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Report/Article Title Scientific Activity Reports and Tables, 1980

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Description Notes Reports on scientific activities, related to phenoxy herbicides and contaminants, being conducted in agencies throughout the government.

DEPARTMENT OF AGRICULTURE

Interagency Work Group on Phenoxy Herbicides and Contaminants

Title of Activity	Funding		
	FY80	FY81	FY82
1. TCDD Residue Monitoring in Deer (Forest Service, Summer 1980)	$1,200*		
2. 2,4-D Human Exposure Study (SEA-AR-NER-BARC-AEQI; December 1980)	85,000		
3. Participation in Study of Herbicides and Spontaneous Abortions being Conducted by SRI International (October 1980)	100,000		

* All data collection completed in FY 79. Only report preparation to be done in FY 80.

NOTE: Proposed Epidemiology Feasibility Study among U.S. Forest Service Employees was cancelled.

ENVIRONMENTAL PROTECTION AGENCY

SCIENTIFIC ACTIVITY REPORT -- FUNDING

Interagency Work Group on Phenoxy Herbicides and Contaminants

Title of Activity	Funding			
	FY80	FY81	FY82	FY83
1. Biodegradation and Carbon Adsorption of TCDD (ORD: Completed)	10 K			
2. National Water Monitoring Survey (OPTS; Ongoing)	300 K*	300K*	300 K*	
3. Health and Nutrition Examination Survey II (OPTS; December 1982)	200 K*	200 K*	200 K*	
4. Microbial Dissimilation of 2,3,7,8 TCDD (ORD; March 1981)	75 K			
5. Hemlock, Mi Study (DMP; November 1980)	30 K**			
6. San Antonio Analyses (DMP; November 1980)	1.5K**			
7. Northwest Human Milk Study (DMP; Completed)	77 K**			
8. Oregon Water and Sediment Study (DMP; September 1980)	38 K**			
9. Region X Deer and Elk Study (DMP; August 1980)	13 K**			

Title of Activity	Funding			
	FY80	FY81	FY82	FY83
10. ALSEA Phase II (DMP: Fall 1980)	15 K**			
11. Wisconsin Soil Study (DMP; Completed)	22 K**			
12. Wisconsin Monkey Study (DMP; October 1980)	39 K**			
13. Oregon Monkey Study (DMP; October 1980)	30 K**			
14. Mississippi Catfish Study (DMP; October 1980)	19 K**			
15. Louisiana Crayfish and Catfish Study (DMP; Fall 1980)	46 K**			
16. Nebraska Adipose Tissue Study (DMP; Completed)	6 K**			
17. Midland Michigan Study (DMP; September 1980)	11 K**			
18. Beef Fat Phase II (DMP; September 1980)	28 K**			

* These monitoring programs analyze for 30-40 different chemical compounds, one of which is the phenoxy herbicide 2,4,5-T

** The DMP, Dioxin Monitoring Program, is an ongoing program within the agency. Each of the individaul studies is completed within a relatively short period of time. The specific studies to be conducted in the future cannot be anticipated

SCIENTIFIC ACTIVITY REPORT -- FUNDING -- HHS

Interagency Work Group on Phenoxy Herbicides and Contaminants

Scientific Activity	Funding ($000)					
	FY80	FY81	FY82	FY83	FY84	FY85
1. Investigation of a leukemia cluster in Madison County, Kentucky allegedly associated with pentachlorophenal-treated ammunition boxes at the Blue Grass Army Depot (NIOSH; July 1981)	10	10	-	-	-	-
2. Bioassay of Octachlorodibenzo-p-dioxin (NIEHS; July 1985)	-	75	75	75	75	-
3. Dioxin registry (NIOSH; June 1983)	75	125	125	125	125 1/	125 1/
4. Investigation of alleged cluster of birth defects in families of Teamsters Union employees of the Long Island Railroad (NIOSH; December 1980)	10	10	-	-	-	-
5. Bioassay of 2,3,7,8-Tetrachloro-dibenzo-p-dioxin for possible carcinogenicity -- dermal study (NCI; Completed)	120	-	-	-	-	-
6. Bioassay of 2,3,7,8-Tetrachloro-dibenzo-p-dioxin for possible carcinogenicity -- gavage study (NCI; Completed)	120	-	-	-	-	-

1/ Funding Dependent on Registry Results

Scientific Activity	Funding ($000)					
	FY80	FY81	FY82	FY83	FY84	FY85
7. Bioassay of a mixture of 1,2,3,6,7,8 and 1,2,3,7,8,9-Hexachloro-dibenzo-p-dioxins for possible carcinogenicity -- dermal and gavage studies (NCI; October 1980)	120	-	-	-	-	-
8. Comparative species evaluation of chemical disposition and metabolism of TCDF in rat, monkey and guinea pig (NCI/NIEHS; Completed)	48	-	-	-	-	-
9. Neurotoxicity of 2,4-D in rodents (NIEHS; March 1981)	9	-	-	-	-	-
10. Studies of the chemical disposition and metabolism of OCDD (NIEHS; May 1981)	14	-	-	-	-	-
11. Effects of "Agent Orange" Components on Male Fertility and Reproduction (NTP; Completed)	95	-	-	-	-	-
12. Mutagenicity Studies of TCDD, 2,4-D 2,4,5-T and Esters of 2,4-D and 2,4,5-T (NIEHS; April 1981)***	20	72	-	-	-	-
13. Implications of low level exposure to dioxins (NIEHS; July 1982)	89	80	-	-	-	-
14. Toxicology of Chlorinated Dibenzo-p-dioxins (NIEHS; January 1981)	81	-	-	-	-	-

***Future studies will be contemplated pending results of these studies.

Scientific Activity	Funding ($000)					
	FY80	FY81	FY82	FY83	FY84	FY85
15. Mechanism(s) of toxicity of the chlorinated p-dioxins (NIEHS; March 1983)	52	54	50	-	-	-
16. Synthesis of analytical standards for dioxin analysis. (NIEHS; September 1981)	100	100	-	-	-	-
17. Dioxin (NIEHS; September 1981)	26	26	-	-	-	-

VETERANS ADMINISTRATION

Interagency Work Group on Phenoxy Herbicides and Contaminants

Title of Activity	Funding		
	FY80	FY81	FY82
1. Review and Analysis of Literature on Phenoxy Herbicides and Dioxin (DMS; December 1980)	$50,000	$25,000	
2. Epidemiology of Agent Orange in Vietnam Veterans (DMS; October 1981)			
a. Contract for Study Design	200,000	300,000	300,000
b. Conduct of Study		3,600,000	
3. TCDD Assay of Human Fat (DMS; Completed)	16,000*		
4. Urinary 6-Hydroxy Cortisol; Physiologic and Pharmacologic Studies (including Agent Orange)	35,000	37,800	37,800
5. Effect of TCDD on Lipid Metabolism	5,100	20,400	20,400

*For both FY79 and FY80

DATE: September 3, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Urinary 6-Hydroxy cortisol; Physiologic and Pharmacologic studies (including Agent Orange).

2. Agency responsible, including agency component(s) directly responsible for activity: Veterans Administration, Department of Medicine and Surgery.

3. Statement of objective(s): Determine the effects of Dioxin on hepatic microsomal enzymes and determine whether altered steroid metabolism can predict exposure.

4. Principal investigator(s): Dr. Norman Ertel, M.D., Chief MED SVC VAMC East Orange.

5. Relationship of activity to other work group activities: Depends on and is a reasonable sequel to previous work. Have already developed a radioimmunoassay for 6 - B - OH Cortisol in urine.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Gas chromatograph - mass spectrometry being used to characterize and measure TCDD in biopsied fat of small group of Vietnam veterans and others. Radioimmunoassay, celite chromatography and High Pressure Liquid Chromatography.

7. Status as of September 3, 1980: Currently investigating safety precautions involved with bringing Dioxin into the hospital.

8. Relevant review process(es), as applicable: Local human safety and R&D committees peer review (merit review board)

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: Do studies in rat liver and check induction of hepatic enyymes (est. time of 6 months once approval is obtained) Human studies will follow rat liver studies.

10. Proposed method(s) for reporting results: Scientific publication

DATE: September 3, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Effect of TCDD on Lipid Metabolism

2. Agency responsible, including agency component(s) directly responsible for activity: Veterans Administration, Department of Medicine and Surgery

3. Statement of objective(s): Study acute and chronic effects of TCDD on plasma lipids and adepal tissue

4. Principal investigator(s): Dewey Dunn, M.D., Assistant Chief, Gastroenterology, VAMC Vanderbilt

5. Relationship of activity to other work group activities: Toxicology Center at Vanderbilt, directed by Dr. Robert Neal

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Lipid chemistry, TLC, GLC, polyacrylamide electrophoresis, ultracentrifugation

7. Status as of September 3, 1980: Paper submitted Biochemical Pharmacology (in guinea pig)

8. Relevant review process(es), as applicable: Merit Review submission approval

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:
1980 - 81-complete studies in rats and rabbits
1981-82 - lipoprotein synthesis and catabolism in rat

10. Proposed method(s) for reporting results: Scientific publication

DATE: August 21, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: TCDD Assay of Human Fat

2. Agency responsible, including agency component(s) directly responsible for activity: Veterans Administration, Department of Medicine and Surgery

3. Statement of objective(s): Evaluation of assay method for possible research use.

4. Principal investigator(s): Lawrence B. Hobson, M.D., Ph.D.

5. Relationship of activity to other work group activities: EPA confirmatory assays of dioxin

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Gas chromatography - mass spectrometry being used to characterize and measure TCDD in biopsied fat of small group of Vietnam veterans and others.

7. Status as of August 12, 1980: The assayist is awaiting EPA results. The paper correlating exposure and symptoms with assay results has been written but may require alterations if the assayist changes his assay paper.

8. Relevant review process(es), as applicable: Reviews have been completed by OTA, NAS, Interagency Work Group and VA Advisory Council and the paper has been modified in accordance with reviewers comments. Reviewers have suggested publication of the clinical paper with or after the paper on analysis.

9. List of key interim project milestones (nature, description, and projected dates of accomplishment) and project completion date: Completion of draft of paper April 4, 1980. Submission for publication when EPA confirmatory results are available.

10. Proposed method(s) for reporting results: Scientific publication

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Epidemiology of Agent Orange in Vietnam Veterans

2. Agency responsible, including agency component(s) directly responsible for activity: Veterans Administration, Department of Medicine and Surgery

3. Statement of objective(s): Characterization of delayed effects of exposure to defoliants.

4. Principal investigator(s): Lawrence B. Hobson, M.D., Ph.D.

5. Relationship of activity to other work group activities: Comparable studies by DOD (Air Force) and DHEW on other groups.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Contract epidemiologist to design study for execution by VA on Vietnam era veterans.

7. Status as of August 12, 1980

8. Relevant review process(es), as applicable: Study design and final results to be reviewed by OTA, NAS, Interagency Work Group, and VA advisory Council.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: See attached

10. Proposed method(s) for reporting results: Scientific publication

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished X

Milestones	1980 Mar.	June	Sept.	Dec.	1981 Mar.	June	Sept.	Dec.	1982 Mar.	June	Sept.	Dec.	1983 Mar.	June	Sept.	Dec.	1984 Mar.	June	Sept.
1. Issuance of RFP	O																		
1. Receipt of study design from epidemiologist & submission to outside groups for review		O	X																
2. Completion of critical reviews of design		O	X																
4. Revision of design			O	X															
5. Receipt ofreviewers Comments on design revision			O	X															
6. final revision and distribution to review groups					X														
7. VACO Agent Orange sub-committee activation		O			X														
8. Selection of participating VAMC's			O		X														
9. Identification of study subjects				O		X													
10. Contacting subjects				O		X													
11. Initial examination of subjects						O	X												
12 Analysis of first set of data subsequent examination of subjects & analysis of second set of data								O		X									
13. Submission of Administrator's first report to Congress							O												

NOTE: Projections beyond dates of initiation of milestones are very tentative pending study design acceptance

O initial projections for milestones made in March 1980.

X Revised projections made in August of 1980.

August 21, 1980

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of Activity: Review and Analysis of Literature on Phenoxy Herbicides and Dioxin.

2. Agency responsible, including agency component(s) directly responsible for activity: Veterans Administration, Department of Medicine and Surgery, Special Assistant to the ACMD (for Agent Orange Affairs).

3. Statement of Objective(s): (a) Development of a comprehensive bibliography of the world's literature on the effects of human health of exposure to phenoxy herbicides and dioxin. (b) Preparation of a list of the major conclusions reached in this literature. (c) Analysis of the relevance of this literature to the resolution of the issue of Herbicide Orange's effects on human health.

4. Principal Investigator(s): This project will be performed by an outside contractor.

5. Relationship of activity to other work group activity: DOD and EPA are also performing a review and analysis of the literature on herbicides and dioxin. The VA's project is mandated by Public Law 96-151.

6. Statement of scientific method(s) to be used, including (as appropriated administrative process(es): The usual methods of assembling bibliographies and analyzing scientific literature will be employed. The project will be performed by an outside contractor chosen by open bidding procedures.

7. Status as of August 12, 1980: Proposals have been received but not yet evaluated. The contracting process is underway. An announcement of the contract will be placed in the Commerce Business Daily in the near future.

8. Relevant review process(es), as applicable: The contractor's progress will be monitored by the Office of Special Assistant to the Chief Medical Director on Agent Orange Affairs.

9. List of key interim project milestones (native, description and projected dates of accomplishment) and project completion date.

	Activity	Estimated Completion Date
a.	Selection of contractor	September 30, 1980
b.	Approval by VA of contractor's approach to project.	October 30, 1980
c.	Submission of contractor's first progress report.	December 1980
d.	Submission of contractor's second progress report.	February 1981
e.	Submission of contractor's third progress report.	April 1981
f.	Completion of Project Report.	July 1981
g.	Submission of Project Report to Congress.	August 1981

10. Proposed method(s) for reporting results: The results will be reported in the form of a monograph.

Date: August 26, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on Phenoxy Herbicides and Contaminants

1. **Title of activity:**

   Herbicide Exposure to 2,4-D and Spontaneous Abortions

2. **Agency responsible, including agency component(s) directly responsible for activity:**

   U.S. Forest Service contract to SRI for $99,950

3. **Statement of objective(s):**

   Examine possible association of the herbicide 2,4-D with the occurrence of human spontaneous abortions in the Pacific Northwest

4. **Principal investigator(s):**

   Robert W. Morgan, SRI, Louise Hofherr, SRI, John Neisess, USFS (235-8209)

5. **Relationship of activity to other Work Group activities:**

   Related to birth effect studies underway

6. **Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):**

   A case control approach involving 100 women who have reported spontaneous abortions and 200 women who have given normal birth. Fathers will be divided into low, medium, and high exposure to 2,4-D

7. **Status as of May 30 , 1980:**

8. **Relevant review process(es), as applicable:**

   Reviewed by Dow, NTP, EPA, CDC

9. **List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:**

   Selection of initial population (6/3/80), Selection of Sample (7/3/80), Case Control Data Collection (9/80), Analysis (9/26/80), Final Report (10/3/80)- these dates are not exact

10. **Proposed method(s) for reporting results:**

    Report to USFS

Title of Activity: Interagency Work Group
Phenoxy Herbicides & Contaminants

Date: August 26, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1980 Mar	Jun	Sep	Dec	1981 Mar	Jun	Sep	Dec	1982 Mar	Jun	Sep	Dec	1983 Mar	Jun	Sep	Dec
Initiation		●														
Mail questionnaires		●														
Validation			●													
Final Report				o												

Date: August 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   TCDD Residue Monitoring

2. Agency responsible, including agency component(s) directly responsible for activity:

   USDA - Forest Service

3. Statement of objective(s):

   To determine levels of 2,3,7,8 tetrachloro-dibenzon-p-dioxin in wild deer feeding in a 2,4,5-T treated area

4. Principal investigator(s):

   Dr. Hugh Black

5. Relationship of activity to other Work Group activities:

   Part of cooperative study to determine 2,4,5-T and TCDD levels and degradation rate in a treated brush field with the University of Cal. (Davis) and the Cal. State Dept. of Food and Agriculture

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   Mass spectrometer

7. Status as of August , 1980:

   TCDD analyses has been completed. Verification analysis of control samples currently underway.

8. Relevant review process(es), as applicable:

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   April 30, 1980 - Analytical data available
   Summer 1980 - Final report available

10. Proposed method(s) for reporting results:

    USDA - Forest Service Report

Title of Activity:

TCDD Residue Monitoring in Deer

Interagency Work Group
Phenoxy Herbicides & Contaminants

Date:

August 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1980 Mar	Jun	Sep	Dec	1981 Mar	Jun	Sep	Dec	1982 Mar	Jun	Sep	Dec	1983 Mar	Jun	Sep	Dec
Area Treated																
First Samples Analyzed																
Second Samples Analyzed																
Report Prepared																

Date: August 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   2,4-D Human Exposure Study

2. Agency responsible, including agency component(s) directly responsible for activity:

   USDA-SEA-AR-NER-BARC-AEQI-Pesticide Degradation Laboratory

3. Statement of objective(s):

   To obtain some baseline information on the amount of human exposure to 2,4-D to applicators under actual conditions in American agriculture

4. Principal investigator(s):

   P. C. Kearney

5. Relationship of activity to other Work Group activities:

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

7. Status as of August , 1980:

   Half of samples have been analyzed for 2,4-D residues

8. Relevant review process(es), as applicable:

   Two revisions after review by USDA, EPA, NAAA, and others

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Completion Date: December 1, 1980

10. Proposed method(s) for reporting results:

    Report to National Pesticide Impact Assessment Program - Dr. S. N. Fertig, Building 1070, BARC-E, Beltsville, Maryland 20705

Title of Activity:

2,4-D Human Exposure Study

Interagency Work Group
Phenoxy Herbicides & Contaminants

Date:

August 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1980 Mar	Jun	Sep	Dec	1981 Mar	Jun	Sep	Dec	1982 Mar	Jun	Sep	Dec	1983 Mar	Jun	Sep	Dec
Sample Collection - Washington	●															
Sample Collection - N. Dak.	●															
2,4-D Analyses Completed			O													
Preliminary Report				O												
Final Report				O												

Date: August 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

National Water Monitoring Survey

2. Agency responsible, including agency components directly responsible for activity:

EPA-Office of Pesticides & Toxic Substances, Survey and Analysis Division--in conjunction with the U.S. Geological Survey

3. Statement of objective(s):

Analyze for various pesticides (including 2,4,5-T and silvex) in water and sediment of streams and rivers throughout the U.S.

4. Principal investigator(s):

F.W. Kutz, Branch Chief within Survey and Analysis Division/EPA Toxicant Analysis Center, Bay St. Louis, Miss.

5. Relationship of activity to other work group activities:

Assist in determining extent and magnitude of problem in the environment

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

1. Screen ester derivatives of samples with electron capture GC
2. If positive, re-extract, make a second ester and analyse
3. If positive, confirm using Halls detector
4. If $>$50ppt, use GC/MS for confirmation

7. Status as of August 1, 1980:

Samples are collected every 3 months, those collected in February '80 have been completed. Work is on those collected in May ' 80.

8. Relevant review process(es), as applicable:

Internal review

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

Samples are collected every 3 months. Analysis is completed 2-3 months following end of sampling.

10. Proposed method(s) for reporting results:

Results are entered into the STORET data base maintained by the Agency and available to users both inside and outside of the government.

Date: August 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

Health and Nutrition Examination Survey II (HANES II)

2. Agency responsible, including agency components directly responsible for activity:

EPA - Office of Pesticides and Toxic Substances, Survey and Analysis Division in conjunction with National Center for Health Statistics

3. Statement of objective(s)

Determine levels of various pesticides in human blood and urine. Urine samples are tested for 2,4,5-T and silvex

4. Principal investigator(s)

5 F.W. Kutz, Branch Chief within Survey and Analysis Division/ Analyses by Texas Tech and Univ. of Iowa

5. Relationship of activity to other work group activities:

Assist in determination of extent and magnitude of problem in humans

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

Shafik, T.M., et al. "Multiple Residue Procedure for Halo- and Nitrophenols, Measurement of exposure to biodegradable pesticides yielding these compounds as metabolites. "Ag & Food Chem 21 (2) :245-298, 1973

7. Status as of August 1 , 1980:

Colection of samples has been completed. 4,700 samples of an anticipated 7,500 have been analyzed.

8. Relevant review process(es), as applicable:

Internal review on our analyses, NCHS, Center for Disease Control and others will also participate in overall review of HANES II.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

Complete analysis of urine samples - December '80
Edit and transfer to computer--Summer '81
Complete this portion of HANES II report--December '82

10. Proposed method(s) for reporting results:

Periodic publication in the literature, as well as final HANES II report.

8. Relevant review process(es), as applicable:

Internal review on our analyses, NCHS, Center for Disease Control and others will also participate in overall review of HANES II.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

Complete analysis of urine samples - December '80
Edit and transfer to computer--Summer '81
Complete this portion of HANES II report--December '82

10. Proposed method(s) for reporting results:

Periodic publication in the literature, as well as final HANES II report.

Date: August 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on Phenoxy Herbicides and Contaminants

1. Title of activity:

   Midland Michigan Study

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Monitoring Program (DMP) and Region V

3. Statement of objective(s)

   Analysis of effluent from Dow Chemical in Tittawabassee River fish

4. Principal investigator(s)

   A. Dupuy (EPA), R. Harless (EPA)

5. Relationship of activity to other work group activities:

   Potential source of TCDD in food supply

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectrometry

7. Status as of August , 1980:

   Initial study complete
   Additional samples being analyzed

8. Relevant review process(es), as applicable:

   Agency DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Complete in Sept.

10. Proposed method(s) for reporting results:

    Report to Region V

Date: August 1 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Louisiana Crayfish and Catfish Study

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Monitoring Program (DMP) and the Survey and Analysis Division

3. Statement of objective(s)

   To determin if native catgish and crayfish are contaminated with TCDD residues

4. Principal investigator(s)

   A. Dupuy (EPA), M. Gross (U of Neb), T. Tiernan (Wright State U)

5. Relationship of activity to other work group activities:

   Possible source of TCDD in food supply

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectrometry

7. Status as of August, 1980:

   Complete

8. Relevant review process(es), as applicable:

   Agency DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Review on Aug 22

10. Proposed method(s) for reporting results:

    Final report
    Scientific publication

Date: August 1 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Nebraska Adipose Tissue Study

2. Agency responsible, including agency components directly responsible for activity:

   Veterans Administration, EPA/Dioxin Monitoring Program (DMP)

3. Statement of objective(s)

   To assist the VA in the analysis of adipose tissue for Vietnam veterans and stateside personnel for the presence of TCDD

4. Principal investigator(s)

   M. Gross (U of Neb), A. Dupuy (EPA), R. Harless (EPA)

5. Relationship of activity to other work group activities:

   Health effects in veterans correlated to exposure and residues

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectrometery

7. Status as of August, 1980:

   Study complete
   Some samples being re-extracted

8. Relevant review process(es), as applicable:

   Reviewed by DMP panelin April
   Reviewed by Interagency Science Panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   None

10. Proposed method(s) for reporting results:

    Final report
    Scientific publication

Date: August 1 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Mississippi Catfish Study

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Monitoring Program (DMP)

3. Statement of objective(s)

   To determine if native and commerically managed catfish accumulate residues of 2,4,5-T contaminat TCDD.

4. Principal investigator(s)

   A. Dupuy (EPA), Tienan (Wright State U), R. Harless (EPA)

5. Relationship of activity to other work group activities:

   Possible sources of TCDD in human food supply

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectroscopy

7. Status as of August , 1980:

   In queue

8. Relevant review process(es), as applicable:

   Agency DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Complete extraction: Sept
   Complete analyese: Oct

10. Proposed method(s) for reporting results:

    Final report
    Scientific publication

Date: August 1 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Oregon Monkey Study

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Monitoring Program (DMP)

3. Statement of objective(s)

   To analyze for the fate and distribution of TCDD in offspring and mothers of mankeys exposed to TCDD.

4. Principal investigator(s)

   W. McNulty (Ore. State Univ), m. Gross (U of Neb), and R. Harless (EPA)

5. Relationship of activity to other work group activities:

   Pharmacohynamics of TCDD in primates

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectroscopy

7. Status as of August , 1980:

   Samples being extracted

8. Relevant review process(es), as applicable:

   Agency DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Complete analyses: Sept
   Complete review: Oct

10. Proposed method(s) for reporting results:

    Final report
    Scientific publication

Date: ~~August 1~~ 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Wisconsin Monkey Study

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Monitoring Program (DMP)

3. Statement of objective(s)

   Monitor for fate and distribution of TCDD in chronically exposed monkeys

4. Principal investigator(s)

   J. Allen (U of Wisc), A. Dupuy(EPA), R. Harless (EPA), M. Gross (U of Neb)

5. Relationship of activity to other work group activities:

   Pharmacohynamics of TCDD in primates

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectroscopy

7. Status as of August, 1980:

   Samples collected and being extracted

8. Relevant review process(es), as applicable:

   Agneyc DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Analysis to be done in Sept
   Review to be done in Oct.

10. Proposed method(s) for reporting results:

    Final report
    Scientific publication

Date: August 1 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Wisconsin Soil Study

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Moniroting Program (DMP) and Hazard Evaluation Division

3. Statement of objective(s)

   To determine if spray drfit of ,2,4,5-T/TCDD on a Wisconsin farm persisted in the soil

4. Principal investigator(s)

   A. Dupuy (EPA), M. Gross (U of Neb), R. Harless (EPA)

5. Relationship of activity to other work group activities:

   Tangential--response to citizen complaint

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectroscopy

7. Status as of August , 1980:

   Complete

8. Relevant review process(es), as applicable:

   Agency DMP review panel complete

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Complete

10. Proposed method(s) for reporting results:

    Rinal report to EPA

Date: August 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Alsea Area Phase II

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Monitoring Program (DMP) and Hazard Evaluation Division

3. Statement of objective(s)

   Possible contamination of water sources with TCDD

4. Principal investigator(s)

   M. Gross (U of Nb), T. Teirnan (Wright State), R. Harless (EPA)

5. Relationship of activity to other work group activities:

   Possible domestic exposure to TCDD

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resoltuation gas chromatography/mass spectroscopy.

7. Status as of August, 1980:

   Samples awaiting analysis

8. Relevant review process(es), as applicable:

   Agency DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Complete analyses in Sept.

10. Proposed method(s) for reporting results:

    Final report

Date: ~~August 1,~~ 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on Phenoxy Herbicides and Contaminants

1. Title of activity:

   Region X Deer and Elk Study

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Monitoring Program (DMP) and Region X

3. Statement of objective(s)

   To determine if deer and elk that range in forested areas where 2,4,5-T is used accumulate TCDD in their tissues.

4. Principal investigator(s)

   A. Dupuy (EPA), T. Tiernan (Wright State U), R. Harless (EPA)

5. Relationship of activity to other work group activities:

   Evidence of tcdd in the environment

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resoltuation gas chromatography/mass spectroscopy

7. Status as of August, 1980:

   Nearing completion

8. Relevant review process(es), as applicable:

   Agency DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   DMP review panel on Aug 22

10. Proposed method(s) for reporting results:

    Final report
    Scientific publication

Date: August 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

Oregon Water and Sediment Study

2. Agency responsible, including agency components directly responsible for activity:

EPA/Dionin Monitoring Program (DMP) and Hazard Evaluation Division

3. Statement of objective(s)

To determin if surface waters used for drinking in forested areas of Oregon contain TCDD

4. Principal investigator(s)

Aubry Dupuy (EPA), M. Gross (U of Neb), and R. Harless (EPA)

5. Relationship of activity to other work group activities:

Possible domestic source of exposure to TCDD

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

High resolution gas chromatography/mass spectroscopy

7. Status as of August, 1980:

Study complete
Review complete

8. Relevant review process(es), as applicable:

Agency DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

Final report scheduled for Sept.

10. Proposed method(s) for reporting results:

Final report
Scientific publication

Date: August 1 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Northwest Human Milk Study

2. Agency responsible, including agency components directly responsible for activity:

   EPA headquarters/Dioxin Monioting Program (DMP) Regions IX and X

3. Statement of objective(s)

   Determination of TCDD residues in juamn milk samples from residents in forested areas of NW

4. Principal investigator(s)

   Aubry Dupuy (EPA), Michael Gross (U of Neb), Bob Harless (EPA/RTP)

5. Relationship of activity to other work group activities:

   Evidence of Human exposure to TCDD

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectroscopy

7. Status as of August, 1980:

   Completed

8. Relevant review process(es), as applicable:

   Agency DMP Review Panel Dec., 1979

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   NA

10. Proposed method(s) for reporting results:

    Preparing for publication in scientific journal

Date: August 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: San Antonio Analyses

2. Agency responsible, including agency components directly responsible for activity: EPA
Dioxin Moniotring Program
Region VI

3. Statement of objective(s)

To determine if TCDD residues are present in soil and garden vegetables

4. Principal investigator(s)

M. Gross (Univ of Nebraska); t. Tiernan (Wright State U)

5. Relationship of activity to other work group activities:

Tangential

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

High resolution Gas chromoatography/Mass spectroscopy

7. Status as of August, 1980:

In Progress

8. Relevant review process(es), as applicable:

DMP chemists and coordinator

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

Completion date Nov., 1980

10. Proposed method(s) for reporting results:

Report to Region VI

Date: August 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Hemlock Mi Study

2. Agency responsible, including agency components directly responsible for activity:
EPA
DMP
Region V

3. Statement of objective(s):

To assist Region V in enforcement actions by analyzing fish and sediment to indicate TCDD contamination

4. Principal investigator(s): M. Gross (U. Nev.) B. Harless (EPA)

5. Relationship of activity to other work group activities:

Tangential

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

HR GC/MS

7. Status as of August , 1980:

8. Relevant review process(es), as applicable:

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: November 1980

10. Proposed method(s) for reporting results:

Report to Region V

Date: ~~August 1~~ 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Microbial Dissimilation of ,2,3,7,8 TCDD

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Office of Research and Development/Industrial Environmental Research Lab--Cinn., Ohio

3. Statement of objective(s)

   Explore possible Biological detoxification procedure for TCDD

4. Principal investigator(s)

   J. Chakrabary (U of ILL Med School, Chicago), M. Salkmoj K-slonen (U of Finland, Helsinki)

5. Relationship of activity to other work group activities:

   Clean-up and disposal

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   Isolation of dechlorination gene from soil bacteria and subsequent incorporation into plasmid of a bacterium which is then incorporated onto a filter.

7. Status as of ~~August~~, 1980:

   Evidence of bacterial metabolism of TCDD obtained.

8. Relevant review process(es), as applicable:

   Internal review

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Periodic interal reports--Final report due in 8 months

10. Proposed method(s) for reporting results:

    EPA publications

Date: ~~August 1~~ 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on Phenoxy Herbicides and Contaminants

1. Title of activity:

   Beef Fat Phase II

2. Agency responsible, including agency components directly responsible for activity:

   EPA/Dioxin Monitoring Program (DMP)

3. Statement of objective(s)

   To determine if cattle grazing on rangeland treated with ,2,4,5-T accumulated TCDD residues in their fat.

4. Principal investigator(s)

   A. Dupuy (EPA), T. Tiernan (Wright State U), R. Harless (EPA)

5. Relationship of activity to other work group activities:

   Possible source of TCDD in food supply

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   High resolution gas chromatography/mass spectrometry

7. Status as of August, 1980:

   Initial analysis complete confirmatory analysis scheduled for Sept

8. Relevant review process(es), as applicable:

   Agency DMP review panel

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

   Completion scheduled for Sept.

10. Proposed method(s) for reporting results:

    Final report
    Scientific publication

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

Investigation of a leukemia cluster in Madison County, Kentucky Allegedly Associated with Pentachlorophenol treated Ammunition Boxes at the Blue Grass Army Depot

2. Agency responsible, including agency component(s) directly responsible for activity:

National Institute for Occupational Safety and Health (NIOSH)
Division of Surveillance, Hazard Evaluations and Field Studies (DSHEFS)
Industry-wide Studies Branch (IWSB)

3. Statement of objective(s):

The initial purpose of this study is to determine if employment at the Blue Grass Army Depot results in an excess risk of developing adult leukemia. If an excess risk is demonstrated, close examination of depot work histories will be conducted in an attempt to establish an etiology such as that alleged with pentachlorophenol which has been used to treat ammunition boxes at the depot.

4. Principal investigator(s):

Patricia A. Honchar, M.S., Ph.D.
William E. Halperin, M.D., M.P.H.
Joe Skaggs, D.V.M., M.P.H.
Kentucky Department of Human Resources

5. Relationship of activity to other work group activities:

This study is investigating a possible association between exposure to pentachlorophenol, which is contaminated with dioxin isomers, and leukemia.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

A case-control epidemiologic methodology is being utilized. All adult leukemia cases residing in Madison County, Kentucky are being located, along with appropriate controls. Ascertainment of any past work history at the depot will be made for both cases and controls to determine if depot employment results in an excess risk of developing leukemia. If a positive association is found, further evaluation of work histories will be conducted to isolate risk factors, if possible.

7. Status as of September, 1980

Case finding is in progress

8. Relevant review process(es), as applicable:

In-house review

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

1. Preliminary meetings with Kentucky State Health personnel and Depot Personnel to define the problem and explore avenues for study.
   October, 1979: Completed

2. Develop protocol for case-control study
   November, 1979: Completed

3. Begin case and control finding
   December, 1979: Completed

4. Complete compilation of cases and controls and submit names to the Army Depot to ascertain which have been depot employees
   October 1980: Projected

5. Receive information back from the depot
   January 1981: Projected

6. Complete data analysis
   June 1981: Projected

7. Final report
   July 1981: Projected

10. Proposed method(s) for reporting results:

Results will be reported to Kentucky Health Department, Blue Grass Army Depot, and Interagency Work Group. If positive, results will be submitted for publication.

Investigation of a Leukemia Cluster in Madison County, Kentucky, Allegedly Associated with Pentachlorophenol Treated Ammunition Boxes at the Blue Grass Army Depot.

Interagency Work Group
Phenoxy Herbicides and Contaminants

Safety and Health
Date Prepared:
March 14, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1979 Sept. Dec	1980 Mar.	June	Sept.	Dec.	1981 Mar.	June	Sept.	Dec.	1982 Mar.	June	Sept.	Dec.	1983 Mar.	June	Sept.	Dec.	1984 Mar.	June	Sept.	Dec.	1985 Mar.	June	Sept.	Dec.
Preliminary meetings	●																								
Develope protocol		●																							
Begin case and control finding			●																						
Complete compilation of cases and controls and submit names to depot					O																				
Receive information back from the depot						O																			
Complete data analysis								O																	
Final report									O																

Date: [illegible]

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:
   Bioassay of Octachlorodibenzo-p-dioxin

2. Agency responsible, including agency component(s) directly responsible for activity: NIEHS-NIH-DHEW

3. Statement of objective(s):
   To evaluate the carcinogenic potential of octachlorodibenzo-p-dioxin

4. Principal investigator(s):
   E.E. McConnell

5. Relationship of activity to other work group activities: Structurally similar compounds have been studied in Environmental Biology Branch.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Acute, subacute and chronic bioassay.

7. Status as of September 1 ,1980: Literature search completed 5/19/80

8. Relevant review process(es), as applicable: Will be reviewed by experimental design group of NCI.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: See attached milestone timetable.

10. Proposed method(s) for reporting results:
    NCI Technical Report
    Possibly scientific journal depending on results.

Note: Please retype or add sheet(s) if more space is nee

Title of activity:

Bioassay of Tetrachlorodibenzo-p-dioxin

Interagency Work Group
Phenoxy Herbicides and Contaminants

NIEHS-NIH-DHEW
Date Prepared:

March 21, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected 0 Accomplished ●

Milestones	1980 Mar.	June	Sept.	Dec.	1981 Mar.	June	Sept.	Dec.	1982 Mar.	June	Sept.	Dec.	1983 Mar.	June	Sept.	Dec.	1984 Mar.	June	Sept.	Dec.	1985 Mar.	June	Sept.	D
Literature Search	●																							
Experimental Design				0																				
Review by Experimental Design Group				0																				
Contract Award						0																		
Acute LD_{50}							0																	
Repeated Dose Study								0																
Subchronic Study										0														
Chronic Study																		0						
Analysis and Interpretation of Results																				0				
Publication of Results																							0	

September 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

Dioxin Registry

2. Agency responsible, including agency component(s) directly responsible for activity:

National Institute for Occupational Safety and Health (NIOSH)
Division of Surveillance, Hazard Evaluations and Field Studies (DSHEFS)
Industry-wide Studies Branch (IWSB)

3. Statement of objective(s):

The objective of this endeavor is to establish a registry of all workers in the U.S. who have been associated with the synthesis of 2,4,5-T. The registry will include work and exposure histories for all registrants. The registry will be utilized initially for a retrospective cohort mortality study, and the workers will be followed prospectively. In the future, an evaluation will be made of the registry to determine if the cohorts can be utilized for studies of morbidity and reproductive outcome.

4. Principal investigator(s):

Patricia A. Honchar, M.S., Ph.D.
William E. Halperin, M.D., M.P.H.

5. Relationship of activity to other work group activities:

This study will contribute information about the long term human health effects of exposure to 2,4,5-T and its contaminant TCDD.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

For the initial retrospective cohort mortality study, workers will be traced historically through the Social Security Administration and other sources as necessary. For deceased workers, cause of death will be determined and coded from death certificates. Rates by cause of death will be age and sex adjusted and compared to worksite controls, state and national rates. Degrees of exposure by number of years exposed and industrial process will be taken into account. Registrants will be followed prospectively and reviewed with additional mortality studies in the future.

7. Status as of September 1, 1980

Discussions with industries and collection of cohorts in progress.

8. Relevant review process(es), as applicable:

Peer review, statistical review, and Interagency work group review to be arranged.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

1. Identify and initially contact all 2,4,5-T synthesizers
October, 1979: Completed

2. Complete collection of all industry records and relevant exposure data
February, 1981: Projected

3. Begin coding demographic data
March, 1980: Completed

4. Begin determination of vital status
October 1980: Projected

5. Finalize coding protocol for work and exposure histories, begin coding and merge with demographic data
June, 1981: Projected

6. Complete determination of vital status
February, 1983: Projected

7. Complete analysis of mortality rates
April, 1983: Projected

8. Final report of initial registry-wide retrospective cohort mortality s
June, 1983: Projected

10. Proposed method(s) for reporting results:

Interim and final results will be submitted for publication

Dioxin Registry

Interagency Work Group
Phenoxy Herbicides and Contaminants

Date Prepared:
March 14, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1979 Sept. Dec.	1980 Mar.	1980 June	1980 Sept.	1980 Dec.	1981 Mar.	1981 June	1981 Sept.	1981 Dec.	1982 Mar.	1982 June	1982 Sept.	1982 Dec.	1983 Mar.	1983 June	1983 Sept.	1983 Dec.	1984 Mar.	1984 June	1984 Sept.	1984 Dec.	1985 Mar.	1985 June	1985 Sept.	1985 Dec.
Identify and initially contact all 2,4,5-T synthesizers	●																								
Complete collection of all industry records and relevant exposure data						O					●														
Begin coding demographic data		●																							
Begin determination of vital status				O																					
Finalize coding protocol for work and exposure histories, begin coding, and merge with demographic data							O																		
Complete determination of vital status														O											
Complete analysis of mortality rates															O										
Final report of initial registry wide retrospective cohort mortality study																O									

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of Activity:

Investigation of all Alleged Cluster of Birth Defects in Families of Teamsters Union Employees of the Long Island Railroad

2. Agency responsible, including agency component(s) directly responsible for activity:

National Institute for Occupational Safety and Health (NIOSH)
Division of Surveillance, Hazard Evaluations and Field Studies (DSHEFS)
Industry-wide Studies Branch (IWSB)

3. Statement of objective(s):

In response to a request for a Health Hazard Evaluation by Teamsters Local 808, this preliminary epidemiologic investigation is aimed at confirming cases and determining whether the rate of birth defects in families of Teamsters who are employed by the LIRR exceeds the expected rate. If an excess is found, a further study may be initiated to investigate the Teamsters' allegations of an association with 2,4,5-T which the LIRR has used in the past to maintain the right-of-way.

4. Principal investigator(s):

Patricia A. Honchar, M.S., Ph.D.
William E. Halperin, M.D., M.P.H.

5. Relationship of activity to other work group activities:

The Teamsters allege that an excess of birth defects is related to exposure to 2,4,5-T.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

A list of live births among the Teamsters' families for the period 1975-1979 has been assembled. Insurance claims files for these individuals will be reviewed and rate(s) of birth defects calculated. The rate(s) will be compared to expected rates as compiled by the CDC Congenital Malformations Surveillance System.

7. Status as of September 1980:

The Teamsters Local is negotiating the retrieval of the needed insurance claims files from their insurance company.

8. Relevant review process(es), as applicable:

In-house review as a NIOSH Health Hazard Evaluation

9. List a [illegible] project milestones (nature, description and projected dates of accomplishment) and project completion date:

   1. Preliminary meetings with the Teamsters Local and LIRR to characterize the workforce, learn about exposures, and explore records systems available for study
      January and February, 1980: Completed

   2. Assemble a list of live births
      February, 1980: Completed

   3. Obtain insurance claims files for live births
      May 1980: Completed

   4. Review claims files, confirm and characterize birth defects, calculate rates
      May, 1980: Completed

   5. Compare with expected rates
      October 1980: Projected

   6. Final report
      December 1980: Projected

10. Proposed method(s) for reporting results:

Results in manuscript form will be presented to the Teamsters, LIRR, and the Interagency Work Group

Title of activity:

Investigation of an Alleged Cluster of Birth Defects in Families of Teamsters Union Employees of the Long Island Railroad

Interagency Work Group
Phenoxy Herbicides and Contaminants

Agency:
National Institute for Occupational Safety and Health

Date Prepared:
March 14, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1980 Mar.	June	Sept.	Dec.	1981 Mar.	June	Sept.	Dec.	1982 Mar.	June	Sept.	Dec.	1983 Mar.	June	Sept.	Dec.	1984 Mar.	June	Sept.	Dec.	1985 Mar.	June	Sept.	Dec.
Preliminary meetings to collect general information	●●																							
Assemble a list of live births	●																							
Obtain insurance claim files		●																						
Review and characterize files; calculate rates		●																						
Compare with expected rates				O																				
Final report					●																			

Date: September 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Bioassay of 2,3,7,8-Tetrachlorodibenzo-p-dioxin for Possible Carcinogenicity (Dermal Study).

2. Agency responsible, including agency component(s) directly responsible for activity: National Cancer Institute/Natio Toxicology Program; Carcinogenesis Testing Program; Prime Contractor, Traco Litco

3. Statement of objective(s): To determine the carcinogenicity of tetrachloro dibenzo-p-dioxin administered to mice by dermal application.

4. Responsible investigator(s): Dr. William V. Hartwell, National Cancer Institute

5. Relationship of activity to other work group activities: Part of a series of chloro-para-dioxins selected fo testing after teratogenic effects were related to the 2,3,7,8-isomer.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Dermal application of acetone suspensions to S Webster Mice through lifetime of test animal under standard bioassay condit

7. Status as of September 1, 1980:
Peer reviewed by NTP ad hoc review committee 6/27/80

8. Relevant review process(es), as applicable: In-house data evaluation March 27, 1980. Submission for peer review by committee to be recommended by Scientific Advisory Board May 1,

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: None

10. Proposed method(s) for reporting results: Carcinogenesis Technical Repor Series

Note: Please retype or add sheet(s) if more space is needed.

Bioassay of 2,3,7,8-Tetrachlorodibenzo-p-dioxin for Possible Carcinogenicity (Final Study).

Interagency Work Group
Phenoxy Herbicides and Contaminants

Date Prepared: March 19, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1980				1981				1982				1983				1984				1985			
	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.
In-house Data Evaluation	●																							
Final Draft of peer review		●																						

Date: September 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Bioassay of 2,3,7,8-Tetrachlorodibenzo-p-dioxin for Possible Carcinogenicity (Gavage Study). (TCDD-Gavage)

2. Agency responsible, including agency component(s) directly responsible for activity: National Cancer Institute/ National Toxicology Program; Carcinogenesis Testing Program; Prime Contractor, Tracor Jitco

3. Statement of objective(s): To determine the carcinogenicity of tetrachlorodibenzo-p-dioxin administered by gavage to rats and mice.

4. Responsible investigator(s): Dr. William V. Hartwell, National Cancer Institute

5. Relationship of activity to other work group activities: Part of a series of chlorodibenzo-dioxins selected for testing after teratogenic effects were related to the 2,3,7,8-isomer.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Administered by gavage to Osborne Mendel rats B6C3F1 mice throughout lifetime studies under standard bioassay conditions

7. Status as of September 1, 1980:

   Peer reviewed by NTP ad hoc review committee 6/27/80

8. Relevant review process(es), as applicable: In-house data evaluation March 27, 1980; submission for peer by committee to be recommended by Scientific Advisory Board May 1, 1980

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: None

10. Proposed method(s) for reporting results: Carcinogenesis Technical Report

Note: Please retype or add sheet(s) if more space is needed.

Title of activity:

Bioassay of 2,3,7,8-Tetrachlorodibenzo-p-dioxin for Possible Carcinogenicity (Cancer)

Interagency Work Group
Phenoxy Herbicides and Contaminants

National Cancer Institute/
National Toxicology Program
Date Prepared:
March 19, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1980 Mar.	1980 June	1980 Sept.	1980 Dec.	1981 Mar.	1981 June	1981 Sept.	1981 Dec.	1982 Mar.	1982 June	1982 Sept.	1982 Dec.	1983 Mar.	1983 June	1983 Sept.	1983 Dec.	1984 Mar.	1984 June	1984 Sept.	1984 Dec.	1985 Mar.	1985 June	1985 Sept.	1985 Dec.
In-house data evaluation	●																							
National Board of peer review		●																						

Date: [illegible]

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Bioassay of a Mixture of 1,2,3,6,7,8 and 1,2,3,7,8,9-Hexachloro-dibenzo-p-dioxins for Possible Carcinogenicity (Dermal Study)

2. Agency responsible, including agency component(s) directly responsible for activity: National Cancer Institute/National Toxicology Program; Prime Contractor, Tracor Jitco

3. Statement of objective(s): To determine the carcinogenicity of a mixture of 1,2,3,6,7,8 and 1,2,3,7,8,9-Hexachloro-p-dioxins administered to mice by dermal application.

4. Responsible investigator(s): Dr. William V. Hartwell, National Cancer Institute

5. Relationship of activity to other work group activities: One of a series of chloro-para-dioxins selected fo testing after teratogenic effects were related to the 2,3,7,8-isomer.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Dermal application of acetone suspensions to Swiss-Webster mice througnout lifetime of test animals under standard bioa conditions.

7. Status as of September 1 ,1980:

   Technical report projected November 1980.

8. Relevant review process(es), as applicable: Reviewed and approved by the Clearinghouse on Environmental Carcinogens February 15, 1980.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: None

10. Proposed method(s) for reporting results: Carcinogenesis Technical Repor Series

Note: Please retype or add sheet(s) if more space is needed.

Date: September 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Bioassay of a Mixture of 1,2,3,6,7,8 and 1,2,3,7,
Hexachloro-dibenzo-p-dioxins for Possible Carcinogenicity (Gavage Stu

2. Agency responsible, including agency component(s) directly responsible for activity: National Cancer Institut
National Toxicology Program; Prime Contractor, Tracor Jitco.

3. Statement of objective(s): To determine the carcinogenicity of a mi
of 1,2,3,6,7,8 and 1,2,3,7,8,9-hexachloro-p-dioxins administered to m
and rats by gavage.

4. Responsible investigator(s): Dr. William V. Hartwell, National Cance
Institute

5. Relationship of activity to other work group activities: One of a series of chloro-para-dioxins select
for testing after teratogenic effects were related to the 2,3,7,8-iso

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Administered by gavage to Osborne Mende
and B6C3F1 mice throughout lifetime of test animals under standard
bioassay conditions.

7. Status as of September 1, 1980:
Technical report projected November 1980.

8. Relevant review process(es), as applicable: Reviewed and approved by the Clearinghouse on Environmen
Carcinogens February 15, 1980.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: None

10. Proposed method(s) for reporting results: Carcinogenesis Technical
Series

Note: Please retype or add sheet(s) if more space is need

Title [illegible]

Bioassay of a Mixture of 1,2,3,6,7,8 and 1,3,7,8,9 Hexachloro-dibenzo-p-dioxins for Possible Carcinogenicity (Dermal and Gavage)

Interagency Work Group
Phenoxy Herbicides and Contaminants

National Toxicology Program
Date Prepared:
March 19, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestone	1980 Mar.	1980 June	1980 Sept.	1980 Dec.	1981 Mar.	1981 June	1981 Sept.	1981 Dec.	1982 Mar.	1982 June	1982 Sept.	1982 Dec.	1983 Mar.	1983 June	1983 Sept.	1983 Dec.	1984 Mar.	1984 June	1984 Sept.	1984 Dec.	1985 Mar.	1985 June	1985 Sept.	1985 Dec.
In-house Data Evaluation	●																							
Final draft of peer review	●																							
Report in publication				O																				

Date: September 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Comparative species evalution of chemical disposition and metabolism of tetrachlorodibenzofuran (TCDF) in rat, monkey, and guinea pi and also in two strains of mice.
   New & Related Activity: Disposition of 1,2,4,6,7,9-hexachlorodibenzofuran (HCDF) begun in rats September 1980.

2. Agency responsible, including agency component(s) directly responsible for activity:

   DHEW/NIH (NTP)/NCI/NIEHS/Environmental Biology Branch

3. Statement of objective(s): To compare the differences between species in the absorption, distribution, metabolism, and excretion of tetrachlorodibenzofura in order to better evaluate the acute and chronic low dose exposure hazards.

4. Principal investigator(s):

   Drs. Linda S. Birnbaum, Gary M. Decad, and H. B. Matthews

5. Relationship of activity to other work group activities: A knowledge of the disposition of TCDF is necessary in order to assess hazards and plan chronic studies. These results may also lead to a better understanding of the toxic mechanisms of TCDD, TCDF, and other halogenated, polyaromatic hydrocarbons.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): ^{14}C-TCDF was administered both orally (at 2 doses and intravenously to male Fischer rats, and intravenously to male Hartley guinea pigs and male Rhesus monkeys. The distribution of radioactivity to the tissues and in the excreta was examined at various time points and the presenc of parent compound or metabolite(s) determined by thin layer chromatography.

7. Status as of September 1, 1980: Disposition study completed; 3 manuscript in preparation; metabolism being further evaluated.

8. Relevant review process(es), as applicable: Intramural review (NIEHS peer review), Peer-reviewed scientific journal

9. [illegible] of [illegible] completion date:

a) October-December 1979: ^{14}C-TCDF is rapidly metabolized to more polar compounds in the rat which are rapidly excreted, via the bile, in the feces.

b) December 1979-February 1980: ^{14}C-TCDF is metabolized to a very small extent by guinea pigs, and very little is excreted. Approximately equal amounts of radioactivity appear in the feces and urine, possibly due to passive redistribution. This lack of metabolism and excretion in the guinea pig explains, at least in part, the previously documented extreme sensitivity of this species to the toxic action of TCDF.

c) January-March 1980: ^{14}C-TCDF is slowly metabolized and excreted from male Rhesus monkeys, in line with the intermediate acute toxicity to this species. Low doses (less than 1/40 of the LD_{50}) result in pathological changes in the meibomian glands of the eyelid, an early marker of toxicity.

d) April-August 1980: Super ^{14}C-TCDF is rapidly metabolized to more polar compounds in the mouse, which are rapidly excreted, via the bile in the feces and to a less extent in the urine. The disposition was compared in two strains of mice, C57BL/6J and DBA/2J, which have different sensitivities to the toxic action of the closely related compound, TCDD. C57, which are very sensitive to TCDD toxicity, clear TCDF more rapidly than DBA, which are relatively resistant. This may be due to the sequestering of TCDF in the adipose tissue of DBA mice, which have over 33% more fat than C57.

e) June-present 1980: Isolation and characterization of metabolites of TCDF have begun for monkey's CCs and rat bile. One metabolite has been purified by HPLC and is awaiting structural determination.

10. Proposed method(s) for reporting results:

Peer-review journals
Scientific meetings

Comparative species evaluation of chemical disposition and metabolism of tetrachlorodibenzofuran (TCDF) in rat, monkey, and guinea pig

Interagency Work Group
Phenoxy Herbicides and Contaminants

Date Prepared: March 17, 1980

SCIENTIFIC ACTIVITY MILLSTONE TIMETABLE

Projected ○ Accomplished ●

Milestones	1980 Mar.	1980 June	1980 Sept.	1980 Dec.	1981 Mar.	1981 June	1981 Sept.	1981 Dec.	1982 Mar.	1982 June	1982 Sept.	1982 Dec.	1983 Mar.	1983 June	1983 Sept.	1983 Dec.	1984 Mar.	1984 June	1984 Sept.	1984 Dec.	1985 Mar.	1985 June	1985 Sept.	1985 Dec.
Rat: ^{14}C-TCDF is rapidly metabolized and excreted in the feces	●																							
Guinea Pig: ^{14}C-TCDF accumulates and very little is metabolized or excreted	●																							
Monkey: ^{14}C-TCDF is slowly metabolized and excreted, primarily in the feces	●																							
Publication of abstract and presentation at FASEB meeting	●		●																					
Preparation and submission of manuscripts			●																					

Date: September 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Pesticides and Chemicals

1. Title of activity:

   Neurotoxicity of 2,4-D in rodents

2. Agency responsible, including agency component(s) directly responsible for activity:

   Laboratory of Behavioral and Neurological Toxicology
   National Institute of Environmental Health Sciences

3. Statement of objective(s):

   To determine whether or not exposure to 2,4-D produces signs of behavioral and/or neurological toxicity in rodents

4. Principal investigator(s):

   C. L. Mitchell

5. Relationship of activity to other work group activities:

   Provide a broad assessment of the biological effects of 2,4-D.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   The acute oral toxicity of 2,4-D in male Fisher rats, approximately 90 days of age, will be determined. Subsequently, rats receiving doses of 1/8, 1/4, or 1/2 of the LD50 will be evaluated in a battery of neurobehavioral tests designed to examine sensory and motor functioning, affective behavior and learning and memory. Special emphasis will be placed on motor functioning and affective behavior. The rats will be examined at the time of peak activity of the compound (as determined by the lethality studies) and at 1 day, 1 week, and 30 days after administration or longer, if effects persist. Further studies, using multiple dosing procedures may be initiated if no neurobehavioral effects are observed following a single sublethal dose.

7. Status as of September 1, 1980

   Test has been completed. Analysis of data in progress.

8. Relevant review process(s), as applicable:

Internal review within the Laboratory of Behavioral and Neurological Toxicology

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

Initiation of dosing - April
Data analysis - May
Further studies if indicated - June-August
Completion - September, 1980

10. Proposed method(s) for reporting results:

Research publication

Title of activity: Neurotoxicity of 2,4-D in rodents

Interagency Work Group
Phenoxy Herbicides and Contaminants

Neurological Toxic. Br., NIEHS

Date Prepared: 3-20-80

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected ○ Accomplished ●

Milestones	1980 Mar.	June	Sept.	Dec.	1981 Mar.	June	Sept.	Dec.	1982 Mar.	June	Sept.	Dec.	1983 Mar.	June	Sept.	Dec.	1984 Mar.	June	Sept.	Dec.	1985 Mar.	June	Sept.	Dec.
Compound received	●																							
Protocols completed		○																						
Initial studies complete		○																						
Secondary testing to begin if necessary				○																				
Secondary testing complete					○																			
Final report						○																		

Tab: [illegible]

SCIENTIFIC ACTIVITY [illegible]

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Studies of the chemical disposition and metabolism of Octachlorodibenzodioxin (OCDD)

2. Agency responsible, including agency component(s) directly responsible for activity:

DHEW/NIH/NIEHS/EBB

3. Statement of objective(s):

To study the disposition of [^{14}C] OCDD in Fischer 344 male rats.

4. Principal investigator(s):

Drs. Gary M. Decad, Linda S. Birnbaum, and H. B. Matthews

5. Relationship of activity to other work group activities:

Initiation of disposition study depends on analysis of purity of ^{14}C-radiolabel OCDD by Chemistry Branch/NIEHS. Data from disposition study will be used to determine doses used by NCI for chronic studies.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

[^{14}C] OCDD will be administered at two dose levels to Fischer 344 male rats to study its absorption and distribution. Tissues will be analyzed for radioactivity and metabolites.

7. Status as of September 1, 1980:

OCDD submitted to Chemistry Branch, NIEHS, for determination of chemical purity.

8. Relevant review process(es), as applicable:

NIEHS peer review.
Review for publication in Scientific Journal.

9. List of the major milestones (nature, description and projected dates of accomplishment) and project completion date:

1) 3-5-80: Custom synthesis of [^{14}C] OCDD achieved and product shipped to NIEHS, EEB.

2) Analysis of chemical purity of OCDD by Chemistry Branch/NIEHS completed 3-24-80.

3) Chemistry branch reported OCDD is not pure and must be purified prior to initiation of disposition study.

4) We are waiting purification of OCDD by HPLC in high hazard room or similar facility prior to initiating study.

10. Proposed methods for reporting results

Scientific meeting and peer reviewed scientific journal.

Title of activity:

Studies of the chemical disposition and metabolism of octachlorodibenzodioxin (OCDD)

Interagency Work Group
Phenoxy Herbicides and Contaminants

Agency: DHEW/NIH/NIEHS/ERB
Date Prepared: 3/17/80 10

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Actions	1980 Mar.	June	Sept.	Dec.	1981 Mar.	June	Sept.	Dec.	1982 Mar.	June	Sept.	Dec.	1983 Mar.	June	Sept.	Dec.	1984 Mar.	June	Sept.	Dec.	1985 Mar.	June	Sept.	Dec.
1) Custom synthesis of [^{14}C] OCDD and purity determination.		O																						
2) Disposition study of [^{14}C] OCDD in rats completed.				O																				
3) Publication of disposition study and abstract for scientific meeting.					O																			
4) Complete determination of metabolism of OCDD, if any.						O																		

Date: September 1, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Effects of "Agent Orange" Components on Male Fertility and Reproduction

2. Agency responsible, including agency component(s) directly responsible for activity: National Toxicology Program, Special Toxicology, Reproduction and Fertility Workgroup

3. Statement of objective(s): This is a probe study in male mice fed large doses of the constituents of Agent Orange to determine effects on fertility and ability to sire normal offspring.

4. Principal investigator(s): Dr. James C. Lamb IV, Dr. John A. Moore, Dr. Thomas Marks, Dr. James Allen

5. Relationship of activity to other work group activities: This workgroup studied toxicity of selected chemicals on male and female reproduction, fertility and development.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): The direct toxic effects of the chemical mixtures are being determined in randomly selected mice during the dosing period and breeding period. Organ weights, appearance, and histopathology are the endpoints of toxicity. Sperm number and morphology are being evaluated in the animals as indices of fertility in these same animals. At the end of the dosing period an additional group of mice are being bred to control female mice. Mating frequency, fertility efficiency, dominant lethality, incidence of congenital variations and malformations, and viability of offspring are being studied. Sister chromatid exchanges are also being measured in an additional group of males.

7. Status as of September 1, 1980: study completed. Technical report completed. Manuscript for publication in preparation.

8. Relevant review process(es), as applicable: Protocol reviewed by selected scientists for scientific merit and safety considerations.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date: Milestones include completion of dosing, breeding of treated males, toxicity evaluation, collection and study of offspring, calculation of data, and preliminary studies on sister chromatid exchanges. Project completion date July 1980.

10. Proposed method(s) for reporting results: Scientific journal(s)

on Male Fertility and Reproduction

Interagency Work Group
Phenoxy Herbicides and Contaminants

Program
Date Prepared: March 19, 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Stones	1980 Mar.	June	Sept.	Dec.	1981 Mar.	June	Sept.	Dec.	1982 Mar.	June	Sept.	Dec.	1983 Mar.	June	Sept.	Dec.	1984 Mar.	June	Sept.	Dec.	1985 Mar.	June	Sept.	Dec.
Treat male mice with compounds	●																							
Breed males to females		●																						
Sacrifice males for toxicological studies		●																						
Collect fetuses for teratological evaluation			●																					
Complete evaluation of fetal skeletons				●																				
Complete data calculations and file report				●																				
Conclude probe of alcohol chromatid exchanges				●				●																

Date: September 1, 1980

[illegible] ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity:

   Mutagenicity Studies of TCDD, 2,4-D, 2,4,5-T and Esters of 2,4-D and 2,4,5-T.

2. Agency responsible, including agency component(s) directly responsible for activity:

   National Institute of Environmental Health Sciences

3. Statement of objective(s):

   To determine the mutagenicity of TCDD, pure 2,4-D and 2,4,5-T, 2,4-D and 2,4,5-T butyl esters and commercial preparations of 2,4,-D and 2,4,5-T in Salmonella typhimurium (Ames Test), Drosophila melanogaster and mammalian (Chinese Hamster Ovary) cells in culture.

4. Principal investigator(s):

   Errol Zeiger, Ph.D., NIEHS

5. Relationship of activity to other work group activities:

   Knowledge of mutagenicity potential of Agent Orange constituent is essential to interpreting if Agent Orange exposure can result in siring abnormal offspring.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   The Salmonella studies will determine the ability of the tested substances to induce point mutations. Drosophila will indicate the induction of sex-linked recessive lethal mutations and reciprocal chromosome translocations. Cultured mammalian cells will indicate the induction of chromosome aberrations and sister chromatid exchanges.

   All chemicals are being tested blind by contract laboratories. The codes will be broken by NIEHS after testing in each laboratory has been completed and a decision made on the mutagenicity of the chemical.

7. Status as of September 1, 1980: Commercial preparation of 2,4-D isooctyl ester (67% DED-WEED LV 69) and 2,4,5-T issooctyl ester (64%, DED-WEED 6V-4T) and pure 2,4-D and 2,4,5-T were tested for mutagenicity in salmonella. No mutagenic activity was seen. TCDD is currently under test in salmonella.

TCDD, 2,4-D and 2,4,5-T are currently under test in drosophila. [illegible] mammalian cells for chromosome aberrations and sister chromatid [illegible]

8. Relevant review process(es), as applicable:

All Salmonella results on TCDD, pure 2,4-D and pure 2,4,5-T should be available by May, 1980. Salmonella results on commercial grades of 2,4-D and 2,4,5-T by June, 1980.

Drosophila results on TCDD, pure 2,4-D and pure 2,4,5-T should be available by November, 1980.

Mammalian cell cytogenetics results on TCDD, pure 2,4-D and pure 2,4,5-T should be available by December, 1980.

At these times, all testing laboratories data will be reviewed by NIEHS EMTDP personnel and a decision will be made on the mutagenicity of the chemicals.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

Salmonella and drosophila results on TCDD should be available by November 1980. TCDD results have been pushed back because of delays in receipt of the chemical. Results with butyl esters of 2,4-D and 2,4,5-T are also pushed back because they must be synthesized by an NIEHS contractor and time originally allocated for this task was insufficient. Mammalian cell cytogenic results should be available by April 1981 because of delays involved in standardizing and validating test protocols in the contract laboratories.

10. Proposed methods for reporting results:

Summarized results and conclusions (plus appended raw data) will be submitted to NTP as they become available.

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Milestones	1980 Mar.	1980 June	1980 Sept.	1980 Dec.	1981 Mar.	1981 June	1981 Sept.	1981 Dec.	1982 Mar.	1982 June	1982 Sept.	1982 Dec.	1983 Mar.	1983 June	1983 Sept.	1983 Dec.	1984 Mar.	1984 June	1984 Sept.
1. Send TCDD to Salmonella & Drosophila contractors	●																		
2. Send pure 2,4-D and 2,4,5-T to Salmonella and Drosophila contractors	●																		
3. Send TCDD, 2,4,5-T to Cultured mammalian cell laboratories				O															
4. TCDD mutagenicity results																			
Salmonella				O															
Drosophila				O															
Cultured mammalian cells					O														
5. 2,4-D, 2,4,5-T mutagenicity results																			
Salmonella			●																
Drosophila				O															
Cultured mammalian cells						O													
6. Send butyl esters to Salmonella labs						O													
7. Butyl esters results																			
Salmonella					O			O											
Drosophila								O											
Cultured mammalian cells																			
8. Send commercial grade 2,4-D and 2,4,5-T to Salmonella contractors	●																		
9. Commercial grade 2,4-D and 2,4,5-T Salmonella results		●																	

Date: [illegible]

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Implications of Low Level Exposure to Dioxins

2. Agency responsible, including agency component(s) directly responsible for activity: National Institute of Environmental Health Sciences; Extramural Program

3. Statement of objective(s): The overall objectives of the project are to evaluate the injurious effects that arise in the adult female primate and her offspring as a result of long term, low level exposure to 2,3,7, 8-tetrachlorodibenzo-p-dioxin and to determine the rate of recovery from these effects once exposure is discontinued.

4. Principal investigator(s): Everson, Merle A., Ph.D.

5. Relationship of activity to other work group activities:

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

Rhesus monkeys will be given diets containing 5.0 and 25 ppt TCDD for 2 years. During this time they will be evaluated clinically. After six months on the diet, they will be bred. Conception rate, abortions, fetal development and neonatal development will be observed. Tissue levels of TCDD will be monitored through periodic fat biopsies. Levels of TCDD in mothers' milk will be determined throughout lactation.

Attempts will be made to rebreed the rhesus females that are receiving 50 ppt TCDD. If sucessful, the females as well as their offspring will be evaluated for abnormalities. Following four months of nursing, the infants will be weaned and evaluated psychologically. If it is impossible to breed the animals that are receiving 50 ppt TCDD, they will be removed from the experimental diet and be given a 6 month recover period prior to additional attempts at rebreeding.

In addition, the 3 surviving animals from the 500 ppt TCDD experiment will continue to be evaluated for recovery from TCDD intoxication. In addition, the animals on the hexachlorodibenzo-p-dioxin will continue receiving 5 ppt in their diet in order to compare the toxicological effects of the two dioxins.

7. Status as of 9/1/80: Current Project Period 08/01/77 through 08/31/82

8. Relevant review process(es), as applicable: Progress report submitted by investigator annually throughout project period. Application for competing renewal at end of project period is reviewed by DRG Initial Review Group (Study Section), by National Advisory Environmental Health Sciences Council, and by Extramural Program staff.

9. List of key interim project milestones: Investigator has essential control over progress in grant-supported research, with thorough scientific and policy review at time of application for competing renewal. Thus milestone prediction within project period is uncertain. Present project period ends August 1982.

10. Proposed method(s) for reporting results: Grant research results generally are disseminated through professional conferences and by publishings in the scientific literature. Investigator also informs supporting institute through annual progress reports and a terminal report at the conclusion of the grant.

Interagency Work Group
Phenoxy Herbicides and Contaminants

Date Prepared: 17 March 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected ○ Accomplished ●

Milestone	1980				1981				1982				1983				1984				1985			
	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.
Current grant project period completed											●													

Date: [illegible]ember [illegible]

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Toxicology of Chlorinated Dibenzo-p-Dioxins

2. Agency responsible, including agency component(s) directly responsible for activity: National Institute of Environmental Health Sciences; Extramural Program

3. Statement of objective(s): The objective is to study the chemistry and biological actions of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related compounds. Interest is in the mechanism of toxicity of these compounds at a molecular level, and their use as a probe in understanding gene expression. In the current funding period the goals have been: 1) to further characterize the structure-activity relationship for the induction of aryl hydrocarbon hydroxylase (AHH) activity by other groups of halogenated aromatic compounds; 2) to further characterize the properties and the biology of the hepatic cytosol binding species which appears to be the receptor or recognition site for the induction of AHH activity; 3) to develop another sensitive assay of microsomal monooxygenase activity.

4. Principal investigator(s): Poland, Alan P., M.D.

5. Relationship of activity to other work group activities:

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

   Investigator is studying the chemistry and biology of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) and related halogenated aromatic compounds. He is interested in the mechanism of toxicity of these compounds at a molecular level, and in their use as probes in understanding gene expressio in the current funding period the goals have been 1) to demonstrate that the toxicity of TCDD and related compounds is mediated through the inductio receptor 2) to develop specific model systems to study TCDD toxicity and 3) to further characterize and partially purify the cytosolic binding protein.

7. Status as of 9/1/80: Current Project Period 09/01/77 through 01/31/81

8. Relevant review process(es), as applicable: Progess report submitted by investigator annually throughout project period. Application for competing renewal at end of project period is reviewed by DRG Initial Review Group (Study Section), by National Advisory Environmental Health Sciences Council, and by Extramural Program staff.

9. List of key interim project milestones: Investigator has essential control over progress in grant-supported research, with thorough scientific and policy review at time of application for competing renewal. Thus milestone prediction within project period is uncertain. Present project period ends January 1981.

10. Proposed method(s) for reporting results: Grant research results generally are disseminated through professional conferences and by supporting institute through annual progress reports and a terminal report at the conclusion of the grant.

Phenoxy Herbicides and Contaminants

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected O Accomplished ●

Items	1980				1981				1982				1983				1984				1985			
	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.
rrent grant project riod completed					O																			

8. Relevant review process(es), as applicable: Progress report submitted by investigator annually throughout project period. Application for competing renewal at end of project period is reviewed by DRG Initial Review Group (Study Section), by National Advisory Environmental Health Sciences Council, and by Extramural Program staff.

9. List of key interim project milestones: Investigator has essential control over progress in grant-supported research, with thorough scientific and policy review at time of application for competing renewal. Thus milestone prediction within project period is uncertain. Present project period ends March 1980.

10. Proposed method(s) for reporting results: Grant research results generally are disseminated through professional conferences and by supporting institute through annual progress reports and a terminal report at the conclusion of the grant.

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Mechanism(s) of Toxicity of The Chlorinated P-Dioxins

2. Agency responsible, including agency component(s) directly responsible for activity: National Institute of Environmental Health Sciences; Extramural Program

3. Statement of objective(s): Numerous cases of poisoning of domestic animals and man by the chlorinated dibenzo-p-dioxins have occurred over the past two decades. In spite of the fact that we have known of the toxicity of these compounds for this period of time, we still do not know the biochemical or pharmacological mechanism(s) by which these compounds exert their toxic effects. The principal objective of these studies is to examine if a relation exists between the induction of an oxido-reductase activity known as DT-diaphorase (E.C. 1.6.99) and the toxicity of the most toxic of these chlorinated dibenzo-p-dioxins, namely, 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).

4. Principal investigator(s): Neal, Robert A., Ph.D.

5. Relationship of activity to other work group activities:

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es):

Investigator will examine whether a relationship exists between the large increase in the activity of a flavoprotein(s) displaying DT-diaphorase activity seen on exposure of rats to the representative chlorinated dibenzo-p-dioxin TCDD and the toxicity of this compound. If progress is made in understanding the biochemical mechanism(s) of toxicity of the representative chlorinated dibenzo-p-dioxin TCDD, investigator will, at some future date, carry out studies examining whether the same biochemical mechanism(s) account for the toxicity of the dibenzofurans and pentachlorobiphenyls such as the 3', 4', 5', 3, 4 isomer.

7. Status as of 9/1/80 : Current Project Period 04/01/77 through 03/31/80

Interagency Work Group
Phenoxy Herbicides and Contaminants

Date Prepared: 17 March 1980

SCIENTIFIC ACTIVITY MILESTONE TIMETABLE

Projected ○ Accomplished ●

stones	1980				1981				1982				1983				1984				1985			
	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.	Mar.	June	Sept.	Dec.
rrent grant project riod completed	●																							

Date: September 3, 1980

SCIENTIFIC ACTIVITY REPORT

Interagency Work Group on
Phenoxy Herbicides and Contaminants

1. Title of activity: Synthesis of selected tetrachlorodibenzo-p-dioxins and related compounds as analytical standards.

2. Agency responsible, including agency component(s) directly responsible for activity: DHHS, NIH, NIEHS, LEC

3. Statement of objective(s): Synthesize 12 selected tetrachlorodibenzo-p-dioxins, and related compounds with chemical purity equal to or greater than 98% and provide unequivocal structure assignment for each compound.

4. Principal investigator(s): Dr. J. D. McKinney
Dr. D. B. Walters

5. Relationship of activity to other Work Group activities: R & D needs with respect to an anlytical method for 2,3,7,8-TCDD for regulatory purposes.

6. Statement of scientific method(s) to be used, including (as appropriate) administrative process(es): Synthetic organic chemistry unequivocal anlytical chemical structure assignment.

7. Status as of September 1, 1980: RFP announced closing date July 1, 1980; anticipate award in FY80.

8. Relevant review process(es), as applicable: Normal research review channels.

9. List of key interim project milestones (nature, description and projected dates of accomplishment) and project completion date:

10. Proposed method(s) for reporting results: Synthetic report and analytical documentation including suff. spectral and other characterization data for structure assignment.