concerned with Superfund site exposures.

In most circumstances of exposure, other than the occupational setting, there are considerable difficulties in documenting the occurrence of exposure and exposure levels. Generally in nonoccupational settings exposures are at low levels, and they are intermittent. Exposure of the population to be studied in the NIOSH dioxin morbidity study is more certain and higher than is generally found. If the results of this study show no adverse health effects, there will be good reason not to initiate any new general population dioxin health effects studies. If the study does show health effects, any new studies which might be indicated can be more effectively focused. ATSDR is under pressure to do more studies relating to Superfund sites. However, if the NIOSH dioxin morbidity study is done, ATSDR will not initiate any new studies until the results of this study are available.

FILE COPY

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE

On September 25, 1984, the Science Panel of the Agent Orange Working Group concluded that, "both the Mortality Study and the Morbidity Study are well designed and carefully considered and should provide useful information on the possible long term effects of industrial exposure to dioxin contaminated products." The Science Panel recommended that both Studies proceed as soon as appropriate resources can be allocated (Tab A).

Both the States of Missouri and New Jersey are collaborators in the study. The State of New Jersey requested Federal assistance to conduct this study in August 1983 (Tab B). In February 1985, the New Jersey Commissioner of Health advised that the study was part of a Civil Action Order (Tab C). EPA has approved funding for the Study and firmly supports the project.

Attached are a detailed appeal statement (Tab D) and a response to the statistical questions raised in the previous review (Tab E).

Donald R. Hopkins, M.D.
Assistant Surgeon General

Attachments
Tab A: Science Panel Recommendations
Tab B: October 1984 Letter from New Jersey
Tab C: February 1985 Letter from New Jersey
Tab D: Detailed Appeal Statement
Tab E: Response to Statistical Questions

cc:
CDC/W
OD
OPPE
NIOSH
CER
ES/PHS

CDC:OD:OPPE:N.W.Axnick: mlj Nov. 8, 1985 Doc.# 3551P; D25206

FILE COPY

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE

ATTACHMENT 4

January, 1987

EXECUTIVE SUMMARY: STUDY OF PERSISTENT HEALTH EFFECTS IN CHEMICAL-HERBICIDE WORKERS AND IN COMMUNITY RESIDENTS OF UNKNOWN EXPOSURE STATUS

EXECUTIVE SUMMARY OF STUDY PROPOSAL

I. Purpose:

The purpose of this cross-sectional morbidity study is to determine whether workers employed at two facilities in the United States experience any long-term health effects as a result of their past exposure to contaminants of chlorophenoxy herbicides particularly 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). The health status of chemical-herbicide workers will be compared to the health status of unexposed individuals matched to the workers by age, race and gender and living at the time of the study within the community of the worker.

II. Study Population:

The study population will consist of all employees of a plant formerly located in Newark, New Jersey who worked in the production of phenoxy herbicides including 2,4,5-trichlorophenoxy acetic acid (2,4,5-T)and 2,4-dichlorophenol (2,4-D) and intermediate products such as 2,4,5-trichlorophenol for 1 or more days between 1946 and 1969, when the plant was closed.

The study population will also include employees of two companies, located in Verona, Missouri who worked in the production of 2,4,5-T, Agent Orange, and hexachlorophene. Both companies operated sequentially between 1968 and 1971 in the same facility and with some of the same employees.

Four hundred ninety seven (497) workers meet the definition of exposure at the New Jersey facility, of which 100 are known to be deceased and 30 are considered to be lost-to-follow-up. A minimum of 306 workers from this facility (80%) are expected to participate.

Ninety (90) workers meet the definition of exposure at the Missouri facility, of whom 4 are deceased. A minimum of 72 workers from this facility (80%) are expected to participate in the study.

A comparison group of approximately 450 persons will be identified from the communities in which the workers reside at the time of the study. The referents will be individually matched to the workers on the basis of age ($\pm$ 5 years), race and sex. Use of community based referents will control possible confounding effects of socioeconomic status.

Wives and former wives of workers and referents will also be interviewed to evaluate the association between occupational exposure to TCDD and decreased fertility in the workers and spontaneous abortions, stillbirths, or congenital malformations in the offspring of male workers.

III. Study procedures:

Information on worker and referent health status will be collected through a comprehensive set of interviews and medical examinations. Interviewer administered questionnaires will elicit lifetime medical history, and detailed occupational and reproductive history of each participant. Medical records will be obtained to verify self-reported health outcomes which have been previously associated with dioxin exposure.

The medical examination will include a general physical, dermatologic and neurologic examinations, pulmonary function tests, chest X-ray (optional), thermal and vibration quantitative sensory tests, nerve conduction velocity test, psychologic and neurobehavioural assessments, delayed hypersensitivity skin tests, electrocardiogram, peripheral pulses, and blood and urine chemistries.

Exposure status of each worker will be assessed using a compilation of data from company personnel and industrial hygiene records and self-reported work histories. Estimates of worker exposure to dioxin will be constructed using company and governmental records of TCDD levels in 2,4,5-T products and in the work environment.

Body burden of 2,3,7,8-TCDD will be measured in the serum of each participant of the medical examination. These data will be used to verify the exposure matrix and to estimate levels of 2,3,7,8-TCDD acquired as a result of workplace exposure.

IV. Analysis

The health outcomes in the exposed workers will be compared to those of the matched referents. The strategy for statistical analysis will involve 1) evaluation of crude associations, 2) stratified analysis, 3) assessment of dose-response relationships, and 4) multivariate analysis.

V. Logistics

The data collection and medical examination components of this study will be conducted under contract by the Lovelace Medical Foundation, Albuquerque, New Mexico. NIOSH has prepared the content-prototype for all questionnaires and all other data collection instruments. The NIOSH Project Director will oversee all contractor activities including interviewing and performance of standardized medical examinations to ensure the quality of the collected data. Data analysis will be conducted by NIOSH under the direction of the Project Director.

The study will be conducted in two phases. Phase I will include the interview and examination of a 80 workers previously employed at the Newark, New Jersey facility, 80 referents, and the interview of a total of 160 wives. The sample of 80 workers will be selected from a stratified random sample of the surviving workers of the New Jersey facility. Phase I began on November 21, 1986. Field work, including interviews and medical examinations will begin about March 1, 1987. Phase I is expected to be completed during September, 1987. Phase II, if conducted, will include the interview and examination of approximately 200 workers from the New Jersey facility, their corresponding referents and wives, and the interview and examination of approximately 90 workers, corresponding referents and wives from the Missouri facility.

Phase II will be initiated after the data collection fo Phase I has been reviewed. The review will be based on three criteria:

1. participation rate in Phase I.
2. completion of exposure model and development of exposure estimates for the entire sample.
3. evaluation of quality and appropriateness of survey instruments.

If data collection for Phase I is successful, Phase II field work will begin approximately in September, 1987, with data collection to be completed approximately in November, 1988. Data generated from both Phases I and II will be collected in a manner such that the data from both phases can be combined in the final analysis.

ATTACHMENT 5

PROTOCOL: DIOXIN MORBIDITY STUDY

PROTOCOL FOR A STUDY OF PERSISTENT HEALTH EFFECTS IN CHEMICAL-HERBICIDE WORKERS AND IN COMMUNITY RESIDENTS OF UNKNOWN EXPOSURE STATUS

Marie Haring Sweeney, M.P.H.
Marilyn A. Fingerhut, Ph.D.
L. Barbara Connally, B.S.
P. Lynne Moody, M.D., M.P.H.

Industry Wide Studies Branch
National Institute for Occupational Safety and Health
and Members of the Dioxin Medical Study Cooperative Group
(NIOSH and the States of Missouri and New Jersey)
Revised April, 1987

TABLE OF CONTENTS

		Page
I.	Introduction	1
II.	Background	1
	A. Suspected toxicity of 2,3,7,8-TCDD to humans	
	B. History of NIOSH's Involvement in Dioxin-Related Research	
III.	Study Design	4-10
	A. Overview of study type and objective	
	B. Description of the study cohorts	
	C. A two-phased study approach	
	D. Referent Selection	
	E. Power Calculations	
IV.	Study Methods	11-22
	A Overview	
	B. Data Collection	
	C.1 Demographic and Occupational Interview	
	C.2 Medical History and Symptom Questionnaire	
	C.3 Medical Examination:	
	C.3.a Components	
	C.3.b. Overview of Testing Schedule	
	C.3.c. General Physical, Dermatological, and Neurological Examinations	
	C.3.d. Quantitative Sensory Test	
	C.3.e. Nerve Conduction Velocity	
	C.3.f. Psychological and Neurobehavioral Test	

C.3.g. Pulmonary Function Test

C.3.h. Laboratory Tests: Blood and Urine

C.4. Female Reproductive Interview

C.5. Quality control assurance

C.5.a. Overview

C.5.b. Examination Standardization Plan

C.5.c. Evaluation of interobserver variation

D. Notification and Follow-up

E. Collection of Medical Records

F. Estimation of Exposure Status

G. Data Management

H. Data Analysis and Analytic Techniques

I. Consideration of Potential Biases

V. Conclusion 22

VI. References 24

Appendix A Chemistry, Toxicity, and Human Health Effects of 2,3,7,8-TCDD-Contaminated Materials

PROTOCOL FOR A STUDY OF CHEMICAL-HERBICIDE WORKERS EXPOSED TO MATERIALS CONTAMINATED WITH 2,3,7,8-TETRACHLORODIBENZODIOXIN

I. Introduction

The dioxins are tricyclic chlorinated phenoxy compounds. Among the 75 isomers, one of the 22 tetra isomers is 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). It is formed as a contaminant of several compounds which have had wide industrial and environmental application, including trichlorophenol (TCP), 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), 2,4,5-T esters, 2,4,5-T amines, 2,4,5-trichlorophenoxypropionic acid (Silvex), Silvex esters and amines, and hexachlorophene.

First produced in the U.S. in the 1940's, the 2,4,5-T-based herbicides were widely used for roadside and railroad right-of-way foliage control, and for eradication of broadleaf species in evergreen forests until 1979, when the Environmental Protection Agency restricted their use. Reports of human exposure to these chemicals began in the late 1940s after an explosion in 1949 at a plant in Nitro, West Virginia. Since that time, research concerning the health effects of such exposure has continued. Subsequent studies and case-reports have suggested that a multiplicity of health effects result from exposure to 2,3,7,8-TCDD-contaminated products and materials.

The U.S. military sprayed approximately 11.2 million gallons of a 50:50 mixture of the butyl esters of 2,4,5-T and 2,4-dichlorophenoxyacetic acid (2,4-D), known as Agent Orange, on Vietnamese forests and crops during the Vietnam War. Environmental contamination with 2,3,7,8-TCDD in the United States was not known to be a problem until the recent discovery of widespread environmental contamination in Missouri, that resulted from application of contaminated waste oil to dusty areas. Even more recently, worksite, neighborhood, and waste disposal site contamination in New Jersey suggest that the problem of environmental contamination has not yet been fully assessed.

II. Background

A. Suspected toxicity of 2,3,7,8-TCDD to humans

Human health effects associated with exposure to the phenoxyherbicides and their contaminants have been reported in several settings, but chiefly in groups occupationally exposed to the manufacture of products containing 2,3,7,8-TCDD as a contaminant. Since the first explosion in a U.S. TCP production

plant in 1949, Kimmig and Schulz (1957), Bauer et al. (1961), Bleiberg et al. (1964), Goldmann (1972), May (1973), and others have described workers affected by acute exposures during industrial accidents occurring in the United States, Europe, and Great Britain. A second source of information is that collected on workers with chronic or sub-acute occupational exposure during the synthesis of herbicides and fungicides, by Poland et al. (1974), May (1982), Walker and Martin (1979), Cook (1980), Ott (1980), Pazderova-Vijlupkova (1981), Crow (1982), and Singer et al. (1982), Zack and Suskind (1980), Suskind and Hertzberg (1984), and Moses et al. (1984). In several of these studies, workers were followed or seen after intervals of 10 to 30 years following exposure.

A series of investigators have documented the medical sequellae of the industrial accident at Seveso, Italy, in which community residents surrounding the factory became ill after exposure to 2,3,7,8-TCDD-contaminated emissions (Reggiani, 1978; Reggiani, 1980; Pocchiari, 1979). In two other discrete incidents, illness attributed to 2,3,7,8-TCDD has been reported. Three laboratory scientists synthesizing pure 2,3,7,8-TCDD displayed health effects deemed related to 2,3,7,8-TCDD exposure, despite careful precautions (Oliver 1975). In 1971, in Missouri, horses, birds, and other farm animals sickened and died, and humans reported illness after exposure in horse arenas sprayed with 2,3,7,8-TCDD-contaminated waste oils (Carter et al. 1975, Kimbrough et al. 1977). Additional studies of other Missouri residents exposed to contaminated soil around their homes, suggest a change in the immune function in the exposed (Hoffman, 1986). The Hoffman study is presently being repeated to verify the findings.

The illnesses or health effects which have been attributed to 2,3,7,8-TCDD or to the substances of which it is a contaminant are many, although some patterns have emerged; and the evidence for the association with 2,3,7,8-TCDD is stronger for some effects than for others. Chloracne, a persistent acneiform eruption associated with exposure to a number of chlorinated hydrocarbons, is certainly associated with 2,3,7,8-TCDD. Porphyria cutanea tarda, neurologic abnormalities, hepatic injury, lipid abnormalities, neurobehavioral alterations, and immunologic dysfunction have also been associated with exposure to dioxin-contaminated materials. Additional effects reported in human populations have included abnormalities of pulmonary function in exposed smokers, gastric ulcer, increased prevalence of coronary vascular disease, Peyronie's disease, impotence, and decreased libido (Suskind 1984). For many of these effects, the epidemiologic data are suggestive but by no means definitive.

In addition to questions about the effects of 2,3,7,8-TCDD in humans following accidental industrial and laboratory exposures or chronic workplace exposures, Swedish studies have implicated 2,3,7,8-TCDD-contaminated herbicides as a risk factor for soft tissue sarcoma in occupationally exposed groups. Vietnam war veterans in the U.S. are concerned about possible carcinogenic and teratogenic effects as a result of their putative exposures to Agent Orange during the Vietnam war. This widespread concern about the Vietnam experience coupled with environmental contamination with 2,3,7,8-TCDD in several areas of the U.S., has fueled medical, government, and public concern over the public health threat of dioxin. (See Appendix A for a more detailed discussion of the toxicology and toxicity of 2,3,7,8-TCDD and contaminated phenoxyherbicides.)

B. History of NIOSH's Involvement in Dioxin-Related Research

NIOSH has had a long-standing interest in the issue of dioxin as an occupational toxicant and carcinogen, because of the animal toxicity of 2,3,7,8-TCDD and relevant human data, and because of 2,3,7,8-TCDD's importance as a contaminant in trichlorophenol production and related chemical processes. Accordingly, NIOSH began in 1979, to accumulate data for a registry, which contains work histories and exposure information about the 7,000 U.S. workers employed in production processes of TCP, 2,4,5-T, hexachlorophene, and pentachlorophenol which is reported to be contaminated with hex-, hepta-, and octa-isomers of dioxin. A study is underway to assess mortality experience of the Registry membership.

The mortality study cannot, however, clarify the issue of long-term phenoxy herbicide and dioxin-related morbidity. It is not clear whether the reported neurologic, hepatic, metabolic, immunologic deficits, and other health effects may be long-term, and no large cohort with an adequately defined range of exposures or an adequate comparison group has been studied to evaluate statistically these hypothesized outcomes. Questions about reproductive impairment remain unanswered, as do questions about carcinogenesis. Because of this plethora of unanswered questions and the development of the Registry, NIOSH has for several years contemplated a future study of morbidity based on the worker populations in the Registry.

There are fourteen plants in the Registry which would theoretically be potential study populations for an examination of long-term morbidity. However, the States of Missouri and New Jersey have requested that NIOSH assist them in an evaluation of the health of workers employed at two chemical-herbicide plants which are located in those states and which are also part of the NIOSH Dioxin Registry.

III. Study Design

A. Overview of Study Type and Objectives

This protocol presents the plan to conduct a cross-sectional epidemiologic study of living workers to evaluate the prevalence of chronic medical conditions related to past exposure to chemicals contaminated with 2,3,7,8-TCDD. The study also includes a longitudinal component to assess overall past exposure to 2,3,7,8-TCDD-contaminated materials and past history of medical conditions. Outcomes of interest will include a number of biological measures of current health status previously reported to be related to 2,3,7,8-TCDD exposure. Additional information to be collected includes medical history, personal habits, and employment history. Certain key medical conditions will be confirmed through medical records. These data will provide concrete information about the current health status and prevalence of diseases or biologically relevant medical effects in this population of workers exposed to 2,3,7,8-TCDD-contaminated materials.

B. Description of the study cohorts

The study population will consist of living individuals from two chemical manufacturing plants located in New Jersey and Missouri. The New Jersey plant located on 80 Lister Street in Newark operated between 1951 and 1969, producing trichlorophenol, chlorinated benzenes, phenoxy herbicides, and other pesticides. The total workforce was about 490 workers. Two studies of some employees of this plant were published, the first by Bleiberg et al. (1964) and the second by Poland (1971). The occurrence of a large number of cases of chloracne throughout the history of the plant, suggests that

2,3,7,8-TCDD exposure was prevalent and ongoing. Although, for a short time, hexachlorobenzene was used at the plant, data to support its role as a chloracnegen is sparse (Taylor, 1978); however, its role as a porphyrogen is well documented (Cripps, 1984). No other suspected chloracnegen was manufactured at the New Jersey plant.

The Missouri plant employed about 90 workers in the production of 2,4,5-T for four months in 1968, and hexachlorophene for two years in 1970-1971. There is no documentation of chloracne in this population. However, recent information indicates plant employees involved in the production of 2,4,5-T and hexachlorophene were exposed to high levels of 2,3,7,8-TCDD (unpublished).

The total study population described above numbers 576. Thirty-five of them are female. As of June, 1986, 448 are believed alive. Where possible, current addresses have been obtained for these

individuals, and death certificates will be obtained for any deceased. Follow-up of the two groups to date indicates that surviving workers from the two plants are presently located in 38 states and territories, with 254 New Jersey workers still living in New Jersey, New York, or Pennsylvania, and 59 Missouri workers still living in Missouri. A comparison of surviving workers who remained in the contiguous geographic area with those who moved away shows that they are similar with respect to date of birth, date of hire, and duration of employment at their respective plants. Despite the wide geographical dispersion of the cohort, we propose to invite to participate in the study all workers from the New Jersey facility and all production workers employed in dioxin-contaminated processes at the Missouri facility .

C. A two-phased study approach

The study will be conducted in two phases. Phase I will include an in-home interview and a medical examination of 80 workers previously employed at the New Jersey facility, 80 matched referents, and the interview of a total of 160 wives. The sample of 80 workers will be selected from a stratified random sample of the surviving workers of the New Jersey facility.

Phase II will include the interview and examination of approximately 200 workers from the New Jersey facility, their corresponding referents and the wives of workers and referents, and the interview and examination of approximately 90 workers from the Missouri facility, their referents, and wives of both workers and of referents.

Data collection for the study will be conducted under contract by the Lovelace Medical Foundation (LMF) and the Research Triangle Institute (RTI). The fixed price nature of the contract dictated that we set minimum levels of achievement for the contractor. If the contractor does not achieve the negotiated levels they will be in default. We set participation limits for the in-home interview and for the medical examination. Thus, for the New Jerssey cohort in Phase I, the contractor must interview no less than 80% of the workers and the referents, and must examine no less than 70% of the workers and 60% of the referents. Therefore, in Phase I, out of 80 workers and 80 referents, 64 workers and 64 referents are to be interviewed, and 56 workers and 48 referents are to be examined. Similarly, in Phase II, for the New Jersey plant cohort, the contractor must achieve the same percentages of interviews and examinations as in Phase I. For the Missouri cohort, the contractor must achieve an 80% participation rate for the in-home interviews and a 60% and 50% participation rate for the workers and referent examinations, respectively. Therefore, 222 New Jersey workers and 222 referents will be interviewed, and 195 workers and 166 referents

will be examined; 72 Missouri plant workers and 72 referents must be interviewed, and 54 of those workers and 45 referents must be examined.

D. Referent Selection

Referents will be selected from the community in which the workers reside at the time of the study, and will be matched to each worker by age, (± 5 years), race, and gender. Follow-up letters will be sent to referents after they have been contacted in-person, to introduce the study and to request their participation.

Referents are selected using a protocol which requires that the interviewer follow standard survey procedures to enumerate households in a specified area, to identify nonexposed individuals who satisfy the specified matching criteria, and to recruit acceptable participants into the study. The method used to construct the selection algorithm is described below.

Before reviewing the selection algorithm, a discussion of the uniqueness of this study is warranted. This study design, which asks a group of individuals with no vested interest in the study objective to travel to a city a great distance from their home, and to take a comprehensive physical examination, has heretofore not been attempted. While other studies have requested participation in examinations away from the participants home, the examination site has been near to their homes (NHANES), or all the participants (exposed and nonexposed) have a readily identifiable bond to the study purpose and objectives, e.g., the CDC Vietnam Veterans Study, the Airforce Ranch Hand Studies, and the Northwestern University Study of pentachlorophenol production workers (the referents were selected from among, nonexposed, long-term workers from the same plant).

Once the assigned worker has been located and interviewed, the interviewer must enumerate all households within the census block of the interviewed worker, beginning in the northeast corner of the census block. During the enumeration process, the interviewer must determine the households within the census block in which nonexposed individuals matching the age, race and sex criteria live. The interviewer must enumerate the neighborhood households until she finds a maximum of 6 individuals who match the worker. Each match is assigned a sequence number according to the location of his/her housing unit in the enumeration process relative to the northeast corner of the census block. The sequence numbers are randomized at RTI and the interviewer must approach the matched individuals in the randomized order. Therefore, the interviewer cannot interview the individual that is most convenient, thus eliminating any selection bias that may occur due to the respondent's availability during a certain time of the day, or by interviewer whim.

Once in the home of the matched nonexposed individual, the interviewer describes the purpose of the study, the requirements of participation, and the benefits to the individuals who participate. Information about the study, including a fact sheet and introductory letters, are left with the potential referent. If the individual agrees to participate, the interviewer will administer the Demographic and Occupational History Questionnaire, describe the medical examination at Lovelace Medical Foundation (LMF) in Albuquerque, New Mexico, and show him/her a brief film about LMF, the exam and Albuquerque.

E. Sample Size

Power Calculations

Power calculations are characteristically conducted prior to the onset of a study to determine the statistical ability of the sample to detect statistically significant increases in the relative risk of hypothesized outcomes, if the increase exists in the studied population. Of the many medical outcomes which have been reported to be related to exposure to dioxin-contaminated materials, we are testing the hypotheses that increases in the following outcomes are related to exposure to dioxin-contaminated materials.: in neurological, hepatic, and dermatologic conditions, elevations in the prevalence of cardiovascular disease and lipid disorders, and adverse changes in the immunologic system. Only a few of these conditions have been examined in well-controlled studies of individuals exposed to dioxin-contaminated materials.

We evaluated the power of our study, to detect as statistically significant, the prevalence of certain conditions reported in two studies of dioxin exposed workers by Suskind (1984) and Moses (1984). The conditions were found in workers involved in the 1949 explosion at a TCP production facility in Nitro, West Virginia. These study populations closely resemble our study group because they were occupationally exposed and are of similar age ranges. Additionally, comparison of the production processes in the New Jersey and Nitro plants suggests that they were very similar. However, these studies had a number of methodological flaws, which may invalidate the study results. Both of the studies were conducted on volunteers, not on all survivors reportedly exposed to TCDD contaminated materials. Neither of the studies confirmed self-reports of medical conditions through objective sources. The Moses study used an inappropriately selected control group: exposed workers who did not have chloracne (Moses, 1984). Because the comparison group in the Moses Study had been exposed to dioxin-contaminated material , and, assuming the outcomes are related to the exposure, it is likely that the prevalence of the examined outcomes is higher than reported (Table III.E.1).

The power estimates for this study were calculated for clinically determined conditions and for history of conditions other than chloracne found to be associated with employment in the 2,4,5-T production area in the Moses and Suskind studies. These conditions include ulcer disease, abnormal pulmonary function, heart disease, neuropathy and decreased libido. Power was not calculated for chloracne because chloracne has not reported in any of the unexposed groups. In addition to outcomes reported in the above epidemiologic studies, there are many other conditions noted in the medical literature which were reported to have occurred subsequent to occupational exposure to dioxin. We will also be testing the hypothesis that these conditions, including hirsutism, porphyria and other liver disorders, immunologic and central nervous system dysfunction, are related to exposure.

Table III.E.2 lists the prevalence ratios for outcomes reported as statistically significantly elevated in the Moses and Suskind studies. Table III.E.1 presents the power in our study to detect the reported prevalence risk ratios. Power was calculated for 358 living workers from the New Jersey plant and 90 workers from the Missouri plant . We used the following assumptions for the calculations: 1) at least 70% of the workers will participate in the exam (N=314) and at least 60% of the referents will participate in the exam (N=268); 2) 20% of the examined workers and referents will be under 50 years old (N=116); 3) 40% of the examined workers and referents will be under 60 years old (N=233); 3) 20% of the examined workers will have chloracne or a history of chloracne; 4) 35% of the examined workers and referents will be current smokers (N=203).

Table III.E.1.

Prevalence Data from Studies of Dioxin Exposed Workers [1,2]
for Statistically Significant Outcomes
Associated with Exposure to Dioxin-Contaminated Materials

Condition	Prevalence in exposed Workers	Prevalence in unexposed Workers	Prevalence Risk Ratio
Ulcer Disease[1]	20.7%	5.5%	3.76
Abnormal Pulmonary function[1] test (FEV1/FVC%)	25.7% (Current) (Smokers)	6.7% (Current) (Smokers)	3.83
Decreased libido[1] (under age 50)	19.6%	5.0%	3.92
Heart Disease (Angina[1] under age 50)	5.9%	1.0%	5.9
Decreased sensation to pin[2] pick (neuropathy)	18%	0	18

[1] Suskind et al. 1984
[2] Moses et al. 1984

Table III.E.2

Power available for selected values of PRR*, Po and n, with alpha = .05, 1 referent per participating New Jersey worker.

Condition	Prevalence* Risk Ratio	Prevalence of condition in unexposed	# of Workers and Referents Examined	Power
Ulcer[1]	4	5.5%	582	100
Abnormal PFT[1] (among smokers)	4	6.7%	203	92
Decreased[1] Libido (Under age 50)	4	5.0%	116	55
Heart Disease[1] (Under age 50)	6	1.0%	116	21
Neuropathy[2]	18	0% (0.01)**	582	100

Based on power calculation by Miettinen
*PRR = Prevalence Risk Ratio based on Suskind[1] and Moses[2] studies
**Limit of program (Rothman and Boice, 1979)

[1] Suskind et al. 1984
[2] Moses et al. 1984

These data suggest that we will have excellent power to detect excesses in ulcer disease, abnormalities in the pulmonary function of current smokers with past exposure to dioxin-contaminated materials, and in peripheral neuropathies. While the power for decreased libido under age 50 and heart disease under age 50 is not as good, we will be able to confirm the presence or absence of the conditions using medical records and clinical data rather than rely on self-reports as the other studies have done and we have an age-matched comparison group for our large over-50 group which the Suskind study did not have. Because we have an appropriately matched unexposed group of referents, serum level of 2,3,7,8-TCDD, and records of confounding exposures, we will be able to relate to exposure status our estimates of the prevalence of the hypothesized conditions found to be in excess. We will also be able to

report on a variety of outcomes never adequately studied in dioxin-exposed groups. These include extensive in vitro studies of immunologic function, the assessment of lipid abnormalities, and the comprehensive determination of central and peripheral nervous system dysfunction and hepatic disorders.

IV. Study Methods

A. Overview

The study will be conducted in two phases. Phases I and II have been described in Section III.C. of this protocol.

Each participant will be contacted by mail and by phone follow-up in order to arrange for an in-person interview, preferably at the participant's home. The interview will include the administration of a questionnaire designed to gather demographic information and occupational history. After completing the demographic and occupational interview, each subject will be invited to participate in the medical examination to be administered at Lovelace Medical Clinic in Albuquerque, New Mexico.

B. Data Collection

1. Demographic and Occupational History Interview

The Demographic and Occupational History Interview will be administered to all workers and referents and will include the collection of demographic information.

The interview is divided into two sections, the first of which is concerned with general demographics, current health and medical history (including hospitalizations and medication histories for living subjects), smoking and alcohol consumption, hobby and home exposures, sunlight exposure, and information on possible chemical exposures during military service in Vietnam.

The second part of this interview, the Occupational History, gathers information about the subject's employment history and about the duties associated with his or her work. This section of the questionnaire is concerned with all jobs the subject may have had for a minimum of six months since his or her sixteenth birthday. Employment information of interest includes dates of employment, and specific job duties and titles, as well as chemical exposures.

A similar interviewing instrument will be administered to the next of-kin of incapacitated and deceased subjects. This questionnaire will be used to probe for the same type of demographic information and occupational history, but will ask about current medical conditions and about medication history for living subjects only. A brief medical history will obtain information on conditions previously associated with exposure to dioxin-contaminated materials.

For workers or potential referents who refuse to complete the Demographic and Occupational History Interview, the interviewer will administer an abbreviated questionnaire to obtain basic demographic information. These data will be used to evaluate response bias, if any, between respondents and non-respondents.

2. Medical History and Symptom Questionnaire

The Medical History Questionnaire and Symptom Questionnaire will be administered at the examination site during the Medical Examination (Section IV.3.). The questionnaire will review the subject's past medical history and current symptoms.

This questionnaire will also include questions about any hospitalizations and any medications the subject may have been prescribed or may have taken since the time of the in-home interview.

A reproductive history segment will also be administered to male workers and female workers and referents, during the Medical History Questionnaire. This portion of the medical history interview will review all of the pregnancies of which the subject has been the mother or father. Information will be obtained about the pregnancy outcomes, conditions which may affect pregnancy outcomes, as well as confounding exposures.

3. Medical Examination
   a. Components:

The Medical Examination consists of the following evaluations:

1) General Physical
2) Dermatologic Examination
3) Neurological Examination
4) Quantitative Sensory Test and Nerve Conduction Velocity
5) Peripheral Pulses
6) Pulmonary Function Test
7) Chest X-Ray
8) Audiometric Test
9) Visual Acuity Test
10) Blood Chemistries
11) Urine Chemistries
12) Electrocardiogram
13) Neurobehavioral Evaluation
14) Psychological Evaluation
15) Delayed hypersensitivity Testing
16) Serum 2,3,7,8-TCDD Evaluation

b. Overview of testing schedule

Participants of the Medical Examination will attend an inbriefing session (DAY #1), during which they will be given information about the examination schedule, and oriented about what they can expect during this segment of their participation period. Physical examinations and lab tests will be scheduled for the day after the subject's arrival at the examination site (DAY #2). Psychological and neurobehavioral testing will occur on DAY #3. Outbriefing by a physician and by a psychologist will also take place on DAY #3, as test results are available.

Prior to the examination, subjects are instructed to refrain from eating red meat taking vitamins, non-prescription medication, and from ingesting alcohol during the three days before the examination. They are also instructed to fast for the 12-hour period preceding the scheduled medical examination and to collect a 12-hour urine sample during the same period.

c. General Physical, Dermatological, and Neurological Examinations

An internist will administer a general screening physical examination. A dermatologist, will administer a detailed examination of the skin to evaluate the presence or absence of conditions previously reported in the literature as dermatalogical sequellae of exposure to dioxin-contaminated substances, chloracne, porphyria cutanea tarda, and skin cancers. A neurologist will administer a directed examination at peripheral nerve function.

d. Quantitative sensory testing

Quantitative sensory testing of vibratory and temperature sensibility provides a quantitative extension of the sensory portion of the neurological examination. Because primarily sensory neuropathic changes are suspected in herbicide/dioxin-exposed individuals, these tests are a logical choice for this study. Such testing provides quantitative sensory thresholds and also tests both large fiber (vibratory) and small fiber (temperature) integrity, which may provide further information about the neurotoxicity of TCDD. These methods provide an excellent and palatable screening tool, such that if participants should decide to refuse nerve conduction testing, they will almost certainly agree to the tactile testing.

e. Nerve Conduction Velocity

Past studies of some dioxin-exposed groups have included nerve conduction studies of various nerves: median motor, median sensory, ulnar motor, peroneal sensory, and sural (sensory).

Parameters which have usually been measured include maximum conduction velocities and amplitudes. Our protocol for electrophysiological testing will include: median motor and median sensory, ulnar motor, peroneal sensory, and sural sensory; maximum conduction velocity with antidromic stimulation and averaging of sensory potentials; distal latency and forearm conduction across the median nerve; and sural conduction velocity velocity with averaging of the stimuli in order to improve the quality of the action potential. The median and sural nerves are chosen for their sensitivity to neurotoxic effects. F-Waves are also generated to detect the presence of radiculopathies often present in older populations.

Instructions for the neurophysiology test have been prepared and instituted. Technicians have been specially trained to provide maximum accuracy and consistency in these and all other testing procedures.

f. Psychological and Neurobehavioral Testing

1.) Because various investigators have reported a variety of neuropsychiatric, affective, and behavioral disorders, including apathy, depression, memory loss, difficulty concentrating, psychomotor retardation, neurasthenia, irritability, and hypomania, in workers exposed to dioxin-contaminated materials, a directed battery of psychological and neurobehavioral tests will be administered to each participant.

2.) Several tests of the computer-administered Neurobehavioral Evaluation System (NES) (Baker, et al. 1985) will also be included in the test battery. The majority of the tests to be used from the NES measure psychomotor skills, such as simple reaction time and psychomotor coordination.

g. Pulmonary Function Testing

Pulmonary function tests will include the measurement of FEV_1, forced vital capacity (FVC), and the calculation of FEV_1/FVC ratio.

h. Laboratory Testing: Blood and Urine

Laboratory tests will measure hepatic function (including lipid metabolism), immunologic function, hematopoetic status, selected endocrine function, urinalyses for urine sediment, for porphyrins, and for enzyme induction. Each participant will be asked to fast for at least 12 hours preceding his or her appointment for the examination. A twelve hour urine collection will be conducted during the 12 hours prior to the commencement of the examination.

Blood and urine will be collected for the following:

1) Blood tests

120ml whole blood will be required from each worker and referent and special collection provisions will be as follows:

One 3ml clot tube (total complement)
Six 15ml SST tubes filled to 13ml volume (for serum)
Three 7ml heparin tube (immunology)
One 3ml sodium heparin tube (platelet verification)
One 3ml EDTA tube (hematology)

A) Hepatic enzymes (gamma glutamyl transpeptidase and SGPT); alkaline phosphatase as an indicator of obstructive disease

B) Lipid profile, including triglycerides, cholesterol, and the HDL lipoprotein fraction

C) Complete blood count including differential and platelet estimation

D) Tests of immunologic capability which will include total lymphocyte and white blood cell count, total T and B cell counts, counts of helper-inducer cells (T4) and suppressor-cytotoxic cells (T8), the helper-suppressor ratio, lymphocyte stimulation by Con A, phytohemagluten, pokeweed, and quantitative immunoglobulins (IgG, IgD, IgM, IgA). Delayed hypersensitivity skin testing for three common antigens (mumps, tetanus, and candida) will be performed on the evening of arrival and read at 24 and 48 hours by a trained reader.

E) Serum levels of testosterone and gonadotropins.

F) Thyroid screen (thyroxine, triiodothyronine, and ratio)

G) Serum B12, folate and amylase, blood lead (potential confounders)

H) 2,3,7,8-TCDD in serum

A relatively recent methodology for the evaluation of the body burden of 2,3,7,8-TCDD has been developed by the Center for Environmental Health at the Centers for Disease Control, and involves the measurement of the level of the dioxin in serum (Patterson et al., 1986). Current methods allow the measurement of parts per quadrillion using 50ml serum.

All subjects will be screened for suitability to participate in the drawing of 105ml (seven 15ml plain clot tubes) whole blood for the purpose of evaluating 2,3,7,8-TCDD in 50ml serum. Subjects who are determined through screening to be at increased risk of adverse effects due to the additional volume of blood to be drawn, will not participate in this phase of blood testing.

2) Urine tests will include:

A) A 12-hour urinary porphyrin profile, including total urinary porphyrins, distribution of uroporphyrins, coproporphyrins, and heptacarboxylic porphyrins, to be done on first morning void collected (with 5 grams sodium bicarbonate and EDTA added to the container).

B) Urinalysis with microscopic examination (to be collected on the morning of the medical exam)

C) Measurement of D-glucaric acid in the urine (assay using 12-hour urine collection)

4. Female Reproductive Interviews

The overall design of the reproductive study is a subset of the morbidity study on the health effects of exposure to 2,3,7,8-TCDD. This component of the larger study will evaluate the reproductive outcomes among the wives and former wives of living individuals previously employed at two facilities which manufactured chemicals contaminated with 2,3,7,8-TCDD.

The comparison group will consist of the wives and former wives of the men identified from the communities in which the workers reside at the time of the study. Information on pregnancy outcomes will be collected by a brief interview with the workers and the non-exposed comparison group, and through detailed telephone interviews with the wives and former wives. Adverse pregnancy outcomes will be verified through medical records. An excess in spontaneous abortions and a decrease in fertility are the primary outcomes of interest.

Similar interviews will take place at the medical examination site with female workers and female referents, and will probe for the same information as that sought from the wives and former wives of male workers and male referents.

5. Quality control assurance

a. Overview

Assurance of quality control can be achieved for nearly all tests. Quality control of medical exams and tests will take three forms: 1) repeats of tests and exams, 2) examining physician standardization, and 3) careful maintenance and calibration of testing equipment.

For quality assurance purposes, approximately 5% of all exams will be repeated, or the exam results reinterpreted. Through the course of the study, statistical correlation of data obtained from repeated/reinterpreted exams with that obtained from the original examination will be done regularly. Correlation data will be reviewed by the NIOSH Project Director and by the contractor's Medical Director. The repeat data will be sent to NIOSH, along with the original data and statistical analysis, for review.

Repeat tests or examinations will be administered by personnel other than those administering the original test or examination. Repeat test data will be part of the medical record and will be reviewed by the contractor's diagnostician prior to the outbriefing session.

While there will be no actual repeat of entire medical histories, a Clinic Manager will monitor the general attitude and manner of examination administration of randomly selected histories, by means of a clinic intercom system.

The following exams will be repeated on randomly selected participants: General Physical, Dermatology, Neurology, Pulmonary Function, Peripheral Vascular, Audiometry and Visual Acuity. Randomly selected Chest X-Rays and Delayed Hypersensitivity tests will be reinterpreted without repeating the tests. All ECG's will be overread by a cardiologist. During Phase I all NCV's, and quantitative sensory test data will be reinterpreted by the neurophysiologist. During Phase II a 10% random sample of these data will be evaluated by the neurophysiologist. All technicians administering tests will be observed at least weekly, and evaluated for method and quality of administration.

Standardization of examining physicians will be assured through the training sessions and by monthly observation and critique sessions. A protocol for certifying that physicians are capable of performing the standard exam is outlined below. The number of examining physicians will be limited, thus allowing greater standardization of data collection.

b. Physical Examination Standardization Plan

A presentation will be made at the training orientation session for physicians by the Project Medical Director or his/her designee. The presentation will discuss the purpose and outline of the study (i.e. logistics, medical exams, outbriefing sessions, data management, quality control, etc.), and the role of standardization in an epidemiological study. Physicians will view the videotape presentation on the purpose and goals of standardization in an epidemiological study. Physicians will also receive a copy of the exam protocol manual and examination forms, and will view the "standard" exam videotape for the medical exam to be performed.

The physician will be videotaped while performing an exam on a professional model, when the physician feels confident about his or her ability to perform the standard exam. This exam will be critiqued by an examining committee consisting of the Medical Director, the Epidemiology Consultant, and the Lovelace Project Director. Upon satisfactory administration of the examination, the physician will be certified to perform participant examinations.

Completion of the training and the certification sessions will be documented by date and appropriately signed on certification forms. Each physician will be critiqued monthly throughout the course of the study for any diversion in examination procedures.

c. Evaluation of interobserver variation

Statistical evaluation of interexaminer variability will be done regularly by Lovelace Medical Foundation, using complete data sets for each examination/test. Statistical analyses will be done using SAS (Statistical Analysis System) software. These data along with the repeat testing data will then be used by Lovelace and NIOSH, for assessing retraining needs of the clinic staff.

NIOSH project staff will also be on-site during the examination period to monitor adherence by the contractor to required quality control measures.

D. Notification and Follow-Up

The outbriefing session at the end of the examination with the physician and the psychologist, will serve as an initial means of individual notification. Participants will receive all available results of the examination and will be encouraged to discuss their examinations, their results, and any recommended follow-up care.

Notification letters will be mailed to participants when all examination results are completed. These letters will include those results which were not available for discussion at the time of the outbriefing session. The letters will list all tests, along with their corresponding test scores, and a list of the ranges for "normal" results. The letters will note any test results which fall outside the normal ranges and explain the significance of such scores. For results which fall significantly out-of-range, participants will be encouraged to seek follow-up care.

For cases of suspected skin cancer determined by dermatological testing, notification will begin during the outbriefing session, and participants will be advised to seek further dermatological care upon returning home. NIOSH will do a follow-up of these participants by means of further follow-up letters and phone calls to identified participants. We will attempt to determine whether follow-up care has been sought by participants and what dermatological care resources are being used. Once a dermatologist or dermatology clinic has been determined, NIOSH will contact that physician or clinic to confirm a date of biopsy and to request pathology to be sent to NIOSH.

E. Collection of Medical Records

Medical and hospital records of all participants (workers, referents, wives and former wives, and their offspring) will be used to confirm certain health conditions reported by and about participants. Participants will be asked to sign authorization forms for the release of medical records. Female participants (workers, referents, wives and former wives) responding to the reproductive interview will be asked for information concerning the health of their children from birth through early childhood. Records of birth and fetal death will be requested from vital statistics offices.

Participants will sign informed consent forms which will document that they have been advised about the benefits and risks involved with participation. Consent forms will also explain the participant's protection of privacy under the provisions of the Privacy Act of 1974, with regard to any information concerning him or her for the purposes of the study. Exceptions to information protected under the Privacy Act will be listed on all consent forms and will also apply to all medical records released concerning the participant.

F. Estimation of Exposure Status

1. Comparison of Biological and Predicted Exposure Levels

Predictive Exposure Matrix

Estimates of potential exposure are currently being constructed for the NIOSH Mortality Study by a NIOSH industrial hygienist

using information from process descriptions; job descriptions; analytic data on 2,3,7,8-TCDD content in substances from various processes, from company records, federal agencies, consulting laboratories, and from the Air Force Agent Orange data base; and industrial hygiene, safety, and medical data from company records. Further refinement of the method will occur after complete work histories have been obtained from workers during the study interviews. These data will provide the information necessary to estimate cumulative level of exposure to 2,3,7,-8 TCDD-contaminated materials over the lifetime of the individual who has worked as an herbicide production worker or in another occupation where exposure to dioxin-contaminated materials was most likely to have occurred.

2. Evaluation of the Predictive Exposure Matrix Using Biological Measurements

   A statistical model will be used to evaluate the predicted Exposure Matrix versus the biological exposure levels. A general linear model will be constructed incorporating the serum level as the dependent variable, the duration of exposure as the independent variable, and years since last employment or exposure as the covariate. Other variables which may be entered into the model include categorical measures of cumulative exposure, as well as other indices, including job duties and biological half-life of 2,3,7,8-TCDD.

G. Data Management

All data collected by the contractors for NIOSH will be conveyed in their original form to NIOSH and on computer tape. Such data will be handled in a manner consistent with that described in the NIOSH Sensitive Data Security Program Manual and the CDC Staff Manual on Confidentiality. While data is retained at NIOSH and handled during the course of data coding and analysis, the data protection provisions will apply.

H. Data Analysis and Analytic Techniques

Data may be classified into three general categories: (1) outcome or dependent variables (such as prevalence of given diseases, nerve conduction velocities, lipid profile, indices of hepatic function, reproductive outcomes, etc.); (2) predictor or independent variables (demographic characteristics, exposure level, alcohol, diabetes, blood lead level, age). The influence of confounders and effect modifiers will be controlled or examined through stratification (when categorical data are examined), through multivariate analysis (general linear models) of continuous data, or through logistic models when necessary. Wherever possible, effect measures such as

prevalence odds ratios and regression slopes will be used to evaluate the contrast between or among exposure groups. Wherever possible, continuous data will be analyzed as continuous data, rather than reduced to categories, in order to preserve maximum precision. In situations with a continuous outcome (NCV) and categories of exposure, analysis of variance may be employed. Analysis preserving the matching scheme will be used whenever possible. In the event that an analysis is desired which will break the matching, there may be a slight loss of efficiency (less power) but this bias should not be substantial.

I. Consideration of Potential Biases

A number of potential biases may impair the validity of an epidemiologic study and complicate interpretation of the results. Those most pertinent here include non-comparability of the study and referent populations, the non-comparability of information collected on the two groups, and confounding exposures. Non-comparability of the study and referent groups has, hopefully, been resolved using the matching criteria as described in the discussion of referent selection (Section III.D.). Even if the comparison group is appropriately chosen, however, bias may nonetheless be introduced if participation rates vary between groups. For example, if the study is presented as a study of workers, exposed persons may be more likely to participate because of their known exposure status. Conversely, unexposed persons may choose not to participate because they have "never been exposed" or may choose to participate because they are either ill or concerned about their health for some reason. A possible result of this second situation might be low participation rates among the controls and/or a sicker-than-normal referent group and a damping of the apparent difference between the exposed and unexposed. Work by Forthofer (1983) on the participants and non-participants in the examination phase of the NHANES II indicates, however, that although concern about health was a motivating factor for examination participation, more serious health outcomes do not appear to be more prevalent in such participants than in non-participants.

The administration of a refusant questionnaire to those workers or potential referents who refuse to participate in the study, will help determine the basic difference between participants and non-participants. This questionnaire obtains a brief demographic profile, as well as general information on health and usual employment.

Two important categories of non-comparable information between groups include so-called recall bias and observation bias. Recall bias for outcomes such as reproductive events may not be avoidable. Although recall bias is a major problem for case-referent studies, it is of

relatively less importance for a medical study which is largely descriptive and in which the use of objective cross-sectional tests and medical records minimizes the effect of such bias for current health status and past medical history. Recall bias is likely to be introduced or enhanced for symptom reporting in the exposed group, if that group knows that its exposure status is important in the study, which will be unavoidable in the current political and journalistic climate. For this reason, the analysis of symptoms will serve chiefly as corroborating evidence in support of more objective outcomes. Observation bias will be eliminated through blinding of examiners to exposure status and confirmation of the condition through medical provider records.

A third source of bias is the presence of extraneous factors which have not been accounted for and which may be differentially distributed among the groups--i.e., confounders. Information on suspected potential confounders will be sought equally in the two groups. We also know, however, that there were potentially confounding exposures at both plants whose effects we will have to control for, if we are to distinguish dioxin-herbicide effect from confounding effect. For example, hexachlorobenzene was manufactured until 1960 at the New Jersey plant. It is a porphyrogen, a neurotoxin, and a questionable chloracnegen. Ethylene oxide has been used at the Missouri plant for a number of years since 1971 and may potentially affect workers employed at the plant after 1971. Ethylene oxide has adverse reproductive effects and is a neurotoxin. We believe that a reasonable approach to this dilemma is by characterization of these exposures as meticulously as possible, utilizing company records, employee reported detailed work histories, and special interviews of long-term employees to obtain a maximally accurate estimate of exposure potential.

V. Conclusion

We have described a cross-sectional, epidemiologic study of workers employed in the past in two plants which manufactured chemicals contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin and an unexposed referent population selected from the community of residence of the workers. The overall purpose of the study is to evaluate the long-term health effects of a range of occupational exposure to dioxin-contaminated substances. Many studies and case-reports have been published about the acute and chronic sequellae of dioxin exposure. However, none have had appropriately selected control populations to evaluate the health consequences of exposure and have not assessed dose-reponse relationships. The comprehensive data collection includes a detailed assessment of previous work and medical histories, collection of clinical data on conditions reported to to be associated with exposure to

dioxin-contaminated materials, obtaining of medical records to document past illnesses, and the objective assessment of exposure to 2,3,7,8-TCDD through a predictive model and through personal serum levels of 2,3,7,8-TCDD. This study should provide the scientific community with the a thorough assessment of exposure-related effects.

VI. REFERENCES

Allen JR, Carstens LA (1967) Light and electron microscopic observations in Macaca mulatta monkeys fed toxic fat. Am. J. Vet. Res. 28: 1613-1629.

Allen JR et al. (1979) Morphological changes in monkeys consuming a diet containing low levels of TCDD. Food, Cosmet. Toxicol. 15: 501.

Armstrong, JS (1975) Monetary incentives in mail surveys. Public Opinion Quarterly 39:111-116.

Bauer M, Schulz KH, Spielberg U (1961). Berufliche vergiftungen bei der herstellung von chlorophenol-verbindungen. Arch. Gewerbepathol. Gewerbehyg. 18: 539-55.

Bleiberg J et al. (1964) Industrially acquired porphyria. Arch. Dermatol. 89: 793-7.

Bond GG et al. (1983) Medical and morbidity surveillance findings among employees potentially exposed to TCDD. Br J Ind Med 40:318-324.

Brunner J and Brunner G (1971) "Are voluntarily unlisted telephone subscribers really different?". Jour. Market. Research VIII: 121-4.

Buu-Hoi NP et al. (1972) Organs as targets of dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin) intoxication. Naturwissenschaflen 59(4): 174-75.

Carter C et al. (1975) Tetrachlorodibenzodioxin: An accidental poisoning episode in horse arenas. Science 188: 738-740.

Cook R et al. (1980) Mortality experience of employees exposed to 2,3,7,8 TCDD. JOM 22(8): 530-32.

Cripps DJ et al. (1984) Porphyria turcica due to hexachlorobenzene: a 20 to 30 year follow-up study on 204 patients. Br J Dermatolog III: 413-422.

Crow, KD (1982) Chloracne. Seminars in Dermatology 1(4): 305-314.

Eriksson M et al. (1979) Case control study on malignant mesenchymal tumors of the soft parts and exposure to chemical substances. Lakartidningen 76: 3872-75.

Faith RE, Luster MI (1979) Investigations of the effects of 2,3,7,8-TCDD on parameters of various immune functions. Ann NY Acad Sci. 320: 564-571.

Favaretti C et al. (1979) Chloracne and general clinical symptoms in a group of subjects 0-14 years of age exposed to TCDD in the area of Seveso. Italian Report-Lombardy Region.

Filippini G et al. (1981) Relationship between clinical and electrophysiological findings and indicators of heavy exposure to 2,3,7,8-TCDD. Scand. J. Work. Environ. Health 7: 257-262.

Findlay, J and Schaible, W (1980) A study of the effect of increased remuneration on response in a Health and Nutrition Examination Survey. Proceedings of the American Statistical Association, Section on Research Methods.

Fleiss, JL (1973) Statistical Methods for Rates and Proportions. John Wiley and Sons, New York. Ch. 3:23-34.

Forthofer, RN (1983) Investigation of non-response bias in NHANES II. Amer. Journal of Epid. 117:4, 507-514.

Goldkin J, Structure-activity relationships for the biochemical effects and the relationship to toxicity, in Halogenated biphenyls, terphenyls, naphthalenes, dibenzodioxins, and related products, ed by R. Kimbrough, Elsevier/North-Holland 1980.

Goldmann PJ (1972) Schwerste akute chlorakne durch Trichlorophenolzersetzungprodukte. Arbeitsmed. Sozialmed. Arbeitshyg. &: 12-18.

Goldstein JA, Linko P, Bergman H (1982) Induction of porphyria in the rat by chronic versus acute exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. Biochem. Pharmacol. 31 (8): 1607-1613.*

Gunn, W. and Rhodes, I. (1981) Physician response rates to a telephone survey: effects of monetary incentive level. Public Opinion Quarterly 45:109-115.

Gupta BN et al. (1973) Pathologic effects of 2,3,7,8-tetrachlorodibenzo-p-dioxin in laboratory animals. Environ. Health Perspect. 5: 125-140.

Gustafsson JA, Ingelman-Sundberg M (1979) Changes in steroid hormone metabolism in rat liver microsomes following administration of 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) Biochem. Pharmacol. 28(4): 497-499.

Hardell L, Sandstrom A (1979) Case control study: Soft-tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br. J. Cancer 39: 711-717.

Honchar P, Halperin W (1981) 2,4,5 trichlorophenol and soft tissue sarcoma, Lancet 1: 268-269.

Hoffman RE et al (1986) Health effects of long-term exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin, JAMA 255:2031-2038.

Huff JE et al. (1980) Long term hazards of polychlorinated dibenzodioxins and polychlorinated dibenzofurans. Environ. Health Perspect. 36: 221-240.

Jirasek L et al. (1974) Acne chlorina, porphyria cutanea and other manifestations of general intoxication during the manufacture of herbicides. Ceskoslovenska Dermatologie 49(3): 145-157.

Kimbrough R et al. (1977) Epidemiology and pathology of a tetrachlorodibenzodioxin poisoning episode. Arch. Environ. Health 32(2): 77-86.

Kincannon, JC (1968), Prediction of the standard MMPI scores from 71 items. J. Consult. Clin. Psychol. 32:319-325.

Knutson JC, Poland A (1980), Keratinization of mouse teratoma cell line KB produced by 2,3,7,8 tetrachlorodibenzo-p-dioxin : an in vitro model of cell toxicity. Cell 22(1): 27-36.

Kociba RJ, Schwetz BA (1982) Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Drug Metab. Rev. 13: 387-406.

Kociba RJ et al. (1976) 2,3,7,8-tetrachlorodibenzo-p-dioxin results of a 13-week oral toxicity study in rats. Toxicol. Appl. Pharmacol. 35: 553.

Kociba RJ et al. (1978) Results of a two-year chronic toxicity and oncogenicity study of 2,3,7,8 TCDD in rats. Toxicol. Appl. Pharmacol. 46(2): 279-303.

Lamb, JC, More JA, and Marks TA (1980), Evaluation of 2,4-D, 2,4,5-T, and 2,3,7,8-TCDD toxicity in C578BL mice: reproduction and fertility in treated mice and congenital malformations in their offspring, National Toxicology Program.

Long term hazards of polychlorinated dibenzodioxins and polychlorinated dibenzofurans (1978) Joint NIEHS/IARC Working group report.
May G (1973) Chloracne from the accidental production of tetrachlorodibenzodioxin. Br. J. Ind. Med. 30: 276-283.

May G (1982) Tetrachlorodibenzodioxin - a survey of subjects ten years after exposure. Br. J. Ind. Med. 39: 128-135.

McConnell EE, Moore JA, Dalgard DW (1978a) Toxicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in Rhesus monkeys (Macacas mulatta) following a single oral dose. Toxicol. Appl. Pharmacol 43: 175.

McConnell EE et al. (1978b) The comparative toxicity of chlorinated dibenzo-p-dioxins in mice and guinea pigs. Toxicol. Appl. Pharmacol. 37(1): 146.

McDaniel, S. and Rao, CP (1980) The effect of monetary inducement on mailed questionnaire response quality. Jour. Marketing Research XVII:265-268.

McNulty WP et al. (1982) Persistence of TCDD in monkey adipose tissue. Fed. Chem. Toxicol. 20: 985-987.

Moses M et al. (1984) Health status of workers with past exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin in the manufacture of 2,4,5-trichlorophenoxyacetic acid: comparison of findings with and without chloracne. Am. Jour. Ind. Med.5: 161-182.

Murray FJ et al. (1979) Three generation reproduction study of rats given 2,3,7,8 TCDD in the diet. Toxicol. Appl. Pharmacol. 50: 241-52.

Neal RA et al. (1982) The toxicokinetics of 2,3,7,8 TCDD in mammalian systems. Drug Metabolism Reviews 13(3): 355-385.

Niwa A, Kumaki K, Nebert DW (1975) Induction of aryl hydrocarbon hydroxylase activity in various cell cultures by 2,3,7,8 tetrachlorodibenzo-p-dioxin . Mol. Pharmacol. 11(4): 399-408.

Ott, MG, Holder B, Olson R (1980) A mortality analysis of employees engaged in the manufacture of 2,4,5 T. JOM 22(1): 47-50.

Oliver RM (1975) Toxic effects of 2,3,7,8 TCDD on lab workers. Br. J. Ind. Med. 31(1): 49-53.

Patterson DG et al. (1987) High resolution gas chromatographic/high resolution mass spectrometric analysis of human serum on a whole weight and lipid basis for 2,3,7,8-tetrachlorodibenzodioxin. Anal Chem (in press).

Pazderova-Vijlupkova J et al. (1981) The development and prognosis of chronic intoxication by tetrachlorodibenzo-p-dioxin in men. Arch. Environ. Health 36.

Poiger H, Schlatter C (1980) Influence of solvents and adsorbents on dermal and intestinal absorption of TCDD. Fd. Cosmet. Toxicol. 18: 477-481.

Poland A, Glover E, Kende AS (1976) Stereospecific, high affinity binding of 2,3,7,8 tetrachlorodibenzo-p-dioxin by hepatie cytosol. Evidence that the binding species is a receptor for induction of aryl hydrocarbon hydroxylase. J. Biol. Chem. 251(16): 4936-4946.

Poland AP et al. (1971) A health survey of workers in a 2,4 D and 2,4,5 T plant. Arch. Environ. Health 22: 316-27.

Reggiani G (1978) Medical Problems Raised by the TCDD Contamination in Seveso , Italy. Archives of Toxicology 40: 161-188.

Rothman KJ, Boice JD (1979) Epidemiological Analysis with a Programmable Calculator. US Dept Health and Human Services: NIH Publication No. 79-1649.

Schantz SL, Barsotti DA, Allen JR (1979) Toxicological effects produced in Non-human primates chronically exposed to fifty parts per trillion 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD) Toxicol. Appl. Pharmacol. 48: A180.

Schwetz BA et al. (1973), Toxicology of chlorinated dibenzo-p-dioxins, Environ. Health Perspect. 5: 87-99.

Singer R et al. (1982) Nerve conduction velocity studies of workers employed in the manufacture of phenoxy herbicides. Environ. Research 29: 297-311.

Smith A et al. (1982) Congenital defects and miscarriages among New Zealand 2,4,5 T sprayers. Arch. Environ. Health 37: 197.

Smith FA, Schwetz BA, Nitschke KD (1976) Teratogenicity of 2,3,7,8 tetrachlorodibenzo-p-dioxin in CF-1 mice. Toxicol. Appl. Pharmacol. 38: 517-523.

Suskind R and Hertzberg V (1984) Human health effects of 2,4,5-T and its contaminants. JAMA 251(18): 2372-2380.

Strik J, Debets F, Chemical porphyria, in Halogenated biphenyls, terphenyls, naphthalenes, dibenzodioxins and related products, ed. by R. Kimbrough, Elsevier/North-Holland 1980.

Taylor, JS. (1979). Environmental chloracne: Update and overview. Ann NY Acad Sci 320: 295-307.

Ton That Tung et al. (1971) Clinical effects of massive and continuous utilization of defoliants on civilians. Vietnamese Studies 29: 53-83.

Van Miller, JP, Lalich JJ, Allen JR (1977) Increased incidence of neoplasms in rats exposed to low levels of 2,3,7,8 tetrachlorodibenzo-p-dioxin. Chemosphere 6(10): 625-632.

WHO Monograph on Chlorinated Dibenzodioxins, August 1977.

Walker A, Martin G (1979) Lipid profiles in dioxin-exposed workers. Lancet i: 446-447.

Ward, A.M. (1983) Investigation of the immune capability of workers previously exposed to 2,3,7,8 tetrachlorodibenzo-p-dioxin (TCDD)--manuscript.
Ward, E (1984) Dissertation. U. of Pennsylvania, Department of Epidemiology.

Zack, J, Suskind R, (1980) The mortality of workers exposed to tetrachlorodibenzodioxin in a trichlorophenol process accident. JOM 22: 11-14.

APPENDIX A

CHEMISTRY, TOXICITY, AND HUMAN HEALTH EFFECTS OF 2,3,7,8-TCDD-CONTAMINATED MATERIALS

Chemistry, kinetics, and metabolism

2,3,7,8-tetrachlorodibenzo-p-dioxin is a lipophilic, chemically stable compound of low volatility (estimated vapor pressure 1.7×10^{-6}) and high melting point (305-306° C). TCDD has been demonstrated to be absorbed through the skin, GI tract, and after intravenous administration (Schwetz et al 1973), and is thought to be absorbed through inhalation as well. Depending on the species, it is distributed to liver, adipose tissue, skin and muscle, brain, testes, and blood. Its biologic half-life, similarly species dependent, ranges from days to more than a year (McNulty, WP et al 1982). It is excreted unchanged in the feces, or conjugated with glucuronides in the urine and bile. Although TCDD is quite persistent with respect to biological systems, it is degraded by UV light (Neal, RA et al 1982).

Toxicologic and Human Health Effects of 2,3,7,8-TCDD

1. Animal Toxicity

There is a large and expanding body of toxicologic literature on TCDD which reveals both its extreme toxicity and its effects on immunologic, hematopoetic, hepatic, and reproductive function, as well as its dermatotoxic, embryotoxic, and carcinogenic properties. A number of excellent reviews of the toxicity of TCDD and related compounds have been published in recent years (eg. Kimbrough ed, 1980; Veterans Administration, 1981, 1984, 1985, 1986) and should be consulted for a more exhaustive discussion of the topic. The chief purpose of this abbreviated review of the toxicology literature will be to underscore the range of toxic effects which have been observed and to identify the chief areas of concern that may have relevance to a cross-sectional medical study of dioxin-exposed workers.

While toxicity varies with species, dose, and length of exposure, animal studies indicate that 2,3,7,8-TCDD is the most potent known chemical toxin. The single acute LD_{50} for several animal species ranges from 0.6 ug/kg body weight in the guinea pig to 5000 ug/kg in the hamster (Kociba 1982). Even when a lethal amount is administered as a single dose, death of the animal occurs only after many days to weeks. Chronic administration of 500 ppt 2,3,7,8-TCDD in the diet of monkeys resulted in a total fatal dose of only 2 ug/kg body weight during a six month feeding experiment, although the single dose LD_{50} for the same species is 50ug/kg (McConnell 1978). There is species variability in the precise biological effects of 2,3,7,8-TCDD, but the general classes of effect or injury include debilitation and wasting, skin lesions, enzyme induction, hepatotoxicity, lymphoid hypoplasia and immunological disturbances,

teratogenesis, fetotoxicity, and carcinogenesis (IARC 1978). Severe thymic atrophy has been observed in all species at doses below lethality. TCDD suppresses several cell-mediated immune functions, including mitogen responsiveness, skin graft rejection, and delayed hypersensitivity reactions (Faith and Luster 1979). Although liver damage after a single fatal dose is not universal, it is marked in rats, mice, and monkeys (Buu-Hoi 1972, Gupta et al 1973, McConnell et al 1978). With subchronic doses in feeding studies, rats and mice exhibited abnormal porphyrin metabolism with slow recovery, or fatty necrosis and altered hepatic architecture (Kociba et al 1976, Goldstein et al 1982). Skin lesions in animals include hyperkeratosis and transformation of sebaceous glands to keratin cysts in mice, rats, and monkeys (Huff et al 1980), and chloracne in rabbits. In macacques fed diets containing various percentages (0.0125% to 10%) of "toxic fat", the dioxin-contaminated substance containing both hexachlorinated dioxins and TCDD which was incorporated into chicken feed and caused an outbreak of chicken-specific illness called "chick edema disease" in 1957, Allen and Carstens (1967) found that all monkey groups developed weight loss, alopecia, generalized edema, depletion of the sternal bone marrow, and vascular degeneration (1967). In 1977, Allen et al fed female rhesus monkeys a diet containing 500 ppt of TCDD (2-3 ug/kg/day), and the monkeys developed alopecia, periorbital edema, thrombocytopenia, anemia, and epithelial hyperplasia and metaplasia of the salivary gland, bile duct, lung, and stomach. Schantz et al observed similar but less severe findings, as well as a decreased ability to bear live young, in monkeys fed a diet containing 50 ppt of TCDD. The precise mechanisms of TCDD toxicity are not known, but speculations have included vitamin A depletion, lipid peroxidation, and endocrine imbalance and direct effects on the hypothalamic-pituitary axis (Gustafson and Ingelman-Sundberg, 1979, Niwa et al 1975). Binding to cytosol receptors with enzyme induction has been proposed as either a mechanism or simply a marker of toxicity, since species susceptibilty to the toxic effects of TCDD corresponds to the genetically-determined degree of receptor binding and enzyme induction (Poland and Glover 1975).

TCDD is teratogenic in certain strains of mice. At doses up to 3 ug/kg body weight in female CF-1 mice, there was no observable effect on live fetuses produced per litter, number of implantation sites, sex ratio, or birth weight, but there was an increased incidence of both cleft palate and dilated renal pelvises in the infant mice. At doses below 0.1 ug/kg, the incidence of fetal abnormalities was deemed comparable to controls (Smith et al 1976 from Kimbrough review article in CDC File). The adverse reproductive effect and fetotoxicity of TCDD was demonstrated in a three generation study of male and female Sprague-Dawley rats administered 0.001, 0.01, and 0.1 ug TCDD/kg. Fertility and offspring survival were reduced in the first generation given 0.1 ug/kg, and doses of 0.01 or 0.1 ug/kg yielded smaller litters, decreased offspring survival, and decreased growth in the second and third generations. The lowest dose group was not different from the control group with respect to these characteristics (Murray et al 1979, as above). In a 1980 simulated Agent Orange study for the National Toxicology Program by Lamb et al, male mice fed TCDD in doses of 0.01 ug/kg showed no adverse reproductive effects when mated with unexposed females.

Mutagenicity is an inconstant finding in bioassays of TCDD, although certain strains of rats do exhibit a slight but significant increase in bone marrow cell chromosomal aberrations after TCDD administration. A number of animal studies of carcinogenicity exist in the current literature, and carcinogenicity has been demonstrated in several species. In an early study by Van Miller et al (1977), the investigators found an overall increase in tumors in the treated group and no tumors in the control group, but small numbers of rats were used. In a larger study by Kociba et al (1978), groups of 100 rats (50 female and 50 male) were fed diets containing the equivalent of 0.001, 0.01, and 0.1 ug TCDD/kg body weight. The investigators observed a dose-dependent effect, with no observed change in the lowest dose group, significantly increased hepatic nodules in female rats in the 0.01 ug group, and a significant increase in carcinomas of the liver, lung, hard palate, nasal turbinates, and tongue, and adenomas of the liver and adrenal cortex, in the 0.1 ug group. In addition to carcinogenic effects, the high dose group exhibited a variety of toxicologic responses, including increased mortality, decreased weight gain, elevated liver enzymes (GGT and SGPT), increased porphyrin excretion, and histologic changes in lymphoid tissue, liver, lung, and blood vessels. More recent studies conducted under the auspices of the National Toxicology Program demonstrated the carcinogenesis of 2,3,7,8-TCDD in both dermal and gavage studies. When applied to the skin of male and female Swiss Webster mice at the rate of 0.005 ug/application three times a week in males, and 0.001 ug in females, administered for 99 or 104 weeks, females exhibited a significant increase in fibrosarcoma of the integument ($p=0.007$), while males exhibited an increase which did not attain statistical significance (National Toxicology Program CAS no. 1746-01-6, no. 201, 1982). In a gavage study of Osborne-Mendel rats and B6C3F1 mice administered doses up to 0.5 ug/kg/week and 2.0 ug/kg/week respectively, rats demonstrated a dose-related increase in follicular cell adenomas of the thyroid which was significant ($p=0.001$) in the high dose group; a dose-related increase in neoplastic nodules of the liver in female rats; and a dose-related increase in hepatocellular carcinomas in both sexes of mice, and follicular cell adenomas of the thyroid in female mice (National Toxicology Program CAS. No. 1746-01-6, no. 209, 1982).

2. Human Health Effects

This review will consider the major clinical findings described in persons exposed to TCDD-contaminated materials to provide a summary of the information on which decisions about the content of the proposed study were based.

Chloracne

The most widely recognized and definitive stigmatum of TCDD exposure is chloracne. While chloracne is not pathognomonic of dioxin exposure--it may result as well from exposure to chlorinated naphthalenes, dibenzofurans, and biphenyls, to tetrachloroazobenzene, and to tetrachloroazooxybenzene--TCDD has been found to be the acnegenic

contaminant of 2,4,5,T and trichlorophenol. Chloracne is not, however, a necessary accompaniment of dioxin exposure: investigators such as Pazderova-Vijlupkova, Poland, and Oliver have observed other health effects now recognized as possibly related to dioxin exposure (such as disordered porphyrin metabolism, hepatic damage, and neurobehavioural disturbances) in persons exposed to dioxin who did not develop chloracne.According to some clinicians (Bleiberg, Poland), chloracne is more likely to appear in, and may be more severe in persons with juvenile acne but it can usually be distinguished from other forms of acne by the distribution of the acneiform eruption, its association with employment or chlorinated polycyclic exposure, and its persistence.

The most common location of chloracne lesions is behind the ears and on the malar crescent just below and lateral to the eye. It may also be found commonly on cheeks, forehead, and neck, but not the nose. The genitals are peculiarly susceptible, and the eruption may also appear on the shoulders, backs, chest, buttocks, and abdomen. The lesions consist of comedones or "blackheads", a scattering of which may be the only manifestation in the mildest cases. With increasing severity, small yellow cysts appear, and increasing numbers of comedones may give the skin a grayish appearance. In very severe cases, large cysts and abscesses form. Scarring and hyperpigmentation typically follow when the lesions heal. Although the chloracnegenic dose in humans has not been established, Schwetz et al (1973) demonstrated that 0.04 ug TCDD in 1 ml benzene applied 5 times a week for four weeks (total dose 0.8 ug) produces an acnegenic response in the ear of a rabbit.

The first identified outbreak of chloracne associated with TCDD occurred in 1949, following the explosion of a trichlorophenol containment vessel in a Nitro, West Virginia plant. One hundred and seventeen workers developed chloracne from the accident, and another 111 were found to have chloracne predating the accident, for a total of 228 cases. Crow (1982) reports finding persistent chloracne in some of the most severely affected workers in 1979, 30 years after the accident, as do Suskind (1984) and Moses et al (1984). Since 1949, hundreds of cases of chloracne in workers around the world have been reported as a consequence of acute or chronic exposure to TCDD-contaminated materials (Huff et al 1980).

No definite dose-effect relationship between the intensity or duration of dioxin exposure and the prevalence or intensity of chloracne has been established in humans. However, in Poland's series (1971), he notes that the most heavily exposed workers were likely to have been maintenance men, and they tended to have the highest prevalence of, and most severe acne. Similarly, the children who developed the most extensive and severe cases of chloracne in the aftermath of the Seveso accident were those actually enveloped in the chemical cloud (Crow 1982). Because an analytic method for measuring TCDD was developed only in 1965, and sampling for dioxins remains technically difficult and expensive, the presence or history of chloracne among those potentially exposed is a useful marker of exposure to dioxins, except in the circumstance of exposure to other chloracnegens.

Hepatotoxicity and Hepatic Porphyria

Although TCDD is profoundly hepatotoxic in some animal species, the extent and persistence of its hepatotoxicty in humans has not been fully defined. Bleiberg (1964) reported "liver dysfunction", abnormal porphyrin metabolism, and abnormal liver biopsies in two New Jersey workers exposed to phenoxy herbicides. In both cases, the biopsy showed hepatocellular necrosis or regeneration and hemofuchsin deposition. In a study in the same New Jersey plant five years later, Poland et al (1971) found no consistent pattern of hepatic dysfunction. May (1973) reported that 5 of 12 British workers had elevated serum transaminases following an explosion in a 2,4,5 trichlorophenol process. Seventy-nine cases of chloracne developed in workers in that same British plant over the ensuing six months, but there is no report in the 1973 article on the hepatic function of those workers. Ten years later, May (1982) followed up all employees of the plant. Forty-one of 46 persons with a definite history of chloracne agreed to participate, 54 other employees with a possible history of dioxin exposure were examined, and 31 management and laboratory personnel with no known dioxin exposure served as "controls". Despite May's contention that there were no abnormalities in the workers except for persistent chloracne in 54% (22 of 41) of those previously affected, his data show a progressive increase in mean serum alkaline phosphatase and triglycerides across the three exposure groups, and an abnormal mean level of gamma glutamyl transferase in the high exposure group. Walker and Martin (1979) found abnormally elevated gamma GT in 5 of 6 TCDD-exposed workers. Pazderova-Vijlupkova (1981) described the Czech experience of a ten year follow-up of dioxin-exposed workers. Among 55 workers examined, liver function tests were "seldom pathological" in the later examinations, although 20% of the workers had exhibited abnormal liver function early in their illness. Filippini et al (1981) found elevated levels of gamma GT, SGOT and SGPT in an undefined number of persons living in the most highly contaminated area after the Seveso accident. Favaretti et al (1979) studied the same population and found that gamma GT, SGPT in blood, and delta amino levulinic acid in the urine (ALA) were significantly elevated in persons with chloracne compared to those without chloracne.

Disorders of porphyrin metabolism occur with exposure to a number of chlorinated hydrocarbons, TCDD and hexachlorobenzene prominently among them. Porphyria cutanea tarda (PCT), the clinical lesion identified with dioxin exposure in several studies, is only the most severe form of acquired hepatic porphyria. Hepatic porphyria is a spectrum of disordered porphyrin metabolism which begins with alterations in the proportions of porphyrin metabolites. Uroporphyrins and heptacarboxylic porphyrins gradually accumulate in the liver, followed by an increase in porphyrin excretion in the urine. In the mildest alteration of porphyrin metabolism, Type A, which is thought to be a normal variant in the population, the coproporphyrin:uroporphyrin ratio remains greater than one (normally, the ratio is 2:1 to 6:1), but 5-15% of the total urinary porphyrins are heptacarboxylic porphyrins. In Type B, the first stage of

deranged porphyrin metabolism which is regarded as pathological, the ratio is reversed, such that the uroporphyrin:coproporphyrin ratio in the urine is greater than 1, 15-20% of the porphyrins are heptacarboxylic, and total urinary porphyrins are above the normal range of up to 200 ug/l. With Type C, called chronic hepatic porphyria or latent PCT, total urinary porphyrins are increased further, and the proportion of uroporphyrins and heptacarboxylic porphyrins continues to rise. Type D or PCT is the fully developed syndrome with elevated uroporphyrins, 65-95% uroporphyrins, and a clinical picture of vesiculobullous eruptions on sun-exposed skin, cola red urine, hirsutism, and hyperpigmentation. An enzymatic defect (suppression of uroporphyrin decarboxylase activity) is the biochemical disorder underlying hepatic porphyria (Strik, Debets, and Koss in Kimbrough 1980).

Both milder disturbances of porphyrin metabolism and florid PCT have been observed in dioxin-exposed workers (Pazderova-Vijlupkova 1981, Bleiberg 1964). Several authors suggest that disordered porphyrin metabolism is a better marker of early and slight dioxin exposure than other liver function tests (Strik, Debets, and Koss in Kimbrough 1980), and porphyria appears to be less persistent than some other dioxin-associated effects, such as chloracne and neurotoxicity (Poland et al 1971, May 1982, Pazderova-Vijlupkova 1981). However, Pazderova-Vijlupkova et al note that all patients with a liver biopsy or necropsy specimen (number undefined) in their series of 55 workers exhibited liver tissue fluorescence with exposure to UV light, even when urinary porphyrins were normal and exposure to TCDD had ceased.

Disorders of Lipid Metabolism

A number of investigators of TCDD-exposed humans, including Poland et al (1971), Jirasek et al (1974) and Pazderova-Vijlupkova (1981), Oliver (1975), Walker and Martin (1979), and May (1982), have demonstrated abnormalities of lipid metabolism in dioxin-exposed workers. Elevated triglycerides, cholesterol, and the pre-beta (VLDL) fraction of plasma lipoproteins have been observed, as have diminished alpha lipoproteins (HDL). The issue of a dioxin-induced predisposition to ischemic vascular disease has also been raised (WHO Monograph on Chlorinated Dibenzodioxins, August 1977).

Neurotoxicity

Although neurotoxicity is a not noted as a feature of TCDD intoxication in animal studies, both central and peripheral nervous system effects have been reported in groups occupationally exposed to TCDD-contaminated materials, and abnormal nerve conduction velocities have been reported among heavily-exposed Seveso residents. Singer et al (1982) provide a review of episodes of TCDD-related human neurotoxicity in their report of electrodiagnostic studies among Arkansas herbicide workers. The following is a summary of that review. Suskind (1950) described symptoms of peripheral neuropathy--pain and weakness predominantly in the lower

extremities--in a group of West Virginia workers exposed to TCDD following an explosion in 1949 (1950), and a nerve biopsy of one affected individual revealed demyelination and fibrosis of the nerve sheaths. Suskind (1953) followed these workers two years later and found symptoms of peripheral neuropathy in 27 of 36. Workers studied by Bauer et al (1961) complained of pain, weakness, and paresthesias in the lower extremities, as well as problems with concentration, memory, and sleep. Bauer also noted apathy and fatigue alternating with bouts of irritability and anger in those affected. Poland et al (1971) found a high correlation between severity of chloracne and hypomania, as assessed by the MMPI, and 7 of 73 workers reported lower extremity fatigue. Ten workers followed for 15 years by Kleu and Goltz (1971) reported persistent fatigue, muscle weakness, and memory loss.

In Goldmann's survey of 42 workers accidentally exposed to TCDD and trichlorophenol (1972), three exhibited signs of peripheral neuropathy, and seven of central nervous system disturbance. Jirasek (1974) and Pazderova-Vijlupkova et al (1981) reported prominent neurotoxicity among their series of 55 workers, and noted that the neurotoxicity appeared as a delayed and persistent effect of TCDD-contaminated materials exposure in workers whose neurophysiologic examinations were normal on the initial examination. Five years after initial exposure, 35 of 36 workers examined by a psychiatrist were described as "depressive" or "neurasthenic". At the time of the final examination 10 years after exposure had ceased, 17 of 55 workers (31%) had "clinical" or "electromyographic" findings consistent with peripheral neuropathy, although the authors provide insufficient information about the comparison group or potentially confounding exposures. In the aftermath of Seveso, Filippini et al (1981) demonstrated slowed nerve conduction velocities in the ulnar and/or peroneal nerves of highly-exposed persons compared with those without evidence of intense exposure, although there are major methodologic and analytical problems with that study. Singer et al (1982) found that phenoxy herbicide workers both with and without chloracne had significantly slowed median and sural nerve conduction velocities when26ompared with "controls", and that duration of employment was the most significant predictor of sural NCV, controlling for age and skin temperature. As with other studies, there are flaws which impair the validity of the results (eg., the workers were employed at the production of 2,4,-D as well as 2,4,5-T, and one or both substances may be neurotoxic; and the referent group was probably not comparable, consisting chiefly of New York lab technicians rather than unexposed Arkansas workers). Moses et al (1984) found 18 cases of sensory neuropathy on physical exam in Nitro workers with a history of chloracne, compared with no cases in persons without chloracne.

Immunologic Changes

Relative to the dramatic and extensive data on immunologic alterations in experimental animals, there is a paucity of information on humans. Reggiani et al (1978) noted a transient decrease in the lymphocytes of

exposed persons at Seveso, although the same authors later reported on 17 Seveso residents in further detail and reported normal immunologic function. May (1982) measured immunoglobulins, T cells, B cells, and PHA response and reports that there were no "clinically significant or abnormal measurements", although no further detail is given. In contrast to these apparently negative findings, an unpublished work by Ward (1983) on the same workers and done concurrently with May demonstrated diminished levels of IgM and IgD and suppressed PHA responsiveness in workers with a history of chloracne and exposure to TCDD-contaminated products ten years earlier. Ward proposed that a larger study of workers exposed in the past to TCDD-contaminated materials would be a valuable contribution to the data on the human immunotoxicity of TCDD.

In a study of Missouri residents who lived near areas where TCDD-contaminated waste oil was spread, Hoffman et al (1986) evaluated the effect of exposure on some characteristics of the immune sytem, including delayed hypersensitivity (DTH), percent of specific peripheral T-cells (T3, T4, T8 and T11), lymphocyte proliferative responses to mitogens, and tetanus toxoid, and allogenic T-cell cytotoxicity. Although the authors report that the frequency of anergy in the exposed participants was significantly higher than that in the unexposed comparison group, 11.6% of DTH readings for the exposed and 5.1% of the DTH readings for the comparison group, were excluded from the analysis. A repeat of this part of the study is currently being conducted. However, Hoffman et at (1986) did find that the T-cell subsets were abnormal in the exposed group relative to the unexposed, though the differences were statistically nonsignificant. These results imply that well-controlled studies are required to clarify these recently identified effects.

Reproductive Disorders

As with the immunologic data, there is little conclusive information about the consequences for fertility, and the teratogenic and fetotoxic effects of human exposure to TCDD. A full review of the literature on the subject is presented in the accompanying Protocol for a reproductive study of chemical-herbicide exposed workers.

Miscellaneous Effects

In addition to the effects described above, abnormalities of pulmonary function in current smokers with past exposure to 2,3,7,8-TCDD-contaminated processes is described by Suskind (1984). Suskind also reports a high prevalence of gastric ulcer in his exposed group of workers, three cases of Peyronie's disease in persons with a past history of chloracne, and elevated prevalences of self-reported coronary heart disease and diminished libido in exposed men under 50 years of age. Moses et al confirmed findings of increased coronary heart disease and decreased libido in younger exposed men in their study of the Nitro cohort (1984).

SELECTED DEMOGRAPHIC CHARACTERISTICS OF WORKER SAMPLE

	Numbers	Percent
Race		
White	69	86%
Black	11	14%
	80	100%
Sex		
Male	78	98%
Female	2	2%
	80	100%
Current Age		
Under 45	5	6%
45 - 49	8	11%
50 - 54	3	6%
55 - 59	14	19%
60 - 64	20	24%
65 - 69	17	18%
70 and older	13	15%
	80	100%
Years Employed at Diamond Shamrock		
Less than 1 year	15	19%
>1 year ≤5 years	26	32%
>5 years ≤10 years	16	20%
>10 years ≤15 years	8	10%
>15 years ≤20 years	11	14%
>20 years ≤25 years	4	5%
	80	100%
Geographic Distribution		
New Jersey	43	54%
Pennsylvania	10	13%
Texas	7	9%
California	3	4%
Florida	4	5%
New York	1	1%
Alabama	1	1%
Arizona	2	3%
Indiana	1	1%
Kansas	1	1%
Kentucky	1	1%
Louisiana	1	1%
North Carolina	1	1%
Maryland	1	1%
Colorado	1	1%
South Carolina	1	1%
West Virginia	1	1%
	80	99%*

* Does not add to 100% due to rounding.

ATTACHMENT 7

An Exposure Matrix for the NIOSH Dioxin Registry

An Updated Protocol and Demonstration of Exposure Estimation for Two Plants

February, 1987

David A. Marlow
Industrial Hygienist
Industrywide Studies Branch
Division of Surveillance, Hazard Evaluations and Field Studies
National Institute for Occupational Safety and Health
Centers for Disease Control
Cincinnati, Ohio

I. OBJECTIVE

To develop and use a systematic procedure for estimating the extent of exposure to dioxin* for a cohort of U.S. production workers and to identify any potentially confounding chemical exposures associated with the plant operations.

II. INTRODUCTION

In 1979, a Dioxin Registry was initiated which defines a cohort of workers who are identified by company records as having worked in the production of chemicals with a known potential for dioxin contamination. Appendix A describes the Dioxin Registry. All U.S. production sites, which produced chlorophenols and phenoxy acid herbicides, with adequate records are included in the Registry because production of these chemicals is not labor - intensive. By including all production sites with adequate records the Registry cohort will be large enough to give adequate statistical power to detect potential work-related mortality in the cohort. The Registry consists of workers from fourteen U.S. production sites. Table 1 lists the types of processes at each site. Building on the exposure rationale presented by Esmen and Corn[1,2] and Gamble and Spirtas,[3] an exposure estimation procedure or matrix for dioxin is presented.

III. DESIGN AND METHODS FOR ESTIMATION OF EXPOSURE

A systematic procedure has been developed in order to assess the extent of potential exposure to dioxin for use in the retrospective

* The term dioxin is a generic term in the text of this report and will refer to 2,3,7,8-tetrachlorodibenzo-p-dioxin and hexachlorodibenzo-p-dioxins.

TABLE 1
SITE NUMBERS AND THEIR PROCESSES
DIOXIN REGISTRY
NIOSH
CINCINNATI, OHIO

	PROCESSES																			
Site Number	Na 245-TCP	245-TCP	245-TCP+	245-T Acid	245-T Acid Ester	245-T Direct Ester	Silvex	Silvex Acid Ester	Silvex Direct Ester	245-T Amines	Formulations	Ronnel	Erbon	PCP	NaPCP	246-TCP	TetCP	Hexachlorophene
01	X			X	X					X	X							
02A	X					X					X							
02B			X															X
03A	X			X	X		X	X		X	X							
03B	X			X	X		X	X		X	X							
04	X					X					X							
05				X	X					X	X							
06	X			X	X					X	X							
07	X			X														
08					X					X	X			X	X			
09	X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	
10			X															
11														X				
12														X			X	
13																		X
14					X					X	X							
Total	8	1	2	7	8	3	3	3	1	8	10	1	1	4	2	1	2	2

Table 1 (continued)

Sodium 2,4,5-trichlorophenate = NaTCP
2,4,5-trichlorophenol = 245-TCP
2,4,5-trichlorophenol+ = 245-TCP+
2,4,5-trichlorophenoxyacetic acid = 245-T Acid
Esters of 245-T Acid = 245T Acid Ester
Direct Esters of 245-T Acid = 245-T Direct Ester
Amines of 245-T Acid = 245-T Amine
2(2,4,5-trichlorophenoxy)-propionic acid = Silvex
Esters of Silvex = Silvex Acid Ester
Direct Esters of Silvex = Silvex Direct Esters
O,O-dimethyl-o-(2,4,5-trichlorophenyl)phosphorothioate = Ronnel
2(2,4,5-trichlorophenoxy)-ethyl 2,2-dichloropropionate = Erbon
Formulations
Pentachlorophenol = PCP
Sodium pentachlorophenate = NaPCP
2,4,6-trichlorophenol = 246-TCP
Tetrachlorophenol = TetCP
2,2'-methylene-bis (2,4,6-trichlorophenol) = Hexachlorophene

+ = ethylene glycol used as raw material instead of methanol

cohort mortality study of U.S. production workers. Using information such as process descriptions, job descriptions, analytical data on dioxin content in substances from the various processes, and industrial hygiene, safety and medical data, estimates of potential exposure to dioxin will be developed. These estimates will reflect the exposure rankings for each individual, relative to the other members of the cohort. Dioxin exposure rankings will be assigned using the following rationale:

(1) the amount of dioxin in a plant product is controlled by the type of process, its operating conditions, and the particular step in the process;
(2) each process has a defined set of tasks that must be performed by workers operating the process;
(3) potential exposure can be assigned to a task in a given plant, if the process, its operating conditions and location in the process where the task is performed are known (this assignment can be aided by industrial hygiene records and data on dioxin content);
(4) the potential for contact with dioxin can be assigned to a worker at a point in time if his job title is known, and the set of tasks that are part of that job are known.

Thus each plant's processes, operating conditions and job definitions will be assessed over the operating life of the plant, so that exposures can be assigned to the study subjects who worked at the plant. The estimation procedure will be broken

down into two phases. The first phase will assess the extent of potential exposure for those workers in the Registry's cohort where industrial hygiene data are available to aid the assessment. The second phase will be to assess the potential exposure to dioxin for those workers in the cohort where no industrial hygiene data were available. The assessments determined in phase two will be based on the similarities of the processes, job descriptions, etc. to those in phase one. This approach is based on the assumption that similar processes with similar operating conditions and job activities will produce similar exposures. Appendix B provides an illustration of the procedure to be used in making the assessments for workers involved in the production of 2,4,5-trichlorophenol, from site nine.

The information used in assessing the extent of potential exposure to dioxin has been collected from several sources. The process descriptions are based on available operation manuals and interviews with knowledgable people who were involved with a process or processes (e.g. foremen and production engineers). Job descriptions were developed from company personnel documents and industrial hygiene records, and union records. The analytical data on dioxin content in substances from various processes was collected from company records, other federal agencies, analytical laboratories, and from the Air Force's Agent Orange data base.[4]

The extent and specificity of the information primarily depends on the company's information for that site and processes included in the Registry. In general, the extent and specificity of the information collected to date reflects the thoroughness of each company's record system for each plant. Table 2 illustrates the information collected as of January 1987.

A. Phase One

The first phase in assessing the extent of potential exposure to dioxin for the Registry's cohort involved the evaluation of the extent of potential exposure to dioxin at those plants where industrial hygiene data were available. In assessing exposures at each plant a two step process was used. (1) The process was evaluated to determine the tasks associated with the process and a directory of uniform tasks (UTs) was developed. (2) A directory of occupational titles (OT) to which the UTs are associated was developed. This permitted assignment of exposure to workers based on their occupational titles.

TABLE 2

EVALUATION OF INFORMATION AND DATA
USED IN EXPOSURE ASSESSMENT
DIOXIN REGISTRY
NIOSH
CINCINNATI, OHIO

Site Number	Operation Years	Number of Years	Process Description	Occupational Title Availability	Job Description	Industrial Hygiene Data	Analytical Data
01	8/51-8/61	18	poor	very poor	none	none	limited
02A	3/68-2/69	1	good	poor/fair	none	none	limited
02B	1/70-1/72	2	good	poor/fair	none	none	limited
03A	1/62-12/70	9	good	poor/fair	good	none	limited
03B	9/71-4/79	7.7	good	fair	good	none	good
04	1/48-8/59 1/63-12/77	24.6	good	good	limited	none	good
05	2/61-12/62	2	good,limited	fair	limited	none	none
06	NC	NC	NC	NC	NC	NC	NC
07	1/38-12/78	40	good	good	poor	limited	limited
08	1/48-12/69	21	good	good	poor	limited	limited
09	1/37-12/80	43	excellent	excellent	excellent	excellent	excellent
10	1/49-6/72	22.5	excellent	excellent	good	none	limited
11	1/58-pres.	26	excellent	good	excellent	good,limited	good, limited
12	1/58-pres.	26	excellent	poor	excellent	poor,limited	good, limited
13	1/51-12/83	32	excellent	poor/fair	good	poor,limited	good, limited
14	NC	NC	poor	poor	poor	none	limited

NC = not yet collected

1. Uniform Tasks (UT) Directories

For each plant included in the Registry a process description was prepared. The process descriptions describe the steps, and operations at each step, that took place throughout a process, and any major changes made and the date of the changes. From the process descriptions, a list of uniform tasks where there was a potential for exposure to dioxin was constructed. These are called uniform tasks (UTs) because they are uniformly required whenever this type of process was operated. These lists of tasks are referred to as UT directories, with each task listed being referred to as a UT. A directory was constructed for each process in the scope of the Registry study at each site and for each time period during which there were no major process changes.

Each UT directory will contain UT codes, UT descriptions, UT time periods, dioxin concentration in the substance involved in the task, the exposure factor, and the UT dioxin rating. The UT code is a number identifying the site and the process. Each UT code has a UT description associated with it. The UT description defines the task being performed. The UT time period is the approximate period of time to perform the task. The assumptions made was that a worker works a shift which is eight hours long. The UT time period is a fraction of the eight hour shift. For example, if a given task takes one hour to perform and is done once per a shift then the UT time period for that task is 0.125. The dioxin concentration in

the substance involved in the task is the geometric mean concentration of dioxin in the substance, and it was derived from the analytical data associated with that process. The analytical data associated with a process was summarized by year and sample type. If an analytical result was reported to be non-detectable (ND) then one half of the limit of detection was used to calculate the geometric mean. The dioxin concentration values are less accurate the earlier in time the analysis was performed. Analytical techniques for measuring dioxin were first developed in 1965 and have steadily improved in the years following.

The UT exposure factor is a weighting factor used to estimate the "cleanliness" or the degree of contamination in the workplace where the task was performed. These numbers were assigned based on knowledge of the nature of the task. Where available, surface wipe sample results were used to provide an external comparison with the estimated exposure factors. The exposure factor is a number between zero and one with zero representing very low probability of contamination in the work area and one representing a very great probability of contamination in the work area. Throughout the entire Registry cohort the amount of industrial hygiene data is limited; however, data are available for plants containing approximately 42% of the cohort (see Table 3). The industrial hygiene measurement data for dioxin is predominately surface wipe samples. A surface was wiped with filter paper, the filter paper was extracted with a solvent, and the solvent extract analyzed for dioxin. There is very little data on

TABLE 3

NUMBER OF WORKERS PER SITE INCLUDED THE DIOXIN REGISTRY
THE DIOXIN REGISTRY
NIOSH
CINCINNATI, OHIO

Site Number	Years of Operation	Number of Workers in Cohort	Percent of Workers in Cohort	Industrial Hygiene Data Available
01	8/51-8/69	470	7.8	No
02A	3/68-2/69	47	0.8	No
02B	1/70-1/72			No
03A	1/62-12/70	350	5.8	No
03B	9/71-4/79	400	6.7	No
04	1948-1959 1963-1977	53	0.9	No
05	2/61-12/62	280	4.7	No
06	ND	85	1.4	ND
07	1938-1978	869	14.5	ND
08	1948-1969	415	6.9	No
09	1937-12/80	2194	36.6	Yes
10	1949-6/72	325	5.4	No
11	1/58-pres.	182	3.0	Yes
12	1958-pres.	156	2.6	Yes
13	1957-12/83	170	2.8	Yes
14	ND	ND	ND	ND
		5996		

ND = not yet determined

airborne dioxin levels. Based on the nature of the processes and work activities, and the physical properties of the materials, it is likely that most of the exposure to dioxin was through skin contact: touching contaminated surfaces, spilling and splashing of substances containing dioxins, and some handling of substances containing dioxins. Drying and flaking operations where dusts and fumes were generated represent situations where inhalation exposure to dioxin could have taken place.

The UT dioxin ratings represent the potential exposure to dioxin for the tasks listed in the UT directories. The UT dioxin rating is based on the concentration of dioxin in the process materials, the frequency and duration of daily contact, and the exposure weighting factor. Therefore, for a given process, UT directory and a given task, a UT dioxin rating will be calculated from the product of the UT time period, multiplied by the dioxin concentration in the substances involved in the task, multiplied by the exposure factor.

2. Occupational Title (OT) Directories

Each process at each plant site included in the Registry was located in a department. Each department had workers with plant specific job titles who performed tasks associated with a process or processes. Therefore a job or occupational title (OT) was associated with a set of tasks in that department.

An OT directory was constructed for each process at each site and for each time period where there were no major process changes. Therefore, there is a matching OT directory for each UT directory. Each OT directory consists of OT codes, the OTs, OT dioxin exposure rating values, and applicable UT codes. The OT codes will be four digit numbers, with the first two digits representing the process, and the second two digits will represent the OT. The OT dioxin exposure rating is the sum of the daily UT dioxin exposure ratings associated with task in the OT.

Having calculated an OT dioxin exposure rating value for each OT through the years of operation for the various processes, the final step was to calculate cumulative dioxin exposure rating values for the workers based on their work histories. These calculations will be performed using the NIOSH Life Table Analysis System.[5] Appendix B provides examples of the procedures used to calculate dioxin exposure ratings for phase one processes.

B. Phase Two

Phase two of the assessment procedure was to calculate the potential exposure to dioxin for those members of the cohort where industrial hygiene data and information were not available. The estimation procedure in phase two was the same as that used in phase one. For each process at each site there was a process description. UT directories were constructed from the process descriptions and contain the same type of information as was provided in the UT directories constructed in phase one. The gaps in the information known about a process in phase two were filled based on the similarities between a process in phase one to the process in phase two. In general, these processes are very similar

to each other throughout the industry. An OT directory also was constructed for each process at each site. The OT directories constructed in phase two contains the same type of information as those constructed in phase one. As in phase one, the OTs in phase two were matched with appropriate UT dioxin rating values to yield OT dioxin exposure rating values which represents the potential exposure to dioxin on a daily basis. Finally, using the NIOSH Life Table Analysis System, cumulative potential exposure rating values will be calculated for the workers based on each person's work history. Appendix C provides a sample of the procedures used to estimate dioxin exposures for a phase two process.

IV. Conclusions

The exposure matrix presents relative potential exposure estimates to dioxin for workers in the Registry cohort. Workers in the cohort can be assigned cumulative potential exposure ratings. The exposure ratings will be used to provide a detailed exposure analysis as part of the effort to determine whether certain mortality outcomes are associated with exposure to dioxin.

REFERENCES

1. Morton Corn and Nurtan A. Esmen: Workplace Exposure Zones for Classifications of Employees Exposure to Physical and Chemical Agents; American Industrial Hygiene Association Journal 40:(1979)

2. Nurtan A. Esmen: Retrospective Industrial Hygiene Surveys. American Industrial Hygiene Association Journal 40:(1979).

3. John Gamble and Robert Spirtas: Job Classifications and Utilization of Complete Work Histories in Occupational Epidemiology. Journal of Occupational Medicine. 18:399(1976).

4. T.O. Tiernan: Analytical and Chemical Support for Herbicide Disposition Activities. U.S. Air Force Contract No. F 41608-76-C-0464.

5. Richard J. Waxweilier, et. al.: A Modified Life-Table Analysis System for Cohort Studies. Journal of Occupational Medicine 25:115 (1983).

Appendix A
THE NIOSH OCCUPATIONAL DIOXIN REGISTRY

THE NIOSH OCCUPATIONAL DIOXIN REGISTRY: A STATUS REPORT*

Marilyn A. Fingerhut, Ph.D.
David A. Marlow
William E. Halperin, M.D., M.P.H.
Patricia A. Honchar, Ph.D.

National Institute for Occupational Safety and Health
Robert A. Taft Laboratories
4676 Columbia Parkway
Cincinnati, Ohio 45226

*This report is an update of the earlier article which appeared in Public Health Risks of the Dioxins, proceedings of a symposium held on October 19-20, 1983 at the Rockefeller University, New York City. Edited by William W. Lowrance. Copyright, The Rockefeller University, 1984. Published by William Kaufmann, Los Altos, California

Presented at the Fifth International Conference on Dioxin, Bayreuth, Federal Republic of Germany, September 16-19, 1985.

The NIOSH Dioxin Registry is a compilation of demographic and work-history information for all U.S. production workers who have synthesized products known to be contaminated with tetrachlorodibenzodioxin (2,3,7,8-TCDD) or the hexachlorinated dibenzodioxins. Currently, there are 14 production facilities and about 7,000 workers in the Registry. The first use of this information is a mortality study for which the comparison group is the U.S. male population. This study will evaluate the causes of death among workers exposed to products contaminated with dioxin.

Table 1 lists the manufactured substances relevant to the Dioxin Registry. Trichlorophenol, the herbicides 2,4,5-T and Silvex, and hexachlorophene are manufactured products which may be contaminated with 2,3,7,8-TCDD. By contrast, pentachlorophenol contains not the 2,3,7,8 isomer but the hexa-, hepta- and octa-chlorinated dioxins. Production workers who made the herbicide 2,4 dichlorophenoxyacetic acid (2,4-D) are not included in the Registry unless they happened to be involved in one of the other processes, because 2,4-D has not been reported to contain 2,3,7,8-TCDD.

Figure 1 illustrates the production processes in which 2,3,7,8-TCDD contamination arises. Tetrachlorobenzene is converted to the product 2,4,5-trichlorophenol (TCP), which is used as a feedstock to generate the herbicide 2,4,5-T. Under conditions of high pressure and temperature and alkalinity, the unintended dioxin contaminants are also generated. The specific isomers of dioxin produced are determined by the position of the chlorines in the reacting compounds. Both 2,4-D and pentachlorophenol are made by a different process, the chlorination of phenol, and the dioxin isomers which contaminate these products do not include the 2,3,7,8-TCDD. Hexachlorophene is made from 2,4,5-trichlorophenol by a process which does not add any additional dioxin to the amount present in the trichlorophenol. The environmental problem in Missouri has resulted from the spraying of oily dioxin wastes which were removed from trichlorophenol prior to its use in synthesizing hexachlorophene.

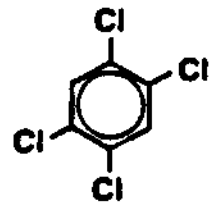
Figure 2 lists the manufacturing sites in the Registry and the years during which they produced dioxin-contaminated substances. We have identified about 7,000 production workers at these 14 chemical plants. To the best of our knowledge, this constitutes all of the manufacturing sites in the United States which synthesized the dioxin contaminated products. There were many other places in the United States where formulation occurred; for example, where 2,4,5-T was mixed with 2,4-D or other substances for sale under a brand name. For logistical reasons, we omitted the formulation sites because most were small facilities with inadequate records there. We have included formulators at the major manufacturing sites who formulated only phenoxy herbicides.

Table 2 illustrates the types of substances produced at each site. Some companies made trichlorophenol and sold it to other companies which used the trichlorophenol to make 2,4,5-T products. We have listed 2,4-D because most of the plants which made 2,4,5-T also made 2,4-D, and many of the workers made both products in the same equipment. Pentachlorophenol was made in four facilities. We will separate the analysis of causes of death in the workers who made pentachlorophenol from the analysis of deaths among workers who made TCP and its derivatives, because the contaminating dioxin isomers are different. We included pentachlorophenol production workers in the Dioxin Registry because there has been very little research on humans exposed to hexachlorinated dibenzodioxins.

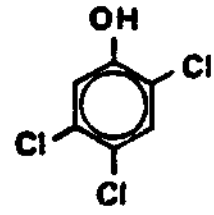
Because the issue of exposure is so important, we have chosen a strict criterion for entrance into the Registry. The requirement is a company record of assignment to a department which made the product of interest, such as 2,4,5-T. The potential for exposure, therefore, is to products contaminated with 2,3,7,8-TCDD or the hexachlorinated dibenzodioxins, not to dioxin alone. Maintenance workers are included in the Registry if they had a record of assignment to the area where the process was located.

We will construct an exposure matrix which estimates the potential for dioxin exposure for each worker by using the following types of information: the product, the process, the operating conditions, temperatures, and solvents. In a number of trichlorophenol facilities accidents occurred during which increased amounts of dioxin were released. We have also gathered detailed information about job descriptions. The fact that an individual worked in the process doesn't necessarily mean that the worker was exposed to any substance. Consider, for example, that in a system involving closed pipes and kettles which require no manual loading, only leakage might be a problem. By contrast, a different potential for exposure exists at another site where the kettles are open or the worker had to shovel out some of the solid material. We also have analyses of dioxin concentrations in the products of various manufacturers.

In the mortality study we will specifically evaluate the following four carcinogenic outcomes which have been suggested in animal and human studies: Additionally, we will use our Life Table Analysis System to evaluate 85 other causes of death. We anticipate that we will complete the study in 1986.

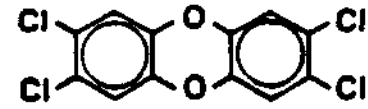


1,2,4,5 - Tetrachlorobenzene

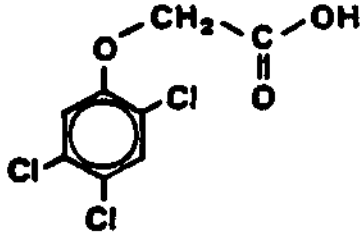


2,4,5 - Trichlorophenol

+

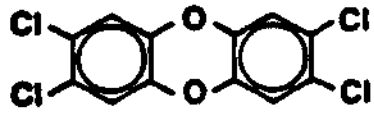


2,3,7,8. - Tetrachlorodibenzo-p-dioxin
present as a contaminant

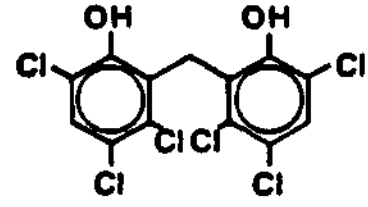


2,4,5 - Trichlorophenoxyacetic Acid

+

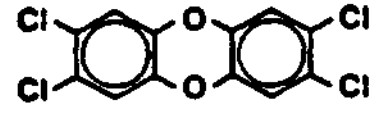


2,3,7,8 - Tetrachlorodibenzo-p-dioxin
present as a contaminant



Hexachlorophene

+



2,3,7,8 - Tetrachlorodibenzo-p-dioxin
present as a contaminant

FIGURE 1

YEARS OF PHENOXY ACID AND CHLOROPHENOL PRODUCTION AT FOURTEEN U.S. PRODUCTION SITES.

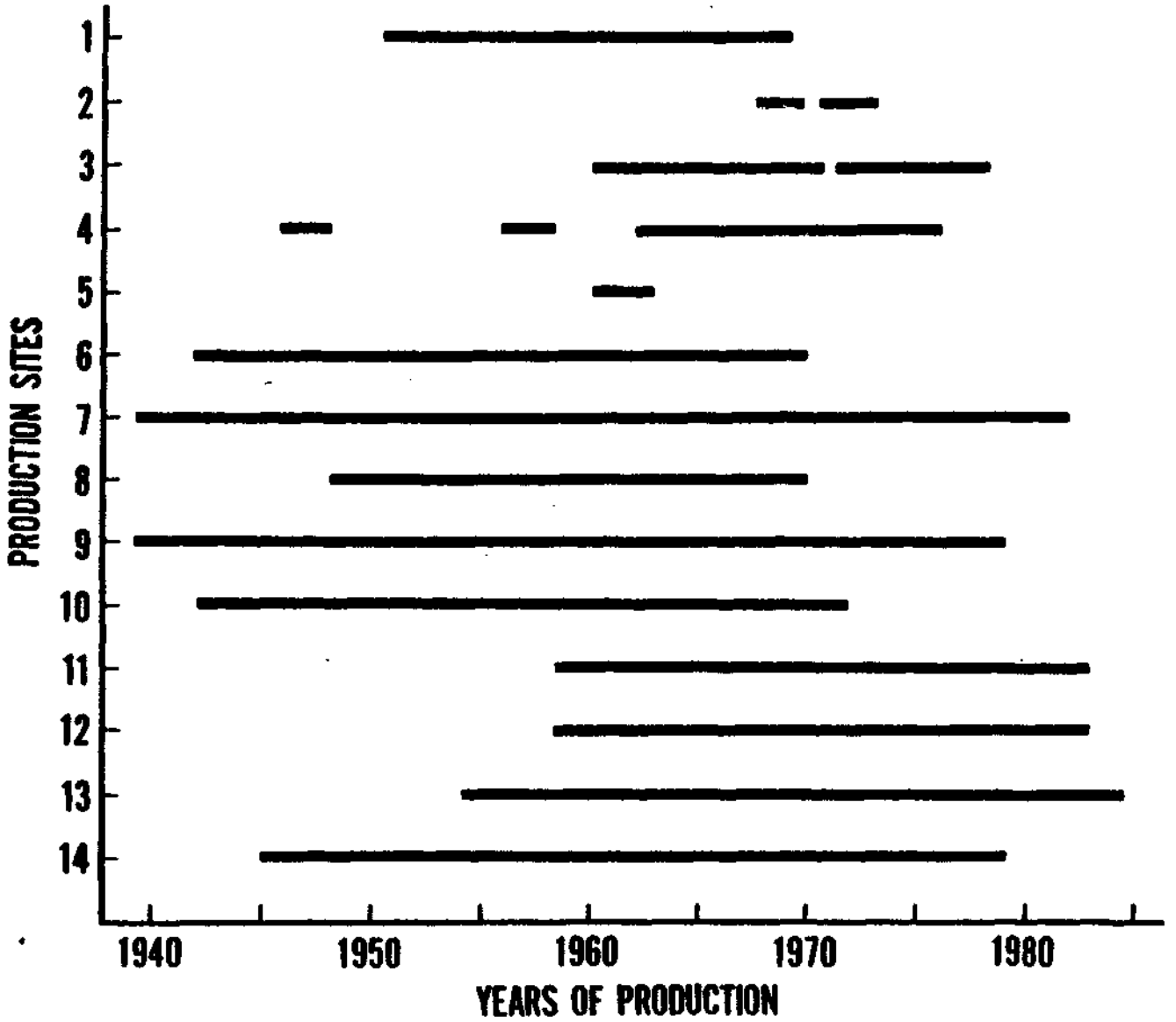


FIGURE 2

TABLE 1

THE RELEVANT SUBSTANCES

MANUFACTURED PRODUCT	DIOXIN CONTAMINANT
TRICHLOROPHENOL 2,4,5-T(ACID, ESTER, AMINE) SILVEX (ACID, ESTER, AMINE) HEXACHLOROPHNE	2,3,7,8-TETRACHLORODIBENZODIOXIN (2,3,7,8-TCDD)
PENTACHLOROPHENOL	HEXACHLORODIBENZODIOXINS HEPTACHLORODIBENZODIOXINS OCTACHLORODIBENZODIOXINS
2,4-D	NONE DICHLORODIBENZODIOXINS TRICHLORODIBENZODIOXINS TETRACHLORODIBENZODIOXINS, (1,3,6,8 or 1,3,6,9)

TABLE 2

PRODUCTION WITH POTENTIAL
FOR DIOXIN CONTAMINATION

PRODUCTION SITES	TCP	T ACID	T ESTERS	T AMINES	SILVEX PRODUCTS	TCP DERIVATIVES	2,4-D PRODUCTS	PCP
01	X	X	X	X			X	
02	X	X				X		
03	X	X	X	X	X		X	
04		X	X	X	X		X	
05	X	X	X	X			X	
06	X		X	X	X		X	
07			X				X	X
08	X	X						
09	X	X	X	X	X	X	X	X
10	X							
11							X	X
12							X	X
13						X		
14			X	X	X			

APPENDIX B

EXAMPLE OF EXPOSURE ESTIMATION PROCEDURE

Introduction

A phase one 2,4,5-trichlorophenol (2,4,5-TCP) production process was examined to demonstrate the dioxin exposure estimation procedure. Site 9, which has excellent records was used to illustrate the process. The 2,4,5-TCP process used as an example began production in 1966 and continued until 1979. The production process was designed and constructed with knowledge that 2,3,7,8-tetrachlorodibenzo(p)dioxin (TCDD) was formed as a contaminant, and no major process changes occurred throughout its years of operation. It was operated such that the formation of TCDD was kept to a minimum and the potential for exposure to the workers to dioxin - contaminated substances was minimized. In addition, an industrial hygiene monitoring program collected surface wipe samples for TCDD throughout the 2,4,5-TCP production process area on a quarterly basis to check for TCDD surface contamination. Presented is a process description of the 2,4,5-TCP process, a list of job titles for workers involved in this process, along with their descriptions, industrial hygiene sampling results and results of dioxin analysis in products, process streams, and waste effluents. Examples are provided to illustrate the process of compiling this information to create Uniform Task (UT) and Occupational Title (OT) directories. In addition, cumulative dioxin ratings will be calculated using sample work histories.

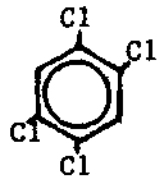
2,4,5-TCP Process Description

2,4,5 TCP was produced in this process using the following raw materials: methanol, caustic soda, 1,2,4,5-tetrachlorobenzene (TCB), and hydrochloric acid (HCl) (aqueous). Water and methanol were used as solvents in various

stages of this process. It was an automated, batch process. A block flow diagram of the process is shown in Figure B - 1 and a plant layout is shown in Figure B - 2.

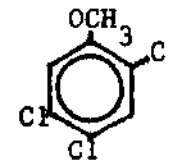
The first step in the process was a three step reaction which occurred in a closed agitated jacketed batch reactor. TCB and methanol were pumped to the reactor and then, while the reaction proceeded, caustic solution was added continuously. Water was used as a solvent. The following sequence of reactions took place, with the dechlorination of TCB being highly exothermic:

$$\underset{\text{(methanol)}}{CH_3OH} + \underset{\text{(caustic)}}{NaOH} \longrightarrow \underset{\text{(sodium methylate)}}{CH_3ONa} + H_2O$$



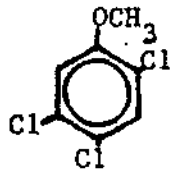
(TCB)

$$+ \; CH_3ONa \longrightarrow$$

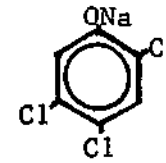


$$+ \; NaCl$$

(2,4,4,-trichloroanisole)



$$+ \; CH_3ONa \longrightarrow$$



$$+ \; CH_3OCH_3$$

dimethyl ether

(sodium 7,4,5-trichlorophenate)

The reaction conditions of this step were an operating temperature of less than or equal to 152°C (a key element in keeping TCDD formation to a minimum) and a operating pressure of less than 300 psig.

The resulting solution contained water, salt, sodium 2,4,5-trichlorophenate (NaTCP), 2,4,5-trichloroanisole (TCA) (because the reaction does not proceed to completion), and methanol (which has been added in excess of the stoichiometrically required amount so that enough would be present to act as

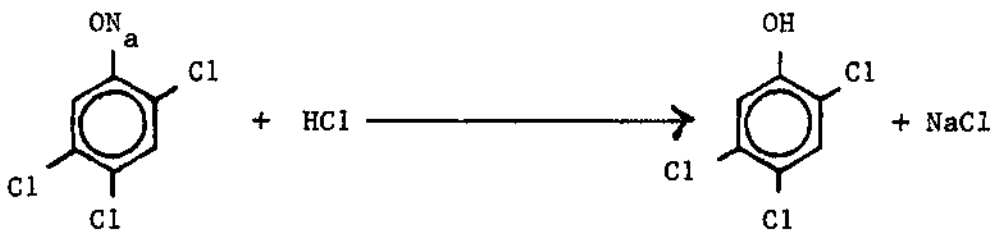
a solvent for the sodium methylate intermediate). The dimethyl ether (DME) by-product was vented to the atmosphere.

The solution was then pumped to the next step in the operation, the decantation. In the decantation vessel two layers were formed, an organic layer consisting mainly of TCA and dioxin, and an aqueous layer containing NaCl, NaTCP, and methanol. This step was operated at a temperature less than 105°C and at atmospheric pressure. The organic layer, or "waste oil," was pumped from the decantation vessel and transferred to a central incineration unit for burning. This was usually accomplished by pumping oil into containers which were hauled to the incinerator. This step was important because it separated the bulk of the dioxin formed from the NaTCP product. Removing the dioxin at this early stage reduced the chances for exposure to dioxin in subsequent steps.

The aqueous product stream of the decanting vessel was pumped to the alcohol recovery operation, the next step in the operation. The alcohol recovery step was a simple distillation which removed most of the methanol from the stream as an overhead product. This was accomplished at a temperature of less than 105°C and at atmospheric pressure. The recovered methanol was recycled to the initial batch reactor where it was used in subsequent batches. The bottoms product, an aqueous solution of salt and NaTCP containing some impurities, was pumped to the phenate stripping operation for further purification. This operation removed "waste oil" from the product stream, by distillation. The "waste oil" removed was disposed of in the same manner as the "waste oil" from the decantation. The product

stream, an aqueous solution of NaCl and NaTCP, was then pumped to the next step in the operation, the acidification reactor.

The acidification of NaTCP to form 2,4,5-TCP was done by adding aqueous HCl to the vessel containing the aqueous solution of NaTCP and NaCl. A reaction between NaTCP and HCl occurred, as shown:



(2,4,5-TCP)

The resulting solution of 2,4,5-TCP, NaCl, water, and any excess HCl was pumped to a decantation vessel where the contents were allowed to settle. Two layers, an organic layer of 2,4,5-TCP which contained some residual NaCl and an aqueous brine containing any excess HCl, were formed and were separated. The 2,4,5-TCP layer was pumped to another vessel where it was mixed with water. The residual NaCl content of the 2,4,5-TCP dissolved in the water, and the vessel contents were then allowed to settle. After the aqueous and organic layers were formed, a second decantation was performed. The "waste brine" (salt water) solutions decanted from each of the last two operations were combined and pumped to a deep well disposal. In later years, the "waste brine" was carbon treated and sent to the waste treatment plant. The TCP product was ready for use in the production of any of the 2,4,5-TCP derivatives or for finishing as a final product.

Description of Job Duties

Two Trichlorophenol (TCP) operators controlled the highly automated 2,4,5-TCP production process per eight hour work shift. Each TCP Operator spent one-half of the work shift controlling the process from the control room panel boards. The other half of the work shift was spent in the process areas, as required, obtaining process samples, checking tank levels, making material transfers and filling tank cars or tank trucks. The Spare and Alternate worked in relief of the TCP Operators and also performed plant maintenance. The Foreman was responsible for overseeing plant operations. The Senior Production Engineer performed the duties of a Foreman in the plant in addition to engineering necessary for plant projects. Table B-1 lists the various occupational titles along with their description of tasks and materials encountered.

Industrial Hygiene Sampling Methods and Results

Surface wipe samples were taken to evaluate workers' potential exposure to TCDD by skin contact with contaminated work surfaces. Sample locations were chosen to represent surfaces which workers might or must contact to occupy and operate the 2,4,5-TCP production process. The technique consisted of wiping approximately 100 square centimeters of surface with a dry filter paper (Whatman #2 5.5 cm) with as much pressure as could be applied without tearing the filter paper. The contaminants on the filter paper were extracted with a solvent and analyses were conducted with vapor phase chromatography (VPC) or gas chromatography-mass spectroscopy (GC/MS) analytical techniques.

Surface wipe samples collected throughout the years the 2,4,5-TCP production process operated are summarized in Table B2. The surface wipe sample results listed in Table B-2 have been summarized by year and the following areas: waste oil dempster area; reactor area; lab area; control room; lunchroom; locker room; and shop area; anisole decantation area; packaging area; 2,4,5-TCP finishing area; and intermediate storage/methanol recovery/waste treatment area. A total 906 surface wipe samples were collected and analyzed for TCDD with 19% (175 out of 906) having detectable quantities of TCDD measured. The limit of detection of TCDD varied from 0.1 to 1.0 micrograms per wipe (ug/wipe) throughout the years summarized in Table B-2. The minimum detectable quantity of TCDD measured was 0.1 ug/wipe, measured at one time or another in all categories. The maximum detectable quantity of TCDD measured was 60.0 ug/wipe, measured in the reactor area in 1977.

Analytical Dioxin Measurements of Products, Process Streams & Waste Effluents

Analytical dioxin measurements in products, process streams, and waste effluents are summarized in Table B-3. The sample results were summarized by year, analyte (TCDD) and sample type (product, process stream or waste effluent). The summary statistics used were the number of sample results; the number of non-detectable (ND) sample results; the limit of detection (LOD); the GM of the sample results when ND=LOD/2; the minimum detectable sample result; the maximum detectable sample result and the GM of the detectable sample results. For the 2,4,5-TCP process the analytical dioxin

data were categorized into three sample types, 2,4,5-TCP (product), NaTCP (process stream) and TCP waste (waste effluents). The results of this summarization were used to calculate the UT dioxin ratings.

Exposure Factors

The UT exposure factors are values assigned to the tasks based on the "cleanliness" or degree of contamination in the work area where these tasks are performed. The factors range from zero to one, and are intended to weight the exposure rating based upon the likelihood that the dioxin - containing material had escaped containment and was present in the plant environment. For example, the point in the production process where the task was performed was an important consideration(e.g., workers adding raw materials to a reactor were assigned a factor of 0, since no dioxin had been formed at this stage of the process). The nature of the process was also considered, for example, product flaking and bagging operations were assigned factors of 0.5 to 0.75 since material transfer operations such as these present a high potential for release of the product to the atmosphere. Centrifuge operations were assigned a factor of 0.5 because the process was not completely contained, and the operators used manual tools to plow dioxin - containing material from surfaces. To evaluate these assigned values, the exposure factors were compared to the summarized surface wipe sample results. Tables B-4 through B-9 compare exposure factor for the various areas of the process to the geometric mean (GM) of the surface wipe sample results for those areas for the years 1972, 1973, 1975, 1976, 1977 and 1978 respectively. The GM of the surface wipe samples was calculated

such that the LOD/2 was used for the ND results. Table B-10 is an overall comparison of the exposure factor to GM of the surface wipe samples.

Uniform Task Directory

UT directories have been constructed for Sites Nine's 2,4,5-TCP process for the years 1970, 1972 through 1978 in Tables B-11 through B-18. A total of twenty tasks are listed in the directories. The UT times listed for the various tasks were obtained from an indepth industrial hygiene survey report conducted in 1978. The UT material TCDD concentrations were obtained from the data list in Table B-3. These data were abstracted and summarized from through review of records kept for Site Nine. The product of the UT time, UT material dioxin concentration and the exposure factor yields the UT dioxin ratings. These values are shown in the last columns of Table B-11 through B-18 and are the values which were used to calculate the Occupational Title dioxin exposure ratings.

Occupational Title Directory

Having constructed UT directories for the 2,4,5-TCP process, Occupational Title (OT) directories were constructed for each year. Tables B-19 through B-26 show the OT directories for the years 1970, 1972 through 1978, respectively. Found in these directories are the OT codes which are four digit numbers that uniquely relate to specific occupational titles. The OT dioxin exposure ratings are obtained as the sum of the appropriate UT dioxin

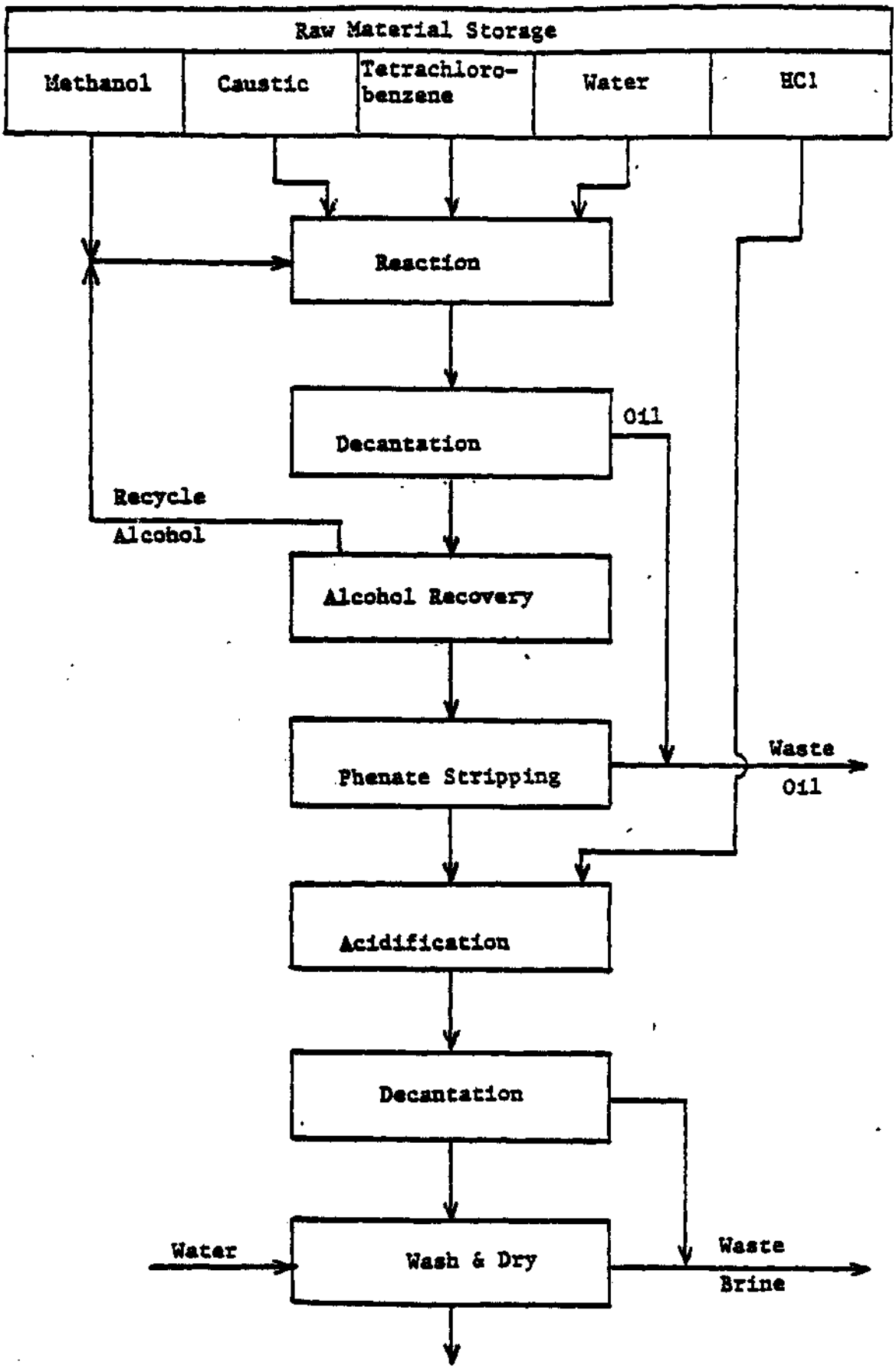
ratings for all job tasks which constitute the total work assignments for the occupational title. The UT codes which are associated with the UT ratings are listed in the last column of the OT directories. The Occupational Title rating is obtained for each Occupational Title by summing all tasks included in the daily work assignment of the person holding that title. For example, as shown in Table B-22, the Trichlorophenol Operator(OT1043) received an exposure rating in 1974 of 51.265 X 10^{-3}. This was obtained by summing the exposure ratings for the Uniform Tasks 10.1 to 10.14 as listed in Table B-14. The OT dioxin exposure rating listed in the OT directories represents the dioxin exposure rating for the occupational titles listed for each day of a given year. Overall the OT dioxin exposure ratings for the Tichlorophenol Operator ranged from 5.595 X 10^{-3} to 56.58 X 10^{-3}, while for the Utility Man (Spare) these ratings ranged from 8.421 X 10^{-3} to 143.1 X 10^{-3}. The Superintendent's OT dioxin exposure rating, which were the lowest among the various occupational titles, ranged from 0.142 X 10^{-3} to 4.469 X 10^{-3}.

Other Processes at Site Nine

Examples of UT and OT directories for an old NaTCP process, a 2,4,5-T acid process and a 2,4,5-T acid ester process are shown in Tables B-27 through B-32. Table B-27 is the UT directory for the 2,4,5-T acid and 2,4,5-T acid ester process for the 1965. Table B-28 is the OT directory for these processes and years. Tables B-29 and B-30 are the UT and OT directories for these processes for the year 1970. Tables B-31 and B-32 are the UT and OT directories, respectively, for an old NaTCP process for the year 1965. All

of these directories were constructed in the same manner as the directories for the 2,4,5-TCP process. Comparisons of OT dioxins exposure ratings for the Trichlorophenol Operator in the old NaTCP process to the 2,4,5-TCP process show that for the old NaTCP process the values were substantially higher than those values associated with Trichlorophenol Operator from the 2,4,5-TCP process. Similarly, the OT dioxin exposure rating for the 2,4,5-T acid and 2,4,5-T acid ester process were higher than the OT ratings listed for the 2,4,5-TCP process. The result should be expected since dioxin levels were higher in these processes than they were for the 2,4,5-TCP process.

Figure B-1
SITE NINE
2,4,5-Trichlorophenol Block Flow Diagram
1966-1979



SITE NINE

2,4,5-Trichlorophenol Plant Layout

1966-1979

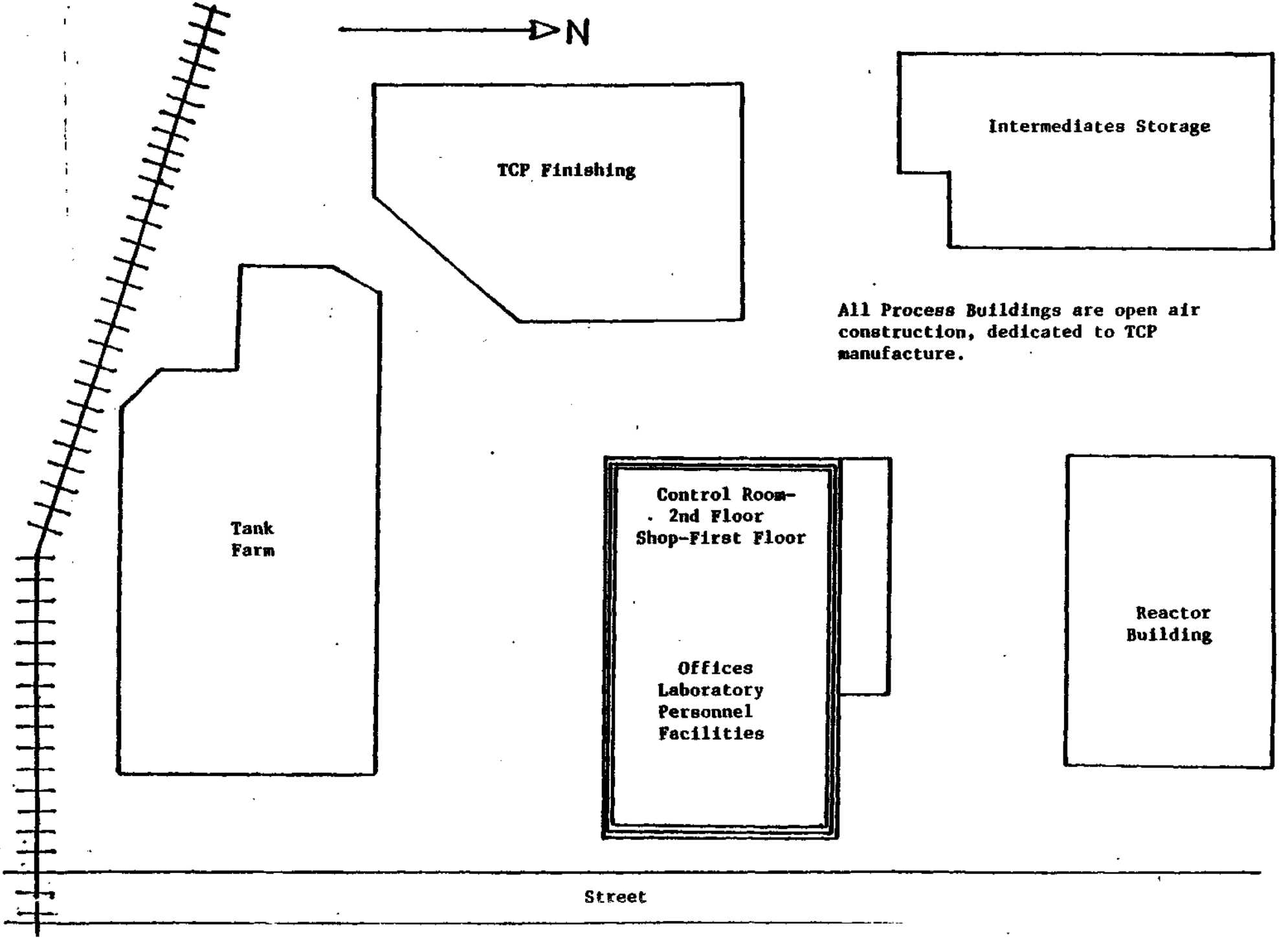


TABLE B-1
SITE NINE

2,4,5-TCP PRODUCTION PROCESS WORKERS' JOB
DESCRIPTION AND MATEIALS ENCOUNTERED

JOB TITLE: Operator (outside man 4 hr/shift)

Materials Encountered: 50% NaOH, tetrachlorobenzene, methanol, sodium trichlorophenate, trichloroanisole, 32% HCl, 2,4,5-trichlorophenol, TCDD (as impurity), 10% NaCl, Dimethyl ether, water softener, Mogul WS-164 corroslion inhibitor, Karl Fisher regents, ortho dichlorobenzene.

Description of Operation	Frequency	Total Time In Hours
Takes readings and surveys equipment	2/shift	1 hr.
Samples acid and basic brine streams and checks pH	2/shift	1 hr.
Sample MeOH reflux and shot tank, checks for H20 with Karl Fisher	2/shift	1/2 hr.
Transfer product and makes stick measurement	daily	1 hr.
Loads tank cars of trichlorophenol	1/week	2 hr.
Unloads methanol trucks (samples and identified raw material)	2/week	1 hr.
Receives tetrachlorobenzene (stick measures storage tank)	2/day	10 min.
Sets valves, starts and stops pumps		
Empties ortho scrubber	1/month	1/2 hr.
Samples anisole storage tank	1/week	5 min.
Performs minor maintenance and line unplugging as directed by supervisor		

JOB TITLE:

TCP Operator (inside man 4 hr/shift

Materials Encountered: 4 amino antipyrene reagent, potassium hexacyanide reagent, sodium tetraborate buffer.

DESCRIPTION OF OPERATION	FREQUENCY	TOTAL TIME IN HRS.
Checks cooling tower water for trace phenolics using amino antipyrene method	2/shift	15 min.
Takes readings and adjusts instruments, relays info to man in field	8/shift	
Initiates loading of reactors and starts up of equipment	as directed	
Operations is remote from chemical handling area	--	

TABLE B-1 (continued)
SITE NINE
2,4,5-TCP PRODUCTION PROCESS WORKERS' JOB
DESCRIPTION AND MATERIALS ENCOUNTERED

JOB TITLE:

Utility-Spare (covers TCP Operator classification inside and out)

Materials Encountered: Same as TCP Operator, plus Mogul Ag-460, Biocide, Mog CT.601 organic dispresent.

Description of Operation
Performs TCP operators functions either inside or outside depending upon need at the time.
Performs necessary minor maintenance including unplugging of lines (tetra, TCP, anisole area not common).
Repairs leaks and replaces worn mechanical equipment.
Responsible for the addition of water treatment chemicals to cooling tower for prevention of corrosion, solids and algee accumulation (Frequency: 1-7 weekly; Total Time: 15-20 min. each].

JOB TITLE:
Alternate (Covers both Utility man and TCP Operator (inside and outside) jobs.

Materials Encountered: Same as TC Operator and Utilityman classification.

Description of Operation:

Same as utilityman and TCP Operator when performing those tasks. Spends about 70% of his time as an Operator (35% inside and 35% outside) and the remaining 30% as a Utilityman.

JOB TITLE:
Superintendent

Materials Encountered: Same as TCP Operator and Utilityman

Description of Operation

Oversees trichlorophenol plant operation, indirectly involved.
Exposure to chemicals low to moderate relative to TCP operators.

TABLE B-1 (continued)
SITE NINE
2,4,5-TCP PRODUCTION PROCESS WORKERS' JOB
DESCRIPTION AND MATERIALS ENCOUNTERED

JOB TITLE:
Sr. Production Engineer

Materials Encountered: Same as TCP Operator and Utilityman

Description of Operation

Similar as Foreman Classification

JOB TITLE:
Foreman

Materials Encountered: Same as TCP Operators and Utilityman

Description of Operation

Oversees trichlorophenol plant operations under the direction of the plant superintendent, makes majority of on spot judgements regarding repairs and methods. Writes permits for vessel entries and line openings, and supervises said activities.
Spends about 90% of time in plant. Exposure to chemicals moderate relative to TCP Operators.

JOB TITLE:
Sr. Production Office Assistant

Materials Encountered: 2,4,5-Trichlorophenol, trichloroanisole, TCDD (as impurity)

Description of Operation

Delivers 4 oz. sample bottles of above materials to laboratory [Frequency: daily; Total Time: 1 hr/day; (sealed bottles)].
Assuming there is no breakage, there is no exposure what so ever.
Classification is least likely to encounter chemical hazards.

Table B-2
Site Nine
Surface Wipe Sample Summary
2,4,5-TCP Process

Site Nine IH Data

Year	Sample Description	Analyte	Sample Type	No. of Samples	No. of NDs	LOD	GM when ND=0	GM when ND=LOD/2	GM when ND=LOD	Min Det Sample	Max Det Sample	GM Det Samples	Units
1977	Anisole decantation area	TCDD	W	4	2	<0.1	0.4	0.6	0.5	0.1	3	0.5	ug/wipe
1978	Anisole decantation area	TCDD	W	4	0	---	3.5	7.1	7.1	0.5	25	3.5	ug/wipe
1979	Anisole decantation area	TCDD	W	5	2	<0.1	0.9	0.9	0.9	0.2	3.7	1.3	ug/wipe
1969	Control room area	Chloracnegen	W	1	1	NFR	---	---	---	---	---	---	REFR
1970	Control room area	TCDD	W	2	1	<1.0	0.4	0.7	1.0	1	1	1.0	ug/wipe
1971	Control room area	TCDD	W	4	2	<0.19*	0.04	0.1	0.2	0.06	0.2	0.11	ug/wipe
1972	Control room area	TCDD	W	4	3	<0.07*	0.01	0.04	0.06	0.07	0.07	0.07	ug/wipe
1973	Control room area	TCDD	W	3	3	<1.0	---	---	---	---	---	---	ug/wipe
1975	Control room area	TCDD	W	1	1	<0.05	---	---	---	---	---	---	ug/wipe
1976	Control room area	TCDD	W	3	3	<0.15*	---	---	---	---	---	---	ug/wipe
1977	Control room area	TCDD	W	4	4	<0.2*	---	---	---	---	---	---	ug/wipe
1978	Control room area	TCDD	W	2	2	<0.1	---	---	---	---	---	---	ug/wipe
1979	Control room area	TCDD	W	1	1	<0.1	---	---	---	---	---	---	ug/wipe
1969	Intermediate storage	Chloracnegen	W	1	1	NFR	---	---	---	---	---	---	REFR
1970	Intermediate storage	TCDD	W	2	2	<1.0	---	---	---	---	---	---	ug/wipe
1971	Intermediate storage	TCDD	W	4	2	<0.19*	0.03	0.50	1.00	0.03	0.18	0.07	ug/wipe
1972	Intermediate storage	TCDD	W	3	2	<0.06*	0.002	0.08	0.11	0.01	0.01	0.01	ug/wipe
1975	Intermediate storage	TCDD	W	3	3	<0.1	---	---	---	---	---	---	ug/wipe
1977	Intermediate storage	TCDD	W	27	24	<0.2*	0.01	0.08	0.15	0.1	0.4	0.2	ug/wipe
1979	Intermediate storage	TCDD	W	4	2	<0.1	0.04	0.08	0.15	0.1	0.1	0.1	ug/wipe
1969	Lab area	Chloracnegen	W	4	4	NFR	---	---	---	---	---	---	REFR
1970	Lab area	TCDD	W	8	5	<1.0	0.3	0.7	1.0	1	1.5	1.1	ug/wipe
1971	Lab area	TCDD	W	16	11	<0.19*	0.01	0.08	0.14	0.02	0.2	0.05	ug/wipe
1972	Lab area	TCDD	W	16	11	<0.08*	0.02	0.04	0.07	0.01	0.3	0.07	ug/wipe
1973	Lab area	TCDD	W	12	12	<1.0	---	---	---	---	---	---	ug/wipe
1975	Lab area	TCDD	W	4	4	<0.05	---	---	---	---	---	---	ug/wipe
1976	Lab area	TCDD	W	13	12	<0.12*	0.01	0.05	0.09	0.5	0.5	0.50	ug/wipe
1977	Lab area	TCDD	W	19	18	<0.2*	.00	0.07	0.14	0.1	0.1	0.1	ug/wipe
1978	Lab area	TCDD	W	18	16	<0.1	---	---	---	---	---	---	ug/wipe
1979	Lab area	TCDD	W	7	7	<0.08*	---	---	---	---	---	---	ug/wipe
1969	Locker room area	Chloracnegen	W	1	1	NFR	---	---	---	---	---	---	REFR
1970	Locker room area	TCDD	W	2	1	<1.0	0.4	0.7	1.0	1	1	1.0	ug/wipe
1971	Locker room area	TCDD	W	4	3	<0.19*	0.01	0.08	0.14	0.04	0.04	0.04	ug/wipe
1972	Locker room area	TCDD	W	4	3	<0.07*	0.01	0.04	0.06	0.06	0.06	0.06	ug/wipe
1973	Locker room area	TCDD	W	3	3	<1.0	---	---	---	---	---	---	ug/wipe
1975	Locker room area	TCDD	W	1	1	<0.05	---	---	---	---	---	---	ug/wipe
1976	Locker room area	TCDD	W	3	3	<0.15*	---	---	---	---	---	---	ug/wipe
1977	Locker room area	TCDD	W	12	12	<0.1*	---	---	---	---	---	---	ug/wipe
1978	Locker room area	TCDD	W	14	14	<0.1	---	---	---	---	---	---	ug/wipe
1979	Locker room area	TCDD	W	9	9	<0.07*	---	---	---	---	---	---	ug/wipe
1969	Lunchroom area	Chloracnegen	W	1	1	NFR	---	---	---	---	---	---	REFR
1970	Lunchroom area	TCDD	W	2	1	<1.0	0.4	0.7	1.0	1	1	1.0	ug/wipe
1971	Lunchroom area	TCDD	W	4	2	<0.19*	0.04	0.10	0.15	0.02	0.3	0.08	ug/wipe
1972	Lunchroom area	TCDD	W	4	3	<0.07*	0.01	0.04	0.06	0.08	0.08	0.08	ug/wipe
1973	Lunchroom area	TCDD	W	3	3	<1.0	---	---	---	---	---	---	ug/wipe
1975	Lunchroom area	TCDD	W	1	1	<0.05	---	---	---	---	---	---	ug/wipe
1976	Lunchroom area	TCDD	W	5	5	<0.17*	---	---	---	---	---	---	ug/wipe
1977	Lunchroom area	TCDD	W	15	15	<0.2*	---	---	---	---	---	---	ug/wipe
1978	Lunchroom area	TCDD	W	10	10	<0.1	---	---	---	---	---	---	ug/wipe
1979	Lunchroom area	TCDD	W	6	6	<0.06*	---	---	---	---	---	---	ug/wipe
1971	Packaging area	TCDD	W	2	1	<0.18	1.8	1.8	1.8	5	5	5.0	ug/wipe
1972	Packaging area	TCDD	W	4	4	<0.08*	---	---	---	---	---	---	ug/wipe
1973	Packaging area	TCDD	W	2	2	<1.0	---	---	---	---	---	---	ug/wipe
1975	Packaging area	TCDD	W	1	1	<0.1	---	---	---	---	---	---	ug/wipe

Table B-2
cont.

Site Nine IH Data

Year	Sample Description	Analyte	Sample Type	No. of Samples	No. of NDs	LOD	GM when ND=0	GM when ND=LOD/2	GM when ND=LOD	Min Det Sample	Max Det Sample	GM Det Samples	Units
1976	Packaging area	TCDD	W	2	0	---	1.7	3.0	3.0	0.4	7.6	1.7	ug/wipe
1977	Packaging area	TCDD	W	1	0	---	0.4	0.4	0.4	0.4	0.4	0.4	ug/wipe
1978	Packaging area	TCDD	W	1	1	<0.1	---	---	---	---	---	---	ug/wipe
1969	Reactor area	Chloracnegen	W	4	4	NFR	---	---	---	---	---	---	REFR
1970	Reactor area	TCDD	W	9	7	<1.0	0.1	0.6	1.0	1	1.2	1.1	ug/wipe
1971	Reactor area	TCDD	W	21	15	<0.22*	0.01	0.08	0.15	0.02	0.6	0.13	ug/wipe
1972	Reactor area	TCDD	W	27	20	<0.07*	0.01	0.04	0.08	0.03	0.2	0.08	ug/wipe
1973	Reactor area	TCDD	W	29	28	<1.0	0.01	0.49	1.02	2	2	2	ug/wipe
1975	Reactor area	TCDD	W	9	9	<0.1*	---	---	---	---	---	---	ug/wipe
1976	Reactor area	TCDD	W	26	24	<0.14*	0.007	0.06	0.11	0.25	0.4	0.32	ug/wipe
1977	Reactor area	TCDD	W	27	23	<0.2*	0.5	0.5	0.5	0.1	60	1.4	ug/wipe
1978	Reactor area	TCDD	W	36	29	<0.1*	0.04	0.06	0.07	0.05	7	0.3	ug/wipe
1979	Reactor area	TCDD	W	33	30	<0.1*	0.01	0.03	0.06	0.06	2.1	0.2	ug/wipe
1969	Shop area	Chloracnegen	W	1	1	NFR	---	---	---	---	---	---	REFR
1970	Shop area	TCDD	W	3	1	<1.0	0.9	1.1	1.4	1	2.5	1.6	ug/wipe
1971	Shop area	TCDD	W	4	2	<0.34*	0.2	0.3	0.4	0.34	0.7	0.49	ug/wipe
1972	Shop area	TCDD	W	7	6	<0.08*	0.003	0.04	0.08	0.06	0.06	0.06	ug/wipe
1973	Shop area	TCDD	W	6	6	<1.0	---	---	---	---	---	---	ug/wipe
1975	Shop area	TCDD	W	3	3	<0.12	---	---	---	---	---	---	ug/wipe
1976	Shop area	TCDD	W	7	5	<0.17*	0.09	0.2	0.2	0.4	0.8	0.57	ug/wipe
1977	Shop area	TCDD	W	20	15	<0.2*	0.04	0.1	0.2	0.1	1.2	0.3	ug/wipe
1978	Shop area	TCDD	W	14	11	<0.1	0.005	0.05	0.09	0.1	0.1	0.1	ug/wipe
1979	Shop area	TCDD	W	10	9	<0.09*	0.01	0.05	0.09	0.2	0.2	0.2	ug/wipe
1971	TCP finishing area	TCDD	W	2	1	<0.2	1.4	1.5	1.6	4	4	4.00	ug/wipe
1972	TCP finishing area	TCDD	W	4	2	<0.1	0.20	0.24	0.27	0.32	0.98	0.56	ug/wipe
1973	TCP finishing area	TCDD	W	3	3	<1.0	---	---	---	---	---	---	ug/wipe
1976	TCP finishing area	TCDD	W	17	10	<0.21*	0.2	0.2	0.3	0.18	3.2	0.52	ug/wipe
1977	TCP finishing area	TCDD	W	29	25	<0.1*	0.02	0.04	0.1	0.1	1.2	0.3	ug/wipe
1978	TCP finishing area	TCDD	W	16	11	<0.1	0.1	0.1	0.1	0.1	1	0.4	ug/wipe
1979	TCP finishing area	TCDD	W	7	6	<0.08*	0.004	0.04	0.08	0.08	0.08	0.1	ug/wipe
1969	Waste oil dempster area	Chloracnegen	W	4	3	NFR	---	---	---	1	1	---	REFR
1970	Waste oil dempster area	TCDD	W	15	9	<1.0	0.4	0.7	1.1	1	5.1	1.6	ug/wipe
1971	Waste oil dempster area	TCDD	W	39	23	<0.29*	0.07	0.14	0.22	0.02	3	0.18	ug/wipe
1972	Waste oil dempster area	TCDD	W	42	24	<0.08*	0.10	0.11	0.12	0.02	6.1	0.24	ug/wipe
1973	Waste oil dempster area	TCDD	W	26	24	<1.0	0.2	0.5	0.9	6	11	8	ug/wipe
1975	Waste oil dempster area	TCDD	W	5	5	<0.1	---	---	---	---	---	---	ug/wipe
1976	Waste oil dempster area	TCDD	W	23	19	<0.11*	0.08	0.1	0.2	0.8	2.8	1.13	ug/wipe
1977	Waste oil dempster area	TCDD	W	38	30	<0.1*	0.2	0.2	0.3	0.1	13	0.9	ug/wipe
1978	Waste oil dempster area	TCDD	W	24	16	<0.1	0.3	0.3	0.3	0.1	29	0.3	ug/wipe
1979	Waste oil dempster area	TCDD	W	10	8	<0.09*	0.01	0.05	0.10	0.07	0.2	0.1	ug/wipe

Table B-3

Site Nine Analytical Dioxin Data: 2,4,5-TCP Process

Year	Sample Descript	No. of Samples	No. of NDs	LOD	GM when ND=LOD/2	Min Det Sample	Max Det Sample	GM Det Samples	Units
1967	2,4,5-TCP	162	162	<1.0	---	---	---	---	ug/g
1968	2,4,5-TCP	81	81	<1.0	---	---	---	---	ug/g
1970	2,4,5-TCP	57	54	<0.49*	0.248101	0.63	1.3	0.923655	ug/g
1971	2,4,5-TCP	143	65	<0.36*	0.095906	0.01	0.1	0.034985	ug/g
1972	2,4,5-TCP	92	67	<0.036*	0.02	0.01	0.06	0.03	ug/g
1973	2,4,5-TCP	260	251	<0.02196*	0.004	0.003	0.05	0.021	ug/g
1974	2,4,5-TCP	272	262	<0.16*	0.01	0.02	0.04	0.03	ug/g
1975	2,4,5-TCP	97	94	<0.0101*	0.005	0.01	0.06	0.023	ug/g
1976	2,4,5-TCP	182	154	<0.011*	0.005	0.0005	0.05	0.015	ug/g
1977	2,4,5-TCP	142	133	<0.014*	0.002	0.006	0.02	0.011	ug/g
1978	2,4,5-TCP	274	269	<0.0099*	0.005	0.001	0.01	0.002	ug/g
1971	Na TCP reactor	15	5	<0.42*	0.23	0.09	1.1	0.26	ug/g
1972	Na TCP reactor	5	4	<0.05	0.01	0.1	0.1	0.1	ug/g
1973	Na TCP reactor	22	18	<0.03*	0.01	0.03	0.3	0.07	ug/g
1974	Na TCP reactor	19	6	<0.03*	0.03	0.02	0.12	0.03	ug/g
1975	Na TCP reactor	3	2	<0.01	0.01	0.08	0.08	0.08	ug/g
1976	Na TCP reactor	65	21	<0.00905*	0.01	0.006	0.09	0.02	ug/g
1977	Na TCP reactor	84	25	<0.01	0.01	0.01	0.09	0.02	ug/g
1966	TCP tars	16	0	---	34.7	1	170	34.7	ug/g
1967	TCP tars	80	0	---	47.6	12	108	47.6	ug/g
1970	TCP tars	6	0	---	60.4	0.5	190	60.4	ug/g
1971	TCP tars	12	1	<0.5	15.0	1.175	188	17.0	ug/g
1972	TCP tars	61	1	<0.2	0.6	0.1	12	0.7	ug/g
1973	TCP tars	27	0	---	4.5	0.2	140	4.5	ug/g
1974	TCP tars	6	3	<6.9	7.3	10	20	15.2	ug/g
1975	TCP tars	1	0	---	0.68	0.68	0.68	0.68	ug/g
1976	TCP tars	2	0	---	8.3	8.3	8.3	8.3	ug/g
1977	TCP tars	22	5	<0.09*	1.9	0.1	10	2.8	ug/g
1978	TCP tars	15	3	<0.1	1.8	0.005	6	2.5	ug/g

Table B-4

Site Nine 2,4,5-TCP Process: Exposure Factor and Surface Wipe Comparison 1972

Process Area	No. of Wipes	% Det. Wipe	Exposure Factor	GM of Wipe	Material TCDD conc
Control room area	4	0.25	0.00	0.04	0.016
Intermediate storage	3	0.33	0.25	0.08	0.015
Lab area	16	0.31	0.25	0.04	0.117
Locker room area	4	0.25	0.00	0.04	0.016
Lunchroom area	4	0.25	0.00	0.04	0.016
Packaging area	4	0.00	0.25	<0.08*	0.016
Reactor area	27	0.26	0.25	0.04	0.015
Shop area	7	0.14	0.25	0.04	0.117
TCP finishing area	4	0.50	0.25	0.24	0.016
Waste oil dempster area	42	0.43	0.50	0.11	0.636

Table B-5

Site Nine 2,4,5-TCP Process: Exposure Factor and Wipe Surface Comprison 1973

Process Area	No. of Wipes	% Det. Wipe	Exposure Factor	GM of Wipe	Material TCDD conc
Control room area	3	0.00	0.00	<1.0	0.004
Lab area	12	0.00	0.25	<1.0	0.749
Locker room area	3	0.00	0.00	<1.0	0.004
Lunchroom area	3	0.00	0.00	<1.0	0.004
Packaging area	2	0.00	0.25	<1.0	0.004
Reactor area	29	0.03	0.25	0.49	0.014
Shop area	6	0.00	0.25	<1.0	0.749
TCP finishing area	3	0.00	0.25	<1.0	0.004
Waste oil dempster area	26	0.08	0.50	0.50	4.454

Table B-6

Site Nine 2,4,5-TCP Process: Exposure Factor and Wipe Surface Comparison 1975

Process Area	No. of Wipes	% Det. Wipe	Exposure Factor	GM of Material Wipe	TCDD
Control room area	1	0	0.00	<0.05	0.005
Intermediate storage	3	0	0.25	<0.1	0.013
Lab area	4	0	0.25	<0.05	0.120
Locker room area	1	0	0.00	<0.05	0.005
Lunchroom area	1	0	0.00	<0.05	0.005
Packaging area	1	0	0.25	<0.1	0.005
Reactor area	9	0	0.25	<0.1*	0.013
Shop area	3	0	0.25	<0.12	0.120
Waste oil dempster area	5	0	0.25	<0.1	0.680

Table B-7

Site Nine 2,4,5-TCP Process: Exposure Factor and Surface Wipe Comparison 1976

Process Area	No. of Wipes	% Det. Wipe	Exposure Factor	GM of Wipe	Material TCDD conc
Control room area	3	0.00	0.00	<0.15*	0.005
Lab area	13	0.08	0.25	0.05	1.390
Locker room area	3	0.00	0.00	<0.15*	0.005
Lunchroom area	5	0.00	0.00	<0.17*	0.005
Packaging area	2	1.00	0.25	2.97	0.005
Reactor area	26	0.08	0.25	0.06	0.012
Shop area	7	0.29	0.25	0.15	1.390
TCP finishing area	17	0.41	0.25	0.22	0.005
Waste oil dempster area	23	0.17	0.50	0.12	8.300

Table B-8

Site Nine 2,4,5-TCP Process: Exposure Factor and Surface Wipe Comparison 1977

Process Area	No. of Wipes	% Det. Wipe	Exposure Factor	GM of Wipe	Material TCDD conc
Anisole decantation area	4	0.50	0.50	0.43	1.938
Control room area	4	0.00	0.00	<0.2*	0.002
Intermediate storage	27	0.11	0.25	0.08	0.012
Lab area	19	0.05	0.25	0.07	0.033
Locker room area	12	0.00	0.00	<0.1*	0.002
Lunchroom area	15	0.00	0.00	<0.2*	0.002
Packaging area	1	1.00	0.25	0.40	0.002
Reactor area	27	0.15	0.25	0.49	0.012
Shop area	20	0.25	0.25	0.12	0.033
TCP finishing area	29	0.14	0.25	0.04	0.002
Waste oil dempster area	38	0.21	0.50	0.25	1.938

Table B-9

Site Nine 2,4,5-TCP Process: Exposure Factor and Surface Wipe Comparison 1976

Process Area	No. of Wipes	% Det. Wipe	Exposure Factor	GM of Wipe	Material TCDD conc
Anisole decantation area	4	1.00	0.50	7.1	1.822
Control room area	2	0.00	0.00	<0.1	0.005
Lab area	18	0.00	0.25	<0.1	0.310
Locker room area	14	0.00	0.00	<0.1	0.005
Lunchroom area	10	0.00	0.00	<0.1	0.005
Packaging area	1	0.00	0.25	<0.1	0.005
Reactor area	36	0.19	0.25	0.07	0.012
Shop area	14	0.21	0.25	0.09	0.310
TCP finishing area	16	0.31	0.25	0.1	0.005
Waste oil dempster area	24	0.33	0.50	0.3	1.822

Table B-10

Site Nine 2,4,5-TCP Process: Exposure Factor and Surface Wipe Comparison 1972-1979

Process Area	Years	No. of Wipes	% Det. Wipe	Exposure Factor	GM of Wipe	Material TCDD conc
Anisole decantation area	77-79	13	0.69	0.50	1.92	2.788
Control room area	72-79	24	0.17	0.00	0.04	0.006
Intermediate storage area	72-79	43	0.19	0.25	0.07	0.015
Lab area	72-79	113	0.15	0.25	0.05	0.295
Locker room area	72-79	52	0.06	0.00	0.04	0.006
Lunchroom area	72-79	50	0.08	0.00	0.04	0.006
Packaging area	72-79	13	0.31	0.25	0.42	0.006
Reactor area	72-79	217	0.15	0.25	0.14	0.015
Shop area	72-79	74	0.22	0.25	0.11	0.295
TCP finishing area	72-79	78	0.26	0.25	0.16	0.006
Waste oil dempster area	72-79	222	0.29	0.50	0.18	2.788

Table B-11

Site Nine 2,4,5-TCP Process: Uniform Task Title Directory 1970

Task Code	Task Decription	Task Time	Task TCDD Conc.	Mat. Exposure Factor	Task Dioxin Rating
10.1	Take readings & survey outside equipment	0.0625	0.248	0.32	0.0050
10.2	Sample 2,4,5-TCP & basic brine streams & check pH	0.0625	0.248	0.25	0.0039
10.3	Sample MeOH reflux and shot tank	0.0625	0.248	0.25	0.0039
10.4	Transfer 2,4,5-TCP & make stick measurements	0.0625	0.248	0.25	0.0039
10.5	Load Tank cars with 2,4,5-TCP	0.0250	0.248	0.25	0.0016
10.6	Unload MeOH truck, collect samples & identify raw material	0.0125	0.000	0.00	0.0000
10.7	Receive TCB & stick measure storage tank	0.0104	0.000	0.00	0.0000
10.8	Empty ortho scrubber	0.0014	60.400	0.25	0.0211
10.9	Sample anisole storage tank	0.0010	60.400	0.50	0.0314
10.10	Set valves,start & stop pumps	0.0625	0.248	0.32	0.0050
10.11	Perform minor maintenance & line unplugging	0.0625	20.629	0.28	0.3610
10.12	Check cooling tower water for phenolics	0.0156	0.248	0.25	0.0010
10.13	Take readings & adjust instruments	0.1250	0.000	0.00	0.0000
10.14	Initiate loading of reactor & start-up equipment	0.0625	0.000	0.00	0.0000
10.15	Repair leaks & replace worn mechanical equipment	0.1250	20.629	0.32	0.8252
10.16	Add water treatment chemicals to cooling tower	0.0083	0.248	0.25	0.0005
10.17	Oversee 2,4,5-TCP plant operations, infrequently in plant	0.0813	0.248	0.25	0.0050
10.18	Oversee 2,4,5-TCP plant operations, frequently in plant	0.7313	0.248	0.25	0.0453
10.19	General work throughout plant	0.7313	0.248	0.25	0.0453
10.20	Deliver 2,4,5-TCP samples to lab	0.1250	0.248	0.25	0.0078

Table B-12

Site Nine Uniform Task Title Directory: 2,4,5-TCP Process 1972

UT Code	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	UT Exposure Factor	UT Dioxin Rating
10.1	Take readings & survey outside equipment	0.0625	0.220	0.32	0.0044
10.2	Sample 2,4,5-TCP & basic brine streams & check pH	0.0625	0.015	0.25	0.0002
10.3	Sample MeOH reflux and shot tank	0.0625	0.015	0.25	0.0002
10.4	Transfer 2,4,5-TCP & make stick measurements	0.0625	0.016	0.25	0.0003
10.5	Load Tank cars with 2,4,5-TCP	0.0250	0.016	0.25	0.0001
10.6	Unload MeOH truck, collect samples & identify raw material	0.0125	0.000	0.00	0.0000
10.7	Receive TCB & stick measure storage tank	0.0104	0.000	0.00	0.0000
10.8	Empty ortho scrubber	0.0014	0.636	0.25	0.0002
10.9	Sample anisole storage tank	0.0010	0.636	0.50	0.0003
10.10	Set valves,start & stop pumps	0.0625	0.220	0.32	0.0044
10.11	Perform minor maintenance & line unplugging	0.0625	0.220	0.28	0.0039
10.12	Check cooling tower water for phenolics	0.0156	0.015	0.25	0.0001
10.13	Take readings & adjust instruments	0.1250	0.000	0.00	0.0000
10.14	Initiate loading of reactor & start-up equipment	0.0625	0.000	0.00	0.0000
10.15	Repair leaks & replace worn mechanical equipment	0.1250	0.220	0.32	0.0088
10.16	Add water treatment chemicals to cooling tower	0.0083	0.015	0.25	0.00003
10.17	Oversee 2,4,5-TCP plant operations, infrequently in plant	0.0813	0.220	0.25	0.0045
10.18	Oversee 2,4,5-TCP plant operations, frequently in plant	0.7313	0.220	0.25	0.0402
10.19	General work throughout plant	0.7313	0.220	0.25	0.0402
10.20	Deliver 2,4,5-TCP samples to lab	0.1250	0.016	0.25	0.0005

Table B-13

Site Nine Uniform Task Directory: 2,4,5-TCP Process 1973

UT Code	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	UT Exposure Factor	UT Dioxin Rating
10.1	Take readings & survey outside equipment	0.0625	0.009	0.32	0.0002
10.2	Sample 2,4,5-TCP & basic brine streams & check pH	0.0625	0.014	0.25	0.0002
10.3	Sample MeOH reflux and shot tank	0.0625	0.014	0.25	0.0002
10.4	Transfer 2,4,5-TCP & make stick measurements	0.0625	0.004	0.25	0.0001
10.5	Load Tank cars with 2,4,5-TCP	0.0250	0.004	0.25	0.00003
10.6	Unload MeOH truck, collect samples & identify raw material	0.0125	0	0	0.0000
10.7	Receive TCB & stick measure storage tank	0.0104	0	0	0.0000
10.8	Empty ortho scrubber	0.0014	4.454	0.25	0.0016
10.9	Sample anisole storage tank	0.0010	4.454	0.5	0.0023
10.10	Set valves,start & stop pumps	0.0625	0.009	0.32	0.0002
10.11	Perform minor maintenance & line unplugging	0.0625	1.491	0.28	0.0261
10.12	Check cooling tower water for phenolics	0.0156	0.014	0.25	0.0001
10.13	Take readings & adjust instruments	0.1250	0	0	0.0000
10.14	Initiate loading of reactor & start-up equipment	0.0625	0	0	0.0000
10.15	Repair leaks & replace worn mechanical equipment	0.1250	1.491	0.32	0.0596
10.16	Add water treatment chemicals to cooling tower	0.0083	0.014	0.25	0.00003
10.17	Oversee 2,4,5-TCP plant operations, infrequently in plant	0.0813	0.009	0.25	0.0002
10.18	Oversee 2,4,5-TCP plant operations, frequently in plant	0.7313	0.009	0.25	0.0016
10.19	General work throughout plant	0.7313	0.009	0.25	0.0016
10.20	Deliver 2,4,5-TCP samples to lab	0.1250	0.004	0.25	0.0001

Table B-14

Site Nine Occupational Title Directory: 2,4,5-TCP Process 1974

UT Code	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	Task Exposure Factor	UT Dioxin Rating
10.1	Take readings & survey outside equipment	0.063	0.018	0.32	0.0004
10.2	Sample 2,4,5-TCP & basic brine streams & check pH	0.063	0.027	0.25	0.0004
10.3	Sample MeOH reflux and shot tank	0.063	0.027	0.25	0.0004
10.4	Transfer 2,4,5-TCP & make stick measurements	0.063	0.008	0.25	0.0001
10.5	Load Tank cars with 2,4,5-TCP	0.025	0.008	0.25	0.0001
10.6	Unload MeOH truck, collect samples & identify raw material	0.013	0.000	0.00	0.0000
10.7	Receive TCB & stick measure storage tank	0.010	0.000	0.00	0.0000
10.8	Empty ortho scrubber	0.001	7.343	0.25	0.0026
10.9	Sample anisole storage tank	0.001	7.343	0.50	0.0038
10.10	Set valves,start & stop pumps	0.063	0.018	0.32	0.0004
10.11	Perform minor maintenance & line unplugging	0.063	2.459	0.28	0.0430
10.12	Check cooling tower water for phenolics	0.016	0.027	0.25	0.0001
10.13	Take readings & adjust instruments	0.125	0.000	0.00	0.0000
10.14	Initiate loading of reactor & start-up equipment	0.063	0.000	0.00	0.0000
10.15	Repair leaks & replace worn mechanical equipment	0.125	2.459	0.32	0.0384
10.16	Add water treatment chemicals to cooling tower	0.008	0.027	0.25	0.0001
10.17	Oversee 2,4,5-TCP plant operations, infrequently in plant	0.081	0.018	0.25	0.0004
10.18	Oversee 2,4,5-TCP plant operations, frequently in plant	0.731	0.018	0.25	0.0033
10.19	General work throughout plant	0.731	0.018	0.25	0.0033
10.20	Deliver 2,4,5-TCP samples to lab	0.125	0.008	0.25	0.0003

Table B-15

Site Nine Uniform Task Directory: 2,4,5-TCP Process 1975

UT Code	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	UT Exposure Factor	UT Dioxin Rating
10.1	Take readings & survey outside equipment	0.0625	0.009	0.32	0.00018
10.2	Sample 2,4,5-TCP & basic brine streams & check pH	0.0625	0.013	0.25	0.00020
10.3	Sample MeOH reflux and shot tank	0.0625	0.013	0.25	0.00020
10.4	Transfer 2,4,5-TCP & make stick measurements	0.0625	0.005	0.25	0.00006
10.5	Load Tank cars with 2,4,5-TCP	0.025	0.005	0.25	0.00003
10.6	Unload MeOH truck, collect samples & identify raw material	0.0125	0	0	0.00000
10.7	Receive TCB & stick measure storage tank	0.0104	0	0	0.00000
10.8	Empty ortho scrubber	0.0014	0.68	0.25	0.00024
10.9	Sample anisole storage tank	0.00104	0.68	0.5	0.00035
10.10	Set valves,start & stop pumps	0.0625	0.009	0.32	0.00018
10.11	Perform minor maintenance & line unplugging	0.0625	0.233	0.28	0.00408
10.12	Check cooling tower water for phenolics	0.0156	0.013	0.25	0.00005
10.13	Take readings & adjust instruments	0.125	0	0	0.00000
10.14	Initiate loading of reactor & start-up equipment	0.0625	0	0	0.00000
10.15	Repair leaks & replace worn mechanical equipment	0.125	0.233	0.32	0.00932
10.16	Add water treatment chemicals to cooling tower	0.0083	0.013	0.25	0.00003
10.17	Oversee 2,4,5-TCP plant operations, infrequently in plant	0.08125	0.009	0.25	0.00018
10.18	Oversee 2,4,5-TCP plant operations, frequently in plant	0.73125	0.009	0.25	0.00165
10.19	General work throughout plant	0.73125	0.009	0.25	0.00165
10.20	Deliver 2,4,5-TCP samples to lab	0.125	0.005	0.25	0.00016

Table B16

Site Nine Uniform Task Directory: 2,4,5-TCP Process 1976

UT Code	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	UT Exposure Factor	UT Dioxin Rating
10.1	Take readings & survey outside equipment	0.062	0.008	0.32	0.00016
10.2	Sample 2,4,5-TCP & basic brine streams & check pH	0.062	0.012	0.25	0.00019
10.3	Sample MeOH reflux and shot tank	0.062	0.012	0.25	0.00019
10.4	Transfer 2,4,5-TCP & make stick measurements	0.062	0.005	0.25	0.00008
10.5	Load Tank cars with 2,4,5-TCP	0.025	0.005	0.25	0.00003
10.6	Unload MeOH truck, collect samples & identify raw material	0.012	0.000	0.00	0.00000
10.7	Receive TCB & stick measure storage tank	0.010	0.000	0.00	0.00000
10.8	Empty ortho scrubber	0.001	8.300	0.25	0.00291
10.9	Sample anisole storage tank	0.001	8.300	0.50	0.00432
10.10	Set valves,start & stop pumps	0.062	0.008	0.32	0.00016
10.11	Perform minor maintenance & line unplugging	0.062	2.772	0.28	0.04651
10.12	Check cooling tower water for phenolics	0.015	0.012	0.25	0.00005
10.13	Take readings & adjust instruments	0.125	0.000	0.00	0.00000
10.14	Initiate loading of reactor & start-up equipment	0.062	0.000	0.00	0.00000
10.15	Repair leaks & replace worn mechanical equipment	0.125	2.772	0.32	0.11088
10.16	Add water treatment chemicals to cooling tower	0.008	0.012	0.25	0.00002
10.17	Oversee 2,4,5-TCP plant operations, infrequently in plant	0.061	0.008	0.25	0.00061
10.18	Oversee 2,4,5-TCP plant operations, frequently in plant	0.731	0.008	0.25	0.00146
10.19	General work throughout plant	0.731	0.008	0.25	0.00146
10.20	Deliver 2,4,5-TCP samples to lab	0.125	0.005	0.25	0.00016

Table B-17

Site Nine Uniform Task Directory: 2,4,5-TCP Process 1977

UT Code	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	UT Exposure Factor	UT Dioxin Rating
10.1	Take readings & survey outside equipment	0.062	0.007	0.32	0.00014
10.2	Sample 2,4,5-TCP & basic brine streams & check pH	0.062	0.012	0.25	0.00019
10.3	Sample MeOH reflux and shot tank	0.062	0.012	0.25	0.00019
10.4	Transfer 2,4,5-TCP & make stick measurements	0.062	0.002	0.25	0.00003
10.5	Load Tank cars with 2,4,5-TCP	0.025	0.002	0.25	0.00001
10.6	Unload MeOH truck, collect samples & identify raw material	0.012	0.000	0.00	0.00000
10.7	Receive TCB & stick measure storage tank	0.010	0.000	0.00	0.00000
10.8	Empty ortho scrubber	0.001	1.938	0.25	0.00068
10.9	Sample anisole storage tank	0.001	1.938	0.50	0.00101
10.10	Set valves,start & stop pumps	0.062	0.007	0.32	0.00014
10.11	Perform minor maintenance & line unplugging	0.062	0.651	0.28	0.01139
10.12	Check cooling tower water for phenolics	0.015	0.012	0.28	0.00005
10.13	Take readings & adjust instruments	0.125	0.000	0.00	0.00000
10.14	Initiate loading of reactor & start-up equipment	0.062	0.000	0.00	0.00000
10.15	Repair leaks & replace worn mechanical equipment	0.125	0.651	0.32	0.02604
10.16	Add water treatment chemicals to cooling tower	0.008	0.012	0.25	0.00002
10.17	Oversee 2,4,5-TCP plant operations, infrequently in plant	0.081	0.007	0.25	0.00014
10.18	Oversee 2,4,5-TCP plant operations, frequently in plant	0.731	0.007	0.25	0.00126
10.19	General work throughout plant	0.731	0.007	0.25	0.00128
10.20	Deliver 2,4,5-TCP samples to lab	0.125	0.002	0.25	0.00006

Table B-18

Site Nine Uniform Task Directory: 2,4,5-TCP Process 1976

UT Code	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	UT Exposure Factor	UT Dioxin Rating
10.1	Take readings & survey outside equipment	0.062	0.008	0.32	0.00016
10.2	Sample 2,4,5-TCP & basic brine streams & check pH	0.062	0.012	0.25	0.00019
10.3	Sample MeOH reflux and shot tank	0.062	0.012	0.25	0.00019
10.4	Transfer 2,4,5-TCP & make stick measurements	0.062	0.005	0.25	0.00008
10.5	Load Tank cars with 2,4,5-TCP	0.025	0.005	0.25	0.00003
10.6	Unload MeOH truck, collect samples & identify raw material	0.012	0.000	0.00	0.00000
10.7	Receive TCB & stick measure storage tank	0.010	0.000	0.00	0.00000
10.8	Empty ortho scrubber	0.001	1.822	0.25	0.00064
10.9	Sample anisole storage tank	0.001	1.822	0.50	0.00095
10.10	Set valves,start & stop pumps	0.062	0.008	0.32	0.00016
10.11	Perform minor maintenance & line unplugging	0.062	0.613	0.28	0.01073
10.12	Check cooling tower water for phenolics	0.015	0.012	0.25	0.00005
10.13	Take readings & adjust instruments	0.125	0.000	0.00	0.00000
10.14	Initiate loading of reactor & start-up equipment	0.062	0.000	0.00	0.00000
10.15	Repair leaks & replace worn mechanical equipment	0.125	0.613	0.32	0.02452
10.16	Add water treatment chemicals to cooling tower	0.003	0.012	0.25	0.00002
10.17	Oversee 2,4,5-TCP plant operations, infrequently in plant	0.081	0.008	0.25	0.00016
10.18	Oversee 2,4,5-TCP plant operations, frequently in plant	0.731	0.008	0.25	0.00146
10.19	General work throughout plant	0.731	0.008	0.25	0.00146
10.20	Deliver 2,4,5-TCP samples to lab	0.125	0.005	0.25	0.00016

Table B-19

Site Nine 2,4,5-TCP Process: Occupational Title Directory 1970

OT Code	Occupational Title	OT Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
1010	Superintendent	0.504	10.17
1011	Assist. Superintendent	0.504	10.17
1040	Foreman	4.534	10.18
1035	Utility Man Class 1	107.468	(10.1+10.2+...+10.14)*.569+10.15+10.16
1043	Trichlorophenol Operator	43.665	10.1+10.2+...+10.14

Table B-20

Site Nine 2,4,5-TCP Process: Occupational Title Directory 1972

OT Code	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
1010	Superintendent	0.447	10.17
1011	Assist. Superintendent	0.447	10.17
1040	Foreman	4.022	10.18
1035	Utility Man Class 1	0.842	(10.1+10.2+...+10.14)*.569+10.15+10.16
1043	Trichlorophenol Operator	1.408	10.1+10.2+...+10.14

Table B-21

Site Nine 2,4,5-TCP Process: Occupational Title Directory 1973

OT Code	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
1010	Superintendent	0.018	10.17
1012	Techn. Supr.	0.165	10.18
1035	Utility Man Class 1	3.863	(10.1+10.2+...+10.14)*.569+10.15+10.16
1043	Trichlorophenol Operator	1.545	10.1+10.2+...+10.14

Table B-22

Site Nine 2,4,5-TCP Process: Occupational Title Directory 1974

OT Code	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
1010	Prodn. Superintendent	0.037	10.17
1040	Foreman	0.329	10.18
1035	Utility Man Class 1	6.379	(10.1+10.2+...+10.14)*.569+10.15+10.16
1043	Trichlorophenol Operator	5.126	10.1+10.2+...+10.14
1046	Loader Lorry Operator	0.329	10.6+10.7+10.14+10.19

Table B-23

Site Nine 2,4,5-TCP Process: Occupational Title Directory 1975

OT Code	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
1010	Prodn. Superintendent	0.018	10.17
1040	Foreman	0.165	10.18
1035	Spare (Utility Man Class 1)	1.253	(10.1+10.2+...+10.14)*.569+10.15+10.16
1043	Trichlorophenol Operator	0.560	10.1+10.2+...+10.14
1046	Loader Lorry Operator	0.165	10.6+10.7+10.14+10.19

Table B-24

Site Nine 2,4,5-TCP Process: Occupational Title Directory 1976

OT Code	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
1010	Prodn. Superintendent	0.016	10.17
1013	Sr. Prodn. Engineer	0.146	10.18
1040	Foreman	0.146	10.18
1035	Spare (Utility Man Class 1)	14.310	(10.1+10.2+...+10.14)*.569+10.15+10.16
1043	Trichlorophenol Operator	5.658	10.1+10.2+...+10.14
1046	Loader Lorry Operator	0.146	10.6+10.7+10.14+10.19

Table B-25

Site Nine 2,4,5-TCP Process: Occupational Title Directory 1977

OT Code	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
1010	Superintendent	0.014	10.17
1011	Prodn. Superintendent	0.128	10.18
1040	Foreman	0.128	10.18
1035	Spare (Utility Man Class 1)	3.393	(10.1+10.2+...+10.14)*.569+10.15+10.16
1043	Trichlorophenol Operator	1.383	10.1+10.2+...+10.14

Table B-26

Site Nine 2,4,5-TCP Process: Occupational Title Directory 1978

OT Code	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
1010	Superintendent	0.016	10.17
1013	Sr. Productin Engineer	0.146	10.18
1040	Foreman	0.146	10.18
1035	Spare (Utility Man Class 1)	3.204	(10.1+10.2+...+10.14)*.569+10.15+10.16
1043	Trichlorophenol Operator	1.316	10.1+10.2+...+10.14
1041	Alternate	1.883	1035*.30+1043*.70

TABLE B-27

te Nine Uniform Task Directory: 2,4,5-T Acid and Acid Ester Process 1965

de	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	UT Exposure Factor	UT Dioxin Rating
.1	Operate 2,4,5-T reactor	0.500	0.50	0.25	0.0625
.2	Sample 2,4,5-T reactor	0.063	0.50	0.25	0.0078
.3	Wash 2,4,5-T reactor	0.063	0.50	0.25	0.0078
.4	pH sampling	0.063	0.50	0.25	0.0078
.5	Operating TCP recovery system	0.031	0.50	0.25	0.0039
.6	Bleach titer sampling	0.125	0.50	0.25	0.0156
.7	Operate drier	0.200	0.56	0.50	0.0560
.8	Clean hammer mill	0.050	0.56	0.75	0.0210
.9	Label packages	0.156	0.56	0.25	0.0219
.10	Package 2,4,5-T acid	0.375	0.56	0.50	0.1050
.11	Rake 2,4,5-T acid	0.063	0.56	0.50	0.0175
.12	Sample acidifiers	0.031	0.56	0.25	0.0044
.13	Operae 48" wheel	0.469	0.56	0.25	0.0656
.14	Plow 48" wheel	0.188	0.56	0.50	0.0525
.15	Air chip 48" wheel	0.094	0.56	0.50	0.0263
.16	Operate 48" wheel box	0.063	0.56	0.25	0.0088
.17	Operate 40" wheel	0.470	0.56	0.25	0.0657
.18	Plow 40" wheel	0.094	0.56	0.50	0.0263
.19	Operate 40" wheel box	0.094	0.56	0.25	0.0131
.20	Air chip 40" wheel	0.094	0.56	0.50	0.0263
.21	Load esterifier	0.125	0.56	0.25	0.0175
.22	Operate esterifier	0.438	0.53	0.25	0.0580
.23	Sample esterifier	0.062	0.50	0.25	0.0078
.24	Wash esterifier	0.062	0.53	0.25	0.0082
.25	Transfer esters to tank farm	0.062	0.50	0.25	0.0078
.26	Oversees processes,	0.609	0.52	0.25	0.0792

Table B-28

te Nine Occupational Title Directory: 2,4,5-T Acid and Acid Ester Process 1965

de	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
70	Foreman	7.92	70.25
71	Alternate	14.97	avg(7073,7074,7075,7076)
73	2,4,5-T Reactor Operator	8.98	70.1+70.2+70.3+70.4+70.5+70.6
74	Na 2,4,5-T Wheel Operator	11.39	70.17+70.18+70.19+70.20
75	2,4,5-T Acid Wheel Operat	16.63	70.12+70.13+70.14+70.15+70.16
76	2,4,5-T Drier Operator	21.95	70.7+70.8+70.9+70.10+70.11
84	2,4,5-T Ester Operator	9.93	70.21+70.22+70.23+70.24

TABLE B-29

te Nine Uniform Task Directory: 2,4,5-T Acid and Acid Ester Process 1970

de	Uniform Task Decription	UT Time	UT Mat. TCDD Conc.	UT Exposure Factor	UT Dioxin Rating
.1	Operate 2,4,5-T reactor	0.500	0.26	0.25	0.0325
.2	Sample 2,4,5-T reactor	0.063	0.25	0.25	0.0039
.3	Wash 2,4,5-T reactor	0.063	0.24	0.25	0.0038
.4	pH sampling	0.063	0.26	0.25	0.0041
.5	Operating TCP recovery system	0.031	0.24	0.25	0.0019
.6	Bleach titer sampling	0.125	0.24	0.25	0.0075
.7	Operate drier	0.200	0.24	0.50	0.0240
.8	Clean hammer mill	0.050	0.24	0.75	0.0090
.9	Label packages	0.156	0.24	0.25	0.0094
.10	Package 2,4,5-T acid	0.375	0.24	0.50	0.0450
.11	Rake 2,4,5-T acid	0.063	0.24	0.50	0.0075
.12	Sample acidifiers	0.031	0.24	0.25	0.0019
.13	Operae 48" wheel	0.469	0.24	0.25	0.0281
.14	Plow 48" wheel	0.188	0.24	0.50	0.0225
.15	Air chip 48" wheel	0.094	0.24	0.50	0.0113
.16	Operate 48" wheel box	0.063	0.24	0.25	0.0038
.17	Operate 40" wheel	0.470	0.24	0.25	0.0282
.18	Plow 40" wheel	0.094	0.24	0.50	0.0113
.19	Operate 40" wheel box	0.094	0.24	0.25	0.0056
.20	Air chip 40" wheel	0.094	0.24	0.50	0.0113
.21	Load esterifier	0.125	0.24	0.25	0.0075
.22	Operate esterifier	0.438	0.24	0.25	0.0263
.23	Sample esterifier	0.062	0.23	0.25	0.0036
.24	Wash esterifier	0.062	0.24	0.25	0.0037
.25	Transfer esters to tank farm	0.062	0.23	0.25	0.0036
.26	Oversees process,	0.609	0.24	0.25	0.0365

Table B-30

te Nine Occupational Title Directory: 2,4,5-T Acid and Acid Ester Process 1970

de	Occupational Title	Occupational Title Dioxin Exposure Rating (1E-02)	Uniform Task Codes Associated with the Occupational Title
70	Foreman	3.65	70.25
71	Alternate	6.49	avg(7073,7074,7075,7076)
73	2,4,5-T Reactor Operator	4.61	70.1+70.2+70.3+70.4+70.5+70.6
74	Na 2,4,5-T Wheel Operator	4.88	70.17+70.18+70.19+70.20
75	2,4,5-T Acid Wheel Operat	7.13	70.12+70.13+70.14+70.15+70.16
76	2,4,5-T Drier Operator	9.49	70.7+70.8+70.9+70.10+70.11
84	2,4,5-T Ester Operator	4.46	70.21+70.22+70.23+70.24

TABLE B-31

SITE NINE
UNIFORM TASK DIRECTORY
NaTCP PROCESS 1965

UT CODE	UNIFORM TASK	UT MAT. TIME	UT TCDD	UT EXPO. FACTOR	UT DIOXIN RATING
01.1	Drain TCB line	.008	0	0	0
01.2	Collect crude NaTCP	.083	2.2	.75	0.13695
01.3	Operate stripper column	.438	2.2	.5	0.4818
01.4	Drain organic from stripper column	.031	1828.8	1	56.69281
01.5	Prepare sodium methylate solution	.062	0	0	0
01.6	Operate coil reactor	.438	2.2	.5	0.4818
01.7	Transferred product	.125	2.2	.5	0.1375
01.8	Preform minor maintenance	.062	915.5	1	56.73

TABLE B-32

SITE NINE

OCCUPATIONAL TITLE
NaTCP PROCESS 1965

OT CODE	OCCUPATIONAL TITLE	OT DIOXIN EXPOSURE RATING (1E - 02)	UTs ASSOCIATED WITH OT
0144	TCP Mixer Operator 01.7	5744.9	01.1+01.2+01.3+0.4+01.5
0143	Reactor Operator	5734.9	01.2 + 01.6 + 01.8

APPENDIX C

EXAMPLE OF EXPOSURE ESTIMATION PROCEDURE
PHASE II

To illustrate the procedure for estimating the OT dioxin exposure ratings for a phase 2 (facilities where no industrial hygiene data is available) process, UT and OT directories have been constructed for NaTCP and 2,4,5-T acid process at Site One. Table C-1 is the UT directory for the NaTCP process which operated at Site One, for 1965. The uniform tasks listed in Table C-1 were obtained from an operating manual for the process. The UT times listed the Table C-1 were estimated using the operating manual and the similarities between this process and the old NaTCP process at Site Nine. The UT material dioxin concentration were obtained from analytical data provided by the company which operated Site One. The values reported in the UT material dioxin concentration column are the geometric mean values of analytical data, with ND results being equal to the LOD/2. UT exposure factors were assigned based on the similarities between this process and the old NaTCP process at Site Nine and from accounts detailed in monthly reports obtained from the company. Table C-2 is the OT directory for the NaTCP process which operated at Site One, for 1965. The methods used to calculate the OT dioxin exposure ratings were the same those used for OT directories for Site Nine (Appendix B).

Similarly UT and OT directories Table C-3 and C-4, respectively, were constructed for the 2,4,5-T acid process at Site One. As was the case with the UT directory for the NaTCP process (Table C-1) uniform tasks and UT times were obtained from operating manuals for the 2,4,5-T acid process and comparisons between the 2,4,5-T acid process at Site One to the 2,4,5-T acid process at Site Nine. Table C-4, the OT directory for the 2,4,5-T acid process at Site One, was constructed in the same manner as previous OT directories.

Comparisons of OT dioxin exposure ratings for the TCP Mixer Operator and the Reactor Operator from Site Nine (Table B-32) are somewhat higher than those ratings obtained for the Trichlorophenol Operator from Site One (Table C-2). Comparison of OT dioxin exposure ratings for the 2,4,5-T Reactor Operator and 2,4,5-T Acid Wheel Operator (Table B-28) are similar to those ratings obtained for the 2,4,5-T Reactor Operator and 2,4,5-T Centrifuge Operator from Site One (Table C-4).

TABLE C-1

SITE ONE
UNIFORM TASK DIRECTORY
NaTCP PROCESS 1965

UT CODE	UNIFORM TASK	UT TIME	UT MAT. TCDD CONC.	UT EXPOSURE FACTOR	UT DIOXIN RATING
02.1	Load autoclave reactor	.125	0	.5	0
02.2	Load autoclave reactor	.250	20	.75	3.75
02.3	Collect reactor samples	.062	20	.75	0.93
02.4	Operate MeOH recovery system	.062	0	.5	0
02.5	Operate anisol still and product recovery system	.125	73	1	9.125
02.6	Operate monel screen filter	.062	46.5	.5	1.442
02.7	Transfer NaTCP product	.062	20	.5	0.62
02.8	Perform minor maintenance	.062	46.5	1	2.888

TABLE C-2

SITE ONE
OCCUPATIONAL TITLE PROCESS 1965

OT CODE	OCCUPATIONAL TITLE	OT DIOXIN EXPOSURE RATING	UTs ASSOCIATED WITH OT
0243	TCP Operator	18.75	02.1+02.2+02.3+02.4 02.5+02.6+02.7+02.8

TABLE C-3

UNIFORM TASK DIRECTORY
2,4,5-T ACID PROCESS 1965

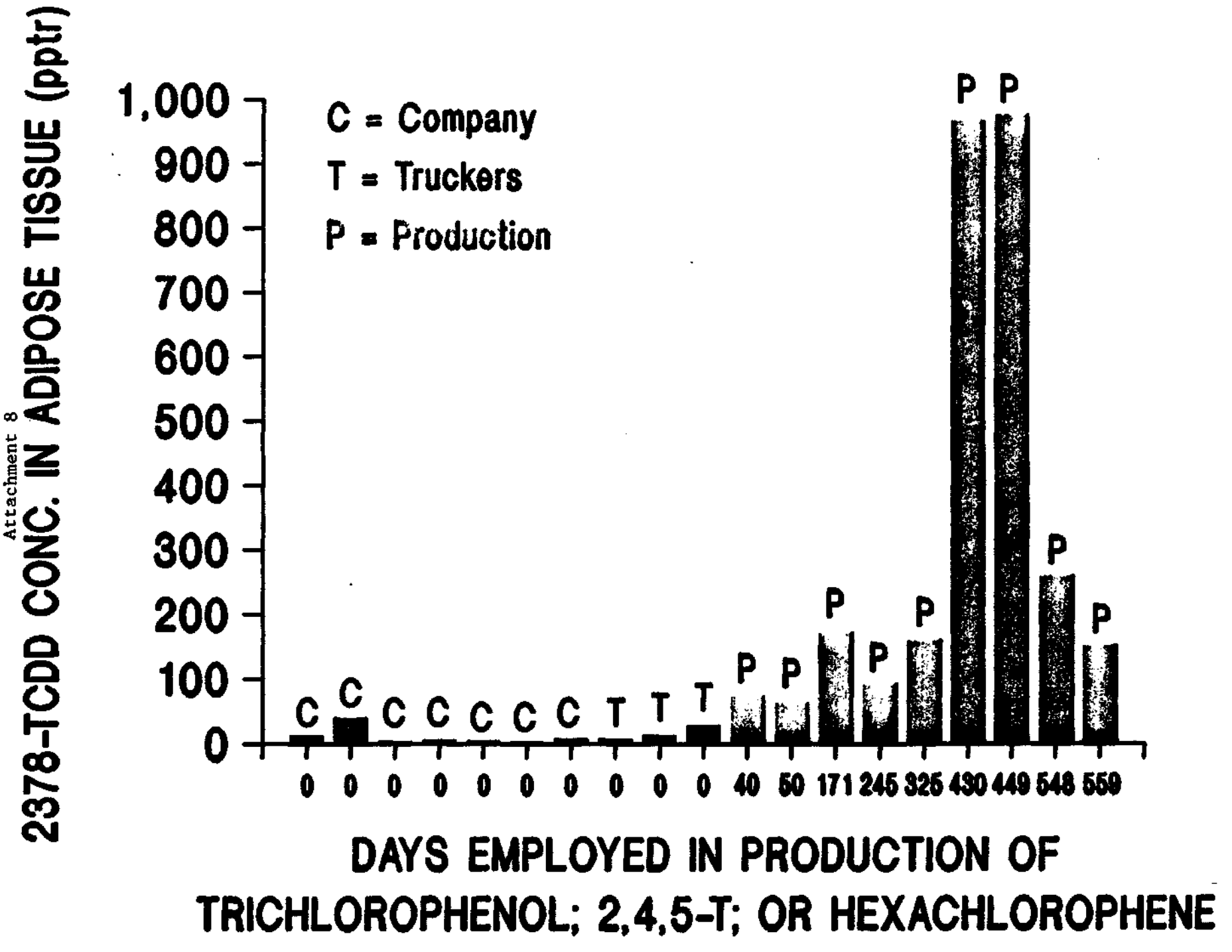
UT CODE	UNIFORM TASK	UT TIME	UT TCDD	EF	UT TCDD RATING
40.1	Load condensation reactor	.125	20.0	.5	1.25
40.2	Operate condensation reactor	.437	11.1	.5	2.425
40.3	Collect reactor samples	.062	11.1	.5	0.344
40.4	Operate NaCl & unreacted organic filtration	.125	20.1	.75	1.875
40.5	Operate reslurry tank	0.125	11.1	.5	.694
40.6	Operate acidification tanks	0.25	11.1	.25	.694
40.7	Operate 2,4,5-TCP recovery and decanter	0.25	20.0	.25	1.25
40.8	Operate wash columns	0.125	11.1	.5	0.694
40.9	Perform minor maintenance	.062	15.6	1	0.967

TABLE C-4

SITE ONE
OCCUPATIONAL TITLE DIRECTORY
2,4,5-T ACID PROCESS 1965

OT CODE	OCCUPATIONAL TITLE	OT DIOXIN EXPOSURE RATING	UTs ASSOCIATED WITH OT
4073	2,4,5-T Reactor Operator	6.861	40.1+40.2+40.3+40.4+40.9
4075	2,4,5-T Centrifuge Operator	7.840	40.5+40.6+40.7+40.8+4-.9

Attachment 8



ATTACHMENT 9

Table 1

Participation of Workers in the In-Home Interviews

as of April 1, 1987

		N
1.	Workers Requested to Participate in the in-home interview.	73
2.	Worker interviews completed.	68 (includes 5 proxy interviews)
	Workers deceased.	2 (proxy interviews)
	Workers medically unable to complete the in-home interview.	3 (proxy interviews)
3.	Workers refused interview.	3
4.	Overall participation rate as of April 1, 1987.	93.2% (68/73)
5.	Worker interviews scheduled but not completed as of April 1.	2
6.	Anticipated participation rate.	95.9% (70/73)

Table 2

Participation of Workers in the Medical Examination
as of April 1, 1987

		N
1.	Workers invited during interview to participate in Medical Exam (does not include 2 deceased).	66
2.	Workers scheduled for or completed medical examination.	52
3.	Workers to be scheduled for examination	5
4.	Workers refused medical examination.*	9
5.	Participation rate for completed exam as of April 1, 1987.	78.8% (52/66)
6.	Anticipated participation rate	86.4% (57/66)

* Reasons for refusals:

Physically or mentally incapacitated	5
Unavailable due to work conflict	1
Unavailable (other reasons)	1
Refused	2

Table 3

Participation of Referents in the In-Home Interview and Medical Examination as of April 1, 1987

		N		
1.	Total number of workers for whom referents have been sought	44		
2.	Number of matched referents agreeing to participate in the interview and the examination.	44	(100%)	
3.	Total number of matched individuals requested to participate in the interview and the examination.	101		
4.	Total # matched individuals requested to participate / # participating referents =	101 / 44	=	2.3

ATTACHMENT 10

Table 1
NUMBER AND PERCENT OF REFERENTS AND NON RESPONDENTS
BY CURRENT ANNUAL INCOME

Table 2
NUMBER AND PERCENT OF REFERENTS AND NON RESPONDENTS
FOR CURRENT HEALTH STATUS

Table 3
NUMBER AND PERCENT OF REFERENTS AND NON RESPONDENTS
BY EDUCATION STATUS

Table 4
NUMBER AND PERCENT OF WORKERS AND REFERENTS
BY CURRENT ANNUAL INCOME

Table 5
NUMBER AND PERCENT OF WORKERS AND REFERENTS
FOR CURRENT HEALTH STATUS

Table 6
NUMBER AND PERCENT OF WORKERS AND REFERENTS
BY EDUCATION STATUS

Table 1

NUMBER AND PERCENT OF REFERENTS AND NON RESPONDENTS
BY CURRENT ANNUAL INCOME

	REFERENTS		NONRESPONDENTS	
ANNUAL INCOME	N	%	N	%
lt 10,000	4	10.5	2	11.1
10,000-19,999	8	21.1	5	27.8
20,000-29,999	12	31.6	4	22.2
30,000-39,999	6	15.8	1	5.6
40,000-49,999	2	5.3	3	16.7
50,000+	5	13.2	3	16.7
refused	1	2.6	0	0

X^2+3.785 df=6 p=.71

Table 2

NUMBER AND PERCENT OF REFERENTS AND NON RESPONDENTS
FOR CURRENT HEALTH STATUS

	REFERENTS		NONRESPONDENTS	
CURRENT HEALTH STATUS	N	%	N	%
EXCELLENT	13	34.2	6	33.3
GOOD	17	44.7	7	38.9
FAIR	6	15.8	2	11.1
POOR	2	5.3	2	11.1
NO ANSWER	0	0	1	5.5

$X^2=3.039$ df=4 p=.55

Table 3

NUMBER AND PERCENT OF REFERENTS AND NON RESPONDENTS
BY EDUCATION STATUS

EDUCATION STATUS	REFERENTS		NONRESPONDENTS	
	N	%	N	%
1-8 YEARS	7	18.4	3	16.7
9-12 YEARS	17	44.7	9	50.0
VOCATIONAL/TECHNICAL SCHOOL	3	7.9	0	0
SOME COLLEGE	11	28.9	6	33.3

X^2=1.701 df=3 p=.63

Table 4

NUMBER AND PERCENT OF WORKERS AND REFERENTS

BY CURRENT ANNUAL INCOME

	WORKERS		REFERENTS	
ANNUAL INCOME	N	%	N	%
1t 10,000	7	11.1	4	10.5
10,000 - 19,000	13	20.6	8	21.1
20,000 - 29,999	8	12.7	12	31.6
30,000 - 39,999	13	20.6	6	15.8
40,000 - 49,999	10	15.9	2	5.3
50,000+	9	14.3	5	13.2
refused	3	4.8	1	2.6

$x^2 = 5.735$ df = 6 p = .45

Table 5

NUMBER AND PERCENT OF WORKERS AND REFERENTS

BY CURRENT HEALTH STATUS

	WORKERS		REFERENTS	
HEALTH STATUS	N	%	N	%
Excellent	14	22.2	13	34.2
Good	28	44.4	17	44.7
Fair	15	23.8	6	15.8
Poor	6	9.5	2	5.3

$x^2 = 5.933$ df = 3 p = .12

Table 6

NUMBER AND PERCENT OF WORKERS AND REFERENTS

BY EDUCATION STATUS

	WORKERS		REFERENTS	
EDUCATION STATUS	N	%	N	%
1 - 8 years	7	11.0	7	18.4
9 - 12 years	28	44.4	17	44.7
Vocational/Technical School	2	3.2	3	7.9
Some College	26	41.3	11	28.9

$x^2 = 3.217$ df = 3 p = .36