Description Memo from Ford to Christofano re: Samples for acute oral toxicity studies.

Exhibit #P0503

PIN #	01450-1
Date	28-Jul-66
Author	JOHN P FRAWLEY
Addressee	OETTEL & DIELEMAN, RIEN PHILLIPS, R.C. & CHRISTOFANO, E.E. TAVES, N.A. & 3 OTHERS

Description Cover letter from Frawley to Oettel for samples sent to BASF for analysis of dioxin content as discussed in September of 1965.

Exhibit #P0508

PIN #	06346-51
Date	23-Aug-66
Author	J A NOONE
Addressee	HERCULES EMPLOYEES
Description	Minutes of NACA meeting on August 23, 1966.

Exhibit #P0509

PIN #	06339-44
Date	23-Aug-66
Author	C L DUNN
Addressee	FILE
Description	Handwritten notes of Dunn of NACA meeting of August 23, 1966.

Exhibit #P0510

PIN #	01246 29-37
Date	26-Aug-66
Author	R DIELEMAN
Addressee	FRAWLEY, J.P. & PHILLIPS, H.C.

Description Letter from Diehlman to Frawley reports on visit of Oettel at BASF and attaches the 1955 report by Oettel re: 1953 exposure; report has evidence compelling punitive

15522

damages: no summary possible.

Exhibit #P0511

PIN #	13970-86
Date	01-Sep-66
Author	HERCULES CORP
Addressee	GOVERNMENT
Description	Contract between Government and Hercules, Inc. (DSA-400-67-C-1633), effective date September 1, 1966,. 437,000 gal. AO for $2,923,530 from 10/1/66 to 6/1/67; free from defects.

Exhibit #P0516

PIN #	06362-5
Date	27-Sep-66
Author	C L DUNN
Addressee	FILE
Description	Minutes of NACA meeting of 09/27/66.

Exhibit #P0517

PIN #	01985-6
Date	01-Oct-66
Author	HERCULES CORP
Addressee	HERCULES
Description	Dechlorination Manual - "CAUTION!!! Do not let temperature get above 170 degrees and do not let pressure get above 315 pounds."

Exhibit #P0525

PIN #	00000
Date	19-Oct-66
Author	JOHN P FRAWLEY
Addressee	OETTEL & SCOTT, R.B. PHILLIPS, R.C. & DIELEMAN, R. TAVES, M.A. & FORD, J.J.
Description	Letter from Frawley to Oettel of BASF re: bioassay for dioxin and Hercules rejecting new efforts to determine a new method; (Dow) reports positive results with samples of 2,4,5-T acid containing 1 ppm dioxin.

Exhibit #P0526

PIN #	06366-70
Date	25-Oct-66
Author	C L DUNN
Addressee	
Description	Minutes of NACA meeting on October 25, 1966.

Exhibit #P0527

PIN #	06366-70
Date	25-Oct-66
Author	C L DUNN
Addressee	
Description	Handwritten notes of Dunn on NACA meeting of October 25, 1966.

Exhibit #P0532

PIN #	31639-50
Date	03-Nov-66
Author	BIOTEST LABORATORIES
Addressee	HERCULES
Description	Biotest Laboratories report to Hercules, Inc. on acute oral toxicity studies on three materials.

Exhibit #P0534

PIN #	00000
Date	04-Nov-66
Author	INC HERCULES
Addressee	
Description	Esterification manual; essential materials; formulas.

Exhibit #P0563

PIN #	06399-401
Date	18-Jan-67
Author	C L DUNN
Addressee	

Description Minutes of NACA meeting of January 18, 1967.

Exhibit #P0567

PIN # 15034-44
Date 27-Jan-67
Author K WILDER
Addressee EAGAN, J. & GIVENS, K.T.

Description Memo from Wilder to Eagan re: visit to U.S. Army phosphate development works, Muscle Shaols, Alabama; describes usage in VN, 2-4 applications, 30 days apart.

Exhibit #P0587

PIN # 17060-1
Date 23-Feb-67
Author K T GIVENS
Addressee TRAUB, JOHN L. & COPELAN, J.G.
EAGAN, J.M. & YATES, R.T.
RENO, P.J. & 2 OTHERS

Description Letter from Givens to Traube re: Hercules' proposal of building a new plant.

Exhibit #P0601

PIN # 08406-10
Date 28-Mar-67
Author G E LYNN
Addressee USDA
Description Lynn speech to USDA re: collect data on toxicity pertinent to use of phenoxy herbicides.

Exhibit #P0604

PIN # 01247
Date 29-Mar-67
Author P OETTEL
Addressee FRAWLEY, JOHN P.
Description Letter from Oettel to Frawley re: photographs of people with acne.

Exhibit #P0607

PIN #	017052-4
Date	03-Apr-67
Author	K T GIVENS
Addressee	YATES, R.T. & RENO, P.J. EAGAN, J.M. & MILLER, J. COPELAN, J.G. & 4 OTHERS
Description	Letter from Givens re: Orange Production, Edgewood Arsenal.

Exhibit #P0612

PIN #	06411-15
Date	20-Apr-67
Author	C L DUNN
Addressee	
Description	Minutes of NACA meeting of April 20, 1967.

Exhibit #P0619

PIN #	06422-3
Date	11-May-67
Author	G E LYNN
Addressee	HAZLETON LAB.
Description	Letter from Lynn to Hazleton Lab., Inc. re: verbal arrangement of 04/20/67 between Lynn and Hazleton to prepare petitions for negligible tolerances for use on crops for phenoxy herbicides.

Exhibit #P0620

PIN #	06420-1
Date	12-May-67
Author	G E LYNN
Addressee	MEMBERS NACA & NOONE, J.A. HALEY, DENIS
Description	Memo from Lynn re: NACA and Hazleton meeting of May 11, 1967.

Exhibit #P0630

PIN # 32493-4
Date 08-Jun-67
Author EMIL E CHRISTOFANO
Addressee FANCHER, OTIS & SIDWELL, A.E.
DUNN, C.L. & SCOTT, R.B.

Description Letter from Christofano to Fancher re: Hercules Project No. 67-13; liver damage studies; toxicity of three materials to rabbits.

Exhibit #P0635
PIN # 03904-5
Date 29-Jun-67
Author JOHN P FRAWLEY
Addressee OETTEL, PROF. H. & DIELEMAN, R.
PHILLIPS, H.C. & SCOTT, R.B.
DUNN, C.L. & SIDWELL, A.E.

Description Letter from Frawley to Oettel re: Columbian study. "I agree with you that this report is very disturbing." States that 2,4,5-T acid and ester are significantly more toxic than TCP.

Exhibit #P0638
PIN # 32452-62
Date 30-Jun-67
Author J M EAGAN
Addressee WILDER, H.E. & FRAWLEY, J.P.

Description Memo from Eagan to Wilder re: chloracne cases in Columbia, South America.

Exhibit #P0640
PIN # 14692-704
Date 06-Jul-67
Author C W CARTY
Addressee HERCULES
Description Letter from Carty to Hercules Powder Co., Inc. demonstrates private industry's input in reviewing commentary and affecting redrafting of government specs. at government's request.

Exhibit #P0641

PIN #	15600-13
Date	11-Jul-67
Author	W W RAYNOLDS
Addressee	WILDER, H.E.
Description	Memo re: July 6, 1967 letter of Carty's to Hercules Powder Co., Inc.

Exhibit #P0644

PIN #	32149
Date	18-Jul-67
Author	MITCHELL R ZAVON
Addressee	CHRISTOFANO, E.E.
Description	Letter of Zavon to Christofano re: his request for a meeting regarding comparative industry study of employees.

Exhibit #P0646

PIN #	32148
Date	28-Jul-67
Author	EMIL E CHRISTOFANO
Addressee	ZAVON, M. & EAGAN, J.M. SIDWELL, R.
Description	Letter from Christofano to Zavon rejecting proposed study.

Exhibit #P0649

PIN #	15392-94
Date	11-Aug-67
Author	A E SIDWELL
Addressee	EAGAN, J.M. & SCOTT, R. WILDER
Description	Memo from Sidwell to Eagan re: "Orange quality problem - recites that Hercules has produced nearly 15,000,000 pounds of Agent Orange since November 15, 1964.

Exhibit #P0650

PIN #	06436-7

15528

Date 17-Aug-67
Author G E LYNN
Addressee NACA MEMBERS
Description Memo from Lynn to Members of Industry Task Force on Phenoxy Herbicide Tolerances re: 2,4,5-T formulations.

Exhibit #P0653
PIN # 31918
Date 28-Aug-67
Author A E SIDWELL
Addressee
Description Appropriation Request signed by A.E. Sidwell re: infrared spectrophotometer.

Exhibit #P0657
PIN # 15468-9
Date 02-Sep-67
Author A L TREISBACK
Addressee WILDER
Description Handwritten notes from Treisback to Wilder re: "quality, purity, and chemistry of our operation."

Exhibit #P0660
PIN # 15454-6
Date 05-Sep-67
Author M A TAVES
Addressee EAGAN, J.M. & RENO, P.J.
TURK, E. & SCOTT, R.B.
GIVENS, K.T. & 3 OTHERS

Description Memo from Taves to Eagan re: "Orange" Analysis; Govt. does not know components in products which are known to Hercules; before advising Govt., Hercules will study.

Exhibit #P0663
PIN # 15443-6
Date 07-Sep-67
Author R B SCOTT

15529

Addressee TAVES, M.A. & CLARK, W.H.
GIVENS, K.T. & EAGAN, J.M.
TURK, E. & 2 OTHERS

Description Memo from Scott to Taves re: Orange; testing September 5, 1967.

Exhibit #P0664
PIN # 15449-50
Date 07-Sep-67
Author E T GIVENS
Addressee EAGAN, J.M. & YATES, R.T.
RENO, F.J. & 3 OTHERS

Description Memo from Givens to Eagan re: NACA's proposed guidelines.

Exhibit #P0666
PIN # 15903-4 101
Date 12-Sep-67
Author J M EAGAN
Addressee
Description Notes of Eagan re: Synthetics Dept. Proposed Meeting, etc.

Exhibit #P0669
PIN # 14716
Date 19-Sep-67
Author UNKNOWN
Addressee
Description Notes.

Exhibit #P0671
PIN # 13903-4
Date 26-Sep-67
Author K T GIVENS
Addressee EAGAN, J.M. & SCOTT
COPELAND, J.G. & TURK, E.
YATES & 2 OTHERS

Description MEMO RE: "ORANGE QUALITY"

15530

Exhibit #P0677

PIN #	32150
Date	10-Oct-67
Author	E E CHRISTOFANO
Addressee	DUNN, C.L. & EAGAN, J.W. WILDER, H.E. & SIDWELL, A.E.
Description	Memo from Christofano to Dunn re: Dr. Zavon at Kettering Lab doing a prospective study of 15 - 20 year duration.

Exhibit #P0683

PIN #	06475-9
Date	17-Oct-67
Author	C L DUNN
Addressee	
Description	Minutes of meeting of October 17, 1967 - NACA

Exhibit #P0685

PIN #	02986PLUS
Date	25-Oct-67
Author	R B SCOTT
Addressee	VANDOVENIER, W. & COPELAND, J.C. CRITTENDEN, K.D. & EAGAN, J.M. GIVENS, K.T. & 2 OTHERS
Description	Letter from Scott to Vandovenier and copy of proposed specifications for herbicide Orange; cover letter for 10/24, proposed specs as drafted by Hercules.

Exhibit #P0698

PIN #	06549
Date	27-Nov-67
Author	C L DUNN
Addressee	MEMBERS NACA
Description	Letter from Dunn to members of NACA re: conference with USDA.

Exhibit #P0699

PIN #	06547-8
Date	27-Nov-67
Author	C L DUNN
Addressee	HAYS, HARRY & IRVING, ARS ANDERSON, USDA & DANIELSON, ARS
Description	Letter from Dunn to Hays requesting Extension for 1 year beyond 12/31/67 for cancellation date at registrations of 2,4-D and 2,4,5-T and others.

Exhibit #P0702

PIN #	06554-56
Date	08-Dec-67
Author	C L DUNN
Addressee	FDA & USDA
Description	Letter from Dunn to FDA on behalf of NACA Industry Task Force on phenoxy herbicide tolerance.

Exhibit #P0703

PIN #	06580-1
Date	12-Dec-67
Author	C L DUNN
Addressee	FDA & USDA
Description	Letter from Dunn to FDA similar to letter of 12/8/67.

Exhibit #P0708

PIN #	15514
Date	27-Dec-67
Author	A E SIDWELL
Addressee	LOWE, L.E.
Description	Memo from Sidwell to Lowe re: Factor "X" unknown, still at 8.5%.

Exhibit #P0710

PIN #	06584

15532

Date 29-Dec-67
Author HAROLD G ALFORD
Addressee HERCULES
Description Letter from Alford at USDA to Dunn at Hercules re: 11/27 request granted until 1/1/69.

Exhibit #P0715
PIN # 14671-8
Date 02-Jan-68
Author K T GIVENS
Addressee WILDER & K.E.
CRITTENDEN, E.D. & RENO, P.J.
EAGAN, J.M.
& SCOTT, R.B.

Description Memo from Given to Wilder re: New contract - Herbicide Orange; Hercules participation in reviewing and redrafting proposed government specs with portions of contract attached.

Exhibit #P0716
PIN # 06592-98
Date 04-Jan-68
Author UNKNOWN
Addressee
Description Minutes of meeting of NACA meeting of January 4, 1968.

Exhibit #P0718
PIN # 14664-70
Date 10-Jan-68
Author A E SIDWELL
Addressee EAGAN, J.M. & CRITTENDEN, E.D.
GIVENS, K.T. & RENO, D.J.
SCOTT & WILDER

Description Memo from Sidwell to Eagan re: "New Contract, Orange" detailing critiques and suggested changes - "you will remember that we have the unsolved problem of compound 'x' in the butyl and ester. . ."

Exhibit #P0721

PIN #	15478-9
Date	11-Jan-68
Author	K T GIVENS
Addressee	WILDER, H.E. & CRITTENDEN, E.D. EAGAN, J.M. & RENO, P.J.
Description	Memo and attachment from Givens to Wilder re: use of imported 2,4,5-T; refers to authority to use imported 2,4,5-T for Agent Orange production.

Exhibit #P0724

PIN #	17041
Date	20-Jan-68
Author	A E SIDWELL
Addressee	TAVES, M.A. & EAGAN, J.M. SCOTT, R.B. & WILDER, H.E. FISHER, J.R. & TECH. FILE
Description	Memo re: Compound "X" in Production n-Butyl-T.

Exhibit #P0727

PIN #	15474-6
Date	25-Jan-68
Author	K T GIVENS
Addressee	COLLNS, G.F. & CRITTENDEN, E.D. EAGAN, J. & SCOTT, K. WILDER, N.E.
Description	Letter from Givens to Collins demonstrating Hercules' role in preparation and drafting of specs.

Exhibit #P0730

PIN #	17050
Date	29-Jan-68
Author	K T GIVENS
Addressee	WILDER
Description	Memo from Givens to Wilder re: Herbicide Samples; use of foreign 2,4,5-T acids.

Exhibit #P0731

PIN #	15400
Date	29-Jan-68
Author	A L TREISBECK
Addressee	GIVENS, K.T. & EAGAN, J.W. SCOTT, R.B. & SIDWELL, A.E.
Description	Memo re: Orange Analyses; Contract DSA-400-67-C-8314; changing specs.

Exhibit #P0739

PIN #	13706
Date	20-Feb-68
Author	R W HUSTON
Addressee	TREISBACK, A.L.
Description	Note from Huston to Treisback re: being below specs.

Exhibit #P0748

PIN #	15344-55
Date	27-Feb-68
Author	GEORGE F COLLINS
Addressee	HERCULES POWDER
Description	Letter from Collins of Defense Supply to Hercules; enclosing copies of a review purchase description for herbicide orange; requesting Hercules' comments.

Exhibit #P0749

PIN #	06669
Date	29-Feb-68
Author	CHIPMAN BALES
Addressee	MCCOLLISER, RON
Description	Letter from Bales at Chipman Chemical Co. to McCollister re: subacute toxicity data requested by FDA.

Exhibit #P0753

PIN #	15343-53
Date	04-Mar-68

15535

Author K T GIVENS
Addressee SCOTT, R. & TREISBACK, A.L.

Description Memo from Givens to Scott and Treisback re: demonstrating Govt's acceptance of Hercules' changes in specs.

Exhibit #P0754
PIN # 06670
Date 04-Mar-68
Author C L DUNN
Addressee BAKER & HEW

Description Letter from Dunn to Baker at HEW re: Pesticide Petition 8F0676 for negligible residues of the herbicide.

Exhibit #P0759
PIN # 06691-2
Date 08-Apr-68
Author HEW BAKER
Addressee DUNN, C.L. & ARS
USDA
Description Letter from Baker at HEW to Dunn re: Hercules' inability to establish tolerances as requested; Hercules may amend or withdraw petition.

Exhibit #P0761
PIN # 06701
Date 15-Apr-68
Author C L DUNN
Addressee NACA MEMBERS & KRAUSCHE, K
CANKIN, R.A.
Description Memo from Dunn to NACA members re: 2,4,5-T petition; re: 4/8/68 letter.

Exhibit #P0762
PIN # 06700
Date 15-Apr-68
Author C L DUNN
Addressee BAKER, HEW & MCCOLLISTER, D.D.

15536

BALES, I.W. & KRAUSCHE, K.
HOLSING, G. CARL & NACA

Description Letter from Dunn to Baker at HEW request NACA's pesticide petitions for negligible residue of herbicide MCPA be withdrawn without prejudice.

Exhibit #P0765

PIN # 15389
Date 09-May-68
Author A L TREISBACK
Addressee EAGAN, J.W. & GIVENS, K.T.
SCOTT, R.B. & SIDWELL, A.E.
BENNETT, T.
Description Memo from Treisback to Eagan re: Recovered Acids - Addenda; government rewriting specs as requested by Hercules.

Exhibit #P0766

PIN # 15342
Date 09-May-68
Author GOVT
Addressee GIVENS, K.T.
Description Teletype message from Government on Hercules letterhead for Givens re: changes in tolerances (for percentage of 2,4-D and 2,4,5-T in Agent Orange); 810,000 gal. @ 7.25 per gal. for $5,872,500 offer; delivery at 90,000 gal. per month from 6/68-2/69.

Exhibit #P0767

PIN # 15390-4
Date 09-May-68
Author A L TREISBACK
Addressee EAGAN, J. & GIVENS, E.
SCOTT, R. & SIDWELL, A.
BENNETT, T.
Description Memo from Treisback to Eagan re: Recovered Acids; Orange quality problems and reference to attached letter of August 11, 1967.

Exhibit #P0768

PIN #	15395
Date	09-May-68
Author	A L TREISBACK
Addressee	GIVENS & EAGAN, J. BENNET, T.
Description	Memo from Treisback to Givens re: Orange; imported 2,4,5-T.

Exhibit #P0774

PIN #	15288-319
Date	05-Jun-68
Author	K T GIVENS
Addressee	TREISBACK, A.L. & CRITTENDEN, E.D. EAGAN, J.M. & RENO, P.J.
Description	Memo from Givens to Treisback re: "Orange" Contract; attached new contract; 90,000 gal. per month from 6/30/68-2/28/69 for $5,872,500; free from defects; attached copies of 2/23/68 specs and amendment of 4/11/68.

Exhibit #P0776

PIN #	13664
Date	11-Jun-68
Author	A S SIDWELL
Addressee	TREISBACK, A.L.
Description	Memo from Sidwell to Treisback re: Conference on Contract DSA-400-68-C-6093; conference with government.

Exhibit #P0778

PIN #	13662-3
Date	12-Jun-68
Author	K W HUSTON
Addressee	TREISBACK, A.L. & BUMP, R.A. BENNETT, T. & RAY, F.H. PENNOCK, J.G. & FISHER, J.R.
Description	Memo from Huston to Hercules employees re: DSA Contract DSA-400-68-C-6093; meeting

with government to discuss and agree on contract.

Exhibit #P0799
PIN # 15245
Date 18-Sep-68
Author R W HUSTON
Addressee BUMP, R.A. & PAMRY, S.A.
GIVENS, K.T. & TREISBACK, A.L.
SIDWELL, A.E. & 2 OTHERS

Description Memo from Huston to Bump re: Documents - "Orange" Contract.

Exhibit #P0808
PIN # 04030-1
Date 16-Oct-68
Author EMIL E CHRISTOFANO
Addressee ROWE, V.K.
Description Letter from Christofano to Rowe re: bioassay methods inconsistant and usefulness as a test for dioxin is questionable.

Exhibit #P0816
PIN # 18121
Date 08-Nov-68
Author TREGLIA
Addressee HERCULES
Description Memo from Treglia at Dept. of Army to Hercules re: invitation to comment on proposed specs - suggestions that may result in a savings to Govt.

Exhibit #P0818
PIN # 06888
Date 03-Dec-68
Author ALFORD
Addressee DUNN, C.L.
Description Letter from Alford at USDA to Dunn re: Extension of Registrations for 2,4,5-T acid; Dunn's letter of 10/29/68; extends

date for finite tolerances to 1/1/70.

Exhibit #P0824

PIN #	25992-4
Date	30-Dec-68
Author	J CHRISTOFANO
Addressee	DUNN, C.L. & OTHERS
Description	Memo from Christofano to Dunn re: Dioxin studies; biotest lab report on dioxin studies; studies inconsistent and inconclusive.

Exhibit #P0870

PIN #	DOW754889
Date	25-Nov-69
Author	J E JOHNSON
Addressee	
Description	Page two of Johnson report.

Exhibit #P0890

PIN #	01540-2
Date	16-Jan-70
Author	J J FORD
Addressee	TAVES, M.A. & SCOTT, R.B. DUNN, CL.L & WALKER, J. CONNER, A.
Description	Memo from Ford to Taves re: analysis of 2,4,5-T Acid for "Dioxin" Content; further development indicated; 4-6 weeks to evaluate proposed modifications.

Exhibit #P0911

PIN #	26964
Date	24-Feb-70
Author	J P FRAWLEY
Addressee	
Description	Notes of Frawley re: findings of cleft palate.

15540

Exhibit #P0923

PIN #	01588-9
Date	19-Mar-70
Author	J J FORD
Addressee	TAVES, M.A. & SCOTT, R.B. DUNN, C.L. & WALKER, J.F. CONNER, A.Z. & SIDWELL, A.E.
Description	Memo from Ford to Taves re: Analysis of 2,4,5-T Acid for "Dioxin" Content; retesting of old samples produced in 1965; attached chart shows dioxin content as high as 3.5 ppm in 1965.

Exhibit #P0938

PIN #	03877
Date	10-Apr-70
Author	J G COPELAND
Addressee	
Description	Synthetics Dept. R&D Newsletter of Copeland; ". . . dioxin, which is highly toxic, a severe skin irritant, and a suspected teratogen."

Exhibit #P0942

PIN #	04032
Date	15-Apr-70
Author	R B SCOTT
Addressee	DUNN, C.L. & PIERCE, H.F. LEMONS, E.W. & GIVENS, K.T. FRAWLEY, J.P. & 2 OTHERS
Description	Memo from Scott to Dunn reL: 2,4,5-T Analyses.

Exhibit #P0959

PIN #	04034-5
Date	10-Jun-70
Author	JOHN J FORD
Addressee	PETERSON, R. & KOPKINS SCOTT, R. & TAVES, M.A.
Description	Memo from Ford to Peterson re: Separation of the Toxic Contaminant 2,3,7,8-TCP from

2,4,5-TCP acid; dioxin is a highly toxic contaminant; teratogenic effects recently attributed to 2,4,5-T may be due to dioxin contaminant.

Exhibit #P0980
PIN # 27817-18
Date 23-Nov-70
Author JOHN P FRAWLEY
Addressee HIGGIN, JOHN C.
Description Memo from Frawley to Higgin discussion whether teratology was associated with dioxin; government agency sponsoring study not familiar with toxicity of dioxin; Surgeon General declared 2,4,5-T hazard to health; 2,4,5-T banned.

Exhibit #P0981
PIN # 27349
Date 24-Nov-70
Author J P FRAWLEY
Addressee DUNN, C.L.
Description Memo from Frawley to Dunn re: completed Bionetics study on 2,4,5-T.

Exhibit #P0993
PIN # 27396-402
Date 26-Jan-71
Author JOHN P FRAWLEY
Addressee WILSON
Description Letter from Frawley to Wilson, Advisory Committee on 2,4,5-T; lack of hazard presented; Hercules acknowledges past history of U.S. and Germany.

Exhibit #P0994
PIN # 27462
Date 17-Feb-71
Author J P FRAWLEY
Addressee DUNN, C.L. & COPELAND, J.G.
PIERCE, H.F. & GIVENS, K.T.
OTHERS

Description Memo from Frawley to Dunn re: Dosing Error in Bionetics Study on 2,4,5-T; mistake in bionetics report and what they should do.

Exhibit #P0999

PIN # 27656
Date 30-Mar-71
Author JOHN P FRAWLEY
Addressee WILSON, JAMES G. & MEMBERS ADVISORY COMMITTEE & ON 2,4,5-T

Description Letter from Frawley to Wilson on Advisory Committee on 2,4,5-T suggesting the restriction of dioxin content ". . . to a safe level."

Exhibit #P1006

PIN # 03579
Date 01-Jun-71
Author GEORGE H HOPKINS
Addressee SIDWELL, A.E. & FORD, J.J.
SCOTT & GIVENS, K.T.
DUNN, C.L.
Description Memo from Hopkins to Sidwell and Ford re: Removal of "Dioxin" from Silvex and removal of "Dioxin" from 2,4,5-T; patent in removal process.

Exhibit #P1007

PIN # 03576-8
Date 03-Jun-71
Author A E SIDWELL
Addressee HOPKINS, GEORGE H. & SCOTT, R.B.
GIVENS, K.T. & DUNN, C.L.
TREISBACK, A.L. & 2 OTHERS

Description Memo from Sidwell to Hopkins re: Removal of "Dioxin" from Silvex.

Exhibit #P1011

PIN # 27741
Date 29-Jul-71

15543

Author R STEHL
Addressee DOW
Description Analytical Laboratories report of July 29, 1971; 4/4/71 sample tested and Hercules rated it 0.18 ppm and Dow rated it less than 5 ppb.

Exhibit #P1015
PIN # 27788-9
Date 28-Oct-71
Author D D MCCOLLISTER
Addressee WEIR, ROBERT J.
Description Letter from McCollister to Weir re: importance of not publishing difference and how to describe difference of 0.18 ppm v. 0.005 ppm.

Exhibit #P1021
PIN # 01740
Date 15-Nov-71
Author W C KENYON
Addressee TAVES, M.A. & HALL, R.T.
FORD, J.J.
Description Memo from Kenyon and Shearer to Taves re: reports of Dow on 2,4,5-T from Hercules; attempted explanation.

Exhibit #P1029
PIN # 01754-5
Date 17-Jan-72
Author D D MCCOLLISTER
Addressee HART, E. ROSS
Description Deposition of A.E. Sidwell taken on April 18, 1980;

Exhibit #P1089
PIN # 00000
Date 28-Apr-80
Author UNKNOWN
Addressee
Description Trial testimony of A.E. Sidwell.

Exhibit #P1105

PIN #	00000
Date	02-May-83
Author	UNKNOWN
Addressee	
Description	Affidavit of Charles L. Dunn date 05/02/83.

Exhibit #P0025

PIN #	DS00017892
Date	
Author	F R KENNEDY
Addressee	SAVAGE & CORT
Description	Memorandum dated March 20 [year illegible] from F. R. Kennedy to S. Savage, New York Sales, stating that the suspect batch samples from the suspect batches have been segregated and put aside for safekeeping. He also reports that Dr. Bleiberg said that he had been contacted, had asked for follow-up materials, and had not done anything more when these materials (photographs of the affected personnel) were not forthcoming.

Exhibit #P0026

PIN #	DS00001061
Date	
Author	F GORDON STEWARD
Addressee	
Description	Staff memorandum of unclear date from F. Gordon Steward reporting on technical operations for the month of April, 1967. The report notes that the use of porosities to filter dioxins was not very encouraging, but that the carbon filter seemed to be effective. Plugging seemed to be a continuing problem.

Exhibit #P0027

PIN #	DS 22713
Date	
Author	UNKNOWN
Addressee	
Description	SCRATCH PAD NOTES REGARDING LETTER OF 10/9/64.

Exhibit #P0028

PIN #	24673
Date	
Author	UNKNOWN
Addressee	

15546

Description OPERATING COMMENTS PLANT TECHNICAL JUNE, 1969.

Exhibit #P0029

PIN #	27928
Date	
Author	PAUL GROSS, MD
Addressee	DIAMOND ALKALI CO
Description	JANUARY, 1960, SEVENTH REPORT ON EVALUATION OF CHLORACNE.

Exhibit #P0074

PIN #	DS00022493
Date	290655
Author	J M YORK
Addressee	SCOVILLE & INGLEY BURTON & KIRP
Description	Memorandum dated June 29, 1955 from J. M. York, MD, to L. P. Scoville concerning chloracne at the Newark plant. Recites visit by the author to the plant, where fumes were noxious but of unknown toxicity. Describes chloracne and its mechanisms, stating that there is really no cure, and further stating that a case has to be seen to appreciate how socially debilitating it can be. Recommends sending some of the worst cases to a Dr. Marion B. Sulzberger in New York city, but further recommends that this be deferred until the plant is cleaned up or it will be an illusory remedy. Also recommends that better physical examinations be given to employees so that blood and liver damage can be assessed.

Exhibit #P0080

PIN #	DS00008854
Date	30-Aug-55
Author	GEORGE H BURRIS
Addressee	ROSENFELD & BURTON FROWNE & PORTER TOWLE & OTHERS
Description	Technical Memorandum dated August 30, 1955, from G. H. Burris and M. Rosenfeld to Mr.

15547

J. Burton describing the methods used to establish absorption curves to identify the impurities in 2,4,5-T by means of chromotography. Suggests that the curve is close to the curve established for dichlorosorcinol, but allows that a polychlorinated diphenyl ether compound may also be indicated in small amounts.

Exhibit #P0081

PIN #	DS00024253
Date	23-Sep-55
Author	J BURTON
Addressee	GLEISSNER & BROWNE TOWLE
Description	Memorandum dated September 23, 1955, from J. Burton to Dr. B. D. Gleissner reporting on toxicology tests run on rabbits by the Industrial Toxicological Laboratories. The tests on crude TCP showed that reactions to the August production samples existed but were less serious than reactions to May production samples. This indicated that they were on the right track in lower autoclave temperatures, according to the author, but that that alone would not solve the problem.

Exhibit #P0093

PIN #	DS00019554
Date	20-Oct-56
Author	JACOB BLEIBERG
Addressee	J BURTON
Description	Letter dated October 20, 1956, from Dr. Jacob Bleiberg to Mr. J. Burton summarizing his recommendations concerning chloracne at the Newark plant. He notes that the probable chloracnogen is a chlorinated di-phenyl. For Prophylaxis purposes, he recommends cleanliness and special soaps. For treatment he recommends using creams, but suggests looking for systemic disorders as well. The report contains numerous recommendations concerning diet, etc.

15548

Exhibit #P0100

PIN #	DS00008217
Date	21-Jun-57
Author	J BURTON
Addressee	GUIDI & BROWNE

Description Memorandum dated June 21, 1957, from J. Burton to R. Guidi and referenced to a file, 2,4,5-TCP Process Development. Memo outlines the need to double TCP production and to eliminate chloracne impurities. Also wants to run at a lower pressure as a safety matter. Explores various suggestions for accomplishing these objectives from an engineering point of view.

Exhibit #P0103

PIN #	DS00017415
Date	18-Sep-57
Author	D J PORTER
Addressee	BURTON & LUKES SUTTER & CLEVELAND

Description Memorandum dated September 18, 1957 from D. J. Porter at Painesville to J. Burton at Newark reporting on meeting with Dr. Kudesus of Boehringer to discuss acquisition of know-how for production of penta- chlorophenol. Told Kudesus that since the work of Al Hirsch and Irving Rosen "several years ago" and the more recent work of Jack Jenney and Al Lewis, they had no indication of chloracne trouble. Dr. Kudesus said he would send them a copy of his report on the problem which had caused them to shut down one of their plants and, in the meantime, he identified the culprit with a diagram which is reported in the memorandum. It was said that the material is not formed if the triTCP autoclave temperature is kept below 155 degrees C, and if the caustic mixture is not more than 120 C. Writer suggests trying this in the TCP plant in view of the problems there.

Exhibit #P0105

PIN #	DS00022024

Date 11-Oct-57
Author D J PORTER
Addressee GUIDI & BURTON
LUKEE
Description Memorandum dated October 11, 1957 from D. J. Porter to R. A. Guidi reporting the forwarding of a transalation of a memo from C. H. Boehringer Sohn, Ingelheim, reiterating comments previously made "some time back" by Dr. Kudesus of Boehringer. Cover letter suggests that if there are problems running a syline at Newark, a test could be done at the autoclave at Painesville. The attachment advises of the steps in the reaction where acnegen can be seen to be formed, and of the further steps (principally temperature control) that can be used to minimize that risk.

Exhibit #P0106
PIN # DS 27915
Date 19-Dec-57
Author MARIAN L WESTRICK, PHD
Addressee J. BURTON
Description SIXTH REPORT ON EVALUATION OF CHLORACNE - NOV 1957

Exhibit #P0115
PIN # 000000
Date 19-Sep-58
Author DONALD M PURDY
Addressee DIAMOND ALKALI & MANK EDWARD

Description Agreement dated September 10, 1958 by employee, Donald M. Purdy, to assign any patent for work done for Diamond to Diamond.

Exhibit #P0128
PIN # DS00017413
Date 30-Sep-59
Author THORNTON HOLDER
Addressee BURTON & BRUMBAUGH
BORROR & EVERSON
PORTER & GOYB

15550

Description Internal Diamond Memorandum dated September 30, 1959 reporting information from Boehringer that they had not had a chloracne case for several years by reason of changes in process and a major overhaul of their factory. The memo notes that Boehringer continued to have liver cases several years after clearing up their chloracne problems.

Exhibit #P0137

PIN #	DS00010807
Date	20-May-60
Author	THORNTON HOLDER
Addressee	SCOVILLE & HONOUR

Description Memorandum dated May 20, 1960 from Thornton F. Holder to L. P. Scoville referring to differences in accidents at Newark and at Ingelheim and stating that he would be willing to use his offices to have a meeting with Boehringer (Cela) if that was desireable.

Exhibit #P0140

PIN #	DS00008450
Date	21-Jun-60
Author	J BURTON
Addressee	BORROR & GUIDI LINDEMANN & SCOVILLE WEINER

Description Confidential Memorandum dated June 21, 1960 from J. Burton to J. A. Borror reporting on laboratory work concerning the 2,4,5-T process. The memo suggests that yields are satisfactory at a 2:2 mol ratio. Identifies information on Newark that chlorinated dyphenyl ethers are the probable cause of chloracne. Suggests that if lab results cannot be duplicated at the plant, then the recommendation is to increase the caustic ratio rather than the heat of reaction because higher temperatures promote chloracnegen (chlorinated diphenyl ethers) formation. The memo suggests that a dilutent might be used to moderate the reaction also.

Exhibit #P0141

PIN #	DS00022022
Date	23-Jun-60
Author	J J BURTON
Addressee	CONRAD & DELL CELA
Description	Copy of a letter dated June 23, 1960 from J.Burton to Herr. Conrad and Dell of Cela describing in some detail Diamond's process, experience, their attempts to understand how to avoid future explosions and their request for a similar exchange of information from Cela.

Exhibit #P0145

PIN #	DS00021951
Date	10-Aug-60
Author	NONE BOEHRINGER SOHN
Addressee	BORROY
Description	Letter from illegible person at Boehringer Sohn to J. A. Borror, Diamond Alkali Company dated August 10, 1960 describing in detail their process [CELA] for processing TCP to avoid chloracnegens. Asks for confidential exchange of information on the subject. Refers to September 20, 1957 letter addressed to Plainsville, Ohio.

Exhibit #P0161

PIN #	DS00011518
Date	06-Mar-62
Author	R L ANNIS
Addressee	EVERSON & CROSS DUNNING & ENTEMANN HIRSCH & OTHERS
Description	Memorandum dated March 6, 1962 from R. L. Annis to H. E. Everson with a wide distribution list reporting on progress of 2,4-D and 2,4,5-T Process Studies. The studies look toward expansion of production outputs. The report states a revised 2,4-D process has been virtually completed, and that it is hoped that a 2,4,5-T process can

be developed from that process, but notes that this will require higher temperatures and higher pressures. The report is emphatic that the plant will require updating at some expense for the new processes. No mention is made of health considerations.

Exhibit #P0166

PIN #	24256
Date	11-May-62
Author	W GOODLOE
Addressee	R. A. GUIDI & R. F. LINDEMANN
Description	UNSIGNED MEMO BY W.GOODLOE TO R. A. GUIDI DATED 11 MAY 1962 ADVISING ALL CHLORACNE SAMPLES (14) PREPARED AS REQUESTED & READY FOR SHIPMENT TO MELLON INSTITUTE. DESCRIPTION OF EACH SAMPLE ATTACHED.

Exhibit #P0171

PIN #	DS 27937
Date	07-Jun-62
Author	JAMES M MC NERNEY
Addressee	DR. GUIDI
Description	8TH REPORT ON EVALUATION OF CHLORACNE.

Exhibit #P0178

PIN #	DS00017412
Date	09-Jul-62
Author	K L CHANDLER
Addressee	GUIDI & WEINER
Description	Memo dated July 9, 1962 from Chandler to Guidi reporting that Riverdale Chemical and Quaker City Tree had serious complaints aobout chloracne associated with Diamond's product and asking whether there is a likelihood that these incidents will recur.

Exhibit #P0185

PIN # DS00019539
Date 06-Nov-62
Author H C BAISALO
Addressee HILL W C & BAISALO H C
GUIDI R A
Description Confidential Memorandum re Chloracne containing what appears to be the outline of a speech concerning the chloracne problem and which is dated November 6, 1962. Document is incomplete as we have it.

Exhibit #P0186
PIN # DS0000715
Date 10-Nov-62
Author EUGENE BAK
Addressee BRAUN & GOODLOE
WEINER & GUIDI
HILL & OTHERS

Description Detailed report concerning existing processes for 2,4-D and 2,4,5-T and making recommendations for changing processes for economy. Report is prepared by Eugene Bak with the assistance of Daniel Braun and William Goodloe, and is signed by Hill and Guidi.

Exhibit #P0193
PIN # DS00008832
Date 07-Jan-63
Author RF LINDEMANN
Addressee HILL
Description Memorandum dated January 7, 1963 from R. F. Lindemann to W. E. Hill, Jr. reporting on his effort to identify the impurities in 2,4,5-T and TCP. States that the chromotograph of the impurity is close to the basic chemical, but with a slightly higher boiling point.

Exhibit #P0201
PIN # DS00017405
Date 15-Feb-63
Author R A GUIDI

15554

Addressee WEINER
Description Memorandum dated February 15, 1963 from R. A. Guidi to H. S. Weiner re: forwarding an article given to him by Dr. Bleiberg suggesting the development of porphyria from the ingestion of hexachlorobenzene. Memo notes presence of porphyrins in urine samples collected from workers and at a level indicating liver disturbance. Says the article will set off the health authorities and that Bleiberg is already in contact with Dr. Birmingham for advice.

Exhibit #P0206
PIN # DS00017400
Date 25-Mar-63
Author H S WEINER
Addressee GUIDI & WILKERSON

Description Confidential Memorandum from H. S. Weiner to R. A. Guidi dated March 25, 1963 re: "Chloracne." The memo refers to a March 20 memo and states that USPH should not be allowed to visit the plant unless a full program concerning the visit is developed with Diamond's medical advisor and Marty Wilkerson. The memo suggests that thought be given to the possibility that the visit might be used as a sensational event in the news- papers.

Exhibit #P0208
PIN # DS00024455
Date 27-Mar-63
Author RICHARD W MCBURNEY
Addressee JARVIS & BROWN
OCIDI
Description Memorandum dated March 27,1963 from Richard W. McBurney, MD, to Frank W. Jarvis in Cleveland. It notes the history with chloracne and states that recent articles have convinced Dr. Bleiberg that they may also be dealing with a liver problem. The letter states that the only way to begin to solve the problem was to renovate the old plant, subject to available financing.

Exhibit #P0211

PIN #	DS00017963
Date	09-Apr-63
Author	GUILLERMO
Addressee	CECIL
Description	Translation of a letter written in Spanish on April 9, 1963 by Leon R. Guillermo of Quimor to L. L. Cecil, Jr. re: "Problem in the Application of Weed Killers". The communication informs Mr. Cecil that workers in the Bucaramanga area have suffered severe reactions after using Diamond's 2,4-D and 2,4,5-T products.

Exhibit #P0212

PIN #	DS00019524
Date	11-Apr-63
Author	R A GUIDI
Addressee	WILKERSON & BROWN MCBURNEY
Description	Memo dated April 11, 1963 from R. A. Guidi to M. F. Wilkerson reporting on a visit of Drs. Key and Birmingham to Newark. Memo encloses a copy of a report from McBurney to Jarvis previously prepared. Guidi reports that two men are to be admitted to Beth Israel Hospital for further tests, "with specific emphasis on the kidneys and liver."

Exhibit #P0222

PIN #	DS00017940
Date	02-May-63
Author	R J MARRESE
Addressee	GUIDI R A & KING, J. O. CHANDLER E. L. & L L CECIL
Description	Confidential Memorandum dated May 2, 1963 from R. J. Marrese to Larry L. Cecil arguing that the Quimor incident did not involve a product quality question as much as a personal hygiene factor.

15556

Exhibit #P0223

PIN #	DS00017939
Date	08-May-63
Author	L L CECIL
Addressee	CLAGHORN & CREAMER KNOBLOCK & CLAIR
Description	Memorandum dated May 8, 1963 from L. L. Cecil to D. A . Claghorn, Herbicides, Columbia, forwarding materials for confidential consideration.

Exhibit #P0227

PIN #	DS00019506
Date	20-May-63
Author	JACOB BLEIBERG
Addressee	GUIDI & DIAMOND NEWARK
Description	Letter from Dr. Jacob Bleiberg to Guidi at Shamrock reporting findings of liver damage among plant workers in Newark. The letter suggests the source of the problem is the old factory building.

Exhibit #P0229

PIN #	DS00019523
Date	31-May-63
Author	R A GUIDI
Addressee	MC BURNEY & BROWN CORT
Description	MEMO OF FINAL HOSPITAL REPORT RE: 2 CASES

Exhibit #P0230

PIN #	DS00019518
Date	07-Jun-63
Author	R W MCBURNEY
Addressee	GUIDI & BROWN CORT
Description	Memorandum dated June 7, 1963 from Dr. McBurney to Mr. Guidi advising that workers affected by plant contamination no longer should be hospitalized since there is no treatment that can really help them, apart from removal from the contamination. Dr. McBurney opinions that the company's

decision to renovate the old building will go far toward solving this problem.

Exhibit #P0231

PIN #	DS 19520
Date	10-Jun-63
Author	R A GUIDI
Addressee	DR. R. MC BURNEY & C.R. BROWN J. S. CORT, JR. & F. R. KENNEDY
Description	I-O MEMO SUBJECT CHLORACNE - MEDICAL REPTS ON AN UNK.

Exhibit #P0247

PIN #	DS00017393
Date	14-Aug-63
Author	R W MCBURNEY
Addressee	GUIDI & BROWN JARVIS
Description	Letter from Richard W. BcBurney MD dated August 14, 1963 to Raymond A. Guidi recommending a urine test for persons affected by chloracne.

Exhibit #P0248

PIN #	DS00017392
Date	01-Oct-63
Author	J CORT
Addressee	KENNEDY
Description	Memo from J. S. Cort, Jr. to F. R. Kennedy, dated October 1, 1963 asking if urine tests had been started.

Exhibit #P0255

PIN #	DS00017390
Date	25-Nov-63
Author	F R KENNEDY
Addressee	CORT
Description	Memorandum dated November 25, 1963 from F. R. Kennedy to J. S. Cort, Jr. in Cleveland sending a copy of the notice that was posted telling the employees they were all

going to be given urine checks.

Exhibit #P0272

PIN #	DS00019479
Date	05-Mar-64
Author	J S JR CORT
Addressee	MCBURNEY RICHARD & MASEK E J
Description	Memorandum dated March 5, 1964 from J.S. Cort, Jr. to Dr. Richard McBurney (cc. to Masek-legal) asking whether a purchaser of raw TCP should be warned of health hazards.

Exhibit #P0273

PIN #	DS00019480
Date	06-Mar-64
Author	RICHARD W MCBURNEY
Addressee	CORT & MASEK
Description	Internal Memorandum dated March 6, 1964 from Dr. Richard W. McBurney, M.D. to J. S. Cort, Jr., stating that TCP is a definite chloracne hazard to workers. It states that the customer may or may not be aware of this, and defers to the legal department (Mr. Masek) the issue of what duty there is to tell them.1, 11, but suggests that the obligation exists anyway. Responds to a memorandum of March 65, 1964

Exhibit #P0275

PIN #	DS00017895
Date	17-Mar-64
Author	S B HONOUR
Addressee	QUIMOR LTDS & CORT GILES & PURDY
Description	Letter dated March March 17, 1964 from S. B. Honour to Guillermo Leon R. at Quimor acknowledging receipt of his letter of March 2d and saying that tests show that the samples of the product being questioned are identical to other batches of Diamond's product. Nonetheless, the letter

says that the matter has been turned over to Diamond's insurance representative and that it has also agreed to take back all questioned product provided its drums are in marketable condition.

Exhibit #P0276

PIN #	DS00017893
Date	18-Mar-64
Author	LEX CREAMER
Addressee	DIAMOND ALKALI & NEW YORK
Description	Memorandum dated March 18, 1964 from Lex Creamer to "New York" reporting on 2,4,5-T outbreaks in Bucaramangea, Cali and Medellin, and describing the severity of those outbreaks. States that distributor, Quimor, is in joeopardy because of bad publicity.

Exhibit #P0277

PIN #	DS L7890
Date	20-Mar-64
Author	S B HONOUR
Addressee	JOHN BINGHAM, V P & QUIMOR LTDA
Description	LETTER RECOMMENDING BINGHAM ACT AS CONSULTANT & CONTACT DR. DIAZ.

Exhibit #P0278

PIN #	DS00017888
Date	23-Mar-64
Author	UNKNOWN
Addressee	CECIL
Description	Letter dated March 23, 1964 (incomplete) from Alexander & Alexander, insurance brokers, to Lawrence Cecil, Jr., Sales Manager, Agricultural Chemicals, Diamond Alkali Company, advising that American Foreign Insurance Association had given assurances to their Bogota representative that matters were in hand, and assuring Diamond that instructions had been given to keep the identity of the American manufacturer a secret.

15560

Exhibit #P0279

PIN #	17888
Date	23-Mar-64
Author	C W GILES
Addressee	LAWRENCE L. CECIL & D. M. PURDY DIAMOND ALKALI
Description	LETTER REGARDING DIAMOND'S PRODUCT LIAB. INSURANCE

Exhibit #P0280

PIN #	19474
Date	23-Mar-64
Author	J S JR CORT
Addressee	J.A. FLOBECK & F.R. KENNEDY R. W. MC BURNEY & E. J. MASEK
Description	REGULATIONS RE HANDLING TRICHLOROPHENOL OR ITS SODIUM SALT.

Exhibit #P0281

PIN #	DS00017865
Date	25-Mar-64
Author	C W GILES
Addressee	CECIL LAWRENCE & PURDY D M DIAMOND ALKALI
Description	Letter dated March 25, 1964 from C. W. Giles, Asst. Vice President, Alexander & Alexander, to Lawrence L. Cecil, Jr., Sales Manager for Agricultural chemicals at Diamond Alkali reporting a request from American Foreign's Mr. George W. Arenas that the sample from "assurd's distributor" be tested by an independent laboratory.

Exhibit #P0282

15561

PIN #	117865
Date	25-Mar-64
Author	C W GILES
Addressee	LAWRENCE L. CECIL & SALES MANAGER AGRICULTURAL CHEM. & DIAMOND ALKALI

Description SIGNED COPY OF LTR 3/25/64 RE PROD LIAB INS8

Exhibit #P0284

PIN #	DS00017885
Date	08-Apr-64
Author	L L CECIL
Addressee	CORT & KENNEDY

Description Confidential Memorandum dated April 8, 1964 from L. L. Cecil, Jr., to J. Cort in Cleveland and referring to Mr. Kennedy's letter of March 31. The Memo states that the Kennedy letter is possibly incorrect because no "formal" complaints were ever filed and investigated. States, however, that "we feel obligated" to tell you that Lex Creamer has advised "by way of conversation" that there are more problems, especially in El Salvador.

Exhibit #P0285

PIN #	DS17885Y
Date	08-Apr-64
Author	L L CECIL, JR
Addressee	J. CORT & F R KENNEDY

Description UNSIGNED COPY OF MEMO DATED 4/8/64 BY CECIL TO CORT.

Exhibit #P0287

PIN #	DS00017881
Date	20-Apr-64
Author	L L CECIL
Addressee	QUIMOR LTDA & CORT ALEXANDER & A

Description Letter dated April 20, 1964 from L. L. Cecil, Manager, Agricultural Chemicals, to Quimor, Ltda. [Attn: Guillermo] authorizing return of 1,725 gallons of weedkiller from Columbia and $907.12. Requests expedited handling.

15562

Plaintiffs respectfully submit the following initial list of witnesses in conformity with paragraph IV.(B)(1) of the Magistrate's Pre-trial Order No. 17.

Dr. Arthur W. Galston	Eaton Professor of Botany, Department of Biology, New Haven, CN.: Dr. Galston is a plant physiologist; observed devastation of Vietnam; general causation; toxicity of tcdd to plants and humans; persistence of tcdd in ecosystem and bioaccumulation in human fatty tissue; Dr. Galston will also testify that there were other herbicides available in the 1960's that did not contain dioxin and could have defoliated the areas that 2,4,5-T was used to defoliate. See curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1/2 day.
Dr. Alastair W.M. Hay	Department of Chemical Pathology, University of Leeds, Leeds, England: Dr. Hay is a biochemist and general lecturer; author of The Chemical Scythe, Lessons of 2,4,5-T and Dioxin, Disaster Research In Practice Series, 1982, Plenum Press, New York and London; generic causation on toxicity of tcdd to man; specific causation on toxicity to Vietnam veterans exposed to Agent Orange; observed devastation of Vietnam countryside; Dr. Hay will also testify that there were other herbicides available in the 1960's that did not contain dioxin and could have defoliated the areas that 2,4,5-T was used to defoliate. Dr. Hay will further testify that based upon his research and expertise, those who made the decisions with respect to the use of herbicides in Viet Nam were at the highest levels of Government, probably the Secretary of Defense and/or the

President. See curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1-1 1/2 days; Cross examination estimated 1-1 1/2 days.

Dr. Deborah Barsotti — Professor of Toxicology, Philadelphia College of Pharmacy and Science, Philadelphia, PA.: Dr. Barsotti is a professor of toxicology; substantial personal research on halogenated aromatic hydrocarbons, including 2,3,7,8 tcdd or dioxin, and its teratological effects on animals and humans; general causation on toxicity, reproductive toxicity, fetotoxicity, gonadotoxicity, and embryotoxicity of tcdd; see curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 3/4 day; Cross examination estimated 3/4 day.

Dr. Ellen Silbergeld — Chief Toxicologist, Environmental Defense Fund, Washington, D.C.: Dr. Silbergeld is an environmental scientist and toxicologist; chief toxicologist for the Environmental Defense Fund; Research scientist in Reproductive Toxicology for National Institute of Health; general causation expert on the extreme toxicity, neuro-toxicity, reproductive toxicity, and carcinogenicity of Agent Orange and tcdd; specific causation on the birth defects of Kerry Ryan, and Michael and Chad Jordan, as related to and caused by their respective fathers exposure to Agent Orange in Vietnam; see curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1 day.

Dr. Alan Scott Levin — 450 Sutter, Suite 1138, San Francisco, CA.: Dr. Levin is a medical doctor who has done considerable research on the immune system;

15564

general causation expert on the extreme toxicity of tcdd and Agent Orange and its adverse health effects such as; chloracne, liver and systemic disorders; chemically induced immune disregulation; neurological disorders; reproductive disorders; and cancer; specific causation expert on the causal relationship of the various Agent orange/dioxin related adverse health effects upon the individual representative class plaintiffs themselves; see curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 3/4 day; Cross examination estimated 1/2 day.

Dr. Ronald Kerman — Department of Surgery, University of Texas Medical School, "UTMS", 6431 Fannin, Houston, TX.: Dr. Kerman is Chief of Cellular Immunology at University of Texas Medical School at Houston; general causation expert on the extreme toxicity of tcdd and the immuno-toxicological effects on humans; see curriculum vitae, all summaries, with references and documents attached; deposition of Dr. Kerman has not been taken to date. Direct examination estimated 3/4 day; Cross examination estimated 1/2 day.

Dr. Maureen Hatch — Professor of Epidemiology, Columbia University, New York, NY.: Dr. Hatch is an epidemiologist at Columbia University; general causation regarding reproductive epidemiology and toxicology of Agent Orange and its dioxin, tcdd, and their specific applicability to miscarriages and congenital malformations (birth defects) in wives and children of Vietnam veterans; see curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1 day.

Dr. Marvin Legator — Professor of Environmental Toxicology, University of Texas Medical School, Galveston, TX.: Dr.

	Legator is a toxicologist with special emphasis on reproductive toxicology and environmental toxicology; general causation expert on the extreme toxicity and carcinogenicity of tcdd; specific causation on the causal relationship between exposure of the representative class plaintiffs and miscarriages experienced by their wives and the congenital malformations of their children; see curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1 day.
Dr. Peter Orris	Division of Occupational Medicine, Cook County Hospital, Chicago, IL.: Dr. Peter Orris is practicing physician, specializing in internal medicine; general causation regarding tcdd intoxication of Vietnam veterans and diagnosis of tcdd syndromes; specific causation of illnesses of representative class plaintiffs as being the result of their Agent Orange exposure; see curriculum vitae, all summaries, with references and documents attached; deposition testimony of Dr. Orris is in the process of being completed and will be in the possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1 day.
Dr. Ronald Codario	1427 South Broad Street, Philadelphia, PA.: Dr. Codario will testify to acute and chronic toxicity of herbicides and tcdd in animals and humans as a medical doctor; general causation of adverse health effects of these herbicides and the extremely toxic tcdd; specific causation expert on the causal relationship between the Agent Orange herbicides and tcdd exposure of representative class plaintiffs and their resulting illnesses and disease processes; see curriculum vitae, all summaries, with

	references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1 day.
Dr. John Garofalo	847 Old Lancaster Road, Bryn Mawr, PA.: Dr. Garofalo is a medical doctor, who specializes on the immune system; general causation expert on the effects of Agent Orange herbicides and tcdd on the immune system; specific causation on the causal relationship of the adverse health effects in the representative class plaintiffs; see curriculum vitae, all summaries, with references and documents attached; deposition testimony will be in the possession of all parties as soon as it has been completed. Direct examination estimated 1 day; Cross examination estimated 1 day.
Dr. Ernest Baran	833 Andorra Road, Lafayette Hills, PA.: Dr. Baran is a practicing psychiatrist specializlizing in electrodiagnostic testing of the peripheral and central nervous system, including somatosensory evoked potentials; general and specific causation expert on toxicity on Agent Orange herbicides and tcdd in the nervous system; see curriculum vitae, all summaries, with references and documents attached; deposition testimony will be in the possession of all parties as soon as it is completed. Direct examination estimated 3/4 day; Cross examination estimated 3/4 day.
Dr. Herbert Kaye	Department of Psychology, State University of New York at Stonybrook, Stonybrook, N.Y.: Dr. Kaye is a psychologist who has performed a battery of neurometric tests on the representative class plaintiffs, which testing system he has developed; general and specific causation expert on the toxic effect of Agent Orange herbicides and tcdd and chemicals and their ability to

	alter the neurometric responses; see curriculum vitae, all summaries, with references and documents attached; deposition testimony will be in the possession of all parties as soon as it is completed. Direct examination estimated 3/4 day; Cross examination estimated 3/4 day.
Dr. Raymond Singer	402 East 90th Street, Suite 6B, New York, N.Y.: Dr. Raymond Singer is a neurotoxicologist and neuropsychologist who will appear as a general and specific causation expert on the extremely harmful and toxic effects of Agent Orange herbicides and tcdd on the human nervous system and the representative class plaintiffs; see curriculum vitae, all summaries, with references and documents attached; deposition testimony is in the possession of all parties. Direct examination estimated 3/4 day; Cross examination estimated 3/4 day.
Dr. Lennart Hardell	Department of Oncology, University Hospital, Umea, Sweden.: Dr. Hardell has a Ph.D. and M.D. and is an oncologist; he has performed epidemiology studies which evaluate the increased risk to humans for the development of various types of cancer from exposure to phenoxy herbicides such as the Agent Orange herbicides contaminted with tcdd; general and specific causation expert; see curriculum vitae; all summaries, with references and documents attached; deposition of Dr. Hardell will be in the possession of all parties as soon as it has been completed. Direct examination estimated 1 day; Cross-examination estimated 1 day.
Dr. Marvin Schneiderman	6503 East Halbert Road, Bethesda, Maryland.: Dr. Schneiderman is a Clement Associates Senior Science Advisor with principal

	responsibilities in biostatistics, epidemiology, risk assessment, and health surveillance; special qualifications in cancer research; general and specific causation expert; see curriculum vitae; all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1 day; Cross-examination estimated 1 day.
Dr. Theodore Sterling	Department of Computer Science, Simon Fraser University, Burnaby, British Columbia, Canada: Dr. Sterling is a professor of computer science at Simon Fraser University, Vancouver, British Columbia, Canada with specialties in mathematics, statistics, and epidemiology; general causation expert on the analyses concerning the effects of 2,3,7,8 tcdd, phenoxy herbicides, including Agent Orange and their impurities on humans; see curriculum vitae; all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 3/4 day; Cross-examination estimated 3/4 day.
Dr. Janet Springer	Environmental Protection Agency, Washington, D.C.: Dr. Springer is a biostatistician for the Environmental Protection Agency who has testified as to her work on dioxin risk model and the use of animal data to extrapolate for the risk of developing cancer in humans at EPA; see curriculum vitae and deposition testimony which is possession of all parties. Direct examination estimated 3/4 day; Cross examination estimated 1/2 day.
Dr. Debdas Mukerjee	Environmental Criteria & Assessment Office, Environmental Protection Agency, Cincinnati, Ohio: Dr.

	Mukerjee is the document manager for the EPA, and responsible for the publication of the draft dioxin documents for the Offices of Air Quality, Solid Waste, and Water in the EPA, (at this time, only the Office of Water Regulations and Standards, Ambient Water Quality Criteria for 2,3,7,8 - Tetrachlorodibenzo-p-dioxin, has been published in final form); see deposition testimony, and exhibits attached thereto, and documents in the process of being produced by the government in the possession of all parties. Direct examination estimated 1/2 day; cross examination estimated 1/2 day.
Dr. Vernon Houk	Center For Disease Control, National Institute For Occupational Safety and Health, Atlanta, Georgia: Dr. Houk is the Director of Center of Environmental Health for the Center of Disease Control (CDC) Atlanta, Georgia, and has conducted and is conducting investigations with cooperation of the States for the identification of dioxin contaminated sites in the United States; initiating clean-up procedures; prevention of future exposure of residents to dioxin in the environment in order to protect the public health from an extremely potent toxic substance "2,3,7,8 tcdd"; he has developed models to make risk assessments for residents of the United States exposure to dioxin; general causation expert on toxicity of tcdd; persistence in soil and in the environment; adverse health effects; see deposition testimony and exhibits attached thereto in possession of all parties. Direct examination estimated 3/4 day; cross examination estimated 1/2 day.
Dr. Steven Bayard	Cancer Assessment Group, Environmental Protection Agency, Washington, D.C.: Dr. Bayard is

	Orange in Vietnam; his physical pain and mental anguish; see deposition testimony and exhibits attached thereto in the possession of all parties. Direct examination estimated 1-1 1/2 days; Cross examination estimated 1 day.
Michael Ryan	Plaintiff. 73 University Heights Drive, Stonybrook, New York: Michael Ryan will testify to his exposure to Agent Orange in Vietnam; his physical condition, illnesses, injuries, and damages resulting from said exposure; the extreme emotional trauma resulting from the birth of his daughter Kerry with over 22 birth defects; his daughter's illness, malformations, injuries and damages; the tragedy reeked upon his family; see deposition testimony and all exhibits attached thereto in the possession of all parties. Direct examination estimated 1-1/2 days; Cross examination estimated 1 day.
Maureen Ryan	Mother of Plaintiff Kerry Ryan, and spouse of Plaintiff Michael Ryan. 73 University Heights Drive, Stonybrook, New York. Maureen Ryan, wife of Michael Ryan, and mother of Kerry Ryan, will testify as to the devastation upon her family, their illnesses, conditions, and injuries and damages as a result of her husband's exposure to Agent Orange in Vietnam; see deposition testimony in the possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1/2 day.
Kerry Ryan	Plaintiff. 73 University Heights Drive, Stonybrook, New York. Final decisions from both defendants and plaintiffs as to whether any deposition will be attempted, and as to whether Kerry can testify have not been made. Plaintiffs reserve all rights, however, to introduce Kerry to the Court and jury and to present demonstrative evidence such as "day in the life of" films and

	biostatician and biochemist with the cancer assessment group of the EPA and responsible for the testing of tcdd and the chemicals which contain it, which was the most toxic chemical of all 54 chemicals tested by EPA; general causation expert; see deposition and exhibits attached thereto in possession of all parties. Direct examination estimated 3 hours; Cross examination estimated 3 hours.
Dr. Umberto Saffiotti	National Cancer Institute, Washington, D.C.: Editor, New York Academy of Science Journal; Dr. Saffiotti is general causation expert, and will testify to the carcinogenicity, mutagenicity, fetotoxicity, acneigenicity, and teratogenicity of 2,3,7,8 tcdd in animals and humans; see deposition testimony and exhibits attached thereto in possession of all parties. Direct examination estimated 1 1/2 hours; Cross examination estimated 1 hour (Caveat: should plaintiffs elect to use deposition testimony the time taken will be less than 1 hour total).
Dr. K. Diane Courtney	Environmental Protection Agency, Washington D.C. and working at Triangle Park, Maryland Laboratories: Dr. Courtney is general causation expert with special emphasis on the toxic effects of dioxin on animals while working for EPA; see deposition testimony and exhibits attached thereto in possession of all parties. Direct examination estimated 3/4 day; Cross examination estimated 1/2 day.
Richard Christian	United States Army, Agent Orange Task Force, Pentagon, Washington, D.C.: Richard Christian is in the U.S. Army and is responsible for charting the exposure of all Vietnam veterans to Agent Orange and the other phenoxy herbicides sprayed in Vietnam while comparing the location

	and movement of all military units with the spray missions and plotting them on grid coordinates; general causation expert; see deposition testimony and exhibits attached thereto which deposition has not been completed as yet and will be in the possession of all parties prior to trial. Direct examination estimated 1 day; Cross examination estimated 1/2 day.
Dr. Philip Landrigan Safety and Health,	Center for Disease Control, National Institute for Occupational Safety and Health,Cincinnati, Ohio: Dr. Landrigan is with the Center for Disease Control, National Institute for Occupational Cincinnati, Ohio and is currently performing a risk assessment for occupationally exposed workers to dioxin and chlorinated phenols; see deposition testimony and exhibits attached thereto in possession of all parties. Direct examination estimated 1/2 day; Cross examination estimated 2 hours.
Dr. Donald Barnes see deposition testimony	Office of Pesticides & Toxic Substances, Environmental Protection Agency, Washington, D.C.: Dr. Barnes is a biochemist. He has done extensive review of the scientific literature on dioxins and participated in the Peer Review of the EPA draft documents; and exhibits attached thereto in the possession of all parties. Direct examination estimated 1/2 day; Cross examination estimated 2 hours.
George Ewalt	Plaintiff. 4351 Lauriston, Philadelphia, PA.: George Ewalt will testify to his individual exposure, as well to his research and mapping of the spray missions in Vietnam for Agent Orange, White, and Blue, and the locations of the various army units in which he and the other plaintiffs were exposed to Agent Orange herbicide; Ewalt will testify

	to basal cell carcinoma and other injuries and damages he has sustained as a result of his exposure to Agent Orange; Ewalt will describe his experience in Vietnam and the description of the effects of the defoliants; see deposition testimony of Ewalt with all production of documents attached thereto as exhibits (including photographs) and prior testimony of Ewalt before Senator Spector in Philadelphia, Penn. Direct examination estimated 1-1 1/2 days; Cross examination estimated 1 day.
Dan Jordan	Plaintiff. 7212 Sir Gawain, Austin, TX.: Dan Jordan will testify to his individual exposure in Vietnam to herbicide "Agent Orange", his research on the chemical compound, his experience while stationed in the U.S. Army, in Vietnam, his injuries and diseases and damages resulting from his exposure to Agent Orange in Vietnam while serving his country; see deposition testimony of Plaintiff and all exhibits attached thereto and/or produced for the defendants in Austin, Texas. Direct examination estimated 1-1 1/2 days; Cross examination estimated 1 day.
Donna Jordan	Plaintiff. 7212 Sir Gawain, Austin, TX.: Donna Jordan, wife of Dan Jordan, and mother of Michael and Chad Jordan, will testify to her husband's physical problems since his exposure to Agent Orange in Vietnam, her miscarriage; and the birth of her deformed children Chad and Michael as a result of her husband's exposure to Agent Orange; she will describe the permanent and substantial mental pain and anguish, as well as the physical injuries and other damages her family has sustained as a result of Agent Orange; see deposition testimony and all exhibits attached thereto and/or produced for the defendants. Direct examination estimated 1/2 day; Cross examination estimated 1/2 day.

Chad Jordan	Plaintiff. 7212 Sir Gawain, Austin, TX.: Chad Jordan, age 13, will testify as to his own physical malformation, condition, and the physical problems resulting therefrom; see deposition testimony in possession of all parties. Direct examination estimated 1 hour; Cross examination estimated 1/2 hour.
Michael Jordan	Plaintiff. 7212 Sir Gawain, Austin, TX.: Michael Jordan, age 11, will testify as to his own physical malformation, condition and the physical problems resulting therefrom; see deposition testimony in possession of all parties. Direct examination estimated 1 hour; Cross examination estimated 1/2 hour.
Danny L. Ford	Plaintiff. 3507 St. Anthony Road, Temperance, Michigan: Danny Ford served in infantry in Vietnam and will discuss his experience in Vietnam and in army; Ford will describe the conditions in Vietnam, his exposure to areas that had been defoliated; his problems, physical and mental as a result of his exposure to toxic herbicides and specifically Agent Orange; his physical diseases, injuries and damages resulting from this exposure; see deposition testimony in possession of all parties, and all exhibits attached thereto, including photographs taken while plaintiff was in Vietnam. Direct examination estimated 1-1 1/2 days; Cross examination estimated 1 day.
David G. Lambiotte	Plaintiff. 44 Westover Road, Newport News, Virginia: David Lambiotte has sustained basal cell carcinoma and lymphitic lymphoma as a result of his exposure to Agent Orange in Vietnam; Lambiotte will testify as to his physical and emotional problems, his injuries and damages as a result of his exposure to Agent

	such other proper evidentiary techniques as become appropriate with respect to Kerry as a witness in her own behalf. Direct examination, if any would be extremely brief; estimated cross examination - none.
	Caveat: Demonstrative evidence such as "day in the life" film would take 1-2 hours to present (estimated).
Dr. Thomas Aboud	c/o Toledo Clinic, Toledo, Ohio: Mrs. Ford's cardiologist treated Danny Ford for hypertension; would testify to medical conditions, health and damage questions. Approximate length of direct testimony is 2 hours. Cross examination, 1/2 hour.
Edward E. Adams	Termination Contracting Officer, Defense Supply Agency, Defense Contract Administration Services Office (DCASO), 1136 Washington, St. Louis, MO.: testimony on issues of one or more of the defendants' failure to warn, procedures re government contract services and personal dealings with one or more defendants in these regards; Has not yet been deposed. Direct testimony and cross examination cannot be estimated at this time due to lack of deposition.
Irene Antonik	812 Sussex, Austin, Texas; Texas disability officer and friend of Jordans' will offer testimony on health and damages issues from personal knowledge; has not yet been deposed. Direct examination estimated 2 hrs; Cross examination estimated 1/2 hour.
Eugene Bak*	Defense Supply Agency Termination Contracting Officer, 200 Mill Street, Bellville, New Jersey: testimony on issues of one or more of the defendants' failure to warn of toxicity of the Agent Orange herbicides; witness has been deposed;
	Direct examination estimated 1-1 1/2 hours; Cross examination estimated 1/2 hour.

Donald Barnes	Government causation expert from Environmental Protection Agency will testify on issues of general causation; has recently been deposed, but as of this writing, deposition transcript has not been abstracted due to press of time in preparing other portions of this pre-trial order. A more specific summary of the witness' testimony will be contained in first amended pre-trial order to be filed.
E.E. Baumgartner	Inspector, Defense Contract Supply Agency Office, Little Rock AFB, Arkansas: Testimony regarding government relationship with supplies of Hercules, Incorporated as it pertains to failure to warn issues; witness has not yet been deposed. Direct and Cross examination lengths impossible to estimate at this time.
R.E. Baynard	Monsanto government products supervisor, 231 Jeffrey Lane, Newtown Square, PA. 19073: Testimony re health problems among workers and failure to warn issues; toxicity knowledge re end product; has not yet been deposed; therefore length of Direct and Cross examinations presently impossible to estimate.
Jeannie Beavers	Flower Hospital, Personnel Department, Sylawia, Ohio: Personal observations regarding effects on plaintiff Danny Ford of his illness, both as to physical and emotional pain and suffering and hospital and business strains caused by illness; Direct examination estimated 1 hour; Cross examination estimated 10 minutes.
Billie Marie Bell Personal observations	4404 Bonnie Drive, Ft. Worth, Texas: regarding health and development throughout life, both pre and post Vietnam service of Danny Jordan. This witness is his mother; Direct examination estimated 1 1/2 hours; cross examination estimated 15

minutes.

Cloyci G. Bell	4404 Bonnie Drive, Ft. Worth, Texas: Personal observations regarding the health and damages issues as they pertain to Plaintiff Danny Jordan. This witness is his step-father. Direct examination estimated to be maximum of 1 hour; cross examination expected to be very brief.
Bell Telephone of PA	1 Park Way, Philadelphia, Pennsylvania: Records of employment and working history, to be presented to the extent necessary by an individual to be chosen from the company; to the extent such live testimony is required, plaintiffs will include such witness as soon as identified by the company in up-date or amendment to pre-trial order. Examination expected to be very brief or subject of a request for stipulation from defendants; if no stipulation achieved, maximum estimated direct examination 1 hour; Cross examination estimated maximum 1/2 hour.
Wilton B. Bills	Contract Officer, Defense General Supply Center, Richmond, VA: Information regarding the contract negotiating process pertaining to all defendants, but esp., Dow and Hercules; has not yet been deposed; therefore presently impossible to estimate length of direct or cross examinations.
Peter S. Bing, M.D.*	9700 Pico Boulevard, Los Angeles, CA.: Former White House Staff Member. Although Dr. Bing has been deposed, plaintiffs may call him as a live witness at trial for the purpose of explaining the preparation of the President's Science Advisory Committee Report regarding the Use of Pesticides in the United States; relevant to lack of government knowledge; Direct examination estimated 1 hour; cross examination estimated 1/2 hour.

Etcyl H. Blair	4 Crescent Court, Midland, MI.: Vice President, Dow Chemical, and Director of Health and Environmental Sciences; has been deposed; He has been employed by the Company since 1951. Dr. Blair will testify as to his involvement with the use and production of herbicides by the Dow Chemical Company. In addition, he will testify as to his involvement with various committees of Dow such as the Risk Assessment Committee. We are currently awaiting the transcript of the second day of the Blair deposition so that we can include any additional supplemental material as may be indicated and required.
Direct examination	estimated 2 hours; cross examination estimated 1/2 hour.
John Blish	Defense Fuel Supply Agency, Washington, D.C.: Information regarding negotiation, fulfillment, and termination of government contracts; witness' particular responsibilities related to Diamond Shamrock Corporation; has not yet been deposed; therefore presently impossible to estimate length of direct and cross examinations.
A.A. Block	Chemical Inspector, Defense Contracting Ageny Supply Region (DCASR), Quality Assurance Representative, Kansas City, Missouri: Information relative to the inspection of herbicides supplied relative to inspection practices, and procedures actually employed, with particular knowledge of T H Agriculture & Nutrition Company; has not yet been deposed; therefore presently impossible to estimate length of direct or cross examinations.
Joseph L. Bolton	Chemical Inspector, Defense Contracting Administrative Services Region (DCASR), 500 South Ervay St., Dallas, TX. 75201: Information re; inspection and acceptance of deliveries, with particular

	knowledge of Hercules, Incorporated, and general knowledge of procedures employed from time to time during herbicide delivery periods; has not yet been deposed; therefore presently impossible to estimate length of direct or cross examinations.
Jack Borrer	12920 Wellswood Trail, Chesterland, Ohio: former Diamond Shamrock employee having testimony relevant to severe contamination of company's manufacturing plant and end product with knowledge of health hazards. If this witness cannot be produced, plaintiffs will append a page and line summary of his deposition to their next submission. Expected length of testimony less than 1/2 day.
Al Bothwell	610 Hudson Terrace, Newport News, Virginia; friend of David Lambiotte's - health and damage witness; total testimony less than 1 1/2 hours.
James E. Bowers	313 N. Midwest Boulevard, Midwest City, Oklahoma: Defense Supply Agency, Administrative Contract Officer, Defense Contracting Services Office, Kansas City, MO.(during relevant periods): particular knowledge regarding contracts of government with T H Agriculture & Nutrition; has not yet been deposed; therefore presently impossible to estimate length of direct of cross examinations.
Daniel Braxton	Address to come; George Ewalt's foreman.
Dave Bunin	Philadelphia, Pennsylvania; professional economist who will evaluate damages of individual plaintiffs. Expected length of testimony 1/2 day.
Emil Christofano	Hercules Towers, Wilmington, Delaware.; Deposed February 9 & 10th, 1984; Expert and Fact Witness; Industrial Hygienist at Hercules

	since approximately 1957; his job responsibility from 1964 through 1975 was to be aware of health hazards possibly presented to employees or to persons handling the product or to persons at risk as product would be used by the customer. The health hazard (nature, magnitude or extent of the injury) can be dependent upon the amount of exposure (and strength of the poison) at a given time; the frequency of exposure, and the route or method of exposure (tender skin, tough skin, oral, breathing, etc.). He will testify to the matters in and the exhibits to his deposition. He has no knowledge of anybody at Hercules ever informing anybody in the government of the existence of dioxin in the 2,4,5-T product. He denies ever receiving knowledge tha the 2,4,5-T produced by Hercules in 1965 contained any measurable dioxin. Estimated length direct testimony 1 1/2 hours; Examination by defendant's unknown, but assume 30 minutes.
J. G. Copeland, Jr.	Assistant General Manager, '64 Gen. Mgr. Synthetics,'65-72 of Hercules; Plaintiffs note that Mr. Copeland's deposition was scheduled for 3/30/84, but continued with the agreement of all defendants due to the witness's inability to appear (a tree fell on his house in a storm). After his deposition has been taken and the transcript received and reviewed, plaintifffs will update this portion of the pre-trial order accordingly. Plaintiffs are not now certain if Mr. Copeland will be a live witness or a deposition witness. The Exhibit List will also be amended accordingly, depending upon developments at the deposition.
George and Marge Crawfis	49 Heck Rd., Kennessaw, Georgia; Dan Ford's brother and sister-in-law; overall physical, emotional and financial conditions suffered by Fords. Total testimony time 1-2 hours.

Owen and Betty Crawfis	61-83 Whiteford Center Rd., Toledo, Ohio; Mrs. Ford's parents to testify to Dan's physical and emotional conditions, his medical treatment, personality changes, increasing stress, job difficulties, wage losses, and effects on the Ford family. Total testimony time 1-2 hours.
Bill Curtis	c/o CBS News, 524 West 57th Street, New York, New York; Eyewitness observations as to the condition of the country of Vietnam, extent of residual defoliation, photographic exhibits. Expected length of total testimony 1/2 day.
Charles L. Dunn	Wilmington, Delaware; First employed at Hercules, 1942 as a chemist & was Manager of regulatory affairs from 1960 through 1965 and then became manager of Ag Chemicals development until 1969. From August, 1966 he served as Hercules' representative on the INdustry Task Force on Phenoxy Herbicides, National Agriculture Chemicals Association (NACA) and became Vice Chairman in August, 1966 and Chairman from October 17, 1967. The task force duties were to represent industry before the Department of Agriculture and the Department of Health, Education & Welfare. To augment the safety of current registration practices, the Secretary of Agriculture selected a panel from the National Academy of Sciences to re-evaluate toxicological data on pesticides and NAS recommended a system of negligible residue tolerances be established. Notwithstanding the legal duty imposed by regulations and law (said duty well known to Dunn, Hercules, NACA & the task force & each of its members (all of the defendants herein being members) & by the past common and accepted practices of the industry generally thedefendants, specifically, the fact of Agent Orange contamination with dioxin in

	the 2,4,5-T was not only not made known to the government (Department of Agriculture, HEW, U.S. Military); the fact of contamination by dioxin was intentionally, maliciously, & for the purpose of greed, secreted from the government through the individual and concerted acts and conduct of members of the Task Force. Because Mr. Dunn is presently under Hercules contract to perform consulting services, he was produced for his discovery deposition on 4/28/83 at Hercules' offices in Wilmington, and was again produced for further deposition on March 8, 1984 (the latter transcript has not yet been received). In view of the Court's discussion on April 2, 1984, it is assumed the court will order Mr. Dunn to be presented for live testimony. If not, plaintiffs will promptly indicate the testimony to be read from the transcripts. Mr. Dunn will testify to all documents marked as exhibits at his depositions on file herein, and dated 5/2/83. He will testify to the March 24, 1965 meeting among the manufacturers, the conspiracy growing therefrom, his knowledge of the hazard, of Hercules pre-1966 production of 2,4,5-T & the hazards of products of others (with which Hercules' was mixed.) Direct examination estimate at 3 hours; Examination by defendants presumed at 1 hour.
J.M. Eagan	45 Cypress Marsh Dr., Hilton, Head, S.C.; deposition taken 3/30/84; Plaintiffs provide the following, however, on a non-binding basis, subject to amendment and augmentation: Mr. Eagan was formerly Hercules' Assistant Director of Operations, Synthethics,(1961-65) and Director of Operations (1965-68); will testify concerning the manufacture of and manufacturing processes for 2,4,5-T, Agent Orange, and phenoxy-herbicides; Hercules' Jacksonville Arkansas plant; Knowledge concerning dioxin

	toxicity, and health hazards of dioxin and 2,4.5-T; detection and reduction of dioxin; sales to government, defendant's failure to advise or warn the government; registration of the herbicide; sales to Dow; purchase and use of foreign 2,4,5-T; issues re proposals concerning government plant at Muscle Shoals, Alabama, production at Edgewood Arsenal; the government's analyses of Agent Orange as to the % of 2,4-D and 2,4,5-T; specifications and contracts for herbicide orange; Hercules' business records (attached to deposition and to be added to Exhibit list where necessary) are documents which may be referred to and discussed ; plaintiffs reserve the right to notice his appearance as a live witness until further supplementation or waiver or order of court.
George W. and Eunice Ewalt, Sr.	731 Penn Pines Blvd., Clifton Heights, Pennsylvania; George Ewalt's parents will testify concerning the health and damages issues pertaining to this plaintiff.
John J. Ford	15 Winterbury Circle, Wilmington, Delaware;
Hercules chemist;	expert and fact witness; Deposed at Hercules' office February 9, 1984; Designed and used the dioxin detection method and measuring system; will testify to matters covered in deposition and exhibits therein identified. Will demonstrate that Hercules' pre, 1966 product contained well in excess of 1 part per million and that testing equipment not valuable below 1 ppm. The test results of Hercules generally showed a greater amount of dioxin than Dows testing allegedly revealed. Though Hercules recognized its testing methods were inadequate and perhaps unreliable; they did nothing to attempt to improve them until after government

	decertified 2,4,5-T; Examination by plaintiffs approximately 1 1/2 hour; examination by defendants unknown but assumed to be 1/2 hour.
Kerry Ford	6507 Secore Drive, Lambertville, Michigan; health and damage witness; total testimony 1 hour.
Jeanette Ford	6507 Secore Drive, Lambertville, Michigan; health and damage witness; total testimony 1 hour.
Ray Ford	13478 South Country Line Highway, Ottowa Lake, Michigan; health and damage witness; total testimony 1 hour.
Rose Ford	13478 South Country Line Highway, Ottowa Lake, Michigan; health and damage witness; total testimony 1 hour.
John P. Frawley	Wilmington, Delaware; Ph. D. Biological Chemistry; Deposed March 8, 1983, and February 7 & 8, 1984; Testified in deposition and at trial of Vertac case as described more fully under witness A.E. Sidwell; will testify to matters included in the above proceeding & the attached exhibits; "its the most toxic man made chemical in my opinion, that has been detected so far, and because if it's extreme toxicity, we have to look for it in parts per trillion and parts per billion range..." It is more toxic than strychnine, arsenic or thalidomide...."at 559 parts per billion I would consider that to be a potentiontial health hazard... I would not consider it safe to walk on barefoot." Regarding the level that might be considered safe, he testified that "I think I'd consider 10,000 parts per trillion as getting significant and this would be 10 parts per billion" (and further, would be .01 parts per million.) He has urged that a standard should be set which would allow 1 ppm dioxin, but this has been rejected as too

	Mr. Kenaga was a prime contact within Dow for Uniroyal personnel, as well as having substantial knowledge concerning the toxicity and environmental persistence of dioxin. Testimony length 2 hours.
Francis Kennedy	2711 Bernadett Lane, Houston, TX; Mr. Kennedy was the Diamond Shamrock Plant Manager of the Newark plant from 8-1-63 to 9-9-68, which plant experienced numerous and severe health problems among its workers; he was deposed on 1-21-83; generally, his testimony will focus on knowledge of Newark's health problems from 1954 to 1968 which he characterizes as a serious problem; was attendee at the Dow March 24, 1965 meeting; knowledge of dioxin, its toxicity and danger to human health; he supervised Newark's dioxin detection and removal program and will establish the dioxin levels for the months and years he was manager; on failure to warn and product defect isssues, and the claim of confidential knowledge of manufacturing processes. Although no longer employed, plaintiffs claim he should be produced as a live witness.
Carl & Carla King	33-42 Romaker, Toledo, Ohio; closest friends of the Danny Fords; she was with Chris when learned of cancerous condition of Danny's leg and will testify on health, pain, suffering, and other damage issues. Total length of testimony 1 1/2 hours.
Harry E. Soehner	Uniroyal employee since 1933 (retired in 1974), was in charge of safety supervision. First heard of dioxin in 1961 and learned that it caused chloracne, and learned in 1968 that Dioxin was a potential carcinogen; will describe the fact that he attended many meetings at Uniroyal relative to the health risks of the chemical. He is being listed in this live witness list, however, it is anticipated that on amendment of this pretrial order, he

will be transferred to the deposition witness list. It is impossible to presently comply with the requirement to give a page and line referenced summary for that purpose, since his deposition was taken so recently that the transcript has not yet been received.

Edward Hager — A technical associate with Uniroyal, Ltd. formerly in research and development at the Elmira plant. first heard of the dioxin problem in 1965 subsequent to the memo received from Dow. Prior to that memo he was aware that it caused Chloracne. Learned that dioxin was in fact a carcinogenic in the Seventies. States that Uniroyal did no testing to determine dioxin content at end product line. Testified that technology was available during the mid-1960's to better analyze for dioxin content. States that Uniroyal didn't feel it was necessary to perform tests during the manufacturing process. He is listed on the live witness list, however, it is anticipated that upon amendment of the pretrial order that he will be listed as a witness by deposition. It is impossible to comply with the requirement to give a line and page summary of this witnesses testimony as his deposition was taken so recently that a copy of the transcript is presently unavailable.

William Shipley — Witness began working for Uniroyal in 1950 as an assistant control chemist. Presently he is in commercial development. Claims he did not know of the term dioxin until after Love Canal in 1981. Presently the Environmental Liason between Uniroyal, Ltd., Elmira Plant and the Canadian Government. He is listed on the live witness list, however, it is anticipated that upon amendment of the pretrial order that he will be listed as a witness by deposition. It is impossible to comply with the requirement to give a line and page summary of this witnesses

testimony as his deposition was taken so recently that a copy of the transcript is presently unavailable.

Taylor H. Evans — Evans started with Uniroyal, Ltd. in 1943 and holds a Ph.D. in Chemistry. He attended the Dow meeting at Midland on 8/3/65 to discuss the Dioxin problem. He was aware of the Hoechst Plant industrial accident in Germany where two workers died and others had liver damage. He did not reveal his knowledge of the "Dioxin Problem" to the Safety Supervisor at the Elmira Plant learned at the Dow Midland meeting on 8/3/65. In a memo prepared concerning the Dow meeting he noted that Dow said that no product containing dioxin should be sold and that no discussion regarding the problem should be had outside of the division. He is listed on the live witness list, however, it is anticpated that upon amendment of the pretrial order that he will be listed as a witness by deposition. It is impossible to comply with the requirement of a line and page summary of his testimony as his deposition was taken so recently that a copy of his transcript is presently unavailable.

Lucien G. Maury — 29 Brandywine Road, Wilmington, Delaware; Hercules, V.P. of Technology; research chemist; Manager, synthetics research, 1961-64; Manager Corporate research 1964-67; Assistant Director of Research 1967-71; Ph. D. Chemistry. Not aware of product 2,4,5-T and did not know anything about potential of contaminant; because of his positions, he would have been expected to have been informed of a possible toxic material but he was not - no information regarding dioxin ever came to him; Examination of plaintiff approx. 45 minutes; Examination by defendants unknown, but assume 15 minutes.

Robert Bates Scott — 609 North DuPont Road, Wilmington, Delaware, 19807; currently employed

Leonard Davenport	3104 Warbler Drive, Montgomery, Alabama; to be asked to testify to the circumstances of the loading, unloading spraying and defoliation as he observed it take place when he was in Vietnam; expected length of testimony 1 1/2 hours.
Mr. Larry List	P.O. 18 Birchrunville, Pennsylvania 19421; will be asked to testify to his observations of the spraying and its affect upon men he observed having reactions to it during his tour of duty in Vietnam. expected length of testimony 1/2 hour.
Mr. Charlie Hartz, decd.	Excerpts from his video taped deposition will be offered with respect to his observations of the spraying and defoliation process during his tour of duty.
JOHN WILDER TUKEY	PSAC Member from 1960 to 1963. Also a member of the ad hoc panel on herbicides. First knowledge of dioxin is in 1969. Whether this witness is produced live or through deposition excerpts awaits ruling of Court.
CHARLES H. TOWNES	1988 SAN ANTONIO AVE, BERKELEY, CALIF. Member, Science Advisory Board of Air Force(1958-1961), Vice President and Director of Research of the Institute for Defense Analysis (1959-1961). No discussion of health effects of herbicides prior to 1970. Whether this witness is produced live or through deposition excerpts awaits ruling of Court.
WILLIAM MC ELROY	9651 BLACK GOLD RD., CALIF. Member of PSAC Panel on the use of Pesticides. Does not recall any chemical company coming forward to report health effects of 2,4,5-T, and did not consult with PHS on the matter. Whether this witness is produced live or through deposition excerpts awaits ruling of Court.

	traveled to by foot and by vehicle, and the conditions of their unit while in these various locations. Less than 1/2 day total testimony.
BETTY SMAYDA	1809 Rapids Road, Hiram, Ohio. Betty Smayda, a long-time friend and busines associate of Mrs. Danny Ford, will testify to Danny Ford's physical and emotional conditions, his behavior changes and increasing stress, the resultant time and wages lost in Danny Ford's work, and the overall emotional and financial strains on the Ford family. Less than 1/2 day total testimony.
TERRY AND JEANNETTE FORD	6507 Secor Road, Lambertville, Michigan. Terry and Jeannette Ford will testify to the Ford family's physical, emotional and financial strain which they observed as Danny Ford's brother and sister-in-law. Less than 1/2 day total testimony.
RAY AND ROSE FORD	13478 South County Line Highway, Ottawa Lake, Michigan. Danny Ford's parents will testify to his behavioral changes, physial conditions, increasing stres and the subsequent financial and emotional strain on the Ford family. Less than 1/2 day total testimony.
JUDY McKINLEY	1899 Rapids Road, Hiram, Ohio. As a long-time friend and business associate of Christina Ford, Judy McKinely will testify to Danny Ford's emotional and physical conditions, behavioral changes, stress and the resulting financial and emotional strains suffered by the Ford family. Less than 1/2 day total testimony.
ROBERT SNODGRASS	Huntington, W. Virginia; In the same gun section as Danny Ford, Robert Snodgrass will testify to the various locations of their unit, including the recently defoliated areas they travelled by both vehicle and foot, as well as the conditions of their unit in the various areas. Less than 1/2 day total testimony.

DAN TWISS	Woodland Street, Sylvania,Ohio. Dan Twiss, the Union Committeeman at Jeep Corporation and long-time friend of Danny Ford, will testify to the lost time and reduced wages of Danny Ford's work as a result of his physical condition. Less than 1/2 day total testimony.
JANE WARD	3527 M.151, Temperance, Michigan. As the Fords' neighbor, Jane Ward will testify to the time and wages lost from both Danny Ford and Christine Fords' jobs as a result of Danny Ford's medical condition. Less than 1/2 day total testimony.
SHERRY MOSHER	184335 Westchester Road, Toledo, Ohio. As the Manager of Christina Ford's business, SherryMosher will testify to Danny Ford's physical condition, the amount of time that Christina Ford has missed from work as a result of Danny Ford's condition and subsequently, the amount of business and wages lost in her absence. Less than 1/2 day total testimony.
HARRY HOLLAND	1626 Dryden Way, Crofton, MD; As a friend of David Lambiotte's before, during and after his stay in Vietnam, Harry Holland will testify to David's behavioral changes, increased stress, irritability and other emotional changes. Less than 1/2 day total testimony.
MICHAEL LAMBIOTTE	18 Milford Rd., Newport News, Virginia; As David Lambiotte's brother, Michael Lambiotte will testify to David Lambiotte's emotional and behavioral changes, increased stress and depression since his return from Vietnam. Less than 1/2 day total testimony.
RICHARD SCOTT	11 White Oak Drive, Newport News, Virginia; As David Lambiotte's high school friend, after spending time with David Lambiotte in Vietnam and after being David Lambiotte's roommate after Vietnam, Richard

	Scott will testify to David Lambiotte's attitude, behavior and emotional changes, his increased stress and his depression. Less than 1/2 day total testimony.
HENRY SADLER	Melbourne Beach, Florida. As David Lambiotte's neighbor and friend before and after Vietnam, Henry Sadler will testify to David Lambiotte's behavior and attitude changes, his increased irritability, depression and stress. Less than 1/2 day total testimony.
DR. SALTER	97 York Street, York, Maine; David Lambiotte's treating physician will testify to David as scientist and toxicologist; chief toxicologist for the Environmental Defense Fund; Research scientist in Reproductive Toxicology for National Institute of Health; general causation expert on the extreme toxicity, neuro-toxicity, reproductive toxicity, and carcinogenicity of Agent Orange and TCDD; mechanisms for the male-mediated birth defects; specific causation on the birth defects of Kerry Ryan, and Michael and Chad Jordan, was related to and caused by their respective fathers' exposure to Agent Orange in Vietnam; see curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1 day.
GEORGE AND MARGE CRAWFIS	49 Heck Road, Kennessaw, GA; Mrs. Dan Ford's brother and sister-in-law. Will testify to the overall physical, emotional and financial conditions suffered by the Fords which they observed as close relatives. Total testimony less than 1/2 day.
JOHN CRAWFIS	1179 Beach ValleyRoad, Atlanta, Georgia. Mrs. Ford's brother, John Crawfis, will testify to Danny Ford's emotional and physical conditions, the effect of his

	physical condition upon his employment and subsequently, upon the Ford family's overall financial status. Total testimony less than 1/2 day.
OWEN AND BETTY CRAWFIS	61-83 Whiteford Center Road, Toledo, Ohio. Mrs. Ford's parents will testify to Dan's physical and emotional conditions, his medical treatment, his personality changes and increasing stress, the limitations created by his physical condition in his job, the subsequent wage loss as a result of these limitations, and the effects of these conditions on the Ford family. Total testimony less than 1/2 day.
Ronald Moody	c/o 65 Rodman Oval, New Rochelle NY 10805; Witness was a Ranch Hander and will testify to the practice and procedures of Operation Ranch Hand and the resultant exposures to Ranch Handers and other troops. Total testimony less than 1/2 day.
William Duffield	1115 Greenhill Lane, Box 485, Phoenixville, Pennsylvania 19460; He will testify concerning exposure of the plaintiffs and identify certain photographs.
Theodore C. Sorensen	345 Park Ave., New York, New York; Mr. Sorensen was a member of the White House staff during the Kennedy administration and may testify that President Kennedy made the initial decision to undertake defoliation in Viet Nam and neither he nor President Kennedy or anyone on his White House staff, as far as he knew, was aware that the herbicides were contaminated with dioxin and potentially posed adverse health hazards to human beings. Direct Examination estimated 1/2 day; Cross examination estimated 1/4 day.
Lawrence O'Brien	New York, New York; Mr. O'Brien was a member of the White House staff during the Kennedy administration and may testify that President Kennedy made the initial decision to

	undertake defoliation in Viet Nam and neither he nor President Kennedy or anyone on his White House staff, as far as he knew, was aware that the herbicides were contaminated with dioxin and potentially posed adverse health hazards to human beings. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
John Siegentholeau	Nashville, Tennessee; Mr. Siegentholeau was a former member of Attorney General Robert F. Kennedy's staff and may testify that Kennedy made the initial decision to undertake defoliation in Viet Nam and neither he nor Kennedy or anyone on his staff, as far as he knew, was aware that the herbicides were contaminated with dioxin and potentially posed adverse health hazards to human beings. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Bill Moyers	c/o P.B.S., 475 L'enfant Plaza, Washington, D.C. 20024; Mr. Moyers was a member of the White House staff during the Johnson administration and may testify concerning decisions regarding the deployment of herebicides in Viet Nam and neither he nor President Johnson or anyone on his White House staff, as far as he knew, was aware that the herbicides were contaminated with dioxin and potentially posed adverse health hazards to human beings. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Josh Valenti	Motion Pictures of America, Washington, D.C.; Mr. Valenti was a member of the White House staff during the Johnson administration and may testify that President Johnson made the initial decision to undertake defoliation in Viet Nam and neither he nor President Johnson or anyone on his White House staff, as far as he knew, was aware that the herbicides were contaminated

	with dioxin and potentially posed adverse health hazards to human beings. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Marvin Watson	Dallas Baptist Univ., Dallas, Texas; Mr. Watson was a member of the White House staff during the Johnson administration and may testify that President Johnson made the initial decision to undertake defoliation in Viet Nam and neither he nor President Johnson or anyone on his White House staff, as far as he knew, was aware that the herbicides were contaminated with dioxin and potentially posed adverse health hazards to human beings. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Walter Nastow	Lyndon Johnson Library, Austin, Texas; Mr. Nastow was a member of the White House staff during the Johnson administration and may testify concerning the White House decision making process from time to time relative to the deployment of herbicides in South East Asia and neither he nor President Johnson or anyone on his White House staff, as far as he knew, was aware that the herbicides were contaminated with dioxin and potentially posed adverse health hazards to human beings. Direct examination estimated 1/2 day; Cross examination extimated 1/4 day.
Joe Califano	Washington, D.C.; Mr. Califano was a member of the White House staff during the Johnson and Carter administrations and may testify concerning decisions regarding the herbicide program and neither he nor President Johnson, President Carter or anyone on his White House staff, as far as he knew, was aware that the herbicides were contaminated with dioxin and potentially posed adverse health hazards to human beings. Direct examination estimated 1/2 day; Cross examination

	estimated 1/4 day.
Mr. Bourland	Address being furnished by the Government. Dr. will testify that he was with the U.S. Army Biological Laboratories and will testify that in preparing the specifications for Agent Orange, Mr. C.H. Russell from Monsanto provided the basic specifications for Agent Orange and that the government relied upon the defendants to have done the testing to insure that the product was safe for use. He will further testify that the contract and dealings imposed upon the defendant have minimal and general requirements leaving substantial discretion in the defendant as to how the Agent Orange would be designed, formulated and manufactured. His deposition was taken and the pretrial order will be supplemented with the deposition line and page summary soon after the copy is transcribed and delivered to us. Plaintiffs' examination approximately 1/2 day; Defendants' cross approximately 1 hour.
Mr. Pearson	Address being furnished by the Government. Dr. will testify that he was with the U.S. Army Biological Laboratories and will testify that in preparing the specifications for Agent Orange, Mr. C.H. Russell from Monsanto provided the basic specifications for Agent Orange and that the government relied upon the defendants to have done the testing to insure that the product was safe for use. He will further testify that the contract and dealings imposed upon the defendant have minimal and general requirements leaving substantial discretion in the defendant as to how the Agent Orange would be designed, formulated and manufactured. His deposition was taken and the pretrial order will be supplemented with the deposition line and page summary soon after the copy is transcribed and delivered to us. Direct

	examination estimated 1/2 day; Cross examination estimated 1/4 day.
Paul Ignatius	Washington, D.C.; Government procuring his address; He was Assistant Secretary of Defense for Installation and Logistics and was General Stanwix Hay's immediate superior. He may testify live and will probably corroborate Gen. Stanwix-Hay's testimony that Secretary of Defense or President were ultimate decision makers with reference to Agent Orange and that no information concerning dioxin or adverse health effects passed up to the Secretary of Defense. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Albert E. Hayward	(address being provided by the Government) He was Chief of the Program Coordination Office at Ft. Detrick. He will testify that at the first "Defoliation Conference" with the Defendants in 1963 at the United States Army Biological Laboratories, it was understood by all that the defoliation program in Southeast Asia would not be conducted in the usual way whereby the Government gives specific and rigidly enforced specifications but that the companies would be given broad and wish latitude in specifying, formulating and manufacturing the defoliants to be used. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
George Collins	Address being provided by the government; he was a contracting officer with respect to several of the Defendants' contracts with the government. He may confirm Hayward's testimony and will confirm that Defendants failed to warn of any hazards in their Agent Orange products. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. Daniel Teitlebaum	Denver Clinic, 701 East Colax

	Avenue, Denver, Colorado; Dr. Teitlebaum is clinical toxicologist and occupational, environmental, and preventive medicine specialist. He will testify about the labelings, warnings, precautions, and advice that should have been used or given by the Defendants with respect to the Agent Orange and about the use of protective clothing, safety gear, safety systems, medical surveilance and other systems, tools, and techniques which could have reduced the risks to those who served in Viet Nam. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. Gary Bokken	340 East Canyon View Drive, Tuscon, Arizona 85704; Dr. Bokken is a human factors and safety engineer. He will testify that considering the predictable human component involved in the use of the herbicides in Viet Nam, and the foreseeable uses and misuses of the product, the Defendants should and could have taken a lot of steps to eliminate or reduce the risks, including issuance of warnings, implementation of safety programs, and special training of the troops. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. William B. Retollick	1432 Johnny's Way, Westchester, Pennsylvania 19380; Dr. Retallick is a Chemical Processing Engineer and he will testify that it was the state of the art, and the Defendants could and should have utilized processes to reduce the dioxin content in the end product. Exhibit references include the flow data sheets from this defendant which were filed with the Court in response to plaintiffs' interrogatories. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. James O. Rasmusson	1582 W. 5th Place, Golden, Colorado 80403; Dr. Rasmusson is a specialist in analytical chemistry,

	instrumentation, general chemistry and environmental chemistry. He will testify that it was the state of the art in the 1960's and the precedent manfacture and sale of Agent Orange would have dictated that the product be tested through gas chromotography and other means to determine the levels of dioxin therein were too high. As an analytical Chemist he will discuss the chemical structure of TCDD and the phenoxy herbicides and their various chemical properties. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. R. Kenneth Godwin	1447 W. Maxermillion Place, Wuscon, Arizon 85704; Dr. Godwin is a public policy analyst at the University of Arizona where his fields of expertise are environmental policy and the relationships between the bureaucracy and decision making. He will testify concerning the relationships between the various governmental agencies including the USDA, NIH, DOD, and other agencies dealing with toxic substances or and the Secretary of Defense and/or the President had the ultimate authority to use or continue to use herbicides in S.E. Asia. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. Clifton D. Crutchfield	7321 N. La Oester Ave., Tuscon, Arizona 85704; Dr. Crutchfield is an industrial hygienist and will testify about the hazard control that should have been suggested and implemented in the form of an overall program by the Defendants in concert with the Government. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. Stephen Wyall	Economics and Finance Dept., Univ. of Houston, Houston, Texas; Dr. Wyalt is a specialist in economics and will evaluate each of the Plaintiffs' economic loss. He will also analyze the financial worth of the Defendants as such information

	may be relevant to punitive damages. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. Douglas Muster (if allowed)	University of Houston, Houston, Texas; Dr. Muster is a mechanical and safety engineer. He will testify about the transport or safety experiences and safety audits in the workplace to place of use by the purchaser or end-user; he will also testify about equipment changes and process modifications that will help reduce the hazards in the end product; and about what constitutes an adequate warning for the Government to have been able to make a proper risk-utility apportionment decisions. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Dr. Rupert Burtan (if	Dr. Burtan is a doctor of occupational and environmental medicine. He will analyze the feasibility of warning the end-user, the solider in the field, in this case and of adopting a monitoring program suitable to that adopted by the Ethyl Corporation with respect to the ethyl lead. Direct examination estimated 1/2 day; Cross examination estimated 1/4 day.
Charles Dishner	401-A Capitol Landing Road, Williamsburg, VA. Vietnam Veteran will testify to conditions and circumstances related to spraying of Herbicide Orange in Vietnam at times relevant to the Representative Plaintiffs. Direct examination approximately 1/2 day; cross-examination 1/4 day.
A.J. Philo	2475 Pinson Highway, Tarant, AL. Vietnam Veteran will testify to exposures of David Lambiotte to Agent Orange, and will authenticate certain photographs. Direct examination approximately 1/2 day; cross- examination 1/4 day.
Billie Newton	35 Town and Country Road, Leeds, AL.

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	Vietnam Veteran served with David Lambiotte will testify to exposure of said plaintiff to Herbicide Orange and will authenticate certain photographs. Direct examination approximately 1/2 day; cross-examination 1/4 day.
Deborah Nelson	2804 Jefferson Drive, Alexandria, VA. After being friends with, and after living with David Lambiotte, Deborah Nelson will testify concerning her observations of said plaintiff's physical and emotional conditions, including her knowledge of his seizure disorder, severe night sweating, stress, increased irritability, cancer and other medical conditions. Direct examination approximately 1/2 day; cross-examination 1/4 day.
Thomas Raftery	2221 56th Drive, Brooklyn, NY. Vietnam Veteran who served with Plaintiff Michael Ryan will testify to Michael's significant weight loss and illness while in Vietnam as well as to the physical terrain of defoliated areas where Michael Ryan served while on Advanced Party missions. Plaintiffs' examination less than 1/2 day; defendants' examination brief.
Thomas Portagallo	106 Evans Road, Brookline, MA. Vietnam Veteran who served with Plaintiff Michael Ryan. He will testify concerning Michael Ryan's physical condition while in Vietnam, including his drastic weight loss, and other medical conditions. He will also attest to the physical terrain of the defoliated areas travelled by Michael's Advanced Party. Direct examination approximately 1/2 day; cross-examination 1/4 day.
Al Bothweel	610 Hudson Terrace, Newport News, VA. As a friend of David Lambiotte in high school, while they both served in Vietnam, and presently, Al Bothweel will testify to the changes in David's physical and emotional

	conditions before Vietnam to the present, including his increased stress, irritability, cancer, seizure disorders, and additional medical conditions. Direct examination approximately 1/2 day, cross-examination 1/4 day.
Walter Jones, Jr.	915 West Wilson Avenue, Chicago, Illinois; Mr. Jones worked at Hercules' Jacksonville Arkansas herbicide plant, in 1967 and 1968, and will testify concerning his observations and knowledge regarding the Plant's operations, including, but not limited to Agent Orange, wastes and waste disposal and workers' health problems, including his own. Estimated time of direct testimony is 1-2 hours, cross examination is unknown, possibly 1/2 hour.
FRED FALANA	Address to come; As a member of Danny Ford's unit, Fred Falana will testify to the various locations which their unit was assigned, including recently defoliated areas traveled to by vehicle and often by foot, as well as the conditions of their unit in these various locations in Vietnam.
CAPT. FARMER	Address to come; Captain Farmer will testify to the assigned locations of Danny Ford's unit, including the defoliated areas traveled to by foot and by vehicle, and the conditions of their unit while in these various locations.
BETTY SMAYDA	1809 Rapids Road, Hiram, Ohio. Betty Smayda, a long-time friend and busines associate of Mrs. Danny Ford, will testify to Danny Ford's physical and emotional conditions, his behavior changes and increasing stress, the resultant time and wages lost in Danny Ford's work, and the overall emotional and financial strains on the Ford family.
TERRY AND JEANNETTE FORD	6507 Secor Road, Lambertville, Michigan. Terry and Jeannette Ford

	will testify to the Ford family's physical, emotional and financial strain which they observed as Danny Ford's brother and sister-in-law.
RAY AND ROSE FORD	13478 South County Line Highway, Ottawa Lake, Michigan. Danny Ford's parents will testify to his behavioral changes, physial conditions, increasing stres and the subsequent financial and emotional strain on the Ford family.
JUDY McKINLEY	1899 Rapids Road, Hiram, Ohio. As a long-time friend and business associate of Christina Ford, Judy McKinely will testify to Danny Ford's emotional and physical conditions, behavioral changes, stress and the resulting financial and emotional strains suffered by the Ford family.
ROBERT SNODGRASS	Huntington, W. Virginia; In the same gun section as Danny Ford, Robert Snodgrass will testify to the various locations of their unit, including the recently defoliated areas they travelled by both vehicle and foot, as well as the conditions of their unit in the various areas.
DAN TWISS	Woodland Street, Sylvania,Ohio. Dan Twiss, the Union Committeeman at Jeep Corporation and long-time friend of Danny Ford, will testify to the lost time and reduced wages of Danny Ford's work as a result of his physical condition.
JANE WARD	3527 M.151, Temperance, Michigan. As the Fords' neighbor, Jane Ward will testify to the time and wages lost from both Danny Ford and Christine Fords' jobs as a result of Danny Ford's medical condition.
SHERRY MOSHER	184335 Westchester Road, Toledo, Ohio. As the Manager of Christina Ford's business, SherryMosher will testify to Danny Ford's physical condition, the amount of time that Christina Ford has missed from work as a result of Danny Ford's

	condition and subsequently, the amount of business and wages lost in her absence.
HARRY HOLLAND	1626 Dryden Way, Crofton, MD; As a friend of David Lambiotte's before, during and after his stay in Vietnam, Harry Holland will testify to David's behavioral changes, increased stress, irritability and other emotional changes.
MICHAEL LAMBIOTTE	18 Milford Rd., Newport News, Virginia; As David Lambiotte's brother, Michael Lambiotte will testify to David Lambiotte's emotional and behavioral changes, increased stress and depression since his return from Vietnam.
RICHARD SCOTT	11 White Oak Drive, Newport News, Virginia; As David Lambiotte's high school friend, after spending time with David Lambiotte in Vietnam and after being David Lambiotte's roommate after Vietnam, Richard Scott will testify to David Lambiotte's attitude, behavior and emotional changes, his increased stress and his depression.
HENRY SADLER	Melbourne Beach, Florida. As David Lambiotte's neighbor and friend before and after Vietnam, Henry Sadler will testify to David Lambiotte's behavior and attitude changes, his increased irritability, depression and stress.
DR. SALTER	97 York Street, York, Maine; David Lambiotte's treating physician will testify to David as scientist and toxicologist; chief toxicologist for the Environmental Defense Fund; Research scientist in Reproductive Toxicology for National Institute of Health; general causation expert on the extreme toxicity, neuro-toxicity, reproductive toxicity, and carcinogenicity of Agent Orange and TCDD; mechanisms for the male-mediated birth defects; specific causation on the birth defects of Kerry Ryan, and Michael

	and Chad Jordan, was related to and caused by their respective fathers' exposure to Agent Orange in Vietnam; see curriculum vitae, all summaries, with references and documents attached; deposition testimony in possession of all parties. Direct examination estimated 1 day; Cross examination estimated 1 day.
William T. Thompson, III*	Mr. Thompson, Theresa Buckley, Leo Crivello, Mr. D. Hallek, Cecil McGill, Dr. Ernest Valasco, Dr. A.J. Reichas, Dr. Raymond Simpson, the custodian of records, American Mutual Liability Insurance Co., St. Louis, Missouri, Contracting Officer George Collins, Contracting Officer William Fenner and Mr. Thompson, are all witnesses relative to Thompson Chemical Corporation which the defendants reserve the right to call as witnesses in their case in chief; a page and line summary of Mr. Thompson's deposition will be provided in the event the plaintiffs do not wish him to testify as a live witness; the others, having not yet been deposed, remain to be determined.
James Gutshall	6307 Jackson Street, Philadelphia, Pennsylvania 19135; will testify to his observations concerning the actual spraying and defoliation of Vietnam; he is a veteran who travelled extensively in defoliated areas; total time of testimony estimated at 2 1/2 hours.
William J. Ezzi	833 4th Street, Camden, New Jersey 08103; will be asked to testify to identify photographic exhibits and as to his observations of defoliations in Vietnam. He is a veteran who was there during the spraying; estimated time of testimony less than 1/2 day.
John Flite	6544 Windsor, Philadelphia, Pennsylvania 19142; a former helicopter crew member will testify concerning the defoliation as it occurred; estimated total time of

	testimony 1 1/2 hours.
Major Lawrence Hondich	212 Flynn Drive, El Paso, Texas; will be asked to testify concerning the defoliation process and to identify and explain aerial and other photos of Vietnam during the defoliation. Anticipated length of testimony less than 1/2 day.
Ret. Mstr. Sgt. James Gregory	5561 Wadsworth, El Paso, Texas 79924; will be asked to testify to his observation of the defoliation process as it occurred in Vietnam. Anticipated length of testimony 1/2 hour.
William J. Eaves	10207 Summer Road, Philadelphia, Pennsylvania 19116; will be asked to testify to his observation of the defoliation as it occurred in Vietnam when he was present; expected length of testimony 1/2 hour.

safety of the plant, the spokesman in labor grievances at Nitro and acknowledged that his objective was to produce as much 2,4,5-T as possible.

Agreed that when Monsanto began producing 2,4,5-T for sales to the Government, certain quality speicifications were most entirely relaxed and there were subsequent gains in rate.

During his tenure at Nitro, Dotson was concerned about the health and safety of his workers at the 2,4,5-T plant. However, he never attempted to find out any more about dioxin - all he knew was that the 2,4,5-T did contain dioxin, although he knew that dioxin was toxic.

During his tenure as Production Supervisor, the amount of 2,4,5-T being produced significantly increased and when hel left, there were three shifts per day producing 2,4,5-T and the plant was producing that product 24 hours.

Transcript of November 2, 1983; p11,116&12;p12,116-12&22-25;p13,112-5;p14,112-8&17-25;p15,112-5&7-17&19-25;p16,111-23;p17,113-9&13-17;p18,111-2&17-25;p19,1112-14;p21,1113-18;p25,115-11;p26,118-9;p28,1116-23;p29,116-22;p31,1115-18;p34,1122-25;p35,1110-12;p39,111-8;p41,112-25;p43,1115-25;p44,111-5;p46,1117-19;p47,111-15;p51,1116-19;p52,115-8;p54,1119-21;p57,1117-24;p58,1110-23;p59,1120-22;p60,1116-25;p61,111-25;p62,111-14;p63,112-25;p64,111-6;p65,1113-25;p66,111-4;p67,111-2&15-25;p70,119-11;p71,111-5&9-14;p72,114-7;p73,1124-25;p75,111-12;p76,1111-17;p78,116-8&22-25;p79,111-10;p80,119-18&21-24;p81,116-10;p83,113-10&15-23;p86,1115-25;p88,1123-25;p89,111-12&23-25;p90,1119-24;p94,113-6;p95,114-25;p96,11;p98,111-8&18-21;p103,1123-25;p104,111-18;p106,112-6&24-25;p107,111-4&8-19;p108,111-6;p109,112-7;p110,1110-25;p111,111-24;p112,111-2&9-13&17-25;p113,111-2&8-25;p114,1121-24;p115,1111-24;p116,1113-21;p117,15-9&12-18;p118,111-24;p122,1120-24;p127,1112-23;p128,1115-24;p129,113-14;p131,112-25;pp132-13

9;p140,111-6;p142,1116-20;p143,111-5
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Verne Rhodes

2120 Windport Lane, St. Louis, Missouri.
Verne Rhodes born April 6, 1939, is a present Monsanto employee having been so employed for the past 22 years. He received a Bachelor in Chemical Engineering from Georgia Tech and a Master of Business Administration from West Virginia University. His present position at Monsanto is Manager Markets and Products, Paper Resins. His yearly salary is $61,000 plus benefits.
In April of 1966, he became Production Supervisor of the 2,4,5-T plant. Buildings 92 and 51 were combined. He was Production Supervisor for a 3 year period and went into the 2,4,5-T plant about eight hundred times over the years. He terminated the position in April of 1969.
Answered the esterification process of 2,4,5-T did not take place at Nitro but at Krumrich where it was thereafter shipped. The product when it left Nitro looked like a brown powder with various size grains, some finer than sand, some larger than sand with a hydrocarbon smell.
The first time hears the word dioxin is in the 70's and probably in 1977. He became involved with herbicides as an Assistant Production Supervisor in 1963 or 1964.
Recalls meeting with Udell when Udell showed him a glass vial and indicated that it was highly toxic. Udell mentioned that he had been given an analytical technique by Dow.
The chlroacne that he saw was much more severe than pimples. Many people that worked around the Nitro unit had it on their face so prominently that it would look like their eyes were permanently blackened. Pimples on the workers. He had seen chloracne lesions under the skin as large as his thumb.

Postules were present on some of the people who had the chloracne.
Hearing how toxic dioxin was from Udell, he has no recollection of doing anything to investigate the extent of that toxicity. Never recalls researching either by experiment or by reading to ascertain further information on dioxin. He never heard the word dioxin being used at Monsanto all during the 1960's. Dioxin in the 2,4,5-T was a major concern of his and his people were worried about trying to eliminate it. Although he was concerned for the workers' safety, he was not concerned for the consumers.
Never remembers asking a worker with chloracne if the worker had any other medical problems, nor does he remember reading any medical reports in which worker problems were claimed. Agrees that at one point almost every worker at theT plant had chloracne.
Nitro had five customers of 2,4,5-T acid. These were the larger chemical companies. Customers included Ag-Chem and their Krumrich plant. He doesn't know whether there is any safe level of dioxin in 2,4,5-T. Does not remember the size or the frequency of the lots being tested for dioxin.
Mr. Rhodes got chloracne in the fall of 1966 and he has had it for almost eighteen years and still has it.
Agrees that in January of 1969, Monsanto still hadn't solved the problem of getting the dioxin out of 2,4,5-T.
Transcript of February 17,1984; p5,119-25;p6,111&21-25;p7,111-6&18-25;p8,111-3;p9,115-25;p10,111-5&21-25;p11,111-9&21-25;p12,111-15&21-25;p13,111-3&11-25;p15,116-25;p16,111-3&6-25;p17,111-2&8-9&13-24;p18,111-25;p19,111-15&18-25;p20,113-8&11-25;pp21-33;p34,111-12&21-25;pp35-36;p37,111-5&19-23;p38,116-23;p40,1114-23;p44,1115-20;p59,1118-25;pp60-79;p80,111-19;p83,1114-25,p88,18-25;p89,111-2;p90,111-16;p92,114-25;p93,111-3&20-25

;p94,111-4;p95,115-15;p97,113-12;p10
1,1117-21;p102,1123-25;p103,111-21;p
104,1112-25;p105,1117-25;p106,111-23
;p107,111-16;p108,113-7;p109,1119-25
;p111,114-7;p112,119-25;p112,111-4;p
114,117-21;p116,111-7&11-24;p117;p11
8,111-9&22-25;p122,115-25;p123,111-2
0;p126,114-25;p127;p128,111-13;p130,
1116-22;p132,1115-25;p133,111-4&15-2
5;p134,111-13;pp135-137;p138,111-6&1
7-25;p139,114-25;p140,114-23;p141,11
2-25;p142,111-2&19-25;p143,111-22;p1
44,111-15;p148,112-13;p149;p150,1110
-25;p151,111-18;p152,1121-25;p153;p1
54,111-21;p155,111-12;p162,1120-25;p
163,111-13;p164,111-4&18-25;p165,113
-14&18-20;p167,113-9;p169,112-6;p171
,115-25;p172,1111-17.

Dexter Sharp

13042 Weatherfield Drive, St. Louis, Missouri: Dexter Sharp is a present employee of Monsanto having been so employed for 33 years and possessing the present title of Director of Environmental Science Formulations. He is a Ph.D. in Chemistry. Salary $86,000 per year.

In 1963 he became Group leader in the Agricultural Division, working under Dr. Stephens and Dr. Speziale. He was a Group leader to 1968. His resonsibility was to direct a group of Chemists in Process chemistry developing technical chemical basis for manufacturing the proess which comrises all the conditions necessary to obtain a final product. Dr. Sharp was working on the 2,4,5-T Research Project in 1964 1965 and learned about the presence of dioxin in the 2,4,5-T from Dr. Stephens. Dr. Stephens told him that dioxin was a very toxic material.

He heard at that time that a certain amount of dioxin would kill half of the test animals at a certain dosage and therefore Dr. Stephens told him it was highly toxic. Other than looking up the word chloracne in a dictionery he never did nay research or investigation of any kind in connection therewith.

The workers were paid a premium to work at the T plant beause of

potential chloracne problems.
When he was told by Dr. Stephens that the impurity was dioxin, he knew that dioxin was highly toxic. Felling from that day until the present time has not changed.
He was thereafter given a sample of dioxin
from Dr. Stephens. Dr. Stephens also told him that dioxin was a toxic material. He was William Udell's superior. Acknowledges that Monsanto knew in 1965 how to analyze dioxin content T acid. Knew that Monsanto was selling 2,4,5-T to the Government in 1965 and he knew then that that 2,4,5-T contained dioxin. He agreed that dioxin was a highly toxic impurity in animal oral tests. At that time they were sellng T to the Government, which they knew contained dioxin, he knew of animal tests that resulted in death to the animals. Knowing the above, he nevertheless did not tell the Government that there was dioxin in the Agent Orange because not being a toxicologist, it wasn't his responsibility.
He did not know whether it was someone else's job to tell the Government. He also didn't tell the Government because he had no contact with the Government and he would not have known to whom to speak.
However, if he had known with whom to speak in the Government he still would not have told that person that the Agent Orange contained dioxin.
Until March of 1968, neither he nor those working under him had recommended any procedures in the manufacturing process, that would eliminate or reduce dioxin in the T acid.
As one who attained a Ph.D. in Chemistry, who taught graduate and undergraduate students chemistry in college and who geared his career in chemistry, he was not able to name any chemicals made by man that had a greater degree of toxicity than dioxin.
He reported the results of his

analytical proedures indicating the amount of dioxin to John Stephens. Sharp's Research Group analyzed the dioxin content of samples of Monsanto's final batches of 2,4-D. He was aware of the animal toxicological tests which revealed that dioxin was highly toxic to animals and perhaps to humans.
Transcript of October 20,1983; p35,112-16;p42,117-14;p47,1119-48;p48;p50,1116-25;p51,111-12;p54,112-18;p58,116-25;pp59-87;p88,111-23;p89,13;p95,121;p96,114-23;p100,115-9;p105,114-21;p107,117-25;p108,1117-19;p112,1111-25;p116,1114-16;p117,1115-18;p128;p130,17;p136,1115-21;p146,114-8.

John A. Stephens

800 North Lindbergh Boulevard, St. Louis, Missouri
Mr. Stephens is presently employed by the Monsanto Company as Director of World Wide Operations for the Agricultural Products Company Research Division. He received a Bachelers, B>A>, and Masters Degree in Chemistry and a Ph.D. in Organic Chemistry. His present salary is $86,000 per year plus benefits.
1961 to 1963, he was the Group leader in Process Research in Agricultural Division and from 1963 to 1969, was the Manager of Chemistry Research.
1961 his position was Group Leader Process Research. He was required to supervise the activities that were going on to support the manufacturing proess. Their goals included the attempted reduction of manufacturing costs, job operating problems to solve quality problems in relation and packaging problems.
1963 he became Manager of Research for Chemistry. At that time Dexter Sharp became group leader working under him.
1964 or 1965 it was called to his attention that dioxin contained in their 2,4,5-T. They received a letter from Dr. Kelly. When Dr. Kelly sent Dr. Stephens a sample of dioxin, at that time he was informed that dioxin was highly toxic and was

warned to take certain safety precausions when handling it. He was told not to touch it with his bare hands.

The Medical Department had an obligation to test for toxic effects an they normally would inform Research of the test results. They had an obligation to tell Research about any toxic effecs. Test them and tell
them the effects.

If a product that Monsanto manufactured had a toxic impurity, two different organizations, research and manufacturer had an obligation to attempt to remove the toxic impurity. Research would tell manufcturer what was wrong and manufactureer would hopefully attempt to do it. Howver, they weren't successful in cleaning up the 2,4,5-T process for a number of years.

At the same time or within a few days thereafter he got the dioxin sample from Dow. He also had received the Dow analytical proess. Dr. Kelly stated that the analytical process was received by him from Dow. He then gave the Dow method and Dow sample to members of his research staff with instructions to analyze it. Monsanto thereafter developed a method of analytical determination of dioxin in the T. With respect to the analytical process within less than a day they were able to find out whether a particular lot produced contained dioxin and to what extent.

He contined to have discussions with Russell, the Director of Product Quality Control from 1963 to 1974 to inform Russell as to what was happening in his research.

Stephens acknowledged that if the temperature were higher, that would result in a grater amount of dixoin. Further agreed that the dioxin concentration in the autoclaves was highly sensitive to temperature with a slight increase in temperature resulting in a significant increase

of dioxin.
Acknowledges it was Mr. Udell's responsibility to supervise the project to reduce the dioxin in the T. Never had a knowledge or realization or belief that there was a safe level of dioxin in the 2,4,5-T acid and Monsanto was never operating under a type of maximum dioxin level. As of September of 1965 Monsanto had an analytical process to determine the dioxin content of the T.
Acknowledges that they anted to reduce the dioxin content at that time because Dr. Kelly of the Medical Department stated that the contaminant was toxic. He reeived that information directly from Dr. Kelly and disseminated the information through Reseach. Kelly told him that he had been to a meeting at Dow. That Dow had agreed to give Monsanto the analytical method and a sample of dioxin. It was his feeling that the reason that Dow was doing that was that "it had something to do with the whole picture that was around Agent Orange."
Acknowledges that at the time of the Kelly discussions he knew that the T acid that they were selling was going into Aget Orange that was being used in Vietnam.
Assumed that the product was going to be sprayed by aerial spray or by hand and it was Monsanto's assumption that it would be sprayed both by hand and through the air. The method by which Agent Orange was to be applied in Vietnam was not considered in any determination as to whether or not or what they should hae done with respect to the dioxin in the product. Also the existence or non-existence of that dilutent in Agent Orange never influenced him in any manner with regard to his actions in connection with the dioxin content of the T.
It was Mr. Speziale's communication that first prompted him to reduce the dioxin content. Speziale's

conversation - he told Dr. Stephens that he received information from Mr. Arvan or Mr. Rumor, the commercial people that they wanted the material eliminated because it as toxic. Speziale told Stephens about what was in the literature and they looked through the literature. He and Mr. Speziale went through the chemical literature, found a couple of references, one in German.
Assumed that the greater the dioxin content, the greater the potentiality for hazardous effect and that assumption has never changed.Assumed that AGent Orange being used in Vietnam would come into contact with some people. Knew in 1965 that their product had dioxin. Knew that the product was being sold to the Government. Did not tell the Government or suggest the Govt. be notified. The reason he did not suggest the Govt. be notified was that he had no contact with the Govt. Then says that the reason that he did not tell the Govt. that the product had a toxic component was "because it was someone else's responsibility." He did not know whose responsibility it was nor did he ever inquire as to whose responsibility it was.
Acknowledgd that the butyl ester of T was contaminated with dioxin and the intermediate products were contaminated with dioxin as well. Stated that Dr. Kelly said worker contact with the intermediate products presented a hazard to workers and he believed Dr. Kelly.
workers in the 2,4,5-T facytory had safety shoes ad safety gloves and safety glasses to avoid contact with the 2,4,5-T and intermediates that were contamineated with dioxin, in order to prevent worker harm from the contaminated 2,4,5-T it was suggested that they wear protective clothing.
He acknowledges that when the workers came into contact with the end product they still are required to maintain the same safety

equipment, however, he was not concerned with what happened to the people coming into contact with the product after it left the hands of the workes, although he agrees that there was knowledge of worker harm up through the final stage of the manufacturing product.
The end product still contained dioxin. The end product was as contaminated when it left the factory as it was when the workers had to deal with it on the prodution line and the only reason that he did not inform anyone else of the toxic problems with respect to the end product was that he as not an authority on toxicity. The only authority in the company was Dr. Kelly but he never spoke to Dr. Kelly about the problems that could be caused to the ultimate consumers.
Agreed that if you increase the temperature, you ncrease the dioxin and if you hold theproduct in the autoclave longer, you increase the dioxin. He assumed that although there is a worker problem there is not aprospective customer problem because noone had ever told him it was a problem and he doesn't remember whether anyone told him it wasn't a problem. Agreed that chloracne resulted in tiny bumps. However, assumed that dioxin exposure caused a few bumps and nothing more. Kelly told him that chlorance meant a few bumps on the skin. Never asked the cause of chloracne nor did he ask how long chloracne lasted.
Never researched or questioned about chloracne.
Never assumed the Government had a process to test 2,4,5-T for dioxin, nor did he receive from the Govt. any indication that they knew that the 2,4,5-T that Monsanto was selling to the Govt. had dioxin.
In the Kelly letter that informed Dr. Stephens about dioxin, kelly told them that it was a very toxic material that should be handled with caution. Dr. Stephens never

attempted to find out anything about the toxic effecs of dioxin at any time up to 1973.
Claimed that Russell, the Director of Quality Control determined which lots of T were to be tested for dioxin content.
He had no reason to disbelieve that in 1968 he was averaging 40 ppm in he T acid.
As a consequence of Dr. Kelly's letter, he treated dioxin as a highly toxic component.
Agreed that during the time he was attempting to reduce the content of dioxin of T they continued to sell to the Govt and realized in 1965 that the T that they were selling to the Govt. was going to be used in Vietnam.
Transcript of October 17,1983; p5,1111-14&18-20;p6,118&15&23-24;p7, 13;p10,110;p11,1114-15&22-23;p12,111 2-13;p13,16&13&24-25;p15;118&14;p17, 112-6;p18,113;p20,1112&20-25;p21;p23 ,113-9;p33,111-7;p35,114-23;p37,1120 -21;p41,114-6;p42,113-11;p43,1115-19 ;p48,1115-23;p49,111;p50,1120-25;p51 ,111-14;p52,1112-25;p53,111-12;p54,1 12-6&13-21;p55,1114-15;p58,112-19;p6 2;p63,14;p65,124;p79,1118-20;p81,115 -8;p91;111;p95,119-11;p96,1115-22;p9 7,1113-24;p101,124;p102,112-6;p103,1 13;p105,1112-20;p107,118-10&20-25;pp 108-109;p110,116-9&15-20;pp111-112;p 113,12;p114,12&9-12&22-25;p115,p2-12 ;p116,1110-15;p117,114-6&&17-25;p118 ;p119,110;p121,114;p122,125;p124,116 -21;p125,119-23;p126,1111-15;p128,11 17-24;p131,1114-20;p132;p133,112-6;p 124,1110-23;p136,1120-21;p138,112;p1 41,1118-22;p142,116-25;p143,111-12&1 9-21;pp144-148;p149,1119-24;p150,111 -4;p159,1112-25;p160;p161,1111;p163, 1112-25;p164;p165,113;p166,1120-25;p 167,1113-15;p168,111-8;p169,118;p170 ,12;p171,116-18;p175;p176,111-24;p17 7,11;p178,116-25;p179;p180,111-11;p1 82,16;p184,120;p187,1116-22;p190,117 -13;p191,1116-22;p192,1114-25;p193,1 121-25;p194,111-23;pp195-196;p205,11 2&6-11;p206,1113&21-24;p207,11;p208, 118-10;p209,111-21;p218,115-25;p219, 11&21-25;p220,11;p221,11-9.

William R. Udell

60 Tealwood, Creve Coeur,Missouri
Mr. Udell is a present employee of Monsanto Co., having been so employed for approx. 35 years. He received his B.S. and Master's Degree in Chemistry and in 1960, was employed by the Agricultural Division Research Department.
Author of several documents in connection with attempted improvements in the 2,4,5-T process.
First heard about dioxin in the mid-1960's and agrees that the acute toxicity of dioxin cannot be overly emphasized. His understanding of the word toxic means to cause death.
He recommended to employees that they wear safety glasses and gloves and a face shield to minimize expousre and to avoid thepossibility of causing death when in contact with dioxin.
Agreed that the incidence of chloracne was almost universal with workers engaged in the 2,4,5-T manufacturing process. Knew in the mid-60's that problems similar to Nitro and Badische occurred with other manufacturers.
Knew about Dow's analytical process to determine existence of dioxin in T and received it in 1965.
Analyzed samples of the 2,4,5-T manufactured during the 1950's and ever since the late 50's claimed that the dioxin content then averaged 10 ppm, but in 1965, averaged 50 ppm. Believed the dioxin formed almost entirely during the period in the autoclave reaction. Felt that because dioxin killed animals it had the potentiality to kill humans as well.
Knew that the Govt. was buying Monsanto's 2,4,5-T.
He never prepared a procedure for the analysis of dioxin in Monsanto's T and does not believe that anyone else in Monsanto did so either.
Acknowledges that dioxin content in 1965 was 35 ppm in 1968 36 ppm and about the same through January of 1979.

using it. He was repsonsible to put the cost factors for Orange together and then recommend the price. Acknowledges that the Govt. had promulgated rules restricting 2,4,5-T in lakes, ponds, ditch banks or drainage ditches - don't go near susceptible crops and liquid formulations not to be used around a home and recreational area.
Thinks he learned in 1969 that his 2,4,5-T acid had a dioxin impurity, but never told anyone. Acknowledged that dioxin was toxic but never attempted to find out the end level. Has no idea of the dioxin tolerance, although assumes there was. When he knew in 1969 there was a toxic impurity in the product, it was then he went to Cecil Russell. Russell told him that they had a procedure to analyze 2,4,5-T for dioxin, but does not recall the ppm specifications.
Believed Monsanto was testing 2,4,5-T for dioxin in 1969, but never saw the test results.
He relied on the peole who delivered the product, but never knew how the product was made - he never worked at the plants.
Never knew how much dioxin they had in the product. Never asked about an analytical process to determine dioxin because it wasn't his job to ask and never asked whether they had a process to remove the dioxin because that wasn't his job.
Hears in 1964 or 1965 - worker health problems in 2,4,5-T plant.
Transcript of May 3,1983 p6,123;p9,116-15&17-18;p10,1118-20;p12,1115-21;p15,1112-15;p16,1111-12;p18,111-2&12-13;p19,115-8&16-17;p20,1118-25;p21,111-17;p23,112-19&23-24;p24,112-4&20-21;p25;12;p27,112-11&14-16;p30,111-8;p34,1112-19;p36,16;p38,116-11&15-16&24-25;p39;1-12&21;p40,17;p41,1115-25;p42,111-10;p50,1118-21;p51,111-6;p54,111-18;p58,118-17;p59,113-25;p60,114-8&15-23;p61,118-22;p62,1119-23;p63;p64,111-8;p72,1115-18;p73,111-4;pp74-75;p77,1123-25;p78,111-3;p79,119-12&16;p82,116&16-25;p83

,18;p85,112-19;p86,1110-19;p90,1119-23;p94,116-11;p95;p96,111-15;p97,114-25;p98,111-7&16-17;p101,113-7;p104,111-2;p105,1110-25;p106;p107,111-24;p108,1111-18;p110,18;p111,119-12;p113,17&11;p114,122;p117,15;p118,114;p120,1120-22;p126,1111-13;p127,111-6;p128,1119-23;p129,11;p140;p148,1119-24;p151,1118-20;p153,1113-15;pp157-158;p159,113-4;p160,117-8;p162,1116-20;p163;p170,114;p173,1122-25;pp174-178;p179,111-12;p180,112-8&17-25;pp181-183;p184,111-18;p190,113-7;p191,1114-25;p192,113;p193,121;p195,1122-25;p196,111-13;p200,116-19;p201,112-15;p203,1124-25;p204,11;p206,1124-25;p207,111-19;p209,111-5;p211,1117-15;p212,111-13;p219,1111-21&24-25;p220,111-8&17-23;p224,1117-19;p225,118;p226,1110-25;p227;p228,111-16&21-25;p229,111-13;p232,113-25;p233,111-16&25;p235,1110-11;p236,1127-19;p244,11;p246,1117-19;p255,1115-19;p258,1122-25;p259;p260,111-19;p261,125;p264,1124-25;p265;p266,111-4;p268,1111-16.

James E. Springgate

13060 East Sunset Drive, Los Altos Hills, California:

James Springgate is a present employee of Monsanto and is the President of Monsanto's Electronic Materials Company. He has been employed by Monsanto for the past 34 years and originally transferred to Nitro in 1962 as the Manufacturing Superintendent of Organic Division Products. He was the Plant Manager of the Monsanto Plant from 1964 through 1968. He became involved with herbicides in 1964 and his overall responsibilities as Plant Manager included personnel safety, labor relations, service facilities maintenance and construction for the entire plant. He recalls having 700 to 800 employees.

His responsibilities included reviewing with the superintendent of personnel the medical doctor and the safety director, worker health problems. The medical doctor was Richard Wallace.

Met on amonthly basis during the time that he was Plant Manager to

discuss medical complaints of the workers.
Has a recollection of workers complaining about health problems other than a skin condition but doesn't remember where that came from. During the time that he was there, the chloracne problems in 64-68 were decreasing from the prior four years.
The total of the chloracne problems for the four years before he got there was greater than for the four years he was there.
He continued to have conversations with Dr. Kelly one to two times per year concerning worker health problems in the 2,4,5-T plant.
During 1964 to 1968 reviewed approximately 100 medical files of 2,4,5-T workers who had chloracne during that time. Does not remember whether the 100 workers with chloracne had other complaints as well.
Knew in 1964 that the 2,4,5-T was being sold to the Govt. for use in Vietnam but did not know whether it was going to come into contact with American soldiers.
Hears about dioxin and heard that it was a highly toxic impurity in Monsanto's 2,4,5-T but does not remember when he heard it.
It was the responsiblity of the AGricultural Manufacturing Management Team to eliminate a toxic content from a product.
2,4,5-T workers were getting paid extra for working in the Plant because there was a high incidence of chloracne among the workers and many workers did not chose to work there. The additional wages were an incentive for the workers to work.
Although claims not to recall whether he was ever told during the time that he was at Nitro that dioxin was in the 2,4,5-T.
Transcript of October 27, 1983. p5,1115-22&24-25;p6,8-9&17-24;p7,111-17;p8,1123-25;p9,111-9&11-13;p10,112-5;p13,111-6;p14,15;p15,1118-24;p16,1113-17;p18,112-4&6-7&9-19;p21,119-

11;p21,112-13;p22,118-19;p23,1113-22;p24,118-16&23-25;p25,115-25;p26;p27,111-21;p28;p29,112-4&21-25;p30,113-7&22-25;p31,116-10;p32,112-6;p34,117-20;p35,119-23;p36,1112-20;p39,113-25;p40;p41,111-12;p44,1111-22;p47,1119-22;p48,11;p50,1121-25;p51,111-6;p52,111-5;p53,18;p54,111-7&13-18;p56,1113-25;p57,111-2&16;p59,1111-22;p60,1111-21;p61,111-5&6-18;p62,115-8&9-14;p63,1110-17;p65,1123-25;p66,111-5;p67,111-19;p69,1115-21&21-25;p71;p72,111-16;p78,1120-25;p79,111-14;p81,12;p82,19;p83,115-7&21-25;p84,111-21;p85,1111-25;p86;p87,111-22;p89,1117-25.

Jack Strum

712 Short Spoon Circle (city and state not available through transcript):
Jack Strumm was a Monsanto employee from 1965 to 1970. When he was hired he was hired at Nitro, West Virginia and his position was Technical Service Engineer, his responsibility was to carry out projects assigned by the Group Leader, normally involving improvements in rate, quality, yield and other processes. In 1969 he became Production Supervisor, initially for 2,4,5-T.
His obligation included a responsibility to increase the production of pounds per hour of 2,4,5-T from the years 1965 to 1969.

Met with Vernon Rhodes in the summer of 1964 or 1965, with regard to 2,4,5-T.
Does not remember from whom he first heard about dioxin. Thinks he first heard late 1966 or 1967. He, himself, had contacted chloracne, had it primarily on his face for five or six years. He has no knowledge of anyone missing work because of chloracne. When he heard about dioxin he eventually began a series of experiments for the purpose of reducing the amount of dioxin. Never attempted to learn as much as he could about dioxin.
Acknolwedges that dioxin was

contaminant in 2,4,5-T. Contaminant dioxin developed in the process at some point before it left the 2,4,5-T plant. Their studies indicated that high temperatures and long time periods at those temperatures tended to increase the amount of dioxin in the trichlorophenol. He first learned of dioxin contamination in the T shortly after learned about dioxin.
The pressure was basically controlled by the temperature and if you increase the temperature, you proportionally would increase the pressure. The lower the temperature the slower the reaction.
The dioxin level was much lower the latter part of the 1960's.
There was a time that Monsanto attempted to speed up the manufacturing process in order to meet requirements. This was sometime around 1967. He had no thought of whether to be concerned or not with dioxin to the end user, his concern with dioxin was to the people who worked in the 2,4,5-T unit. He did not know of anyone who had an obligation to convey the fact that dioxin was the contaminant in the 2,4,5-T which was being sold to end users.
Toxicity to him means poisonous and poisonous menas that if you ingest it it will kill you.
His recollection is that they had no analytical method to determine dioxin content until 1967.
Did not share information regarding the Monsanto's process to reduce dioxin with anyone in the Govt.
Transcript of December 16, 1983: p6,115-6;p7,111-13;p8,111-8;p9,116-8 &14-17;p10,118-25;p11,113-6&23-25;p12,111-3&8-25;p13,111-4;p15,119-24;p16,111-9;p17;p19,111-13;p21,115-19;p23,115-25;p24;p25,111-5;p26,116-25;p27,1112-25;p28,111-24;p34,1111-25;p35,111-3;p36,1113-18;p38,111-4;p44,1114-25;p45;p46,111-4;p46,119-12&15-18;p47,115-13&24-25;p48,111-2;p49,1112-15&24-25;p50,111-12;p51;p52,111-5&13-21&25;p53,111-9;p54,1123-25;p55,111

-5;p57;p59,111-9&16-22;p61,1116-21;p62,111-6&15-25;p63,111-6&13-18&25;p64,111-8;p65,116-25;p66,111-22;p67,1123-25;p68,111-6;p70,125;p69,1117-19;p71,111-5;p72,1112-15;p74,1122-25;p76,111-11&14-17&20-24;p77,112-25;pp78-80;p81,111-4&17-25;p82,114-19&23-25;p83,111-4;p89,111-3;p93,1117-25;p94,111-21;p95,1120-24;p98,1121-25;p99,114-6;p101,118-11;p103;p104,111-5&8-25;p105,113-11;p106,112-25;p107;p108,111-18;p109,115-11&20-25;p110,114-25;p111;p112,111&6-12;p113,1121-25;p114,1112-20;p115,113-5&13-15&21-25;p116,111-8;p118,116-23;p120,115-16;p121,1110-11&15-25;p122,111-16;p123,1110-13;p124,1116-25;p125,111-10&18-25;p126,111-10&17-25;p127,111-8;p128,1116-22;p133,1120-25;p134;p135,1120-25;p136,111-4;p142,111-10&14-18;p145,1110-18;p146,1111-16;p147,114-25;p148,1114-25;p149,111-16;p151,1112-22;p154,1118-25;p155,113-16;p156,112-10;p160,114-25;p161,111-7;p163,111-7;p164,1111-25;p165,111-4&20-24;p171,1123-25;p172,111-23;p175,1114-19;p176,115-16;p177,1116-25;p178,111-2&20-25;p179,111-2;p180,116-17;p181,1115-19;p184,1124-25;p185,111-20.

A. John Speziale

311 North Umberland Avenue, Redwood City, California 94061:
A. John Speziale was the Director of Research of the Agricultural Chemical Division from 1963 to 1979 and was employed by Monsanto from 1948 to 1979. Mr. Speziale is presently a consultant to Monsanto. Paid pursuant to Contract, receiving $500 per day guaranteed, 8 days per month. He became Director of Research in 1963 and first became aware of the dioxin impurity in 2,4,5-T around 1965. When he heard about it he gave Mr. Udell, a chemist, instructions to go to the literature and find out all he could about the compound and structure formation toxicity and to find out what the company knew about it. When he learned about dioxin he was told that it was a toxic substance and he considered as a priority matter to find out about dioxin.

Thereafter, he realized from the Chemical Literature that dioxin was highly toxic. In accordance with his instructions, either Sharp or Udell developed an analytical method to determine the presence of dioxin in 2,4,5-T.

From 1965 to 1970 Mr. Speziale reported that he informed the Monsanto Operating Committee of his progress or lack of progress in reducing the dioxin content in 2,4,5-T. The Operating Committee consisted of various department heads or directors.

Around 1969, he wrote to Prof. Baldeshweiler in Washington, forwarding to him Monsanto's analytical methods for the detection of dioxin.

Prof. Baldeschwieler was an advisor to Dr. Lee DuBridge, the President's Science Advisor, whose testimony clearly infers that the Govt. did not have a dioxin detection analytical process at that time. Dr. Baldeschweiler was the sole outside person that Mr. Speziale communicated with concerning 2,4,5-T during the 1960's.

As the Director of Research, his responsibility was to administer and manage the research in the Agricultural Research Dept. which had about 120 people. From 1963 until 1970 he communicated with Dr. Kelly of the Medical Department, approx. one per month, in which Research forwarded written summaries of anything having to do with toxicology.

When he received the assignment in 1963, Dexter Sharp and Bill Udell were the leaders in connection with resolving the problems with the T process.

The work on the project went on until 1969. It was from one or more of his Research chemists that he first heard the word dioxin. Says he found out in 1966 or 1967 that it was highly toxic. Probably learned in 1964 to 1965 that Monsanto was selling 2,4,5-T to the Govt.

When he found out that dioxin was highly toxic, that is when he told the research section to get it out of the product. In August of 1969, Monsanto discontinued the production and sale of 2,4,5-T.
Always agreed with the statement that the concentrations of dioxin in the trichlorophenol was equal to the concentrations of the dioxin in the 2,4,5-T acid produced from the trichlorophenol. Probably heard in the early 1950's that the workers in the 2,4,5-T plant in Nitro were receiving more money than the other workers, because it was a more hazardous operation in the T plant. Never attempted to determine if there were any worker problems in the T manufacturing process other than chloracne.
He knew in Septemer of 1965 that dioxin was in the T and that dioxin was highly toxic and he then initiated a program to get the dioxin out of his T.
He was interested in the dioxin reduction program because of any prospectie harm that could occur either to the workers or to the public. He thereafter denied concern over consumer problems with regard to the workers, he acknowledged that he never asked anyone at Nitro wherther there were any other problems on the T line other than chlorance. With regard to the customers he never made the determination as to whether or not the product was toxic or non-toxic to humans. He never told the Govt. that the 2,4,5-T he was making had a toxic contaminant.
When he got the communication from Dr. Baldeschweiler, he asked Udell and Sharp to give him the analytical method and the chromatograms so they could send them to Baldeschweiler. When he met with Udell and Sharp he told them to institute process work to reduce dioxin in the product, to determine where and how it was being formed and to remove it from the product if possible to the lowest

possible limits.
With respect to the process, agrees that a slight increase in temperature results in an increase in dioxin. Agreed that dioxin in the 2,4,5-T process was the formation of a hazardous by-product. Assumed that he kept Dr. Kelly informed of research related to dioxin since it was Kelly's responsibility a Medical Director to know about this because that is the way the company operated. Kelly's responsibility to Medical Director to be aware of the safety of workers, users, customers. Knowledge that during 1968 to 1969, some people said there was a certain level that was safe and some people said there was no level that was safe.
He knew the product was being used in Vietnam. Knew that it was being sprayed, did not assume one way or the other that it was being sprayed diluted or undiluted.
Transcript of October 26, 1983; p5;p7,1122-23;pp9-10;p11,120;p12,1117-25;p24,1115-25;p25,111-13;p26,112-7;p27,119-24;p28,115-25;p29,111-10;p31,112-7&13&16-25;pp32-35;p37,1117-25;p38,111-21;p40,1110-18;p41,1114-20;p45,118;p47,1117-25;p48,111-5;p51,1111-24;p52,125;p53,115,p56,112-10;p57,117-25;p58,111-16;p60,1123-25;p61,111-4&13-21;p63,1112-19;p64,119;p67,12;pp68-69;p70,112&19;p71,13;p74,114-19;pp75-76;p77,1120-24;p79,118-25;p80,111-23;p81,125;p82,111-13;p83,1114-25;p84;p85,119-14;p87,1124-25;p88,111-7&14;p89,119-25;p90,111-15;p91,118-18;p96,111-9;p99,121;p100,12;p110,111-7;p111,115-21;p116,1124-25;pp117-119;p124,114-25;p125;p126,111-16;p128,1119-25;p133,1114-25;p134,119-15;p137,1121-25;p138,111-4;p140,1119-24;p142,115-14;p143,111;pp146-149;p154,1121-25;pp155-157;p159,1113-18;p163,1115-25;p167,118-17;p168,113-9;p169,113-25;p170,111-18;p172,1119-25;p173,112-24;p176,111-11:p178,13;p180,13.

Jane Lewis

Washington, D.C.: Jane Lewis was

assigned during the years 1966-68 by both her superiors and people outside of her division and even outside the Department of Commerce, the find chemical compounds necessary for the production of Agent Orange. Her main problems in this are was in finding tetrachlorobenzene (TCB). Only two domestic producers, Dow and Hooker, existed at the time. Dow did not cross-sell to the industry, Hooker did. This ingredient was needed to produce trichlorophenol (TCP), which in turn, was needed in the production of 2,4,5-T. Other interests wanted TCB as well. Jane Lewis' job was basically to see the military have as much 2,4,5-T as possible. She admits that she was told by some purported Dow employee that Dow had linked chloracne to workers exposed to dioxin in the manufacturing process of 2,4,5-T. However, she said this is all she ever learned of potential health hazards from the defendant companies (all of whom she dealt with). Moreover, she never conveyed this information to anyone in DOD or any other office or branch of the Government.

Transcript of deposition:
p.7 ll 1-19; p.7 ll 20-23; p.7 ll 24-25;
p.8 ll 1-11; p.8 ll 14-23; p.8 ll 24-25; p.9 ll 1-2; p.9 ll 3-12; p.9 ll 13-19; p.9 ll 20-25; p. 10 ll 1-4; p.10 ll 9-20; p. 10 ll 21-25; p.11 ll 1-3; p.11 ll 4-19; p.11 ll 20-25; p. 12 ll 1-10; p.12 ll 11-20; p. 12 ll 21-25; p. 13 ll 1-17; p. 13 ll 18-25; p. 14 ll 1-11; p.14 ll 13-21; p.15 ll 9-25; p.16 ll 1-15; p.17 ll 1-7; p.17 ll 10-21; p.17 ll 20-25; p.18 ll 1-15; p.19 ll 1-10; p.19 ll 11-15; p.20 ll 1-10; p.20 ll 11-15; p.21 ll 1-25; p.22 ll 1-25; p.23 1-3; p.23 ll 12-25; p.24 l 1; p.24 ll 11-18; p.25 ll 8-25; p.26 ll 1-25; p.27 ll 1-5; p.27 l 16; p.28 l 25; p.29 l 17; p.32 l 15; p.60 ll 18-25; p.61 ll 1-25; p.62 ll 1-25; p.63 ll 1-25; p.64 ll 1-25; p. 65 ll

1-25; p.66 ll 1-25; p.67 ll 1-25; p.68 ll 1-25; p.69 ll 1-9; p.69 ll 11-25; p.70 ll 1-20; p.71 ll 24-25; p.72 ll 1-3; p.72 ll 13-25; p.73 ll 1-25; p.74 ll 1-2; p.75 ll 4-25; p.76 ll 1-2; p.76 ll 10-13; p.76 ll 17-25; p.77 ll 1-25; p.78 ll 1-7; p.79 ll 1-25; p.80 ll 1-25; p.81 ll 1-22; p.81 ll 24-25; p.82 ll 1-25; p.83 l 1; p.83 ll 9-25; p.84 ll 1-5; p.84 ll 11-15; p.85 ll 1-25; p.86 ll 1-25; p.87 ll 1-25; p.88 ll 1-13; p.88 ll 18-25; p.89 ll 1-3; p.89 ll 11-25; p.90 ll 1-25; p.91 ll 1-25; p.92 ll 1-9; p.92 ll 17-18; p.93 ll 8-15; p.94 ll 14-25; p.95 ll 1-12; p.96 ll 12-25; p.97 ll 1-22; p.98 ll 14-25; p.99 ll 1-4; p.100 ll 1-15; p.101 ll 6-17; p.101 l 25; p.102 l 19; p.103 ll 1-3; p.114 ll 14-23; p.115 ll 4-12; p.116 ll 2-4; p.117 ll 6-12; p.118 ll 2-4; p.119 ll 8-13; p.120 ll 17-25; p.21 ll 1-25; p.11 ll 1-19; p.123 ll 1-23; p.124 ll 6-14; p.124 ll 21-25; p.125 l 5; p.125 ll 14-21; p.126 ll 6-21; p.127 ll 11-17; p.127 ll 22-25; p.128 l 1; p.147 ll 19-20; p.149 ll 2-4; p.152 ll 18-25; p.153 ll 1-22; p.154 l 17; p.155 ll 3-24; p.156 ll 13-22; p.157 ll 1-24; p.159 ll 5-6; p.159 ll 1-17; p.160 ll 1-25; p.161 ll 1-17; p.165 ll 24-25; p.166 ll 1-4; p.182 ll 12-23; p.183 ll 5-7; p.185 ll 12-25; p.186 l 5-25; p.187 ll 11-25; p.188 ll 1-25; p.189 ll 1-10; p.189 ll 15-25; p.190 ll 1-4; p.190 ll 19-25; p.191 ll 12-25; p.192 l 6; p.193 ll 19-24; p.194 ll 3-11; p.194 ll 22-25; p.195 ll 1-23; p.195 ll 7-16.

ELMER P. WHEELER

110 Cool Springs Drive, Camden, South Carolina.
Mr. Wheeler is a past employee of Monsanto having been employed almost 28 years from 1947 through 1976 as an Industrial Hygenist. His testimony will include his conclusions with regard to systemic injuries seen in Monsanto workers as a result of dioxin contamination, realization in 1960 that dioxin was

the causative agent of Nitro and Badishe worker health problems, knowledge of the toxcity of dioxin health experience of Monsanto workers, contacts with representatives from other chemical companies, numerous observations concerning etiology of health hazards.
Transcript of March 1, 1984:

p.6 ll 8-25; p.7 ll 12-13; p.7 ll 17-25; p.8 l 1; p.9 ll 22-25; p.10 ll 1-24; p.15 ll 17-21; p.23 ll 15-22; p.24 ll 14-25; p.25 ll 1-25; p.26 ll 1-25; p.27 ll 1-25; p.28 ll 1-14; p.29 ll 4-25; p.30 ll 1-25; p.31 ll 1-6; p. 31 ll 13-25; p.32 ll 1-25; p.33 ll 1-25; p.34 ll 1-25; p.35 ll 1-25; p.36 ll 1-25; p.37 ll 1-25; p.38 ll 1-12; p.38 ll 19-25; p.39 ll 1-25; p.40 ll 1-6; p.40 ll 18-25; p.41 ll 1-25; p.42 ll 1-25; p.43 ll 1-25; p.44 ll 1-25; p.45 ll 7-25; p.46 ll 1-25; p.47 ll 1-25; p.48 ll 1-15; p.48 ll 24-25; p.49 ll 1-6; p.49 ll 12-25; p.50 ll 1-13; p.53 ll 21-25; p.54 ll 7-14; p.56 ll 13-25; p.57 ll 1-25; p.58 ll 1-25; p.59 ll 1-25; p.60 ll 1-14; p.61 ll 8-25; p.62 ll 1-25; p.63 ll 1-18; p.63 l 25; p.64 ll 1-25; p.65 ll 1-25; p.66 ll 4-25; p.67 ll 1-25; p.68 ll 1-25; p.69 ll 1-25; p.70 ll 11-25; p.71 ll 1-15; p.72 ll 1-25; p.73 ll 1-25; p.74 ll 1-25; p.75 ll 1-19; p.75 ll 22-25; p.76 ll 1-25; p.77 ll 1-25; p.78 ll 1-25; p.79 ll 1-25; p.80 ll 1-4; p.80 ll 24-25; p.80 ll 1-14; p.82 ll 11-25; p.83 ll 1-10; p.84 ll 20-25; p.85 ll 1-22; p.86 ll 7-25; p.87 l 1; p.88 ll 9-25; p.89 ll 1-5; p.89 ll 12-25; p.90 ll 24-25; p.91 ll 1-25; p.92 ll 1-25; p.93 ll 1-25; p.94 ll 1-13; p.94 ll 18-25; p.95 ll 1-25; p.96 ll 1-25; p.97 ll 1-25; p.98 ll 1-25; p.99 ll 1-25; p.100 ll 1-25; p.101 ll 1-13; p. 101 ll 16-25; p.102 ll 1-25; p. 103 ll 1-25; p.104 ll 9-25; p.105 ll 1-11; p.105 ll 1-11; p.105 ll 22-25; p.106 ll 1-6; p.106 ll 16-21; pg.106 ll 23-25; p.107 ll 1-7; p.108 ll 20-25; p.109 ll 1-25;

p.110 ll 1-2; p. 110 ll 18-25; p.111 ll 1-25; p.112 ll 1-8; p.112 ll 13-25; p. 114 ll 1-8; p.116 ll 3-25; p.117 ll 1-25; p.118 ll 1-25; p.119 ll 1-25; p.120 ll 1-25; p.121 ll 1-25; p.122 ll 1-25; p.123 ll 1-25; p.124 ll 1-25; p.125 ll 1-25; p.126 ll 1-25; p.127 ll 1-25; p.128 ll 1-11; p.129 ll 3-25; p.130 ll 1-25; p.131 ll 3-17; p.131 l 25; p.132 ll 1-25; p.133 ll 1-25; p.134 ll 1-7; p.135 ll 5-25; p.136 ll 1-25; p.137 ll 1-4; p.137 ll 24-25; p.138 ll 1-25; p.139 ll 1-10; p.139 ll 21-25; p.140 ll 1-25; p.141 ll 1-25; p.142 ll 1-25; p.143 ll 17-25; p. 144 ll 1-25; p.145 ll 1-25; p.146 ll 1-25; p.147 ll 1-25; p.148 ll 1-25; p.149 ll 1-25; p. 150 ll 1-25; p.151 ll 1-24; p.152 ll 8-25; p.153 ll 1-25; p.154 ll 2-25; p.155 ll 1-25; p.156 ll 1-25; p.157 ll 1-21; p.159 ll 1-25; p.160 ll 1-25; p.161 ll 14-25; p.162 ll 1-25; p.163 ll 1-5; p.164 ll 8-10; p.165 ll 1-25; p.166 ll 1-25; p.167 ll 1-25; p.168 ll 1-25; p.169 ll 1-12; p.171 ll 18-25; p.172 ll 1-25; p.173 ll 24-25; p.174 ll 1-4; p.175 ll 1-25; p.176 ll 1-14; p.176 ll 22-25; p.177 ll 1-25; p.180 ll 20-25; p.181 ll 1-8; p.181 ll 18-25; p.183 ll 1-25; p.183 ll 4-25; p.184 ll 1-5; p.184 ll 21-25; p.185 ll 2-19; p.186 ll 21-25; p.187 ll 1-10; p.190 ll 21-25; p.191 ll 1-17; p.192 ll 4-25; p.193 ll 1-25; p.194 ll 1-25; p.195 l 1; p.195 ll 24-25; p.196 ll 1-25; p.197 l 1; p.198 ll 1-25; p.199 ll 1-25; p.200 ll 1-25; p.201 ll 1-25; p.202 ll 1-23; p.203 ll 8-25; p.204 ll 1-9; p.204 ll 13-25; p.205 ll 1-25; p.206 ll 1-25; p.207 ll 1-11; p.208 ll 8-25; p.210 ll 11-25; p.211 ll 1-25; p.212 ll 1-25; p.213 ll 1-22; p.216 l 25; p.218 ll 1-25; p.219 ll 1-14.

PAUL F. HOFFMAN, PhD.

1202 Lake Shore Drive North, Barrington, Illinois.
Dr. Hoffman is a past Monsanto employee, was the Product Manager

for pesticides group from 1961-1965. Testimony will include facts relevant to marketing and sale of 2,4,5-T herbicides.
Transcript of November 22, 1983:
p.5 ll 12-18; p.9 ll 1-6; p.14 l 25; p.15 ll 1-9; p.22 ll 3-10; p.24 ll 21-25; p.26 ll 14-25; p.27 ll 1-15; p.43 ll 19-25; p.44 ll 1-4; p.44 ll 20-25; p.45 ll 1-5; p.48 ll 20-25; p.49 ll 1-16; p.50 ll 11-25; p.51 ll 1-2; p.55 ll 7-13; p.57 ll 6-13; p.60 ll 21-25; p.61 ll 1-25; p.62 ll 1-10; p.63 ll 1-10; p. 63 ll 20-25; p.64 ll 1-22; p.74 ll 5-12; p.80 ll 24-25; p.81 ll 1-6; p.102 ll 2-25; p.103 ll 1-3; p.104 ll 22-25; p.105 l 1; p.107 ll 9-13; p.117 ll 20-25; p.118 ll 1-9; p. 119 ll 18-25; p.120 ll 1-18; p.130 ll 2-11; p.130 l 25; p.131 ll 1-25; p.132 ll 1-5; p.134 ll 3-14; p.139 ll 15-25; p.140 ll 1-12; p.141 ll 14-25; p.142 ll 1-6; p.143 ll 6-25; p.144 ll 1-25; p.145 ll 1-25; p.146 ll 1-25; p.147 ll 1-15; p.147 ll 21-25; p.148 l 1; p.149 l 25; p.150 ll 1-12; p.150 ll 23-25; p.151 l 2; p.151 ll 23-25; p.152 ll 1-8; p.152 ll 20-25; p.153 ll 1-11; p.153 ll 15-25; p.154 ll 1-25; p.155 ll 1-25; p.156 ll 1-5; p.156 ll 9-23; p.157 ll 12-25; p.158 ll 1-5; p.162 ll 5-25; p.163 ll 1-25; p.164 ll 1-4; p.165 ll 11-25; p.166 ll 1-25; p.167 ll 1-25; p.168 ll 1-25; p.169 ll 1-9; p.174 ll 8-25; p.175 ll 1-5; p.175 l 25; p.176 ll 1-9; p.187 ll 5-25; p.188 ll 1-5; p.191 ll 11-25; p.192 ll 1-25; p.199 ll 1-25; p.194 ll 1-25; p.195 ll 1-25; p.196 ll 1-25; p.197 ll 1-25; p.205 ll 11-25; p.206 ll 1-25; p.207 ll 1-3; p.207 ll 16-25; p.208 ll 1-7.

JOHN S. BUSH, JR.

2232 North Military Road, Arlington, Virginia 22207:
Mr. Bush is a past Monsanto employee commencing his employment for them in 1962 and terminating in 1972. In 1963, he bacame Manager Government Marketing whose function it was to act as a liason between Monsanto and

the Government. It was his understanding that Agent Orange was not required to be free from hazardous effects to humans. It was he who was the Monsanto - Government contact.
Transcript of February 22, 1983:
p.5 ll 7-22; p.8 ll 9-11; p.9 ll 4-19; p.10 ll 6-23; p.11 ll 1-5; p.11 ll 16-25; p.12 ll 6-25; p.13 ll 1-20; p.14 ll 12-25; p.15 ll 1-17; p. 16 ll 2-7; p.16 ll 10-14; p.18 ll 20-25; p.19 ll 1-8; p.19 ll 21-25; p.20 ll 1-6; p.20 ll 21-25; p.21 ll 1-4; p.21 ll 11-25; p.22 ll 1-25; p.23 ll 1-2; p.24 ll 15-19; p.25 ll 1-3; p.25 ll 6-9; p.25 ll 21-25; p.26 ll 1-21; p.27 ll 13-15; p.27 ll 17-18; p.27 ll 23-25; p.28 ll 1-4; p.29 ll 3-25; p.30 ll 1-8; p.31 ll 3-6; p.31 ll 9-15; p.31 ll 18-25; p.32 ll 1-16; p.33 ll 5-25; p.34 ll 3-19; p.35 ll 21-25; p.36 ll 1-25; p.37 ll 1-12; p.39 ll 7-25; p.40 ll 1-25; p.41 ll 1-15; p.42 ll 18-25; p.43 ll 1-6; p.44 ll 2-25; p.45 ll 1-25; p.46 ll 1-10; p.47 ll 11-13; p.49 ll 14-22; p.50 ll 3-15; p.50 ll 24-25; p.51 ll 1-17; p.51 ll 22-24; p.52 l 1; p.52 ll 7-17; p.52 ll 19-25; p.53 ll 1-3; p.56 ll 4-16; p.57 ll 10-25; p.58 ll 1-25; p.59 ll 2-5; p.59 l 8; p.68 ll 7-25; p.69 ll 1-17; p.71 ll 17-25; p.72 ll 1-2; p.72 ll 5-7; p.72 l 11; p.73 ll 17-21.

William P. Schambra

1411 West Saint Andrews, Midland MI.: Retired Dow employee, with responsibility for negotiating contracts between Dow and others, including the U.S. Government; his testimony relates to his negotiation of contracts for R&D work with Dr. Minarick and Dr. Darrow of the Army Chemical Corp. and that he cannot recall discussing the toxicity of any herbicide at any of the Defoliation conferences that he attended and did not discuss the same with either Dr. Minarick or Dr. Darrow; He also did not discuss health problems encountered by Dow workers with any government

1984
include;p.5,111-2;p.6,116-13&18-25;p.7,6-25;p.8,111-8;p.13,1116-25;p.14,111-25;p.15,111-25;p.16,111-23;p.18,1111-20&22-25;p.19,111-12&14-16&21-25;p.20,111-5&9-17&20-25;p.21,111-25;p.22,111-25;p.23,111-7&13&16-19&23-25;p.24,111&5-25;p.25,111-10&12-18&20-25;p.26,111-4,p.28,112-25;p.29,111-13&15-25;p.30,111-5&17-25;p.31,111-14&16-25;p.32,111-16&20-25;p.33,111-18&21-25;p.34,111-25;p.35,111-20&24-25;p.36,111-25;p.37,111-14&19-25;p.38,111-25;p.39,111-25;p.40,111-25;p.41,111-9&11-25;p.42,111-22&24-25;p.43,111-9&13-25;p.44,111-11&22-24;p.45,111-7&9-24;p.46,112-6&10-11&14-25;p.47,111-2&5-6&8-17&25;p.48,111-4&8&10-19;p.49,1116-18&22-25;p.50,111-6&8-22;p.52,118-25;p.53,111-2,13-25;p.54,114-25;p.55,111-3&5-10&12-25p.56,111-6,7-19,22-25;p.57,111,7-15,18-23,25;p.58,111-15,19-15;p.59,111-2,4-25;p.60,111-25;p.61,111-15,19-25;p.62,111-14,19-25;p.63,111-11.13-20,22-25;p.64,112-10,13,23-25;p.65,111-13,15-23,25;p.66,116-10,12-16,18-25;p.67,111-25;p.68,111-2,9-11,13-22,25;p.69,111-5,7-10,12-25;p.70,111,3-6,7-12,18-22,24,25;p.71,111-18,p.72,111-23,25;p.73,111-25;p.74,1,3,16-20,22-25,p.75,111-6,14-25;p.76,111-22-24-25;p,77,111-3,7-15,17-25;p.78,111-25,p.79,111-4,6-25;p.80,111-16,22-25;p,81,111-4,7-14,17-22,24-25;p.82,111-8,10-12,14-25;p.83,111-4,6-17,19-22;p,84,1116-18,20-25;p,85,111-25;p,86,111-25;p,87,111,3-23,25;p,88,111-10,13-19,21;p,89,115-7,9,13-21;p,90,14-16;p,94,1115-25;p,95,1110-10.

A. E. Sidwell

1804 West Road, Jacksonville, Arkansas: Director of Chemical Research - Plant Manager, Hercules' Jacksonville plant which produced Hercules' 2,4-D and 2,4,5-TCP & 2,4,5-T; His deposition and attached exhibits will be offered as indicated. He also testified in deposition and at trial concerning the same subjects in Arkansas Department of Pollution Control & ecology, USA & Others vs. Vertac Chemical, Hercules, Inc. & others;

U.S. Dist. Ct., Eastern District of Arkansas, Western Division, Civil #L.R.-C-80-110, and was represented by counsel in both hearings; His testimony relates to his expertise in chemistry, his knowledge of 2,4,5-TCP and 2,4,5-T, and the contaminant TCDD, how and when dioxin is created in the process of manufacture, how its creation can be minimized & how it can be removed (at least in part) by a toluene extraction process: He will also testify to the testing methods available & as used by Hercules and the confidentiality of the entire subject of the presence of dioxin in Agent Orange. He will also testify re "compound X" which they delivered to the government without knowing what it was. Further, he will testify that he participated in preparing and amending the government specification for 2,4,5-T and that the government never rejected a Hercules request for a change in the contract or its specifications; Excerpts from his deposition in this litigation, taken March 6, 1984, will include, P.11 L. 19 - P.12 L. 11; P.17 L.17 - P.18 L.20; P.26 L.3 - P.49 L.9; P.50 L.7 - P.56 L.17; P.59 L.13 - P.69 L.12; P.71 L.3 - P.102 L.17; P.106 L.9 - P.106 L.22; P.108 L.11 - P.109 - L.6; P.110 L.17 - P.111 L.10; P.112 L.1- P.112 L. 11; P.119 L.24 - P.126 L.15; P.129 L.9 - P.132 L.4; P.132 L.6 - P.132 L. 12; P.136 L.12 - P.136 L.16; P.138 L.16 - P.141 L.3; P.147 L.2 - P.148 L.2 (ex 3); P.148 L.4 - P.148 L.20 (ex 4); P.158 L.4 - P.162 L.21 (ex 5); P.162 L.22 - P.166 L.21 (ex 6); P.166 L.22 - P.169 L.16 (ex 7); P.169 L.18 - P. 174 L.7 (ex 8); P.174 L.8 - P.177 L.19 (ex 9); P.178 L.2 - P.179 L.10 (ex 10); P.179 L.12 - P.186 L.10 (ex 11); P.186 L.15 - P.191 L.10 (ex 12); P.191 L.11 - P.194 L.25 (ex 13); P.195 L.1 - P.195 L.23 (ex 14); P.201 L.6 - P.206 L.1 (ex 15); P.206 L.18 - P.217 L.6 (ex 16); P.217 L.7 - P.227 L.21).

PETER G. ARVAN

4475 Laguna Place, Boulder,Colorado; Mr. Arvan is a past employee of Monsanto having worked for them from 1949 through 1978. In 1960, he became Director of Product Sales in the Agricultural Chemical Division and was Assistant General Manager of that division from 1964 - 1968. It was Mr. Arvan's suggestion that a substantial amount of Agent Orange that Monsanto sold to the Government had previously been purchased by Monsanto from the Government. It should be noted that a second deposition of Mr. Arvan was recently held - that transcript is not yet available.

Transcript of November 28, 1983: P.5 L. 14-25; P.6 L. 1-2; P.6 L.10-25; P.7 L. 1-5; P.14 L. 1-14; P.31 L.13-25; P.32 L. 1-25; P.33 L. 1-25; P.35 L. 1-25; P.36 L. 1-25; P.37 L. 1-21; P.39 L. 14-23; P.40 L. 9-25; P.41 L. 1-2; P.41 L. 12-25; P.42 L.1-25; P.43 L. 1-5; P.43 L. 22-25; P.44 L.1-3; P.45 L. 7-25; P.46 L. 1-25; P.47 L. 1-6; P.47 L. 23-25; P.48 L. 1-11; P.48 L. 25; P.49 L. 1-8; P.49 L.22-25; P.50 L. 1-4; P.52 L. 1-25; P.53 L. 1-10; P.56 L. 17-25; P.57 L. 1-6; P.60 L. 1-5; P.61 L. 7-13; P.65 L. 15-25; P.66 L. 1-9; P.66 L. 21-25; P.67 L. 1-25; P.68 L. 4-6; P.69 L. 3-6; P.70 L. 4-11; P.71 L. 6-19; P.72 L. 3-18; P.73 L. 2-13; P.75 L. 16-25; P.76 L. 1; P.78 L. 24-25; P.79 L. 1-6; P.81 L. 16-25; P.82 L. 1-3; P.87 L. 11-25; P.88 L. 22-24; P.91 L. 23-25; P.92 L. 9-12; P.92 L. 17-18; P.94 L. 12-25; P.95 L. 1; P.97 L. 25; P.98 L. 1-2; P.102 L. 8-19; P.123 L. 17-25; P.127 L. 25; P.128 L. 1-6; P.129 L. 19-25; P.130 L. 1-8; P.132 L. 18-25; P.133 L. 1-25; P.134 L. 1; P.134 L. 9-14; P.135 L. 17-25; P.136 L. 1-4; P.155 L. 1-25; P.156 L. 1-11; P.157 L. 1-11; P.158 L. 1-10; P.158 L. 18-25; P.159 L. 1-24; P.160 L. 5-15; P.165 L. 7-25; P.166 L. 1-17; P.172 L. 17-25; P.173 L. 1-25; P.174 L. 1-25; P.175 L. 1-7; P.181

L. 3-13; P.182 L. 21-25; P.183 L. 1-25; P.184 L. 10-25; P.185 L. 1-25; P.187 L. 17-25; P.188 L. 1-3; P.189 L. 6-25; P.190 L. 1-25; P.191 L. 1-25; P.193 L. 3-25; P.194 L. 1-25; P.195 L. 1-25; P.196 L. 1-25; P.197 L. 1-25; P.198 L-25; P.199 L. 1-25; P.200 L. 1-25; P.201 L. 1-25; P.202 L. 1-25; P.203 L. 16-25; P.204 L. 1-2; P.205 L. 1-25; P.206 L. 1-6; P.207 L. 1-25; P.208 L. 1-20; P.214 L. 14-25; P.215 L. 15-25; P.218 L. 3-6; P.218 L. 21-25; P.219 L. 1-25; P.220 L. 1-9; P.235 L. 1-25; P.236 L. 1-7; P.236 L.19-25; P.237 L. 1-6; P.242 L. 1-25; P.243 L. 1-25; P.250 L. 12-25; P.251 L. 1-4.

HERBERT YORK

6110 CAMINO DE LA COSTA, LA JOLLA, CA. Deposed August 3, 1983. He was a physicist and chief scientist of ARPA and was the first director of defense research and engineering. Was a member of PSAC 1957-58, 1964-65. PSAC Vice Chairman from February 1965-67. Does not recall the PSAC briefing on defoliants discussing potential toxicity to humans. Only remembers defoliation discussed with reference to reducing ambushes. No recollection of mention of contaminant in Agent Orange during PSAC tenure and unaware of any health hazards associated with defoliants. P 6, L 17-25; p pp. 7-10, all; p 16, L 20-25; p 17, all; p 21, L 12-25; p 22, all; pp 23-24, all; p 25, L 3; p 29, L 18-24; p 30, L 20-25; p 31, L 1-8; p 34, L 8-25; p 36, L 6-25; p 37, L 1-16; p 40, L 9-25; p 41, all; p 42, all; p 43, all; p 45, L 17-25; p 47, L 3-17; p 48, L 9-15; p 49, L 1-18; p 55, L 5-16, 22-25; p 56, all; p 57, all; p 58, all; p 59, all; p 60, L 1-16; p 61, L 5-8; 63, L 12-25; p 64, L 1-22; p 65, L 15-25; p 67, L 23-4; p 68, L 1-2, 24-25; p 69, all; p 70, L 1-11; p 81, L 9-17; p 132, L 8-24; p 134, L 1-25; p 135, L 1-25; p 136, all; p 137, all; p 138, all; p 139, L 1-15.

JEROME B. WIESNER

61 SHATTUCK RD, WATERTOWN, MA.

PSAC Memember (1958-1967); Chairman (1961-1964); and Member of NSC (1961-1964). Never discussed dioxin in the context of a meeting. No presentations on chloracne or use of herbicides in Southeast Asia.

P. 6, L 10 to p. 15, L 20; p. 16, L 1 to p. 28, L 10; p. 30, L 4 to p. 31 L 5; p. 31, L 17 to p. 32, L 20; p. 33, L 1 to p. 35, L 12; p. 35, L 23 to p. 36, L 1; p. 36, L 6 to p. 36 L 6; p. 36, L 12 to p. 38, L 9;

p. 38, L 15 to p. 39, L 15; p. 39, L 24 to p. 39, L 25; p. 40, L 11 to p. 40, L 15; p. 41, L 4 to p. 45, L 23; p. 46, L 16 to p. 46, L 19; p. 47, L 1 to p. 47, L 17; p. 47, L 22 to p. 48, L 7; p. 48, L 14 to p. 48, L 15; p. 49, L 10 to p. 50, L 1; p. 50, L 11 to p. 63, L 3; p. 65, L 7 to p. 65, L 12; p. 69, L 9 to p. 70, L 3; p. 70, L 21 to p. 70, L 25; p. 71, L 17 to p. 72, L 23; p. 75, L 9 to p. 76, L 4; p. 76, L 17 to p. 78, L 12; p. 78, L 21 to p. 81, L 21; p. 82, L 1 to p. 85, L 2; p. 85, L 17 to p. 91, L 9; p. 91, L 18 to p. 93, L 9; p. 93, L 25 to p. 94, L 4; p. 94, L 15 to p. 94, L 21; p. 95, L 6 to p. 95, L 13; p. 95, L 22 to p. 109, L 2.

FRANK H. WESTHEIMER — 3 BERKELEY STREET, CAMBRIDGE, MASS.

On Ground Warfare, Educational & Research Development and Chemical and Biological Warfare Panels of PSAC. Discussed herbicides in CW context, but did not discuss health problems associated with them. P6,L6 to p20, L5;p20,L12 to p24,L6; p24, L17 to p41, L14; p41, L23 to p45, L3; p52, L14 to p57, L1; p57,L18 to p61,L7; p61,L22 to p67, L20; p69,L6 to p72,L2; p72,L9 to p72,L22; p73,L5 to p74,L4; p75,L8 to p82,L10; p82,L23 to p85,L23; p87,L8 to p91,L5; p92,L13 to p92,L24; p93,L10 to p94,L16; p96,L9 to p96,L23; p99,L7 to p99,L18;

James O. King — P.O. Box 900 Alpharetta, Georgia; Former employee Diamond Shamrock; excerpts from transcript of deposition; p. 8, LL 7, 12 & 16; p. 9, LL 17 & 22; p. 11 L 20; p. 12, L 5; p. 22, LL 7 & 11; p. 24, LL 7 & 17; p. 26, L 13; p. 27, LL 4 & 15; p. 28, L 16; p. 29, LL 3, 7, 16 & 19; p. 30, L 17; p. 31, L 5; p. 34, L 25; p. 35, LL 7 & 8; p. 36, LL 3 & 10; p. 37, LL 19 & 25; p. 40, L 2; p. 42, LL10 & 18; p. 43, LL 9, 20 & 23; p. 44, L 10; p. 45, LL 15, 18 & 22; p. 48, 12, 17, 18 & 21; p. 50, L 17; p. 51, L 11; p. 52, L 20;

p. 53, LL 1, 10 & 25; p. 57, LL 6, 10, 16, 18, 23 & 25; p. 58, LL 13 & 16; p. 59, L 15; p. 60, L 23; p. 66, L 11; p. 69, L 22; p. 70, LL 16 & 25; p. 71, L 25; p. 73, L 17; p. 79, LL 6 & 19; p. 81, LL 10 & 24; p. 84 LL 1 & 9; p. 85, L 22; p. 86, L 15; p. 87, LL 1 & 22; p. 88, LL 1 & 7; p. 94, LL 3 & 23; p. 95, LL 3 & 8; p. 98, LL 2 & 7; p. 104, LL 11 & 19; p. 109, L 12; p. 110, LL 1 & 25; p. 111, L 12; p. 112, LL 11 & 22; p. 114, L 19; p. 115, LL 1, 10 & 16; p. 117, L 23; p. 118, LL 1, 12, 15, 21, 23 & 24; p. 119, L 3; p. 122, LL 19 & 24; p. 123, LL 2 & 7; p. 124, L 25; p. 125, LL 5 & 25; p. 126, L 19; p. 127, LL 1 & 19; p. 129, LL 4 & 14; p. 130, L 25; p. 132, L 8; p. 145, LL 9 & 24; p. 147, LL 4, 9 & 19; p. 148, L 6; p. 152, LL 10 & 18; p. 156, L 25; p. 157, L 8; p. 162, L 23; p. 164, L 16; p. 168, L 23; p. 170, LL 7, 16 & 22; p. 172, L 23; p. 173, L 23; p. 180, L 9; p. 195, L 2; p. 196, LL 4 & 17; p. 198, LL 10 & 20; p. 203, LL 9 & 15; p. 208, L 16; p. 214, L14; p. 215, L 24.

George C. Kempson

143 South Gore, Webster Groves, Missouri.
George Kempson is a past employee of Monsanto and was employed by Monsanto from 1955 - 1975. From 1960 - 1964, he was a District Manager of the Agricultural Division and from 1964 through 1968, he was the Director of Marketing. He receives a pension from Monsanto of approximately $11,000 - $12,000/year. Never told anyone outside of Monsanto that the product that they were selling was contaminated with dioxin. Never did any research or requested any research while at Monsanto about dioxin. Members of the marketing department who had monthly meetings about 1963 or 1964 included the general manager, the assistant general manager and directors of marketing, manufacturing, research, administration, development and personnel. He attended those

meetings when he became Director of Marketing. Never was apprised of any worker health problem in the 2,4,5-T manufacturing plant and claims to have heard the word chloracne for the first time several years ago. Not aware of does not recall that the 2,4,5-T workers refused to work in that plant and were given bonus pay in order to induce them to work. Spoke to Dr. Emmet Kelly quite often, but Kelly never advised him that 2,4,5-T workers had problems nor did Kelly advise him that the 2,4,5-T ws contaminated with dioxin. The monthly committee meetings above referred were called the number one committee meeting. If before 1965 he knew that T was contaminated with a chloracnegen, had marketing been informed it would have come from research. Claims that research would have stopped it there and if it effected human beings or animals or so forth, that would have been discussed with medical and if proven, they would have stopped it. Assuming that a great deal of the product had already gone out to the market with the contaminant, he is prositive that they (marketing) would have been asked to recall the product promptly. He was involved in contract negotiations between Government and Monsanto with regard to Monsanto supplying D and T. He approved the Government purchasing orders when they came in. Doesn't remember if Monsanto had a contract. He did not deal directly with the Government - it was Redd Zorsch. Zorsch and Hoffman knew the specifications of T and D. He was Zorsch's superior and Zorsch kept him apprised of the negotiations between Government and Monsanto regarding purchases of herbicides. Claims that he knew of no other company that was producing 2,4,5-T. Acknowledges that there is a possibility Russell could have suggested to the Government what the specifications should be in

Missouri.
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Transcript of January 20, 1984:
p.49 L. 6-25; p.46 L. 1-8; p.52 L. 22-25; p.53 L. 1-16; p.54 L. 7-20; p.57 L. 3-25; p.58 L. 1-15; p.59 L. 12-25; p.60 L. 1-25; p.61 L. 1-2; p.61 L. 21-25; p.62 L. 1-5; p.63 L. 12-25; p.64 L. 1-25; p.65 L. 1-25; p.66 L. 1-23; p.67 L. 6-25; p.68 L. 1-25; p.69 L. 1-25; p.70 L. 1-24; p.72 L. 13-25; p.73 L. 1-25; p.74 L. 1-25; p.75 L. 1-25; p.76 L. 1-25; p.77 L. 21-25; p.78 L. 1-25; p.79 L.

	1-4; p.81 L. 15-25; p.82 L. 2-25; p.83 L. 1-25; p.84 L 1-24; p.86 L. 1-25; p.87 L. 1-25; p.88 L. 1-25; p.99 L. 9-18; p.101 L. 2-22; p.103 L. 19-25; p.104 L. 1-25; p.105 L. 1-8.
Donald K. Ballman*	722 Revelle Drive, La Jolla, California; Former Vice-President, Marketing Division, Dow Chemical during the mid-60's, and claims no relcollection of any relevant matters. In fact, he disclaims any specific knowledge of and/or responsibility for Dow's government sales, despite being copies on numerous relevant exhibits; Deposition taken November 1, 1983; p.6,1118-25;p.7,111-3;p.12,115-25;p.13,111-20;p.14-114-8;p.15,116-22;p.16,1112-18;p.17,1113-25;p.18,1112-22;p.19,1112-18;p.21,112-4&24-25;p.22,111-25.
Eugene D. Crittenden, Jr.	908 Dupon Road, Wilmington, Delaware, 19807, was deposed February 10, 1984; Vice-President of International Division of Hercules; Substance of testimony; Director of Sales in Synthetics for Hercules, May, 1966 until October, 1967 and then Assistant General Manager, synthetics, until July, 1968. He never heard of the contaminant dioxin until the Seveso accident in 1976. Excerpts include, p.5,LL6-p.8,LL21; p.16,LL16-p.17,LL16;p.17,LL25-p.19,LL14;p,19,LL15-p.21,LL14.
J. K. Leasure	Rural route No. 2, Box 157, Makanda, Illinois; Former employee of Dow, was a researcher in the application of herbicides and the development thereof from approx. 1955-1966 at Dow; Research group leader involved in screening and early testing of chemical materials to find out if they had any apparent utility as herbicides; in about 1964, became "responsible for government contract

22-24;p. 56, LL 1-13 & 15-25; p. 57 LL 1-8, 18-23 & 25; p. 58, LL1, & 12-13 & 17-25; p. 59, LL 1; p. 60, LL 13-25; p. 64, LL18-20 & 24-25; p. 65, LL 1-10; p. 67, LL23-25; p. 66, LL 1-7;12-20;p.69, LL 15-25; p. 70, LL1-5 & 12-18;

Albert E. Hayward

5716 Jefferson Blvd., Braddock Heights, Maryland 21714; he was Director of the Program coordination office at the U.S. Army Biological Laboratories at Fort Detrick; he will testify that at the first "Defoliation Conference" with the defendants in 1963 at the U.S. Army Biological Laboratories it was understood by all that the defoliation program in Southeast Asia would not be developed in the usual military industrial collaboration but rather reliance on the experience and knowledge of the various commercial producers would be significant; and he will further testify that he first heard that Agent Orange might be contaminated with Dioxin in 1969; p. 8, LL 10-11 & 12-14; p. 9, LL 7-10 & 23-25; p. 10, LL 1-3 & 11-14; p. 11, LL 14-19; p. 12, LL 1-3, 12-16 & 17-23; p. 13, LL 6-11 & 19-25; p. 14, LL 1-4, 9-12, 13-16, 17-19, & 20-22; p. 15, LL 3-6, 14-21; p. 16, LL 2-6, 10-12, 13-15, 16-22, 23-24 & 25; p. 17, LL 1-2 & 21-25; p. 18, LL 1-2, 10-12 & 19-23; p. 19, LL 3-6, 7-11, 19-21 & 24-25; p. 20, LL 4-8, 9-10 & 16-17; p. 21, LL 1-6; p. 23, LL 12-14; p. 24, LL 7-8, 9-12, 13-15 & 24-25; p. 25, LL 1, 14-17 & 23-25; p. 26, LL 2, 3-5, 6-9 & 10-16; p. 27, LL 11-12, 13-14, 15-19 & 20-25; p. 28, LL 1-5, 9-15 & 18-25; p. 29, LL 1-3, 4-7, 11-17 & 18-25; p. 30, LL 1-3 & 13-20; p. 31, LL 1-5 & 13-15; p. 32, LL 1-5; p. 34, LL 21-25; p. 35, LL 1-2 & 16-23; p. 36, LL 8-13, 14-18 & 19-23; p. 37, LL 5-7, 13-14, 15-18 & 19-21; p. 38, LL 3-4, 15-19 & 20-22; p. 39, LL 4-10; p. 40, LL 10-17 & 18-21; p. 41, LL 4-7, 8-12, 13-15 & 20-25; p. 42, LL 1-3, 9-16, 17-21 & 25; p. 43, LL 1, 2-3, 4-10, 14-17,

21-23 & 24-25; p. 44, LL 1-6 & 20-25; p. 45, LL 1, 2-7, 8-9, 17-20 & 21-22; p. 46, LL 1-4, 8-11, 12-15, 16-21 & 24-25; p. 47, LL 1-2 & 18-21; p. 48, LL 2-6, 10-12, 17-21 & 22-24; p. 49, LL 12-16, 17-22 & 23-25; p. 51, LL 5-6, 21-23 & 6-11; p. 53, LL 7-11 & 25; p. 54, LL 1-4, 5-9, 13-17 & 18-20; p. 55, LL 3-8; p. 56, LL 21-24; p. 57, LL 8-11 & 21-25; p. 58, LL 1-6, 7-14 7 15-19; p. 59, LL 14-18 & 22-25; p. 60, LL 1-13 & 7-12; p. 61, LL 2-6, 7-11 & 22-25; p. 62, LL 1-5; p. 63, LL 14-16 & 17-24; p. 64, LL 11-12, 13-17 & 20-22; p. 65, LL 1-3, 4-11, 12-20 & 21-25; p. 66, LL 1-2, 3-11 & 19-25; p. 67, 1 & 21-25; p. 68, 1-3, 8-10 & 14-18; p. 70, LL 9-13, 14-16 & 22-24; p. 71, LL 2-7, 8-11 & 12-17; p. 72, LL 6-8; p. 73, LL 5-13, 14-17 & 18-23; p. 74, LL 11-16 & 17-25; p. 75, LL 2-5; p. 76, LL 1-12, 13-16 & 17-25; p. 77, LL 3-18, 19-22 & 23-25; p. 78, LL 2-7, 8-12, 13-17 & 22-25; p. 79, LL 6-9, 10-12, 13-16 & 17-18; p. 80, LL 3-4, 8-10 & 21-23; p. 81, LL 14-16, 17-20 & 21-25; p. 82, LL 1-3, 4-6, 12-14, 15-19, 20-23 & 24-25; p. 83, LL 1, 2-4, 5-6 & 12-15; p. 84, LL 2-10 & 16-18; p. 85, LL 4-8, 9-13, 14-16, 17-23 & 24-25; p. 86, LL 1-3, 5-15, 16-19 & 20-21; p. 87, LL 1-7, 11-14, 15-23 & 24-25; p. 88, LL 1-2, 7-11 & 12-14; p. 89, LL 4-5, 10-11, 12-13, 17-18 & 19-21; p. 90, LL 2-6, 14-16 & 17-21; p. 91, LL 10-18; p. 92, LL 19-22 & 23-25; p. 93, LL 1-4; p. 94, LL 12-16, 19-22 & 23-25; p. 95, LL 1-3, 4-10, 11-15 & 16-19; p. 96, LL 13-18; p. 97, LL 11-15, 16-18 & 19-21; p. 98, LL 6-12; 16-20 & 21-23; p. 99, LL 5-8, 9-15, 16-22; p. 100, LL 4-9, 10-13, 14-16, 17-22 & 23-25; p. 101, LL 1-4, 7-10, 11-14 & 18-25; p. 102, LL 1-6 & 7-12; p. 103, LL 20-25; p. 104, LL 1-4 & 24-25; p. 105, LL 1-10; p. 106, LL 5-7, 16-18 & 23-25; p. 107, LL 1-2 & 21-25; p. 108, LL 1-2; p. 109, LL 9-11; p. 110, LL 21-24; p. 111, LL 18-21; p. 112, LL 14-22 & 23-25; p. 113, LL 1-6 & 7-17; p. 114, LL

	14-25; p. 115, LL 1-2 & 3-11; p. 117, LL 11-15 & 16-25; p. 118, LL 1-5, 15-19 & 16-25; p. 119, LL 1-4, 11-16 & 19-25; p. 120, LL 18-21; p. 121, LL 15-17; p. 123, LL 1-10 & 21-24; p. 124, LL 1 & 2-12; p. 125, LL 5-12, 13-19 & 20-25; p. 126, LL 1-7, 11-16 & 23-25; p. 127, LL 1-7, 8-15, 16-20 7 21-23; p. 128, LL 3-6, 8-11 & 12-16; p. 129, LL 8-10, 11-14 & 15-16; p. 130, LL 9-12 & 14-17.
RAYMOND A. GUIDI	420 Essex Place, Memphis, TN.: Former assistant Diamand Shamrock plant manager who will testify concerning health problems in Diamond Shamrock's plant, and knowledge of toxicity of end product and process details relating to that company.
	p. 14 LL 20-25; p. 15 LL 1-7; p. 15 LL 8-15; p. 15 LL 22-25; p. 16 LL 1-3; p.16 LL 4-25; p. 17 LL 14-25; p. 18 LL 1-9; p. 19 LL 12-18; p. 19 LL 22-25; p. 20 LL 1-11; p. 21 LL 9-16; p. 22 LL 24-25; p. 23 LL 1-4; p. 49 LL 7-25; p. 24 LL 10-25; p. 25 LL 1; p. 22 LL 2-17; p. 23 LL 14-20; p. 26 LL 9-24; p. 27 LL 2-15; p. 28 LL 1-16; p. 30 LL 14-20; p. 30 LL 21-25; p. 31 LL 1; p. 32 LL 10-25; p. 36 LL 1-15; p. 39 LL 2-7; p. 39 LL 20-25; p. 40 LL 1-14; p. 40 LL 16-21; p. 44 LL 3-14; p. 44 LL 14-25; p. 45 LL 1-6; p. 41 LL 4-14 p. 45 LL 11-14; p. 43 LL 19-23; p. 38 LL 10-14 p. 40 LL 16-21; p. 45 LL 15-25; p. 46 LL 1-14; p. 46 LL 14-22; p. 46 LL 23-25; p. 47 LL 1; p. 47 LL 2-6.
Francis Kennedy	Address not shown on transcript; Mr. Kennedy started with Diamond in 1953 and became plant manager in Newark in 1963. He was first familiar with serious health hazards in Newark Plant in 1954 and until 1968 when transferred to Cleveland. Will testify as to purpose of Midland meeting, Dow's dioxin detection procedures, relation between dioxin content and health hazards, and dioxin levels of Diamond's product.

p. 26 LL 1-2; p. 27 LL 23-25; p. 48 LL 12-19; p. 44 LL 14-25; p. 45 LL 1-10; p. 48 LL 16-24; p. 50 LL 3-8; p. 53 LL 3-25; p. 54 LL 1-1; p. 55 LL 23-25; p. 56 LL 1-3; p. 57 LL 25; p. 58 LL 1-9; p. 61 LL 15-18; p. 53 LL 3-25; p. 54 LL 1-19; p. 71 LL 1-20; p. 105 LL 1-4 and LL 18-23; p. 113 LL 3-8; p. 115 LL 3-19; p. 115 LL 3-19; p. 116 LL 23-25; p. 117 LL 1-12; p. 127 LL 14-25; p. 128 LL 7-25; p. 129 LL 1-6; p. 129 LL 7-20; p. 132 LL 7-12; p. 132 LL 6-25; p. 135 LL 14-17; p. 135 LL-14; p. 206 LL 20-25; p. 207 LL 1-22; p. 207 LL 19-22; p. 138 LL 24-25; p. 139 LL 1-18, P139 l 14-25, P140 l 1-2, p. 142 LL 1-25; p. 143 LL 1-3; p. 143 LL 19-25; p. 145 LL 9-21; p. 70 LL 4-11; p. 71 LL 1-11; p. 66 LL 19-25; p. 67 LL 1-6; p. 67 LL 7-14; p. 124 LL 22-25; p. 123 LL 1-9; p. 45 LL 11-18; p. 98 LL 6-20; p. 209 LL 1-5; p. 149 LL 2-20; p. 152 LL 18-25; p. 153 LL 1-3; p. 156 LL 7-21; p. 104 LL 11-16; p. 103 LL 15-25; p. 104 LL 1-10; p. 104 LL 7-25; p. 105 LL 1-23; p. 109 LL 19-25; p. 110 LL 1-16; p. 77 LL 9-21; p. 77 LL 22-25; p. 166 LL 17-25; p. 167 LL 1-4; p. 177 LL 24-25; p. 178 LL 1-25; p. 179 LL 1-12; p. 179 LL 14-16; p. 183 LL 8-16; p. 180 LL 14-20; p. 182 LL 12-16; p. 182 LL 17-22; p. 181 LL 10-19; p. 185 LL 3-14; p. 185 LL 15-17; p. 184 LL 16-19; p. 188 LL 14-25; p. 189 LL 1-5; p. 129 LL 12-15; p. 193 LL 4-2; p. 194 LL 1-25; p. 193 LL 12-14; p. 198 LL 3-5, p. 202 LL 7; p. 203 LL 5-25; p. 206 LL 1; p. 204 LL 2-3; p. 202 LL 12-14; p. 204 LL 4-10; p. 19 LL 2-25; p. 220 LL 1-4; p. 218 LL 21-25; p. 211 LL 1-10; p. 219 LL 1; p. 220 LL 22-25; p. 211 LL 1-10; p. 221 LL 9-11.

Eugene A. Cutright

1474 Maplewood Drive, Macon, Georgia. Deposition taken January 18, 1984. He is a past employee of Monsanto, having been employed by them from 1957 to 1969. His involvement with 2,4,5-T occurred from 1966 to 1969 when he was the

Production Supervisor at Nitro. He is a chemical engineer and testified concerning 2,4,5-T process and analysis. Analytical tests for dioxin was not done on a regular basis but only for "special cases" - research efforts. Attempted to set tentative permissable dioxin levels at 10ppm. Was aware of process and equipment malfunctions. P 6, L 5-9, 19-25; p 7, L 1-8; p 9, L 7-8, 13-20, 25; p 10, L 1-6, 9-11, 22-25; p 11, L 1,2, 7-25; p 12, L 1, 6-10; p 44, L 14-16; p 46, L 12-25; p 47, L 1-4, 16-25; p 49, all; p 50 L 1-6; p 52, L 3-25; p 53 all; p 54, L 1-7; p 55, L 5-7, 19-25; p 56, L 1-13; p 57 all; p 58, L 1-10, 20-25; p 59 all; p 60, L 1-21; p 61, L 3-25; p62 L 3-8, 13-18, 25; p 63 all; p 64 all; p 65, L 1-5, 11-22; p 66 all; p 67 all; p 69 all; p 70, L 1-5, 21-25; p 71, L 1-14, 20-25; p 72, L 1-9; p 73 L 16-24; pp. 74-75 all; p 76, L 1-8, 20-25; p 77, L 5-25; p 78 all; p 79 L 1-23; p 80, L 6-7; p 81 all; p 82, L 1-9; p 84, L 13-25; p 85, L 1-15; P 88, 6-10; p 89, L 6-25; pp. 90-94 all; p 95, L 1; p 96, L 21-25; p 97, L 1-17; p 98, L 12-25; p 100, L 8-25; p 101, L 1-2; p 104, L 4-25; p 105, L 10-14; p 106, L 5-25; p 107, L 1-11; p 109 all; p 110, L 1-18; p 111, L 7-24; p 112, L 9-25; p 113-114 all; p 115, L 1-12; p 118, L 3-16; p 119, L 10-21; p 120, L 20-25; p 121, L 1-8, 22-25; p 122, L 1-9; p 124, L 1-6, 18-24; p 126, L 15-18; p 127, L 9-13, 22-25; p 128 all; p 129, L 18-22; p 131, L 7-25; p 132, L 1-23; p 133, L 13-25; p 134, L 1-3; p 135, L 6-25; pp. 136-139 all; 140, L 13-25; 141, L 1-8; p 143, L 8-16; p 144, L 17-25; p 145, L 3-15; p 146, L 11-25; p 147, L 1-5; p 148, L 12-25; p 149, L 1-16; p 150, L 9-11, 14-15, 22-25; p 151, L 2-8, 24-25; p 152, L 1-14; p 157, L 19-25; p 158, L 1-11, 19-25; p 159, L 1-15; p 161, L 9-22; p 162, L 1-5.

John W. Tukey 115 Arreton Rd, Princeton, New

15649

Jersey. Deposition taken October 3, 1983. Member of President's Science Advisory Committee from 1960-1963. First heard term dioxin in 1969. Had no recollection of any specific herbicides being employed in Vietnam. Member Herbicide Panel. P 7, L 21-25; p 8, L 1-25; p 9, L 4-25; p 10, L 1-25; p 11, L 1-5; p 13, L 14-25; p 14, L 14-25; p 15, L 1-15; p 23, L 3-25; p 24, all; p 25, L, all; p 26, L 10-25; p 27, L 1-20; p 28, L 3-25; p 29, L 1-3; p 30, L 8-13, 24-25; p 31, L 1-25; p 32, L 1-3, 10-25; p 33, L 3-21; p 34, L 3-25; p 35, L 1-5, 16-24; p 36, L 4-6, 16; p 48, L 8-25; p 49, 1-2; p 54, 10-25; p 55 all; p 56, L 1-8, 18-25; p 57, L 1-25; p 58, all; p 59, L 1-12, 17-18, 25; p 60, all; p 61, all; p 62, all; p 63, L 1-8; p 64, L 4-25; p 65, L 1-17, 22-25; p 66, L 1-20; p 67, L 13-25; p 68, L 1-20; p 70, L 20-24; p 72, L 7- 25; p 73, all; p 74, L 1-13; p 75, L 10-13; p 78, all; p 79, L 1-9; p 81, L 1-19.

Herbert York

6110 Camino De La Costa, La Jolla, CA. Deposed August 3, 1983. He was a physicist and chief scientist of ARPA and was the first director of defense research and engineering. Was a member of PSAC 1957-58, 1964-65. PSAC Vice Chairman from February 1965-67. Does not recall the PSAC briefing on defoliants discussing potential toxicity to humans. Only remembers defoliation discussed with reference to reducing ambushes. No recollection of mention of contaminant in Agent Orange during PSAC tenure and unaware of any health hazards associated with defoliants. P 6, L 17-25; p pp. 7-10, all; p 16, L 20-25; p 17, all; p 21, L 12-25; p 22, all; pp 23-24, all; p 25, L 3; p 29, L 18-24; p 30, L 20-25; p 31, L 1-8; p 34, L 8-25; p 36, L 6-25; p 37, L 1-16; p 40, L 9-25; p 41, all; p 42, all; p 43, all; p 45, L 17-25; p 47, L 3-17; p 48, L 9-15; p 49, L 1-18; p 55, L 5-16, 22-25; p

Dr. Steinman	"
Dr. Barbara Crockett	"
Dr. Cooke	Danny Ford
Dr. Horvath	"
Dr. Schafer	"
Dr. Keichel	"
Dr. Sternfeld	"
Dr. Dr. Mewborn	"
Dr. Hawkins	"
Dr. Clark	"
Dr. Schachner	"
Dr. Susan K. Blew	Jordan Family
Dr. H. R. Melch	"
Dr. Karamat Choudhry	"
Dr. C. S. Patterson	"
Dr. William Bernell	"
Dr. Charles Crane	"
Dr. R. K. Gaines	"
Dr. W. L. Stewart	"
Dr. H. B. Follander	"
Dr. Stephen Youngberg	"
Dr. Geesbrecht	"
Dr. Dwight Pierson	"
Dr. Allan Sonstein	"
Dr. Rambie Briggs	"
Dr. Steven J. Senevy	"
Dr. James Aston	"

15051

Dr. L. Lee Lankford	"
Dr. James E. Way	"
Dr. Philip Kingery	"
Dr. Thomas O. Tiernan	"
Dr. I. L. Van Zandt	"
Dr. V. Rhoades	"
Dr. Funnell	"
Dr. Hall	"
Dr. Edward C. Rainey	"
Dr. Stephen G. Maddox	"
Dr. Hugh Warren	Treating Physician for David Lambiotte
Dr. Delvyn C. Case	"
Dr. Kellet	"
Dr. B. Voss Neal	"
Dr. James E. Kopp	"
Dr. Barry Salter	"
Dr. John Q. A. Mattern	"
Dr. Peter Law	"
Dr. John Wirth	"
Dr. George Sigalos	"
Dr. George Brown	Treating physician Ryan
Dr. Fred Mehlop	"
Dr. Richard Kubick	"
Dr. Robert DiNapoli	"
Dr. Judith Chown	"
Dr. Michael Sampson	"
Dr. Wilten Fritz	"

15652

Dr. Oscar Schwartz	"
Dr. Ronald Carr	"
Dr. Walter Silver	"
Dr. Morton Glaser	"
Dr. Bertram Cohen	"
Dr. David Baker	"

* The above treating physicians have not yet been deposed and may be called either live or by way of deposition testimony to be taken in the future.

ROBERT S. McNAMARA — 1800 K Street, Washington, D.C. 20006; Robert McNamara was Secretary of Defense, January 1961, through March, 1968; he will testify that he was unaware of any health hazards posed by 2,4,5-T and further that he neither had nor received any communication from other government agencies as to any health hazards of 2,4,5-T. And had he known of any health hazards, he would have pursued the matter.
P.9 L.16; P.10 L. 14; P.11 L. 25; P.12 L.1-12; P.13 L.20-25; P.14 L.25; P.15 L.23; P.16 L.5; P.20 L. 1-8; P.21 L.22; P.22 L.9-14; P.22 L. 15; P.23 L. 4-15; P.23 L. 21-25; P.24 L.1-3; P.25 L.22; P.25 L.25; P.26 L. 1-4; P.26, L. 5-12; P.26 L.22-25; P.27 L. 1-1-; P.27 L. 16-19; P.28 L.25; P.30 L.1-11; P.30 L.12-19; P.30 L.20-25; P.31 L. 1-4; P.32 L.18-19; P.32 L.24-25; P.34 L.1-4; P.35 L. 8-19; P.36 L.23-25; P.40 L.15-25; P.40 L.15-25; P.41 L. 1-9; P.42 L.24-25; P.43 L.1-5; P.44 L.13-23; P.45 L. 15-25; P.51 L. 10-25.

JOHN ANGEL — Box 78, Yellville, Arkansas; Various titles over the years including Research Chemist at Jacksonville, Arkansas Plant of Reasor Hill Corporation, 1950-1959.

15653

From 1950-1959, Mr. Angel was a research chemist at Reasor Hill Corp.'s Jacksonville Plant, where he analyzed materials and products, including, 2,4,5-T, and did process research work on the process for producing 2,4,5-T with Dr. Sidwell. During the period of 1950 - 1959, a number of herbicide production workers in the Jacksonville Plant had chloracne. During that period, he also learned of Monsanto's industrial accident in their 2,4,5-T process at Nitro, West Virginia, and learned of Thompson Hayward Chemical Co.'s industrial accident in their plant. He was aware that TCP caused chloracne several years before he began working with Thompson Chemical Co. in 1963.
Deposition designations: P.10 L.16 - P.10 L.23; P.14 L.16 - P.15 L.1; P.16 L. 1 - P.16 L.4; P.16 L.17 - P.17 L.9; P.17 L.25 - P.18 L.13; P.19 L.7 - P.20 L.3; P.21 L.5 - P.23 L.2; P.23 L.9 - P.24 L.25; P.29 L.3 - P.30 L.8; P.41 L.3 - P.41 L.15; P.56 L.18 - P.57 L.8.

GENERAL MAXWELL TAYLOR

General Taylor was Chairman of the Joint Chiefs of Staff from 1962 through 1964 and was the Ambassador to Vietnam. Although General Taylor admits knowing of the defoliation program, he repeatedly asserted his lack of knowledge of the harmful effects of Agent Orange. He also repeatedly asserted that he never had any communications, to and from, concerning possible harmful effects of Agent Orange with either Federal Agencies or Chemical Companies. The Brief Cross-examination by defense attempted to establish that Gen. Taylor was more involved with policy rather than the overall conduct of the military operation. The distinction would tend to diminish the significance of his lack of knowledge and communication concerning Orange's harmful effects. Aside from this, the impact of his testimony was lack of knowledge of

the military. Disclaimer of knowledge prior to 1969. Gen. Taylor stated to the best of his recollection that he never heard of defoliation program being discussed either by Presidents Johnson or Kennedy. The witness became aware, sometime after 1962 while serving as Chairman of the Joint Chiefs, of the defoliation program and of the use of commercial herbicides. The program's purpose was to clear undergrowth to prevent ambush and to destroy food sources. Gen. Taylor stated that the defoliation program's purpose was not to harm human beings, American Personnel or Enemy. The witness stated that everone assumed that the herbicides deployed were non-toxic. He also did not recall if McNamara informed him of any possible harm posed by the herbicides. After becoming Ambassador to Vietnam in 1965, the witness along with McNamara, visited Vietnam at least 5 times. He reported that during these visits and attendant briefings at Westmoreland's Headquarters, there were no discussions concerning Americans becoming sick as a result of being in areas that were sprayed. Gen. Taylor responds that in his capacity as a military representative of the President and Chairman of the Joint Chiefs, he never received any information from any source of the harmful effects of deployed chemicals. Gen. Taylor further reported of not hearing complaints that herbicides were causing harm while serving as Ambassador to Vietnam from 1964 - 1965. Gen. Taylor was not aware of AAAS study which indicated that Orange could cause birth defects as of December, 1969. He was never during any of his positions advised by any Department of Agriculture Representative of the harmful effects of Orange. The witness, from 1966-1969, was President of the Institute of Defense Analysis. He had contact with Dr. McDonald and to

the best of Gen. Taylor's recollection, he had no discussions with MacDonald and to the best of Taylor's recollection, he had no discussions with MacDonald concerning the harmful effects of Agent Orange or Dioxin. Witness reports not having oral or written communication with the following Government Agencies concering Orange's harmful effects: U.S. Public Health Service; Food and Drug Administration; Surgeon General; NCI; HEW; EPA; Edgewood Aresenal; Fort Detrick Crops Division; Advanced Research Project Agency; U.S.Army Chemical Corps., Naval Medical Research Institute; Marine Corps Chemical Branch; Air Force Systems Command. In his capacity as Ambassador to Vietnam, Gen. Taylor reports that he was not advised concerning a Dow meeting in Midland, Michigan in 1965, to discuss chloracne problem associated with defoliation program. He expressly stated that he was never in contact at any time with any chemical company.
P.12 L.21-25; P.13 L. 16-25; P.14 L.10-18; P.15 L.13-25; P.17 L.22-25; P.18 L.22; P.20 L.24-25; P.21 L.1-6; P.21 L.18-22; P.28 L.11-25; P.24 L.15-20; P.25 L.14-24; P.26 L.1-25; P.27 L.1-25; P.28 L.1-25; P.22 L.11-23; P.23 L.1-19.

PAUL WARNKE

Mr. Warnke served as Assistant Secretary of Defense for International Security Affairs from 1967 to 1969. He testified to his lack of knowledge of any health hazards associated with Agent Orange. He further testified that in spite of his awareness of the Herbicide Program, he was unaware of the specific names of the herbicides. His testimony indicates that he was not informed specifically of all aspects of the herbicide program in his capacity as Assistant Secretary of Defense. It can be inferred, therefore, that Government knowledge of Agent Orange

Toxicity was minimal or fragmented within specific agencies. Mr. Warnke also testified about daily morning meeting with McNamara and there was no discussion of Orange's toxicity. He also testified as to his lack of communication to and from other government agencies concerning this matter. Mr. Warnke did not recall any issue arising regarding the use of herbicides in Vietnam while he was an Assistant Secretary for Defense from 1967 - 1969. He became aware that a herbicide program was being utilized in South East Asia, but was unaware who made the decision to deploy herbicides. He became aware of deployment program while serving as General Counsel in 1966-1967. Mr. Warnke wsa not aware that Agent Orange was a specific herbicide being deployed. In addition, he did not recall ever hearing the term while at the Defense Department. The witness reports of not receiving any notice either oral or written, from any chemical company, relating to defoliation agent's potential health hazards. He also reports not receiving any communication of adverse health effects of Agent Orange from any representative: 1) U.S. Public Health Service 2) FDA 3) Surgeon General 4) NCI 5)HEW 6) EPA 7) Edgewood Arsenal 8) Fort Detreick 9) The Advanced Research Project Agency 10) U.S. Army Chemical Corps. 11) The Naval Medical Research Institute 12) U.S. Marine Corps. Chemical Branch 13) Air Force Systems Command 14) or Interagency task force on the subject of herbicides or pesticides. Mr. Warnke also did not recall seeeing or reading a Rand Corp. report from 1967 that indicated the Herbicides were deadly to humans as well as to plants. He reported lack of personal knowledge of a December 29, 1967, Joint Chiefs of Staff report to McNamara that herbicides were non-toxic to humans. The witness recalls study being

conducted relating to defoliation program's efficiency. However, he did not recall any conversation or investigation with regard to human beings. The witness was never assigned any project concerning the defoliation program in Vietnam and reported that to his knowledge, purpose of defoliation was never to harm humans. Mr. Warnke reported, based upon his experience of the general decision making process, that the decision to deploy herbicides would have emanated from the Joint Chiefs. The Joint Chiefs would have brought it to the Secretary of Defense, who would have brought it to the President. The ultimate decision to employ herbicides would be made by the President. Based upon his experience, decision with regard to any changes in the conduct of warfare during his tenure to the President. However, the witness did not know if ultimate decision was made by the President. He also reported that Secretary of Defense McNamara would hold daily morning staff meetings to discuss the War's progress and says that he discussed the herbicide program with Secretary McNamara. Mr. Warnke reports that the only hazards discussed at these daily meetings were the ecological or agricultural impact of the defoliation program. There were no discussions concerning health hazards to humans. Mr. Warnke recollected that there were never any discussions at these daily meetings concerning who established "Agent Orange" specifications, or whether the Chemical Companies met those specifications. No Governmental Agency or subdivision thereof ever advised Mr. Warnke of a possible health hazard to "Agent Orange". Although Mr. Warnke served under Presidents Johnson and Nixon, he does not recall having any conversations with either President regarding Ageny Orange's possible toxicity to humans. He believes

that the Secretary of Defense had authority to terminate or initiate defoliation and expressly stated that he didn't believe that anyone in lower levels had such authority. Secretary McNamara never told witness that he had received an ARPA Report indicating that deployed herbicides were toxic to humans.
P. 10 L.6-14; P.11 L. 8-16; P.13 L. 11; P.13 L.25; P.19 L.16 - P.24 L.5; P.29 L.23 - P.30 L.14; P.31 L.8-16; P.32 L.11-18; P.39 L.4-7; P.48 L.17-22; P.11 L.19 - P.12 L.1; P.12 L. 8-15; P.15 L.23 - P.16 L.9; P.17 L.5 - 9; P.17 L.10-18; P.24 L.6-11; P.33 L.6-13; P.33 L.18 - P.34 L.9; P.35 L.14 - P.36 L.11; P.48 L.4-16.

VI

ISSUES TO BE PROVED

Plaintiffs are not required to present a statement of such issues with this submission at this time.

A complete statement of issues to be proved will be filed in conformity with the Magistrate's Pre-trial Order No. 17.

VII

DISPUTED ISSUES OF FACT AND LAW

Plaintiffs are not required to present a statement of such issues with this submission at this time.

A complete statement of such issues will be filed in conformity with the Magistrate's Pre-trial Order No. 17.

Respectfully Submitted,

PLAINTIFFS' MANAGEMENT COMMITTEE

By Stephen J. Schlegel
Stephen J. Schlegel

Exhibit #P0288

PIN #	DS00017880
Date	22-Apr-64
Author	J S CORT
Addressee	CECIL & KENNEDY
Description	Memorandum from J. S. Cort, Jr. dated April 22, 1964 from J. S. Cort, Jr. to L. L. Cecil, Jr. reminding him that any materials returned from Columbia are to be inspected for tampering and samples taken for chemical testing.

Exhibit #P0289

PIN #	DS00018061
Date	27-Apr-64
Author	MARCELLUS POWERS
Addressee	QUEMOR LIMITADA & BONFIELD HOPKINS JACKSON JAMERSON
Description	Report dated April 27, 1964 from Hazelton Laboratories, Incorporated, Falls Church, Va., to Quimor Ltda. concerning toxicology of samples furnished by Quemor. The Report, written by Dr. Marcellus Powers, DVM, concludes that the materials were, in fact, toxic.

Exhibit #P0290

PIN #	DS00017879
Date	27-Apr-64
Author	WARREN M ALGEO
Addressee	CECIL & SAVAGE HONOUR
Description	Memo dated April 27, 1964 from Warren M. Algeo, Columbia, to L. L. Cecil stating that the problem in Valle del Cruce is not as serious as in Modellin 1, and suggesting that if the latter problem could be resolved the problem would be in hand.

Exhibit #P0297

PIN #	DS00018059
Date	01-Jun-64

15660

Author C W GILES
Addressee HONOUR & PURDY

Description Letter dated June 1, 1964 from Alexander & Alexander (C.W. Giles, AVP) to S. B. Honour at Diamond returning copy of Cecil letter and stating that the government report had been received and would be transmitted, but that it indicated that there was a product fault.

Exhibit #P0299
PIN # DS00018081
Date 02-Jun-64
Author D M PURDY
Addressee CRICHLAY A & CORT
HONOUR & KENNEDY
MASAK

Description Memorandum dated June 2, 1964 from D. M. Purdy to A. Critchlay concerning Product Liability claims in South America. The writer suggests that the problems in South America could be traced to a single batch. Otherwise, it is estimated that claims will be from $5,000 to $10,000. The writer suggests that distributors be advised that all claims should be reported to insurance carriers.

Exhibit #P0301
PIN # DS00018057
Date 04-Jun-64
Author CECIL
Addressee CORT & HONOUR
PURDY & SAVAGE

Description Memo dated June 4, 1964 from Cecil to the File stating that Quimor's letter of May 15, 1964 was only a statement of what might happen after the government investigation was finished. The letter suggests that Quimor could sue, but really doesn't prefer that course of action.

Exhibit #P0303

15661

PIN # DS 17384
Date 10-Jun-64
Author JOHN WHITTLEMAN
Addressee WILLIAM CARGO
Description INTER OFFICE MEMO - CHLORACNE COSTS

Exhibit #P0304
PIN # DS17383
Date 12-Jun-64
Author W A CARGO
Addressee C. R. BROWN
Description MEMO REGARDING ANNUAL COSTS OF CHLORACNE

Exhibit #P0309
PIN # DS00011398
Date 15-Jul-64
Author J J PIRRONE
Addressee CORT & BRUMBAUGH
EVERSON & SCHULDT
HONOUR & SAVAGE

Description Memorandum dated July 15, 1964 from Pirrone to Cort reporting on negotiations with Cela to obtain know-how on reducing acnegin in TCP.

Exhibit #P0317
PIN # DS00008800
Date 21-Aug-64
Author VAN C CAYTON
Addressee KENNEDY & CORT
WILKERSON
Description Memorandum from Van C. Cayton to F. R. Kennedy dated August 21, 1964 asking what data is available to substantiate claim on patent application that new TCP process reduces Chloracne causing compounds.

Exhibit #P0318
PIN # DS00017367
Date 01-Sep-64

15662

Author C R BROWN
Addressee TILLMAN & CORT
KENNEDY & MASEK
THOMPSON
Description Memorandum dated September 1,1964 from C.R. Brown to A. B. Tillman and a large distribution list, advising that Dr. McBurney has sent along three articles on porphyria, which is old hat to Bleiberg and McBurney and some others, but which was new to himself and, he thought, to the addressees. States that this will be expensive in terms of insurance premiums. Reports hopefully on the efforts of John Cort to obtain know-how from a German company on the matter and of a forthcoming trip by Dr. McBurney to Germany at which a visit is to be arranged.

Exhibit #P0321
PIN # DS 17367
Date 10-Sep-64
Author C R BROWN
Addressee A. B. TILLMAN & J. S. CORT
F. R. KENNEDY & E. J. MASON
D. L. THOMPSON
Description UNSIGNED MEMO DATED 091064 FROM BROWN TO TILLMAN, ET. AL.

Exhibit #P0322
PIN # ILLEGIBLE
Date 11-Sep-64
Author F R KENNEDY
Addressee CAYTON & CLEVELAND
CORT & WILKERSON

Description Memorandum from Kennedy to Cayton in response to his inquiry of August 31 seeking backup data on statement in patent application and stating that pre-1960 data was too poorly kept to be able to produce charts showing changes in health experience after using the new process.

Exhibit #P0328

15663

PIN # DS00018205
Date 21-Oct-64
Author B KRIENKE
Addressee CHEMICAL BANK & LEON CHANG
MORRIS ABE
Description Letter from B. Krienke, Agricultural Chemicals, Diamond Shamrock to Chemical Bank, dated October 21, 1964, instructing the bank to accept $6,045.60 4,570.50 against a $10,616.10 draft due to a credit for returned materials. A postscript to the letter, signed by Morris Abe, states that Quimor Ltda. is entitled to a credit for 1,000 gallons of of 2,4-D and 2,4,5,-T herbicides.

Exhibit #P0330

PIN # DS00022683
Date 06-Nov-64
Author D J PORTER
Addressee EVERSON & GALLOWAY
LIMPEL & MCCALLAN
SCHULDT
Description Memorandum dated November 6, 1964 from D. J. Porter to a distribution list forwarding a letter of the same date from Porter to Contracting Officer, U.S. Army, Biological Laboratories, Fort Detrick, sending proposal to participated in a one year study of the effects on biological activity of combining a number of chemical herbicidal compounds and adjuvants, as per an invitation letter dated October 9, 1964. Letter brags about facilities available for the project.

Exhibit #P0337

PIN # DS00017997
Date 04-Dec-64
Author S B HONOUR
Addressee GILES & CORT
PURDY & SAVAGE

Description Memorandum dated December 4, 1964 from S. B. Honour to C. W. Giles, Assistant Vice President of Alexander & Alexander, Inc. Acknowledges receipt of November 24, report letter, and states that it would be a

15684

mistake for the AFIA representative to settle individual workers' claims and that Quimor had a point in suggesting settlements' with the employers.

Exhibit #P0347

PIN #	DS 17978
Date	28-Dec-64
Author	C W GILES
Addressee	R F INGEGNERI & LEGAL DEPT AMER. FOREIGN INS. & ASSN.
Description	LTR FROM GILES TO INGEGNERI RE BOGOTA CLAIMS D.A.

Exhibit #P0348

PIN #	DS 17980
Date	29-Dec-64
Author	C W GILES
Addressee	S. B. HONOUR & DIV. SALES MANAGER DIAMOND ALKALI
Description	LETTER REGARDING PRODUCTS LIAB. BOGOTA, COLOMBIA

Exhibit #P0354

PIN #	DS 22677
Date	13-Jan-65
Author	P H SCHULDT
Addressee	FILE & L E LIMPEL D J PORTER
Description	SIGNED COPY INTER OFFICE CORRES. 1/13/65

Exhibit #P0384

PIN #	DS00018145
Date	08-Mar-65
Author	S B HONOUR
Addressee	QUIMOR LTDA & GUILLERMO LEON GILES & PURDY
Description	Letter dated March 8, 1965 from Honour to Quimor forwarding check for claims and requesting a quitclaim.

15665

Exhibit #P0407

PIN #	DS 379
Date	19-Mar-65
Author	V K ROWE
Addressee	EMMET KELLY MD & DR. J. WILKENFELD MR. RAYMOND VERHOEZE & MR. FRANCIS KENNEDY DR. ED CHANDLER & DR. JOHN P. FRAWLEY
Description	LTR OF ROWE TO KELLY ET. AL. RE 2,4,5-T MEETING.

Exhibit #P0411

PIN #	DS 12615
Date	25-Mar-65
Author	E L CHANDLER
Addressee	JOHN CORT JR. & F.P. KENNEDY J. O. KING & M. F. WILKERSON
Description	I-O MEMO RE 3/24/65 MEETING ON 2,4,5-T TOXIC IMPURITIES.

Exhibit #P0421

PIN #	12609
Date	30-Mar-65
Author	F R KENNEDY
Addressee	J R CORT, JR.
Description	I-O MEMO RE CHLOROACNE - DOW MEETING.

Exhibit #P0429

PIN #	DS00018120
Date	27-Apr-65
Author	C W GILES
Addressee	HONOUR & PURDY DIAMOND ALKALI
Description	Letter dated April 27, 1965 from C. W. Giles. AVP Alexander & Alexander to S. B. Honour of Diamond Alkali paying $1,611.90 in reimbursement for Quimor claims.

15666

Exhibit #P0430

PIN #	DS 17355
Date	27-Apr-65
Author	T S JR CORT
Addressee	F R KENNEDY
Description	MEMO OF 4/27/65 FROM CORT TO KENNEDY RE CHLORACNE.

Exhibit #P0440

PIN #	DS 24633
Date	11-Jun-65
Author	W A GOODLOE
Addressee	MR. E. BAK
Description	MONTHLY REPORT FOR MAY 1965

Exhibit #P0446

PIN #	DS00024548
Date	09-Jul-65
Author	W A GOODLOE
Addressee	BAK
Description	Memorandum dated July 9, 1985 from W. A. Goodloe to E Bak reporting chromotographic assays of residuals after filtering TCP. Report shows that 10% solfiltration is required to keep residual below 1ppm.

Exhibit #P0447

PIN #	0000
Date	09-Jul-65
Author	W A GOODLOE
Addressee	E. BAK
Description	MONTHLY REPORT JUNE 1965 RE P-DIOXIN PROJECT.

Exhibit #P0449

PIN #	DS 18090
Date	15-Jul-65
Author	GEORGE RATHGABER
Addressee	S.B. HONOUR & SALES MANAGER DIAMON ALKALI & D.M. PURDY

15687

Description LETTER RE PRODUCTS LIABILITY, BOGOTA COLOMBIA

Exhibit #P0460

PIN #	DS 2454
Date	20-Sep-65
Author	W A GOODLOE
Addressee	
Description	LABORATORY ANALYSIS REPORT RE T-ACID LEVELS.

Exhibit #P0466

PIN #	DS00018235
Date	19-Nov-65
Author	LEON R GUILLERMO
Addressee	COPETE ALBERTO & AFIA COLIMBIANO LTD DIAMOND INTERAM & RESTREPO HUMBERTO
Description	Letter from Quimor, Ltd. to AFIA Colombian, Limited, dated November 19, 1965 outlining complaints in relation to the toxicity of the product, which it had independently tested Hazeltine, and outlining the dollar value of its complaint.

Exhibit #P0477

PIN #	DS00018227
Date	01-Feb-66
Author	B B HONOUR
Addressee	QUIMOR LIMITADA & GUILLERMO
Description	Letter dated February 1, 1966 from S. B. Honour to Guillermo Leon R. of Quimor Limitada, stating that his January 28 letter was received and that it has been brought to the attention of Mr. Savage, General Manager-International Division and Mr. J.S. Cort, Jr., General Manager - Agricultural chemicals Division, and stating that they have to wait for Mr. Savage to come back from a trip before they can give him an answer.

15668

Exhibit #P0481

PIN #	DS00024628
Date	23-Mar-66
Author	W A GOODLOE
Addressee	STEWARD & KENNEDY
Description	Memorandum dated March 23, 1966 from W. A. Goodloe at Newark to F. G. Steward reporting on analysis of TCP using different filtration methods. Shows production TCP evidenced levels of 56 to 10 ppm, from December of 1965 through March of 1966. The Memorandum also shows that dilution results in minimal dioxin content. The Memo is denominated an "Interim Report."

Exhibit #P0482

PIN #	DS 24628
Date	23-Mar-66
Author	W A GOODLOE
Addressee	F. G. STEWARD
Description	INTERIM REPORT - DIOXIN STUDY.

Exhibit #P0483

PIN #	DS00012690
Date	06-Apr-66
Author	J C KELLY
Addressee	KING & KENNEDY GUIDI
Description	Memorandum dated April 6, 1966 by J. C. Kelly to J. O. King reporting that after submitting a sample of technical 2,4,5-T , Dow said they would not buy it because they felt that using Diamond's material would resurrect their chloracne problem.

Exhibit #P0496

PIN #	DS 21663
Date	30-Jun-66
Author	UNKNOWN
Addressee	
Description	ASSIGNMENT OF PATENT PERKINS ET AL TO DIAMOND ALKALI

Exhibit #P0501

PIN #	DS 951
Date	13-Jul-66
Author	F GORDON STEWARD
Addressee	
Description	OPERATING COMMENTS JUNE, 1966.

Exhibit #P0512

PIN #	DS 967
Date	07-Sep-66
Author	E BAK
Addressee	
Description	OPERATING COMMENTS - PRODUCTION - AUGUST, 1966.

Exhibit #P0522

PIN #	DS00021969
Date	12-Oct-66
Author	BOEHRINGER
Addressee	WARBURGTON & DIAMOND CLEVELAND
Description	Letter from C. H. Boehringer Sohn dated October 12, 1966 to Diamond threatening to challenge a proposed patent unless Diamond signs a stipulation (not annexed to the exhibit).

Exhibit #P0542

PIN #	DS1005
Date	23-Nov-66
Author	R A GUIDI
Addressee	F. R. KENNEDY & R. L. URBANOWSKI GORDON STEWARD
Description	MONTHLY TECHNICAL REPORT.

Exhibit #P0558

PIN #	ILLEGIBLE
Date	09-Jan-67

15670

Author JJ LUSARDI
Addressee STEWARD & KENNEDY
BAK & GOODLOE

Description Memorandum dated January 9, 1967 from J. J. Lusardi to F. G. Steward, reporting on experiments with different types of filters in an attempt to remove the 2,3,7,8-TCDD impurity from the production line.

Exhibit #P0559
PIN # DS23332
Date 09-Jan-67
Author J J LUSARDI
Addressee F G STEWARD & F R KENNEDY
E BAK & W A GOODLOE

Description INTERIM REPORT OF EXPERIMENTAL WORK FOR TCP PURIFICATION.

Exhibit #P0585
PIN # DS 3367
Date 20-Feb-67
Author J S JR CORT
Addressee FILE & R A GUIDI

Description RESUME OF "ORANGE" NIAGARA FALLS MEETING 2/17/67.

Exhibit #P0608
PIN # DS00001046
Date 12-Apr-67
Author F GORDON STEWARD
Addressee
Description Staff document originated by F. Gordon Steward and dated April 12, 1967 which outlines operations at the 2,4-D and 2,4,5-T lines. States that the TCDD removal filtration system is successful and that the carbon filter is being tested for further evaluation.

15671

Exhibit #P0628

PIN #	DS00001074
Date	07-Jun-67
Author	F GORDON STEWARD
Addressee	
Description	Staff Memorandum by F. Gordon Steward reporting on technical operations for the month of May, 1967. Reporting on a continuing effort to evaluate the effectiveness of different filtration systems, the report states that the use of small disposable filters as the primary means of TCP purification does not appear possible and that the filters still plug up rapidly. The use of a carbon filter, although it too plugs, is being considered and shows some promise. Heating in the vicinity of the plub did not see seem to work.

Exhibit #P0642

PIN #	DS00016917
Date	12-Jul-67
Author	F R KENNEDY
Addressee	CORT & GUIDI
Description	Technical Memo examines recently issued specification for Agent Orange. Dated July 12, 1967. Principal complaint is that by requiring mixing to be done by volume instead of weight, Diamond will have to come up with more "T" in the mixture than it had planned. Refers to a previous document issued by Newark, possibly a draft specification.

Exhibit #P0643

PIN #	DS00001084
Date	12-Jul-67
Author	F GORDON STEWARD
Addressee	
Description	Staff Memorandum prepared by F. Gordon Steward on July 12, 1967. With regard to filtration of TCP, states that experimental tower has been set up and seems to be working and that tests were being conducted to see what the saturation point of the carbon filters were so that cycles could be

15072

designed.

Exhibit #P0645
PIN # DS 23266
Date 20-Jul-67
Author D R GEAMAN
Addressee F.G. STEWARD & F.R. KENNEDY
E. BAK & W. A. GOODLOE
L.M. SZENDREY
Description I-O CORRES. RE FILTRATION OF CHLORACNEGENS FROM 10% TCP.

Exhibit #P0648
PIN # DS 1095
Date 09-Aug-67
Author F GORDON STEWARD
Addressee
Description OPERATING COMMENTS PLANT TECHNICAL JULY 1967.

Exhibit #P0668
PIN # DS00001107
Date 13-Sep-67
Author F GORDON STEWARD
Addressee
Description Staff memorandum prepared by F. Gordon Steward on or about September 13, 1967. Reports that an analysis of the last runs made at the lab column showed that it was removing the dioxin from the TCP and that, under laboratory conditions, the effluent from the tower benzine in the wash could remove 75% of the dioxin from 10 times its volume of effluent. In a plant setting, they would expect 5 times the ration, and it was concluded that this was not acceptable, so the program was being scrapped.

Exhibit #P0680
PIN # DS00001119
Date 11-Oct-67

15673

Author F GORDON STEWARD
Addressee
Description Staff Memorandum concerning plant technical operations prepared by F. Gordon Steward on October 11, 1967. Report indicates that plant purification unit is operating successfully, producing TCP with dioxin contents of less than 1ppm. States that a real control on this factor was delayed because instrumentation was not completed in the new facility.

Exhibit #P0688
PIN # DS00018206
Date 31-Oct-67
Author S S SAVAGE
Addressee HONOUR & SARREY

Description Memorandum from S. S. Savage dated October 31, 1967 in Bogota to S. B. Honour stating that ROBLEDO HERMANOE is the last claim from the debacle and that, although AFIA is handling their claim, there is the matter of two 55-gallon drums that they were holding for evidence and that they want to return. Savage reports that he assured Quimor that they would "work something out" if they had to credit the customer.

Exhibit #P0692
PIN # DS00001129
Date 08-Nov-67
Author F GORDON STEWARD
Addressee
Description Staff Report prepared on November 8, 1967 by F. Gordon Steward concerning technical operations at the Newark Plant. Under "TCP" it is reported that the carbon tower was converted from a batch operation to a flow operation, but through use of a specific gravity controller. TCP flow was controlled manually and tended to plug up. Checks of dioxin levels made during the month were reported to be "satisfactory."

Exhibit #P0696

PIN #	DS 2917
Date	10-Nov-67
Author	R A GUIDI
Addressee	F. R. KENNEDY & J.C. KELLY
Description	I-O MEMO FROM GUIDI TO KENNEDY - SEND "ORANGE" SAIGON.

Exhibit #P0719

PIN #	DS 1156
Date	10-Jan-68
Author	F GORDON STEWARD
Addressee	
Description	OPERATING COMMENTS PLANT TECHNICAL DEC. 1967.

Exhibit #P0736

PIN #	DS00001169
Date	07-Feb-68
Author	F GORDON STEWARD
Addressee	
Description	Staff Memorandum prepared on February 7, 1968 by F. Gordon Steward concerning technical operations at the Newark plant. The Memorandum reports that, although the TCP purification unit continued to operate in a satisfactory manner mechanically, they were continuing to get higher-than-desired-p-dioxin levels, averaging 3.0 in ppm in January and 2.8 ppm in December.

Exhibit #P0745

PIN #	DS00003446
Date	26-Feb-68
Author	F R KENNEDY
Addressee	GUIDI
Description	Memorandum dated February 26, 1968 from F. R. Kennedy to R. A Guidi concerning residues collecting in the dump pit north of the Process Building. States an analysis showing dioxin levels of 75 ppm, and another dioxin of 16.6 ppm. Notes precautions being taken with workers at site. Also says that the assay is about

the same as the TCDD content of Diamond's production TCP before the "clean up." States that this will go down as the clean up progresses.

Exhibit #P0764

PIN #	DS00001206
Date	08-May-68
Author	F GORDON STEWARD
Addressee	
Description	Staff Memorandum dated May 8, 1968 and prepared by Gordon Steward. Gordon Steward summarizing plant operations from a technical point of view during the month of May, 1968. The Memorandum reports that the operation of the TCP purification unit "satisfactory", with dioxin levels running at about 1.8 ppm average for the month. The principal contaminants are reported to be, still, "unknowns."

Exhibit #P0777

PIN #	DS 1219
Date	11-Jun-68
Author	F GORDON STEWARD
Addressee	
Description	OPERATING COMMENTS, PLANT TECHNICAL, MAY, 1968.

Exhibit #P0796

PIN #	DS 1253
Date	11-Sep-68
Author	F GORDON STEWARD
Addressee	
Description	OPERATING COMMENTS, PLANTS TECHNICAL, AUGUST, 1968.

Exhibit #P0806

PIN #	DS 17181
Date	04-Oct-68
Author	M F WILKERSON
Addressee	H. HOCHBERG & J.A. WILSON

15678

	R. A. GUIDI & C. L. TROPH J. O. KING
Description	I-O CORRESPONDENCE TASK FORCE MEETING WELDON SPRINGS.

Exhibit #P0819

PIN #	19437
Date	03-Dec-68
Author	R W MD MC BURNEY
Addressee	WILLIAM F. BARTHAL & DEPT HELTH, EDUC. WELFARE
Description	HOW TO ASSIST RE PORPHYRIA CUTANEA TARDA & CHLORACNE.

Exhibit #P0820

PIN #	DS00001285
Date	11-Dec-68
Author	F GORDON STEWARD
Addressee	
Description	Staff Memorandum on Newark technical operations for the month of November, 1968 prepared by F. Gordon Steward on or about December 11, 1968. The cleaning tower for TCP did not work well and was producing 9.3 ppm after cleaning. The carbon bed was to be replaced when materials were received. The memorandum reports on efforts to analyze dirt around the plant for dioxin and also to divert contamination from vents at the TCP unit area.

Exhibit #P0832

PIN #	1297
Date	07-Jan-69
Author	F GORDON STEWARD
Addressee	
Description	OPERATING COMMENTS, PLANT TECHNICAL, DECEMBER, 1968.

Exhibit #P0841

PIN #	DS00024724
Date	12-Feb-69

Author F GORDON STEWARD
Addressee
Description Staff Report on Plant Technical Operations for the Month of January, 1969 , prepared by F. Gordon Steward on or about February 12, 1969. Under the heading "TCP" it is reported that the dioxin content at the tower was greater than 10 ppm, which was reduced to less than 1 ppm after changing the carbon bed.

Exhibit #P0842
PIN # 24724
Date 12-Feb-69
Author F GORDON STEWARD
Addressee
Description OPERATING COMMENTS, PLANT TECHNICAL, JANUARY, 1969.

Exhibit #P0857
PIN # 10302
Date 13-Aug-69
Author F GORDON STEWARD
Addressee
Description OPERATING COMMENTS PLANT TECHNICAL JULY 1969.

Exhibit #P0866
PIN # DS 24611
Date 24-Nov-69
Author R A GUIDI
Addressee F G STEWARD & F. R. KENNEDY
Description I-O CORRES. NEWARK PLANT HEALTH SURVEY MAN. FOR PUBL.

Exhibit #P0882
PIN # DS00024544
Date 23-Dec-69
Author F GORDON STEWARD
Addressee KENNEDY
Description Memo dated December 23, 1969 from F. Gordon

15678

Steward at Newark to F. R. Kennedy at Cleveland reciting history of efforts to identify and eliminate the chloracnegen, now known to be TCDD , from their TCP. Shows dioxin content by quarters from 1968 through 1969, disclosing that in December of 1968 the product had a 9 ppm which the report argues was due to a labor-management dispute that caused the carbon tower not be to be cleaned.

Exhibit #P0969

PIN #	DS 12557
Date	22-Jul-70
Author	F R KENNEDY
Addressee	DR. JACOB BLEIBERG
Description	LTR FROM KENNEDY TO BLEIBERG NOTING FREQUENCY OF SYMPTOMS

Exhibit #P0971

PIN #	12558
Date	04-Aug-70
Author	JACOB BLEIBERG, MD
Addressee	DIAMOND SHAMROCK
Description	LTR FROM BLEIBERG TO KENNEDY RE "PERMANENT DISEASE"

Exhibit #P1008

PIN #	DS 17442
Date	25-Jun-71
Author	DL THOMPSON
Addressee	C. T. BALDEMA & C. R. BROWN F. G. STEWARD & C. H. GILBERT F. I. SCHICK
Description	I-O MEMO RE NEWARK WORKMEN'S COMPENSATION.

Exhibit #P1045

PIN #	10526
Date	25-Jun-73
Author	E A LAVERGNE

15679

Addressee DR. HANS KOCH
Description LTR STATED USE OF DR KOCH'S PATENTED PROCESS.

Exhibit #P1053
PIN # DS24599
Date 22-Nov-75
Author F GORDON STEWARD
Addressee D.M. PURDY & F. R. KENNEDY
R. W. MC BURNEY
Description I-O MEMO N.J. STATE DEPT. OF HEALTH SURVEY FORMER PERSONNEL

Exhibit #P1088
PIN # 00000
Date 18-Apr-80
Author UNKNOWN
Addressee
Description DEPOSITION OF A.E. SIDWELL TAKEN 4/18/80

15680

Exhibit #P0030

PIN #	C 61055
Date	
Author	G J MACLEAN
Addressee	DAVIDSON J H
Description	Article by G. J. MacLean and J. H. Davidson, Research and Development, Dow Chemical Company, re: Diagnosis of Disorders in Pastured Livestock.

Exhibit #P0031

PIN #	CO52415
Date	
Author	VI AINSLEE
Addressee	CANADA CUSTOMS
Description	Form prepared by Uniroyal (1966) Ltd., Chemical Division, Elmira, Ont. for Canada Customs for shipment of 126 drums (6868.26 gals) via C.N.R. to Gulf Outport, Mobile , Alabama.

Exhibit #P0032

PIN #	J 668
Date	
Author	GEORGE F COLLINS
Addressee	UNITED STS RUBBER CO & DCASR
Description	Contract for herbicides (Incomplete).

Exhibit #P0033

PIN #	J 936
Date	
Author	UNKNOWN
Addressee	UNKNOWN
Description	Incomplete contract for purchase of herbicides with Uniroyal Chemical Div. of Uniroyal , Inc., undated.

Exhibit #P0034

PIN #	000
Date	
Author	UNKNOWN

Addressee
Description Contract between Thompson Chemical & US & all extensions or renewals concerning the furnishing of AO or any herbicide containing 2,4,5-T to US government. (THESE DOCUMENTS ARE NOT YET AVAILABLE, BEING OBTAINED THROUGH CUSTODIAN OF RECORDS OF US GOVERNMENT. CONTRACTS ARE DATED 4/19/67 & 5/2/68.)

Exhibit #P0035
PIN # THOMPSON-15
Date
Author UNKNOWN
Addressee
Description Organizational chart of Thompson-Stearns-Rogers project (Weldon Springs Chemical Plant).

Exhibit #P0036
PIN # THOMPSON-16
Date
Author UNKNOWN
Addressee
Description Curriculum vitae of various players involved in Thompson-Stearns-Rogers project (Weldon Springs).

Exhibit #P0037
PIN # 0002
Date
Author R L DRUVA
Addressee
Description Sundry notes of Stern-Rogers showing the total knowledge on part of Thompson-Stearns-Rogers people concerning dioxin and its potential adverse health effects.

Exhibit #P0038
PIN # 0003
Date

15682

Author UNKNOWN
Addressee
Description Notes on conversations and interviews by Environmental Protection Agency, document 192059, subject; Thompson Chemical Company", revealing interviews by agents of the EPA of the United States govt. concerning waste disposal and going into knowledge of Thompson Chemical concerning 2,4,5-T.

Exhibit #P0039
PIN # JUS0071
Date
Author UNKNOWN
Addressee
Description Unidentified handwritten document with colums of figures.

Exhibit #P0132
PIN # THOMPSON-11
Date 17-Jan-60
Author F VARGAS
Addressee
Description Notes of meetings dated January 17, 1960 concerning concerning 2,4,5-T and the fact that dioxin is produced as a bi-product of 2,4,5-T, causing "chloracne and liver damage."

Exhibit #P0144
PIN # C 61054
Date 22-Jul-60
Author UNKNOWN
Addressee ELMIRA, ONT. & 5
Description Page 7 of memorandum re:hygene.

Exhibit #P0241
PIN # J 4279
Date 19-Jul-63
Author UNKNOWN
Addressee

15683

Description Military Specification for Herbicide: n-butyl 2,4-Dichlorophenoxyacetate, dated July 19, 1963.

Exhibit #P0242

PIN #	JUS0056
Date	19-Jul-63
Author	UNKNOWN
Addressee	UNKNOWN
Description	Military specificatin for normal butyl ester of 2,4-D dated July 19, 1963.

Exhibit #P0271

PIN #	021565
Date	15-Feb-64
Author	W BRAUN
Addressee	BUCKELY
Description	Cover slip for translation of W. Braun article done on May 27, 1966 of article written in 1959 by Trans. Chem Inc.

Exhibit #P0451

PIN #	CO56196
Date	10-Aug-65
Author	T H EVANS
Addressee	GRD & HAT WYH & TDM CRH & OTHERS
Description	Memo dated August 10, 1965 reporting on visit to Dow facility in Midland by T. H. Evans. Bears "Received" stamp of A.L.Gorman.

Exhibit #P0514

PIN #	J 469
Date	23-Sep-66
Author	JOHN EVANS
Addressee	UNITED STATES
Description	Herbicide contract DSA-400-67-C-1635 between USA and United States Rubber Company Chemical Div. for 150,000 gallons to be delivered on or before June 1, 1967,

with all attachments.

Exhibit #P0518

PIN #	J 253
Date	06-Oct-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICE
Description	Acceptance form for 5451 gallons herbicide.

Exhibit #P0519

PIN #	J 265
Date	06-Oct-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER
Description	Acceptance form for 5451 gals. herbicide dated Oct. 6, 1966.

Exhibit #P0520

PIN #	J 241
Date	06-Oct-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICE
Description	Acceptance Form dated Oct. 6, 1966 for 5451 gals. of herbicide.

Exhibit #P0521

PIN #	J 228
Date	07-Oct-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER
Description	Acceptance dated October 7, 1966 for 5451 gallons of herbicide.

Exhibit #P0523

PIN #	J 220
Date	17-Oct-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER
Description	Acceptance form dated October 17, 1966 for

5451 gallons of designated herbicide.

Exhibit #P0524

PIN #	J 211
Date	17-Oct-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER
Description	Acceptance form dated October 17, 1966 for 5451 gallons of designated herbicid.

Exhibit #P0528

PIN #	J 202
Date	25-Oct-66
Author	R J JEFFERY
Addressee	DCASR & DISBURSING OFFICER
Description	Acceptance form for 5451 gallons of designated herbicide dated October 25, 1966.

Exhibit #P0529

PIN #	J 196
Date	01-Nov-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER
Description	Acceptance of 5451 gallons of designated herbicide dated November 1, 1966.

Exhibit #P0530

PIN #	J 190
Date	01-Nov-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER
Description	Acceptance Form for 5451 gallons of herbicide dated November 1, 1966.

Exhibit #P0531

PIN #	J 184
Date	01-Nov-66
Author	H J FICHT

Addressee DCASR & DISBURSING OFFICER
Description Acceptance Form for 5451 gallons of herbicide dated November 1, 1966.

Exhibit #P0536
PIN # J 177
Date 09-Nov-66
Author H J FICHT
Addressee DCASR & DISBURSING OFFICER BOSTON
Description Acceptance form for 5451 gallons of herbicide dated November 9, 1966.

Exhibit #P0537
PIN # J 171
Date 09-Nov-66
Author H J FICHT
Addressee DCASR & DISBURSING OFFICE BOSTON
Description Acceptance of 5451 gal of herbicide dated November 9, 1966.

Exhibit #P0538
PIN # J 165
Date 09-Nov-66
Author H J FICHT
Addressee DCASR & DISBURSING OFFICER BOSTON
Description Accpeptance of 5451 gals of herbicide dated November 9, 1967.

Exhibit #P0539
PIN # J 159
Date 21-Nov-66
Author H J FICHT
Addressee DCASR & DISBURSING OFFICER BOSTON
Description Acceptance for 5451 Gallons of herbicide dated November 21, 1966.

15887

Exhibit #P0540

PIN #	J 153
Date	21-Nov-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER BOSTON
Description	Acceptance for 5451 gals of herbicide dated November 21, 1966.

Exhibit #P0541

PIN #	J 147
Date	21-Nov-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER BOSTON
Description	Acceptance for 5451 gals of herbicide dated November 21, 1966.

Exhibit #P0543

PIN #	J 141
Date	28-Nov-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICER BOSTON
Description	Acceptance form for 5451 gallons of herbicide dated November 28, 1966.

Exhibit #P0544

PIN #	J 135
Date	28-Nov-66
Author	H J FICHT
Addressee	DCASR & CONTRACTING OFFICER BOSTON
Description	Acceptance form for 5451 gallons of herbicide dated November 28, 1966.

Exhibit #P0545

PIN #	J 129
Date	28-Nov-66
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICE

15089

BOSTON
Description Acceptance for 5451 gals of herbicide dated November 28, 1966.

Exhibit #P0546
PIN # J 123
Date 28-Nov-66
Author H J FICHT
Addressee DCASR & DISBURSING OFFICER
BOSTON
Description Acceptance form dated November 28, 1966 for 5451 gallons of herbicide.

Exhibit #P0550
PIN # J 117
Date 05-Dec-66
Author H J FICHT
Addressee DCASR & DISBURSING OFFICE
BOSTON
Description Acceptance form for 5451 gals of herbicide dated December 3, 1966.

Exhibit #P0551
PIN # J 111
Date 05-Dec-66
Author H J FICHT
Addressee DCASR & DISBURSING OFFICE
BOSTON
Description Acceptance form dated December 5, 1966 for 5451 gallons of herbicide.

Exhibit #P0552
PIN # J 104
Date 06-Dec-66
Author H J FICHT
Addressee DCASR & DISBURSING OFFICE
BOSTON
Description Acceptance for 7523 gallons of herbicide dated December 6, 1966.

Exhibit #P0561

PIN #	DOW751871
Date	15-Jan-67
Author	V K ROWE
Addressee	BUCKLEY & MC COY DIXON & HOLDER SILVERSTEIN
Description	Letter dated February 15, 1967 from V. K. Rowe to M.S. Buckley forwarding translations of "Clinical Observations About The Origin of Chloracne" and "Industrial Poisoning in the Manufacture of Chlorophenol Compounds". Mr. Rowe states he believes the reference to 2,4-D is incorrect and that the problem is confined to 2,4,5-T.

Exhibit #P0568

PIN #	J 657
Date	27-Jan-67
Author	GEORGE F COLLINS
Addressee	FAIRCLOUGH, W A & US RUBBER CO
Description	Negotiated Contract for 40,000 gallons of herbicide dated January 27, 1967 to be delivered on or before March 31, 1967.

Exhibit #P0574

PIN #	DOW 751874
Date	03-Feb-67
Author	WJ MCCOY
Addressee	ROWE, V.K. & CORBIN, W.L. PLETCHER, D.E. & GOWELL, J.H.
Description	Dow document 751874 memo dated 02-03-67 from McCoy to Roe, subject "Thompson Chemical Company", which included notation that Buckley of Thompson had phoned asking for recommendations for medical treatment for employees believed suffering from chloracne contracted during manufacture of 2,4,5-T.

Exhibit #P0575

PIN #	DOW751874
Date	03-Feb-67

15099

Author W J MC COY
Addressee ROWE & CORBIN
FLETCHER & GOWELL
Description Memo dated February 3, 1967 from W. J. Mc Coy to V. K. Rowe reporting that M. S. Buckley of Thompson Chemical had phoned asking for reporting a severe chlorancne problem and saying they were using Hooker's TCP. Asked for Dow's recommendations re: medical treatment. Notes they are a competitor but maybe advice would be be in order.

Exhibit #P0581
PIN # 751872,3
Date 15-Feb-67
Author VK ROWE
Addressee DIXON, WILLIAM E' & CORBIN, W.L.
PLETCHER, D.C. & COWELL, J.H.
MCCOY, W.J. & HOLDER,B. B.
Description Dow Doc. No. 751872 memo dated 02-05-67 from Rowe to Dixon of Dow re: internal memo relating Marion Buckley's phone call asking for info & guidance in cleanup after trichloraphenol accident.

Exhibit #P0582
PIN # 751871
Date 15-Feb-67
Author VK ROWE
Addressee BUCKLEY, M.S. & MCCOY, W.J.
DIXON, W.R. & HOLDER, B.B. M.D.
SILVERSTEIN, L.
Description

Exhibit #P0583
PIN # DOW751872
Date 15-Feb-67
Author V K ROWE
Addressee DIXON & CORBIN
FLETCHER & GOWELL
MC COY & HOLDER
Description Memorandum dated February 15, 1967 from V. K. Rowe to William E. Dixon, Bioproducts Division, reporting on calls from Buckley for help. Asked for advice and help on

what to do in cleaning up instruments, and was given limited information. Also received articles in the public literature. Did not ask for information on how assay of residuals made, so did not volunteer. Similarly, had little understanding of total toxicological activity, and so it was not volunteered.

Exhibit #P0599

PIN #	J 761
Date	21-Mar-67
Author	GEORGE F COLLINS
Addressee	US RUBBER CO & DCASR
Description	Change to Contract DSA-400-67-C-5959 dated March 21, 1967 making Chief, DCASD, Hartford, Conn., the contracting officer.

Exhibit #P0611

PIN #	UNKNOWN
Date	19-Apr-67
Author	GEORGE F COLLINS
Addressee	MITCHELL & THOMPSON CHEMICALS
Description	Herbicide contract dated April 19, 1967.

Exhibit #P0615

PIN #	J 899
Date	02-May-67
Author	GEORGE F COLLINS
Addressee	UNIROYAL CHEMICAL
Description	Modification of contract dated May 2, 1967 changing specifications for drum markings.

Exhibit #P0616

PIN #	J 95
Date	10-May-67
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICE BOSTON
Description	Acceptance for 5451 gallons of herbicide dated May 10, 1967.

15892

Exhibit #P0865

PIN #	0003
Date	22-Nov-69
Author	T A TREGLIA
Addressee	THOMPSON-STEARNS & ROGER, INC. JOHN GERETY, US ARMY
Description	Letter from T. A. Treglia to Thompson-Stearns-Roger, Inc. dated Nov. 22, 1968 concerning the Weldon Springs Project.

Exhibit #P0958

PIN #	C 61149
Date	09-Jun-70
Author	T D MURPHY
Addressee	WATT BERRY J & GREEN CROSS PRODUCTS SHERWIN-WILLIAMS CA & MONTREAL,QUE
Description	Letter dated June 9, 1970 from T. D. Murphy to Berry J. Watt of Green Cross Products of Sherwin- Williams of Canada, Ltd. discussing that the 1 ppm standards originated with equipment limitations and that it is not a government standard.

Exhibit #P0963

PIN #	C 61052
Date	15-Jun-70
Author	E WANLESS
Addressee	THOMSON H A & UNIROYAL LTD. CHEMICAL DIVISION & ELMIRA, ONTARIO
Description	Methodology for detecting residues.

Exhibit #P0965

PIN #	C 61051
Date	23-Jun-70
Author	WP COCHRANE
Addressee	THOMSON HUGH & CONTROL CHEMIST UNIROYAL LTD. & ELMIRA ONT.
Description	Reply to inquiry re: residues.

Exhibit #P0973

15693

Exhibit #P0617

PIN #	J 83
Date	10-May-67
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICE BOSTON
Description	Acceptance for 5451 gallons of herbicide dated May 10, 1967.

Exhibit #P0618

PIN #	J 74
Date	10-May-67
Author	H J FICHT
Addressee	DCASR & DISBURSING OFFICE BOSTON
Description	Acceptance for 5451 gallons of herbicide, dated May 10, 1967.

Exhibit #P0621

PIN #	J 929
Date	17-May-67
Author	GEORGE F COLLINS
Addressee	FAIRCLOUGH & UNIROYAL CHEM DIV UNIROYAL INC
Description	Contract for 50,000 gallons herbicide to be shipped by June 30, 1967. Contract is dated May 17, 1967 and is a negotiated contract.

Exhibit #P0624

PIN #	J 82
Date	23-May-67
Author	M JEFFERY
Addressee	DCASR & DISBURSING OFFICE BOSTON
Description	Acceptance of 5451 gallons of herbicide, dated May 23, 1967.

Exhibit #P0625

15684

PIN # C056178
Date 11-Aug-70
Author H A THOMSON
Addressee GORMAN, A & MURPHY, TOM
CHUNG, Y
Description Memorandum dated August 11, 1970 from H. A. Thomson to Gorman, Murphy, and Chung relating to the problems of identifying dioxin in chlorophenols through gas chromotography. Attempts to identify peaks. Notes results of cooperative tests and concludes that "our" material has about 10 ppm.

Exhibit #P0997
PIN # 061319
Date 18-Mar-71
Author A H GORMAN
Addressee GRD & WJH
PCT & FMH
HAT & OTHERS
Description Confidential internal memorandum dated March 18, 1971 from A. H. Gorman to a large circulation list entitled "2,4,5-T - Uniroyal Position." The memorandum outlines Uniroyal's history with 2,4,5-T and the "Agent Orange" Program, highlight---lighting defensive factors, the 1 ppm standard, assurances from suppliers, and inability to control field applications.

Exhibit #P0998
PIN # C 60801
Date 19-Mar-71
Author A H GORMAN
Addressee PCT & GRD
WEH & FMH
HAT & OTHERS
Description Internal Memorandum dated March 19, 1971 from A.H. Gorman to a wide variety of persons forwarding material on phenoxy herbicides and suggesting how calls about health problems should be handled.

15695

PIN # J 4715
Date 23-May-67
Author R JEFFERY
Addressee DCASR & DISBURSING OFFICE
BOSTON
Description Acceptance of 7413 gallons of herbicide, dated May 23, 1967.

Exhibit #P0673
PIN # 605
Date 29-Sep-67
Author SIEGAL IND TSTG LABS
Addressee THOMPSON CHEM
Description Eighty-three separate and dated reports showing the moisture content of samples of Thompson Chemical batches.

Exhibit #P0693
PIN # THOMPSON-7
Date 08-Nov-67
Author INTER OFFICE MEMO THOMPSON CHEM
Addressee
Description Interoffice Memo 110867 involving discussions w/ Kolker of Montrochem & again demonstrating the involvement of the Thompson Chemical people in the Thompson-Sterns-Rogers project & the knowledge concerning how the 2,4,5-T is manufactured, the problems, etc.

Exhibit #P0722
PIN # THOMPSON-9
Date 15-Jan-68
Author D W NORBERG
Addressee
Description 1 page report dated January 15, 1968 by D. W. Norberg of Stearns-Rogers entitled "Engineering Status Report".

Exhibit #P0723
PIN # THOMPSON-
Date 16-Jan-68

15696

Author UNKNOWN
Addressee
Description Minutes of meeting concerning Thompson-Stearn-Rogers project, including Thompson & Buckley of Thompson Chemical dated 01-16,17,18 &19 showing total involvement of Thompson Chemical people, particularly Bill Thompson & M.S. Buckley, with respect to knowledge of 2,4,5-T, its manufacturing process, hazards, etc.

Exhibit #P0725
PIN # 0000
Date 22-Jan-68
Author MONTROCHEM PROCESS MEETING
Addressee
Description 01-22-68 Memo "Process Meeting w/ Montrochem Consultants showing Thompson & Buckley of Thompson Chemical & Norberg & Angell of Stearns-Rogers & Bill Boyer present. Shows total involvement & knowledge of Buckley & Thompson in direct contravention to Thompson's sworn testimony. Plaintiff's position that this demonstrates Thompson's testimony has no credibility, in addition to establishing knowledge of Thompson Chem. concerning product, its contaminant, dioxin & potential health hazards & risks.

Exhibit #P0735
PIN # THOMPSON-6
Date 05-Feb-68
Author DEV CORP MONTROCHEM
Addressee STEARNS-ROGERS CORP.
Description 02-05-68 Expense Statement of Montrochem submitted by Montrochem to Stearns Rogers, showing Messrs. Colker & Burton of Montrochem or Stearns met with Messrs. Angell & Buckley on 12-27-67 concerning "review design plans for Weldon Springs project.

Exhibit #P0743
PIN # JUS0011

15697

Date 23-Feb-68
Author UNKNOWN
Addressee UNKNOWN
Description Purchase description for Herbicide Orange (Not a Mil-Spec) dated 2February 23, 1968.

Exhibit #P0746
PIN # THOMPSON-10
Date 26-Feb-68
Author JOHN BURTON
Addressee DONALD NORBERG & M. BUCKLEY
C.KOLKER
Description Letter from John Burton, consulting chemical engineer to Donald Norberg of Stearns-Rogers corporation, attaching a memorandum concerning 2,4,5-T process description; this letter shows carbon copy to Mr. Buckley of Thompson Chemical.

Exhibit #P0760
PIN # JUS0012
Date 11-Apr-68
Author UNKNOWN
Addressee UNKNOWN
Description Purchase description for Orange II.

Exhibit #P0772
PIN # UNKNOWN
Date 24-May-68
Author W A FENNER
Addressee THOMPSON
Description Contract dated May 24, 1968 signed by W. A. Feener for the government and Thompson Chemical Company for herbicide.

Exhibit #P0781
PIN # C 77065
Date 22-Jun-68
Author F M HAGER
Addressee RMN & GPD
JCRW & KGP
WME & CDMCC

15888

Description Minutes of Development Committee Meeting of June 22, 1968 1968 of Uniroyal (1966) Ltd., Chemical Division Elmira, Ontario Development Department, prepared by F. M. Hager. Reports that vapor-phase oxidation of 2,4-D has not been successful to date and promises continuing work. Identifies direct production of 2,4-D and 2,4,5-T as a "Top Priority" project.

Exhibit #P0817

PIN #	THOMPSON-13
Date	26-Nov-68
Author	HOWARD J BUCHHOLTZ
Addressee	
Description	Memo of conference concerning Weldon Springs chemical plant dated 11-26-68, showing Thompson & Buckley.

Exhibit #P0823

PIN #	THOMPSON-14
Date	19-Dec-68
Author	M S BUCKLEY
Addressee	DEPT. OF ARMY & J.N. MCLAGAN LARRY BECON
Description	Letter on Stearns-Rogers stationery dated December 19, 1968, signed by M. S. Buckley of Thompson-Stearns-Rogers concerning manufacture of 2,4,5-T and again showing total involvement of Thompson Chemical.

Exhibit #P0840

PIN #	THOMPSON-14
Date	07-Feb-69
Author	R L JR ANDERSON
Addressee	
Description	Memorandum dated Feb. 7, 1969 entitled "Minutes of Meeting concerning termination of DA CONTRACT... WELDON SPRINGS CHEMICAL PLANT..." This memorandum discusses termination of Weldon Springs project and again shows Thompson Chemical's involvement.

15699

Exhibit #P1012

PIN #	JUS0007
Date	16-Aug-71
Author	R STAHL
Addressee	TATEM & KELLY AFB
Description	Analysis by Dow of Gulfport batches for dioxin. Handwritten onto the analysis, which is dated August 16, 1971, is an identification of the origin of the batches tested.

Exhibit #P1106

PIN #	THOMPSON-5
Date	16-Sep-83
Author	CORP STEARNS ROGER
Addressee	MONTROCHEM & DEVELOPMENT CORP.
Description	Purchase order dated 09-16-83 under heading Stearns Rogers Corp. to Montrochem Dev. Corp. concerning "Thompson-Stearns-Rogers Project" & generally showing total involvement of Thompson Chemical in the Stearns-Rogers project.

Exhibit #P1134

PIN #	5870-4
Date	01-Jan-01
Author	UNKNOWN
Addressee	SUSKIND, M.D., R.R. & OETTEL, M.D., H. WHEELER, E.P. & WEGER,L.C.
Description	Document describes meeting held at the Kettering Laboratory and Dr. Oettel sharing with representatives of Monsanto knowledge he possessed regarding Badische incident. Photographs of individuals with chloracne were exchanged by the parties.

Exhibit #P1135

PIN #	256691-700
Date	01-Jan-01
Author	VERALD ROWE
Addressee	UNKNOWN
Description	HAZARDS IN HANDLING HERBICIDES

Exhibit #P1136

PIN #	2183-95
Date	01-Jan-01
Author	UNKNOWN
Addressee	NONE
Description	GD BACKROUND INFORMATION RE: PROBLEMS AT MONSANTO

Exhibit #P1137

PIN #	002183-23095
Date	01-Jan-01
Author	ROWE
Addressee	UNKNOWN
Description	Article written by Dr. Rowe entitled "Health Hazards Associated with Handling and Use of Herbicides."

Exhibit #P1138

PIN #	006005
Date	07-Oct-01

15701

Author R EMMET KELLY
Addressee ILLEGIBLE
Description Letter from Kelly, M.D. re: Medical History of 2,4,5-T Manufacture; contamination at Nitro.

Exhibit #P1139
PIN # 00000
Date 10-Oct-10
Author KRISIK, H; JONES, L
Addressee
Description A Technique for Testing Acnegenic Potency in Rabbits, applied acnegen 2,3,7,8-TCP; written by Linn Jones and Helen Krizek.

Exhibit #P1140
PIN # 00000
Date 10-Oct-10
Author K H SCHULZ
Addressee
Description Occupational Chloracne Caused by Aromatic Cyclic Esthers written by K.H. Schulz.

Exhibit #P1141
PIN # DOW21310-481
Date 01-Aug-50
Author V K ROWE
Addressee UNKNOWN
Description TOXICITY OF 2,4-D AND 2,4,5-T

Exhibit #P1142
PIN # DOW256691-00
Date 01-Feb-52
Author V K ROWE MD
Addressee NONE
Description HLTH HAZDS ASS. W/ HANDLNG AND USE OF HERB.

Exhibit #P1143

15702

PIN # DOW536347-54
Date 01-Jan-54
Author V K ROWE ET AL
Addressee NONE
Description TOXLOG INF REGARDING D & T EFFTS ON LIVESTOCK

Exhibit #P1144
PIN # DOW750691-93
Date 09-Dec-55
Author VERALD ROWE
Addressee J.W.BRITTON & L. SOUTHWICK
K.C. BARRONS & J.E. JOHNSON
W.W. ALLEN
Description Letter discusses problems with reddon, with request for applications testing to agricultural and biochemical research attached dated 11/22/55. Routine toxicological study revealed that reddon produced a skin response in rabbits typical of those materials which produced acne -form dermatitis in man. It is stated that Reddon is not a satisfactory product for Dow to distribute to the General public. The responsible ingredient and the substitted indegredient have been deleted from the memo. Ten ingredients have been deleted from the memo.

Exhibit #P1145
PIN # 278600-01
Date 26-Oct-56
Author VERALD ROWE
Addressee H.H. GAY
Description Memo is claimed to be a summary of toxicological information that Dow has on Esteron 245. One of the active ingredients is stated to be 2,4,5-T. Claims that outside lab test on 200 humans revealed "... no primary irritation or any hypersensitivity." Letter states that "... we can only guess at what might appear in humans.", and refers to two other reports on toxicity of 2,4,5-T type herbicides and a study on "... Acute and Chronic Toxicity in Dogs." with respect to 2,4-D and 2,4,5-T. Page two, paragraph two lines 3,4,5 & 6 appear to have been deleted by

15703

someone.

Exhibit #P1146

PIN #	DOW568816-18
Date	11-Feb-57
Author	DR WEYLAND
Addressee	DOW
Description	Weyland's experience is that the chloracne exciting effect on impurities is formed if trichlorophenol sodium or other alkali salts is prepared from trichorophenol, purified and worked up further.

Exhibit #P1147

PIN #	278591
Date	21-Jun-57
Author	VERALD ROWE
Addressee	R.O. FLETCHER & D. L. CONNER H. H. GAY, MD & R. H. ASHWORTH
Description	Memo contains Rowe's comments regarding a claim that a pilot in Seattle had been exposed to esteron 44 that caused illness. Memo denies that a pilot spraying the product could be exposed to enough of the product to cause any illness and that no systemic toxicology from such activity could be obtained according to Dow's knowledge. Also, that it is difficult to believe that normal aerial application with due regard to safety could cause any illness.

Exhibit #P1148

PIN #	DOW278588
Date	01-Oct-57
Author	HAROLD M GAY MD
Addressee	UNINTELLIGABLE & ROWE, V K BRYANT, C A
Description	LTR FRM GAY ESTRON 99 NOT THE CAUSE OF USERS RASH

Exhibit #P1149

PIN #	00000
Date	03-Feb-59
Author	ALKALI DIAMOND
Addressee	BAK, EUGENE
Description	Signed employee patent agreement of Eugene Bak; Bak agreed to treat as confidential all information he acquired in the course of his employment with Diamond; included in this restriction was knowledge of all procedures, specifications and secret processes.

Exhibit #P1150

PIN #	286577
Date	22-Sep-59
Author	E WIFFEN
Addressee	DR. MILLER & DR. MOONEY MACDONALD & ROWE WILSON
Description	Letter to Miller states that Dow of Canada does not presently have sufficient information regarding the possibility of detrimental effects on the human pancreas following exposure to Esteron brush killers. States letter will be forwarded to Biochemical group for discussion and that Rowe will contact Miller.

Exhibit #P1151

PIN #	278576
Date	18-Oct-59
Author	HAROLD GORDON
Addressee	MILLER & MOONEY ROWE & WIFFEN
Description	Letter from Gordon to Miller states that Dow's biochemical research laboratories conducted a study regarding the effect of esteron on the human pancreas which revealed no relationship between exposure to the chemical and damage to the pancreas. Also according to their knowledge no evidence of intoxication would lead them to believe that the pancreas is subject to injury by Esteron exposure.

15705

Exhibit #P1152

PIN #	278574
Date	11-May-60
Author	VERALD ROWE
Addressee	H.H. GAY & D.L. CONNER
Description	Letter refers to a request from Mr. Bain about information which could be used in defense of a claim that Esteron 44 had caused a cancerous growth on the neck. Rowe claims that Dow has no information from results of t evaluations or field studies which would indicate that Esteron 44 could produce cancerous growths and states that Esteron is not responsible.

Exhibit #P1153

PIN #	DS00008587
Date	18-Oct-60
Author	J A BORROR
Addressee	GUIDI, R.A. & SIEMONEIT, J.R. WEINER, H.S.
Description	Confidential Memo from Borror to Guidi. Borror mentioned Diamond's exchange of correspondence with Boehringer relative to the production of TCP. He also commented on severe liver damage that resulted from a plant explosion in Germany that had been producing TCP.

Exhibit #P1154

PIN #	DOW750814-27
Date	01-Jun-61
Author	KEN OLSEN
Addressee	DOW & MCINTYRE, H H PERKINS, R P & GAY,MD H H OTHERS
Description	Dow biochemical research laboratory's document entitled, "Results of Range Finding Toxicological Tests on Esteron 2,4,5-O.S." (Replacement for Present Formulations M-1257)

15706

Exhibit #P1155

PIN #	DOW382172
Date	22-Jun-61
Author	JOSEPH V KLAUDER
Addressee	ROWE, V.K.
Description	Letter from Klauder, M.D. to Rowe re: final result of rapcated insult patch test with 1 per cent aqueous solution of Kurosal SL; performed on 50 subjects; 3 times weekly 12 consecutive times; no cutaneous reaction; no evidence of primary irritant, fatiguing, or allergic reaction.

Exhibit #P1156

PIN #	DOW382169-71
Date	20-Jul-62
Author	V K ROWE
Addressee	
Description	Letter of report summarizing Toxicological Information Concerning KUROSAL SL and KUROSAL G by V.K. Rowe, letter attached from Rowe to Wiffen re: above.

Exhibit #P1157

PIN #	DS00008832-3
Date	07-Jan-63
Author	R F LINDEMAN
Addressee	HILL, W.E. & GUIDI, R.A. ROSENFELD, M. & GOODLOE, W. KENNEDY, F.R.
Description	Memo from Lindemann to Hill re: TCP and T-Acid Impurities; Lindemann recites the findings relative to impurities found in Diamond's TCP and T-acid.

Exhibit #P1158

PIN #	DOW008172-4
Date	05-Mar-63
Author	C P O'HARE
Addressee	GORDON, DR.H.L. & ROWE, V.K. KRAMER, C.G. & SILVERSTEIN, L.G. HOLDER, B.B. & 5 OTHERS
Description	Letter from O'Hare to Gordon, M.D. re:

15707

washing as a prophylactic measure to control folliculities produced in the rabbit ear by repeated applications of various concentrations of symmetical TCDD; Results: washing quite ineffective; delays the formation of folliculitis.

Exhibit #P1159
PIN # DS00024442-9
Date 28-Mar-63
Author KEY, M M; BIRMINGHAM, D J
Addressee
Description Dermatoses Investigation conducted by Donald J. Birmingham and Marcus M. Key; occupational health research; chloracne in production of 2,4,5-T in workers.

Exhibit #P1160
PIN # DS0324761-3
Date 29-Mar-63
Author C E MINARIK
Addressee FILES
Description Memorandum for Record from Minarik re: Criteria for Selection of Defoliation and/or Vegetation Control Agents.

Exhibit #P1161
PIN # DS1266-94
Date 26-Apr-63
Author FRANK L BAUER
Addressee
Description Minutes of meeting on April 26, 1963 at Edgewood Arsenal to discuss and evaluate the toxicity of 2,4-D and 2,4,5-T compounds with particular emphasis on use of these materials in military operations as herbicides.

Exhibit #P1162
PIN # DS00019520
Date 10-Jun-63
Author R A GUIDI

15708

Addressee MCDURNEY, R. & BROWN, C.R.
CORT, J.S. & KENNEDY, F.R.

Description Interoffice correspondence from Guidi to McDurney re: Chloracne; Guidi advised that Kennedy would keep Dr. McBurney informed relative to his discussions with Mr. Bleiberg about the worker's medical reports.

Exhibit #P1163
PIN # DS00018043-4
Date 18-Jun-64
Author S B HONOUR
Addressee GILES, C.W.

Description Letter from Honour to Giles at Alexander & Alexander; Honour requested Giles to initiate settlement of the workers' claims without waiting for the outcome of the government's investigations which he felt would favor the workers. He also mentioned the increasing pressure of unsatisfied claimants on Quimor.

Exhibit #P1164
PIN # DOW724316-23
Date 01-Oct-64
Author HYMAS, T A; ROWE, V K
Addressee
Description "Summary of Toxicological Information on 2,4-D and 2,4,5-T Type Herbicides and an Evaluation of the Hazards to Livestock Associated with Their Use" by V.K. Rowe and T.A. Hymas; toxicological information on the use of 2,4-D and 2,4,5-T for use as control of undesirable vegetation.

Exhibit #P1165
PIN # DOW129844-46
Date 22-Feb-65
Author D E PLETCHER
Addressee DOEDENS, J. D.
Description Summary of meeting (VK Rowe present) to discuss knowledge of exciter components in

15709

Dow 2,4,5-trichlorophenol, potential hazards, possible effect on Dow image, legal implications, and possible quarantine (not considering economic impact).

Exhibit #P1166

PIN #	DOW170736
Date	26-Feb-65
Author	DAVID M GROTH
Addressee	UPTON, EDWIN T.
Description	Letter from Groth to Upton re: samples requested; results on own techniques used for separation.

Exhibit #P1167

PIN #	DS00012602-3
Date	26-May-65
Author	F R KENNEDY
Addressee	CORT, J.
Description	Interoffice memorandum from Kennedy to Cort re: Chromotograph Progress Report; Kennedy was keeping Cort, Manager of the Division, advised of the latest developments in Newark's dioxin detection and removal program.

Exhibit #P1168

PIN #	21745-48
Date	22-Jun-65
Author	DOW
Addressee	NONE
Description	Dow document describing the analytical method to determine 2,3,7,8 - Tetrachlorodibenzo-p-Dioxin in 2,4,5-Trichloropheloxyacetic acid by gas-liquid chromatography bearing Monsanto Bate's number.

Exhibit #P1169

PIN #	J4061-4068
Date	10-Aug-65
Author	T EVANS

15710

Addressee UNKNOWN
Description Paper explains the dioxin and Dow midland meeting. Document suggest that the problem should not be discussed outside the division at present and that Dow suggested that no 2,4,5-T products containing dioxin should be sold. Describes the effects of dioxin and different tests performed and the results. It is stated that Dow has developed a process to remove the dioxin by a treatment of the 2,4,5-T acid with benzene but would not disclose what the process was.

Exhibit #P1170
PIN # 00000
Date 01-Jan-66
Author CARSTENS L A; ALLEN J R
Addressee
Description "Electron Microscopic Alterations in the Liver of Chickens Fed Toxic Fat" written by James R. Allen and Laurine A. Carstens.

Exhibit #P1171
PIN # 74270-83
Date 15-Aug-66
Author G M DOWNARD
Addressee MONSANTO CO. & SIDO, ROBERT

Description This document indicates that the USDA refused to register Monsanto's 2,4-D/2,4,5-T Butyl Ester Brush Killer. The document also contains numerous enclosures regarding the aforementioned matter.

Exhibit #P1172
PIN # 74365-91
Date 03-Nov-66
Author G ROBERT SIDO
Addressee USDA
Description Packet of documents regarding Monsanto's modified renewal application for the product known as 2,4,5-T Ester Brush Killer, filed with the USDA for the purpose of registering this product.

15711

Exhibit #P1173

PIN #	JUS947-8
Date	01-Jan-67
Author	DALE UNINTELLIGBLE
Addressee	NONE
Description	Document entitled "Memorandum For Deputy Chief of Staff , systems & Logistics, USAF, Subject: Herbicide Orange".

Exhibit #P1174

PIN #	21390-91
Date	28-Mar-67
Author	C H RUSSELL
Addressee	DOLIN, O. E. & BALDERSON, PHIL CUTRIGHT, E. A. & DUNLAP, W. P. STEPHENS, J. A.
Description	Semichronic oral toxicity of 2,4-Dichlorophenoxyacetic Acid to rats prepared for Dow Biochemical Research Dept. Indicates while data on results of toxicologuical tests on 2,4,5-T acid is omitted from the document.

Exhibit #P1175

PIN #	DS00016934-5
Date	05-Jul-67
Author	C W CARTY
Addressee	CORT, J.S.
Description	Letter from Carty at Dept. of Army to Cort; Carty requested Diamond to review and comment on the enclosed copy of the proposed military specification, Agent Orange II and Orange III. He was looking for constructive suggestions that could be incorporated into the specifications.

Exhibit #P1176

PIN #	00000
Date	01-Sep-67
Author	CARSTENS L A ALLEN J R
Addressee	

15712

Description "Light and Electron Microscopic Observations in Macaca Mulatta Monkeys Fed Toxic Fat" written by J.R. Allen and L.A. Carstens.

Exhibit #P1177

PIN # DOW 278589
Date 05-Oct-67
Author C BRYANT
Addressee V.K. ROWE & DR. GAY

Description Memo from Bryant to Rowe suggesting that Rowe answer inquiry from Mrs. Ernest Stahmer of Oklahoma. Rowe suggests in memo to Dr. H.H. Gay that Gay answer the letter of Mrs. Stahmer.

Exhibit #P1178

PIN # 93-4
Date 11-Oct-67
Author C H RUSSELL
Addressee ZORCH, C P & CAYARD, D E
DAVIS, A F & FISCHER, D R
STEPHENS, J A
Description Document in which Russell openly admits that he wrote the specifications for Agent Orange.

Exhibit #P1179

PIN # 21492
Date 03-Nov-67
Author R ATKINSON
Addressee SPRINGGATE & KELLOGG
DOLIN & CUTRIGHT
RHODES & HOWELL

Description Memo states natcp production step is limiting production of 2,4,5-T acid and suggests that purchasing outside natcp would allow for greater production of 2,4,5-T acid at the Nitro plant. A savings of $98,000.00 per year is predicted.

15713

Exhibit #P1180

PIN #	21389
Date	11-Oct-68
Author	F HELMER
Addressee	R.A. ATKINSON & W.R. UDELL E.A. CUTRIGHT & O.E. DOLIN V.L. RHODES & J.C. STRUM
Description	Report on Na 2,4,5-T cake washing to improve color and residual TCP.

Exhibit #P1181

PIN #	00000
Date	16-Nov-68
Author	G R HIGGINBOTHAM
Addressee	HUANG, ANITA & FIRESTONE, DAVID VERRETT, JACQUELINE & RESS, JOHN CAMPBELL, A.D.
Description	Story in "Nature" called Chemical and Toxicological Evaluations of Isolated and Synthetic Chloro Derivatives of Dibenzo-p-dioxin; written by Higginbotham Huang, Firestone, Verrett, Ress, Campbell.

Exhibit #P1182

PIN #	DS00012604-5
Date	19-Dec-69
Author	F R KENNEDY
Addressee	BALDESCHWEILER, J. & EISLER, MILTON
Description	Letter from Kennedy 2,4,5-T submitted to to Baldeschweiler re: Bionetics Corp.

Exhibit #P1183

PIN #	148293-5
Date	11-Mar-70
Author	LAWRENCE FISHBEIN PHD
Addressee	FALK, DR HANS L
Description	Document indicates that members of the 2,4,5-T industry met with various governmental agencies and discussed "Chlorophenols and Chlorodibenzodioxins". Dr. Linn (Dow) indicated that no

15714

teratological changes or lesions were observed when using T with a level of .5ppm. Dr Kolbye stated that even clean 2,4,5-T is a teratological hazard. Tests have shown that purified T as well as T with 4ppm caused a high rate of mortality .

Exhibit #P1184

PIN #	74316-64
Date	29-Jun-70
Author	G ROBERT SIDO
Addressee	USDA
Description	Packet of documents regarding Monsanto's request for an amendment of a registration regarding the product known as 2,4-D/2,4,5-T Amine Brush Kill.

Exhibit #P1185

PIN #	74480-29
Date	10-Jul-70
Author	G ROBERT SIDO
Addressee	ALFORD, HAROLD G & USDA
Description	This is a packet of documents regarding the USDA's suspension of the registration of the product known as 2,4,5-T Low Volitile Ester Brush Killer.

Exhibit #P1186

PIN #	76737-843
Date	23-Jul-70
Author	PSAC
Addressee	BALDERSWIELER, J D & MACLEOD, COLIN M BRADY, NYLE & FARBER, EMMANUEL WILSON, JAMES G & OTHERS
Description	This document is the PSAC's draft report on 2,4,5-T.

Exhibit #P1187

PIN #	7039-7040

Date 13-Nov-70
Author ROBERT MUELLER
Addressee CHARLES ZORSCH & MONSANTO

Description Document entitled, "Summary of Toxicological Information on 2,4-D and 2,4,5-T Type Herbicides and an Evaluation of the Hazards to Livestock Associated with Their Use."

Exhibit #P1188
PIN # 74416-79
Date 21-Dec-70
Author A E CONROY II
Addressee MONSANTO CO.
Description Packet of documents mailed by the EPA regarding Monsanto's labeling numerous products containing 2,4-D or 2,4,5-T.

Exhibit #P1189
PIN # 00000
Date 15-Jan-71
Author CHARLES ZORSCH
Addressee GEORGIA PACIFIC & REX BLACK
WERNER HARRIS
Description Letter from the Medical Director at Dow which advises a user of Esteron 99 that the skin irritation is not related to the use of that product.

Exhibit #P1190
PIN # 00000
Date 01-Mar-71
Author SMITH POLAND
Addressee
Description A Health Survey of Workers in a 2,4-D and 2,4,5-T Plant with special attention to chloracne, porphyria cutanea tarda, and psychologic parameters; written by Poland, Smith, Metter, Possick.

Exhibit #P1191

15716

PIN # 74284-98
Date 24-Feb-72
Author G ROBERT SIDO MON CO
Addressee USDA
Description Packet contains various documents regarding Monsanto's request of th USDA for a registration renewal of their product known as 2,4,5-T Isooctly Ester Tech Grde.

Exhibit #P1192
PIN # 74392-03
Date 01-Mar-72
Author ROBERT SIDO MON
Addressee USDA
Description Packet of documents regarding Monsanto's renewal registration of the product known as 2,4,5-T Butyl Ester Technical Grade.

Exhibit #P1193
PIN # DS22629-32
Date 20-Nov-72
Author J J LUKES
Addressee LAVERGNE, E.A. & FISH, G.L.
O'LEARY, K.J. & IRANI, R.R.
FILES
Description Interoffice memorandum from Lukes to Lavergne re: Recovery of D&T from Agent Orange; cited the proposed progress for the recovery of saluble 2,4-D butyl esther and 2,4,5-T acid from Agent Orange. The potential advantages as well as the disadvantages of such a program were reviewed.

Exhibit #P1194
PIN # DS00021570-1
Date 23-Jan-73
Author A WHYTE
Addressee GALLUP, W.A. & CRYBERG, R.L.
JANZ, W.A. & LASCO, R.H.
LAVERGNE, E.A. & FILES

Description Memo from Whyte to Gallup re: Progress Report, January, 1973; Progress report on the dioxin removal from Agent Orange.

Exhibit #P1195

PIN #	00000
Date	01-Sep-73
Author	DAVID FIRESTONE
Addressee	
Description	"Etiology of Chicken Edema Disease" written by David Firestone.

Exhibit #P1196

PIN #	00000
Date	01-Sep-73
Author	STEHL R H CRUMMETT W B
Addressee	
Description	"Determination of Chlorinated Dibenzo-p-dioxins and Dibenzo-p-furans in Various Materials" written by W.B. Crummett and R.H. Stehl.

Exhibit #P1197

PIN #	00000
Date	01-Sep-73
Author	BRADY T P LANGER H G
Addressee	BRIGGS, P.R.
Description	"Formation of Dibenzodioxins and Other Condensation Products from Chlorinated Phenols and Derivatives" written by H.G. Langer, T.P. Brady, and P.R. Briggs.

Exhibit #P1198

PIN #	DOW5593-95
Date	08-Jul-74
Author	DD MCCOLLISTER
Addressee	M. LENG & W. CRUMMETT J. DAVIDSON & P. GEHRING GETZENDANER & JENSEN, ET AL
Description	FIRST MEMO IS FROM MCCOLLISTER TO LENG DIRECTING THAT LENG LETTER OF 7/3/74 IS NOT TO BE SENT OUT UNTIL IT IS KNOWN WHAT EPA'S POLICY IS GOING TO BE WITH RESPECT TO

15718

HANDLING THE RESIDUE TOLERANCE PETITION. SECOND MEMO FROM LENG TO MCCOLLISTER AGREES TO HOLD THE LETTER BUT QUESTIONS WHETHER DOW IS OBLIGATED TO SUBMIT PERTINENT INFORMATION TO RESIDUES AND TOXICOLOGY. SAYS NOT INFORMING GOVERNMENT ABOUT TCDD IN 2,4,5-T IS WHAT GOT THEM IN TROUBLE IN THE FIRST PLACE & THAT WITHHOLDING INFORMATION ONLY MAKES THE GOVERNMENT THINK DOW IS TRYING TO HIDE SOMETHING FROM THEM. LETTER STATES THAT DISMISS OF PUBLIC HEARING BY EPA DOES NOT MEAN THERE ARE NO PROBLEMS AND REQUESTS ADDITIONAL DATA TO PREPARE AMENDMENT OF 2,4,5-T REPORT AND NOTES THEY HAVE NO TOLERANCES FOR 2,4,5-T .

Exhibit #P1199

PIN #	294508
Date	11-Sep-74
Author	RENATE D KIMBROUGH
Addressee	DIRECTOR & CLINICAL CHEMISTRY DIVISION
Description	Memorandum from Kimbrough to Director of Clinical Chemistry Division re: Microscopic Examination of Livers and Ear Lobes of Rabbits; cc: Dr. Meath, Dr. Carter, Dr. Falk, Mr. Barthel, Dr. Liddle, Dr. Clinn.

Exhibit #P1200

PIN #	294510
Date	06-Nov-74
Author	JOHN H RICHARDSON
Addressee	CARTER, COLEMAN D. & HEATH BARTHEL
Description	Letter from Richardson to Carter re: Animal Studies with 2,3,7,8-TCDD.

Exhibit #P1201

PIN #	000000
Date	01-Apr-79
Author	EPA DRAFT
Addressee	EPA
Description	This document is the preliminary draft of an EPA study entitled, "Dioxins: Sources, Transport, Exposure, and Control."

15719

Exhibit #P1202

PIN #	JUS 312 94-6
Date	28-Aug-80
Author	FRANK S. SERDY
Addressee	EPA - R.J. TAYLOR
Description	Letter to EPA from Monsanto requesting EPA cancellation of all 2,4-D registrations held by Monsanto, removal of Monsanto from list of data submitters and producer of this chemical.

Exhibit #P1203

PIN #	JUS 312 88
Date	03-Dec-80
Author	FERIAL S BISHOP
Addressee	MONSANTO COMPANY
Description	Letter from U.S. Environmental Protection Agency regarding notice sent on September 23, 1980, notifying of intent to cancel registrations of certain EPA products including certain Monsanto 2,4-D, 2,4,5-T products.

Exhibit #P1204

PIN #	DS1266-94
Date	26-Apr-83
Author	FRANK L BAUER
Addressee	
Description	Minutes of meeting on April 26, 1963 at Edgewood Arsenal to discuss and evaluate the toxicity of 2,4-D and 2,4,5-T compounds with particular emphasis on use of these materials in military operations as herbicides.

Exhibit #P1205

PIN #	DS00003810-1
Date	27-Jun-83
Author	E L CHANDLER
Addressee	PIERSON, P.G. & LINDEMANN, R.F.

15720

KENNEDY, F.R.

Description Letter from Chandler to Pierson. Chandler submitted a recommendation for the government specifications for Agent Orange relative to the free acid.

Exhibit #P1206

PIN # 001564
Date 14-Sep-65
Author Agricultural Research - St. Louis
Addressee Take, E F (Nitro) & Dunlap,W P
Stephens,J A & Sharp,D B
Description Analysis of four autoclave batches indicates that, although it was previously known (April, 1965) that the concentration of TDD in the TCP is approximately equal to the concentration of TDD in T-acid produced from the TCP, during April 1965 it was observed that production of TDD rose to an all-time high, and it has remained much higher than the previous norm.

15721

IV. B. Plaintiffs respectfully submit the following initial list of documents in response to paragraph IV. (E) (2) of Magistrate's Pretrial Order No. 17. Plaintiffs reserve the right to amend this list in conformity with the schedule for filing the amendment to this Pretrial Order and the final form.

Plaintiffs refer all counsel in connection with this list to all Rule 26 (B)(4)(a)(1) statements and summaries together with attachments thereto which have been filed previously some of which will be filed in amended form in conformity with the Magistrate's ruling in those regards.

The documents are, as follows:

Exhibit #P0002

PIN # 19
Date
Author B P MCNAMARA
Addressee
Description McNamara, B.P., Summary of toxicity Data of Phenoxyacitates.

Exhibit #P0003

PIN # 48
Date
Author G LAWTON
Addressee
Description Lawton, G. "E.300 Chloracne Study."

15722

Exhibit #P0004

PIN # 69-80

Date

Author VARIOUS VARIOUS

Addressee

Description Sixth, Fourteenth, Second, Seventh, Ninth, Tenth Eleventh, Twelfth, Thirteenth, Fifteenth, Sixteenth, Seventeenth, Quarterly Progress Reports to National Cancer Institute, Program of Carcinogenesis Studies, from Bionetics Research Laboratories, Inc.

Exhibit #P0005

PIN # 56

Date

Author D W GOLDSTEIN

Addressee

Description Goldstein, D.W. "Chloracne from Marketing Herbicide."

Exhibit #P0006

PIN # 56

Date

Author LOUIS SCHWARTZ

Addressee G.O. NELSON

Description Letter from Louis Schwartz to G.O. Nelson dated May 11, 1949.

15723

Exhibit #P0007

PIN # 88

Date

Author UNKNOWN

Addressee

Description Unlisted Drugs list.

Exhibit #P0008

PIN # 89

Date

Author BENJAMIN WITTEN

Addressee

Description Title page, pages 202-205 and page 308 of Edgewood Arsenal Technical Report 4210 "The Search for Toxic Chemical Agents: by Benjamin Witten.

Exhibit #P0040

PIN # 00

Date 01-Jan-01

Author REVIEW V A

Addressee PUBLISHED & BIBLIOGRAPHY
DIOXIN

Description Article entitled "Veteran's Administration review of literature on herbicides, including phenoxy herbicides and associated dioxins," two volumes which comprise a fairly comprehensive search of the

15724

literature regarding herbicides which may be offered in whole or in part, at least be

certain articles cited therein may be used at time of trial.

Exhibit #P0043

PIN #	47
Date	01-Jan-43
Author	L SCHWARTZ
Addressee	
Description	Schwartz, L., "An Outbreak of Halowax Acne ('Cable Rash') Among Electricians," 122 JAMA 158-61 (1943).

Exhibit #P0049

PIN #	58
Date	16-Aug-49
Author	LOUIS SCHWARTZ
Addressee	G.O. NELSON
Description	Letter from Louis Schwartz to G.O. Nelson dated August 16, 1949.

Exhibit #P0050

PIN #	00
Date	05-Dec-49
Author	WILLIAM ASHE

Addressee SUSKIND, RAYMOND & REPORT ON MONSANTO

Description This report is dated December 5, 1949 from Dr. Wm. Ashe and Dr. Raymond Suskind (Dermatologist) to Monsanto Management, and the Kettering Laboratory in Cincinnati, Ohio and demonstrates acute neurotoxic, systemic, and dermatological disorders to workers exposed to TCDD also shows immune disregulations following exposure.

Exhibit #P0051

PIN # 00
Date 19-Dec-49
Author G D NELSON
Addressee ASHE, WM MD
Description Letter criticizes Ashe's initial reporting of the serious injuries of Monsanto workers at 2,4,5-T Plant following incident in autoclave.

Exhibit #P0052

PIN # 00
Date 27-Dec-49
Author WILLIAM ASHE
Addressee NELSON, G D
Description Letter regarding Ashe's response to the company's (Monsanto) criticism of his findings RE Workers seriously injured at

the 2,4,5 -T Plant in Nitro, West Virginia in 1949.

Exhibit #P0064

PIN #	00
Date	01-Jan-53
Author	WILLIAM ASHE
Addressee	SUSKIND
Description	This report dated 1953 summarizes the findings of Dr. William Ashe and Dr. Raymond Suskind on the 1949 incident at Nitro Plant in West Virginia; both Doctors are listed at the Kettering Laboratory in the Department of Preventive Medicine and Industrial Health, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

Exhibit #P0073

PIN #	00
Date	06-Jun-55
Author	WILLIAM ASHE
Addressee	SUSKIN, RAYMOND
Description	This document clearly reflects in 1955 Monsanto's characterization of 2,4,5-T and its dioxins as chemically intoxicating, characterized by acneform skin lesions, hepatitis, disturbed lipid metabolish , peripheral neuropathy, and probably mild central nervous system involvement.

15727

Exhibit #P0085

PIN # 63
Date 01-Jan-56
Author P DUGOIS
Addressee COLOMB, H.

Description Dugois, P. and Colomb, H., "Chloracne from 2,4,5-Trichlorophenol,"63 BULLETIN DE LA SOCIETE FRANCAISE 262-63 (1956) (translation).

Exhibit #P0095

PIN # 00
Date 01-Jan-57
Author J KIMMIG
Addressee SCHULTZ, K H

Description PUBLISHED IN DERMATOLOGICA VOL. 115:540-546 (1957)

Exhibit #P0104

PIN # 01
Date 01-Oct-57

15728

Author VON J KIMMIG

Addressee SCHULZ, K.H.

Description Kimmig, J., Schulz, K.H., "Berufiche Akne (sog. Chlorakne) durch chlorierte aromatische zyklische Ather", and English Translation, "Occupational Chloracne Caused by Aromatic Cyclic Ethers," 115 DERMATOLOGICA 540-46 (1957).

Exhibit #P0117

PIN # 11

Date 01-Jan-59

Author M TOMITA

Addressee UEDA, S. & NARISADA, M.

Description Tomita, M., Ueda, S., Narisada, M., "Studies on the Dibenzo-ppdioxin (Diphenylene Dioxide) Derivatives XXVII. Synthesis of Polyhalodiobenzo-p-dioxin" (1959).

Exhibit #P0129

PIN # 21

Date 05-Oct-59

15729

Author F HOFFMANN

Addressee

Description Extract of Report on Trip to Europe, Hoffmann, F., October 5, 1959.

Exhibit #P0130

PIN # 21

Date 05-Oct-59

Author F HOFFMANN

Addressee

Description Report on Trip to Europe, Hoffmann, F. October 5, 1959.

Exhibit #P0151

PIN # 00

Date 01-Jan-61

Author ET AL BAUER

Addressee

Description Article by BAUER published in "FUER GEWERBEPATHOLOGY UN GEWERBEHYGIN" VOL. 18:538-555.

Exhibit #P0152

PIN # 36

15730

Date 01-Jan-61
Author A YARTZOFF
Addressee

Description Yartzoff, A., et al., "Studies of the Chick Edema Factor, II. Isolation of a Toxic Substance" (1961).

Exhibit #P0162
PIN # 25
Date 08-Mar-62
Author J W BROWN
Addressee

Description Brown, J. W., "Preliminary Report of Vegetational Spray Tests" (March 8, 1962).

Exhibit #P0175
PIN # 02
Date 26-Jun-62
Author E L JONES MD
Addressee HELEN KRIZEK, PH.D.

Description Jones, E.L., Krizek, H., "A Technic for Testing Acnegenic Potency in Rabbits, Applied to the Potent Acnegen 2,3,7,8-Tetrachlorodiobenzo-p-Dioxin,"

J. INVESTIGATIVE DERMATOLOGY 511-17 (1962).

Exhibit #P0180

PIN # 31
Date 04-Aug-62
Author HAROLD BROWN
Addressee SECY OF DEFENSE

Description Memorandum from Harold Brown to the Secretary of Defense dated August 4, 1962.

Exhibit #P0181

PIN # 90
Date 07-Sep-62
Author ROBERT J GOODLOW
Addressee ARMY CH.RES.DEV.LAB

Description September 7, 1962 memo from Robert J. Goodlow to Commanding Officer, U.S. Army Chemical Research and Development Laboratories.

Exhibit #P0182

PIN # 91
Date 28-Sep-62
Author B WITTEN
Addressee ARMY CH.RES.DEV.LAB

Description September 28, 1962 memo from B. Witten to Commanding Officer, U.S. Army Chemical Research and Development laboratories.

Exhibit #P0183

PIN # 92
Date 04-Oct-62
Author D W FALCONER
Addressee

Description October 4, 1962 memo from D.W. Falconer to Commanding Officer, U.S. Army Chemical Research and Development Laboratories.

Exhibit #P0184

PIN # 93
Date 15-Oct-62
Author ROBERT J GOODLOW
Addressee ARMY CH.RES.DEV.LAB

Description October 15, 1962 memo from Robert J. Goodlow to Commanding Officer, U.S. Army

Chemical Research and Development
laboratories.

Exhibit #P0187

PIN # 49
Date 28-Nov-62
Author DAVIS W GOLDSTEIN
Addressee KEY, MARCUS M

Description Letters from Davis W. Goldstein to Marcus
M. Key dated November 28, 1962, December
17, 1962, and April 5, 1963.

Exhibit #P0188

PIN # 94
Date 29-Nov-62
Author ROBERT J GOODLOW
Addressee ARMY CH.RES.DEV.LAB

Description November 29, 1962 memo from Robert J. Goodlow to Commanding Officer, U.S. Army
Chemical Research and Development
Laboratories.

Exhibit #P0189

PIN # 27
Date 01-Dec-62
Author JA COATES
Addressee POLLACK, H & SHARPE, L
ROBERT PHELPS

Description Coates, J., Sharpe, L., Pollack, H., "The Present Status of Chemical Control of Vegetation in Relation to Military Needs" (December, 1962) including distribution letter by Robert Phelps.

Exhibit #P0190

PIN # 95
Date 10-Dec-62
Author B WITTEN
Addressee ARMY CH.RES.DEV.LAB

Description December 10, 1962 memo from B. Witten to Commanding Officer, U.S. Army Chemical Research and Development laboratories.

Exhibit #P0191

PIN # 28
Date 11-Dec-62
Author NONE HEASTON

Addressee

Description Heaston, "Chemical Control of Vegetation"
(December 11, 1962).

Exhibit #P0209
PIN # 50
Date 27-Mar-63
Author MARCUS M KEY
Addressee GOLDSTEIN, DAVIS W.

Description Letter with attachments from Marcus M. Key
to Davis W. Goldstein dated March 27, 1963.

Exhibit #P0210
PIN # 44
Date 28-Mar-63
Author D J BIRMINGHAM
Addressee KEY, M.M.

Description Birmingham, D.J., Key, M.M., "Dermatoses
Investigation" (March 28, 1963).

Exhibit #P0214

PIN # 51
Date 19-Apr-63
Author MARCUS M KEY
Addressee GOLDSTEIN, DAVIS W.

Description Letter from Marcus M. Key to Davis W. Goldstein dated April 19, 1963.

Exhibit #P0217

PIN # 65
Date 22-Apr-63
Author MARCUS M KEY
Addressee MCCRANEY, H.C.

Description Letter from Marcus M. Key to H.C. McCraney dated August 22, 1963.

Exhibit #P0218

PIN # 52
Date 25-Apr-63
Author NONE NONE
Addressee U.S. DEPT OF LABOR

Description Letter to U.S. Department of Labor dated April 25, 1963.

Exhibit #P0219

PIN # 10
Date 26-Apr-63
Author COL FRANK L BAUER
Addressee

Description Minutes of a Meeting held to Discuss and Evaluate the Toxicity of 2,4-D and 2,4,5-T compounds, with appendices, dated April 26, 1963.

Exhibit #P0224

PIN # 15
Date 09-May-63
Author NONE AGENDA
Addressee PSAC & THE PENTAGON

Description Tentative Agenda for Meeting of the PSAC, The Pentagon, Washington, D.C., May 9, 1963 with attachments. Attachments include BRIEFING TO PRESIDENT'S SCIENTIFIC ADVISORY COMMITTEE 9 MAY 1963 BY CBR AGENCY PERSONNEL ON POSSIBLE HEALTH HAZARD OF

PHENOXYACETATES AS RELATED TO DEFOLIATION

OPERATIONS IN VIETNAM

Exhibit #P0225

PIN # 04

Date 15-May-63

Author SCI ADVIS COMM PRESIDENTS

Addressee

Description President's Science Advisory Committee "Use of Pesticides" (May 15, 1963).

Exhibit #P0228

PIN # 53

Date 27-May-63

Author NONE NONE

Addressee KEY, MARCUS M.

Description Letter to Marcus M. Key dated May 27, 1963.

Exhibit #P0243

PIN # 23

Date 29-Jul-63

Author J C WARD

Addressee

Description Meeting of Subcommittee on Herbicides, July 29, 1963 by Ward, J.C.

Exhibit #P0244

PIN # 24

Date 30-Jul-63

Author R G MCCALL

Addressee ALVELLINO, J.D.

Description Memo for Record, July 30, 1963 from McCall, R.G. and Avellino, J.D.

Exhibit #P0246

PIN # 64

Date 09-Aug-63

Author H C MCCRANEY

Addressee MARCUS M. KEY

Description Letter from H.C. McCraney to Marcus M. Key dated August 9, 1963.

Exhibit #P0251

PIN # 26
Date 10-Oct-63
Author P OLENCHUCK
Addressee

Description Olenchuck, P. "Evaluation of Herbicide Operation in the Republic of Vietnam" (October 10, 1963).

Exhibit #P0261

PIN # 00
Date 01-Jan-64
Author ARTHUR W GALSTON
Addressee

Description Book published by Dr. Galston on plant physiology, Prentice-Hall, 1st edition, 1961; 2d edition 1964, 3rd edition, 1980

(with P.J. Davies and R.L. Satter).

Exhibit #P0262

PIN # 61
Date 01-Jan-64
Author NONE NONE
Addressee LETTER TO EDITOR

Description Letter to the editor "New Weed Killers Produce Chloracne," 189 JAMA 66-67

15741

(1964).

Exhibit #P0296

PIN # 85
Date 28-May-64
Author KENNETH KOPPLE
Addressee GRANITO, CHARLES

Description May 28, 1964 letter from Kenneth Kopple to Charles Granito.

Exhibit #P0298

PIN # 03
Date 01-Jun-64
Author JACOB BLEIBERG MD
Addressee MARVEN WALLEN, MD & ROGER BRODKIN, MD
I.R. APPLEBAUM, MD

Description Bleiberg, J., Wallen, M., Brodkin, R., Applebaum, I.L., "Industrially Acquired Porphyria," 89 ARCHIVES OF DERMATOLOGY 793-97 (1964).

Exhibit #P0310

PIN # 86
Date 18-Jul-64

Author GERHARD CLOSS

Addressee GRANITO, CHARLES

Description July 18, 1964 letter from Gerhard Closs to Charles Granito.

Exhibit #P0311

PIN # 87

Date 21-Jul-64

Author CHARLES GRANITO

Addressee CLOSS, GERHARD

Description July 21, 1964 letter form Charles Granito to Gerhard Closs.

Exhibit #P0312

PIN # 45

Date 24-Jul-64

Author D H GROTH

Addressee

Description Groth, D.H., "Microscopic Changes in Rabbits Secondary to Application of Various Pesticides to their Ears" (July 24, 1964).

Exhibit #P0335

PIN # 54
Date 03-Dec-64
Author DAVID H GROTH
Addressee UPTON, E.T.

Description Letters from David H. Groth to E.T. Upton dated December 3, 1964, and February 26, 1965.

Exhibit #P0340

PIN # 55
Date 11-Dec-64
Author EDWIN T UPTON
Addressee GROTH, DAVID H.

Description Letters from Edwin T. Upton to David H. Groth dated December 11, 1964, January 14, 1965, February 17, 1965 and June 2, 1965.

Exhibit #P0353

PIN # 46
Date 12-Jan-65
Author D H GROTH

Addressee

Description Groth, D.H., Project Development and Approval "Identification of the Toxic Factor in 2,4,5-trichlorophenoxyacetic Acid (2,4,5-T)" (January 12, 1965).

Exhibit #P0397

PIN # 73255

Date 17-Mar-65

Author EMMET KELLY

Addressee STEPHENS, JOHN

Description This letter was passed around monsanto, to Dr. Paul Hoffman, and others as initialed on letter, and shows knowledge of TCDD being by Dow and Monsanto the "most toxic compound they (Dow) has ever experienced." Instructions to lab to use extreme caution in handling, since even trace amounts 200ppb have caused cholacne in rabbits. This further shows they could detect dioxin in the parts per billion range in 1965.

15745

Exhibit #P0474

PIN # 59
Date 01-Jan-66
Author M M KEY
Addressee BIRMINGHAM, D.J.

Description Key, M.M., Birmingham, D.J., "Occupational Chloracne", INTERNATIONAL CONGRESS ON OCCUPATIONAL HEALTH 752-55 (1966).

Exhibit #P0475

PIN # 62
Date 01-Jan-66
Author D J BIRMINGHAM
Addressee

Description Birmingham, D.J., "Preventable Occupational Dermatoses, "12 ARCH ENVIRON HEALTH 639-43 (1966).

Exhibit #P0556

PIN # 00
Date 01-Jan-67
Author J R ALLEN
Addressee CARSTENS, L A

15746

Description Paper entitled "Light Electron Microscope Investigations in Macaca Mulatta Monkeys Fed Toxic Fat." American Journal of Vet. Res. 28: 1513-1526.

Exhibit #P0557

PIN # 33
Date 01-Jan-67
Author NONE NONE
Addressee

Description Portion of 1967 CHECO Report.

Exhibit #P0590

PIN # 22
Date 24-Feb-67
Author A P BEUTEL
Addressee HEBBELER, JAMES W

Description Letter to James W. Hebbeler from A.P. Beutel dated February 24, 1967.

15747

Exhibit #P0627

PIN # 82

Date 01-Jun-67

Author NONE NONE

Addressee

Description Edgewood Arsenal Research Laboratories SOP NO 70-3 dated June 1, 1967, and Appendices A-H.

Exhibit #P0632

PIN # 32

Date 25-Jun-67

Author NONE NONE

Addressee

Description Portion of the DI7AF Report on Ranch hand Operations, June 25, 1967.

Exhibit #P0672

PIN # 20

Date 26-Sep-67

Author A P BEUTEL

Addressee FREDERICKS & ANDERSON, ANDREW W SHEAD, C.G. & KRATZ, W. J.

15748

Description Letters to Fredericks with attachement, Andres W. Anderson, C. G. Shead and W. J. Kratz from A. P. Beutel, dated September 26, 1967.

Exhibit #P0674

PIN # 09
Date 01-Oct-67
Author W L ZIELINSKI
Addressee FISHBEIN, L.

Description Zielinski, W.L., Fishbein, L. "Gas Chromatographic Measurement of Disappearance Rates of 2,4-D and 2,4,5-T Acids and 2,4-D Esters in Mice, "15 J. AGR. FOOD CHEM. 841-44 (1967).

Exhibit #P0675

PIN # 17
Date 01-Oct-67
Author R BRETTS
Addressee DENTON, F.

Description Bretts R. and Denton F., "An Evaluation of Chemical Crop Destruction in Vietnam,"

October, 1967.

Exhibit #P0687

PIN # 18

Date 30-Oct-67

Author JAMES A HEBBLER

Addressee G.L. QUINN

Description Memorandum from James A. Hebbeler to G.L. Quinn "Comments on Rand Herbicide Reports" October 30, 1967).

Exhibit #P0705

PIN # 34

Date 15-Dec-67

Author LT COL SHADE

Addressee

Description Handwritten note of telephone call from Lt. Col. Shade dated December 15, 1967.

Exhibit #P0714

PIN # 37

Date 01-Jan-68

Author ET AL G R

Addressee

Description Preliminary draft and final version of Higginbotham, G.R., et al., "Chemical and Toxicological Evaluations of Isolated and Synthetic Chloro Derivatives of Dibenzo-p-dioxin, "222 NATURE 702-03 (1968).

Exhibit #P0789

PIN # PB-223159

Date 01-Aug-68

Author RESEARCH LABS BIONETICS

Addressee US DEPT OF COMMERCE & FOR NCI

Description Volume I entitled "Evaluation of Carcinogenic, Tera-Togenic, and Mutagenic Activities of Selected Pesticides and Industrial Chemicals, Bionetics Research Labs, Inc. Prepared for National Cancer Institute, And Under The Department of Commerce, National Technical Information Service; Volume I evaluates the carcinogenic risks to animals and man.

13751

Exhibit #P0790

PIN #	PB-223160
Date	01-Aug-68
Author	RESEARCH LABS BIONETICS
Addressee	VOLUME II & FOR NCI

Description Volume II entitled "Teratogenic Study in Mice and Rats" prepared by Bionetics Labs, Inc. for the National Cancer Institute, shows clear teratogenic effects in two species of rodents which led to the military suspension of spraying in Vietnam.

Exhibit #P0791

PIN #	PB-223161
Date	01-Aug-68
Author	RESEARCH BIONETICS
Addressee	FOR NCI & VOLUME III MUTAGENIC EFFECTS

Description Volume III of Bionetics Report Prepared for National Cancer Institute entitled "Mutagenic Study".

15752

Exhibit #P0828

PIN # 00

Date 01-Jan-69

Author E MRAK

Addressee

Description Paper entitled "Report of the Secretary's Commission on Pesticides and their Relationship to Environmental Health." U.S. Department of Health, Education, and Welfare, Washington,D.C.

Exhibit #P0829

PIN # 30

Date 01-Jan-69

Author J R M INNES

Addressee

Description Innes, J.R.M, et al., "Bioassay of Pesticides and Industrial Chemicals for Tumorigenicity in Mice: A Preliminary Note, "42 J. NAT'L CANCER INST. 1101-14 (1969).

15753

Exhibit #P0830

PIN # 35

Date 01-Jan-69

Author NONE NONE

Addressee

Description Contaminants Branch DFCT, "Current Status of the Chick Edema Factor Problem" (1969).

Exhibit #P0863

PIN # 08

Date 29-Oct-69

Author DR LEE A DUBRIDGE

Addressee

Description Press Release dated October 29, 1969 by Office of Science and Technology re: Restrictions on the use of 2,4,5-T

Exhibit #P0873

PIN # 39

Date 09-Dec-69

Author J W COOKE

Addressee

Description Memorandum of Conference, December 9, 1969

by Cooke, J.W.

Exhibit #P0895

PIN # 43
Date 28-Jan-70
Author NONE NONE

Addressee

Description Summary of Meeting January 28, 1970 re: Chick Edema Factor.

Exhibit #P0899

PIN # 40
Date 06-Feb-70
Author A D CAMPBELL

Addressee

Description Memorandum of Conference, February 6, 1970,

"Analysis of Chick Edema Factor in Pesticides," by Campbell, A.D.

Exhibit #P0901

PIN # 12
Date 07-Feb-70
Author T WHITESIDE

Addressee

Description Whiteside, T., "A Reporter at Large: Defoliation," THE NEW YORKER (February 7, 1970).

Exhibit #P0906

PIN # 41
Date 11-Feb-70
Author NONE NONE
Addressee

Description Summary of February 11, 1970 meeting on Chick Edema as an Industrial Checmical Contaminant.

Exhibit #P0913

PIN # 13
Date 05-Mar-70
Author T WHITESIDE
Addressee EDITOR OF NEW YORKER

Description Whiteside, T., "Letter to the Editor," THE NEW YORKER (March 5, 1970).

Exhibit #P0916

PIN # 38
Date 11-Mar-70
Author LAWRENCE FISHBEIN
Addressee DR. HANS L. FALK

Description Memorandum from Dr. Lawrence Fishbein to Dr. Hans L. Falk, "Meeting on Chlorophenols" (March 11, 1970).

Exhibit #P0920
PIN # 16
Date 17-Mar-70
Author DR E J BURGER
Addressee DR LEE A DUBRRIDGE

Description MISSING DOCUMENT

Exhibit #P0943
PIN # 14
Date 15-Apr-70
Author DR JESSE STEINFELD
Addressee SENATE SUBCOMMITTEE

Description Hearing on the effects of 2,4,5-T on man and the environment before the subcommittee on Energy Natural Resources, and the Environment of the Senate Committee on

Commerce, 91st Cong., 2d Sess. 167-89 (April 1970) (Statement of Dr. Jesse Steinfeld).

Exhibit #P0957

PIN # 81
Date 05-Jun-70
Author DR BERNARD JANDORF
Addressee DIR RESEARCH LABS & OTHERS

Description June 5, 1970 memorandum from Dr. Bernard Jandorf to Director of Research Laboratories, and memo routing slip dated June 10, 1970 from Dr. Jandorf to Dr. B. McNamara.

Exhibit #P0964

PIN # 14.1
Date 17-Jun-70
Author DR NED D BAYLEY
Addressee BYERLY, DR T.C.

Description Hearing on the Effects of 2,4,5-T and Related Herbicides on Man and the Environment Before the Subcommittee on Energy, Natural Resources, and the

15758

Environment of the Senate Committee on Commerce, 91st Cong., 2d Sess. 1-89 (June 17, 18, 1970) (Statements of Dr. Ned D. Bayley and Dr. T.C. Byerly).

Exhibit #P0987

PIN # 00
Date 01-Jan-71
Author A R ISENSEE
Addressee JONES, G E

Description Paper entitled "Absorption and translocation of root and foliage applied 2,4-dichlorophenol, 2,7-dichlorodibenzo-p-dioxin, and 2,3,7,8-tetrachlorodibenzo-p-dioxin. J. Agric. Food Chem. 19(6): 1210-1214.

Exhibit #P0988

PIN # 00
Date 01-Jan-71
Author K D COURTNEY
Addressee MOORE, J A

Description Published in the Toxicology and Applied Pharmacology, 20:396-403.

15759

Exhibit #P0989

PIN # 00

Date 01-Jan-71

Author G L SPARSCHU

Addressee ET AL

Description Paper entitled "Study of the Teratogenicity of 2,3,7,8-TCDD in the Rat." Food and Cosmetic Toxicology, 9:405-412, by Dow scientists.

Exhibit #P0990

PIN # 00

Date 01-Jan-71

Author R ROLL

Addressee

Description Paper entitled "Investigation of the Teratogenic Mechanism of 2,4,5-T With Mice" Food and Cosmetic Toxicology.9:671-676.

Exhibit #P0996

PIN # 06

15760

Date 11-Mar-71
Author DR COLIN M MACLEOD
Addressee BALDESCHWEILER,JD & BRADY, NYLE C
FARBER, EMMANUEL & KOTIN, PAUL
MACMAHON, BRIAN & OTHERS

Description Panel on Herbicides of the President's Science Advisory Committee, "Report on 2,4,5-T" (March 11, 1971)

Exhibit #P1024
PIN # 00
Date 01-Jan-72
Author P C KEARNEY
Addressee WOOLSON, A & ELLINGTON, C P JR

Description Persistence and metabolism of chlorodioxins in soils, Environ. Sci. Technol. 6(12): 1017-1019.

Exhibit #P1025
PIN # 00
Date 01-Jan-72
Author M L LENG
Addressee

Description Paper entitled "Residues in milk and meat

15761

and safety to livestock from the use of phenoxy herbicides in pasture and rangeland." Down Earth 28(1):12-20.

Exhibit #P1026

PIN # 00
Date 01-Jan-72
Author MATTHEW MESELSON
Addressee WESTING, ARTHUR H. & CONSTABLE, J D

Description Paper of presentation entitled "Background material relevant to presentations at the 1970 meeting of AAAS. United States Congressional Record. 118:6807-6813.

Exhibit #P1027

PIN # 00
Date 01-Jan-72
Author D NEUBERT
Addressee DILLMAN, I

Description Paper entitled "Embrytoxic Effects in Mice Treated With 2,4,5-T and 2,3,7,8-TCDD." Arch. Pharmacol. 272:243-264.

15762

Exhibit #P1035

PIN # 00
Date 01-Jan-73
Author R BAUGHMAN
Addressee MESELSON, M

Description Paper entitled:"Analytical Method for Detecting TCDD(dioxin): levels of TCDD in samples from Vietnam." Environmental Health Perspectives. 5:27-83.

Exhibit #P1036

PIN # 00
Date 01-Jan-73
Author P C KEARNEY
Addressee WOOLSON, E A & ISENSEE, A R
HELLING, C S

Description Paper entitled "Tetrachlorodibenzo-p-dioxin in the environment: sources, fate, and decontamination." Environ. Health Perspect. 5:273-277.

Exhibit #P1037

PIN # 00
Date 01-Jan-73
Author TON THAT TUNG
Addressee

Description Paper entitled "Le Cancer Primaire du Foie Au Viet-Nam." Chirurgie. 99:427-436.

Exhibit #P1038
PIN # 00
Date 01-Jan-73
Author ARTHUR H WESTING
Addressee

Description Report entitled "AAAS Herbicide Assessment Commission." Science 179:1278-1279.

Exhibit #P1039
PIN # 00
Date 01-Jan-73
Author B A SCHWETZ
Addressee ET AL

Description Chapter concerning the extreme toxicity of the TCDD molecule.

Exhibit #P1040

Pin # 00
date 01-jan-73
Author J B Greig
Addressee ET AL
Description Article published in Food and Cosmetics Toxicology Vol. 11, 585-595.

Exhibit #P1041

PIN # 00
Date 01-Jan-73
Author D NEUBERT
Addressee ZENS, P & ROTHENWALLNER, A
MERKER, H J

Description Paper Entitled: "A survey of the embrytoxic effects of TCDD in mammalian species." Environ. Health Perspect. 5:67-79.

Exhibit #P1042

PIN # 00
Date 01-Jan-73
Author J A MOORE
Addressee ET AL

Description Paper entitled "Postnatal Effects of Maternal Exposure to 2,3,7,8-TCDD.

15765

Environmental Health Perspectives.

5:81-95.

Exhibit #P1043

PIN # 60
Date 01-Jan-73
Author J B GREIG
Addressee

Description Greig, J.B., et al., "Toxic Effects of 2,3,7,8-Tetrachlorodibenzo-p-dioxin,ED. COSMET. TOXICOL. 585-95 (1973).

Exhibit #P1044

PIN # 00
Date 01-Jan-73
Author F A SMITH
Addressee ET AL

Description Published in Environmental Health Perspectives 5:81-85.

Exhibit #P1046

PIN # 42
Date 12-Sep-73
Author D FIRESTONE

15766

Addressee

Description Memorandum from Firestone, D., "Dioxins"
(September 12, 1973).

Exhibit #P1047
PIN # 00
Date 01-Jan-74
Author A LANG
Addressee EDITOR & NAT'L ACA. SCI.
WASH., D.C.

Description Paper as titled

Exhibit #P1048
PIN # 00
Date 01-Jan-74
Author J G VOS
Addressee MOORE, J A

Description Article entitled "Suppression of Cellular
Immunity in Rats and Mice by Maternal Treatment of 2,3,7,8-TCDD." Internal
Archives Of Allergy and Applied Immunology.
47:777-794 (1974)

15787

Exhibit #P1051

PIN # 00

Date 01-Dec-74

Author ROBERT BAUGHMAN

Addressee THESIS

Description Paper entitled "Tetrachlorodibenzo-Para-Dioxins in the Environment. Highresolution Mass Spectrometry at the picogram Level." Published and filed at Harvard University Library; Matthew Meselson Chairman

Exhibit #P1052

PIN # 00

Date 01-Jan-75

Author A R ISENSEE

Addressee JONES, G E

Description Paper entitled "Distribution of 2,3,7,8-TCDD in aquatic ecosystem." Environ. Sci. Technol. 9(7):668-672.

Exhibit #P1054

PIN # 00

Date 01-Jan-76

Author ARTHUR H WESTING

Addressee

Description Paper entitled "Ecological Consequences of the Second Indochina War." Stockholm International Peace Research Institute. Almquist and Wiksell. Stockholm, Sweden.

Exhibit #P1055

PIN # 00
Date 01-Jan-76
Author DIANE COURTNEY

Addressee

Description Published in BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY,16:674-681.

Exhibit #P1056

PIN # 00
Date 01-Jan-77
Author J R ALLEN
Addressee BARSOTTI, DEBORAH A. & VAN MILLER, J P ABRAHAMSON, L J & LALICH, J J

Description Paper entitled " Morphological changes in monkeys consuming a diet containing low levels of 2,3,7,8-

tetrachlorodibenzo-p-dioxin." Food Cosmet.
Toxicol. 5:401-410.

Exhibit #P1057

PIN #	00
Date	01-Jan-77
Author	J P VAN MILLER
Addressee	LALICH, J J & ALLEN, J R

Description Paper entitled "Increased incidence of neoplasms in rats exposed to low concentrations of 2,3,7,8 tetrachlorodibenzo-p-dioxin." Chemosphere.
10: 625-632.

Exhibit #P1058

PIN #	00
Date	01-Jan-77
Author	THOMAS WHITESIDE
	Addressee

Description Newspaper article entitled "A Reporter at Large; the pendulum and the toxic cloud."
New Yorker. July 25, 1977, pp 30-55.

15770

Exhibit #P1059

PIN # 04
Date 01-Mar-77
Author ALAN P POLAND MD
Addressee DONALD SMITH MD & GERALD METTER
PAUL POSSICK MD

Description Poland, A.P., Smith, D., Metter, G., Possick, P., "A Health Survey of Workers in a 2,4-D and 2,4,5-T Plant," 22 ARCH. ENVIRON. HEALTH 316-27 (1971).

Exhibit #P1062

PIN # 00
Date 01-Jan-78
Author ARTHUR H WESTING
Addressee

Description Paper entitled "Ecological Considerations regarding 2,3,7,8-tetracholordibenzo-p-dioxin." Ecological Bulletin (Stockholm) 27:285-294.

15771

Exhibit #P1063

PIN # 00
Date 01-Jan-78
Author E E MCCONNELL
Addressee ET AL

Description Published article of the extreme toxicity of TCDD

Exhibit #P1064

PIN # 00
Date 19-Jan-78
Author MATTHEW MESELSON
Addressee O'KEEFE, P & BAUGHMAN, ROBERT

Description Paper entitled "The Evaluation of Possible Health Hazards from TCDD in the Environment." Symposium on the use of Herbicides in Forestry. Arlington, Virginia. 21-22 February, 1978.

Exhibit #P1065

PIN # 00
Date 01-Jun-78

Author WHO IARC
Addressee MONOGRAPH & WORLD HEALTH ORG.

15772

Description International Agency for Research on Cancer, Sponsored by the World Health Organization Study on Polychlorinated Dibenzo-P-Dioxins and Polychlorinated Dibenzofurans.

Exhibit #P1067

Pin # 00
date 04-sep-78
Author Thomas Whiteside
Addressee

Description Article in magazine on the effects of defoliation in Vietnam and the massive spraying of herbicidal poisons.

Exhibit #P1068

PIN # 00
Date 01-Jan-79
Author L A SHADOFF
Addressee HUMMEL, R A & LAMPARSKI, L
DAVIDSON, J H

Description Paper entitled "A search for 2,3,7,8-TCDD in an environment exposed annually to 2,4,5-trichloro-phenoxyacetic acids ester(2,4,5-T) herbicides." Bulletin

15773

Environ. Contam. Toxicology. in press.

Exhibit #P1069

PIN # 00
Date 01-Jan-79
Author ARTHUR W GALSTON
Addressee

Description Article which described the persistence of TCDD in the soil, the fact that TCDD does bioaccumulate in the human fat tissue and milk, and the harm to our entire ecosystem from this extremely toxic substance.

Exhibit #P1070

PIN # 00
Date 01-Jan-79
Author R E FAITH
Addressee LUSTER, M I

Description TCDD is immunosuppressive

Exhibit #P1071

15774

PIN # 00
Date 01-Jan-79
Author ARTHUR GALSTON
Addressee

Description Plants, People and Politics. Bio. Science 20-7:405-410.

Exhibit #P1078
PIN # DOW33791-836
Date 01-Nov-79
Author ALVIN ET AL YOUNG
Addressee PUBLISHED

Description Paper entitled "Herbicide Orange Site Treatment and Environmental Monitoring":

Summary Report and Recommendations for Naval Construction Batallion Center, Gulfport, Mississippi, dated November, 1979.

Exhibit #P1079
PIN # 00
Date 01-Jan-80
Author ARTHUR W GALSTON
Addressee

description Book describing the life, death and

15775

diseases of the green plant including their sex lives and reproduction cycles, and their cancers.

Exhibit #P1080

PIN # 00
Date 01-Jan-80
Author ARTHUR W GALSTON
Addressee

Description Article entitled "Herbicides" in Academic American Encyclopedia. Arete Publishing Co., Inc., Princeton Forrestal Center, Princeton, New Jersey.

Exhibit #P1081

PIN # 00
Date 01-Jan-80
Author ARTHUR W GALSTON
Addressee KAUR-SAWHNEY, R

Description Article published in What's New in Plant Physiology. 11:5-8.

15776

Exhibit #P1082

PIN # 00
Date 01-Jan-80
Author ARTHUR GALSTON
Addressee KAUR-SAWHNEY, R & FLORES, H E

Description Paper entitled "Polyamine-induced DNA synthesis and mitosis in oat leaf protoplasts." published in Plant Physiology. 65:368-371.

Exhibit #P1083

PIN # 00
Date 01-Jan-80
Author CINCINNATI EPA
Addressee R AND D

Description Document published by the Research and Development Office of EPA Concerning the "Most Toxic Chemical Ever Synthesized by Man" Dioxin (2,3,7,8-TCDD).

Exhibit #P1084

PIN # 00
Date 01-Jan-80
Author PHILLIP E ENTERLINE
Addressee

15777

Description Published in Chest 78:2, AUGUST, 1980.

Exhibit #P1090

PIN # 29

Date 06-May-80

Author PHILIP HANDLER

Addressee GEN MURPHY A CHESNEY

Description Review of U.S. Air Force protocol: Epidemiological Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicide Orange (1980) with cover letter from Philip Handler to General Murphy A. Chesney dated May 6, 1980.

Exhibit #P1093

PIN # 90035

Date 27-Apr-81

Author WILLIAM GAFFEY

Addressee ROUSH, G JR MD & ET AL

Description Report on Dr. Moses report on Selikoff Study, while the reporter notes the abmornal clinical findings is careful to

15778

describe them as "Anti-Climatic."

Exhibit #P1094

Pin # 00

Date 24-Jun-81

Author Raymond Singer

Addressee ET AL 7 PUBLISHED

Description Paper entitled "Nerve Conduction Velocity Studies of Workers Employed in the Manufacture of Phenoxy Herbicides." Academic Press, Inc., Environmental Research 29:297-311(1982).

Exhibit #P1095

PIN # 00

Date 29-Jul-81

Author FIFRA EPA

Addressee DOCKET SHEET

Description All testimony and exhibits produced during the EPA'S cancellation hearing under FIFRA may be used at time of trial by plaintiffs.

15779

Exhibit #P1097

PIN # 00

Date 01-Jan-82

Author ALASTAIR HAY

Addressee

Description A comprehensive history of the manufacture of chlorinated phenoxy herbicides in the United States and abroad;the chemistry, biochemistry, and manufacturing processes of these chemical compounds; the spraying of these herbicides in massive quantities during the war in Vietnam; other documented human exposures; the harmful and toxic effects resulting from exposure to Agent Orange, 2,4,5-T and dioxin.

Exhibit #P1100

PIN # 00

Date 01-Jan-83

Author BIBLIOGRAPHY DIOXIN

Addressee CHRONOLOGICAL ORDER

Description These articles may be used in plaintiffs'

prima facie case.

Exhibit #P1101
PIN # 00
Date 01-Jan-83
Author MAUREEN HATCH
Addressee DOCTORAL THESIS

Description Dr. Hatch has submitted at her deposition a copy of her doctoral thesis at Columbia University on the Reproductive Toxicity of TCDD.

Exhibit #P1102
PIN # 00
Date 06-Jan-83
Author SOLID WASTE EPA
Addressee PUBLISHED DRAFT

Description Draft document prepared for the EPA Office of Solid Waste and Emergency Response, by the Environnmental Criteria and Assessment Office, Cincinnati, Ohio 45248 entitled "Health and Environmental Effects for: Tetra, Penta and

15781

Hexachlorodibenzo-p-dioxin."

Exhibit #P1103

PIN # 00
Date 07-Jan-83
Author AIR QUALITY EPA
Addressee DRAFT PUBLISHED

Description An overview on the health problems associated with dioxin, including the routes of possible human exposure, laboratory animal data, and conclusions of the extreme toxicity of the substance known as 2,3,7,8-TCDD or dioxin. Paper entitled "Research and Development, Health Assessment Document on Dioxin for the Office of Air Quality, Planning, and Standards, prepared by the Environmental Criteria and Assessment Office, Cincinnati, Ohio 45248.

Exhibit #P1104

PIN # 00
Date 07-Jan-83
Author WATER OFFICE EPA

15782

Addressee DRAFT PUBLISHED

Description 1983 Draft of EPA Document prepared for Office of Water Regulations and Standards by the Environmental Criteria and Assessment Office, Cincinnati, Ohio 45248 after Peer Review in July 1983.

Exhibit #P1108
PIN # 00
Date 01-Jan-84
Author ARTHUR GALSTON
Addressee UNPUBLISHED

Description Chapter submitted on the auxin-like effects of TCDD on plants; the devastation of the Vietnamese countryside from the spraying of herbicide Orange during the Vietnam War; extrapolation from plants to humans in assessing the horrible risks of the spraying of massive quantities of 2,4,5-T contaminated products.

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Exhibit #P1109

PIN #	00
Date	01-Jan-84
Author	ALASTAIR HAY
Addressee	MURPHY, SEAN & ROSE, STEVEN

Description Book describing the devastation of the use of manufactured poisons which are indiscriminately sprayed on the third world.

Exhibit #P1110

PIN #	00
Date	01-Jan-84
Author	BIBLIOGRAPHY HAY
Addressee	LIST OF CITATIONS & LIST OF BOOKS LIST OF ARTICLES & BY HAY BY OTHERS

Description The attached references are cited in Dr. Hay's summaries and curriculum vitae and will form the basis of Dr. Hay's testimony.

Exhibit #P1111

15784

PIN # 00
Date 01-Jan-84
Author MARVIN SCHNEIDERMAN
Addressee LIST OF CITATIONS & LIST OF ARTICLES BY AUTHOR & BY OTHERS

Description Dr. Schneiderman has cited references upon which he may rely in whole or in part in forming his opinions.

Exhibit #P1112

PIN # 00
Date 01-Jan-84
Author ELLEN SILBERGELD
Addressee LIST OF CITATIONS & LIST OF ARTICLES BY AUTHOR & BY OTHERS

Description Silbergeld has submitted numerous references, including her own original works and the works of others which will form in whole or in part the basis of her opinions at trial.

Exhibit #P1113

PIN # 00
Date 01-Jan-84

15785

Author RONALD KERMAN
Addressee LIST OF CITATIONS & LIST OF ARTICLES BY AUTHOR & BY OTHERS

Description Dr. Kerman has submitted comprehensive lists of references including his own articles and those of others which will form in whole or in part the basis of his opinions.

Exhibit #P1114
PIN # 00
Date 01-Jan-84
Author ALAN LEVIN
Addressee LIST OF CITATIONS & LIST OF ARTICLES BY AUTHOR & BY OTHERS

Description Dr. Levin has submitted a comprehensive list of references including his own works and those of others which will form the basis in whole or in part of his testimony.

Exhibit #P1115
PIN # 00
Date 01-Jan-84
Author ALAN LEVIN

15786

Addressee SPOHN, RICHARD & CHAPTER OF BOOK SUBMITTED & FOR PUBLICATION

Description Chapter of book submitted by Dr. Alan Levin for approval to the board of Medical Quality Assurance by the Society for Clinical Ecology (Northern California Chapter).

Exhibit #P1116

PIN # 00
Date 01-Jan-84
Author ALAN LEVIN
Addressee MEDICAL RECORDS & OTHER PATIENTS

Description Self Explanatory

Exhibit #P1117

PIN # 00
Date 01-Jan-84
Author MARVIN LEGATOR
Addressee LIST OF CITATIONS & LIST OF ARTICLES BY AUTHOR & BY OTHERS

Description Dr. Legator has submitted an extensive list of references including his own work and

15787

those works of others upon which he will base his opinions and his testimony in whole or in part.

Exhibit #P1118

PIN #	00
Date	01-Jan-84
Author	MARVIN LEGATOR
Addressee	NOTEBOOK & DIOXIN CITATIONS EXHIBIT DEPOSITION

Description Dr. Legator has submitted his personal notebook of dioxin citations and abstracts which was an exhibit to his deposition and in possession of all parties.

Exhibit #P1119

PIN #	00
Date	01-Jan-84
Author	LENNART HARDELL
Addressee	LIST OF CITATIONS & BY AUTHOR PUBLISHED

Description Dr. Hardell has submitted an extensive list of his own scientific articles which will

form the basis of his opinions, as well as his underlying 25,000 pages of questionnaires to the defendants.

Exhibit #P1120

PIN #	00
Date	01-Jan-84
Author	RAYMOND SINGER
Addressee	LIST OF CITATIONS & LIST OF ARTICLES BY AUTHOR & BY OTHERS PUBLISHED
Description	Dr. Singer has submitted a list of references including his own work and the work of others which will form the basis of testimony and the basis of his opinions in

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AGNEW V DOW
MOYER V DOW

DOW 746900
MN0069799

MIDLAND, MICHIGAN
July 25, 1967

W. J. McCoy
Bioproducts Sales
BPC

cc: W. L. Corbin, BPC

2,4,5-T FORMULATIONS

I appreciate very much your note of 7/17/67 in which you informed me that some Diamond material has apparently caused serious skin problems among people applying the material. This goes along with a report that recently appeared in the South American literature which states that materials of this nature have also been noted to have caused similar difficulties. I am enclosing a copy of this publication for your information.

It would appear that our predictions of a few years ago are beginning to come to pass, unfortunately. Frankly, I am mighty glad that we took the position we did.

Please continue to keep me informed as best you can.

28

V. K. Rowe
Biochemical Research Laboratory
1803 Building

pgw

bcc: V. K. Rowe (2)
Correspondence

OFFICE COPY

Biochemical Research Laboratory

The Dow Chemical Company

HLORACNE PROBLEM AT
'ORT SASKATCHEWAN PLANT,
OW CHEMICAL OF CANADA

File: T2.1-18-2
Date: 3/21/69
By: L. G. Silverstein

DOW 746398
MN 0697994

Signed _____ Date 3-27-69

Checked _____ Date 3-28-69

PROBLEM

Workmen in Fort Saskatchewan have experienced chloracne. here may be another skin rash problem related to the weed killer peration but this has not been diagnosed definitely by a physician.

FINDINGS

1. An acnegen was found to be present in some process samples, specifically the Dowicide G product in the reactor and the Dowicide G product at the packaging location. In addition, a sample of crude dichlorophenol showed slight to moderate activity, and the caustic insolubles in the G Liquor settling tank showed severe acnegenic activity in the rabbit test.

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2. No acnegenic activity was found on a series of wipe tests taken in the G and weed killer building.

3. Laboratory studies on the decomposition of chlorinated phenols have indicated the definite possibility of an acne hazard from overheated or decomposed materials.

RESTRICTED: for use within The Dow Chemical Company only.

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CONCLUSIONS

1. There is not enough exposure during normal operations to active materials to explain the degree of chloracne seen in workmen at Fort Saskatchewan.

2. The housekeeping observed and in the wipe samples I collected during my visit in October of 1965 indicated satisfactory housekeeping in the penta and weed killer plant.

3. Unusual exposure from maintenance or clean-out of equipment such as the dryer, or from accidents such as overheating of the dryer may have caused the severity of skin reaction noted in the workmen.

4. Personal cleanliness is of primary importance in avoiding skin problems and minimizing their severity once encountered. The instructions on the second page of the operator's manual for Fort Saskatchewan should be followed conscientiously: "Dow will provide a complete change of clothing for each operator, each day. This clothing including shoes, hats and gloves must be left in the lockers provided. To assure adequate cleanliness and hygiene, a shower must be taken by each operator prior to his leaving the Company premises at the end of each shift."

Discussions during my visit in October, 1965, indicated that this procedure had been relaxed or at least not enforced by

DOW 746399

supervision. It is my firm opinion that this is the most important step that management can take toward improving the situation.

5. Any unusual exposure should require immediate and thorough shower and change of clothes from the skin out to minimize the probability of injury. If exposure to airborne fume or dust, for example from the dryer during clean-out, is to be encountered, an air supplied hood should be a required item of clothing. Men should not be allowed to work in the vicinity of such an unusual exposure unless they too are protected from inhalation of the airborne material.

6. A clinical definition of the skin rash described by Kasanovich would be very helpful in determining if there is a second problem on the weed killer side.

7. Skin condition of the workmen afflicted should be followed clinically in order to determine if progress is being made in eliminating the skin condition.

MTD 746400

DISCUSSION

"Dowicide bumps," or chloracne, is a skin condition characterized by blackheads and bumps appearing on the face of the individual afflicted, sometimes spreading to other parts of the body. The condition has been recognized for many years as an occupational hazard in the production of Dowicides, especially Dowicide G (sodium pentachlorophenate).

Fort Saskatchewan Dowicide production plant has experienced an outbreak of chloracne in its workmen. Tests on process samples from Fort Saskatchewan are summarized in Table 1.

A series of wipe tests in the Fort Saskatchewan plant are summarized in Table 2. All wipes were free of activity indicating that at the time of the survey housekeeping was good.

The mild activity of process and product samples, and the lack of the activity in wipe samples, plus the physical nature of the most likely exposure; that is, the solid Dowicide G; make it difficult to rationalize the severity of the chloracne in workmen at Fort Saskatchewan if their exposure was "routine," that is, to the normal process materials during normal operation of the plant.

On the other hand, the [illegible] response to the caustic solubles in the G Liquor Tank and the [illegible] of animal response decomposition products of Dowicide G in the laboratory study

DOW 7464401

summarized in Table 3 indicate the possibility that nonroutine exposures to overheated Dowicide G or its fumes either during malfunction of the dryer or to the residue in cleaning out the dryer, or perhaps cleaning out the G Liquor settling tank may have brought on the pronounced chloracne in the persons affected.

From the description of his rash by Peter Kasanovich there may be a second skin problem related to the weed killer operation. This needs clarifying by a clinical examination of the men. According to Peter Kasanovich the rash appears and disappears rather promptly and is related to working and being off work on week-ends. This is not characteristic of chloracne. It does sound like a rash which occurred in Midland many years ago and was associated with 2,4-D production. When a bleaching step was added to the 2,4-D process to remove odor and color the rash disappeared along with improvement of the product.

Careful attention to housekeeping and personal cleanliness may eliminate this problem.

DOW 749402

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...mple ...mber	Sample Descriptions	Animal Responses Folliculitis	Burn	No. of Appl.	Days Exposure	µg TCBD/gm VPC Analysis	Re...
1	Crude DCP from reactor	None	Yes	3	24		tested
	Same, 50% in $CHCl_3$	Sl-Mod	Yes	4	11	<1	100% da...
2	Still bottoms from SBS	None	Yes	3	38		
	Same, 50% in $CHCl_3$	None	Yes	4	24	<1	100% da...
3	...ector effluent from bottom pot	None	No	15	24		
	...me, 50% in $CHCl_3$	None	No	17	38	<1	100% da...
4	...illed still bottoms from V-20	None	Yes	3	38		
	..., 50% in $CHCl_3$	None	Yes	4	38	<1	100% da...
	...ol mixed dichlor tank	None	Yes	2	38		
		None	Yes	1	38	<1	100% da...
	...a	None	Yes	1	24		
		None	Yes	4	3...		100% da...
	...a fines	Sl-Mod	Yes	3	11		
	..., 50% in $CHCl_3$	Slight	Yes	4	11	1...	100% da...
	...a beads	None	Yes	4	24		
	Same, 50% in $CHCl_3$	Slight	Yes	4	14	13	100% da...
	Penta 95-105 from reactor	Slight	Yes	2	...		
	Same, 50% in $CHCl_3$	Slight	Yes	3	...	80	100% da...
	Dow 7 to G batch 104	Slight	Yes	2	1...		
	Same, 50% in $CHCl_3$	Slight	Yes	2	1...	6	100% da...
	Unoiled penta from flaker (65405)	None	No	19	2...		
	Same, 50% in $CHCl_3$	Slight	Yes	3	1...	13	100% da...

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Table 2. PORT SASKATCHEWAN WIPE SAMPLES -- 10/5/65 --
L. G. SILVERSTEIN

Penta Side and Control Room

1. Dowicide 7 bagging -- handles.
2. Dowicide G bagging -- handles.
3. Door to warehouse -- handles.
4. Handrail to second floor, north end of 151 Building.
5. Floor -- doorway between washroom and "clean" locker room.
6. Floor -- doorway between plant and locker rm.
7. G classifier platform.
8. Floor -- center of first fl. in 151 Building.
9. Valves near phenate tank head.
10. Pipe near landing, north stairway of 151 Building.
11. Latch of penta reactor sample box.
12. Handles of flaker parts.
13. Operator's desk -- penta reactor room, second floor.
14. Drier -- handles.
15. Door to control room from penta reactor room.
16. Benchtops in control room.
17. Operator's desk and clip boards, control room.
18. Tools in drawer -- control room.
19. Valve handles in G reactor dike area, southwest corner of 151 Bldg.
20. G reactor -- handles, second floor outside.

Weed Killer Side

21. Stair treads -- first floor going up (caked with tar).
22. Handrail, first to second level.
23. Valves and handles on R-304, second floor.
24. Sample hood, second floor -- front lip and valve handles.
25. Valve handles on LUWA evaporator, third level.

DOW 748404

Table 3. LABORATORY STUDIES ON THERMAL DECOMPOSITION OF CHLOROPHENOLS

Sample Number	Sample Description	No. Appl./ No. Days	Rabbit Response
1	Sodium 2,4-dichlorophenate residue	10/19	Moderate
2	Sodium 2,4-dichlorophenate fume condensate	13/22	Sl-Mod
3	Sodium o-chlorophenate, fume condensate	14/21	Sl-Mod
4	Dowicide F fume condensate	7/11	Severe
5	Dowicide G fume condensate	14/21	Severe
6	Sodium 2,4-dichlorophenate control	16/22	None
7	Sodium 2,4-dichlorophenate held 7 hours at 150°C	16/22	None
8	Sodium 2,4-dichlorophenate held 7 hours at 170°C	8/11	Slight
9	Dowicide G control	16/22	None
10	Dowicide G held 7 hours at 170°C	10/14	Slight
11	Dowicide G residue from overheated sample from 265 Building, below grate in fluid bed dryer	12/13	Moderate

DOW 749405

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TOXICOLOGY RESEARCH LABORATORY
HEALTH AND ENVIRONMENTAL RESEARCH
DOW CHEMICAL U.S.A.
MIDLAND, MICHIGAN 48640

TESTIMONY FOR THE 2,4,5-T HEARING

by

V. K. Rowe

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INTRODUCTION

The purpose of this testimony is to provide background information that will be useful in considering the testimony from Dow and other scientists. 1) It will state briefly some of the basic concepts in toxicology. 2) It will outline the history of toxicological and environmental health research in The Dow Chemical Company. 3) It will discuss the development and use of toxicological and related data. 4) It will describe the development of Dow toxicological information on 2,4,5-trichlorophenoxy acetic acid (2,4,5-T) and 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) up to 1970.

It will not include a discussion of the studies that have been conducted since 1969 as they will be presented by others.

DOW 760560

I) Basic Concepts of Toxicology

Webster defines toxicology as "a science that deals with poisons and their effect on living organisms, with organisms, with substances otherwise harmless that prove toxic under particular conditions and with the clinical, industrial, legal or other problems involved."

Webster defines Toxicity as "the quality, state, or relative degree of being toxic or poisonous." It is worthy of note that Webster recognizes a relative degree of toxicity, because this concept is too often overlooked in evaluating "toxic hazard", or the probability of an untoward effect occurring. This latter concept is recognized in the definition of toxicology.

Further, there is no such thing as a nontoxic material. All materials are toxic--it is only a matter of how much and under what conditions they are encountered that determine whether a real-life hazard exists. In industrial toxicology, we are continuously determining both the qualitative and the quantitative aspects of materials to cause adverse effects. Based on such basic information and with knowledge of conditions of use, it is possible, within reason, to predict the consequences of given situations. Thus a material may be quite appropriate (safe) for a particular application but be

DOW 7605611

quite inappropriate (hazardous) for another application. In other words, the risk is judged to be acceptable or unacceptable depending upon circumstances. The toxicity of the material has not changed--it is the same in both situations but the likelihood of excessive exposure is different in the two situations, being too great in the second situation. Toxicologists are well aware that toxicity information developed in animal studies cannot always be used to assess directly what may occur in man. Nevertheless, based upon my experience in the field of toxicology, I can only conclude that predictions based on appropriate animal studies have been remarkably accurate and have served mankind well.

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II) History of Dow Toxicological and Related Research

It was only a relatively short time ago, say 45 to 50 years ago, that what we think of as "industrial toxicology" or perhaps more appropriately termed "preventive toxicology" was nonexistent for all practical purposes. "Forensic or diagnostic toxicology" was, of course, well known but its capabilities were severely limited as measured by standards of today. Organized laboratories for determining the toxicity of substances before the fact were not known. Medical people took care of persons after the fact. There was little preventive industrial medicine, because there was little toxicological data upon which to base a preventive medical program. That was the state of the art in 1933 when Dow hired its first biochemist, Dr. Don D. Irish, because the

late Dr. Willard H. Dow, son of the founder of our company, in his far-sighted way, thought that someone trained in the biological-chemical area ought to be useful to a chemical company. Less than a year later, a fatal accident occurred as a result of an acute skin exposure to a chemical. Dr. Irish identified the culprit as phenol, studied its effect on animals both qualitatively and quantitatively, and set-up operating procedures and an educational program designed to prevent any reoccurrences. Dr. Dow charged Dr. Irish with the responsiblity of examining new and old materials so that the unexpected would not occur. Thus, the Toxicology Laboratory of The Dow Chemical Company was born and it has flourished ever since under essentially the same but broadened charter and with the full support of Dow Management.

DOW 760563

By 1936, Dr. Irish had outgrown his garage and construction shanty laboratory and was given a wing in a new laboratory building. These facilities served us well for almost 20 years.

In 1955, we moved into a completely new building of about 40,000 square feet dedicated wholly to biochemical research, including 14,000 square feet for toxicological research. In 1960, another new building, approximately 5200 square feet, a dog kennel capable of handling 200 dogs was added. The

need for toxicological data continued to grow and in 1966-1967 Dow built a new 30,000 square foot 1.1 million dollar building committed wholly to toxicology. In January 1974, ground was broken for an additional 47,000 square feet of laboratory space. This new space, costing approximately 4 million dollars was dedicated in May 1975 giving Dow, at Midland, Michigan one of the finest and most modern toxicology research facilities anywhere in the world. As of January 1976, our present staff in toxicology consists of 109 persons. The present staff includes 20 persons with the doctorate degree including 7 who also have the DVM degree, 28 with baccalaureate or masters degree, 5 non-degree specialists, 22 working toward their baccalaureate, 23 animal caretakers, a secretarial staff or 8 and 3 high school student co-ops. In addition, we have a staff of 20 industrial hygienists associated with our laboratory, 6 of whom are fully certified by the American Board of Industrial Hygiene, and 8 industrial physicians located in Midland. Also, we have a sizable Pathology and Toxicology Research Laboratory associated with our pharmaceutical business located in the Indianapolis, Indiana area and a new Biomedical-Toxicology Laboratory at our Texas Division in Freeport, Texas.

DOW 1605641

About 1937, it became obvious that if we were to effectively apply our toxicological information, we needed to know more about the actual environmental conditions. This meant careful analysis of the workroom environment for the presence of excessive amounts of chemical substances, heat, ionizing and nonionizing radiation, noise or any other condition with which we might be concerned. Such environmental studies have developed into what is now called industrial hygiene. The Dow Industrial Hygiene Laboratory developed as a part of the Toxicology Research Laboratory.

DOW 760565

As toxicology and industrial hygiene evolved in the direction of control of the environmental health problem of Dow's working people, we developed close cooperation with the Medical Department and Safety Department. It is obvious that the studies of environmental circumstances by industrial hygienists needed to be coordinated with medical surveillance of the people in that environment. While the safety engineers emphasized mechanical hazards, the industrial hygienists emphasized chemical hazards and other physical stresses. It is obvious that the interests of the four groups, Toxicology, Industrial Hygiene, Medical and Safety are quite inter-related and complement one another toward a common goal, a safe place to work.

As soon as we were developing effective toxicological information and knowledge of the environmental circumstances within our production plants, it became obvious that this type of information would be useful to our customers as well. As the years passed, such information on our products became more and more important. It is interesting to note that in the mid-thirties we almost never received an inquiry on the handling problems of a particular chemical but by the forties, such requests were common, and by the fifties, it was usually one of the first pieces of information requested on a material, particularly, if it was new to the inquirer. Today, such information is not merely requested, it is demanded, not only by the customer as a condition of doing business, but by governmental regulatory agencies prior, in many instances, to doing business in certain areas.

Earlier I spoke about toxicology and industrial hygiene evolving as needed to meet problems in occupational or environmental health. The very same thing has happened in all of the areas of science with which I am familiar. What this really means is that our tools of the trade have become sharper and sharper and I have no doubt that this will continue. I have no question that the techniques we view as being sophisticated today, will be commonplace in 2 or 3 years and many of them will be obsolete in 5-10 years.

UCW 60066

This is the pattern of scientific progress. For example, the need to develop a laboratory test to identify materials with a capacity to cause chloracne in man was recognized early in our laboratory's history because some of the workmen were experiencing mild cases of the disease. The disease was not a new one, having been identified in Germany in 1899 although it was referred to as folliculosis caused by chlorinated hydrocarbons. In the following years, there were occasional reports of chloracne but in 1937, several articles were published relating to the development of chloracne and liver injury caused by exposure to higher chlorinated naphthalenes and biphenyls. No method was then known by which materials having this property could be identified. Consequently, we began searching for such a method that we could use to test new chemicals for their chloracnegenic potential. This research resulted in the development of the "rabbit ear test", a description of which we published in the January, 1941 issue of Industrial Medicine. It was entitled 'THE RESPONSE OF RABBIT SKIN TO COMPOUNDS REPORTED TO HAVE CAUSED ACNEFORM DERMATITIS and was authored by E. M. Adams, D. D. Irish, H. C. Spencer and V. K. Rowe.

The response of the rabbit ear to chloracnegens is characterized by a thickening of the ear, excessive exfoliation having a granular consistency and most characteristically enlarged

DOW 7605G7

hair follicles from which keratin and sebaceous matter may be expressed leaving pits up to 1-2 mm in diameter. This "rabbit ear test" is still used in our laboratory and in many others as well. It is a very reliable test which has stood the test of time. It served us well in dealing with the problem we had in 1964 in the production of 2,4,5-trichlorophenol.

Another excellent example of science's response to need is in the field of analytical chemistry. I remember well my trying, about 30 years ago, to get the analytical specialists to give me results with a sensitivity of 1 ppm of an organic compound. They threw up their hands in despair and usually said that they probably could get to 100 ppm, they might be able to go to 10 ppm but 1 ppm was out of the question. Nevertheless when there was a recognized need for greater sensitivity, it was accomplished. Just a very few years ago we considered analytical methodology with a sensitivity of one part per billion as extreme, and it was. Now, in some areas, we are talking about parts per trillion. The same situation prevails in toxicology. Our methodology has improved along a road parallel to that of the analytical chemists. Some of the methodology used a few years ago is inadequate by today's standards, some that is adequate today will be inadequate a few years hence, and so it will be as time goes on--as the needs develop, science will find a way to meet those needs.

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In all cases, methodology is only a tool employed to generate data. The application of such data in the solution of real life problems requires a knowledge of the limitations of the data, a knowledge of the real-life situations to which the data is to be applied, and the exercise of good judgment based on the rule of reason.

I have spoken about Dow's commitment to toxicology, industrial hygiene and medical surveillance programs. I want also to describe a related effort which has as its objective the conservation of the quality of our environment. Late in 1969, the Dow Board of Directors decided that not enough was being done to avoid introducing undesirable materials into the environment. It decided to accelerate Dow's efforts in this area by appointing a company wide Ecology Council. Many of Dow's top executives were members of this council. In rapid succession, ecology councils were created in manufacturing areas and in product departments. These councils were charged with the responsiblity of examining everything within their domain to determine whether it constituted a problem if released to the environment and if so, to correct the situation in the best way possible. This charge encompassed products, with consideration being given to the various uses of a product, by-products and wastes.

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Thus Pollution Abatement became the watchwords of the production managers and Product Stewardship became the watchwords for research, development and sales personnel.

Many problems and questions were generated. Where solutions were readily apparent, corrective action was instituted. As expected there were many situations identified where there was no data available and hence an unknown existed and questions could not be answered.

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In an effort to bring the technology and expertise available within Dow to bear on this problem, Dr. J. E. Johnson, then Vice President and Director of Research and Development, speaking for both Dow Corporate Management and Dow Chemical U.S.A. announced on April 21, 1971, the creation of an Environmental Testing Advisory Board, dubbed ETAB for short. The announcement stated the objectives as follows:

> The board will serve as Dow's technical authority advising all functions and management levels on the possible environmental effects of products and new or changed processes. It will also advise on registration requirements and on customer and public environmental safety needs.
>
> The board will function under the broad direction of the company Ecology Council.
>
> Specifically, the board will:
>
> --establish standardized test procedures. These procedures will be useful to determine and predict possible environmental effects of experimental and existing products and new or changed processes.

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--assess capabilities of both Dow and non-Dow laboratories and identify those best able to conduct specific environmentally related experiments.

--serve as a repository for data acquired from studies conducted outside of Dow.

--help interpret experimental results.

--provide advice and recommendations concerning environmental testing matters.

The ETAB board was interdisciplinary in character and consisted of persons who had the best knowledge available about the problems the board was asked to solve. Many subcommittees were formed under the leadership of board members and work commenced. In January of 1972, a compilation of the best methodology available entitled "ETAB - Environmental Testing Manual" was issued. This manual describes procedures to be followed in assessing environmental effects and describes about 150 tests that can be used to help evaluate such factors as toxicity, bioaccumulation, movement, and stability of materials. During the next several months, a team(s) experienced in the use of the manual to solve environmental related problems conducted training courses for many Dow groups in many Dow locations in the United States and Canada. Concurrently,with the development of the manual, the board or members of the board met one or two days a week with various groups needing help to deal with their problems. The philosophy of the board was that it should be an advisory body and not a policing body; the responsiblity and accountability for the various materials, whether they be wastes

or products was placed squarely on the shoulders of line supervision. This advisory effort pioneered by company officials and expedited through ETAB has succeeded in instilling a high degree of awareness and concern by Dow managers at all levels. It has resulted in a tremendous reduction in the amount of undesirable materials getting into the environment.

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I am relating all of this history and philosophy for one purpose--to show that The Dow Chemical Company has been and is committed to the development of toxicological, industrial hygiene, environmental, and medical data that will permit it to successfully and profitably produce products that can be handled and used safely, be environmentally acceptable, and at the same time provide a safe place for its employees to work.

III) Development and Use of Toxicological and Related Data

With more and more demands for information, the complexity of the problems of environmental health control increases. There are no simple, pat answers to the following questions: What is healthful? What is unhealthful? What is desirable? What is undesirable? We have much more knowledge today on which to base a reasonable judgment but we must be flexible to adjust to constantly changing circumstances and constantly advancing knowledge.

How do we get the information on which to base a reasonable judgment? There are certain basic toxicological tests that have been prescribed by various regulatory agencies to meet regulations under the Federal Hazardous Substances Act, the Federal Insecticide, Fungicide and Rodenticide Act and others. Such studies are usually relatively simple and their purpose is to identify acute or short-term hazards associated with handling or use. When considering materials for uses such as direct additives for food, residues in food from agricultural practice, residues in food from processing procedures and drugs for long-term use, comprehensive toxicological studies are required by the regulatory agencies. (EPA and FDA) I will not discuss the intricacies of a complex toxicological study but I can sketch a few principles to give you some notion of what is done today. The design of the study will be determined by the depth of the question(s) to be answered and may involve anywhere from one to several species of animals, from a few to hundreds of each species, a few weeks to years of treatment and observations and from a few hundred to several hundred thousands of dollars.

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First, we must expose our animals in ways which are pertinent to the manufacture, handling and use of the material in question. In an accidental spill, it may be splashed on the skin or in the eyes, or it may be breathed as an air dispersion. Also,

it may be ingested, usually accidentally as in a case of mistaken identity. To evaluate the hazards of such situations, animals are given the material orally in single or a few repeated graded doses, their eyes and skin are exposed to various concentrations for various periods of time. The results are useful in predicting the likely effect on humans from similar exposure.

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In the work area, the material may be encountered as an isolated event or a single exposure, or it may be contacted repeatedly or continuously in fluctuating amounts during the 8-hour workday and a 5-day workweek for a working lifetime. As a general or public air pollutant, it may be contacted repeatedly or continuously in fluctuating amounts during a 24-hour day and a 7-day week for an indefinite period of time. If the material in question is likely to be encountered as a part of the air one breathes for an extended period of time, then animals are subjected to the material in the air they breathe. The amount in the air and pattern and duration of the exposure are selected to simulate real-life as well as exaggerated conditions. If the chemical is likely to find its way into food or potable water, it may be ingested daily for an indefinite period of time. Under such

conditions, its safety is evaluated by putting it in the food or water of a colony of one or more species of animals for a lifetime or several generations. If a material is likely to be encountered by pregnant women, it may be further evaluated by administration to pregnant female animals during the gestational period to determine any effect on the embryo and fetus. The permutations and combinations are many and in order to answer the critical questions one must develop his experimental program with a knowledge of the properties of the substance and of the conditions of manufacturing and anticipated use.

In discussing general approaches to toxicological problems, I have not dealt with specific observations that are routinely made or that can be made if needed to answer specific questions. Perhaps a few comments to these points would be appropos. In all long-term or lifetime studies it is routine to follow growth and behavior, to do periodic blood counts and clinical chemistry determinations on blood and urine, to autopsy all dying or dead animals, weigh the major organs, and examine grossly and microscopically many tissues, usually 25 to 30 from each animal. The ultrastructure of individual cells as seen under the electron microscope is examined more and more frequently even though the significance of subtle deviations from normal are not always interpretable.

The purpose of all these studies is to detect any deviations between the treated and untreated animals. If deviations are found, they may suggest the need for special studies on those particular organs or tissues; thus the conduct of any comprehensive toxicological study is subject to additions or deletions depending upon continuing observations and the need for additional data to explain how and why the material does what it does. Chemical analyses of tissues are frequently done to determine if residues of the test chemical per se or a metabolite(s) have accumulated in tissues during the course of treatment.

The primary, but not the only, objective of lifetime studies is to determine carcinogenicity and to relate this, if it is detected, to dosage.

Mutagenicity, or the capacity of a material to induce genetic or inheritable changes, is of considerable concern today and will be henceforth. Animals on lifetime experiments can be studied cytogenetically for changes in their chromosomes in an effort to detect mutagenic potential. Other tests for mutagenicity such as the dominant lethal test or some variation of a host-mediated test, because of their singular nature, must be carried out apart from lifetime studies.

Another parameter of toxicity which may or may not be measured as a part of a lifetime study is an assessment of reproductive ability. In such studies, the animals are permitted to reproduce through three generations while being subjected to the material under test. The results reflect the stress of a particular dosage upon ability to conceive, gestate, deliver viable normal young, and nurse and raise the young.

Teratological studies are widely used today to determine the capacity of materials to interfer in one way or another with the intrauterine development of embryos and fetuses. The test material is administered by an appropriate route to pregnant females, usually mice, rats, hamsters or rabbits at varied dosage levels and at various times during pregnancy. The effects are determined by examination of the fetuses taken by caesarean section the day prior to the normal delivery date and sometimes by examination of pups a week or more after natural delivery. Data from such studies are particularly useful in the evaluation of safety of drugs that may be taken by pregnant humans or on chemicals to which the expectant mother may be subjected in her employment or normal living.

Another parameter of toxicity that is receiving considerable attention today is the effect of defined and/or controlled stresses upon behavior, innate or conditioned. The results of such

studies can sometimes demonstrate very subtle neurologic effects that would otherwise go undetected in conventional toxicological studies.

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As we proceed down the road from art to science, we are becoming more and more cognizant of the importance of studying the metabolic and pharmacokinetic patterns of materials. Such studies can tell us how the intact animal body deals with a substance, and provide answers to such essential questions as:

1) What biochemical transformations of the material occur in the body and how are these influenced by dosage?
2) How is the material excreted and how fast?
3) Does it or a metabolite accumulate in the body?
4) Does the material interfere with a particular vital function of a biochemical nature?
5) What animal species is most like man in its mechanism for dealing with the substance?
6) Which species is the best for toxicological studies?

As a part of any comprehensive toxicological evaluation, information relative to the pharmacological activity of the material should be obtained. This is usually done on

specially treated animals or upon isolated organ systems. Such studies are essential to understanding the mode of action of a material and they are a great help to the physician who may be called upon to treat a case of excessive exposure.

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In essence, the objectives of a toxicological study on animals are to describe the effects caused by various intensities of exposure measured in terms of the parameters of exposure, dosage, frequency, and duration. With such information in hand the toxicologist can make predictions as to the safety of a particular situation if he knows the pattern and intensity of expected exposure.

Here is where the industrial hygienist comes in. It is his job to determine the intensity and pattern of exposure to be anticipated in a new situation or in one that exists in an ongoing situation. With both the toxicological data and the industrial hygiene data in hand, the physician, who is always in the picture, is in a position to make a better assessment of the health of the people involved. He may even be able to improve on the medical surveillance program and thereby generate more meaningful data.

With all of the data derived from the three sources, toxicology, industrial hygiene and medicine in hand, decisions such as the following can be made:

1) it is safe to continue operations as they are;

2) modifications must be made in operations or equipment to reduce exposure;

3) more toxicological, industrial hygiene and/or medical data are needed;

4) a continuous monitor of the work environment needs to be installed; or

5) go out of business.

I have described briefly the 'closed-loop' interactions of the toxicologist, the industrial hygienist and the industrial physician as we have practiced it for years at Dow. My experience tells me that the solving of problems related to environmental health requires multidisciplinary cooperation not only between those professions mentioned above, but also between analytical specialists, design engineers, operating engineers, plant superintendents, top management and most important, employees.

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Essentially, the same situation exists when the end use of products is considered. The toxicologist has been involved for years but in more and more situations the industrial hygienist is asked to go forth into the "field" where products are used or wastes disposed of and measure the potential for exposure. For the most part, this is a new dimension for the industrial hygienist and even newer for the physician, but we will see more and more of it in the future because such information is essential to the proper assessment of safety.

As I am sure everyone can appreciate, all of these activities are expensive. Since resources in terms of man-power, laboratory facilities and money to pay for the work are always limited, we have to use our best judgment as to where we deploy our resources. In making such judgments, we have to consider the potential for exposure, the possibility that such exposure will occur and the value of the ultimate product. If we are to proceed, an affirmative answer must be forthcoming to the question, can the product support the necessary research, construction, monitoring, and surveillance program? We have considered such questions as they relate to the subject of this hearing. The answers will be forthcoming as our case develops.

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IV) The Development of Dow Toxicological Information on 2,4,5-T and TCDD up to 1970

With this background, I should like to trace for you the early work we have conducted on 2,4,5-T and TCDD and try to relate this with the sequence of events that have impinged so heavily upon the toxicology problems related to these compounds.

The compound, 2,4,5-trichlorophenoxyacetic acid, (2,4,5-T) was evaluated by the Department of Defense at Fort Detrick during the early part of World War II and found to be an effective herbicide. Dow was aware of this and in 1945 2,4,5-T was subjected to limited toxicological studies. The conclusion from these studies were: 1) that 2,4,5-trichlorophenoxyacetic acid has a moderate acute oral toxicity and is slightly irritating to the skin of rabbits; 2) that excessive exposure to the dust of either the free acid or the salt would be likely to cause skin irritation; 3) that exposure to dilute solutions, such as these used in practical application, would not be expected to cause trouble except among those who persist in spraying themselves or who do not take the necessary precautions to

prevent prolonged contact with the material; and 4) that reasonable handling precautions which will prevent ingestion and prolonged skin contact with the material should suffice to prevent serious trouble.

A paper published in the Botanical Gazette (June, 1946) revealed that 2,4,5-T was one of the more effective herbicidal materials discovered. There was little interest in 2,4,5-T until 1947 when Dow researchers found that it was a very effective herbicide for unwanted stands of wild blackberry. About the same time, Tam of Hawaii, reported it was highly herbicidal towards Lantana, a nuisance shrub infesting pastures. These two reports stimulated much work by agricultural research people interested in weed and brush control.

In 1948, The Dow Chemical Company obtained registration of 2,4,5-T (June 10, 1948) (Reg. No. 464-069) for control of herbaceous and woody plants growing in rangeland, pastures, fence rows, farm lands and right-of-ways.

When Dow elected to manufacture 2,4,5-T, we were immediately concerned with the possiblity that an impurity could be present in the 2,4,5-trichlorophenol used to make 2,4,5-T and that this might cause chloracne problems. Our concern

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stemmed from the fact that in our research on the chloracne problem some years before we had learned that the waste tars from the manufacture of 2,4,5-trichlorophenol contained chloracnegens.

As early as 1944, Dow was using the rabbit ear test to monitor the waste oils from the 2,4,5-trichlorophenol process. The impurities were concentrated in these oils and we had learned that when the waste oils were low in acnegenic activity the impurities in the 2,4,5-trichlorophenol were correspondingly low. Thus, when Dow became interested in manufacturing 2,4,5-T in 1948 we were sensitive to the potential for a chloracne problem in the product.

In 1949, we again conducted toxicological studies on our 2,4,5-T and there was no evidence of any acnegenic response in the rabbit-ear test. The results of the skin application study was summarized as follows: "When 2,4,5-trichlorophenoxy-acetic acid as a 10% solution in butyl carbitol acetate was applied repeatedly to the rabbit ear and bandaged repeatedly to the shaven abdomen, a slight simple irritation developed in both instances." During the next few years, there was much toxicological work done on 2,4,5-T because of its wide utility and general interest. The rather extensive literature to 1954 together with the results of work from our laboratory

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to that date which dealt with ingestion were summarized and published in 1954 in the American Journal of Veterinary Research, Vol. XV, No. 57, Oct. 1954, pp 622-629. The article is entitled SUMMARY OF TOXICOLOGICAL INFORMATION ON 2,4-D AND 2,4,5-T TYPE HERBICIDES AND AN EVALUATION OF THE HAZARDS TO LIVESTOCK ASSOCIATED WITH THEIR USE by V. K. Rowe, M.S. and T. A. Hymas, D.V.M. The Summary and Conclusions were as follows:

1) The acute oral LD50 values for 2,4-D, 2,4,5-T and their various derivatives commonly used in herbicidal preparations fall in the range of 300 to 1000 mg/kg for rats, mice, guinea pigs, and rabbits. Generally, dogs are more susceptible and chicks are more tolerant of this type of material. On a weight basis, the toxicity to cattle appears to be quite similar to the toxicity to ordinary laboratory animals

2) The acute oral LD50 values for commercial formulations of 2,4-D and 2,4,5-T type materials are approximately proportional to their content of active ingredient. The "inert ingredients" do not appear to contribute materially to the oral toxicity of the formulations.

3) Data available indicate that the 2,4-D and 2,4,5-T type herbicides have a low chronicity.

4) MCP (2-methyl-4-chlorophenoxyacetic acid) and silvex (2-(2,4,5-trichlorophenoxy)propionic acid) and their herbicidal derivatives appear to be slightly less toxic than the corresponding 2,4-D and 2,4,5-T type materials.

5) The hazard to livestock and wildlife associated with the use as recommended of herbicides containing 2,4-D, 2,4,5-T, MCP, and silvex is negligible. It should be recognized, however, that toxic amounts of these materials can be obtained if animals have access to spray tanks or other containers of the materials.

Early information from the FDA laboratories was not included in this article so I shall summarize it in the following paragraph.

In 1952, Dr. A. J. Lehman, Chief of Division of Pharmacology of the U. S. Food and Drug Administration published conclusions from 30-week feeding studies done in their laboratories on 2,4,5-T. This information appears under the title "Chemicals in Foods:A Report to the Association of Food and Drug Officials on Current Developments. Part II. Pesticides. Section III. Subacute and Chronic Toxicity, published in Association of Food and Drug Officials of the United States, Vol XVI, No. 2 April 1952, page 49. In a subsequent article in the same series "Section V, Pathology" published in October 1952, page 130, he states with respect to 2,4,5-T under the heading "Gross Effects", "5000 ppm not tolerated; no effect from 1000 ppm" and under "Histopathological Changes", "Negative. None of the characteristic hepatic cell changes seen with the chlorinated insecticides".

During the ensuing several years, we had no appreciable trouble with chloracne so we just kept on doing what we were doing. During this time, however, we had several visitations and inquiries from foreign manufacturers of 2,4,5-trichlorophenol trying to learn why we weren't having

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chloracne problems and they were. I am not sure that we really knew except that they had had runaway reactions and we had not.

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In 1957, as a result of studies of the consequences of one of these episodes, Kimmig and Schulz of the University Clinic of Dermatology, Hamburg-Eppendorf, Germany disclosed in an article entitled "Occupational Chloracne caused by Aromatic Cyclic Ethers published in Dermatologica, 115, 1957, pp 540-546 that 2,3, 6,7-tetrachlorodibenzodioxin formed in the manufacture of 2,4,5-trichlorophenol was the likely cause of the chloracne in workmen making the chemical. (Later, a change in the numbering system for dibenzodioxin revised the 2,3,6,7-designation to 2,3,7,8-). This discovery was subsequently confirmed by other groups of investigators studying outbreaks of chloracne in workers involved in runaway reactions in the manufacture of 2,4,5-trichlorophenol.

In 1964, several Dow workers developed chloracne and the bioassay program showed that the chloracne potential of the waste oil from the 2,4,5-trichlorophenol process had unknowingly built up to a danger point. Exposure to this waste oil was the cause of the acne in the workmen, not exposure to trichlorophenol. The plant was shut down immediately. Bioassays

of Dow 2,4,5-trichlorophenol and 2,4,5-T being produced at that time were negative for a chloragnegen, but the waste oil from the production of 2,4,5-trichlorophenol was very strongly acnegenic in the rabbit ear test. The principal offending impurity was isolated and identified in the waste oil as 2,3,7,8-tetrachlorodibenzo-p-dioxin, TCDD. This confirmed the findings of Kimmig and Schulz. By early 1965, technology had progressed to the point where Dow was successful in developing a gas chromatographic method for TCDD with a sensitivity of 1 ppm in 2,4,5-trichlorophenol and 2,4,5-T. (Sensitivity has since been improved markedly.)

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When the difficulty was encountered in 1964, Dow notified the Michigan Department of Health, the Institute of Industrial Health, University of Michigan and various other health oriented individuals in private medicine and industry. In addition, Dow called a meeting of the other 2,4,5-T manufacturers in March, 1965 to describe the health hazard and share test procedures and analytical standards with them.

The closing down of our manufacturing operation caused great concern among our customers, because 2,4,5-T was already in short supply. Dow elected to buy raw material with which to make its final products. However, we insisted that a specification be placed on any 2,4,5-T or 2,4,5-trichlorophenol purchased stipulating that neither could contain more than 1.0 ppm of the impurity, TCDD. We tested samples from all potential suppliers and found only one who could meet these specifications.

and produce the amount of material we needed to meet our contracts. Needless to say, they received our business. It is interesting to note that we assayed each carload of material we received and one carload was returned to the supplier as unacceptable because it contained an excess of TCDD.

Dow rebuilt its plant and brought it on stream in 1966 and since that time has had a self-imposed manufacturing specification for 2,4,5-trichlorophenol and for 2,4,5-T. From 1965 to 1970, this specification was less than 1 ppm TCDD. This concentration did not cause a positive response in the rabbit ear test, was the least amount that could be detected then by analytical methods available and was a level, which in our judgment, was safe for use. As analytical technology has improved and manufacturing procedures have improved, specifications have been lowered. For example, the specification with respect to TCDD in Dow 2,4,5-T was lowered from 1 ppm to 0.5 ppm in 1970 and to 0.1 ppm for the 2,4,5-T acid in February of 1972 and for the esters in June of 1972.

On October 29, 1969, Dr. Lee A. DuBridge, Science Advisor to the President and Executive Secretary of the President's Environmental Quality Council was informed of an unreleased report from Bionetics Laboratory that 2,4,5-T was teratogenic and this caused him to announce that a "coordinated series

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of actions are being taken by the agencies of the Government to restrict the use of the weed-killing chemical 2,4,5-T". The announcement continued "Although it seems improbable that any person could receive harmful amounts of this chemical from any of the existing uses of 2,4,5-T and while the relationships of these effects in laboratory animals to effects in man are not entirely clear at this time, the action taken will assure safety of the public while further evidence is being sought".

The next day, October 30, 1969, an article appeared in the Washington Post and other newspapers announcing "The White House ordered restriction of the herbicide 2,4,5-T," and reference was made to the Bionetics' report. This newspaper article was the first information most producers, formulators and users received relative to the test results.

Following the DuBridge announcement, The Dow Chemical Company, as a producer of 2,4,5-T, became concerned about the quality of the material used in the Bionetics' study. This concern stemmed from the knowledge that 2,4,5-T manufactured by some companies might contain several parts per million of the highly toxic contaminant TCDD. In view of Dow's knowledge of the low mammalian toxicity of Dow 2,4,5-T and the absence of reports of increased incidence of birth defects in cattle

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or sheep grazing rangelands sprayed with 2,4,5-T, Dow found it difficult to believe that any practical hazard existed from the registered uses of 2,4,5-T. It was suspected that if the material tested contained excessive amounts of TCDD, this could be responsible for the observations. It, therefore, became important to learn of the quality of the 2,4,5-T tested and to gain additional evidence as soon as possible as to whether TCDD itself could be responsible and would 2,4,5-T meeting specification as made by Dow (<1 ppm TCDD) cause similar birth abnormalities. In order to expedite solving this problem, Dr. Dale Lindsay, Associate Commissioner for Science of FDA, was asked by Dow if a conference could be arranged with appropriate individuals in U. S. Dept. of Health Education and Welfare (HEW) and the National Cancer Institute (NCI) to discuss this problem and to develop protocols for tests designed to provide answers to our questions and concerns and which would be acceptable to FDA and NCI scientists. Dr. Lindsay asked Dr. McLaughlin of the FDA to arrange a meeting which was held November 25, 1969. Present at this meeting were Dr. I. Mitchell and Dr. R. Bates of NCI; Dr. J. McLaughlin, FDA; Dr. J. E. Johnson, D. D. McCollister, Dr. V. B. Robinson and V. K. Rowe of Dow. Dow revealed to the Government people its knowledge of TCDD and its concern about the purity of

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the sample of 2,4,5-T used in the Bionetics' tests. Dr. Mitchell was asked to identify the test procedure by which Dow could reexamine 2,4,5-T and the suspected contaminant. Dr. Mitchell replied that tests with Sprague-Dawley rats would be the best procedure for reconfirmation and further stated that, for the purpose, it would be superior to a test with mice.

Dow offered to underwrite the cost of confirmatory experiments in the laboratories of the National Institute of Health, in the laboratories of a third party (independent of Government or Dow) or in the Dow laboratories open to observation at any time by personnel of the Department of HEW.

Dr. Mitchell stated that he would have confidence in the work if it were done in Dow laboratories. Dow agreed to repeat the Bionetics' work with Sprague-Dawley rats using Dow 2,4,5-T of regular production grade. If this study yielded positive results the Bionetics' results would be confirmed. If the results were negative it would be necessary to run further tests on graded levels of the contaminant and on refined 2,4,5-T. It was agreed that Dow would provide samples of 2,4,5-T and 2,3,7,8-tetrachlorodibenzo-p-dioxin to the National Institute of Environmental Health Science laboratories at

Research Triangle Park, North Carolina. Robinson and Rowe of Dow were asked to visit the NIEHS laboratories in order to confer with them concerning the details of the test methods to be used.

On December 1, 1969, Dr. Johnson of Dow met with Dr. DuBridge and Dr. Buckley of the OST (Office of Science and Technology) to apprise them of the possibility of a contaminant in the sample tested by Bionetics and also of the information known to Dow. At this meeting, the plan for additional testing as discussed with Drs. McLaughlin, Bates, and Mitchell also was presented. Dr. DuBridge stated that he would be interested in further information as it developed and was willing to consider new evidence when it was available.

On December 11, 1969, Drs. V. B. Robinson and V. K. Rowe met with Drs. Falk, Courtney, and Gaylor at the Research Triangle Park and discussed with them the design of a teratological study to be conducted on TCDD and Dow regular production 2,4,5-T. Agreement on the design of the experiment was easily achieved and was followed in the Dow studies.

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At this meeting, Dr. Courtney of the NIEHS Laboratory provided a 2 gm sample of the 2,4,5-T used by the Bionetics Laboratory. This sample was examined at Dow with the following results:

1) Rabbit ear tests showed a strongly positive reaction characteristic of TCDD.
2) Analysis by gas liquid chromatography indicated the presence of 27±8 ppm of TCDD (2,3,7,8-tetrachlorodibenzo-p-dioxin).

On December 23, 1969, J. E. Johnson, G. E. Lynn and J. C. Hansen of Dow met with Secretary of Agriculture Hardin and reviewed Dow's activity in the 2,4,5-T case.

On December 29, 1969, Dr. E. H. Blair and others from Dow made a presentation to Dr. Burger and others of the Office of Science and Technology, relative to the chemistry, the Dow process for manufacture of 2,4,5-T, and the methods used to control the levels of the contaminant TCDD.

By January 12, 1970, enough progress had been made in the Dow teratological study in rats with Dow production grade 2,4,5-T to make a report to Dr. Egeberg, Assistant Secretary for Health and Scientific Affairs, Dept. of Health, Education and Welfare. Copies were sent to other involved persons in HEW and USDA. This report showed that Dow regular production-grade 2,4,5-T did not cause birth defects as determined

by gross examination of fetuses from pregnant rats fed 24 mg/kg/day on days 6-15 of gestation. The dosage levels used were those selected in consultation with Drs. Falk, Courtney, and Gaylor of NIEHS. Furthermore, Dow was able to report to Dr. Egeberg that a pilot study with pregnant rabbits fed the same Dow production grade 2,4,5-T had not caused birth defects. The late Dr. H. L. Richardson, Food and Drug Administration pathologist, was present and observed the fetuses taken by caesarean section from the rats in the studies just described.

On February 17 and 18, 1970, the animals in our teratological studies on TCDD were autopsied and the fetuses examined in the presence of the late Dr. H. L. Richardson of the FDA and Dr. C.T.G. King of NCI. The results suggested that some of the teratogenic effects reported in the Bionetics' study may well have been due to the high content of the impurity, TCDD, in the sample of 2,4,5-T which was studied.

On February 24, 1970, V. K. Rowe presented a summary of our teratology studies to people from FDA and other concerned governmental groups in Washington.

DOW 760595

On March 17, 1970, the final reports of the Dow studies were presented before the Society of Toxicology in Atlanta, GA, entitled TERATOGENIC STUDY OF 2,4,5-TRICHLOROPHENOXYACETIC ACID IN THE RAT by J. L. Emerson, D. J. Thompson, C. G. Gerbig, and V. B. Robinson, The Dow Chemical Company, Zionsville, Indiana and STUDY OF TERATOGENICITY OF 2,3,7,8-TETRACHLORO-DIBENZO-p-DIOXIN IN THE RAT by G. L. Sparschu, F. L. Dunn, and V. K. Rowe, The Dow Chemical Company, Midland, Michigan.

DOW 760596

On April 17, 1970, J. E. Johnson, E. H. Blair, G. E. Lynn, and V. K. Rowe appeared before the Senate Committee on Commerce, Subcommittee on Energy, Natural Resources and Environment chaired by Senator Hart of Michigan. Dr. Johnson summarized for the Committee the uses, benefits, and hazards associated with the herbicide. He paid special attention to the toxicological information available on 2,4,5-T and 2,3,7,8-tetrachlorodibenzo-p-dioxin, and told of the work in progress.

During and since 1970, there have been a great number of toxicological and related studies conducted. Others from Dow and elsewhere will be discussing these in detail in subsequent presentations.

VKR
January 1970

a Dow Canada

BACKGROUNDER

L / Chemical Canada Inc.
P.O. Box 1012, Sarnia, Ont. N7T 7K7

Contacts: Don Stephenson 519-339-3599
Wayne Wolski 519-339-3384

Contributors: Dr. Richard Wilson, Harvard Univ.
(as reported in Weed Science Society
of America "Newsletter" October 1981)

Date: June 30, 1982

Release no. 155

THE RISK IN SPRAYING 2,4,5-T HERBICIDE

Environmental activist groups have been demanding the ban of 2,4,5-T on the premise that it increases the risk of developing tumors.

Dr. Richard Wilson, a Harvard scientist, disputes the 2,4,5-T and tumors theory, however, he recently calculated the risks associated with spraying 2,4,5-T and found that if a person worked at applying 2,4,5-T with a backpack sprayer for 5 days a week, 4 months a year for 30 years his/her chances of developing a tumor would be 0.4 per million. Those conditions would represent a probable exposure level far greater than the general populace, even if they lived in a spray zone.

In comparison, other risks associated with developing a tumor are:

	Chances Per Million
Sunbathing	5,000.0
Smoking cigarettes	1,200.0
Being in a room with a smoker	10.0
Drinking one can of diet soda with saccharin/day	10.0
Drinking milk with aflatoxin or eating four tablespoons of peanut butter/day	10.0
Drinking one can of beer/day	10.0
Eating 1/4 lb. charcoal broiled steak/week	0.4

31

15843

DOW CHEMICAL CANADA INC.
Modeland Road, P.O. Box 1012, Sarnia, Ontario, N7T 7K7

August 19, 1982

File - Spray Program
Duplicate copy

Mr. T. S. Thompson, Ph.D.
Public Affairs Manager
New Brunswick Electric Power Commission
527 King Street
Fredericton, New Brunswick E3B 4X1

Dear Mr. Thompson:

The attached letter and documents pertaining to the safety of phenoxy herbicides were sent yesterday to the enclosed list of Atlantic Provinces daily and weekly newspaper editors as well as two magazines covering the region. No broadcast media were covered because the complexity of the information does not lend itself to 60-second explanations.

The letter of transmittal is self-explanatory. The point is that there is a great deal of scientific evidence attesting to the safety of these products and there is no substance to alarmist claims.

Please feel free to use the information enclosed in any appropriate manner. Extra copies of any item are available by calling my office in Sarnia (519-339-3131), our agricultural chemicals sales representative in our Halifax sales office (902-429-5623), or write to either location.

We hope our initiative will lead to more balanced news coverage of the safety issue and result in a better informed public.

Yours very truly,

Harold Major /kan

Harold W. Major
Manager, Government Relations
Agricultural Chemicals

/kan

15844

DOW CHEMICAL CANADA INC.
Modeland Road, P.O. Box 1012. Sarnia, Ontario, N7T 7K7

August 18, 1982

News Editor
The Daily News
446 Main Highway
Halifax, N.S. B4C 2S9

Dear Sir:

Recently the phenoxy herbicides 2,4-D and 2,4,5-T have been "in the news" in the Atlantic Provinces because of allegations that their use for brush and weed control in forestry and on right-of-ways involves significant risk to human health and the environment.

These pressures have resulted in some suspensions of proposed herbicide applications until "further study" can be undertaken, particularly in Nova Scotia. That has unfortunately strengthened some people's belief that the risk may indeed be real.

In view of the current controversy, we thought you might like to have information which summarizes what the world's scientific community knows about the health and environmental impact of these two herbicides. We also thought you might be interested in knowing the relative risk that these compounds pose versus other risks people readily accept.

In actual fact, so much is known about the effect of these two herbicides after more than thirty years of research and use that it is reasonable to say they pose thousands of times less risk to human health than sunbathing, for example!

The herbicide most recently in question is Esteron*3-3E, a Dow product which, in its concentrated form before dilution for use, is 42 percent 2,4-D, 40 percent 2,4,5-T, a small amount of an emulsifier, and the rest light furnace oil. This concentrate is diluted for actual spraying at ground level by mixing it with about 140 times its volume of water. This is a low volatile formulation which minimizes evaporation and drift.

It isn't necessary for you to read all the information enclosed (just skim the summaries and conclusions sections) to gain an insight into the huge body of data that exists on the effects of 2,4-D and 2,4,5-T. Moreover, government-approved application rates embody an additional hundred-fold safety factor.

(more...)

*Trademark of The Dow Chemical Company

If I can help you understand and interpret all this science for your readers, please give me a call collect (519-339-3599) in Sarnia.

Yours very truly,

D. R. Stephenson
Director of Corporate Communications

/kan

Enclosures:

(1) "The Risk In Spraying 2,4,5-T Herbicide" - Dr. Richard Wilson, Harvard University, as reported in Weed Science Society of America newsletter, October '81. Dow Canada Backgrounder #155, June '82.

(2) "A Summary Of Pertinent 2,4-D Facts" - Backgrounder #159, Dow Canada, July '82 (supported by a bibliography of 134 literature references).

(3) "The Phenoxy Herbicides, Second Edition" - Published by the Council for Agricultural Science and Technology, August '78 (Note Summary on pg. 1, para's. 4 & 5). (Cites over 190 literature references).

(4) "What 56 World-Renowned Scientists From Eight Nations Say About The Safety Of The Herbicide 2,4,5-T" - Backgrounder #160, Dow Canada, July '82 (based on the results of the June '79 three-day Dispute Resolution Conference On 2,4,5-T, Arlington, Virginia. Journalists can obtain a copy of the complete 102-page report from Dow Canada).

(5) "The Safety Of The Herbicides 2,4-D And 2,4,5-T" - Forestry Commission Bulletin #57, United Kingdom, 1977; by D.J. Turner, B.Sc., Ph.D. et al, (Cites 242 literature references). (Note Summary on pg.4 and conclusions on pgs. 39-41).

(6) "On the Matter of Dioxins In Our Environment" - Backgrounder #131, Dow Canada, December 1980.

V - RESULTS FOR ALL CAUSES OF DEATH

Results of the analyses for all causes of death combined (i.e. total mortality) are set out below, for the total cohort, and for two sub-groups of the total cohort, namely those with year first sprayed of 1959 or later and those with year first sprayed of 1958 or earlier. These two sub-groups were selected since there is evidence which suggests that diesel oil and used transformer oil was routinely mixed with the herbicide in 1959 and later years. If this is the case, these two sub-groups would have been exposed to a different range and mix of toxic agents.

Total Cohort

The SMR for the total cohort, for all durations since first exposure to the herbicide, is 154 (CI 126 to 188), based on 98 actual deaths versus 63.55 expected.

The corresponding results broken down by durations since first exposure to the herbicide are set out in Table 1 below.

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TABLE 1

**ACTUAL AND EXPECTED DEATHS,
FOR TOTAL COHORT,
BY DURATION SINCE FIRST EXPOSURE**

Duration (Years)	Deaths		SMR	CI
	Actual	Expected		
0 - 4	6	4.47	134%	49% - 292%
5 - 9	8	5.95	134%	58% - 264%
10 - 14	12	7.91	152%	79% - 266%
15 - 19	14	9.95	141%	77% - 237%
20 - 24	19	11.09	171%	103% - 267%
25 - 29	25	10.32	242%	157% - 358%
0 - 9	14	10.42	134%	73% - 225%
10 - 19	26	17.86	146%	95% - 215%
20 - 29	44	21.41	206%	150% - 277%
30 and over	14	13.86	101%	55% - 170%
25 and over	39	24.18	161%	114% - 220%
20 and over	58	35.27	164%	125% - 214%
15 and over	72	45.22	159%	125% - 201%
All durations	98	63.55	154%	126% - 188%

Therefore, for the total cohort, statistically significant excess mortality is observed for all causes of death for all durations combined (SMR = 154, CI 126 to 188), for durations 20 to 24 years (SMR = 171, CI 103 to 267), 25 to 29 years (SMR = 242, CI 157 to 385), 20 to 29 years (SMR = 206, CI 150 to 277), 15 years and over (SMR = 159, CI 125 to 201), 20 years and over (SMR = 164, CI 125 to 214) and 25 years and over (SMR = 161, CI 114 to 220).

DOW–APPENDIX A

PART I

THIS COMPLETES

YOUR MARKED

DOCUMENTS

19–Nov–92

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1431

ROUTING

AG. CHEM.	ALRAT						Phenol	SOLVENT	T. O. D. D.	OTHER
								12.50-13-22		2 4D

FIRM NAME (IN FULL—DO NOT ABBREVIATE) INDIVIDUAL DIVISION OF COMPANY, IF ANY — INDUSTRY

STREET — CITY — ZONE — STATE — SALES OFFICE

PERSONS INTERVIEWED AND POSITIONS

(Mr.)	ADDRESS NO.	FIELD	DOW	PHONE	DATE CALLED	DATE WRITTEN	FIELD CALL
		3				2/23/53	23

ACTION — RECORD — SALES OFFICE

DOW.1 551474

"SALES RECORD"

MAR 25 AM 10:14

MN0732280

MARKET DATA

CONSUMPTION DATA OBTAINED DURING THIS CALL

PRODUCT (USE PRICE BOOK NAME)	ESTIMATED ANNUAL REQUIREMENTS			PROSPECTIVE OR UNSATISFIED QTY.	END USE CODE
	DOW QUANTITY	COMPETITION			
		COMPETITOR	QUANTITY		

OTHER INFORMATION

2. [illegible] that to date they have purchased [illegible] allocation for the 1952 season. This means that they will be able to [illegible] their entire chemical weed control spraying program [illegible] They report that they will handle this work as they have in [illegible] as also the hands of the contractors. They will [illegible] their own [illegible]. The bulk of the business will be handled by Penn Line Service of Scottdale, Pa. and the Tree Preservation Company of Pittsburgh, Pa. Other smaller contracts will go to the Quaker City Tree Company of Philadelphia, the Asplundh Tree Expert Co. of Jenkintown, Pa., the Davey Tree Expert Company, and to a few other contracts which will be decided later. Mr. Thorp expects that a very big share of the chemicals used on the right-of-way in 1952 will be Dow materials. All of the above mentioned contractors are for foliage spraying

2. These people in addition to doing contract work, are also purchasing Dow Esteron Brush Killer and Esteron 245 for their maintenance departments. This material is being applied by their own crews to plant and local right-of-way areas in and around their plant sites.

3. These people are still vitally interested in developing a program of basal bark spraying. Mr. Thorp expects that they will be doing some of this after the regular foliage spraying is the answer this. They will also do some experimental plantings this [illegible]

15851

DOW 1 551475

// Attention: R. K. Perry and H. L. English - A very serious adverse publicity situation seems to have arisen on some of the P.P.&L. lines. It was the purpose of the writer meeting with the above mentioned men to discuss this problem to see if we could come up with some answer. While talking with Mr. Emery he advised that this problem had recently arisen and Mr. Robert Batey of American Chemical Paint and others were called in consultation. It seems as though one Mr. R. L. Angst, Sports Editor of the Pottsville, Pa. journal published several articles to the fact that many dead rabbits were found along P.P. & L. right-of-ways where they had been sprayed by "poisonous" chemicals. Of course P.P.&L.'s publicity department jumped on this right away in an attempt to correct the situation. Apparently in an open meeting attended by Mr. Batey, P.P.&L. people, State Forestry people and local sports clubs , this question arose and Mr. Batey advised all present that there was no such thing as killing rabbits and they must be wrong. Of course this was the wrong approach and right a way all of them felt that probably the Power line companies and the chemical companies were trying to pull the wool over their eyes. Since Mr. Angst's articles have appeared in the Pottsville paper, some of the national sport writers have taken up the hue and cry as it seems to be quite a nice controversial subject for them to get into! The writer observed several exchanges of correspondence between the National President of the Outdoor Writers Association of American and some of the local sports clubs in the Pennsylvania area served by Penna. Power and Light. Inasmuch as these writers do not know anything about chemical weed controls they have naturally assumed that all of the materials are poisonous and are thereby creating a serious hazard to wild life of the community.

As a result of a recent meeting the above mentioned people decided that they would turn their problem over to one Professor English of Pennsylvania State College who is apparently an expert on game animal diseases. They all agreed to abide by Dr. English's recommendations.

During the course of our discussion it was the writer's question that perhaps Dr. English of Penn State and one of the representative members of the outdoor writers association could be interested in taking a trip to our Midland, Michigan plant in order to observe the toxicological laboratories and the various procedures which we go through to insure positive safety for the use of these materials to our own personnel and to people who are using them. Inasmuch as American Chemical Paint apparently do not have too much toxicological information which they developed themselves it might be to Dow's advantage to press this point at this time. I would appreciate receiving any comments that Mr. Rowe or Mr. Smith might have in this regard.

DOW 1 551397
MN07 3280

MIDLAND
February 22, 1961

F. E. Ouellette
Labeling and Product Regulating Section
47 Building

TOXICOLOGICAAL INFORMATION ON A NUMBER OF PRODUCTS SUITABLE FOR APPLICATION FOR REGISTRATION IN NEW ZEALAND

Here is the information you wished for the registration of these products in New Zealand. I shall give the toxicity data; the rest you can get from the literature I am sure.

Vidden D

Vidden D has a moderate acute oral toxicity; the LD_{50} value for rats is 0.40 g/kg with 10/20 confidence limits of 0.31 to 0.54 g/kg. Eye contact tests on rabbits resulted in marked pain, moderate conjunctival irritation and transient corneal injury; healing occurred within two - three days. No appreciable skin irritation occurred in rabbit skin tests if Vidden D was applied so that it could evaporate normally. However, when confined, a moderate irritation occurred upon several hours contact. Repeated prolonged contact when confined resulted in a burn. In skin absorption studies rabbits survived 0.4 g/kg of body weight. Higher doses were not run because of the severe burn produced at both 0.2 and 0.4 g/kg levels. When rats were exposed for one hour to 1000 ppm of Vidden D, one of ten rats died; seven of ten died when exposed for two hours. At 400 ppm (2 mg/l) both a two and one hour exposure caused the death of one of ten rats. Signs of eye irritation were immediate; definite indications of upper respiratory irritation and lachrymation appeared in about one hour. Human tests indicate that the threshold of odor for most people is probably no greater than three to five ppm. A tentative threshold limit value for repeated daily exposures of one ppm has been suggested.

Fumazone (1,2-dibromo-3-chloropropane)

Fumazone has a high acute oral toxicity; the LD_{50} value for various species of animals ranges from 0.06 to 0.41 g/kg of body weight with chicks the most susceptible and mice the most resistant. Eye contact tests on rabbits resulted in moderate pain and mild transitory conjunctival irritation. Healing occurred in two to three days. In skin contact

studies on rabbits Fumazone caused only a mild irritation if the exposure was short, but it caused a burn on prolonged contact. Fumazone is readily absorbed through the skin; the LD_{50} value for rabbits being about 0.5 g/kg of body weight. When inhaled Fumazone was found to be high in toxicity to rats. The LC_{50} values are approximately; for one hour, 370 ppm; for two hours, 232 ppm; four hours, 154 ppm; and for eight hours, 100 ppm. A seven hour exposure to 50 ppm caused adverse effects but the animals recovered slowly. The tentative threshold limit value suggested for repeated exposure to Fumazone is below 1 ppm. Human volunteers reported that 1.7 ppm of Fumazone was detectable but not unpleasant. (See also data sheet entitled "Summary of Toxicological Information and Practical Considerations in the Handling and Use of 1,2-Dibromo-3-Chloropropane (Fumazone)".

DOW 1 5513398

Zytron

See Dow Crab Grass Killer information sheet entitled "Information for Research Workers Dow Crab Grass Killer".

Carlon

Carlon has a low acute oral toxicity, the LD_{50} value for rats is approximately 4.0 g/kg of body weight. It was found to cause essentially no effect when in contact with the eyes of rabbits. In skin tests on rabbits, Carlon caused mild irritation and some scaliness. In the skin tests conducted, there were no symptoms of absorption through the skin observed.

Dowpon

See data sheets entitled "Toxicological Information Relative to Dowpon or Radapon" and "Summary of Toxicological Information, Practical Considerations in the Handling and Use and First Aid Measures, Dalapon, Sodium Salt".

Baron

See data sheets entitled "Summary of Toxicological Information, Practical Considerations in Handling and Use and First Aid Measures" and "Properties, Health Hazards and Precautions For Safe Handling Baron".

Kuron

For data see data sheets entitled "Summary of Toxicological Information and Practical Considerations in the Handling and Use of Kuron, a Brush Killer Formulation" and "Properties, Health Hazards and Precautions For Safe Handling Kuron".

DOW 1 5513399

Dowfume MC-2, because it may be considered to be chlorized methyl bromide, may be considered to have the same degree of toxicity as methyl bromide. The toxicity data on methyl bromide and, therefore, on Dowfume MC-2 may be summarized as follows:

Dowfume MC-2 is a gas at ordinary temperatures, therefore, there is no problem from ingestion. Direct eye contact with the liquid has been shown to be capable of resulting in considerable discomfort, transitory conjunctival irritation and corneal injury. Skin contact with the liquid may result in a burn especially if confined. The vapors of Dowfume MC-2 are very irritating to the eyes, causing lachrymation. They are also highly toxic. Rats survived a one hour exposure to 1000 ppm and an eight hour exposure to 260 ppm. Rabbits have been shown to be more resistant than rats to Dowfume MC-2. As an overexposure to chloropicrin is unlikely, the principal hazard from inhalation of Dowfume MC-2 is that presented by methyl bromide. The suggested threshold value for repeated prolonged exposures to methyl bromide is 20 ppm.

For handling precautions, see the enclosed bulletin entitled "Dowfume MC-2."

Dowfume EB-15

Dowfume EB-15 has a moderate acute oral toxicity; the LD_{50} values for laboratory animals range from 0.12 to 0.32 g/kg of body weight. Eye contact with the liquid may result in moderate to severe pain, moderate conjunctival irritation and minor corneal injury. Healing should be complete in several days. A single short skin contact should cause no more than minor irritation; prolonged or frequently repeated exposures such as may occur when wearing contaminated clothing or shoes may cause severe pain, blistering and a burn. Dowfume EB-15 is high in acute toxicity by skin absorption; the LD_{50} for rabbits is approximately 0.2 g/kg of body weight. The vapors of Dowfume EB-15 are high in acute toxicity; the LC_{50} for rats is 600 ppm for a one hour exposure, 500 ppm for a two hour exposure. The suggested threshold limit values for single exposures are as follows:

75 ppm for a 7 hour exposure
300 ppm for a 1 hour exposure
1500 ppm for a 0.1 hour exposure

See also the enclosed reprint entitled, "Toxicity Study of a Spot Fumigant".

[illegible] similarity; the LD_{50} value [illegible] 0.25 g/kg of body weight. Eye contact tests on rabbits showed that Promerge is capable of causing a severe burn of the eye resulting in possible permanent [illegible] of vision. A single short skin contact, [illegible] minor irritation. A prolonged or frequently repeated skin contact may result in a burn especially when confined to the skin. However, the main hazard from skin contact is that of absorption through the skin. Promerge is highly toxic by skin route; the LD_{50} for rabbits being in the range of 25 to 50 mg/kg of body weight. Incidently Promerge, even in very small amounts, stains the skin upon contact.

Spray concentrations of Promerge, diluted with water as directed (10 and 5,), are capable of causing only minor eye and skin irritation. However, such concentrations may be absorbed through the skin in toxic amounts.

I hope the above is helpful to you in preparing the information in these documents suitable for registration purposes in New Zealand. If, however, you encounter some difficulty, let me know.

-Mark A. Wolf-

Mark A. Wolf
Biochemical Research Laboratory
1701 Building

MAW/mmd

Enclosures

DOW 1 551400

15856

THE DOW CHEMICAL COMPANY

DOW 1 551259
MN0732 90

Midland, Michigan
December 19, 1958

V. H. Kahn
Biochemical Research
CBV Building

cc:
L. E. Coulter
J. E. Coleman
C. J. Kintz
E. E. Hollingsworth
E-8,9th Floor Dale

This is a request for work to evaluate the safety of Esteron 44 as an aquatic herbicide:

1. Human oral administration tests for human. Since this formulation is to be used in water at a concentration of 5.0 p.p.m. (2 p.p.m. active) normally a dilute aqueous solution should be tested.

2. 96-hour TLm and chronic feeding studies on the active ingredient of Esteron, propylene glycol (C$_3$H$_8$O$_2$ to [illegible] and other esters of 2-(2,4,5-trichloro-phenoxy)propionic acid.

This work should be completed as soon as possible and before May 1, 1959. We are planning to withhold a Release to Sales for use as an aquatic herbicide until this work is completed. Charge Account 1640.

Very truly yours,

G. E. Lynn
Agricultural Chemical Research

1jl

15857

A TALK GIVEN BY DR. DON D. IRISH IN BIOCHEMICAL RESEARCH DEPARTMENT CONFERENCE ROOM, 1701 BUILDING, ON JANUARY 18.1967

MN062926

I am using many illustrations from Toxicology because I think they apply more in the toxicological area, of course. This is rough, and off-the-cuff. I did make some notes to keep me at least a little close to the facts and I'm going back further in history than the Biochemical area.

H. H. Dow, who was the founder of company, (I didn't know him, I came here just after he died) was very interested in the biological area in spite of the fact that he was, I guess everything else from an electrician, to a chemist, to an electrochemist, to whatever you want to call it. He got very interested in the agricultural area and grew a nice orchard out here; he used to take apples to national shows and win prizes. His interest, of course, affected The Dow Chemical Company slightly (as you would expect), and we got into the agricultural chemical business by making some old standby materials that have been known as long as there have been agricultural chemicals--lead arsenate, Paris Green, and sulphur--powdered sulphur. I doubt if many of you have ever even heard of Paris Green. It was a copper arsenical material. A fellow by the name of Kellogg, I don't remember which laboratory he occupied part of the time, I guess Chemical Engineering, was sort of a leg man for the agricultural area. He went into the Dow orchard and tried things out.

Dr. Hale--William J. Hale--was an interesting person, as I discovered after I got here. He was also interested in the agricultural area. He started quite a commotion nationally by something he called the farm chemurgy, which means trying to interlock the chemical industry with the

agricultural area by using the agricultural materials for chemical purposes and vice versa--using chemicals in the agricultural area. (There's a national conference on the subject.) He was the Director of the Organic Research Laboratory up until somewhere around 1950. As he moved up to the front office, Edgar Britton moved in to be the Director of Organic Chemistry. Edgar Britton was also interested in the biological field, particularly the agricultural field. He had the notion of synthesizing nicotine or something close thereto. Nicotine was a very important contact insecticide in those days. Well, he gave up on nicotine, but he got into some quite unrelated organic structures, particularly the nitrophenols. They were tested at universities and had some activities of interest.

There was also a group of relatively economic byproducts of our phenol process that had microbiological activities. That was another area of possibility here. Michigan State University microbiologists had tested these materials. (Didn't amount to much on the market in those days.) There was enough interest in this area that Edgar Britton of the Organic Laborato , suggested to a chap named Lindley Mills--no longer here--that they set up a small group to do a little work in this area in the Organic Laboratory. About 1931, Bill Allen, who is now Manager of Marketing in a byproducts area, came in. He largely worked in the agricultural area. And Bruce Fayerweather, down in the Patent Department, came in also as a microbiologist, from Michigan State. These people--there are a couple more of them there but I thought--you don't know them anyway--they started the concept of what we call today TS&D--Technical Service and Development. They'd take chemicals that

were made in various places in The Dow Chemical Company and they'd run out to the Agricultural Experiment Station at the University and have them tested and see if they could get Dow Sales to sell them. It was just sort of a "feeling beginning", if you wish. Then, in 1935 this group moved out of Research and into the Sales Department. They started what reall·· is called today Tech. Service and Development.

Now at an earlier date, in the early thirties sometime, Dr. Hale (Billy Hale as we called him) tried to convince Willard Dow that we ought to have a Biochemistry outfit. Actually, why should we have a biochemist? I can only guess that he was thinking in terms of broadening the base, the disciplinary base of research at Dow. We had organic chemical engineers, physical chemists and physicists, and a few things of this sort. In any case, Willard Dow was receptive and started probing around. I met John Grebe about that time and John was looking around, so—I was working for a drug company at that time—it seemed sort of interesting, so we got together on the deal. That was in the spring of 1933. So, I managed to disconnect my former relationships and get here in August 1933. I came in, and I was taken to Willard Dow's office. Not knowing anything about The Dow Chemical Company or their interests, (not knowing anything more about biochemistry than I should, certainly) I said, "What am I supposed to do?" I think his answer was—I believe an important basic thinking—he said, "How do I know? I'm not a biochemist; you're the biochemist. You tell us. There's The Dow Chemical Company. If you can find a place for a biochemist, you're in." I think that's a fair statement of principle around The Dow Chemical Company. It

15860

was then; I think it still is to a degree except, of course, we're much larger and more complex. You're hired to use your brain. You're not just a pair of hands. You're expected to tell Dow Management what is needed in your area. Management can accept it or not, as they please. There are a lot of other factors besides your part; you have to realize this, of course. But they need you to draw conclusions on your part. It's your job to know; to draw a definite conclusion; Management needs the facts and they need the conclusions, along with all the other factors they have to be concerned with, in drawing business conclusions.

DOW 1 2777220

Well, I came in August. Where will we put a laboratory? We didn't know what we were going to do, we didn't know what we wanted. We looked out in this area--and by the way, there was nothing this side of the railroad tracks at that time--there was an old chicory plant out here (this is near where they grew chicory) and nothing else. The West Side Power House, which is an old place now, was a new building then and there was a little extra space out there. We looked at those and wondered how we could build a laboratory in either place. Then John Grebe suggested that he could squeeze a little space in the Physics Laboratory. Now, the Physical Research Laboratory then was occupying what had been the old garage and 48 Building is now the cafeteria. That was the entire area. So John squeezed out a little space for us in there.

Well, at that time a general aspect of day-to-day operations in getting money and getting things, we turned to John as administrative head. Ray Boundy was assistant director there; Jack Chamberlin was also the administrative there, but he spent most of his time actually

working with Dowell problems and trying to cook up fancy electronic instruments for plant control operations. He was largely interested in that area. Willard Dow made it very clear, however, that he wanted a direct report from us on what we were doing and why. So frankly, I reported no closer to Willard Dow than anybody else. Well, we started out talking to people.

What were the valuable fields in this great Dow Chemical Company? I didn't know anything about Dow. Might as well find out what people thought. Well, I got a lot of free advice, as you can expect, although I couldn't go into all the angles of it. Mills' group in the Organic Laboratory had already started to explore these areas. They were very anxious that we get into the agricultural field and microbiology field. Partly, because they were closer to the development--to the Sales--area, and they'd like to see more research, they'd like to see things coming into this area. Not to replace them, not with any transference with, but as a research backup. We could sit in many fields. Too many to mention--I doubt if I could remember all of them. We took to human health, of course, animal health and nutrition, and heaven knows what else.

I was in sort of an innocent mood one time after probing around and listening to people, and I suggested to Willard Dow that we didn't know enough about the problems of handling chemicals. Now you remember that things have changed. We used to make--up until that time we'd been making old chemicals--large quantities to go to large industries. Responsibility was not as great; fact is, we didn't know what we were doing ourselves. But now we had people

synthesizing brand new things and I commented that I didn't think we knew enough how to handle the things and might get into difficulties. He came back with a very direct and very simple answer, "So why don't you do something about it?" That's quite typical of Willard Dow. Well that of course was the start of the idea, at least of toxicology. In fact, not many people did. Toxicology in those days was legal-medical toxicology and largely dealt with analyzing stomachs for arsenic and other jolly things like that. That's about all it was. Nobody conceived of toxicology in the sense that we do today.

Now, of course, we shortly realized, when we got a look at this point of view that we had some concern for our own worker health, and that developed into what we call today "Industrial Hygiene" or "Environmental Research." Let us take a look at each one of these fields and follow the development. I'll take one of them and follow it through and go back to pick up the other.

Get a feel for what we did and why. I'm going to use some anecdotes in here--not because they relate specifically to those fields, that's their source, but largely because I think they give a broader picture of policy and thinking at that time, and I think you'll agree to that. We'll start with agriculture.

They were slow in beginning; it's quite a sizeable field as you know. We worked very close with Bill Allen. Bill first came into the picture, of course, in the Organic Laboratory; he moved into the Sales Department later. And he was quite an important part of the development of the early agriculture area. Most of the work was done, at the time I came here, at the University's experiment

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stations by Mills or Allen contacting these people. Franklin Kagy, who's now in the Walnut Creek Laboratory, was at Ohio State University. He did quite a bit of testing for us at that time. Later moved into the California Division, where he was working with our Sales Department and developed the field station at Seal Beach. At the same time, Walter Duck,a few of you may have known him personally, was at Michigan State University also doing some work for us. His work for us became so dominant over university work that he moved out of the university and down to South Haven, and he set up an experiment station there in the field. Now these people reported to the Chemical Engineering Laboratory. You say, "Well, why?" Well, they were responsible for manufacture, sale--in the sense of development--of agricultural chemicals after they developed the procedure.

Coming back to Midland. We felt, in discussing this thing, that we needed some backup in a more research sense in Midland, and they looked at us in Biochemical Research. Well, 1937, we picked up another biologist --Fred Fletcher--who went to the University of Syracuse--professor there. In 1935, Lefty Lynn, who's now in bioproducts, had come with us from the University of Illinois. His work was not in agriculture at first; it was in microbiology and he did much of the microbiology of the early study of the phenol waste disposal area. By 1939 we figured we needed a more elaborate backup field research in Midland, and we got the farm out on Eastman Road and set up green houses, etc., out there. We got this going and moved in 1940. Lynn moved in as chemist, responsible for the development of these areas; and we sep up entomologists, plant pathologists, and agricultual people out there. Many of the older people in the present bioproducts, you will find, were in that group out there on Eastman Road farm.

Let me give you a couple illustrations of development in this area. But I want you to recognize these are more significant than just the agriculture field; they have a much broader significance, I should say.

Edgar Britton had developed these electrophenols; one of them, di-nitro-secondary-butylphenol, was quiet interesting for the control of plant disease. It killed the fungus, it controlled the disease all right--but it had a little tendency to kill the host plant, too. Now any intelligent plant pathologist would know that's the time to throw the whole thing out. But I want to point out I think there was some rather astute understanding that they took a look at it; it killed plants! Now don't--looking hindsight, looks real simple. Looking ahead is quite different. There were very few materials used at that time as herbicides to control plants. We didn't think that way. But I think it's very astute that there's a "It does what we don't want it to do, so how can we use what it does do?", and developed a pretty good herbicide that was used quite extensively. I know there was a lot of it used in California. I'll bring that up a little later as another illustration.

The next one--a little more complex--I think particularly interesting. In other words, this first one, when it doesn't do what you want it to do, what can you do with what it does do? It's about that simple. Another one, Dr. Hale--Billy Hale--had contact with a young Professor Watley down East. George Ehl (George is now director of Brooklyn Botanical Gardens) had done some very, very excellent research in the area of plant hormones, things that affect or control the growth of plants. It looked very interesting. He came in here as a

consultant and helped us enormously in our laboratory research to become familiar with these things. And we thought, "Now this has wonderful possibilities for the control of plant growth, increasing it, decreasing it, controlling it." And we even got quite enamored with pathenocopic fruit. You didn't have to pollinate the tomatoes, you could put on a little plant hormone--we jokingly talked about a big ad in the Saturday Evening Post with a big red tomato, underneath, "Fatherless tomatoes sired by Dow's Chemical." This was one of our jokes that carried over.

But seriously, we were looking at this sort of thing. Here he was, --and we were not as astute as we were in the case of the herbicide-- a university professor, I think down in Chicago, who suggested an entirely different purpose in other areas. Minute traces of these things were effective, but only a little more than minute traces were exceedingly effective in killing plants. Why didn't we see it? I don't know. But you can imagine when this opened up as a suggestion-- and by the way, he was a consultant to the government and this was thrown into the government area--wide open--you should have seen the scramble. We could spend all morning, fascinating discussion of the patent problems and the chicanery and everything else that went on-- all over the country. The Dow Chemical Company came out on top. Why?

Well, I have three angles that I want to outline. First: We had the field experience with herbicides, with that dinitrophenol complex, and others. We knew something about it--we knew where it was needed, how to market it, and we knew how to use it in the field. Also, we had know-how in the laboratory on plant hormones, not on herbicides--we

understood the basis, we knew what they did. We knew what they did that we wouldn't want them to do. We had backup understanding. And third, the 2,4-D and the 2,4,5-T just played right into our rough product in our production area. We knew how to make it.

Now, many people laughed, like they always do--"You know how to make them? I don't buy that." We needed all three. But we did have this scientific know-how to approach this thing and have maintained our lead in the herbicidal field ever since. I brought this up because I think you should remember that sometimes, in a worthwhile field, you may not have to have complete patent control--but it's nice to have. You may not have to have all the aspects of the thing, but if you understand what it's all about, when it breaks you're in a good position to do a good job of evaluating.

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Let's move on quickly.

Julius Johnson came in 1941 to the Biochemical Laboratory, from Illinois, and we explored with him immediately the possibilities of the human health area, the animal health area. That was right at the beginning of the war and there was a tremendous program--as we were moving into tropical areas--a tremendous program on malaria. We got very much involved in that. Julius was doing the key work in our malaria program at that time. Well, Edgar Britton, of our Organic Laboratory, had become quite intrigued by the essential amino acids. It's an easy game to look back to see these things. They were brand new than. We'd just begun to know a little about them. He developed the means of synthesis of several important essential amino acids. Julius Johnson had done his graduate work with Rose in Illinois--the very foundation of fundamental

research in essential amino acids. Well, Julius came to me one day and he said, "This fellow Britton has developed these things...I think we ought to do something with them." I said, "Fine. What do you want to do?" He said, "I think we ought to look at animal nutrition." "Swell. Let's go."

It was immediately after the war; the malaria program went down. We moved out to what is called "the old bromine plant," at the end of Main Street, in that area which is now occupied by Northwood Institute. It was an old dump, I'll admit. But it was an economic way of moving into the animal field, out away from the rest of town, to see what we could do. So,we developed the second farm--this for animal investigation. Heavily into the chicken area and chicken nutrition, but other animal nutrition, too. And I think this was the foundation of our methionine business and a number of other things, but I won't go into them. It was a break into this field of animal nutrition.

Now, Dow had grown pretty large by then relative to the small company it was when I came here. And to handle all the chemicals--plastics, agricultual chemicals, metals, what not--all in one pot, it was an extraordinary difficult thing. It needed sharp delineation of a field and what it was. Willard Dow had started this idea of setting up product departments. The obligation of knowing a field, knowing what was needed in the field, and serving that field. Well, several of us who were concerned in the agricultural area were pushing very hard that we did set up such a department in the agricultural area. Bill Britton, who was then in charge of the pilot plant area, organic chemicals basically, was put in charge of this group. Mills, who was in biochemistry,

pushed Bill very hard, saying "If you're going to be successful, you have got to move this research into your product department." Now that was not the way things were set up. I think we can say that the Biochemical Laboratory was very inclined to promote this thing and to give up our prerogatives there in order that this be well done, and I think it was. We reorganized this, and moved it there, and Julius Johnson took the position of Director of Research in the agricultural area. Of course this has grown, as you know, into the present Bioproducts Department.

Well. Let's return to 1933 and take a look at microbiology, as time moves. This moved more rapidly than did the agricultural research. It's a bit simpler, you know. The bugs are smaller, and it doesn't take quite as big a field to herd them, and the apparatus is a bit simpler. So we moved in the field, I think, more rapidly for that reason. We had this small group of compounds, we called it Dowicides; we knew they were active in the microbiological field, but we didn't sell many of them. An energetic young chap by the name of Don Ballman came in. You probably know Don now as one of the vice-presidents in the Marketing area. An executive and on the Board of Directors. Don was an energetic young fellow then, and I wonder sometimes if it wasn't a little waggish point of view on the part of our Executive Sales to say they quieted him down by giving him sort of a working post. And, they dumped in these Dowicides. I've got to hand it to Dow, he made something of it and in no uncertain terms. I want to give him a lot of credit for it.

About that same time, about 1935--Don came in 1933, the same time Biochem started--by '35 Mills' group had moved into the Sales Department, Technical Service and Development. Bruce Fayerweather moved to Patent

Department. The whole matter of research, development, sales service, microbiology, everything else, dumped into biochemistry--we had the whole works. Working closely with Don Ballman in the Sales we, I think, succeeded in going places.

Now, as this thing moved, there was a young chap out in Nebraska teaching out there in a medical school--by the name of Edwin Dunn. We captured him and brought him here because we felt that with his broad background in biochemistry, particularly in the enzyme field, he might do something in this microbiology field. Which he did. Primarily because we were interested in preservation again, toying with the area of fermentation (I'll mention a little later), but also we wanted to do some basic biochemical research in the field of enzymes, and this was in the area that he graduated.

We were just going with this business of preservatives field when The Dow Chemical Company acquired a wood displacion plant in Marquette, Michigan (acquired the Cleveland Cliffs Iron Company) became the Cliffs-Dow Company.

Edgar Britton and Willard Dow were very interested in the possibility of converting this cheap wood waste, sawdust, everything else, into sugar and alcohol. Alcohol is a very fundamental chemical raw product and we could get it cheaper. Bill Britton, then in charge of the pilot plant--organic pilot plant--started to set up the pilot plant for fermenting this. Not fermenting--hydrolyzing this wood to sugar, to a sugar solution. And the Biochemical Laboratory took on the job of trying to ferment the resulting mess to produce some kind of a chemical. Ethanol was one that they particularly wanted, but we also looked at propionic acid as an important product at the time and also

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something we could fool with here.

Some very intriguing scientific aspects of this thing, but I won't take time to go into it. I'd say that it was reasonably successful as a new technical angle. However, the economics of the United States at that time--in the thirties--was not particularly exciting. Black strap molasses in waste materials from the sugar industry was very, very cheap. Mostly sucrose but it was fructose, pentose and maltose. So the total picture economically did not look good, so we dropped it.

Well, many people have come and gone in microbiology; many things have been done, and I can't take the time to go into them and I don't think it's important. You can get them from Paul Wolf who's been around here. Paul was one of my fellows that was here (not at the beginning, but came into the act when it was early and been here ever since) and made a major contribution, particularly to the preservatives field.

But there's one area in microbiology that I must mention. We found that pentachlorophenol was a very good wood preservative. Wood rots, got a bad habit of that. And this was an excellent market, and in order to effectively develop this thing we got a group of people who knew wood technology and the wood problem, and as a result we got interested in wood. Interested in wood? Why don't we look at other aspects--it not only rots, the stuff shrinks and swells and bugs eat it, and it burns, and things of this sort. How could we chemically change this thing, which was an economic, light weight, decorative, structural material. This really is the basis of the wood group which split off from the microbiology to put most of their effort into the development of wood and wood products. Fred Meier is familiar with that.

Well, let's go back again. Please understand I'm sketching these

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things pretty fast. I'm going to cover a third of a century in a few minutes. I want to go back to discuss toxicology and environmental research. And, as I promised, I'm going to cut down a lot of this discussion; however, I think there are some very important anecdotes in the development of this that imply much more than toxicology; apply broadly to policy and thinking.

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You remember that I had suggested to Willard Dow that we didn't know enough about our chemicals toxicologically, and he said, "Why don't you do something about it?" Well, I was pretty naive to that suggestion, I want to tell you. I thought we had to know something about the new ones. What I didn't know was that we didn't know very much about the old ones. But leave it at that.

Toxicology and Environmental Research were new to the industry; I mean that literally. I would look back and think, "Oh those horrible people," and how cruel they were. Bill Britton commented that he came to work at The Dow Chemical Company in the mid-twenties and there was no chemical industry in the United States, and he was just about right. There was certain- nothing that amounted to anything in the chemical industry prior to the First World War. Just really beginning in the 1930's. What did we make? Phenol, caustic, chlorine--old, old, old chemicals. We made them in carload lots; we sold them to major chemical companies. We had every assumption--they had every reason to know as much or more about them as we did. Why should we do toxicological work and environmental research in this product thinking? However, things were changing and changing very rapidly. As billy Hale came into the act, now, only at first to develop processes for old chemicals; but then we began to make new ones. Edgar Britton and his gang, and Clarence Boyle was with us, were starting to look at new things, entirely new.

So in time there was a real revolution in the chemical industry. Don't forget, and this was part of it.

Well, we started in a single room in 48 Building, which was the old garage. In order to get an animal out, we pulled a construction shanty up outside where you could climb through the window to get to it easily rather than having to go around to it if you were in a real hurry. We made a comfortable little animal house out of it. The first chamber we used for exposing animals to gas vapors, etc., was a 55-gallon drum; they called it a quick closing drum. You slapped the head on and clamped a metal clamp down, like that. Unclamp it, pull it off again. And it was very handy. We had them out there in the warehouse and just went over and swiped one and brought it over to the laboratory. Good apparatus.

I might comment that the first toxicological investigation, and I confess, extraordinarily crude, on 1.1.1-trichloroethane, known as methyl chloroform, was performed in that drum. And it's still quite surprising. We even carried the animals up to anesthesia day after day after day and they seemed to get along fine. We brought it up again after we had a little better apparatus and a little better means of doing it. _____. Now I might say the first experiments in the field of toxicology were animals. It created more amusement around The Dow Chemical Company than it did serious consideration. We were quite the laughing stock, for certain, in a good natured sense, I agree. Until something serious happened.

This was in early 1934, I think in the spring, or early summer. I came to work on a Friday morning and Dutch Beutel was sitting on my desk. If any of you knew Dutch Beutel, you'd understand this. Dutch is a

chemical engineer, short, stocky, jaw sticking out--swell guy. He moved on...he was then assistant manager at Midland...Willard Dow's assistant. He moved on to develop the Texas plant. He is now in charge of our Government Affairs Department; has been around a long time.

Well, I blinked when I saw Dutch sitting on my desk. He said, "I hear you've been tinkering with a bunch of animals. "Well," he said, "show me what you can do. A man died out in the butylphenol plant last night and we suspect some chemical exposure. Get going." Just like that. That was his way of approcach and I respected him.

So we did get going, believe me. We worked day and night, and week ends, through that week-end. And I might comment Mark Putnam, who was then director of that production division, moved into the laboratory. I think it was typical of The Dow Chemical Company in those days, I think typical today, that their point-of-view was that this kind of accident should not occur. Period. There wasn't any question about it, this wasn't something that you accepted. Now Mark Putnam was not in the way; he was not that sort of person. He was there to be used. He brought Bill Williams in. Bill was in charge of a particular plant area and later was placed in as production manager. Those people were available to me on a moment's notice, day or night, any chemistry in the process.

I went into the plant with Bill Williams and we got samples all over the place. This sort of approach. That's the sort of backup we had. We sent dow drivers all over the state picking up odd animals for us in a whale of hurry, too, because we didn't have enough.

Well, that's quite a bit of a story. But, to end up, we discovered that it was not butylphenol but... and it was not a strange, new and startling thing...by absorption through the skin. I wish I had time to go into the actual accident because it's quite fascinating to recognize how

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people can know something and still not know it. But let's skip it.

I went to Willard Dow. I said, "Now we know what caused it. What more do you need to know--The Dow Chemical Company?" Well, I can almost quote him saying, "Get the information that you need to see that this king of an accident does not occur again in The Dow Chemical Company." He didn't mean phenol. He meant any chemical and he meant it! If you knew Willard Dow, you'd know he meant it.

"Well", he said, "get the equipment, get the people to do this job". Well, that gave me a good excuse and I sneaked down and grabbed Ed Adams and dragged him in in 1934. This accident, I think, tells us quite a bit about Willard Dow and I think about The Dow Chemical Company. And I think it's still true today.

Well, another session a good many years later--I think I must slip in here--it concerns our safety program. Willard Dow didn't like the safety record then. He couldn't figure out why people wanted to hur themselves. He began to suspect that line management didn't believe that Executive Management wanted the operations to be safe; they though they wanted production turned out in spite of anything. He wrote a letter...I wish I had a copy of it--I probably could get it easy enough--it said to all Executive Management and I can summarize it...it said in no uncertain and blunt terms, "If you plant can't be run safely, it won't be run, period." And He meant it. At that time also he established what was called, the Executive Safety Council. And I want to illustrate a point here by...he called Dr. Strosacker.

Dr. Strosacker was a vice president and he was in charge of one of the large areas of production. A very able man; an awfully nice person. Dow said, "Tell you what I'm going to do" and Stro said, "Gee, that's wonderful--I think that's a marvelous idea. I've got just the man in

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my division to represent us." And Willard Dow said, "No he won't. You will direct this. Stro, you're going to be on that Executive Safety Council. I want Management, my management, to know that Executive Management means what it's talking about." And I might say that the chairman of that Executive Safety Council was the vice president and general manager, Mark Putnam. And I might say, also, the plant superintendent who had to show up to that executive meeting and report every accident, and one thing they had to tell them is how...what they had done, and how they would prevent this from every happening again... there wasn't any yes or now about it. And I might say they did not like to show up a second time either, particularly. Well, back to toxicology and biochemistry.

That butylphenol accident, way back in '34 taught us that you need not only to have information, but you needed to convert that into a language useful to a man in the plant. You had to know what was going on in the plant and how they operate. So we got ourselves entangled with that situation and this, of course, is when we woke up to the fact that we had to do something in the area, and it became Industrial Hygiene and Environmental Research.

Nobody knew about industrial hygiene then, shall we say, but we found out about it in a backhanded way. There weren't many people in the country who knew much about it in those days. We found that we had to define the actual environmental circumstances and Ed Adams did much in the evolution...in the beginning of these things. There weren't any texbooks, no simple rules, no real body of previous knowledge in the area; very little equipment. We had to improvise about everything we needed. There were a few standards. Not enough to hid behind.

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It was necessary to take the full responsibility yourself, in drawing conclusions...all by yourself. You didn't have much in the way of technical knowledge or backup. Now line supervision did not necessarily welcome us with open arms, as you might understand. They were a bit afraid we might find something that reflected on the quality of their operation. Now, let's be reasonable and human--they were very human. Very ordinary. Don't forget that times were changing. I thought maybe some people didn't care about human life out there, but I find quite the contrary. And I found some men who did run their plants and ran them well. It's when something changes, when something new comes into the picture that we had a real problem. Well, it took a long history of selling that to plant supervision, I assure you.

About that time Willard Dow got very interested in this and he asked me, he said, "Do you want policing power in the plant?" In other words, the power to close down a plant if something goes wrong. And I said, "No!" And I'm awafully glad I did. The supervisor, if he found he could dump his responsbility on us, would be most delighted. And we did not have the men to be in constant surveillance of every action in the entire plant, I assure you. We figured that it was necessary for that plant supervisor to remain captain of his ship and be fully responsible. We were his technical advisors and assistants. I think Willard Dow wanted exactly that aspect, but he wanted us to come to that conclusion. It made it a little slow in development, but I think much sounder, much stronger, and I think it stands up much better today, don't you Harold? Well I'm going to skip quite a bunch of stuff in here. There's some very fascinating cases in Toxicology that do have a lot of implication but I'm going to jump over them or I won't get done in time for lunch.

Oh, yes. The solvent field. Now this is a bit toxicology, but I want to bring it out because of its importance today to get a feel for how we get into things scientifically.

The Dow Chemical Company had all the backup and raw products and know-how of making a lot of chlorinated hydrocarbons. Of course, we make carbon tetrachloride, trichloroethylene, perchloroethylene, ethylene dichloride, methylene chloride...well, you name it. Anything that was of any use in the field we were in a position to make. Carbon tetrachloride, in those days, was available anywhere, in a drug store, a hardware store. You could take an old can or a pop bottle and go down and get it anyplace...you'd find it in every backyard. I was going to say garage, but also the stable because we didn't all have garages in those days. You people wouldn't understand that. There were other means of transportation besides automobiles.

In fact, you would cringe with horror if you were familiar with the amount of misuse of this material. Small drycleaning establishments used it...they did not have the equipment, they did not have the know-how ...to handle it intelligently. Now, why did they get by with it? Well, there were several reasons, as you people in Toxicology well know, in the phenol area. An individual can tolerate...most individuals can tolerate...a surprisingly large amount of this material for at least a reasonably short exposure. Even continuous exposure, in use, didn't cause obvious difficulties. At least they didn't spot the difficulties in the early days. Partly tremendous individual differences, I must admit. Now. I've known some people...I still know some people--I mean they're still alive today--who have literally wallowed in that stuff. I don't know how they did it...I frankly don't. I suggested to one of them that

couldn't quite understand what in the world all of this stuff was all about, I said, "Would you mind donating your liver and kidneys, when you die, to scientific interests?" He looked a little peculiar when I said that, and said "I'm not so sure they're what they ought to be."

But they were beginning to identify some of the cases, not only the acute problems, I could tell you some instances that occurred during the war and in the early 1930's. . . 1940's, I mean, positively staggering. You could not believe them. In the early '30's this was beginning to stir a bit in the industry, and Henry Fielding Smith, Sr., father of the man we know at Mellon Institute as Henry Smith, did some animal work. He came around to various industries and studied people, and I want to tell you that this work was quite an innovation in its day. He told us a lot about this material and what it could do...came up with a suggestion that we ought to have control over its operation within about 100 ppm concentration. We know today that's rather high but don't forget the perspective the day in which that work was done. I think actually, if the industry hadn't really, and vigorously stuck to this 100 ppm that a lot more live people today . . . and they operated in much better circumstances than they did. The heat was still on carbon tet. We felt the picture was by no means clear and we decided to take a look at this material and several others in their class which I jokingly called the "big four": carbon tet, trichloroethylene, perchloroethylene, ethylene-dichloride.

We originally took ethylene chloride and started to work on it but people at the National Institute of Health had started to work and we knew them well and we said "Well, we'll swap with you". As why should we both do it. Well, I jump over all this rather elaborate investigation, I think actually almost classic in its day. This work has been quoted and respected nationally and internationally. We decided that carbon

tetrachloride must be controlled below a level of 25 ppm and below a time-weighted average of 10 ppm. And I think that after a good many years we can say this was a well justified suggestion. However, (now I see where I got beyond toxicology) we recognized that this meant the death of carbon tetrachloride as a pocket solvent--as a miscellaneous material kicking around.

Well, could you convince people all over the country, all over the world--distributors and handlers, that this meant the death of a solvent they'd used for years? Generations of people had used the stuff. Now you couldn't convince them easily, I assure you. At the same time we were studying these other materials we decidedly got interested in the differential of action quantitively and qualitively of differently chlorinated hydrocarbon materials we picked up on the materials we had as an intermediate that they called methyl chlorofrom--1,1,1,trichloroethylene. Well, believe me, in deciding a relation to other materials we were utterly astounded because it was so low in toxicity. It didn't make any sense at all at that time. We know more about it today, of course. At that point in time, very close to carbon tet--an extra solvent.

We said, "Oh, boy. Somebody's going to run us out of business in carbon tet--let's put another solvent together." Well, do you think you could convince sales people, our distributors, that carbon tetrachloride was dead? Not easily. But, could you convince them that anybody would pay for a thing because it was a little safer, and they said "No" and I think maybe they were right, then.

However, looking back it looks very simple, looking ahead it did not look as simple. I couldn't go into all the contributions of many different laboratories. There's a lot of aspects in getting a solvent on the market--not just toxicity, believe me. This stuff wasn't

inhibited; it reacted on aluminum and heaven knows what else--well, your know the story. It wasn't an easy task but today, as I think you all know, it's a pretty sweet product. Now, I have a moral--it's much more than toxicology--don't weep over a dead horse, get another one to ride. I think that's a good sound basis, industrially and scientifically.

Well, I've had a long story; it was too long. I want to move on.

I want to get in a couple more sermons here. Field of education. Yes, we need to get the facts, but that's not enough. We need to integrate them; need to interpret them, put them in plain language. You must see that the people who need to know, understand it. I don't mean to say that you give it to them. You have to know that they understand it. That means plant supervision, that means workmen, that means customers, general public, anybody that needs to know.

Well, skip along to other areas here to get going.

Publication is another sermon I want to make. Let's go back to ancient history again. Back in the very late '30's we had developed some very interesting scientific research. I went to Willard Dow and asked him what the publication policy should be on this kind of material. This was entirely new to Dow. Pertty new to the industry, really. Now I'm going to confess, I gave him a sales talk. Alarming approach. And with a twinkle in his eye, he chuckled just a little bit and he said, "Well, I'm quite sure" (and he named a few companies--by the way, he was sure right), "will ride on our work," and they did. But he said, "I still think it ought to be out." Then he made a qualification that I want to emphasize to you and I'll repeat it every day if necessary, one qualification: "Know what you're talking about before you publish it." That's a pretty darn good one to look at; and if you'll look at the published literature today, you'll see why. It isn't the pages; it's publication that's important.

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I'd like to add some factors to this that's an addition, but I mean it's an interpretation of the same thing. We don't publish just to publish. We have to be sound scientifically. It has to make a genuine scientific contribution. I think, on the whole, this laboratory has done that, and I think for that reason it has been respected nationally and internationally. It is, wherever you go. I think at the same time, something you can't put your finger on, or can we? We have saved a good many lives. I think we've prevented a good deal of illness. I'm not talking about our own people only. I'm talking about the fact that this information was out and around the world in various places. I think also, that it's been a great deal of value to The Dow Chemical Company in the promotion and development of its products.

And now, I've neglected one of our very important areas--if it is an area; I'm not so sure it is--and you'd like to call it basic research. It's important, perhaps because it's not an area. I think that's one of our sad errors. It's not something isolated over here somewhere in an ivory tower. It's important because it impinges on all areas, and because it is an integral part of all areas, and because it contributes to all these areas. I think that is the important part of basic research. It's not easy to demonstrate basic research by the same kind of anecdotes--I won't take the time anyway. But let's go back and take a little look at the history as I think of this era.

Ed Dunn came here in '34 and we were thinking of the Dowicides pretty serious. But frankly, we were thinking also of the fact that Ed Dunn's graduate work was in enzyme research. I proposed to Willard Dow we ought to look at enzymes as a basic research program. He grinned and he said, "You mean organic catalysts?" and I said, "If you want to call them that," and he just chuckled and said, "Why don't we get going?"

Well, Ed Dunn did do something--did some very interesting work in

UNIT 1 1741

this area; however, unfortunately, as too often happens, (watch this), the immediate pressures of preservatives, fermentation, and heaven knows what else, dominated the picture, and this went down hill as a basic research area. It was displaced.

However, let's see, it was about 1957 we discovered an innocent chap, a good Canadian boy with a bit of experience in England and some other places, by the name of W. Brock Neely--some of you have heard of him. And we managed to get him here in '57 and suggested that he go into this basic biochemical research, particularly the enzyme field--not limited to it by any means, as you know. I won't go into any other areas because you know many of any other areas in which these have been explored. He stayed with it. Not exclusively, but he stayed with the basic area.

Remember we mentioned that one of our earliest considerations of the many things were exploring was human health area. We hadn't done anything about it. We kept probing--what'll we do next? In 1953, we managed to get our hands on an innocent guy by the name of Maynard Chenowith. He'd been consulting with us on some toxicology problems, and some other things--he had a background in toxicology. We figured pharmacology would be a might good consulting area on the part of basic research, toxicology, and on the other areas of the interaction of the environment in man or animals. But I'll admit, too, that personally the primary reason was to act as what I could best call as a 'point of infection', getting us entangled in the area of human health. And I think it's helped to do just that. I don't know that we need to go into the area because it's recent enough that you know most about it. Chen's done a lot of work in the area of blood pressure, Les McCarty in muscular conduction, and Van Dyke, biochemistry of the area. Walt Piper now is giving us other whole areas in this area but I think it did help in

this area, and of course, one very practical aspect that came out of it is a darn good anesthetic. And some excellent basic research on why anesthetic works and how they work.

Now, we always got most of our chemical substances with which we worked from the Organic Laboratory, Physics Laboratory, you name--all over the country. All Dow operations. We still do. We still should. Never forget--you're not an isolated group. You're an integral part of a very, very large research organization. If you don't take advantage of it, too bad. However, by pure chance, and we didn't object at all, we hooked an organic chemist by the name of Clarence Boyle; I guess he didn't know what he was getting into either. At least, a very small group here who could work close to the biologists from the point of view of structure activity relationship, and point of view of specialized syntheses and things of this sort. Well, you know what Clarence has done--in many areas. He jumps off the deep end and does many peculiar things. Developed some interesting organic phosphates that are important in agriculture now and a cute little material to selectively pick out these sea lamphreys in the Great Lakes. Things of this sort. I think more important, however, are the little things day-by-day he does in connection with the biologist which summates into something. It isn't the individual outstanding thing that jumps out, usually. It's sometimes the contribution to the collective genius of the laboratory.

Well, move along. First, basic research is part of all areas of research. Mechanism, actions in toxicology, microbial physiology, biochemistry of micro-organisms and of the action of chemicals and micro-organisms of pharmacology, and so on and so forth. It is not a field--it is an integral part of every operation. And we need this as a fundamental basis for all areas. We must not forget that it is the basis of this work; so, while all along some good basic works for some has been done,

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for heaven's sake, keep it up.

And I think the time flies and I should end my sermon.

Thank you.

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Biochemical Research Department
THE DOW CHEMICAL COMPANY

Subject: RESULTS OF TOXICOLOGICAL TESTS ON 2,4,5-TRICHLOROPHENOXYACETIC ACID

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Att'n: W. C. Dutton (1)
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D. D. Irish (1)
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DOW 7512541 MN0069799

UNIT INDEX

Results of toxicological studies together with handling hazards and precautions for safe handling are given.

INDEX HEADINGS

2,4,5-Trichlorophenoxyacetic acid
Acetic acid: 2,4,5-trichlorophenoxy-,
Phenoxyacetic acid: 2,4,5-trichloro-,

PROBLEM

The widespread handling of 2,4,5-trichlorophenoxyacetic acid made it desirable for us to have a significant amount of toxicological information. Data on the oral toxicity was necessary for presentation to the F.D.A. Hearing on residue tolerances.

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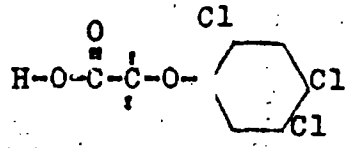
DOW 751255

MATERIAL

Name: 2,4,5-Trichlorophenoxyacetic acid

Formula:

Structural: 

Empirical: $C_8H_5Cl_3O_3$

B.R.D. K No. 4568-4

Source: L. White 267 Bldg.

Reference: Batch 138 (20W-108 SPL 6)

EXPERIMENTAL RESULTS

The acute oral toxicity of 2,4,5-trichlorophenoxyacetic acid for rats, mice, guinea pigs and chicks is given in the attached summary which was presented in evidence at the F.D.A. Hearing. In concluding our testimony on this material we stated,

"Because of the similarity in chemical structure and in toxicity and physiological effect between 2,4-D and 2,4,5-T, it seems that a residue tolerance for the latter on fresh fruits and vegetables should be the same as that established for 2,4-D; it would seem that a residue of 20 p.p.m. would provide a wide margin of safety."

Eye Irritation

When 2,4,5-trichlorophenoxyacetic acid as a 10% solution in propylene glycol was introduced into the eye of a rabbit, it produced marked pain and slight conjunctival irritation immediately. Five hours later, severe conjunctivitis and moderate corneal damage was apparent. This picture remained about the same for two days before healing began. Five days after the exposure mild conjunctivitis and corneal damage was still apparent.

Skin Irritation

When 2,4,5-trichlorophenoxyacetic acid as a 10% solution in butyl carbitol acetate was applied repeatedly to the rabbit ear and bandaged repeatedly to the shaven abdomen, a slight simple irritation developed in both instances.

DOW 751256

SUMMARY

The toxicological properties of 2,4,5-trichlorophenoxyacetic acid may be summarized as follows:

1. The material is moderate in acute oral toxicity for the four species, rat, mouse, cavie, and chick. Of these species the rat seems to be the more resistant and the chick the most susceptible.
2. The material is markedly irritating to the eyes
3. The material is slightly to moderately irritating to the skin upon prolonged exposure.

HANDLING HAZARDS AND PRECAUTIONS FOR SAFE HANDLING

Swallowing

It does not seem likely that 2,4,5-trichlorophenoxy acetic acid can be swallowed accidentally in amounts dangerous to life, although this might be possible if concentrated solutions of the material were available to children. If substantial quantities of the material were to be swallowed by anyone, serious ill effects could be anticipated.

If the material should be swallowed, induce vomiting by giving a common emmetic such as 2 tablespoonfuls of table salt in a glass of warm water. Call a doctor.

15888

Eyes

The 2,4,5-trichlorophenoxyacetic acid is capable of causing serious damage to the eyes. Precautions should be taken when handling this material to prevent possible eye contacts. It is recommended

when handling strong solutions of 2,4,5-trichlorophenoxyacetic acid that goggles, face shield, or other similar device be worn to prevent accidental splashes in the eye. It is believed that the handling of the solid does not present a hazard simply because of its insolubility in aqueous medium.

If the material in any form should get into the eyes, they should be promptly washed with flowing water for at least 15 minutes and medical attention obtained.

DOW 7512257

Skin

Prolonged and repeated contact with the skin may result in irritation. Occasional contacts for short periods are not expected to cause irritation. Strong solutions are no doubt more likely to cause difficulty than the dry solid.

In case of contact wash the exposed area with soap and water. Do not wear clothing or shoes which have been contaminated with solutions of the material.

Inhalation

No studies of toxicity upon inhalation of 2,4,5-trichlorophenoxyacetic acid dust have been made. We believe, however, that in view of the similarity with this material to that of 2,4-dichlorophenoxyacetic acid, that it is unlikely that toxic concentrations of the dust would be inhaled, primarily because of the irritation it will produce upon the upper respiratory passages.

15889

Return to Jary Schneider 1530

THE CHLORACNE PROBLEM - BIOCHEM'S CONTRIBUTION

Date: 3/11/65
File: 7
By: LKS

E. J. K
Cleared

DOW 7475532

SUMMARY

An outbreak of chloracne in Dow workmen in the trichlorophenol process in 199 Building and in 349 Building has resulted in approximately 40 cases of chloracne in Dow people. The outbreak was precipitated primarily by a series of process changes which increased the production of a chloracne-producing impurity in trichlorophenol. Increased exposure to operating and to maintenance personnel also contributed. Much effort by persons in the Analytical Laboratory, the Toxicology Laboratory, and the Environmental Research Laboratory has resulted in the isolation and identification of one impurity which is capable of having caused the difficulty, and has also resulted in control of the exposure situation so that no new cases of chloracne have appeared in the last four months. Some important questions remain to be answered. There is evidence that other compounds than the one already isolated and identified and studied are capable of producing chloracne. Their significance in the trichlorophenol process is not yet known.

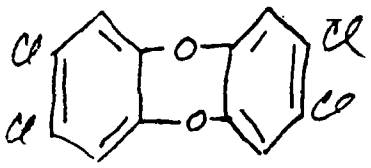
CHLORACNE

Chloracne is a skin disorder characterized by the appearance of black heads and small bumps. These appear first on the face of the individual affected. Depending upon extent of exposure, the skin disorder may spread to other parts of the body. Infection and irritation of the skin rash may cause enough discomfort ~~of the~~

15890

individual to result in time lost from work. This happened in two of the trichlorophenol dust cases.

The materials known to cause chloracne in humans are usually chlorinated complex organic molecules. The compound isolated from trichlorophenol caustic insoluble oil is 2,3,7,8-tetrachloro dibenzo-p-benzodioxin (symmetrical).



DOW 747533

This compound and others which have been shown to cause chloracne have also been shown by animal tests and some human experience in other companies to produce liver damage if the exposure is more extensive. Thus far, no liver injury has been detected by clinical examination of the affected Dow people.

Two aspects of the ailment are distinctive and somewhat frustrating. First, there is a latent period of approximately two months after sufficient exposure before the disorder is evident on the person. Secondly, once a person has contracted chloracne, the recovery period is from about six months to two years for the cases which Dow has encountered. In some instances, the Europeans have encountered recovery periods as long as five years before the man was completely free of the chloracne.

DOW 747534

TOXICOLOGY RESEARCH

In 1941, Adams, Irish, Spencer and Rowe of the Biochemical Research Laboratory published a paper in Industrial Medicine on "The Response of Rabbit Skin to Compounds Reported to Have Caused Acneform Dermatitis". They described ~~the animal~~ a test using the rabbit ear, which has been extremely valuable in the studies of compounds which may cause chloracne in humans. The rabbit appears to be very sensitive to such compounds, but it is non-specific, that is, the folliculitis which occurs in rabbits does not identify the particular agent. Another shortcoming of the rabbit test is the period of time necessary for the folliculitis to develop. There appears to be an induction period of approximately one week for the tetrachlorodibenzo dioxin (hereafter abbreviated TCDD) to produce folliculitis in rabbits regardless of the severity of exposure. There is evidence that unknown acnegens may produce folliculitis in rabbits with a shorter induction period. Before a particular test sample is exonerated, the test is run for four weeks of repeated daily application to the rabbit's ear.

In 1944, research in the Benzene Research Laboratory produced a severe case of chloracne and toxicology studies on animals showed that the probable culprit was a chlorinated double ether produced from the experimental solvent being studied. At this time, samples from the trichlorophenol process were also studied and the caustic insoluble oil was shown to be active by the rabbit ear test. There was no human experience with chloracne in the trichlorophenol production group at that time. The phenate product was shown to be inactive by animal tests.

DOW 747535

In 1955, a number of German manufacturers of trichlorophenol and at least one French company had human experience with chloracne that caused them to shut down production plants and to study the problem. Their studies contributed ~~much~~ to the medical picture and to process improvements, but not much to the toxicology ~~of the~~ situation in industrial hygiene. The Germans ~~did~~ isolated the TCDD and ~~do~~ did some limited animal studies on it and on some chlorinated dibenzofurans (diphenylene oxides) but this was a very limited amount of work. They did even less ~~in the~~ to evaluation ~~of the~~ exposures of their people which led to the injuries.

In 1957, a series of process samples were acquired from 199 and 349 Buildings and tested on animals. The tests indicated that the caustic insoluble oil and coil reactor product in 199 Building were active and that the tar from the color stills in 349 Building was also active. The precautions first recommended in 1945 were re-emphasized. There was still no human injury in the trichlorophenol process.

About 1956, impurities in trichlorophenol produced by Dow and Hooker were isolated and studied by animal test and shown to be inactive ~~in terms of chloracne~~.

Over the years, some samples of end products such as Silvex, Fonnel, and 2,4,5-T acid have been tested on animals and in no case was chloracne activity detected in these products.

In 1962, supervision of 199 Building sent samples from the process & the Toxicology Lab then existing process and from a pilot run ~~of proposed change~~ utilizing a in the ~~process which was~~ a decrease in the caustic concentration, ~~in the starting materials~~. These samples were tested on animals and again

DOW747536

the caustic insoluble oil was shown to be active but no more active in the new process than in the old. The Biochem report reiterated the precautions necessary in handling the oil and the change was made at 199 Building. There was still no human injury.

When the chloracne outbreak occurred in early 1964, many more process samples were tested on animals with particular attention to the caustic insoluble oil. Two samples of this oil were dramatically different, ~~qualitatively~~, than those tested before or since. These two samples killed the rabbits when applied at the same concentration as has normally been used. The oils had to be diluted to 0.1% concentratio before the animals survived and showed folliculitis. The normal test concentration of caustic insoluble oils up to that time had been 10% dilution. Subsequent studies on the TCBD have indicated that the amount of TCBD in these two samples of oil is probably not sufficient to cause the death of the animals. In July of 1964, the rabbit ear test was used for the first time on wipe samples of the building equipment and surfaces at 199 Building. The wipe tests indicated extensive contamination of 199 Building. This test has been repeated periodically to the extent that over 600 animal tests have been run since ~~last~~ July directly related to the chloracne problem.

A representative oil sample was selected in August 1964 to be fractionated in order to isolate and identify the chloracne-producing impurities. Norm Skelly of the Analytical Lab isolated a number of fractions which were identified, among them the TCBD, which was also synthesized by Skelly from dibenzodioxin. The two materials were identical ~~in terms~~ by determination of infrared and melting point, and both showed extreme activity on the examination by

rabbits. Other fractions indicated little or no activity on the animals. The isolated material was utilized by VPC (Vapor Phase Chromatography) to standardize a method for detecting this impurity. Harold Gill's group in the Analytical Laboratory has consistently improved the VPC sensitivity in process samples so that at the present about 1 ppm (parts per million by weight) of TCBD may be detected in various process samples. However, the animal studies have indicated that rabbits are sensitive to TCBD down to approximately 5 ppb (parts per billion by weight), upon repeated application to the ear. The rabbit test remains the most sensitive method of detecting acnegenic activity. ~~However~~, single application studies on TCBD indicate that parts per million are necessary for a response so that VPC does provide a first step in evaluating the hazard from TCBD specifically. Many wipe samples and some process samples have indicated by VPC, unknowns in the region of the TCBD which we suspect are also acnegenic. Samples of chlorinated dibenzofurans were acquired from the K list and run by VPC. These compounds show up on a VPC chromatogram in the same region as some of these unknowns. However, the impurities isolated by Skelly also show up in this same region and were shown to be inactive on animals. The unknowns are truly that, with this evidence of activity, however; many wipe samples with no detectable TCBD but ~~substantial~~ varying amounts of unknowns have shown more activity on the animals than can be accounted for by the low level of ~~dioxin~~ TCBD which may be present. The chlorinated dibenzofurans were tested on animals many years ago and shown to be quite active. Research was abandoned on these products because of their high acnegenic activity. The samples are impure by VPC analysis and have not yet been

DOW 747537

These unknowns appear on VPC chromatograms in the same time periods relative to the known TCBD, as do some of the compounds isolated from the caustic insoluble oil by Stelly, which were inactive on animals.

Samples of impure chlorinated dibenzofurans were run on VPC and some of the peaks coincided with some unknowns which were seen in wipe samples and product samples. Both the Biochem Lab and the Germans have reported animal tests with carcinogenic activity, these compounds which showed. Neither group indicated that the possibility of TCBD contamination of the furans had been ruled out.

DOW 747538

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DOW 1475539

purified and tested again on animals. The possibility exists that these are contaminated themselves by ~~dioxin~~ TCBD. This possibility has not been investigated as yet.

More detail on the results of process sample and wipe sample testing on animals will appear in the sections under specific building numbers.

Studies are now in progress on Dow ~~end~~ products made from Trichlorophenol and those of other manufacturers for acnegenic activity. Thus far, no Dow ~~end~~ products have shown activity on animals while some other manufacturer's end products are showing activity on animals as well as detectable dioxin by VPC analysis. The Analytical Laboratory and the Toxicology Laboratory are presently conducting a project to determine the analytical and animal test limits of sensitivity for TCBD in various Dow products ~~starting~~ made from trichlorophenol. This project is aimed at developing a quality control specification for ~~the dioxin~~ TCBD in consumer products.

199 BUILDING

The first animal test on trichlorophenol process material was conducted in 1945, at which time the caustic insoluble oil was shown to be active. Precautions were recommended at that time. The second animal test took place in 1957. The caustic insoluble oil was again active and the coil reactor product was also active. Other process samples were not active. Precautions were recommended again for handling the oil.

DOW747540

In 1955, the C. H. Boehringer Sohn [redacted] Company in Germany asked for information from the Givaudan Corporation, which company referred the request to Dow. A letter describing the hazards and precautions for safe handling of 2,4,5-trichlorophenol was sent to Boehringer with a data sheet from Biochem enclosed. The letter answered seven specific questions regarding our own plant experience.

In 1957, Boehringer sent Dow and all other known trichlorophenol manufacturers a letter describing the ~~fruits~~ results of their research on chloracne in the trichlorophenol process. The letter described the danger points in the process and the limits which had to be observed in order to avoid producing acne exciter in trichlorophenol and in 2,4,5-T acid. A temperature limit of 150°C for the ~~reaction~~ distillers was emphasized by Boehringer. Which?

In 1962, the ~~above-mentioned animal~~ rabbit ear test indicated that the caustic insoluble oil from a 73% caustic process and from a 24% caustic process were the same in that they both produced folliculitis on animals ~~in~~ with about the same ~~order~~ magnitude of response. The Biochem report reiterated the precautions but stated there was no evidence of increased hazard in the new process.

In July 1963, 199 Building started up on ~~new~~ tetrachlorobenzene which caused line plugging problems and increased exposure of personnel according to the plant superintendent. In November and December of 1963, the plant ran at capacity. The caustic insoluble oil production was above normal, ~~and~~ the oil was drawn off more frequently, and it was also being sampled regularly. The samples were taken to the 199 Bldg lab for freezing point analysis. The temperature at which the plant process was run was also

DOW 0475541

increased (215-225°C)

On January 23, 1964, the first medical report of ~~the~~ a case of chloracne initiated a survey by the Environmental Research Laboratory. ~~On January 23, 1964,~~ The trichlorophenol operator's job was studied closely and a report issued on 2/5/64 recommending changes in the procedure and in personal hygiene habits. Some changes in the oil draw-off equipment and procedure were already initiated before the Environmental Research survey got under way. In the spring of 1964, process equipment changes were made by the Phoenix Sprinkler Company and at this ~~point~~ time, the caustic insoluble oil samples which killed the animals were taken at the plant. In July 1964, the first wipe samples were taken. The building was found to be extensively contaminated. Some air sampling was begun at this time. No activity was found in the air samples. In August 1964, VPC detected ~~tetrachlorobenzodioxin~~ TCBD in the waste oil, the oil was fractionated, ~~the dioxin~~ TCBD was isolated and identified, and was also synthesized. In ~~the~~ August of 1964, ~~more cases of chloracne appeared.~~ SOME Phoenix Sprinkler men, some area shop people, and more 199 Building employees developed chloracne. Wipe samples indicated continued contamination. Extensive clean-up measures were undertaken. Wipe samples showed improvement but not complete elimination of the contamination. ~~Air samples were not active.~~ In late October 1964, there was a flare-up of some existing chloracne cases in 199 Building people. This was brought on by exposure to hot fumes from a screen in the phenate product line. Animal tests showed that this phenate was active and that the screen residue was extremely active. This phenate went to 349 Building and is the probable cause of the

three cases which eventually appeared in 349 Building people. About November 1 1964, very stringent safety precautions were instituted in 199 Building. These included a full-time health supervisor ~~on duty~~ whose job was to review each and every maintenance or installation job ~~in the reactor area~~ to specify the detailed safety procedures which the men should follow. Clean-up activity continued and extensive modifications of equipment and the building of an enclosure around parts of the process took place in November and December of 1964. ~~Literally~~ Over one hundred ~~of~~ outside personnel were involved. Wipe tests indicated improvement in the contamination situation and air samples ~~were~~ showed no activity on the animals.

In 1965, the full-time health supervision continues. VPC analysis is now being used for quality control of the phenate leaving the building. Wipe tests show substantial improvement. However, air samples are beginning to show activity on the animals, although only one air sample thus far has shown detectable dioxin by VPC analysis. A very significant factor is that to the present date, there have been no new cases of chloracne since the institution of the full-ti health supervision and extreme safety precautions. Two cases have appeared at Medical since that date, but both of these have shown that the individuals were in the area and had possible exposure prior to the November 1st date. Since the induction period in people is about two months, and it is now approximately ~~nine~~ five months since the height of activity in 199 Bldg with the many outside personnel, there is evidence that the safety precautions which ~~were~~ used were satisfactory. These precautions are being continued on jobs in 199 Building.

DOW 1475542

349 BUILDING

Sodium trichlorophenate from 199 Building is received ~~by~~ at 349 Building where it is neutralized, ~~which effects~~ effecting a ten-fold concentration of the material to provide crude trichlorophenol. This "wet feed" is ~~sent~~ passed through a drying column; the "dry oil" is then distilled in two color stills.

The first animal tests run on ~~349~~ July samples in 1957 indicated activity only in the tar from the color stills. This was mild activity, less than that demonstrated by the caustic insoluble oil at 199 Building Similar samples taken in early 1964 again showed the tar from the color stills to be active. Samples taken in October 1964 showed activity in the wet feed, in the dry oil and again in the tar from the color stills. The product was still not active on animals. Samples taken in November 1964 showed activity again in the wet feed, the dry oil and the product ~~was~~ were inactive. The degree of activity in the crude materials was less than that in the October samples.

The contaminated phenate ~~mentioned above,~~ found in 199 Bldg at the end of October 1964 was processed by 349 Building. ~~The activities of two~~ two pipe fitters and an operator at 349 In early November ~~involved~~ ed cleaning lines and ~~changing~~ changed valves in lines which had carried the contaminated phenate. The actual exposure that brought on chloracne in the 349 Building personnel is not definitely established but this is the most likely situation which could have caused it.

In early November, Clare Bailey, 349 Building Superintendent, issued a written sheet describing precautions to be taken because of the

poor

DOW 747543

potential hazard. This resulted from the 1964 experience and was promulgated on Bailey's initiative as a precautionary measure. About the first of this year, 1965, objections by workmen to working in 349 caused the adoption of full-scale protective measures in that building in regard to the trichlorophenol process. Further complaints caused the extension of such precautions to the entire reactor room, including the bisphenol process. Wipe tests eventually indicated that the bisphenol process area was free of contamination. In fact, only limited areas of the trichlorophenol section show contamination. Clean-up and further wipe tests are being delayed until process equipment has been moved to a new location outside the work area of 349 Building. Extensive clean-up will be necessary in the alleyway behind 349 because of contamination from the trichlorophenol tar.

A health supervisor is now stationed at 349 Building and full precautions are being taken on any jobs where exposure is possible. Only three cases of chloracne have shown up at 349 thus far, none since the incident in early November.

Composite samples of finished trichlorophenol from 349 have been run on animals at either a 10% or 1% concentration in Dowanol PM. Under these conditions, no finished product from 349 has shown activity on animals. Quite recently, VPC has succeeded in lowering sensitivity for TCBD in trichlorophenol to about 1 ppm. They have since analyzed some retainer samples and found some with detectable TCBD plus unknowns that appear in the same place as the chlorinated benzofurans. These samples were extracted with chloroform for analysis. The chloroform extracts, when placed on rabbits' ears, are showing activity.

DOW 747544

Another tar, the catch-all tar in 349, has shown some slight activity on animals. This is the residue from catch-all distillation for 265 Building. The "catch-all" material itself did not show activity The tar from the dichlor still was not active. Tar, crude product and final product from the Dowicide 3 process are currently being studied on animals. The Dowicide 3 Tar is showing activity Dowicide 3 in the past has been regarded as a potential chloracne-producing material.

DOW 747545

267 BUILDING

Finished trichlorophenol from 349 Bldg is processed in 267 Building to 2,4,5-T acid and to 2,4,5-T esters.

Process samples taken in early 1965 showed no activity with one exception. The residue from the sodium salt filter press showed slight activity on the rabbit ear.

Tests of Wipe sample taken ~~tests~~ in 267 Building are still in progress but show no activity at this date.

Human experience in 267 Building ~~would~~ indicates no problem in the past, but the ~~circumstances of~~ degree of exposure of problem could cause chloracne ~~lead to grave concern over future problems~~ if contaminated materials are processed at 267 Building.

par

265 BUILDING

A number of Dowicides are produced and packaged in 265 Building Pentachlorophenol, tetrachlorophenol, and others are among the products. Penta- and tetra- have long been known to be capable of causing chloracne The human experience at 265 Bldg has indicated no particular problem; only an occasional case of chloracne through the years has been reported at Medical. At the present time, two individuals, an operator and a pipe fitter, have been

DOW 747546

reported to have mild cases of chloracne.

Process samples are currently being studied on ~~the~~ animals. No wipe testing has been done as yet at 265 Building, ~~itself~~.

266 BUILDING

Three cases of chloracne have been reported from 266 Building. None of the processes or materials in 266 Building have been known to cause chloracne in the past. Its proximity to the Dowicide plant ~~has~~ could result in contamination of the area. ~~been investigated by virtue of~~ Wipe tests in 266 Building and process samples from the parahydroxybenzaldehyde process have also been tested on animals since the most significant case is in an operator on this proces None of the process samples were active; only one wipe test (on the mobil elevator in the warehouse section) was active on animals. This elevator has been decontaminated and painted. It is difficult to explain the contact which resulted in these three cases of chloracne.

206 BUILDING

This building has three cases of chloracne in operators who hav worked on the finishing and packaging end of the 6X process. 6X has bee known as a chloracne-producing material for many years. The cases in th building were reported to Medical in the middle of 1964. Study of the finishing end, distillation and drumming-off of 6X, indicated numerous opportunities for exposure. The process was not running on 6X itself, bu on an innocuous material using the same equipment and the circumstances as ~~6X purification.~~ Wipe tests were made of the equipment and area but no 6X was detected in any place. ~~6X is produced in the north end of 206~~ ~~Building.~~ The 6X process equipment has been idle in the north end of 206 all of this equipment and wipe tests on ~~it~~ indicate

15904

DOW 747547

6X contamination. This equipment is presently being cleaned up for other service, precautions are being taken.

The Dowicide 3 process will soon be moved, in its entirety, to 206 Building. Plans have been made to study it thoroughly in its initial operation in 206 Building.

206 Building is a neighbor of 199 Building and for this reason the question of neighborhood contamination from 199 was investigated by means of wipe tests in spots likely to have been contaminated by 199 effluents. None of these wipe tests were active. Some wipe tests at 199 itself indicated a rather quick drop-off of activity with distance from the vent on the roof of 199 which was the source of roof contamination at that building.

1603 BUILDING

Bradley's group in Chemical Physics Research Laboratory has been studying variations of the trichlorophenol process. Two of the group contracted severe cases of chloracne about two and one-half years ago as the result of exposure during laboratory runs. Their former work area in 294 Building and their present work area in 1603 Building were wipe tested and no active samples were found in either place.

Laboratory samples have been submitted by this group occasionally in the last two years, ~~approximately~~. Many of these samples have demonstrated activity on the animals.

474 BUILDING

Widiger's group in the Benzene Research Laboratory has been studying the current trichlorophenol process. Wipe samples have been taken of the work areas in 474 Building. Those that have been completed showed no

activity.

703 BUILDING

The Waste Disposal Department handles the caustic insoluble oil from 199 Building and the tar from 349 Building, both of which are active. Wipe samples have been taken in the tar burner area. Soil samples were also tested and wipe samples of the vertical tar burner are in process. Some activity was found on an area around the tar burner. Waste Disposal has been advised of necessary precautions.

Other possibly contaminated effluents have been discussed with the Waste Water group of Waste Disposal and arrangements made for necessary precautions when called for by work on waste disposal lines.

Larry Silverstein
March 10, 1965

Unit Index

jd

Distribution
Hutchenreuther
Goergen
Stallings
Amstutz
J. Kelly (W. Disposal)
Shannon "
Lueck
Bailey
Levitt

DOW 747548

DOW 746900
MN0069799

MIDLAND, MICHIGAN
July 25, 1967

W. J. McCoy
Bioproducts Sales
BPC

cc: W. L. Corbin, BPC

2,4,5-T FORMULATIONS

I appreciate very much your note of 7/17/67 in which you informed me that some Diamond material has apparently caused serious skin problems among people applying the material. This goes along with a report that recently appeared in the South American literature which states that materials of this nature have also been noted to have caused similar difficulties. I am enclosing a copy of this publication for your information.

It would appear that our predictions of a few years ago are beginning to come to pass, unfortunately. Frankly, I am mighty glad that we took the position we did.

Please continue to keep me informed as best you can.

V. K. Rowe
Biochemical Research Laboratory
1803 Building

pgw

15934

bcc: V. K. Rowe (2)
Correspondence

THE DOW CHEMICAL COMPANY

MIDLAND DIVISION
April 25, 1967

K. E. Coulter
Midland Division Research & Development
566 Building

CHLORACNE RESEARCH PROGRAM

History of Chloracne Incidences at Dow:

Historically, Dow Chemical has been involved in chloracne incidences ever since Dow began the production of chlorophenols. At first, the commercial production of chlorophenols was conducted at 206 Building. During the period 1934-36 there was a severe outbreak among the employees which resulted in an unsuccessful lawsuit. The chloracne incidents were traced back to poor working conditions and the manufacture of Dowicide P. The manufacture of Dowicide P has since been terminated. New and improved working facilities for the Dowicide group were constructed at 265 Building in 1940.

In the late 1930's, Wes Stoesser in 20A lab got a serious chloracne attack from chlorinated diphenylene oxide. Drastic treatments were used to cure this incident and no further work was done on this series of compounds. It is suspected that many of the other incidences of chloracne are caused by chlorinated diphenylene oxides or analogues thereof.

In the next ten years, another unfortunate situation occurred in the chloracne situation. Some of the Dow customers complained about dermatitis and/or chloracne from the use of Dow's Dowicide 3. I understand financial adjustments were made and the production of Dowicide 3 terminated. A purified material of related structure is now sold as Dowicide 31 and 32.

During the period 1940-65, the product 6X (diphenyl oxide chlorinated to the hexa level) was manufactured at 206 Building and at least one severe case of chloracne occurred because of this product. The production of 6X has been terminated.

In the research lab at 172 Building, there were some cases of chloracne from research exposures. In one case, a severe case resulted from the recycling of residues from the manufacture of 2,4,5-trichlorophenol using glycol as a solvent. In another case, several mild cases occurred hydrolyzing polychlorobenzenes using aqueous caustic at high temperature. The Chemical Physics Lab had several incidences of chloracne from the recycling of caustic insolubles in the alcoholic caustic hydrolysis of tetrachlorobenzene.

DOW 15143193

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In 1963, the 2,4,5-trichlorophenol hydrolysis step at 199 Building was modified for economy and safety reasons from the use of 100% caustic to 23% caustic. The rabbit test for chloracnigens in the caustic insolubles obtained from a pilot run at this time indicated that the test response for chloracnigens showed no difference between caustic insolubles obtained by either procedure. During the latter part of 1963, the production department, in order to increase capacity, raised the reaction temperature and increased the throughput. This meant that more caustic insolubles were produced, and more Dempster loadings had to be made. This meant that employees had more exposures to the caustic insolubles, and the caustic insolubles due to the higher temperature had larger concentrations of chloracnigens. Thus the higher concentration of chloracnigens and the more frequent exposure caused many mild incidences of chloracne in 199 Building and two severe cases (LTI's). In 1966, a new process (Boehringer) was put into operation using a batch reactor at low temperature, and so far has operated satisfactorily.

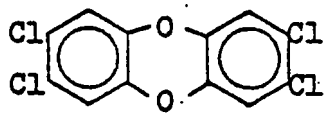
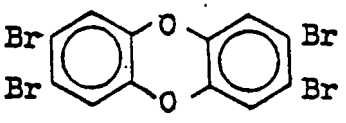
After they started up their Dowicide plant, the Canadians began to experience chloracne incidences in their employees. In Midland, more than half of the Dowicide employees have chloracne of varying intensity and it is impossible to say when or where these incidences occurred.

Research Program in Progress for Chloracne Reduction:

Because of the prevailing existence of chloracne in the Dowicide plants and a sincere desire to reduce or eliminate this, research has been initiated in 1966 on this problem. Progress has been slow due to the complexity of the problem. The problem involves isolation and determination of the identity of the chloracnigens. After being properly identified, work can progress on its reduction or elimination in the process.

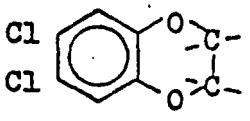
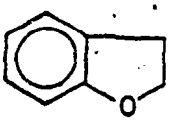
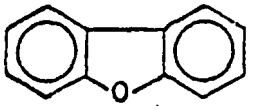
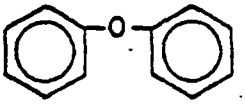
In commenting on chloracne, we must keep in mind that chloracne is a cosmetic evidence of the attack and serious liver damage is an invisible effect of the attack. Rabbit ear tests are a positive sensitive method of determining the chloracne activity of chlorophenol impurities.

Present Knowledge of Chloracnigens:

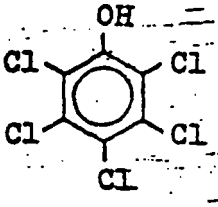
Compound	Activity
	2,3,7,8 Tetrachloro - Very positive Cl_{1-3} - Not active Cl_{5-7} - Possibly some cpds. active Cl_8 - Not active
	Very active

DOW 1514317

15936

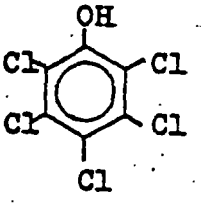
Compound	Activity
	Very active
	Cl_{1-x} - Unknown activity
	Cl_{1-2} - Unknown activity Cl_{3-8} - Some very active
	Cl_{4-8} - Some activity?
	Cl_3 + - Some activity

Materials possessing unexplained chloracne activity:



Some Midland batches are mildly reactive

Many Canadian batches are mildly reactive

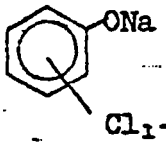
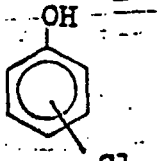


$\xrightarrow{NaOH}$ Dowicide G

All sludges are active

DOW 1514318

15937

Compound	Activity
	All decompositions are active
	Some have activity

Midland Research Program on Chloracne:

The following chloracne activity fractions are being examined for isolation, identification, and minimization of chloracne activity. Unfortunately, due to shortage of technical help, the program is proceeding quite slowly.

1. Dichlorophenol still residue.
2. Pentachlorophenol process samples.
   a. Dowicide 6 and 7 "active" batches.
   b. Dowicide G sludge.
   c. Dowicide G scrubber sludge.

The method of research is to first concentrate the sample (remove chlorophenols); then fractionate by chromatography; test fraction on rabbits, then further fractionate by chromatography, then test fraction on rabbits; etc., then determine structure by micro analysis; then determine method of analysis in original sample; and then investigate process changes which will minimize the chloracnigens in the process.

The Benzene Research Lab and the Biochem Research Lab are collaborating in this project. The Benzene Research Lab does the chemical research and the Biochem Research Lab does the testing on the rabbits on their charge.

Alex Widiger

Alex Widiger
Benzene Research Laboratory
474 Building

je

cc: W. H. Haberstroh, 474 Bldg.
R. C. Sauers, 474 Bldg.
S. L. Bender, 172 Bldg.
E. C. Staehling, 258 Bldg.
L. Silverstein, 1701 Bldg.

15938

DOW 1514319

1600

THE DOW CHEMICAL COMPANY

MIDLAND, Michigan
June 4, 1969

MN0697699

DOW12329000

L. A. Asadorian
Halogens Research Laboratory
768 Building

cc: R. H. Solem, Halogens Research Laboratory, 768 Building
J. F. Mills, Chemicals Laboratory, 335 Building
F. C. Leavitt, Halogens Res. Laboratory, 768 Building
A. E. Schober, Toxicology Laboratory, 1803 Building
V. K. Rowe, Toxicology Laboratory, 1803 Building
F. L Dunn, Toxicology Laboratory, 1803 Building

2,3,7,8-Tetrabromodibenzo-p-dioxin appears to be as potent an acnegen as its chlorine analog, which is known to be the main offending material in the trichlorophenol process chloracne problem of a few years ago. A sample of hexabromodiphenyl oxide was tested in 1965 and a sample of decabromodiphenyl oxide was tested recently. Neither showed a response on the rabbit ear test for chloracne. Dow 6X (hexachlorodiphenyl oxide) has caused chloracne in humans and a response on animals; octachlorodibenzodioxin was inactive on the rabbits.

Because chloracne is a distressing illness which requires a long time to clear up in humans, and because the test data on brominated compounds is so limited, I would recommend that very good personal hygiene and housekeeping habits be followed in working with brominated diphenyl oxides, until further assurance of a lack of hazard is forthcoming from toxicology tests.

I recommend further that, if brominated diphenyl oxides appear to be an important item in Dow's future, more samples be submitted to the Toxicology Laboratory for test and in particular, any process samples from pilot plant or production operations, including waste streams and intermediate points where human exposure may occur. In laboratory tests by Alex Kidiger, chlorinated phenols and their sodium salts subjected to temperatures >150°C produced acnegens. Still bottoms and drier residues from Dowicides production also show acnegenic activity in animal tests.

15939

DOW1737901

I realize that this letter is an inadequate explanation of my concern. For more detailed information on our present knowledge of chloracne please contact me.

L. G. Silverstein
Biochemical Research Laboratory
1701 Building/6-4676

LGS:sjl

NATIONAL AGRICULTURAL CHEMICALS ASSOCIATION

ASSOCIATIONS BUILDING
1145 NINETEENTH STREET, N. W.
WASHINGTON 6, D. C.

TELEPHONE: STERLING 3-2833

1609

JANUARY 22, 1960

DOW 1 3669920

MR. MARVIN BUGH
HEAD LANDSCAPE ARCHITECT
LANDSCAPE DEPARTMENT
INDIANA STATE HIGHWAY DEPT.
STATE HOUSE ANNEX
INDIANAPOLIS, INDIANA

DEAR MR. BUGH:

IT HAS COME TO OUR ATTENTION THAT THE INDIANA STATE HIGHWAY DEPARTMENT IS CONCERNED ABOUT RECENT STATEMENTS ISSUED BY DOCTORS AT THE MAYO CLINIC IN WHICH THEY REPORT ALLEGED EFFECTS ON HUMANS WHO HAVE COME IN CONTACT WITH 2,4-D OR SIMILAR PRODUCTS.

IN RECENT YEARS 2,4-D HAS BEEN ACCUSED OF BEING RESPONSIBLE FOR MANY ILLNESSES AND EVEN HAS BEEN BLAMED IN CAUSING DEATHS IN HUMANS. IN 1957 A WOMAN BLAMED EXPOSURE TO 2,4-D SPRAY AS THE CAUSE FOR HER DEVELOPING ASTHMA. AT THAT TIME WE CONTACTED THE U. S. PUBLIC HEALTH SERVICE TO DETERMINE WHETHER ANY DOCUMENTED INSTANCES OF 2,4-D POISONING HAD BEEN REPORTED. I WOULD LIKE TO QUOTE EXCERPTS FROM A REPLY TO OUR INQUIRY SIGNED BY DR. WAYLAND J. HAYES, JR., MEDICAL DIRECTOR, CHIEF, TOXICOLOGY SECTION, COMMUNICABLE DISEASE CENTER, U. S. PUBLIC HEALTH SERVICE.

> "WE HAVE NO RECORDS OF INJURY TO MAN CAUSED BY 2,4-D OR 2,4,5-T WHEN USED WITHOUT SUICIDAL INTENT.
>
> "MORE RECENTLY WE HAVE HAD AN INQUIRY FROM A PRIVATE PHYSICIAN REGARDING A WOMAN ABOUT 50 YEARS OF AGE, WEIGHING 185 POUNDS, WHO CLAIMED THAT SHE WAS EXPOSED TO A CLOUD OF 2,4-D SPRAY. WITHIN 10 MINUTES AFTER THE EXPOSURE SHE SUFFERED FROM A PARCHED THROAT AND 15 MINUTES LATER HAD DIFFICULTY IN BREATHING SIMILAR TO ASTHMA AND THIS CONDITION HAS PERSISTED UNTIL OCTOBER 31, 1957. THE EXPOSURE WAS SUPPOSED TO HAVE OCCURRED DURING THE FALL OF 1956. THE WOMAN'S HOME WAS ABOUT 150 FT. FROM THE ROAD WHERE THE SPRAYING WAS DONE. SHE WAS IN THE KITCHEN AT THE TIME. SHE

15941

HAD BEEN TOLD BY HER PERSONAL PHYSICIAN THAT SHE HAD AN ENLARGED HEART. IT MAY OR MAY NOT BE THAT THIS CASE IS THE SAME AS THE ONE WHICH YOU REFERRED TO. IF IT IS THE SAME, THE CHANCE THAT THE ILLNESS IS RELATED TO THE EXPOSURE TO HERBICIDES IS REMOTE TO THE POINT OF BEING IMPOSSIBLE.

"AS WE MENTIONED IN OUR LETTER TO THE INSURANCE COMPANY, IT IS NOT POSSIBLE TO EXCLUDE THE POSSIBILITY THAT ONE OR BOTH HERBICIDES MIGHT CAUSE ALLERGY IN A FEW HIGHLY SUSCEPTIBLE INDIVIDUALS. HOWEVER, THE CHANCE THAT ONE OF THESE MATERIALS, OR, IN FACT, ANY MATERIAL, WILL PRODUCE A CONDITION OF CHRONIC ASTHMA WITHOUT FURTHER EXPOSURE IS ABSURD. IT WOULD APPEAR MUCH MORE LIKELY THAT THE WOMAN IS SUFFERING FROM A CONDITION OF CARDIAC ASTHMA AND THAT HER CONDITION IS NOT RELATED TO ALLERGENS OF ANY SORT."

I WOULD ALSO LIKE TO QUOTE FROM A LETTER FROM DR. HAYES IN REFERENCE TO PUBLISHED PAPERS ON THE TOXICITY OF 2,4-D AND/OR 2,4,5-T.

"THREE PAPERS ON THE TOXICITY OF 2,4-D AND/OR 2,4,5-T ARE AS FOLLOWS:

DRILL, V. A., AND HIRATZKA, T.:
TOXICITY OF 2,4-DICHLOROPHENOXYACETIC ACID AND 2,4,5-TRICHLOROPHENOXYACETIC ACID: A REPORT ON THEIR ACUTE AND CHRONIC TOXICITY IN DOGS.
A.M.A. ARCH. IND. HYG. OCCUPATIONAL MED. 7: 61-67, JANUARY 1953.

HILL, E. V., AND CARLISLE, H.:
TOXICITY OF 2,4-DICHLOROPHENOXYACETIC ACID FOR EXPERIMENTAL ANIMALS.
J. IND. HYG. AND TOXICOL. 29:85, 1947

BUCHER, NANCY L. R.:
EFFECTS OF 2,4-DTCHLOROPHENOXYACETIC ACID ON EXPERIMENTAL ANIMALS.
PROC. SOC. EXP. BIOL. MED. 63:204, 1946

"ALL STUDIES WITH THESE COMPOUNDS HAVE SHOWN THAT THEY HAVE A MODERATE TOXICITY FOR EXPERIMENTAL ANIMALS. WE HAVE NO RECORD OF THEIR HAVING PRODUCED SIGNIFICANT INJURY IN MAN WITH THE EXCEPTION THAT ONE SUICIDE WAS CARRIED OUT WITH A LARGE DOSE OF 2,4-D. THE MATERIALS ARE NOT NOTABLE ALLERGENS. IT IS, OF COURSE, NOT POSSIBLE TO EXCLUDE THE POSSIBILITY THAT ONE OR BOTH MATERIALS MIGHT CAUSE ALLERGY IN A FEW HIGHLY SUSCEPTIBLE INDIVIDUALS."

DOW 1 366921

THE FOLLOWING IS A COPY OF A LETTER SIGNED BY DR. MITCHELL R. ZAVON, KETTERING LABORATORY, CINCINNATI, OHIO, WHEN HE WAS ASKED FOR INFORMATION AND COMMENTS ON THE TOXICITY OF 2,4-D AND RELATED CHEMICALS IN LIGHT OF THE MAYO CLINIC REPORT:

"FOR MANY YEARS 2,4-D AND ITS RELATED ANALOGS SUCH AS 2,4,5-T HAVE, AS YOU WELL KNOW, BEEN USED WIDELY AND WITH LITTLE OR NO DIFFICULTY TO THE PERSONS USING THEM. IT HAS LONG BEEN ACCEPTED BY THOSE CONCERNED WITH PESTICIDE TOXICITY THAT THESE PRODUCTS WERE OF VERY LOW TOXICITY. EXPERIENCE OVER THE YEARS HAS TENDED TO CONFIRM THIS IMPRESSION.

"MY PERSONAL EXPERIENCE WITH THE COMPOUNDS HAS BEEN LIMITED BUT WITHIN THESE LIMITS THE ONLY PROBLEMS I HAVE RUN INTO HAVE BEEN NAUSEA AND A FEELING OF FAINTNESS DUE TO THE ODOR. THIS PARTICULAR DIFFICULTY ONLY RESULTED WHEN TRANSFERRING LARGE QUANTITIES OF THE MATERIAL FROM ONE VEHICLE TO ANOTHER. IN FIELD OPERATIONS I HAVE RUN INTO NO DIFFICULTY WHATSOEVER. IN GENERAL THE EXPERIENCE OF OTHERS HAS BEEN SIMILAR TO MY OWN. A RECENT PUBLICATION OF THE DIVISION OF SANITARY ENGINEERING OF THE SOUTH DAKOTA STATE DEPARTMENT OF HEALTH WHICH REPORTED ON A SURVEY DONE COOPERATIVELY WITH THE U.S. PUBLIC HEALTH SERVICE ENTITLED 'REPORT OF AN OCCUPATIONAL HEALTH SURVEY OF AGRICULTURAL AND MANUFACTURING INDUSTRIES IN SOUTH DAKOTA' REPORTS WITH REGARD TO THE TWO PRODUCTS UNDER DISCUSSION THAT ON 112 FARMS SURVEYED 2,4-D WAS USED. 'ALTHOUGH ITS ODOR MAKES IT ANNOYING TO HANDLE, IT IS GENERALLY CONSIDERED TO BE NON-TOXIC AND NON-IRRITATING TO HUMANS. THE LARGE NUMBER OF PERSONS COMING IN CONTACT WITH THIS CHEMICAL WITHOUT ENCOUNTERING DIFFICULTY TENDS TO SUPPORT THIS VIEW. HOWEVER, TWO OF THE FARMERS INTERVIEWED STATED THAT SPRAYING WITH 2,4-D MADE THEM MILDLY NAUSEATED AND ANOTHER THAT IT CAUSED AN EDEMATOUS SWELLING OF HIS GENITAL ORGANS WHICH LASTED ABOUT TWO WEEKS.'

"UNTIL THE RECENT REPORT IN THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION THERE HAD BEEN NO REPORTS OF WHICH I AM AWARE OF ANY PROBLEM OTHER THAN IRRITATION RESULTING FROM THE USE OF THESE HERBICIDES. THE RECENT REPORTS DO NOT PROVE ANYTHING. THEY DO, HOWEVER, SERVE TO ALERT US TO THE POSSIBILITY OF OTHER EFFECTS FROM 2,4-D AND 2,4,5-T. UNFORTUNATELY, ON A NUMBER OF OCCASIONS CLAIMS MADE BY CLINICIANS, WHO ARE MEMBERS OF THE MAYO CLINIC STAFF, HAVE BEEN UNFOUNDED IN THAT THEY RELY COMPLETELY ON THEIR OWN PERSONAL OBSERVATIONS WITHOUT ANY SORT OF CONTROL. THESE OBSERVATIONS ARE EXCELLENT FOR THE PURPOSE OF ALERTING AS TO POSSIBLE EFFECT BUT AS I HAVE SAID THEY DO NOT PROVE THE EFFECT.

DOW 13669922

I AM REASONABLY CERTAIN THAT THERE WILL NOW BE A NUMBER OF REPORTS APPEARING WHICH POINT TO AN ASSOCIATION BETWEEN THESE HERBICIDES AND ANY NUMBER OF NEUROLOGICAL AND/OR HEMOTOLOGICAL DISEASES. UNLESS THE PROOF IS MORE SUBSTANTIAL THAN I HAVE SEEN THUS FAR, I CANNOT ACCEPT THESE CASE REPORTS AS PROOF.

"PERHAPS ANOTHER EXAMPLE MIGHT PROVE TO ILLUSTRATE MY POINT. AT PRESENT I AM INVESTIGATING A CASE OF PARTIAL BLINDNESS ASSOCIATED WITH EXPOSURE TO CARBON TETRACHLORIDE. THOUGH THERE ARE A NUMBER OF CASES IN THE LITERATURE SIMILAR TO THE ONE I AM INVESTIGATING AND I AM QUITE CERTAIN OF THE ASSOCIATION OF THE INDIVIDUAL CONCERNED AND CARBON TETRACHLORIDE, THIS IS NO PROOF OF THE CAUSE OF HIS BLINDNESS. WHAT I WILL DO IS TO WRITE UP THE CASE FOR MEDICAL PUBLICATION IN ORDER TO ALERT OTHERS TO THE POSSIBILITY. IF A SUFFICIENT NUMBER OF CASES WITH THIS ASSOCIATION APPEAR THEN IT MAY WELL BE THAT THERE IS A CAUSE AND EFFECT RELATIONSHIP. THUS FAR I DO NOT CONSIDER THE CAUSE AND EFFECT RELATIONSHIP PROVEN.

"WE MUST REMEMBER THAT ANYTIME VAST NUMBERS OF PEOPLE ARE EXPOSED TO A PRODUCT A CERTAIN PERCENTAGE OF THEM WILL DEVELOP ONE DISEASE OR ANOTHER. TO CONDEMN A PRODUCT BECAUSE OF THIS WITHOUT FURTHER INVESTIGATION WOULD BE THE HEIGHT OF IRRESPONSIBILITY. PATIENTS COMING TO THE MAYO CLINIC ARE IN A SENSE SCREENED FROM A LARGE POPULATION AND THE MERE FACTOR OF ASSOCIATION MAY NOT PROVE A THING BECAUSE OF THE WINNOWING OUT PROCESS THAT HAS OCCURRED PRIOR TO THEIR BEING SEEN AT THE MAYO CLINIC."

I TRUST THE STATEMENTS BY AUTHORITIES QUOTED IN THIS LETTER TOGETHER WITH THE REFERENCES CITED WILL ANSWER QUESTIONS WHICH YOU MAY HAVE CONCERNING 2,4-D AND ITS EFFECTS ON HUMANS. IN OUR OPINION, 2,4-D IS ENTIRELY SAFE TO USE WHEN APPLIED AS DIRECTED.

YOURS VERY TRULY,

/S/ JACK DREESSEN
JACK DREESSEN

JD/NEM

DOW 1366923

foot, was unable to stand and would then sit or lie in an awkward position with spastic limbs, particularly spasm of the hind legs. Other dogs stumbled and rolled on the floor in attempts to right themselves. An occasional dog has shown evidence of irritation or pain when the skin over the back of the neck was grasped. Some dogs, when held [illegible]ers would show extension and crossing of the hind limbs. As the [illegible] of the drug progressed the dogs eventually refused the various [illegible] offered. Occasionally sneezing, rubbing of the eyes and diarrh[illegible]d, but not vomiting.

Such symptoms were also seen i[illegible]t survived a lower dose of 2,4-D for 14 days (Table 1). In th[illegible]he changes were relatively mild and were limited to spasm in the hi[illegible]a slight ataxia.

Marked symptoms were not obse[illegible] dogs receiving 2,4,5-T. The changes were limited to a slight t[illegible]stiffness in the hind legs, with the development of ataxia, in the [illegible]eiving the highest doses. No symptoms were evident in the one d[illegible]l following a single dose of 100 mgm./kg. (Table 1).

Pathology. Changes observed were limited to the gastro-intestinal tract and lungs. Four dogs (Nos. 1,2,4,6) receiving 2,4-D and two (Nos. 13, 17) fed 2,4,5-T showed mild to diffuse redness of the mucosa in the small intestine. In some dogs pneumonia was present. Histologically the above dogs showed some necrosis and inflammation of the intestinal mucosa. One dog (No. 13) had a moderate, diffuse hepatic necrosis. Two dogs (Nos. 13,16) had a mild degree of renal tubular degeneration. In most dogs that died the findings were limited to non-specific changes such as hepatic congestion. In many cases death was probably due to pneumonia which followed the development of anorexia, weight loss and myotonia.

DOW 7123224

II. CHRONIC ORAL TOXICITY

Mortality. All dogs receiving 2, 5 or 10 mgms. of 2,4-D or 2,4,5-T per kilo at body weight survived the 90 day test period. The dogs receiving 20 mgm./kg. of these compounds died during the study. The administration of 20 mgm./kg. in divided doses twice a day produced death in both dogs receiving 2,4,5-T and in one dog receiving 2,4-D (Table 2).

Body Weight. The only significant change in body weight occurred in the animals that failed to survive the study (Table 2). Loss of weight in these dogs began 7 to 12 days before the death of the dog.

General Symptoms. Dogs that survived the oral administration of 2,4-D or 2,4,5-T for 90 days were free of any symptoms.

The three dogs that died while receiving the highest dose of 2,4-D showed signs differing somewhat from those observed in the acute studies. The dogs were quiet, weaker and less responsive than normal. Muscle tonus was higher in the hind legs, particularly on passive extension. The hind legs were held more stiffly than usual when walking and a slight ataxia was present. During the last 2 to 3 days of their survival two of the dogs showed difficulty in chewing or swallowing and eventually even refused a small bolus of canned dog food (usually readily consumed). There was also some oozing of blood from the gums and buccal mucosa. In dogs that died while receiving 2,4,5-T the prominent effects were weakness, slight stiffness in the hind legs, difficulty in the swallowing of food, and in one dog, bleeding from the gums.

Blood count. The administration of 2,4,-D or 2,4,5-T did not have any significant effect on the hemoglobin, red cell, or total white cell count of animals that survived or died during the study. The differential count remained normal in the surviving animals. In three animals that died a terminal fall in the percentage of lymphocytes was observed (Table 3).

DOW 712325

Organ weights. There was no significant change in the weight of the thyroid gland, adrenal gland, heart, liver or kidney in animals that survived the 90 day period of study. In two of the three dogs that died during the administration of 2,4-D there was a slight increase in heart and kidney weight. A similar change was experienced in two of the four dogs that died as a result of 2,4,5-T.

DOW 712326

Gross pathology. Two dogs receiving 2,4-D (Nos. 26 and 34) showed areas of redness in the duodenum. With 2,4,5-T one animal (No. 42) showed a diffusely reddened duodenum and jejunum and dog 48, autopsied on the 59th day demonstrated a generalized icterus.

Microscopic changes. The heart, lungs, thyroid, adrenal, ovary or testes did not demonstrate any significant changes. Three of the dogs receiving 2,4,5-T and two receiving 2,4-D showed an occasional area of focal necrosis in the liver. This finding, however, was not related to either the dose of the compounds or the death of any animal (Table 4) and was judged to be of no significance. The duodenum of dogs 26, 34, 42 and 48 showed varying degrees of hyperemia and some early infiltration of cells in the mucosa. The submucosa and serosa were normal. A slight increase in the number of casts in kidney sections was noted in some dogs (Table 4) but again this was unrelated to dosage and is of doubtful significance.

DISCUSSION

Single large oral doses of 2,4-D administered to dogs may produce signs characteristic of clinical myotonia. This effect of 2,4-D was similar to that observed following injection into various species[5,6]. In addition, some dogs showed signs of irritation and pain when the skin of the back of the neck was grasped, which may indicate meningeal irritation. The extension and crossing of the hind limbs, when lifted by the shoulders, may point to a spinal or central

lesion. Other effects occasionally observed were sneezing, rubbing of the eyes and diarrhea. The effects of 2,4,5-T, previously unstudied, were not as severe, being limited to stiffness in the hind legs and ataxia. The higher doses of either compound produced anorexia and weight loss. Although initial effects may be seen six hours after the compounds are given, the syndrome developed slowly in the dogs and death was delayed, occurring several days after the administration of the compounds.

In the chronic study, the dogs survived doses of 2,5 and 10 mg. of 2,4-D or 2,4,5-T per kilo of body weight without apparent ill effects. However, the daily oral administration of 20 mgm./kg. of 2,4-D produced death in three of four dogs within 18 to 49 days. This delayed death may indicate a cumulative effect of 2,4-D. The signs observed in animals dying from the 20 mgm./kg. dose of 2,4-D differed somewhat from those seen in the acute studies. With the chronic administration, the animals exhibited chiefly a stiffness of the hind legs and ataxia, weakness, difficulty in chewing or swallowing and, occasionally, bleeding from the gums. All four dogs receiving 20 mgm./kg. of 2,4,5-T succumbed between the 11th and 75th day of the study. Toxic effects in these animals consistently included slight muscle spasm and difficulty in swallowing food. Thus, the chronic oral toxic dose for 2,4,5-T in dogs seems to be in the same range as that obtained with 2,4-D. With both drugs, there was a terminal loss in body weight.

Dogs surviving the chronic doses of 2,4-D or 2,4,5-T did not show any significant change in hemoglobin, total blood counts or differential count. In three of the dogs (Nos. 64, 57, 105) that died while receiving 20 mgm./kg. of 2,4-D or 2,4,5-T, there was a definite decrease in the percentage of lymphocytes in the peripheral blood. Hill and Carlisle[6] have observed a fall in the polymorphonuclear leucocyte count in one dog and a decrease in the per cent of lymphocytes in two dogs receiving 50 mgm./kg. of 2,4-D intravenously per day

DOW 7123277

Table 3. COMPETITION EXPERIMENT

DNA on filter	^{32}P-RNA	Unlabelled RNA	RNA bound to filter*
Nuclear DNA	cyt. 25*S*	—	932
Nuclear DNA	cyt. 25*S*	cyt. 25*S*	647
Nuclear DNA	cyt. 25*S*	mit. 23*S*	912
Nuclear DNA	cyt. 17*S*	—	971
Nuclear DNA	cyt. 17*S*	cyt. 17*S*	507
Nuclear DNA	cyt. 17*S*	mit. 16*S*	885

* C.p.m., corrected for background adsorption on to blank filters.

Filters containing 5 μg of nuclear DNA were incubated with 5 μg/ml. of labelled RNA to which 5 μg/ml. of unlabelled RNA was added as indicated. Specific radioactivities: cytoplasmic 25*S* RNA: 10,020 c.p.m./μg; cytoplasmic 17*S* RNA: 11,010 c.p.m./μg.

it is interesting that nucleotide sequences complementary to chloroplast rRNA were found on nuclear as well as on chloroplast DNA of tobacco plants[16].

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Chemical and Toxicological Evaluations of Isolated and Synthetic Chloro Derivatives of Dibenzo-*p*-dioxin

ONE of the toxic compounds known as hydropericardium factor (chick oedema factor) is 1,2,3,7,8,9-hexachlorodibenzo-*p*-dioxin[1]. Because it is highly improbable that these very toxic compounds are naturally occurring components of the fats from which they have been isolated, the question of their origin has aroused speculation.

A clue to the possible origin of hydropericardium factor is found in a report by Tomita *et al.*[2] of the synthesis of polyhalodibenzo-*p*-dioxins: chlorophenols and their salts, when heated, undergo condensation reactions and form chlorinated derivatives of dibenzo-*p*-dioxin. Because of this observation, we studied the pyrolysis of a number of commercially available chlorophenols which are widely used in agriculture and industry, and present results of some preliminary experiments which suggest that hydropericardium factor could arise from certain chlorophenols.

The commercial chlorophenols used in this work were pyrolysed in accordance with the general procedures described[3]. Benzene extracts of the reaction mixtures were fractionated by passing them through an alumina column. Residues of the benzene effluents were extracted with petroleum ether at room temperature, and the petroleum ether was then removed. The resulting products were sufficiently pure in most cases for examination by electron capture gas–liquid chromatography (GLC) and biological testing by the chicken embryo assay[4]. Table 1 shows retention times of the GLC peaks on a 7 foot, 2·5 per cent '*SE*-52' column at 200° C and the results of the chicken embryo assay. Individually isolated hydropericardium factors of known chemical structures were not available for use as standards; consequently, a concentrate from the unsaponifiable fraction of a certain commercial toxic fatty acid material was used as a GLC reference. The unsaponifiable fraction of the fatty acid material was known to contain trace amounts of the hydropericardium factor. The toxic fatty acid material, a by-product obtained from the manufacture of oleic and stearic acids, has been used as a reference in all our previous chemical and biological work[4].

Table 1. EXAMINATION OF CHLOROPHENOL PYROLYSATES

Sample pyrolysed*	R_e at 200° C of components† in pyrolysate	Chicken embryo bioassay	
		μg/egg‡	Per cent mortality§
2,4-Dichlorophenol (R)	1·0	500·0	70
2,4,5-Trichlorophenol (T)	3·5, 6·5	0·25	100
2,4,6-Trichlorophenol (R)	2·6	5·0	50
2,3,4,6-Tetrachlorophenol (T)	8·9, 10·0, 11·2, 17·4, 20·0, 35·0	1·0	100
Pentachlorophenol (R)	35·0	5·0	27
Chlorinated dibenzo-*p*-dioxin	1·0, 1·6, 3·5, 6·5	0·05	100
Reference toxic fat components	1·0, 1·6, 3·5, 6·5, 8·9, 10·0, 11·2, 17·4, 20·0, 35·0	3·0	100

* (R) = reagent grade; (T) = technical grade.
† R_e = retention times of peaks relative to the retention time of aldrin.
‡ 1 μg = 20 p.p.b. in the egg. Sample injected into the air cell of fresh fertile eggs before incubation. Solvents used: ethanol, acetone and chloroform.
§ Embryonic mortality at 21 days. The mortality of non-injected and solvent-injected controls was 10–15 per cent.

The chromatogram of components from the toxic fatty acid material contained a number of peaks of widely varying retention times; four of these peaks had R_e values greater than 10. According to a current electron capture GLC test[4], the presence of one or more GLC peaks with R_e values of 10 or more indicates that hydropericardium factor is present in a fat. The pyrolysate from technical grade 2,3,4,6-tetrachlorophenol was the only product that showed a peak pattern indicating the presence of hydropericardium factor; the peak pattern resembled that displayed by the long retention time components of the reference toxic fat. When tested by the official chick bioassay[4] for hydropericardium factor, the mixture produced the disease at a dietary level of 0·1 p.p.m.

In addition, dibenzo-*p*-dioxin was chlorinated directly in order to prepare 2,3,7,8-tetrachlorodibenzo-*p*-dioxin[5]. This material proved to be extremely toxic in the chicken embryo assay (Table 1), and provided a source for isolation of a trichloro as well as the tetrachlorodibenzo-*p*-dioxin.

The technical grade 2,3,4,6-tetrachlorophenol pyrolysate, chlorinated dibenzo-*p*-dioxin, and components from

15945

the reference toxic fat were each fractionated by preparative GLC (thermal conductivity detection), using a 12 foot × 4 mm column at 250° C packed with 10 per cent 'DC-200' on 60/80 mesh 'Gas Chrom Q'. Isolated components from the 2,3,4,6-tetrachlorophenol pyrolysate and from the chlorinated dibenzo-*p*-dioxin were examined by electron capture GLC and infrared spectroscopy, and were also analysed by mass spectrometry to determine molecular weight and number of chlorine atoms per molecule. Results are recorded in Table 2. The components isolated from the reference toxic fat have not yet been examined spectroscopically.

Table 2. COMPONENTS ISOLATED FROM CHLORINATED DIBENZO-*p*-DIOXIN AND 2,3,4,6-TETRACHLOROPHENOL PYROLYSATE

Mixture	GLC peak No.	R_e at 200° C	Molecular weight	No. of Cl atoms
Chlorinated dibenzo-*p*-dioxin	1	1·8	286	3
	2	3·5	320	4
2,3,4,6-Tetrachlorophenol pyrolysate	1	8·9	386	6
	2	10·0	358	6
	3	11·2	358	6
	4	11·6	388	6
	5	17·4	422	7
	6	20·0	422	7

Infrared spectra of individual components exhibited characteristic absorption bands in the region of 1,330–1,380 cm^{-1} attributed to asymmetric stretching vibration of C—O—C in the dibenzo-*p*-dioxin ring. The two principal compounds isolated from the chlorinated dibenzo-*p*-dioxin were 2,3,7-trichlorodibenzo-*p*-dioxin and 2,3,7,8-tetrachlorodibenzo-*p*-dioxin. The infrared spectrum of the trichloro compound has bands at 870 cm^{-1} and 805 cm^{-1} (1,2,4-substituted benzene), and 860 cm^{-1} (1,2,4,5-substituted benzene). The infrared spectrum of the tetrachloro compound has a strong band at 863 cm^{-1} (1,2,4,5-substituted benzene). The infrared spectrum of the tetrachloro compound matched the spectrum of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin published by Tomita *et al.*[2]. Chicken embryo assay showed that the tetrachloro compound was more toxic than the trichloro compound.

The first four peaks in the chromatogram from the tetrachlorophenol pyrolysate were caused by positional isomers, each containing six chlorine atoms; the fifth and sixth peaks were caused by positional isomers, each containing seven chlorine atoms. A seventh peak in the chromatogram, observed when the sample injection was overloaded, had a retention time identical to that of a sample of octachlorodibenzo-*p*-dioxin prepared by pyrolysis of pentachlorophenol. The presence of pentachlorophenol in technical grade 2,3,4,6-tetrachlorophenol accounts for the formation of the two heptachloro isomers and the octachlorodibenzo-*p*-dioxin.

A fourth hexachloro isomer, in addition to the three expected from pure 2,3,4,6-tetrachlorophenol, is probably caused by the presence of a tetrachlorophenol other than the 2,3,4,6-isomer in the starting material. Infrared spectra of peaks 3 and 4 from the 2,3,4,6-tetrachlorophenol pyrolysate were very similar to published spectra of two hydropericardium factors isolated from a contaminated fat[3].

The components isolated by preparative GLC from the reference toxic fat, the chlorinated dibenzo-*p*-dioxin, and the 2,3,4,6-tetrachlorophenol pyrolysate were analysed by electron capture GLC at 200° C and by the chicken embryo assay. These results are shown in Table 3. The quantity of material in each fraction from the reference toxic fat was estimated on the basis of the weight of sample injected into the preparative gas chromatograph and the number of fractions collected. The amounts of material isolated from the chlorinated dibenzo-*p*-dioxin and 2,3,4,6-tetrachlorophenol pyrolysate were rough estimates based on comparison of GLC peak areas of isolated components and the starting mixtures. Amounts of individual components in the mixtures were estimated from normalized peak area calculations. The data suggest that one hexa

Table 3. GLC ANALYSIS AND EGG EMBRYO ASSAY OF ISOLATED COMPONENTS

Reference toxic fat components		Components from chlorinated dibenzo-*p*-dioxin and 2,3,4,6-tetrachlorophenol pyrolysate		
			Chicken embryo assay†	
R_e at 200° C	Chicken embryo assay* per cent mortality	R_e at 200° C	μg/egg	Per cent mortality
1·0	20			
1·8	20	1·8‡	0·5	15
3·3	100	3·5‡	0·2	100
5·1	40			
6·5	100			
8·9	80	8·9	2·0	30
10·0	80	10·0	1·0	100
		11·2	1·0	100
11·6	100	11·6	0·5	100
17·4	80	17·4	2·5	15
20·0	100	20·0	1·25	100
35·0	40			

* It was estimated that about 20 μg of material was injected into each egg.
† See footnotes 3 and 4, Table 1.
‡ Components from chlorinated dibenzo-*p*-dioxin.

and one hepta-isomer are less toxic than the other isomers. Work is now under way to prepare individual compounds of high purity in sufficient quantities for additional chemical and biological testing.

Reference toxic fat components with low R_e values (less than R_e 8·9) could be due to chloro-organic pesticides and/or lower chlorodibenzo-*p*-dioxins. Additional work is required to identify the compounds responsible for the peaks with low R_e values. The peaks with high R_e values (those equal to or greater than 8·9) correspond to those of the hexachloro and heptachloro positional isomers isolated from the pyrolysate of 2,3,4,6-tetrachlorophenol. The overall results of this work suggest that chlorophenols could be precursors of hydropericardium factor. Commercial chlorophenols are widely used for such diverse applications as contact herbicides, defoliants and termite control agents, as well as for control of microbial attack in the manufacture of a number of products. There are many opportunities for fats and fatty acids, the only products in which hydropericardium factor has been found, to become contaminated. When crude fats and tallows are subjected to heating operations (hydrolysis, distillation) in the production of commercial fatty acids, residues of commercial chlorophenols present in the fat might be converted in part to chick oedema factors. Additional work is required to determine whether hydropericardium factors are formed from residual chlorinated phenols during production of commercial fatty acids. This laboratory is developing methods for detecting chloro mols in fats and fatty acids.

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ACUTE AND CHRONIC TOXICITY OF 2,4-DICHLOROPHENOXYACETIC ACID AND 2,4,5-TRICHLOROPHENOXYACETIC ACID IN DOGS

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15947

Both 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) may act as plant hormones and herbicides[1,2,3,4] and are now being fairly widely used for the control of certain types of weeds on farm land. These herbicides are being sprayed from airplanes on many acres of specialized farms and grazing land. They are present in trade-marked preparations sold at retail for home gardners. With the widespread use of these herbicides, possible toxic effects are important as accidental ingestion may occur or in case food residues are inadvertently encountered.

In an earlier report 2,4-D was mentioned as being non-toxic to animals and man when administered orally[1,4]. The injection of large doses of 2,4-D did, however, produce symptoms in animals which were similar to those seen in clinical myotonia[5]. More detailed observations were reported by Hill and Carlisle who studied the acute and subacute effects of 2,4-D in various species of animals[6]. There are no reports concerning the toxic properties of 2,4,5-T. The present study concerns the acute oral toxicity and chronic oral toxicity of 2,4-D and 2,4,5-T in dogs.

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METHODS

Adult mongrel dogs of both sexes were used. Most of the animals were housed in the laboratory for a period of 2 to 3 months before the study was started. During this control period they were immunized against distemper with the Green vaccine. The dogs were fed a standard stock diet (Friskies) ad libitum. Both 2,4-D and 2,4,5-T were commercial materials with a purity of 98.5% and 98.9% and freezing points of 132.8°C and 150.6°C, respectively.

In the acute studies the calculated dose of 2,4-D or 2,4,5-T was administered as a single oral dose in capsules. The dogs were observed for a period of 14 days at which time survivors were autopsied. In the chronic study the 2,4-D or 2,4,5-T was administered orally in capsules, 5 days a week over a 13 week period. Each capsule was imbedded in a 4 to 5 gram piece of commercial canned dog food, which the animals consumed readily, thus avoiding the continued trauma of the stomach tube. During the study the animals were weighed twice a week. Control blood counts were taken before the administration of the drug, on the 30th

DOW 712322

day and on the 90th day at the completion of the study. Hemoglobin was determined with a photoelectric colorimeter[7]. Upon the death or at the completion of the study, the animals were autopsied. Tissues were taken from the lung, heart, liver, kidney, adrenal, spleen, thyroid and ovary or testes, fixed in 10% formalin, and stained with hematoxylin and eosin.

DOW 712323

RESULTS

I. ACUTE ORAL TOXICITY

Mortality. The effect of single oral doses of 2,4-D or 2,4,5-T on survival for 14 days is shown in Table 1. The deaths were delayed and occurred 2 to 9 days after the compounds were administered. The oral LD_{50} of 2,4-D is approximately 100 mg/Kgm and for 2,4,5-T is in the range of 100 mgm./kg. or higher.

Body Weight. The large oral doses of 2,4-D or 2,4,5-T produced a decrease in body weight (Table 1). Such animals developed various degrees of anorexia and those that died refused even canned dog food towards the end of their survival.

Symptoms. In dogs that died the effect produced by 2,4-D varied from a mild ataxia and stiffness in the hind legs to a definite myotonia. Initial signs were often noted 6 hours after the oral administration of 2,4-D. At this time the animals were more quiet than normal and a slight ataxia was occasionally present. The hind legs were always affected first, the forelegs later or not at all. There was usually a progressive increase in spasm in the hind legs associated with increasing ataxia and some dogs spontaneously extended the hind limbs in a spastic movement lasting a few seconds. The knee jerk was either normal or hyperactive.

In the early stages of acute poisoning with 2,4-D the animals were usually quiet. If the animal was lifted and made to walk the spasm and ataxia were clearly noticed, but when walked for a while the spasm and ataxia tended to decrease. In the later stages of intoxication, the animal, when placed on his

for six days. Repeated injections into mice did not alter the peripheral blood picture[5].

Large doses of 2,4-D intravenously, or in the present study orally, occasionally produced some necrosis in the liver. However, repeatedly administered oral doses produced only a slight and inconsistent focal necrosis of doubtful significance (Table 4). Deaths during the chronic oral administration of 2,4-D or 2,4,5-T were not correllated with significant lesions in the liver, kidney, or other organs examined.

DOW 712328

SUMMARY

1. The acute oral LD_{50} of 2,4-dichlorophenoxyacetic acid (2,4-D) in dogs is approximately 100 mg. per kilo. Doses in this range or higher produce a definite myotonia accompanied by anorexia and weight loss. The acute oral LD_{50} for 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) is in the range of 100 mg. per kilo or higher. Such toxic doses only produced signs of a mild spasticity.

2. All dogs survived the oral feeding of 2, 5 and 10 mg. per kilo of 2,4-D or 2,4,5-T 5 days a week for a period of 90 days. These doses did not produce any symptoms or changes in body weight, organ weight or blood count.

3. Three of the four dogs receiving repeated doses of 20 mg. per kilo of 2,4-D died and all four dogs receiving 20 mg. per kilo of 2,4,5-T died during the study. Toxicity to 2,4-D at this dosage level was accompanied by bleeding from the gums, necrotic changes in the buccal mucosa and some difficulty in chewing and swallowing but only little evidence of

clinical myotonia. A terminal fall in the percentage of lymphocytes was observed in three of the animals.

4. Death during the repeated administration of 2,4-D or 2,4,5-T was not related to pathological changes in the liver, kidney or other organs examined.

DOW 712329

Table I

Effect of single oral doses of 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid in dogs

Dog No.	Dose mg/k	Wt. loss kgm	Symptoms*	+Died day	Mortality
			2,4-D		
1F	400	-0.1	+	2	2/2
2M	400	-0.8	++	3	
3F	250	-1.6	+++	8	
4M	250	-2.0	++	7	3/3
5M	250	-0.4	++	4	
6F	100	-2.5	+	S	
7F	100	-2.0	0	9	
8F	100	-1.7	+	9	2/4
9F	100	-2.4	0	S	
10F	25	0.0	0	S	
11F	25	+0.2	0	S	0/3
12M	25	+0.2	0	S	
			2,4,5-T		
13M	400	-1.1	+	2	1/1
14M	250	-1.4	+	3	1/1
15F	100	-0.5	0	S	
16F	100	-1.0	0	7	1/4
17F	100	-1.0	0	S	
18F	100	-0.4	0	S	
19M	50	+0.3	0	S	
20M	50	-2.3	0	S	0/4
21F	50	+0.1	0	S	
22M	50	-0.6	0	S	

F, female; M, male

+ S = survival for 14 day test period.

* column indicates general severity of symptoms as discussed in text. 0= no change from normal.

DOW 712330

15957

Table 2

Body weight and survival of dogs fed 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid for 90 days

Dog No.	Dose mg/kgm	Weight Initial kgm	Weight Final kgm	Weight Diff. kgm	Day Died
		2,4-D			
23F	none	14.9	16.4	+2.7	S
24F	none	9.3	10.9	+1.6	S
25M	2	6.8	9.5	+2.7	S
26F	2	15.2	13.8	-1.4	S
27M	5	9.5	9.5	0.0	S
28F	5	12.0	12.5	+0.5	S
29M	10	14.7	14.8	+0.1	S
30M	10	11.6	11.9	+0.3	S
31M	10	17.2	17.8	+0.6	S
32M	*20	13.0	13.7	+0.7	S
33F	*20	9.8	5.9	-3.9	49
34M	20	12.2	10.1	-2.1	18
35M	20	13.4	9.7	-3.7	25
		2,4,5-T			
36F	none	7.3	7.7	+0.4	S
37M	none	12.1	14.5	+2.4	S
38F	2	11.3	12.7	+1.4	S
39M	2	8.9	10.0	+1.1	S
40F	5	8.6	8.4	-0.2	S
41M	5	12.3	12.5	+0.2	S
42F	10	12.3	11.5	-0.8	S
43M	10	13.0	12.2	-0.8	S
44F	10	9.8	9.2	-0.6	S
45M	*20	11.8	9.2	-2.6	49
46F	*20	10.5	7.9	-2.6	75
47F	20	14.9	12.7	-2.2	11
48M	20	10.9	8.2	-2.7	59

F, female; M, male

* = daily dose divided and administered 1/2 in A.M., and 1/2 in P.M.

S = survived 90 day test period.

DOW 712331

Repeated feeding of

Table 3

Effect of 2,4-D and 2,4,5-T on hemoglobin, total blood and differential counts

Dog No.	Dose mg/K	Day	Hb gm.%	RBC mil.	WBC	Differential count					Death day
						Neut %	Lymph %	Mon %	Eos %	Eosin %	
Control Dogs											
23F	none	0	13.20	5.72	17,600	56	38	0	0	6	
		30	13.02	5.93	15,600	64	29	0	0	7	
		90	13.70	6.09	13,850	71	27	2	0	0	
24F	none	0	12.80	5.01	10,700	68	11	3	0	0	
		30	14.72	6.66	13,150	79	12	7	0	2	
		90	14.85	6.16	7,100	79	21	0	0	0	
36F	none	0	9.60	5.03	16,100	67	26	1	0	6	
		30	10.75	5.63	13,300	56	16	2	0	3	
		90	12.74	5.82	14,700	81	18	1	0	0	
37M	none	0	12.29	5.53	14,500	55	39	2	0	4	
		30	13.31	5.78	14,900	63	26	4	0	7	
		90	13.95	6.47	6,400	48	51	1	0	0	
2,4-D											
32M	*20	0	10.43	5.02	13,600	64	27	5	0	4	
		30	12.44	6.16	15,400	66	26	4	0	4	
		90	11.52	6.35	12,100	70	28	6	0	0	
33F	*20	0	13.18	5.56	14,850	54	41	2	0	3	
		30	14.46	5.88	9,700	47	46	4	0	3	
		49	14.36	5.67	16,600	79	14	7	0	0	49
34M	20	0	13.20	5.72	15,200	59	44	4	0	3	16
35M	20	0	14.96	6.47	13,150	76	11	1	0	12	
		25	14.59	6.34	9,100	68	27	4	0	1	25
2,4,5-T											
45M	*20	0	12.54	5.35	16,400	72	12	6	0	10	
		30	8.64	3.98	16,450	77	13	3	0	7	
		49	3.98	3.07	6,900	94	4	2	0	0	49
46F	*20	0	12.43	7.10	15,050	63	29	2	0	6	
		30	14.66	6.82	11,200	71	28	0	0	1	75
47F	20	0	12.44	5.73	13,800	63	32	4	0	1	11
48M	20	0	12,48	6.03	16,000	51	44	2	0	3	
		30	12.93	5.81	14,650	78	18	4	0	0	
		59	11.97	6.14	7,175	92	9	1	0	0	59

F, female; M, male

* = daily dose divided and administered 1/2 in A.M. and 1/2 in P.M.

To conserve space only data on control dogs and the highest doses are given.

DOW 712332

15959

Table 4

Histological changes in liver and kidney of dogs fed 2,4-D or 2,4,5-T for 90 days

Dog No.	Dose mgm./kg.	Day Died	Liver		Kidney	
			congestion	Focal necrosis	Casts	Tub. degen.
			2,4-D			
23	none	-	0	0	0	0
24	none	-	0	0	0	0
25	2	-	0	0	0	0
26	2	-	0	0	1+	0
27	5	-	1+	1+	0	0
28	5	-	2+	0	1+	1+
29	10	-	0	0	0	0
30	10	-	0	0	0	0
31	10	-	1+	0	0	0
32	20	-	0	0	0	0
33	20	49	1+	1+	0	0
35	20	25	2+	0	0	0
			2,4,5-T			
36	none	-	0	0	0	0
37	none	-	0	0	0	0
38	2	-	0	0	1+	0
39	2	-	0	0	0	0
40	5	-	0	0	0	0
41	5	-	0	*1+	2+	1+
42	10	-	2+	0	1+	0
43	10	-	0	0	0	0
44	10	-	1+	0	0	0
45	20	49	1+	1+	0	0
46	20	75	1+	1+	1+	0
48	20	59	2+	0	0	0

Tissues graded on basis of 0,1+,2+,3+ and 4+.

* also a 1+ fibrosis.

DOW 712333

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2. VanOverbeek, J., and Vélez, I.: Use of 2,4-Dichlorophenoxyacetic acid as a Selective Herbicide in the Tropics, Science 103: 472-473, 1946.

3. Smith, F. G., Hammer, C. L., and Carlson, R. F.: Control of Ragweed Pollen Production with 2,4-Dichlorophenoxyacetic acid, Science 103: 473-474, 1946.

4. Marth, P. C., and Mitchell, J. W.: 2-4-Dichlorophenoxyacetic acid as a Differential Herbicide, Bot. Gaz. 106: 224-232, 1944.

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6. Hill, E. V., and Carlisle, H.: Toxicity of 2,4-Dichlorophenoxyacetic Acid for Experimental Animals, J. Ind. Hyg. and Toxicol. 29: 85-95, 1947.

7. Evelyn, K. A.: A Stabilized Photoelectric Colorimeter with Light Filters, J. Biol. Chem. 115: 63-75, 1936.

DOW 712334

1631

Toxicity of 2,4-Dichlorophenoxyacetic Acid and 2,4,5-Trichlorophenoxyacetic Acid

A Report on Their Acute and Chronic Toxicity in Dogs

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15962

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TOXICITY OF 2,4-DICHLOROPHENOXYACETIC ACID AND 2,4,5-TRICHLOROPHENOXYACETIC ACID

A Report on Their Acute and Chronic Toxicity in Dogs

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DETROIT

BOTH 2,4-dichlorophenoxyacetic acid (2,4-D) and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) may act as plant hormones and herbicides [1] and are now being fairly widely used for the control of certain types of weeds on farm lands. They are being sprayed from airplanes on many acres of specialized farms and grazing land and are present in trademark preparations sold at retail for home gardeners. With the widespread use of these herbicides, possible toxic effects are important, as accidental ingestion may occur or residues may be inadvertently encountered in food. In an earlier report, 2,4-D was mentioned as being nontoxic to animals and man when administered orally.[1a,d] However, the injection of large doses of 2,4-D in animals produced symptoms similar to those seen in clinical myotonia.[2] More detailed observations were reported by Hill and Carlisle who studied the acute and subacute effects of 2,4-D in various species of animals.[3] There have been no reports concerning the toxic properties of 2,4,5-T. The present study concerns the acute oral toxicity and chronic oral toxicity of 2,4-D and 2,4,5-T in dogs.

EXPERIMENTAL PROCEDURES

Adult mongrel dogs of both sexes were used. Most of the animals were housed in the laboratory for a period of two to three months before the study was started. During this control period they were immunized against distemper with the Green vaccine. The dogs were fed a standard stock diet (Friskies) ad libitum. Both 2,4-D and 2,4,5-T were commercial materials, with a purity of 98.5 and 98.9% and freezing points of 132.8 and 150.6 C., respectively.

In the acute studies, the calculated dose of 2,4-D or 2,4,5-T was administered as a single oral dose in capsules. The dogs were observed for a period of 14 days, at which time the sur-

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From the Department of Physiology and Pharmacology and the Department of Pathology, Wayne University College of Medicine.

1. (*a*) Hildebrand, E. M.: War on Weeds, Science **103**:465-468, 1946. (*b*) van Overbeek, J., and Vélez, L.: Use of 2,4-Dichlorophenoxyacetic Acid as a Selective Herbicide in the Tropics, Science **103**:472-473, 1946. (*c*) Smith, F. G.; Hamner, C. L., and Carlson, R. F.: Control of Ragweed Pollen Production with 2,4-Dichlorophenoxyacetic Acid, Science **103**:473-474, 1946. (*d*) Marth, P. C., and Mitchell, J. W.: 2,4-Dichlorophenoxyacetic Acid as a Differential Herbicide, Bot. Gaz. **106**:224-232, 1944.

2. Bucher, N. L. R.: Effects of 2,4-Dichlorophenoxyacetic Acid on Experimental Animals, Proc. Soc. Exper. Biol. & Med. **63**:204-205, 1946.

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DOW 1 249504

15963

vivors were autopsied. In the chronic studies, the 2,4-D or 2,4,5-T was administered orally in [redacted] days a week over a 13 week period. Each capsule was imbedded in a 4 to 5 gm. pi[redacted] commercial canned dog food, which the animals consumed readily, thus avoiding the co[redacted] of the stomach tube. During the study the animals were weighed twice a we[redacted] blood counts were taken before the administration of the drug, on the 30th day, and [redacted] 90th day at the completion of the study. Hemoglobin was determined with a photoelectric colorimeter.[4] Upon death or at the completion of the study, the animals were autopsied. Tissues were taken from the lung, heart, liver, kidney, adrenals, spleen, thyroid, and ovary or testes, fixed in 10% formalin, and stained with hematoxylin and eosin.

TABLE I.—*Effect of Single Oral Doses of 2,4-Dichlorophenoxyacetic Acid and 2,4,5-Trichlorophenoxyacetic Acid in Dogs*

Dog No.*	Dose, Mg./Kg.	Weight Loss, Kg.	Symptoms†	Death Days‡	Mortality
		2,4-D			
1 F	400	−0.1	+	2	2/2
2 M	400	−0.8	++	2	
3 F	200	−1.8	+++	8	2/2
4 M	200	−2.0	++	7	
5 M	200	−0.4	++	4	
6 F	100	−2.5	+	S	2/4
7 F	100	−2.0	0	9	
8 F	100	−1.7	+	9	
9 F	100	−2.4	0	S	
10 F	25	0.0	0	S	0/2
11 F	25	+0.2	0	S	
12 M	25	+0.2	0	S	
		2,4,5-T			
13 M	400	−1.1	+	2	1/1
14 M	200	−1.4	+	2	1/1
15 F	100	−0.5	0	S	1/4
16 F	100	−1.0	0	7	
17 F	100	−1.9	0	S	
18 F	100	−0.4	0	S	
19 M	50	+0.2	0	S	0/4
20 M	50	−0.9	0	S	
21 F	50	+0.1	0	S	
22 M	50	−0.6	0	S	

* F in this column means female; M, male.
† Column indicates general severity of symptoms as discussed in text. 0 means no change from normal.
‡ S in this column means survived 14 day test period.

RESULTS

1. Acute Oral Toxicity.—(*a*) Mortality: The effect of single oral doses of 2,4-D or 2,4,5-T on survival for 14 days is shown in Table 1. The deaths were delayed and occurred two to nine days after the compounds were administered. The oral L.D. [redacted] of 2,4-D was approximately 100 mg. per kilogram of body weight; for 2,4 [redacted] the range of 100 mg./kg. or higher.

[redacted] Weights. The large oral doses of 2,4-D or 2,4,5-T produced a de[redacted] weight (Table 1). Such animals developed various degrees of an[redacted] those that died refused even canned dog food toward the end of their SURVIVAL.

4. Evelyn, K. A.: A Stabilized Photoelectric Colorimeter with Light Filters, J. Biol. Chem. 115:63-75, 1936.

DOW 1249505

15964

(*c*) Symptoms: In dogs that died the effect produced by 2,4-D varied from a mild ataxia and stiffness in the hind legs to a definite myotonia. Initial signs were often noted six hours after the oral administration of 2,4-D. At this time the animals were more quiet than normal, and a slight ataxia was occasionally present. The hind legs were always affected first; the forelegs later or not at all. There was usually a progressive increase in spasm in the hind legs associated with increasing ataxia, and some dogs spontaneously extended the hind limbs in a spastic movement lasting a few seconds. The knee jerk was either normal or hyperactive.

In the early stages of acute poisoning with 2,4-D, the animals were usually quiet. If the animal was lifted and made to walk, the spasm and ataxia were clearly noticed, but after it had walked for a while, the spasm and ataxia tended to decrease. In the later stages of intoxication, the animal, when placed on its feet, was unable to stand and would then sit or lie in an awkward position with spastic limbs marked particularly by spasm of the hind legs. Other dogs stumbled and rolled on the floor in attempts to right themselves. An occasional dog showed evidence of irritation or pain when the skin over the back of the neck was grasped. Some dogs, when held up by the shoulders, would show extension and crossing of the hind limbs. As the toxic effects of the drug progressed, the dogs eventually refused the various types of food offered. Occasionally, sneezing, rubbing of the eyes, and diarrhea were observed, but not vomiting.

Such signs were also seen in one dog that survived a lower dose of 2,4-D for 14 days (Table 1). In this instance the changes were relatively mild and were limited to spasm of the hind legs and a slight ataxia.

Marked effects were not observed in the dogs receiving 2,4,5-T. The changes were limited to a slight or moderate stiffness in the hind legs, with the development of ataxia in the two dogs receiving the highest doses. No symptoms were evident in the one dog that died after a single dose of 100 mg./kg. (Table 1).

(*d*) Pathology: Changes observed were limited to the gastrointestinal tract and lungs. Four dogs (1, 2, 4, and 6) receiving 2,4-D and two dogs (13 and 17) fed 2,4,5-T showed mild to diffuse redness of the mucosa in the small intestine. In some dogs pneumonia was present. Histologically, the above dogs showed some necrosis and inflammation of the intestinal mucosa. One dog (13) had a moderate, diffuse hepatic necrosis. Two dogs (13 and 16) had a mild degree of renal tubular degeneration. In most dogs that died the findings were limited to nonspecific changes, such as hepatic congestion. In many cases death was apparently due to pneumonia, which followed the development of anorexia, weight loss, and myotonia.

II. Chronic Oral Toxicity.—(*a*) Mortality: All dogs receiving 2, 5, or 10 mg. of 2,4-D or 2,4,5-T per kilogram of body weight survived the 90-day test period. The dogs receiving 20 mg./kg. of these compounds died during the study. The administration of 20 mg./kg. in divided doses twice a day produced death in both dogs receiving 2,4,5-T and in one dog receiving 2,4-D (Table 2).

(*b*) Body Weight: The only significant change in body weight occurred in the animals that failed to survive the study (Table 2). Loss of weight in these dogs began 7 to 12 days before the death of the dog.

(*c*) General Symptoms: Dogs that survived the oral administration of 2,4-D or 2,4,5-T for 90 days were free of any symptoms.

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The three dogs that died while receiving the highest dose of 2,4-D showed signs [illegible] somewhat from those observed in the acute studies. The dogs were quiet, [illegible] less responsive than normal. Muscle tonus was higher in the hind legs, [illegible] on passive extension. The hind legs were held more stiffly than usual when walking, and a slight ataxia was present. During the last two to three days of their survival two of the dogs showed difficulty in chewing or swallowing and eventually even refused a small bolus of canned dog food (usually readily consumed). There was also some oozing of blood from the gums and buccal mucosa.

TABLE 2.—*Body Weight and Survival of Dogs Fed 2,4-Dichlorophenoxyacetic Acid and 2,4,5-Trichlorophenoxyacetic Acid for 90 days*

Dog No.*	Dose, Mg./Kg.	Weight			Death Day‡
		Initial, Kg.	Final, Kg.	Diff., Kg.	
		2,4-D			
23 F	None	14.8	16.4	+2.7	S
24 F	None	9.3	10.9	+1.6	S
25 M	2	6.8	9.5	+2.7	S
26 F	2	15.3	13.9	−1.4	S
27 M	5	9.5	9.5	0.0	S
28 F	5	12.0	12.5	+0.5	S
29 M	10	14.7	14.8	+0.1	S
30 M	10	11.6	11.9	+0.3	S
31 M	10	17.2	17.8	+0.6	S
32 M	20†	13.0	13.7	+0.7	S
33 F	20†	8.0	5.9	−2.9	49
34 M	20	12.2	10.1	−2.1	18
35 M	20	13.4	9.7	−3.7	25
		2,4,5-T			
36 F	None	7.3	7.7	+0.4	S
37 M	None	13.1	14.5	+2.4	S
38 F	2	11.3	12.7	+1.4	S
39 M	2	8.9	10.0	+1.1	S
40 F	5	8.6	8.4	−0.2	S
41 M	5	12.3	12.5	+0.2	S
42 F	10	12.3	11.5	−0.8	S
43 M	10	13.0	12.2	−0.8	S
44 F	10	9.3	8.5	−0.8	S
45 M	20†	11.8	9.5	−2.3	49
46 F	20†	10.5	7.9	−2.6	75
47 F	20	14.0	13.7	−0.3	11
48 M	20	10.9	8.1	−2.7	58

* F in this column means female; M, male.
† Daily dose divided and administered one-half in a. m. and one-half in p. m.
‡ S in this column means survived 90 day test period.

In dogs that died while receiving 2,4,5-T, the prominent effects were weakness, slight stiffness in the hind legs, difficulty in swallowing food, and, in one dog, bleeding from the gums.

([illegible] Blood Counts: The administration of 2,4-D or 2,4,5-T did not have any sig[illegible] on the hemoglobin, red cell count, or total white cell count of an[illegible] survived or died during the study. The differential blood count remained nor[illegible] surviving animals. In three animals that died a terminal fall in the percentage of lymphocytes was observed (Table 3).

(*e*) Organ Weights: There was no significant change in the weight of the thyroid gland, adrenal gland, heart, liver, or kidney in animals that survived the 90-day period of study. In two of the three dogs that died during the administration

15966

of 2,4-D, there was a slight increase in heart and kidney weight. A similar change was noted in two of the four dogs that died as a result of 2,4,5-T.

(*f*) Gross Pathology: Two dogs receiving 2,4-D (26 and 34) showed areas of redness in the duodenum. With the administration of 2,4,5-T there developed in dog 42 a diffusely reddened duodenum and jejunum, while in dog 48, autopsied on the 59th day, a generalized icterus was demonstrated.

TABLE 3.—*Effect of 2,4-D and 2,4,5-T on Hemoglobin, Total Blood, and Differential Counts*

Dog No.*	Dose, Mg./Kg.	Day	Hb, Gm. %	RBC, Mil.	WBC	Differential Count: Neut., %	Lymph., %	Mon., %	Bas., %	Eosin., %	Death Day
					Control Dogs						
28 F	None	0	13.20	5.73	17,200	56	38	0	0	6	..
		20	13.82	5.98	15,600	64	29	0	0	7	..
		90	13.70	6.09	13,200	71	27	2	0	0	..
34 F	None	0	12.80	6.01	10,900	86	11	3	0	0	..
		30	14.72	6.66	13,150	79	12	7	0	2	..
		90	14.86	6.16	7,100	79	21	0	0	0	..
36 F	None	0	9.60	5.06	16,100	67	26	1	0	6	..
		30	10.78	5.63	13,200	56	16	2	0	3	..
		90	12.74	5.82	14,700	81	15	1	0	0	..
37 M	None	0	12.20	5.53	14,500	53	39	2	0	4	..
		30	13.21	5.78	14,800	62	26	4	0	7	..
		90	12.96	6.47	6,400	48	51	1	0	0	..
					2,4-D						
32 M	20†	0	10.48	5.02	13,200	64	27	5	0	4	..
		30	12.44	6.16	15,400	68	26	4	0	4	..
		90	11.52	6.86	13,100	70	26	6	0	0	..
33 F	20†	0	12.18	5.56	14,200	54	41	2	0	3	..
		30	14.46	6.86	9,700	47	46	4	0	3	..
		49	14.36	6.67	16,000	79	14	7	0	0	49
34 M	20	0	13.30	5.72	15,300	50	44	4	0	2	18
35 M	20	0	14.90	6.47	13,150	76	11	1	0	12	..
		25	14.50	6.24	9,100	68	27	4	0	1	25
					2,4,5-T						
45 M	20†	0	12.54	5.35	16,400	72	12	6	0	10	..
		30	8.64	3.98	16,450	77	13	3	0	7	..
		49	8.98	3.07	6,900	94	4	2	0	0	49
46 F	20†	0	12.48	7.10	16,000	62	29	2	0	6	..
		30	14.66	6.86	11,300	71	28	0	0	1	75
47 F	20	0	12.44	5.78	13,800	62	32	4	0	1	11
48 M	20	0	12.48	6.08	16,800	52	44	2	0	2	..
		30	12.98	5.81	14,800	78	18	4	0	0	..
		59	11.97	6.14	7,175	92	8	1	0	0	59

* F in this column means female; M, male.
† Daily dose divided and administered one-half in a. m. and one-half in p. m.
To conserve space, only data on control dogs and the highest doses are given.

(*g*) Microscopic Changes: The heart, lungs, thyroid, adrenal, ovary, or testes did not demonstrate any significant changes. Three of the dogs receiving 2,4,5-T and two receiving 2,4-D showed an occasional area of focal necrosis in the liver. This finding, however, was not related to either the dose of the compounds or the death of any animal (Table 4) and was judged to be of no significance. The duodenum of dogs 26, 34, 42, and 48 showed varying degrees of hyperemia and some early infiltration of cells in the mucosa. The submucosa and serosa were normal.

DOW 1 249508

15967

A slight increase in the number of casts in kidney sections was noted in some dogs (Table 4), but again this was unrelated to dosage and was of doubtful significance.

COMMENT

In the acute studies, single large oral doses of 2,4-D administered to dogs may produce signs characteristic of clinical myotonia. This effect of 2,4-D was similar to that observed after various experimental species had received injections.[2,3] In addition, some dogs showed signs of irritation and pain when the skin of the back of the neck was grasped, which may indicate meningeal irritation. The extension and crossing of the hind limbs, when lifted by the shoulders, may point to a spinal or

TABLE 4.—*Histological Changes in Liver and Kidney of Dogs Fed 2,4-D or 2,4,5-T for 90 Days*

Dog No.	Dose, Mg./Kg.	Death, Day	Liver		Kidney	
			Congestion	Focal Necrosis	Casts	Tub. Degen.
		2,4-D				
23	None	..	0	0	0	0
24	None	..	0	0	0	0
25	2	..	0	0	0	0
26	2	..	0	0	1+	0
27	5	..	1+	1+	0	0
28	5	..	2+	0	1+	1+
29	10	..	0	0	0	0
30	10	..	0	0	0	0
31	10	..	1+	0	0	0
32	20	..	0	0	0	0
33	20	49	1+	1+	0	0
34	20	25	2+	0	0	0
		2,4,5-T				
35	None	..	0	0	0	0
37	None	..	0	0	0	0
38	2	..	0	0	1+	0
39	2	..	0	0	0	0
40	5	..	0	0	0	0
41	5	..	0	1+*	2+	1+
42	10	..	2+	0	1+	0
43	10	..	0	0	0	0
44	10	..	1+	0	0	0
45	20	45	1+	1+	0	0
46	20	75	1+	1+	1+	0
48	20	80	2+	0	0	0

* Also a 1+ fibrosis.
Tissues graded on basis of 0, 1+, 2+, 3+, and 4+.

central lesion. Other effects occasionally observed were sneezing, rubbing of the eyes, and diarrhea. The effects of 2,4,5-T, previously studied, were not as severe, being limited to stiffness in the hind legs and ataxia. The higher doses of either compound produced anorexia and weight loss. Although initial effects may be seen sixty minutes after compounds are given, the syndrome developed slowly in the dog and death was delayed, occurring several days after the administration of the compound.

In the chronic studies, the dogs survived doses of 2, 5, or 10 mg. of 2,4-D or 2,4,5-T per kilogram of body weight without apparent ill effects. However, the daily oral administration of 20 mg./kg. of 2,4-D produced death in three of four dogs within 18 to 49 days. This delayed death may indicate a cumulative effect of 2,4-D. The signs observed in animals dying from the 20 mg./kg. dose of 2,4-D

DOW 1243509

differed somewhat from those seen in the acute studies. With the chronic administration, the animals exhibited chiefly a stiffness of the hind legs and ataxia, weakness, difficulty in chewing or swallowing, and occasionally bleeding from the gums. All four dogs which received 20 mg./kg. of 2,4,5-T succumbed between the 11th and the 75th day of the study. Toxic effects in these animals consistently included slight muscle spasm and difficulty in swallowing food. Thus, the chronic oral toxic dose for 2,4,5-T in dogs seems to be in the same range as that obtained with 2,4-D. With both drugs, there was a terminal loss in body weight.

Dogs surviving the chronic doses of 2,4-D or 2,4,5-T did not show any significant change in hemoglobin, total blood counts, or differential blood count. In three of the dogs (64, 57, and 105) which died while receiving 20 mg./kg. of 2,4-D or 2,4,5-T, there was a definite decrease in the percentage of lymphocytes in the peripheral blood. Hill and Carlisle [3] have observed a fall in the polymorphonuclear leucocyte count in one dog and a decrease in the per cent of lymphocytes in two dogs to which 50 mg./kg. of 2,4-D was administered intravenously each day for six days. In mice which received chronic injections there was no alteration in the peripheral blood picture.[2]

Large doses of 2,4-D administered intravenously or, in the present study, orally occasionally produced some necrosis in the liver. However, the administration of chronic oral doses produced only a slight and inconsistent focal necrosis of doubtful significance (Table 4). Deaths during the chronic oral administration of 2,4-D or 2,4,5-T were not correlated with significant lesions in the liver, kidney, or other organs examined.

SUMMARY

The acute oral $L.D._{50}$ of 2,4-dichlorophenoxyacetic acid (2,4-D) in dogs was approximately 100 mg. per kilogram of body weight. Doses in this range or higher produced a definite myotonia accompanied by anorexia and weight loss. The acute oral $L.D._{50}$ for 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) was in the range of 100 mg. per kilogram or higher. Such toxic doses produced only signs of a mild spasticity.

All dogs survived the oral feeding of 2, 5, or 10 mg. per kilogram of 2,4-D or 2,4,5-T 5 days a week for a period of 90 days. These doses did not produce any symptoms or changes in body weight, organ weights, or blood count.

Three of the four dogs receiving repeated doses of 20 mg. per kilogram of 2,4-D died, and all four dogs receiving 20 mg. per kilogram of 2,4,5-T died during the study. Toxicity to 2,4-D at the dosage level was accompanied by bleeding from the gums, necrotic changes in the buccal mucosa, and some difficulty in chewing and swallowing, but there was only little evidence of clinical myotonia. A terminal fall in the percentage of lymphocytes was observed in three of the animals.

Death during the repeated administration of 2,4-D or 2,4,5-T was not related to pathological changes in the liver, kidney, or other organs examined.

Printed and Published in the United States of America

DOW 1249510

C. R. I. Name: Kuron

Common Name:

DOW 750524

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jd

1219-161 Printed in U.S.A. R11-58

THE DOW CHEMICAL COMPANY

REQUEST FOR SCREENING OR APPLICATION TESTING

DATE: Jan. 2, 1959

A DUPLICATE OF THIS REQUEST SHEET SHOULD ACCOMPANY EACH SAMPLE. DO NOT USE BLUE INK TO FILL OUT THIS FORM. NO ERASURES.

K NUMBER	B. C. FILE NO.	F. R. NO.	OTHER CODE NO.	MOLECULAR FORMULA	M. W.
Sample	2.30 40.9				

NAME (CRI APPROVED)

Kuron - Lot 500458

DOW 750525

STRUCTURAL FORMULA (OR GIVE CONSTITUENTS OF MIXTURES AND POLYMERS)

SUBMITTED BY: V. K. Rowe

SOURCE CHEMIST (IF OTHER THAN SUBMITTER) Sent by L. C. White

LAB. NAME AND LAB. REFERENCE Lot 500458

PREPARATION DATE | SOURCE OUTSIDE OF DOW

REPORT RESULTS TO:

FIRST LITERATURE REFERENCE

PATENT NUMBER | CASE NUMBER | DISCLOSURE NUMBE

STOCK ON HAND | ESTIMATED MFG. COST ¢LB.@ L

AMOUNT SENT TO:

MIDLAND, BIO. & AG. CHEM. | SEAL BEACH | LAKE JACKSON | INFRA - RED | OTHERS (NAME, SUCH AS ORGANIC PROD. DEVELOP., AROMATICS, T.S.&D.; GIVE LOCATION)

PHYSICAL PROPERTIES

THIS SAMPLE

MELTING POINT °C	BOILING POINT AT MM	DENSITY	FLASH POINT	FIRE POINT	EST. PURITY

APPEARANCE, PHYSICAL STATE, COLOR	R. I.	STABILITY (TO PH CHANGE, HEAT, LIGHT, ETC.)	VISCOSITY
Brown liquid			

BEST KNOWN SAMPLE

MELTING POINT °C	BOILING POINT AT MM	DENSITY	FLASH POINT	FIRE POINT	EST. PURITY

APPEARANCE, PHYSICAL STATE, COLOR	R. I.	STABILITY (TO PH CHANGE, HEAT, LIGHT, ETC.)	VISCOSITY

SOLUBILITY AT ROOM TEMPERATURE (DETERMINE WHERE POSSIBLE, OTHERWISE ESTIMATE)

	<1%	1-10%	10-25%	>2
ACETONE				
ETHANOL, 95%				
GASOLINE, REG.				
KEROSENE				
NaOH, 1%				
OIL, S.A.E. NEUTRAL				
WATER				
XYLENE				

PRODUCT STATE: ☐ EXPLORATORY RESEARCH ☐ DEVELOPMENT ☐ TECHNICAL SERVICE (CHEMICAL STAGE SYSTEM CHECK ONE) 1 2 3 4 S. S. R. NO.

SPECIAL PROPERTIES: CHEMICAL REACTIVITY, TOXIC EFFECTS (Suspected or Experienced) OTHERS

TESTS REQUESTED ☐ AGRICULTURAL GENERAL SCREENING ☐ BIOCHEMICAL GENERAL SCREENING ☐ OTHERS

NAME: (LUBE OR PLASTICS ADDITIVES, SURFACTANT, PHARMACEUTICAL - BE SPECIFIC AS POSSIBLE)

SPECIFIC TESTS:

Just for Skin sensitization work as Kuron to Dr. Klauder

☒ TOXICOLOGY TESTS (SEE REVERSE, YELLOW SHEET. ATTACH ANOTHER PAGE FOR OTHER INFORMATION IF SPACE ABOVE IS NOT SUFFICIENT.)

PROCESS:

FORM C-1220 PRINTED IN U.S.A. 81-58

15372

1634

cc: V. K. Rowe (2)
T2.30-40-3
T2.30-40-20
Correspondence

February 27, 1959

Joseph V. Klander, M.D.
1934 Spruce Street
Philadelphia 3, Pennsylvania

Dear Dr. Klander:

Subject: KURON

As per our telephone conversation of February 27, 1959, I have sent you under separate cover samples of the ingredients of Kuron. They are designated as Dowco 134, Dowco 135, Dowco 136, and Dowco 137. I think it would be very important when you recheck the man who showed some response to Kuron to include these materials in the check. I would suggest rechecking as follows:

Kuron at 0.1% in water
Dowco 134 at 0.1% in sesame oil
Dowco 135 at 0.~~05~~% in ~~water~~ 0.05
Dowco 136 at 0.01% in ~~sesame oil~~
Dowco 137 at 0.~~05~~% in ~~sesame oil~~ 0.01

Such a check should tell us which, if any, of these materials is responsible. If no response is obtained, it would seem desirable to increase the concentration of each by a factor of 10 and retest.

If additional costs are involved in these additional checks, they can be justified.

I trust I have made myself clear. If you have any questions, let me know.

Sincerely yours,

V. K. Rowe
Biochemical Research Laboratory
12-634 Building

VKR/vmv

15970

P.S. As I told you, Kuron is used at a concentration of 3 to 4 parts per million or 0.0003 to 0.0004% so our margins are large. Naturally, we want your conclusions to recognize this usage.

DOW 7505 28

DR. JOSEPH V. KLAUDER
1934 SPRUCE STREET
PHILADELPHIA 3

1630

June 22, 1961

Dr. V. K. Rowe
Biochemical Research Laboratory
Dow Chemical Company
Midland, Michigan

Dear Dr. Rowe:

I herewith report final result of repeated insult patch test with 1 per cent aqueous solution of Kurosal SL.

The test was performed on fifty male subjects. A cloth 1 x 3/4 inch attached to an Elastoplast was saturated with the Kurosal solution and immediately placed on the skin. This was repeated three times weekly for twelve consecutive times. Two weeks later a challenging application was made.

As shown in Table I there was no cutaneous reaction after removal of each patch. There was therefore, no evidence of primary irritant, fatiguing or allergenic action.

Yours very sincerely,

Joseph V. Klauder

Joseph V. Klauder, M. D.

JVK:js

RECEIVED
JUN 23 1961
Biochem. Res. Lab.

DOW 531498

REPEATED INSULT PATCH TEST
WITH 1 per cent AQUEOUS
SOLUTION KUPCSAL SL

Subject Number	1	2	3	4	5	6	7	8	9	10	11	12	C
1	-	-	-	-	-	-	-	-	-	-	-	-	-
2	-	-	-	-	-	-	-	-	-	-	-	-	-
3	-	-	-	-	-	-	-	-	-	-	-	-	-
4	-	-	-	-	-	-	-	-	-	-	-	-	-
5	-	-	-	-	-	-	-	-	-	-	-	-	-
6	-	-	-	-	-	-	-	-	-	-	-	-	-
7	-	-	-	-	-	-	-	-	-	-	-	-	-
8	-	-	-	-	-	-	-	-	-	-	-	-	-
9	-	-	-	-	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-	-	-	-	-
14	-	-	-	-	-	-	-	-	-	-	-	-	-
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48	-	-	-	-	-	-	-	-	-	-	-	-	-
49	-	-	-	-	-	-	-	-	-	-	-	-	-
50	-	-	-	-	-	-	-	-	-	-	-	-	-

C - Challenging Application

\- Negative

Joseph V. Kreuder
June 22 1961

COW 531499

K-3948	Silvex	Toxicology Research Laboratory	
-(1)	Toxicity Test	V.K. Rowe	1951
(2)	Acute & Semi Chronic Oral Toxicity in Rats	DD. McCollister	1954
3)	-Skin unit No Report Written - data submitted (1 page)		1965
4)	Pharmacokinetic Profile ... following intravenous administration in Rats	M. Sauerhoff DS1421	1975
5)	The Fate ... following oral administration to humans	M. Sauerhoff	1976

MN073280 DDMD688427

Kelen file - Kurosal SL. 1649

MIDLAND
July 20, 1962

RECEIVED
JUL 20 1962
BIOPRODUCTS DEPT.

E. E. Wiffen
Dow Chemical of Canada
Sarnia, Ontario, Canada

DOW 533170

Dear Ted:

As per our discussion by telephone on the 17th, I have looked up the toxicological data we have on Kurosal SL and Kurosal G. Without going into a lot of detail, I shall attempt to summarize it for you in the following paragraphs.

KUROSAL SL - FORMULATION: M-1845

Acute Oral Toxicity - Rats

When the formulation as a 20% aqueous solution was fed in single doses to rats by intubation, doses of 1 g./kg. were survived and doses of 2 g./kg. were lethal. Apparently then, the LD_{50} for this formulation lies somewhere between 1 and 2 g./kg. We have not attempted to define it more accurately.

Effects Upon the Eye - Rabbit

When the undiluted formulation was introduced directly into the conjunctival sac of the rabbit, the material produced severe conjunctivitis and corneal injury such that impairment of vision might result if such contact were experienced. When a freshly contaminated eye was promptly washed with water, the injury was considerably reduced but still rather serious. When the formulation was diluted to 1% with water, it produced only a very slight transient conjunctivitis.

Skin Contact - Rabbit

When the undiluted formulation was confined to the skin of a rabbit, it produced significant hyperemia, edema and necrosis and there was evidence that absorption through the skin occurred, since the animal treated in this manner died. When the formulation was diluted to 1% in water, repeated and even continuous exposure over a two week period, produced only very slight edema and exfoliation without evidence that toxic amounts were absorbed.

Skin Absorption - Rabbit

In an effort to assess the significance of skin absorption, the cuff technique advocated by the U.S. Food and Drug Administration

15976

was employed. Using a 5% aqueous solution, a 24-hour exposure, and a dosage level of 1 gm./kg. of the K-1845, none of the animals died but there was evidence of irritation and some weight loss.

Skin Irritation and Sensitization Tests on Humans

Kurosal SL was tested for us on 50 human subjects by Dr. J. V. Klauder, M.D., Consulting Dermatologist of Philadelphia, Pennsylvania. He employed the repeated insult technique, 12 applications being made over a three week period plus a challenge application two weeks later. Dr. Klauder selected a 1% aqueous solution as an appropriate test preparation since it was many times the concentration which would ultimately appear in any treated lake or water reservoir. He observed no evidence of primary irritation, fatiguing or allergenic action. A copy of Dr. Klauder's report and a protocol of his studies is attached.

KUROSAL G - FORMULATION: K-1847

Skin Absorption - Rabbit

The dry granules of Kurosal G, 2.0 g./kg., were wet with water and bandaged onto rabbit's bellies using the cuff technique. A very slight hyperemia, edema and necrosis occurred but otherwise there were no untoward physiological responses observed.

In talking with C. E. Lynn about the Kurosal problem this morning, I learned that he had sent to Jim Johnson a copy of our report of a 90-day dietary feeding study on rats. That, together with this information, constitutes the data we have at this time on these materials. I trust it will serve your purposes.

Sincerely yours,

VER

V. E. Rowe
Biochemical Research Laboratory
1701 Building
Phone NE 6-2375

VER/jd

cc: C. E. Lynn
L. L. Coulter

DOW 931790
MN0640351

1666

BC T2.2-139-2

Biochemical Research Laboratory

The Dow Chemical Company

SKIN IRRITATION AND ACNEGENIC PROPERTIES OF VEON® BRUSH KILLER, VEON® 2,4,5-T, TORDON® 101 AND WEEDAR 2,4,5-T AMINE

File T2.2-139-2
Charge 1263
Ref. (See below)
Source Weedar from Amchem
Sub. By G. E. Lynn
Rept. By C. P. O'Hare
K. J. Olson

Signed K. J. Olson Nov. 9, 1965

Signed C. P. O'Hare Nov. 9, 1965

Checked F. Agens 11-9-65

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PROBLEM

It is understood that a customer mixed 1.5 gallons of Tordon 101 Mixture with 2 gallons of Weedar 2,4,5-T Amine (Amchem product) in 100 gallons of water and used it for spraying brush. The customer reports that some of his men developed a skin rash as a result. He claims further that his men used Weedar 2,4,5-T Amine alone with no problem. The specific nature of the rash was not revealed. Whether or not the dermatitis was diagnosed by a competent physician is not known. It was requested that these materials be subjected to the rabbit ear test designed to detect acnegenic properties and to the regular testing program used to evaluate primary skin irritating properties.

In view of the likelihood that some other products might be used with Tordon 101 it was requested that the following testing program be initiated.

1. Untreated control.

2. Tordon 101 Mixture, lot 590685.

RESTRICTED: for use within The Dow Chemical Company only.

DOW 931761

3. Tordon 101 Mixture plus Weedar 2,4,5-T Amine (1.5:2).
4. Tordon 101 Mixture plus Veon 2,4,5-T Amine (1.5:2).
5. Tordon 101 Mixture plus Veon Brush Killer (1.5:2).
6. Weedar 2,4,5-T Amine.
7. Veon 2,4,5-T Amine, lot 870665.
8. Veon 2,4,5-T Brush Killer (lot 8802558880244).

TEST PROCEDURE

All materials and mixtures were applied to the rabbit ear and to the intact and abraded rabbit belly on a repeated daily basis. The materials were placed on the belly areas under a cotton pad and bandaged to assure intimate contact. Three applications were made to the abraded skin. Ten applications were made tothe intact belly and the ear unless prior exposure produced a moderate to severe skin burn. Folliculitis, indicative of acnegenic properties, was evaluated daily in the case of the ears (see Table 1).

Table 1 - RABBIT EAR TEST FOR ACNE (UNDILUTED MATERIALS)

Materials	No. Of Appl.	Days Exposed	Response-Results
Control	0	0	No response.
Tordon 101	10	16	No folliculitis.
Tordon 101 + Weedar 2,4,5-T Amine	10	16	Slight to moderate folliculitis.
Tordon 101 + Veon 2,4,5-T Amine	10	16	No folliculitis.
Tordon 101 + Veon Brush Killer	3	15	No folliculitis.
Weedar 2,4,5-T Amine	10	16	Moderate folliculitis.
Veon 2,4,5-T Amine	10	16	Slight folliculitis.
Veon Brush Killer	10	16	No folliculitis.

15980

DOW 931792

DOW 9317793

The test for chloracne was repeated increasing the number of applications to the ear to 17-19 and the days of observation or exposure to 35. On this study the four products only (not the mixtures) were investigated, undiluted and as 10% solutions in chloroform. A volume of 0.1 cc was applied per dose to the inner ear in all cases. The data are summarized in Table 2.

Table 2 -

Materials	Applied As	No. Of Appl.	Days Exposed	Response-Remarks
Veon Brush Killer	Undiluted	19	35	No response.
Veon Brush Killer	10% in chloroform	19	35	No response.
Veon 2,4,5-T	Undiluted	19	35	Slight folliculitis.
Veon 2,4,5-T	10% in chloroform	19	35	No response.
Tordon 101	Undiluted	17	24	No response.
Tordon 101	10% in chloroform	18	39	No response.
Weedar 2,4,5-T Amine	Undiluted	18	34	Moderate folliculitis.
Weedar 2,4,5-T Amine	10% in chloroform	19	34	Very slight folliculitis.

15962

DOW 931794

DOW 031795

The data recorded in Table 3 summarizes the primary irritating properties of the materials as indicated by the rabbit belly. It will also be noted that the skin response regards folliculitis was also observed. In general it is felt that the rabbit ear is more indicative of acnegenic potential than the belly. In these cases the ear and belly data are consistent with the exception of Tordon 101. All ear studies are negative whereas the belly showed a slight positive reaction. This can be interpreted as meaning that Tordon 101 possesses a very slight potential for producing chloracne. The data indicate that Weedar 2,4,5-T Amine is appreciably more potent than Tordon 101. It is inconceivable that the customer referred to above experienced chloracne with the Weedar-Tordon mixture but not with Weedar alone. None of the materials or combinations were tested as use-dilutions (about 3.5% in water). It is possible under conditions of spraying brush that a skin rash might result from prolonged, excessive contact, even with such dilute solutions of any of the materials. A rash might be of a primary nature or chloracne. A competent dermatologist should be employed to diagnose the nature of the rash.

Veon 2,4,5-T Amine appears also capable of producing slight chloracne although under the conditions of the test the Tordon 101 - Veon mixture did not. This is probably due to a matter of diluting Veon. Further applications would probably have proved positive.

Veon Brush Killer and the Tordon 101 - Veon Brush Killer mixture were negative under the conditions of the chloracne test.

The following summary of primary skin irritating data indicates that all of the materials and mixtures tested are capable of producing skin redness, swelling and even a burn in the undiluted form under repeated, prolonged conditions of exposure. As use-dilutions they are not as likely to produce a rash, but if extensively misused and if clothing were to become contaminated and not changed from day to day, a rash could well result. Good care and cleanliness should be practiced at all times while handling these materials, either undiluted or as sprays.

Table 3 - PRIMARY SKIN CONTACT DATA SUMMARY

Materials	Rabbit Number (Sex)	Condition Of Skin	No. Of Appl.
Control	395 (F)	Intact	0
Tordon 101	364 (M)	Intact	3
Tordon 101	364 (M)	Abraded	3
Tordon 101 + Weedar 2,4,5-T Amine	363 (M)	Intact	3
Tordon 101 + Weedar 2,4,5-T Amine	363 (M)	Abraded	3
Tordon 101 + Veon 2,4,5-T Amine	374 (F)	Intact	3
Tordon 101 + Veon 2,4,5-T Amine	374 (F)	Abraded	3
Tordon 101 + Veon Brush Killer	472 (F)	Intact	3
Tordon 101 + Veon Brush Killer	472 (F)	Abraded	3

continued on next page

1398

(RABBIT BELLY)

Response-Remarks

No irritation observed.

No irritation followed first application, moderate redness, slight burn followed second and moderate burn followed third. Skin healed with moderate scab, scar and redness in 16 days. No folliculitis.

Essentially the same as above.

Essentially the same as above. Very sligh to slight folliculitis.

Essentially the same as above, with extensive scar in 16 days.

Slight redness and edema followed first application. Extensive burn followed third. No folliculitis.

Essentially the same as above with slight scar in 16 days. No folliculitis.

Moderate to extensive redness with moderate swelling and burn followed second application. Skin healed with moderate scar in 15 days. No folliculitis.

Moderate redness and burn followed first application. Burn became extensive. Moderate scar in 15 days. No folliculitis.

Table 3 - continued

Materials	Rabbit Number (Sex)	Condition Of Skin	No. Of Appl.
Weedar 2,4,5-T Amine	373 (F)	Intact	3
Weedar 2,4,5-T Amine	373 (F)	Abraded	3
Veon 2,4,5-T Amine	375 (F)	Intact	3
Veon 2,4,5-T Amine	375 (F)	Abraded	3
Veon 2,4,5-T Brush Killer	359 (F)	Intact	3
Veon 2,4,5-T Brush Killer	359 (F)	Abraded	3

T5585

Response-Remarks

Slight redness followed first application. Extensive with moderate swelling and burn followed third. Extensive scar in 16 days. Moderate to severe folliculitis.

Essentially the same as above. Moderate to severe folliculitis.

Moderate to extensive redness; slight to moderate swelling followed first and second applications; extensive burn followed third. Skin healed with moderate scar in 16 days. Slight folliculitis.

Essentially the same as above. No folliculitis.

Slight redness followed first application. Extensive redness and moderate burn followed second and third; skin healed with slight scar in 21 days. No folliculitis.

Slight redness followed first application. Extensive redness and moderate burn followed second and third; skin healed with slight scar in 21 days. No folliculitis.

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Health Hazards Associated with

Handling and Use of Herbicides

by

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15987

Health Hazards Associated with

Handling and Use of

DOW 882211

THE purpose of this paper is to outline the health hazards associated with the handling and use of some of the herbicides employed widely today.

Before discussing specific materials, the terms "toxicity" and "toxic hazard" should be defined. These terms are not synonomous although they are sometimes thought to be; *toxicity* is a property of matter; it may be defined as the property of causing injury to the living organism by other than mechanical means. *Toxic hazard* may be defined as the likelihood that a substance will cause toxic injury.

Warning properties such as foul odors or tastes, lachrymation, or irritation, which become apparent and highly disagreeable from harmless exposure, tend to prevent the likelihood of serious exposure and thereby reduce the hazard. Similarly, the absence of such properties tends to increase the hazards. Physical properties such as vapor pressure, solubility, dustiness, etc., may either increase or decrease the hazard of a material depending upon how it is handled and used. It follows that a material may be highly toxic and yet may not be particularly hazardous; and conversely, a material may be relatively low in toxicity and yet be quite hazardous.

During the last 10 years, and to some extent during the preceding 10 years, more and more attention has been paid to the effects of herbicides upon human subjects, livestock, and wildlife. The development of new and better herbicides and new uses for old ones has led to a tremendous increase in their use by an increasing number of people and to their use over prolonged periods of time by custom operators. The likelihood of human exposure to these materials, has been increased many fold by these new developments. If these newer materials are to be handled safely, specific directions for their use and specific precautions against misuse must be issued. In other words, specific hazards must be defined and information given on how to avoid hazardous exposure. In order to do this intelligently, facts must be known about the chemical, physical, and toxicological properties of the material, about the form and manner in which it is to be handled and applied, and about the likelihood and magnitude of exposure. Industry has recognized and accepted this responsibility.

To be specific, what health hazards are presented by the various commonly used herbicides? and, how should they be handled in order to insure safety?

Sodium Chlorate

THE principal hazard associated with the use of sodium chlorate as an herbicide is that of fire. Vegetation sprayed or dusted with chlorate constitutes a real fire hazard. Clothing contaminated with dry chlorate is easily ignited. Sodium chlorate is not particularly toxic if ingested and in normal use, the likelihood of ingesting dangerous quantities is remote The material is not particularly irritating to the skin and is not absorbed through the skin in significant amounts; hence, the hazards from topical contact are not serious. Information with regard to its effect upon the eyes is lacking.

Precautions for safe handling should be directed primarily toward the elimination of the possibility of fire and, secondarily, toward the avoidance of unnecessary personal contact.

Although cases of livestock poisoning due to chlorate have been reported, most experience has indicated that when used as recommended, it does not present a hazard to livestock grazing in treated areas (1). Precautions should be taken to spread the solid evenly so as not to leave piles of it available and to avoid leaving containers of the material where stock can get it. Salt-hungry stock are most likely to consume toxic amounts of this material (2).

Borax

AVAILABLE information indicates that the use of borax as an herbicide or soil sterilant does not present significant health hazards. The material is fairly toxic if ingested, but the likelihood of ingestion is small. No special handling precautions are believed necessary.

Experience has indicated that the ordinary use of the material does

15988

Herbicides

by

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not present a hazard to livestock or wildlife.

The combination of sodium chlorate and borax (1 part chlorate and 9 parts borax) essentially eliminates the fire hazard from sodium chlorate. The health hazards of the combination are not believed to be of significance.

Special precautions in handling are not believed to be necessary, since experience has indicated that the material does not present a significant hazard to stock and wildlife.

Arsenicals

THESE materials, (Sodium Arsenite and Arsenic Trioxide) present serious hazards of handling and use probably greater than those of any other herbicide. They are highly toxic and the consequence of accidental ingestion of even relatively small amounts is very likely to be death. When handling or applying these materials, particular care must be taken to prevent ingestion, inhalation of dust or spray, and skin contact. Particular care must be exercised in the disposal of sludge or residues from spraying and of contaminated containers.

The hazard to livestock and wildlife from eating sprayed vegetation or from drinking water contaminated by these materials is serious.

Calcium Cyanamid

HEALTH hazards associated with the use of calcium cyanamid are those resulting from contact with the skin and eyes and from inhalation of dust. The hazard from possible ingestion is of little significance.

Precautions for safe handling should include measures to prevent contact with the skin. When handling dusty material, coveralls which fit tightly at the neck, cuffs, and ankles will be helpful in preventing skin contact, as will wearing a hat. Exposed surfaces of the skin may be protected by covering with a bland oil or appropriate protective cream. The skin should be washed thoroughly at the end of each day. Contaminated clothing should be washed before re-use.

Care must be exercised to prevent cyanamid from getting into the eyes. If this should occur, the eyes should be flushed immediately with an abundance of clean water and medical attention obtained.

The breathing of cyanamid dust should be avoided. A respirator should be worn whenever the breathing of dust cannot be avoided by other means. This is particularly important when exposures are repeated or prolonged.

When the granular form of cyanamid is used, the hazard is reduced significantly.

Herbicidal Oils

NUMEROUS oils have been used as herbicides, alone and in combinations with other materials. However, a discussion of the individual oils is beyond the scope of this paper.

Toxicological information regarding the oils is very meagre. Judging from past experience and what is known of the toxicity of petroleum fractions, certain generalizations are justified. It is likely that the most significant hazard presented by the oils would be that of dermatitis caused by prolonged or repeated skin contact. Contact with the eyes may be quite painful, but serious eye injury is probably not likely. The hazard from ingestion is not usually serious unless such materials are swallowed in substantial quantity. The hazard from inhaling vapors or mists of the oils when used as herbicides is not believed to be serious, mainly because the likelihood of inhaling appreciable amounts in normal use is very small. The hazard from fire should not be overlooked.

Precautions for safe handling should be directed toward the avoidance of prolonged and repeated skin contact. Clothing, particularly shoes, wet with oils should be removed and cleaned before re-use. Heavy mists of oil alone or in combination with other toxicants should not be breathed repeatedly or for prolonged periods; under certain conditions, respiratory protection may be necessary to insure safety.

Ammonium Sulfamate

USE of ammonium sulfamate as an herbicide does not present significant health hazards. This conclusion is based on toxicological studies conducted by Ambrose (3) and is borne out by extensive use over an appreciable period of time without reported injury to either humans or livestock.

No special handling precau-

*Paper presented at Northeastern Weed Control Conference, New York City, January 4, 1952.

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15989

tions are necessary. The material presents no fire hazard.

Pentachlorophenol

HAZARDS attending the use of pentachlorophenol are those of absorption of toxic amounts of the material through the skin, skin irritation, eye irritation, and ingestion (4, 5, 6). There is no fire hazard. The dusts of the free phenol and of the sodium salt and oil or water sprays of either are quite irritating to the nose and eyes, sufficiently so that toxic amounts are not likely to be inhaled. Pentachlorophenol may be absorbed through the skin in toxic amounts from concentrated preparations if contact is extensive and prolonged. The irritating action on the skin will vary considerably with the solvent. In general, strong solutions (10% or more) may cause skin irritation on single prolonged exposure, but contacts of short duration are not likely to irritate. Fine dust or solutions as dilute as 1% may irritate upon prolonged and repeated exposure; if exposures are continued over a considerable period of time, an "acne-like" dermatitis may develop. Special tests conducted on human subjects have suggested that the sodium salt, but not the free phenol, possesses a slight tendency to cause hypersensitivity. These results are interpreted to mean that a very few persons may show increased susceptibility after once having a rather severe rash; in practice, this has not been of importance.

Although pentachlorophenol is rather toxic when swallowed, its use as an herbicide does not ordinarily offer opportunity for sufficient intake to be dangerous.

Its safety in regard to livestock feeding upon freshly sprayed forage has been indicated by Grigsby and Farwell (7).

The hazards associated with the handling and use of pentachlorophenol can be avoided by taking precautions to prevent contact with the skin and eyes. If such contact does occur, the material should be removed promptly by washing. Contaminated clothing or shoes should not be worn. In instances where contact cannot be avoided, the necessary protective clothing should be worn—such as goggles, rubber boots, and rubber gloves.

Dinitrophenols

THE hazards attending the handling and use of the dinitrophenols (Dinitrocresols and Dinitro-o-secondary butylphenol) as herbicides are predominantly related to their acute toxicity (8), to the ability of the skin to absorb them, and to their rapid absorption following inhalation of dust preparations. The dinitrophenols generally do not present a hazard of skin irritation or eye injury; however eye irritation may result from contact with certain preparations. Rarely a person exhibits hypersensitivity to these compounds; if so, that person has no alternative but to avoid them carefully. Some liquid preparations are flammable because of the solvents employed; the dinitrophenols, except for dry sodium cresolate, do not present a fire hazard.

In handling dinitrophenol concentrates, either solutions or dusts, precautions should be taken to avoid skin contact and inhalation. Protective clothing such as coveralls, hat, rubber boots, rubber gloves, and a dust respirator may be required — depending upon conditions. If contact with concentrates should occur, contaminated clothing should be removed promptly and the exposed skin thoroughly cleansed with soap and water.

In applying sprays, prolonged breathing of mist should be avoided. When clothing becomes obviously wet with dilute sprays, it should be removed within a short time and the skin cleansed. It is always advisable to bathe each day after applying spray. It should be remembered that the staining of the skin and clothing by dinitrophenol compounds gives no indication of the quantity absorbed or of the actual hazard involved, but merely shows that there has been some contact with the material.

The improper disposal of sludge or residues left after spraying can present a hazard. These should be disposed of so that they will not be available to animals and so they will not contaminate water supplies or streams.

Residues upon foliage treated as recommended are not hazardous to grazing livestock (1).

2,4-D and Others

THREE other materials, 2,4-Dichlorophenoxyacetic acid, its salts and esters (2,4-D); 2,4,5-Trichlorophenoxyacetic acid, its salts and esters (2,4,5-T); and, 4-Chloro-o-toloxyacetic acid, its salts and esters (MCP), can be considered together because their toxicological properties are very similar and because they are used in essentially the same manner (6,9,10, and 11).

These materials present hazards of eye injury and skin irritation. Dusts and strong solutions are capable of causing appreciable injury to the eyes. Dusts in high concentrations may cause irritation of the upper respiratory tract. Repeated or prolonged contact to concentrated formulations may result in skin irritation, while contact with dilute solutions, such as are used for spraying, could possibly cause irritation of the skin. However, this is highly unlikely except, perhaps, in the unusually susceptible person. As ordinarily handled, these materials are not likely to cause skin irritation, eye irritation, or skin sensitization (6). They are not absorbed through the skin to any appreciable extent, and in the amounts likely to be inhaled, are not hazardous. The ingestion of harmful amounts is not likely.

In themselves, 2,4-D and 2,4,5-T do not constitute a hazard to livestock grazing on treated areas (7). On the basis of laboratory studies, the same is believed to be true of MCP. However, it has been suggested that spraying with 2,4-D and 2,4,5-T may render certain plants toxic or possibly make some toxic plants more palatable or attractive. This subject is presently undergoing considerable study; its practical significance has not been great, but cannot be evaluated fully until more data are available.

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Precautions for safe handling should include measures necessary to prevent dust or concentrated preparations from getting into the eyes and to avoid prolonged and repeated skin contact with concentrates. If contamination of the eyes should occur, they should be flushed promptly with clean flowing water for at least 15 minutes and then medical attention should be obtained.

Sodium Trichloroacetate

SODIUM TCA in concentrated form, presents hazards of skin irritation, eye irritation, and respiratory irritation. The material presents no hazards from ingestion or from absorption through the skin (6). Contact with the dust or spray solution, particularly on the face, results in a pronounced burning sensation but serious injury is not likely unless exposures are severe and prolonged. Inhalation of dust may be painful to the nose and upper respiratory passages, but is not likely to cause serious effects.

Precautions in handling and use should be directed toward avoiding contact with the skin and eyes. Protective clothing such as coveralls with tight fitting neck and cuffs and a hat are effective protection. Contaminated clothing should be removed and washed before re-use. If skin contact occurs, promptly remove the material by washing with water. If the eyes should become contaminated, they should be flushed with clean water for at least 15 minutes and medical attention obtained.

No significant hazard to livestock exists from their eating or contacting sprayed foliage. (7).

IPC Materials

NO appreciable hazards appear to be involved in the use of Isopropyl N.-Phenyl Carbamate (I. P. C.) and Isopropyl N-(3-Chlorophenyl)-carbamate (chloro I. P. C.) as herbicides. They are low in toxicity by ingestion and by inhalation, (12) and are not significantly irritating to the eyes or skin. Although it has been suggested that I. P. C. may be carcinogenic, studies conducted at the National Cancer Institute have failed to substantiate this hypothesis (12).

Methyl Bromide

THE health hazards associated with the use of methyl bromide as a seed bed fumigant for killing weed seeds are those of inhalation of vapor and direct contact of the liquid upon the skin.

Since methyl bromide is a highly toxic, odorless gas (13), the hazard from inhalation is serious. The inhalation of hign concentrations for short periods of time may lead to acute systemic poisoning and even death; the inhalation of lower concentrations repeatedly and for prolonged periods of time may lead to chronic poisoning from which recovery may be slow but complete.

In order to reduce the hazard of inhalation, methyl bromide is now marketed to a large extent for agricultural purposes with chloropicrin added. Chloropicrin is a very strong lachrymator and a small percent of it in methyl bromide serves as a warning agent, thus markedly reducing the possibility that a person will unknowingly expose himself to hazardous amounts of the vapors.

The use of methyl bromide as an herbicide involves mostly outdoor applications. Under such conditions the likelihood of the operator exposing himself to hazardous concentrations of gas is remote, providing he stays on the windward side of the gas. This practice should also be followed in removing tarpaulins and other equipment from fumigated beds.

When methyl bromide is used indoors, the hazards are increased markedly. If good ventilation is lacking, the precautions necessary to insure safety will approach those required for space fumigation.

In case of spills in confined spaces, persons present should vacate immediately and should not reenter until aeration has been accomplished. If it is necessary to enter a significantly contaminated area, a gas mask should be worn.

It should be noted that the lachrymatory effect of chloropicrin disappears a few hours after discharge over soil and will not keep children or animals from crawling under gas retaining covers. Care should be taken to keep children or animals away from treated plots during fumigation and perhaps for 30 minutes after tarpaulins have been removed. It is recommended that workmen also practice such precautions.

There is little likelihood of local skin injury in using methyl bromide except from spilling or discharging the material directly upon the shoes or clothing. Even should this occur, the prompt removal of contaminated clothing will prevent significant injury. Repeated or prolonged contact is likely to result in irritation and blistering. Contaminated clothing, particularly leather shoes, should not be re-used until completely free of the material.

It can be noted from the preceding discussions of the various herbicides used widely today that information of a more specific nature is available upon the newer products than is available, even now, on some of the older products. The reason for this is that information regarding the health hazards of the older herbicides has been derived largely from experience, some of which has been sad. Information regarding the newer products has been and is being derived largely from studies on laboratory animals together with observations made during the field testing of such products.

The practice in industry today is to study the toxicological properties of new products before marketing, yes, even before samples are sent out, so that hazards can be defined and so that precautions necessary to insure safe handling can be given.

Informative precautionary labeling such as appears on essentially every agricultural product and other chemicals marketed today is an example of this practice. It takes directly to the consumer the following information:-

A. Name of product.

B. Signal word designating the de-

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gree of hazard: *Danger! Warning!* or *Caution!*

C. Affirmative statements of the particular hazards of that product in the order of their importance.

D. Precautionary measures covering actions to be taken or avoided.

E. Instructions as to what to do in case of contact or exposure.

If every consumer would read the labels on the products he buys today and would follow the directions given thereon, it is exceedingly doubtful that a single case of ill effects would result from the handling and use of herbicides or other agricultural chemicals.★★

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ACD Project Status Report - Document No. 12850

"WHAT ABOUT KURON?"

by

L. L. Coulter

Agricultural Chemical Development

The Dow Chemical Company

Midland, Michigan

May 21, 1957

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"WHAT ABOUT KURON?"

by

L. L. Coulter

SUMMARY

1. Action of Kuron is similar to that of 2,4-D, MCP and 2,4,5-T. It differs mainly in the slower killing action, particularly of woody stems and in the lesser leaf modification on new growth from minute dosages.

2. It is superior to related chemicals and Ammate for control of oak and maple - possibly more active on basswood and is not dependable on ash, aspen and buckbrush.

3. It is not recommended for basal sprays.

4. "Professional" use on the northern turf for control of henbit and chickweeds as well as associated weeds is recommended.

5. Kuron is the primary product for use in combination with Radapon for over-all control of broad-leaved weeds and grasses.

6. American Chemical Paint Company's "Weedone 2,4,5-T Propionic" is the main competition.

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NOMENCLATURE

When The Dow Chemical Company introduced this product to the trade in 1954, it was thought desirable to have a common name for the chemical* which would not be an addition to the present alphabetical series and which would be a word in itself rather than a series of letters. Accordingly, the name silvex was developed and sponsored by us as the proposed common name. This name has inevitably been caught in the whirlpool of terminology confusion which has resulted from the lack of a definite system for clearing common names. In the absence of a public agency to make a positive certification of a common name, each author and each man involved with silvex has used a different common name, depending on his own ideas. Common names for this product have included "2,4,5-T Propionic", "2,4,5-TP", "2,4,5-TPA", "TP" and "T Propionic". "2,4,5-T Propionic" has been included in the trade name for ACP's product. However, recently the Weed Society of America has approved the use of silvex as a common name for use

*The active ingredient of Kuron is 2(2,4,5-trichlorophenoxy propionic acid).

15934

in official Weed Society of America publications and all Division of Weed Investigations personnel have been requested to use it. This is about as far as anyone can go right now in establishing the common name. In view of this action and in view of the fact that we have sponsored this name, it is important for us to use the common name "silvex" whenever we refer to the chemical. We should encourage all of our co-operators to do the same.

Kuron has been developed and registered as the product name for our formulation containing four pounds acid equivalent per gallon as the propylene and polypropylene glycol butyl ether esters of silvex. This is the name we should use wherever feasible, and the common name should be used only where it is essential to use it in connection with experiment stations and research publications.

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ACTION OF KURON

Kuron is, of course, a growth regulating compound, and its physiological effect on the plant is essentially similar to that of 2, 4-D or 2, 4, 5-T in many respects. Application of Kuron is followed by curling and twisting of the leaves within a short time after application. This is not a wilting action in that the leaves do not become limp as they often do in the case of drought. It is a mechanical turning and twisting of the leaf and should not be associated with wilting in any respect. If plants are growing rapidly, a severe swelling and splitting of the stem may occur where growth is taking place most rapidly. This is similar to the action observed with 2, 4-D or 2, 4, 5-T.

The action of Kuron differs from that of related compounds in two respects which are observable to the relatively untrained eye. These are: (1) speed of action, and (2) leaf modification. In general, Kuron causes a much slower response than 2, 4-D or 2, 4, 5-T. The speed of reaction varies with the environmental conditions and the plants involved. However, the rate of leaf browning is usually slower than it is with 2, 4-D or 2, 4, 5-T. This difference may vary from one to two days up to one to two weeks slower, however, the principal difference in speed of action is not in the rate at which the leaves turn brown but the rate at which the stems are killed. Kuron sprayed brush often retains green stems through the first year following application, and commonly hardwoods such as oak will show green stems with no leaves a year after treatment. This is particularly true if application is made late during the growing season, i. e. after about August 15. This relatively slower action must be pointed out to potential customers to avoid early disappointment, and, in fact, if properly presented it can be established as an asset since it is a common feeling in the industry that slow action is the most lethal action.

Kuron action differs further in that it does not cause the severe leaf modification often associated with 2, 4-D and on occasions with 2, 4, 5-T. Leaf modification is not the curling and twisting of the leaves. It is the complete change in leaf conformation or structure which takes place on new growth developing after the material has been applied. With 2, 4-D, this ordinarily means that leaves which are normally wide or ovate become narrow, distorted, and exhibit what is often called a fern leaf or strap-leaved character. These leaves ordinarily present a botchy appearance caused by a variation in color intensity throughout the leaf, particularly apparent if the leaf is held up to the sunlight. This latter factor is important in conjunction with the effect of drift on crops. The effects of very small amounts of Kuron are much less evident.

Resprouting of Kuron-treated brush is often delayed one to two years more than with 2, 4-D or 2, 4, 5-T. This means that spraying costs can be written-off over a longer period.

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Crop Hazard with Kuron

Coincidental with studies involving the activity of Kuron on brush, studies at Texas A & M Experiment Station, Spur, Texas, and by A. J. Watson at Greenville indicated that Kuron has less drastic effect on cotton than 2, 4-D. These findings undoubtedly gave considerable impetus to the early Kuron development program. Intensive studies, particularly at Greenville, subsequent to these early findings have shown that as far as yield of cotton is concerned, Kuron unit for unit causes less reduction than similar compositions of 2, 4-D. In fact, it seems to be less injurious than Esteron 245, and its effect on yield is essentially comparable to 2, 4, 5-T amine salt, based on the same acid equivalent rate. For practical purposes, Kuron is a safer product to use in cotton areas but it is not a safe product to use. It has to be used with the same precautions that Esteron 245 or Esteron Brush Killer demand, and the essential difference is that ordinarily, if used with the same precautions, the chances of injury are less with Kuron.

One of the main aspects of the effect of Kuron on cotton and other crops is the difference in its physiological effect on the leaves as mentioned above. Since it does not cause the sensational grotesque leaf development from minute amounts such as that caused by 2, 4-D, farmers and others concerned with the crop do not become concerned as a result of a small amount of drift. Actually, in most instances, any amount which will cause a yield reduction will show some effect on plants. In contrast, sufficient amounts of 2, 4-D to cause severe leaf distortion will not necessarily cause yield reduction, but will unnecessarily alert the grower to the drift situation. Incidentally, Kuron injury on leaves where leaf modification does occur is usually manifested by a slight cupping of the leaves, and in some extreme situations, the leaf may become almost tubular.

It has been natural to infer from some of the observations on cotton that Kuron is safer to use in other crop areas. Experimental work that has taken place since the development of Kuron and observations which have been made in conjunction with commerical use, do not support a common concept that Kuron is safe to use in all crop areas, since it can severely injure grapes, tobacco, tomatoes, beans, legumes, etc. Here again it is less likely to cause leaf distortion, leaf modification and hence betray itself. However, for practical purposes, every precaution must be made to keep the drift off the leaves of desirable plants.

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RESIDUAL PROPERTIES OF KURON

The phenoxy compounds, 2,4-D, 2,4,5-T, MCP and silvex are readily attacked by micro-organisms in the soil and hence have limited persistence in most soils. In general, 2,4-D is the least persistent, and silvex is the most persistent of the group. This persistence of silvex is not sufficient to permit its use as a long-term soil sterilant. However, it is enough to prevent annual seedling emergence for a longer period than is obtained with the other phenoxy compounds.

BRUSH CONTROL WITH KURON

Leaf-stem Sprays (Foliage Sprays):

Our initial interest in Kuron developed as a result of its outstanding activity on most species of oaks. This continues to be its greatest asset. It is recognized by most experiment station workers and customers as one of the more active herbicides for control of oaks. It is recommended widely, via air application, to open up rangeland in Missouri, Arkansas, Oklahoma and Texas which has been over-grown with oaks and other trees and brush. When it is compared with 2,4,5-T, it does not always show superior results, however, it usually gives better kill of oak, particularly the white oaks. For example, H. M. Elwell, who has done considerable work with Kuron on oak in the cross-timbered area of Oklahoma, feels that Kuron is quite superior on white oaks (including post oak), but the difference between Kuron and 2,4,5-T is not as consistent on blackjack oak. In contrast, work with ground equipment at Tallahassee, Florida by C. B. Owens has proved conclusively that Kuron is more effective than 2,4-D or 2,4,5-T on turkey oak, which is a member of the red oak group. The Texas Agricultural Experiment Station takes recognition of the greater activity of Kuron over 2,4,5-T on oak in their recommendations for control of scrub and tree oaks by air application: "For the two year spraying program, applications totaling two pounds per acre of silvex (2 quarts of Kuron) or two and one-half pounds per acre of

2, 4, 5-T low volatile esters (2-1/2 quarts of Esteron 245). Initial application of 1-1/4 quarts of (Kuron) per acre or 1-1/2 quarts of 2, 4, 5-T ester are followed in the succeeding year with 3/4 quart (Kuron) or one quart of (2, 4, 5-T) in four gallons of spray solution per acre."

We feel that three quarts to one gallon of Kuron per hundred gallons of water applied with good ground equipment as a thorough drenching spray to wet all stems and leaves completely on all sides is the most effective foliage spray known for control of most oaks. We should recognize this in planning our sales programs and sales pitch, and should not be lead into any feeling of inferiority because of the legendary potency of Ammate on this species. We feel that Ammate offers no advantage on this species or on maple as far as activity is concerned, and Kuron is a much more economical product to use.

Similarly, Kuron is probably the most effective foliage spray on eastern maples such as red maple and hard (sugar) maple. These species dominate most right-of-ways in eastern areas of the United States which have been on a "brush killer" program. We hope that Kuron will ultimately be established as a preferred product in the northwest where vine maple and big leaf maple are a considerable problem, however, at this point information available does not suggest superiority of Kuron over Esteron 245 on these two species.

The general utility of Kuron for mixed brush control is more limited than that of Esteron 245, which has a wider activity spectrum. For practical purposes, Kuron has demonstrated superiority on oaks and maples as discussed above, however, it offers little advantage as a product for use where these species are in the minority. We should not infer from this the generalization that it is not active on other species. For example, it is very effective (similar to Esteron 245) on poison ivy, and has shown promise of controlling bedstraw (Galium mullago) in roadside applications in New York. It will control willows and many other woody species. A few reports indicate that Kuron may give superior control of basswood. This is a species tolerant to most herbicides, and although it fortunately does not occur in great numbers in many localities, it is a common survivor in right-of-ways sprayed with other materials. The evidence is not good enough to warrant statements that Kuron is more effective on basswood than other materials, however, this should be followed up, and we should watch basswood control very closely in all commercial applications where Kuron is used. There do not seem to be other significant species which are relatively more susceptible to Kuron.

Like all phenoxy herbicides and, in fact, like all herbicides, there are some species which are relatively less susceptible to Kuron. These include aspen, buckbrush and ash. Control of aspen in Michigan with Kuron has

DOW 017468

not been equivalent to that obtained with the phenoxy acetic compounds, though, in most instances it has been satisfactory. In Canada, Kuron has failed to give satisfactory control of aspen. Like 2, 4, 5-T, Kuron is virtually selective on buckbrush (Symphoriocarpus) when applied either as a foliage or basal spray. White and green ash are tolerant to applications of Kuron, and while these species have responded erratically in most instances, foliage application has failed to give even terminal kill, while basal spraying has shown no practical results.

Oil-water Emulsions

Very little work has been done with Kuron where amounts of oil in the range of five to ten gallons per hundred gallons of spray have been added to form an oil-water emulsion. The small amount of test work that has been done coupled with some commercial work in Arkansas indicates that we cannot make generalizations with regard to the effect of oil on brush control with different herbicides. There is some evidence that five gallons of fuel oil per hundred gallons of Kuron-water spray may be beneficial. We need more information on this matter. We have never seen any marked reduction in kill when fuel oil has been added. In contrast, we have seen a reduction in root kill when additional oil was added to sprays of Esteron 245 or Esteron Brush Killer.

Basal Sprays With Kuron

We cannot recommend basal sprays with Kuron. For some reason, its specificity becomes more pronounced when it is used as a basal spray, and species which it controls moderately well in foliage sprays or species which are tolerant to Kuron are even more tolerant when it is applied as a basal spray. Such species as oak and maple, which are susceptible to foliage sprays of Kuron, can be killed with basal spraying but it often takes the plants all summer to die. We have not seen any advantage over 2, 4, 5-T in basal sprays in connection with any specific woody plant and we have not encouraged research in this line. However, with our present recommendation of Kuron for industrial sites, it is important for us to obtain more information on basal sprays so that industrial users who have some Kuron on hand and wish to make basal sprays during the winter can be more adequately advised on what to expect.

WEED CONTROL IN TURF

Kuron shows excellent possibilities for weed control in turf where clovers, henbit and chickweeds are a problem. This project has been reviewed

DOW 017469

in ACD Status Report No. 12762, and it has also been reviewed in the Fall, 1956 issue of DOWN TO EARTH. It is recommended only for use on northern grasses only until further information is available on the response of such stoloniferous grasses as Bermuda and St. Augustine. In addition to its activity on 2,4-D-resistant species like clover, henbit and chickweeds, Kuron also has given good control of such common broad-leaves as dandelion and the plantains as compared with 2,4,5-T. The standard recommendation is 1-1/2 quarts per acre, applied uniformly.

At the present time its use on turf is limited to applications by professional turf people. However, recent information, particularly in the Washington, D. C. area, indicates that we may be able to safely recommend Kuron to the home owner, and this should be considered again in time to make plans for the fall use season.

WEED CONTROL IN INDUSTRIAL SITES

Kuron has been selected as our primary broad-leaf weed control agent to be used with Radapon for general vegetation control. It fills the bill here, and selecting one material simplifies our recommendations, our advertising and our sales pitch. In most industrial areas, blackberries or similar species requiring a 2,4,5-T derivative are present, and Kuron will do the job on them. Further, we have less competition with Kuron than any of the other pheroxy products. Kuron has more residual, and thus we expect it to be helpful in suppressing the growth of annual weeds which subsequently come in following treatment with non-soil sterilants. It is probably safer to use in areas where cotton is grown and it is generally less hazardous to use than 2,4-D formulations.

WEED CONTROL IN RICE

Excellent control of rice weeds has been obtained without crop injury or damage to crops close to treated areas by ground and airplane application. Approval of Kuron use was obtained from authorities in rice growing areas on the basis of effectiveness and safety to cotton growing in the vicinity. We obtained clearance through the U. S. D. A. and now, of course, we have the use recommendations on the Kuron label. Its use seems to be most extensive in Arkansas and Louisiana, where it does a better weed control job in comparison with other rice herbicides (2,4-D,MCP and 2,4,5-T) than in the west. In Texas, 2,4,5-T amine and 2,4-D are widely used, and in California it is 2,4-D and MCP. Kuron can be pushed in appropriate areas.

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OTHER USES

Kuron has shown some promise for submergent aquatic weed control. Used at 1-2 ppm., it has given good control of parrot feather and related aquatics. This use is being explored in the east. When this further exploratory work is completed, it should be possible to decide what development activity is needed. In the meantime, we do not have a recommendation for Kuron on this problem and our development effort is not great.

Kuron has been used for spot treatment of bindweed growing in New Mexico and Texas cotton fields. Control of this weed as well as trumpet creeper and red vine has been very good. The prime reason for using Kuron here is its relative safety in cotton areas. Fred Elliott, Texas Extension Cotton Work Specialist, has issued an official release entitled "Binweed Control in Cotton with Kuron and Kerosene". The recommendations are as follows (issued April, 1957): Treat bindweed spots 1/4 acre or less in size. Leave soil in spots undisturbed for the rest of the season. Apply 1-1/2 to 3 gallons "Kuron" in 100 gallons kerosene to foliage and crowns of bindweed in or close to cotton. Start immediately. Destroy crop in spots if necessary. Spray below 8 inches. Use pressure of 5 pounds or less. Inspect spots next day. Spray surviving (missed) plants. Treat new bindweed at emergence for two seasons. Reduce stands of more extensive bindweed infestations by cheaper methods before starting with "Kuron" in oil.

ACP has introduced "ACP Benzac 103-A", for experimental use only, on non-agricultural land for bindweed control. The product contains 24% polychlorobenzoic acids equivalent to 2 pounds per gallon and sells for about $11.50 per gallon. For field application, the use of 20 gallons of product per acre in a water spray is recommended. We believe Kuron-oil or even Kuron-water is just as effective, less hazardous to use from the drift standpoint, and probably more economical. We should carefully watch results with Kuron on bindweed as well as other perennial weed problems. Since silvex is more residual than 2,4-D, Kuron could well become widely utilized as a temporary soil sterilant in heavy applications to control spot infestations of thistle, bindweed, knapweed, hoary cress, leafy spurge, etc.

COMPETITIVE PRODUCTS CONTAINING SILVEX

The herbicidal use of silvex is a Dow development, and very few competitors have seen fit to get into this business. Our prime competitor is the American Chemical Paint Company, who sell a product called "Weedone 2,4,5-T Propionic". This is a formulation similar to ours which contains four pounds acid equivalent per gallon as the butoxy ethanol ester. Insofar as we know, its properties are similar to Kuron and activity is essentially the same. ACP has not actively promoted the use of "Weedone 2,4,5-T Propionic",

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however, they have been successful in obtaining some business which we developed. They do not list their product in their major literature which discusses their various products available for right-of-way brush control, and their policy appears to be merely to carry "Weedone 2,4,5-T Propionic" so that it will be available to pick up whatever sales eventually develop.

Pittsburg Coke and Chemical Company (now Chemagro), formerly carried an iso-octyl ester formulation of silvex under the trade name of Propon 4. Like ACP, they did not actively promote the use of Propon 4, however, they did pick up some sales where acceptance had been developed and utility established. They do not now list this product in their product information sheets, and we feel that they are no longer a competitor as far as silvex is concerned.

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RELATED COMPOUNDS

A close relative of silvex, 2,4-dichlorophenoxy propionic acid, has given excellent control of oak. It seems quite probable that this compound is about as effective as silvex on most species of oak. However, it has only slightly more effect than 2,4-D on maple, which makes it entirely unsatisfactory for control of this species. In addition, its activity spectrum is even more limited than that of silvex, and it would have to be regarded as a compound to be used solely for oak control insofar as we now know. This material was sampled by Agricultural Chemical Development for several years, and in view of the limited activity of the compound, we decided to discontinue sampling. ACP went through a similar process, however, recently they have reactivated this compound. Unless something very striking develops, it is unlikely that this compound will become a commercial product. There is a possibility that ACP might decide to market a product to counteract what they feel is a Dow advantage in the silvex deal.

CONCLUSION

Primary Uses for Kuron Are:

1. Right-of-way brush control where oak and/or maple dominate the population. It is a superior product for this purpose.

2. As an additive to Radapon for broad-leaf weed and brush control in industrial vegetation control.

3. Rangeland brush control by air application in Missouri, Arkansas, Oklahoma and Texas.

4. Weed control in rice.

5. Control of resistant and general weeds in turf by professional users.

6. Bidweed control by spot treatment.

Kuron has had limited development and sales promotion in the past. We can now see clearly where its greatest potential uses are, and while we will always have some competition, the way is open for us to establish this as a good Dow product for special problems, and we should make every effort to push it for specific uses where it excels.

DOW 017473

THE DOW CHEMICAL COMPANY

DOW_1027211

MIDLAND
May 25, 1960

P. Ritty
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Abbott Road Building

COMMENTS ON BULLETIN ENTITLED, "AQUATIC VEGETATION CONTROL WITH KURON" BY MARK G. WILTSE

I have reviewed the bulletin and would like to make the following suggestions in the section entitled, "Safety to User".

Kuron herbicide is low in toxicity and presents a low degree of hazard in handling and use.

When Kuron herbicide was fed by intubation to groups of various animal species, the LD_{50} values were found to be as follows: rat, 1070 mg/kg; guinea pig, 850 mg/kg; rabbit, 850 mg/kg; mouse, 2140 mg/kg and chicks, 2000 mg/kg. From these data, it may be concluded that there should be no problem from ingestion incidental to the handling and use of this product. If large quantities are swallowed, accidentally or willfully, some injury might result. However, the likelihood of serious injury is remote. Nevertheless, Kuron herbicide should not be left where children or livestock have access to it.

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Cattle, sheep, swine, ducks and chickens have consumed water containing Kuron herbicide at 50 ppm over a four week period with no adverse effects as determined by water consumption, body weight gains, and gross observations, including gestation and parturation in sheep. These data indicate that foliage or water treated with Kuron herbicide, as recommended, should not present a hazard from ingestion.

Skin irritation tests conducted upon rabbits have indicated that Kuron herbicide and its dilutions are slightly irritating, upon repeated prolonged contact. In these studies, there was no evidence of absorption through the skin in acutely toxic amounts. The observation of reasonable care and personal cleanliness practices should be adequate to avoid skin difficulties.

Kuron herbicide, when diluted to one per cent with water, caused no primary irritation nor allergenic responses when applied to

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the skin of 50 human volunteers using a repeated insult technique. One subject did develop a mild fatiguing response. In addition, the product was "patch tested" on a second group of 50 human subjects at concentrations up to 50 per cent without cutaneous reaction. Even when applied undiluted to the skin for 2 hours, it caused no skin response. Thus, it may be concluded with a high degree of assurance that when used as directed, this product should cause no skin irritation or skin sensitization responses.

When tested on the eyes of rabbits, Kuron herbicide and its solutions produced moderate pain but only slight irritation. Thus, this product presents no unusual hazards from eye contact. However, suitable eye protection, such as safety glasses, may be worn simply to avoid the discomfort that might result from contact.

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I understand that many local and state laws governing the use of hazardous substances require that all literature giving directions for use must include a copy of the precautionary label. While Kuron is not highly hazardous, I believe this is a good practice and therefore I recommend that the following section be added to the bulletin:

Recommended Precautionary Labeling for Kuron Herbicide

CAUTION

MAY CAUSE SKIN IRRITATION

Avoid contact with eyes, skin and clothing

If there are any questions concerning tne above, please call me.

-Mark A. Wolf

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MAW/jd

cc: L. L. Coulter
M. G. Wiltse

36-B-6607

AQUATIC VEGETATION CONTROL WITH KURON*

11 0141

by Mark G. Wiltse
THE DOW CHEMICAL COMPANY

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Aquatic weed growth has become an increasing problem in recreational waters of the eastern half of the United States. Vegetation has restricted utilization of waters for such purposes as bathing, water skiing, boating, and in some instances has destroyed the normal beauty of aquatic areas. Fish production has often been limited by excessive growth of water weeds. A number of control methods have been employed with varying degrees of success.

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Mechanical contrivances have ranged from under water cutting bars to hand rakes. Although these mechanical methods are often effective for a short time, regrowth from roots or rooting of stem fragments often increases the problem. The method is generally laborious and provides only temporary relief.

Sodium arsenite has been used as a herbicide for several years. In some areas, particularly static waters, this well known chemical has given outstanding results. Principle limitations to its use have been its inherent toxicity, resistance to decomposition and failure to control a broad range of vegetation.

Several workers have been actively evaluating products which would control submerged aquatic weeds and overcome the limitations of previously existing methods. The New Jersey Division of Fish and Game inaugurated a five-year research program in 1951 financed by Dingell-Johnson funds to find an aquatic herbicide (8). In the course of this work, Kuron herbicide was found adaptable to this problem and seemed to offer control comparable to sodium arsenite (8). Kuron contains the active ingredient silvex 2(2-4,5-trichlorophenoxy) propionic acid as the propylene glycol

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butyl ether ester and acts as a plant growth regulator.

Aquatic Weeds Controlled

Early tests indicated that Kuron at 5 quarts per acre foot would control many of the troublesome submerged aquatic weeds in the northeastern United States (1,2,3,4,8). Experimental tests in 1957 and 1958 in several sections of the country evaluated the effectiveness of this concentration on several aquatic weeds. Some tests were conducted at reduced concentrations by certain workers (2). Commercial applications in 1958 and 1959 contributed additional performance information for controlling certain species. The following list summarizes some of the weeds controlled by Kuron.

Aquatic Weeds Controlled by Kuron at 1.25, 2.5 and 5 quarts per acre foot

Kuron 1.25 quarts/acre foot or less (0.5 ppm)

White water lily (Nymphaea spp.)

Pickerel weed (Pontederia cordata L.)

Kuron 2.5 quarts/acre foot or less (1.0 ppm)

Yellow water lily (Nuphar spp.)

Mud Plantian (Heteranthea spp.)

Water Milfoil (Myriophyllum heterophyllum)

Kuron 5 quarts/acre foot or less (2 ppm)

Bladder wort (Utricularia spp.)

Water shield (Brasenia Schreberi)

Coontail (Ceratophyllum demersum)

Fan Wort (Cabomba caroliniana)

Waterweed (Elodea canadensis)

Variable pond weed (Potomogeton diversifolius)

(Potomogeton amplifolius)

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~~Burly Pondweed~~ Naiad	(Najas flexilis)
Spike Rush	(Eleocharis spp.)
Tape grass	(Vallisneria americana)
Water star wort	(Callitriche spp.)
Soft rush	(Juncus effusus)
Bulrush	(Scirpus americanus)
Bur Reed	(Sparganium spp.)

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In some treatments, these weeds were controlled at lower concentrations, but there were not sufficient tests to indicate consistent effectiveness at the lower rates. Treated areas observed two years after treatment indicated a continued control over this period of time. In total treatments on ponds and lakes with Kuron at 5 quarts/acre foot 2 years control has been obtained in some instances.

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Application Technique

Emerged species were controlled in many instances by using Kuron at one gallon per 100 gallons of spray solution applied to the emerged foliage as a thorough wetting spray. The applications for the control of the submerged aquatic weeds were generally applied by diluting the Kuron at 1 gallon in 10 to 40 gallons of water and directing this solution on or into the water. Proportioning pumps were often used to ~~deliver the Kuron solution~~ mix Kuron with lake water and pump it to the booms which would distribute the ~~Kuron~~ solution over a wide swath. Uniform distribution appeared to be desirable to allow a lethal concentration of the Kuron to come in immediate contact with all the vegetative growth.

Injection of the undiluted Kuron formulation was used in some equipment, but on a limited basis.

Environmental Effects

Kuron applications appeared to be most effective if treatments were made during periods of active growth. Treatments applied when water temperatures have been 65°F or higher have been most effective. The water temperature may not influence the reaction of the chemical to a significant degree, but the aquatic weeds may be in their most active growth at these higher temperatures and thus more susceptible. Undoubtedly, the most active growth periods vary for the various aquatic weed species.

Applications with Kuron have been most effective on submerged aquatic plants in lakes and ponds where there is no or limited water movement. Less satisfactory control of some plants has been observed where water currents replace the treated water soon after application. Translocation has been demonstrated in water lilies where applications to the leaf surface has caused a herbicidal effect on the rootstock. However, some aquatic plants have only primative vascular systems which may not be functional and translocation to root areas probably is not important. In these plants, a lethal concentration of Kuron to contact all the vegetative portions of the plant which are capable of growth or reproduction may be required. Adequate water movement around the plant is desirable to allow even distribution of the Kuron around the entire vegetative portion of the plants. Although the exact minimum contact or exposure time required is not clearly defined, 48 to 72 hours exposure to treated water has given control.

Truchelut and Williams (7) compared the effectiveness of Kuron for controlling coontail (Ceratophyllum demersum) in greenhouse tank experiments at three pH levels and three concentrations of calcium ions. Kuron was most effective on

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coontail growing in slightly acid water. It was also more active on coontail growing in water with 250 and 500 ppm of calcium ion than in water with no calcium. In these tests, the effect of calcium was not differentiated from a possible effect of chloride ion which was added in equivalent amounts. Field plot treatments and commercial applications have been only slightly better under acid water conditions compared with treatments to neutral or slightly alkaline water. Perhaps the water pH is only important in water situations with a low level of calcium ions or similar dissolved ions.

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Safety to Fish and Other Aquatic Organisms

The experimental treatments to plots and complete ponds have caused no fish injury at Kuron concentrations of 1.25 to 5 quarts per acre foot. Commerical applications at concentrations of 5 quarts per acre foot or less have given no appreciable fish kill in numerous treatments throughout the country. Slight fish kill has occurred in some instances where applications were made at higher concentrations. The higher concentrations sometimes occurred in shallow areas where the spraying equipment could not operate properly and thus higher concentrations were developed. There has been no fish injury in over 99% of the treatments applied. Rapid incorporation of the spray solution particularly those associated with rates in excess of 5 quarts per acre foot of Kuron should be avoided where fish kill cannot be tolerated.

Pierce (4,5,6) found that Kuron applications had no influence on oxygen content in treated plots. Aquatic weeds treated with Kuron normally decompose slowly, in most situations 10 to 21 days are required for decomposition. This slow decom-

position apparently does not lower the oxygen content of the water. This is a problem with some aquatic herbicides which give rapid kill of weeds. Pierce also reported that Kuron treatments showed no effect on population of benthic organisms represented by the following groups; Annelida, mostly leeches; Mollusca, including 7 species of Gastropoda and 1 species of Pelecypoda (Sphaerium); Amphipoda; Insecta, larvae of mayflies, damsel flies, dragon flies, midges and beetles. Kuron applications temporarily decreased populations of some plankton, but within two weeks after treatment the populations were equal to untreated areas. These plankton consisted of fifty identified species in the following large groups: Myxophyceae, Chlorophyceae, Desmidaceae, Diatomaceae, Flagellata, other Protozoa, Nematoda, Rotifera, Annelida, Crustacea. There was no deleterious effect on large aquatic vertebrates such as frogs and turtles in the treated areas.

Prolific algae growth is often a problem soon after treating aquatic weeds with some aquatic herbicides. Algae growth has not normally occurred until 3 to 4 weeks after Kuron treatment. The delay in appearance of algae apparently is associated with the slow kill of the aquatic weeds and thus the delay in release of nutrients into the water from the decaying vegetation.

Safety to User

Kuron is a relatively safe material to use. When Kuron was fed by intubation to groups of various animal species, the LD_{50} values were found to be as follows: rat 1070 mg/kg; guinea pig, 850 mg/kg; rabbit 850 mg/kg; mouse, 2140 mg/kg and chicken, 2000 mg/kg. Thus Kuron is low in acute oral toxicity.

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~~In other tests~~, Cattle, sheep, ~~swine~~, ducks and chickens consumed water containing 50 ppm Kuron over a four-week period. No adverse effects ~~were demonstrated in any of the species of animals tested as~~ determined by water consumption, body weight gains, and gross observations, including gestation and parturation in sheep.

Results of dermatological studies indicate with a high degree of assurance that Kuron will not cause skin irritation or skin sensitization when used according to label directions.

Generally accepted methods of handling agricultural chemicals associated with good personal cleanliness should be sufficient for the use of Kuron.

maybe put # or safety precautions in application

Effect on Water Use

Kuron may remain in water for 3 to 4 months after treatment where no dilutinn occurs. An 88 acre lake was treated in New York after the water level was lowered 2 feet. No flow occurred through the outlet until 3 months after treatment. In analysis of the lake water 30 days after treatment, 2.4 ppm of silvex from Kuron was present, essentially the same amount that was applied. Analysis of the lake water 70 days after treatment showed 2.1 ppm of silvex present. Samples of water analyzed 100 days after treatment and there after showed no Kuron present. Chemical analysis of the bottom mud indicated no build-up of Kuron. Since Kuron is an organic compound, the components would be expected to be bacteriologically decomposed principally to the elements carbon, hydrogen and oxygen.

Silvex acts as a growth regulating compound on terrestrial broadleafed plants and is used as a stop-drop treatment prior

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to harvest of apples at concentrations of 10 to 20 ppm. Although 2 ppm of silvex as used for aquatic weed control might not cause injury if sprayed on some broadleafed plants, some susceptible species may be affected. Accordingly, it is suggested that water treated with Kuron should not be used for spray purposes or for irrigation during the season of treatment until more information is available on the possible hazards to crops.

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Summary

Kuron is an effective aquatic herbicide on several submerged and emerged aquatic weeds. Applications to still water at 5 quarts per acre foot are suggested for general aquatic weed control. Lower rates are effective on certain species. Conditions for growth, pH and dissolved ion content of water may influence the effectiveness of Kuron. The low mammalian toxicity, slow action, and safety on fish food organisms are desirable properties for Kuron use as an aquatic herbicide.

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THE DOW CHEMICAL COMPANY

DOW_1 027211

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Agricultural Chemical Development
Abbott Road Building

COMMENTS ON BULLETIN ENTITLED, "AQUATIC VEGETATION CONTROL WITH KURON" BY MARK G. WILTSE

I have reviewed the bulletin and would like to make the following suggestions in the section entitled, "Safety to User".

Kuron herbicide is low in toxicity and presents a low degree of hazard in handling and use.

When Kuron herbicide was fed by intubation to groups of various animal species, the LD_{50} values were found to be as follows: rat, 1070 mg/kg; guinea pig, 850 mg/kg; rabbit, 850 mg/kg; mouse, 2140 mg/kg and chicks, 2000 mg/kg. From these data, it may be concluded that there should be no problem from ingestion incidental to the handling and use of this product. If large quantities are swallowed, accidentally or willfully, some injury might result. However, the likelihood of serious injury is remote. Nevertheless, Kuron herbicide should not be left where children or livestock have access to it.

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Cattle, sheep, swine, ducks and chickens have consumed water containing Kuron herbicide at 50 ppm over a four week period with no adverse effects as determined by water consumption, body weight gains, and gross observations, including gestation and parturation in sheep. These data indicate that foliage or water treated with Kuron herbicide, as recommended, should not present a hazard from ingestion.

Skin irritation tests conducted upon rabbits have indicated that Kuron herbicide and its dilutions are slightly irritating, upon repeated prolonged contact. In these studies, there was no evidence of absorption through the skin in acutely toxic amounts. The observation of reasonable care and personal cleanliness practices should be adequate to avoid skin difficulties.

Kuron herbicide, when diluted to one per cent with water, caused no primary irritation nor allergenic responses when applied to

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the skin of 50 human volunteers using a repeated insult technique. One subject did develop a mild fatiguing response. In addition, the product was "patch tested" on a second group of 50 human subjects at concentrations up to 50 per cent without cutaneous reaction. Even when applied undiluted to the skin for 2 hours, it caused no skin response. Thus, it may be concluded with a high degree of assurance that when used as directed, this product should cause no skin irritation or skin sensitization responses.

When tested on the eyes of rabbits, Kuron herbicide and its solutions produced moderate pain but only slight irritation. Thus, this product presents no unusual hazards from eye contact. However, suitable eye protection, such as safety glasses, may be worn simply to avoid the discomfort that might result from contact.

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I understand that many local and state laws governing the use of hazardous substances require that all literature giving directions for use must include a copy of the precautionary label. While Kuron is not highly hazardous, I believe this is a good practice and therefore I recommend that the following section be added to the bulletin:

Recommended Precautionary Labeling for Kuron Herbicide

CAUTION

MAY CAUSE SKIN IRRITATION

Avoid contact with eyes, skin and clothing

If there are any questions concerning the above, please call me.

-Mark

Mark A. Wolf
Biochemical Research Laboratory
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Phone ME 6-2776

MAW/jd

cc: L. L. Coulter
M. G. Wiltse

34-13-66 c.2

DOW 1027213

Midland, Mich.
May 13, 1960

M. G. Wiltse
Ag. Chem. Dev.
ARB

Paper: Aquatic Vegetation Control with Kuron

This paper is approved for outside presentation and publication.

We are retaining 3 copy (ies) for our files.

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~~Propionic acid: 2-(2,4,5-trichlorophenoxy)~~,

Kuron: in Aquatic weed control

weed control: aquatic, with Kuron

sfm

E. Monroe
Applications Liaisor Center

36-B-6602

To be Presented:

To be Published: Dow handouts to interested ACD cooperators from ACD available literature file.

cc: D. M. Plummer
M. Ondrus

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CENTRAL RESEARCH INDEX

566 Building, Midland, Michigan

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In order to safeguard the interest of The Dow Chemical Company and its authors, all talks, papers, publications, articles, news releases, etc. for release outside the company must FIRST BE APPROVED. Technical information must be approved by Midland Central Research Index and other material by the Public Relations Department.

INFORMATION TO BE SUPPLIED AT SOURCE:

Title of Proposed Talk or Publication: **Aquatic Vegetation Control with Kuron**

Authors: **Dr. Mark G Wiltse**

Submitted By: **Dr. Mark G Wiltse** Date: 4-6-60 Deadline Date: 4-22-60

To what process is the information in this paper related?

None Weed Control

Is this information covered by patents -- patent disclosures? ~~Yes.~~

Where and when talk is to be presented:

Not applicable.

RECEIVED EXECUTIVE RESEARCH APR 25 1960

Probable publication or distribution: **500 copies to be made for use as Dow handouts to interested ACD cooperators from ACD available literature file.**

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DOW 1119431

MIDLAND, Michigan
March 26, 1965

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T36.25-66681-6

THE INEFFECTIVENESS OF WASHING AS A PREVENTIVE MEASURE IN THE FORMATION OF FOLLICULITIS IN THE RABBIT EAR FOLLOWING REPEATED APPLICATIONS OF 2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN IN CORN OIL

Problem

To examine the effectiveness of washing with soap and water as a prophylactic measure in the control of folliculitis produced in the rabbit ear by repeated applications of various concentrations of 2,3,7,8-tetrachlorodibenzo-p-dioxin in corn oil. A previous report (T36.25-66681-2) summarized the effect of washing the material from the ear when applied in benzene as a solvent. The material is relatively soluble in benzene. It was of interest to employ similar techniques by applying the dioxin in oil in which it is essentially insoluble.

Materials Used

0.01 Per cent and 0.001 per cent 2,3,7,8-tetrachlorodibenzo-p-dioxin isolated from caustic insoluble oil.

Solvent -- Corn oil
Soap -- Dial
Tap water

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Washing Procedure

Ears were thoroughly washed with rich soap lather for 30 seconds and subsequently rinsed in copious amounts of freely-flowing tap water, after which they were blotted dry with paper towels.

Exposure Times Selected For Study

(1) Five seconds (time taken to uniformly spread solutions described above on rabbit ear).

(2) Two hours.

(3) Four hours.

Experimental Procedure

The effectiveness of washing with soap and water as a prophylactic measure was studied in the lab, by repeatedly applying the solutions described above to rabbit ears -- 0.1 cc/ear/day -- and allowing the material to remain for controlled periods of time before washing. Two animals were used to demonstrate each point represented by a chemical concentration and a particular exposure time. Controls for each chemical concentration and for the solvent were incorporated into the study. A total of 18 animals were used in the evaluation.

Results And Conclusions

Results of this study indicate that concentrations as low as 0.001 per cent 2,3,7,8-tetrachlorodibenzo-p-dioxin in corn oil produced a discernable folliculitis as a result of sixteen applications in 24 da When compared to a previous similar experiment in which benzene was incorporated as the solvent, results indicate that the use of benzene hastens the development of folliculitis.

Under the conditions of the experiment it appears that washing with soap and water is quite ineffective as a preventive measure even when the dioxin is applied in an essentially insoluble form.

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sjl

attachment

Solution Strength	Number Of Applications	Days Exposed	Washed
0.01%	16	24	No
0.01%	14	24	No
0.001%	16	24	No
0.001%	16	24	No
0.01%	11	17	At once
0.01%	14	20	At once
0.001%	16	24	At once
0.001%	16	24	At once
0.01%	7	13	2 hours
0.01%	6	11	2 hours
0.001%	16	24	2 hours
0.001%	14	20	2 hours
0.1%	16	24	4 hours
0.01%	16	24	4 hours
0.001%	16	24	4 hours
0.001%	16	24	4 hours
Corn oil Control	16	24	No
Corn oil Control	16	24	2 hours

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Summary of Results

Ear Appearance	First Appearance of Folliculit	
	Applications	Days Expose
Moderate-severe folliculitis	12	18
Severe folliculitis	12	18
Slight folliculitis	16	24
Slight folliculitis	16	24
Severe folliculitis	9	13
Severe folliculitis	12	18
Slight folliculitis	16	24
Very slight folliculitis	16	24
Severe folliculitis	6	10
Slight folliculitis (Animal died)	6	11
Slight folliculitis	16	24
Severe folliculitis	11	17
Moderate folliculitis	15	21
Moderate folliculitis	15	21
Slight folliculitis	16	24
Slight folliculitis	16	24

O.K.

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NOT FOR OUTSIDE DISTRIBUTION

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DOW 1092087

ACD Project Status Report - Document No. 16793

AQUATIC VEGETATION CONTROL WITH KURON

by

L. L. Coulter

Agricultural Chemical Development
The Dow Chemical Company
Midland, Michigan

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June 16, 1958

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DOW 1092088

AQUATIC VEGETATION CONTROL WITH KURON

by

L. L. Coulter

Summary

Kuron at one gallon per acre foot of water has given excellent control of water milfoil in the east. The potomagetons as a group have been resistant to this dosage. No fish kill has been noted at this rate. This product will not be recommended by The Dow Chemical Company for this use in 1958 but an intensive development program is proposed to define the limitations and provide the basis for labeling in 1959.

Introduction

Kuron has been evaluated for emergent and submergent aquatic weed control by a number of experiment stations during the last two years. Investigation has been most intensive in New Jersey. The work there was reviewed by Roy Younger of the New Jersey Fisheries Commission in the spring issue of DOWN TO EARTH. Some of the results have been rather spectacular, and in the absence of any other truly satisfactory aquatic herbicide, Kuron has naturally stirred up a great deal of interest, particularly in the eastern areas where the problem is severe. This interest has been intensified by the several papers[1,2,3] on the use of Kuron which have been published this winter and by the discussions which have taken place in the various weed conferences and fishery society meetings. With this interest manifested, it is logical to expect that many people with aquatic weed problems will be interested in the use of Kuron for aquatic weed control during 1958, and we will be under pressure to supply Kuron recommendations and guidance for its use. This report is prepared to bring together the information that we have and to point out certain information that we do not have in order to facilitate proper handling of the anticipated inquiries. A section is also devoted to the development program and its objectives.

---

1. "A Preliminary Report On Controlling Aquatic Vegetation in New Jersey With Kuron", Younger, Roy R. DOWN TO EARTH 13:4, Spring, 1958.
2. "Aquatic Weed Control in Kentucky and Preliminary Research With Certain Herbicides Used For Their Control", Charles C. Bowers, Proc. N.C.W.C.C., December, 1957.
3. "The Effect of the Weedicide Kuron Upon the Flora and Fauna of Two Experimental Areas of Long Pond, Dutchess County, N.Y. Pierce, Madeline E. Proc. N.E.W.C.C., January, 1958.

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Performance

Kuron is applied in a manner which permits the build up of a given concentration in the water of the entire treated area. Thus, a dosage of two ppm is an application of Kuron sufficient to give a concentration of two ppm of silvex equivalent in the entire pond or lake. Obviously, the concentration in the spray tank is of little significance.

Many emergent and submergent aquatic plants have been reported satisfactorily controlled with Kuron at concentrations of two ppm acid equivalent or less. These are: white water lily, Nymphaea; yellow water lily, Nuphar; mud plantin, Heteranthera; waterweed, Anacharis; water milfoil, Myriophyllum; bladderwort, Utricularia; arrowhead, Sagittaria; water shield, Brasenia; fanwort, Cobomba; wild celery, Vallisneria; coontail, Ceratophyllum. Of this group, water milfoil or Myriophyllum and white pond lily, Nymphaea are probably the most susceptible.

The Potamogetons appear to be quite tolerant to Kuron. Unfortunately, this is a major aquatic genus, and while it has not been the dominant trouble species in New Jersey, it is in some areas, and it could rapidly become a real problem after the more susceptible species have been controlled with Kuron. We do not have sufficient information to know what concentrations are required to control Potamogeton. In fact, there is some doubt that this weed can be practically controlled with Kuron. Duck weed, Lemna minor, is tolerant to Kuron as it is to most herbicides. Some satisfactory control has been reported by multiple application within one or two day periods so that as the plants are shifted about the pond new plants which were previously protected from an application can be sprayed. However, even with this promise, we cannot feel that Kuron is going to be the answer to duck weed.

It has not shown any promise as an algaecide.

Speed of Action

The reaction of most plants to Kuron, particularly submerged weeds, is very slow. It ordinarily requires at least seven days before response is noted, and at the end of two to three weeks, some open areas may be evident as a result of a "settling" of the weeds. Milfoil usually disintegrates in about three weeks, and in about one month control is obvious and there may be a breaking off of large masses of plant tissue which float ashore. This slow action is desirable from a biological standpoint, since the gradual decomposition of organic matter does not create an oxygen shortage in the water as may happen when vegetation is killed quickly and the entire mass disintegrates within a short period. This can happen when sodium arsenite is used and may be accompanied by high

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fish mortality as a result of low oxygen supply. From the selling point of view, of course, slow action may be somewhat undesirable since most folks are anxious to get results quickly.

Nature of Action

Kuron probably has the same physiological effects on aquatic weeds that it has on terrestrial plants. However, the manner of getting it into the plant is quite different since most of the growth is submerged. Thus, by building up a concentration of Kuron in the water surrounding it, a plant is literally bathed in herbicide, and even though translocation, which may be very limited in these primitive plants, may not occur, lethal action can take place through absorption over the entire exposed area of the plant.

We do not know if aquatic weeds as a group are more susceptible to Kuron than they are to other phenoxy growth regulators. However, we feel that one of the reasons that Kuron has been more effective is that it is more persistent in water than either 2,4-D or 2,4,5-T. This has been reported earlier by Barrons in GH Report, "The Relative Persistence of Six Substituted Phenoxy Aliphatic Acids in Pond Water", dated February 28, 1951. This work showed conclusively that 2,4-D and 2,4,5-T both decompose rapidly in pond water containing active micro-organisms, while Kuron persists. This has been verified by analysis of test areas last summer, where no change in Kuron content was indicated two months after treatment. This longer persistence gives a longer and more continuous exposure of plants to the herbicide.

Methods of Application

In most of the work that has been reported to date, Kuron has been diluted at a ratio of 1-40 in the spray tank, and then this diluted spray has been applied to the surface of the water. This has been effective on both emergent and submergent species, however, presumably there are several other methods which might be used to apply Kuron. These would include injection beneath the water surface, if feasible, and spraying over the surface with other dilutions that would be practical for various types of equipment. In any case, the main thing is to attempt to build up a lethal concentration in the water. There is no evidence that emergent species such as lily pads are controlled better if the surface is sprayed as compared with the injection below the surface. However, in many cases this would be the most feasible way to make the application. Methods of injecting the chemical directly into the water without pre-mixing are being investigated.

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Toxicity

Fish - There has been no significant fish kill in any of the reported field tests. Laboratory data indicates that if fish are exposed to Kuron at concentrations of seven or more parts per million, considerable mortality can occur. In field work where applications as high as five parts per million have been made, no evidence of fish kill has been seen. We feel that there is a reasonable margin of safety based on the field experience to date. Conceivably, some fish could be killed if trapped in areas of high concentration. Some research workers have reported that fish caught in Kuron treated water were completely free of any flavor change, and as far as they were concerned, there was no change in quality as a result of Kuron treatment. However, one report, and some laboratory findings, indicate that Kuron treatment can affect fish quality. Therefore, more information is needed before definite statements are made. On the basis of acute oral toxicity data, we do not expect Kuron, used in the suggested manner, to be harmful to livestock.

Plankton

Present evidence indicates that Kuron does not effect pond plankton. However, this group of pond flora and fauna is sufficiently complex and important that we should encourage more research on this aspect of Kuron use.

OTHER HAZARDS CONNECTED WITH KURON USE

Vegetation Surrounding Ponds

In two years of experience in New Jersey, no effects have been noted on trees or other vegetation growing on the banks of treated ponds. Therefore, there is reason for hope that we may not have a problem. However, it is important to realize that many of the places where Kuron ultimately may be used will be on estates or other resort developments where vegetation around the pond border may be dense and valuable. We must consider injury to be a possibility until we have more conclusive evidence that there is or is not a hazard.

Contamination of Irrigation Water

Any time an herbicide is put into water that is ultimately going to be used on desirable plants, there is a possible hazard to plants that are sprayed or irrigated. We know that if this concentration is applied to the more succulent vegetable crops or to flowers, we can expect trouble, and in view of the uncertainties

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of the situation, we would have to recommend that Kuron treated water should not be used for any irrigation or spraying purposes.

Potable Reservoirs

One of the aquatic weed problems in the east is in potable water reservoirs. Kuron can cause an off flavor in water, and we cannot recommend its use in this type of a situation. We hope that some of the water reservoir people will evaluate this problem for themselves so ultimately the product could be cleared. Actually, they would want to do much of their own work regardless of what we do here, and we will have to depend largely on them to make the decision.

Suggestions for 1958 Use

This is a new field for the Agricultural Chemical Department. We have some reason to believe that we have a winner (though an unprotected product). This new field may be fraught with hazards, some of which we have yet to recognize. We should not let our limited success so far lead us to become blind to these possible hazards, and our 1958 program has to be pursued cautiously. Kuron will not be recommended for aquatic weed control by The Dow Chemical Company in 1958. The following suggestions are offered for those conducting evaluations of the product.

For control of such aquatic weeds as water milfoil, Myriophyllum, fanwort, Cabomba; white water lily, Nymphaea, use one gallon of Kuron per acre foot of water (i.e., a pond one acre in surface area and one foot deep would require one gallon of Kuron. If it averaged five feet deep, it would require five gallons of Kuron). In addition: Treat small areas not entire lakes. Avoid bathing areas. Don't treat water used for watering livestock, irrigating or spraying crops or for human consumption. Avoid lakes with valuable shade trees or other plantings on the pond margins.

Application can be made early in the growing season, after weed growth is well underway, in any safe manner which will give uniform distribution over or under the water surface. This concentration will not control most weeds in the potamogeton group, and other species may be resistant.

1958 PROGRAM

Agricultural Chemical Development

A full scale development program on the product Kuron is planned for 1958. This will be designed to get the following

DOW 1092094

information where feasible:

(1) Spectrum of activity; (2) limitations in use; (3) additional information on toxicity to adult fish, fingerlings, egg masses and plankton; (4) feasibility of injection type equipment; (5) general areas of utility; (6) best time for application; (7) persistence in the water; (8) hazards of use; (9) possible effect on taste of water and/or fish and (10) duration of control.

The aquatic weed control field is a new one to Dow, and now that we have Kuron, we have a good opportunity of developing more know-how in this field, making some sales, and laying the ground work for development and sales methods for new products which may be coming down the line. Kuron could well be just a starter in this field.

There are a number of possibilities in using silvex in forms other than Kuron. These include granular (acid or ester), amine salts, etc. We cannot overlook potential competition from related compounds such as 2,4-D which is now being sold (daringly) by another company. This competition may be expected to "flood" the research organizations with many types of related materials in 1958. We should watch the resulting experiments closely. In the meantime, we have a good record of field successes with Kuron which is a commercial product. We should agressively pursue its development in 1958. We will, of course, do sufficient basic work on granulars so that we can move in that direction if it appears desirable later.

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Dow Chemical Co.
EPA Hearing
Submissions Re: Cancellation - Volume 2

DOW 1151718

16. "Petition for the Establishment of Tolerances for the Pesticide Chemical, (2,4,5-T) on Raw Agricultural Commodities", Sec. C: Full Reports of Investigations re: 2,4,5-T, 12/8/67.

(1) Summary of 11 tests on safety of 2,4,5-T (A-K below)

(2) Conclusion:

-more data on 2,4,-D than 2,4,5-T is available, but indications are that two materials are comparable; acute oral toxicity of both in lab animals is in same range, 300-1000 mg/kg.

-long history of usefulness not produced evidence of unusual toxicity.

A. "Acute Oral Toxicity of 2,4,5-T to Rats, Mice, Guinea Pigs and Chicks", Rowe, McCollister and Spencer, (Dow, 1950).

(1) Single oral doses (administered by stomach tube) of 2,4,5-T as a 10% suspension in olive oil, to mixed sex group of rats, mice and guinea pigs, 3% solution in olive oil given to chicks.

(2) Symptons of poisoning = ataxia, myotonia; death at highest dosage levels; doses ranged from 0.1 - 1.0 grams/kg.

(3) LD 50's:

rats	=	0.500	grams/kg.
mice	=	0.389	"
guinea pigs	=	0.381	"
chicks	=	0.310	"

(4) 2,4,5-T significantly more toxic to chicks than to rats.

B. "Toxicity of 2.4-D and 2,4,5-T - a report on their acute and chronic toxicity in dogs", Drill and Hiratzka, 1953. ("There have been no reports concerning the toxic properties of 2,4,5-T").

(1) Experimental Procedures: adult mongrel dogs of both sexes

used, fed "Friskies" ad lib, commercial 2,4-D and 2,4,5-T used.

-single oral dose administered in capsules. Survivors autopsied after 14 days (acute studies).

-oral administration in capsules imbedded in 4-5 gram piece of commercial canned dog food, 5 days/wk for 13 weeks (chronic studies).

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(2) Results of Acute Studies:

(a) 2,4-D:

-400 mg/kg caused death in 2/2 dogs in 2-3 days following administration.

-250 mg/kg - death in 3/3 in 4-8 days

-100 mg/kg - 2/4 died in 9 days, 2 survived to 14th day

- 25 mg/kg - no deaths, all 3 survived to day 14

(b) 2,4,5-T:

-400 mg/kg - 1/1 died on day 2

-250 mg/kg - 1/1 died on day 3

-100 mg/kg - 1/4 died on day 7, 3 survived to day 14

- 50 mg/kg - no deaths, all survived to day 14

(c) Oral LD_{50} for 2,4-D = approx. 100 mg/kg; for 2,4,5-T, = 100 mg/kg or higher

(d) Body weight - decrease with larger doses of both 2,4-D and 2,4,5-T; these animals developed anorexia, those that died refused food towards end.

(e) Symptoms: ataxia, stiffness in hind legs, myotonia

16030

(f) Pathology: gastrointestinal changes - redness of mucosa in small intestine, some necrosis and inflammation, hepatic necrosis, mild renal tubular degeneration. Most deaths due to nonspecific changes - hepatic congestion, many cases of death due to pneumonia.

(3) Results of Chronic Studies:

(a) Mortality -

-2,5,10 mg 2,4-D or 2,4,5-T/kg: all dogs survived 90-day test period

-20 mg/kg of compounds: all dogs died during study

(b) Body Weight - loss in weight occurred significantly only in those animals that died

(c) Symptoms - survivors were free of any symptoms; in both 2,4-D and 2,4,5-T dead, weakness, leg stiffness, difficulty in swallowing food, bleeding from gums

(d) Blood Count - only change observed = fall in % of lymphocytes in 3 animals that died.

(e) Organ Weights - no change in survivors; in 2 of 3 2,4-D deaths, slight increase in heart and kidney weight, similar change in 2 of 4 2,4,5-T deaths.

(f) Gross Pathology - 2,4-D: 2 dogs showed areas of redness in duodenum; 2,4,5-T: one dog showed diffusely reddened duodenum and jejunum, another demonstrated a generalized icterus.

(g) Microscopic Changes - 5 cases of focal necrosis in the liver (not related to dosages nor death, thus, of no significance). Some duodenal hyperemia, some early infiltration of cells in the mucosa. Submucosa and serosa were normal. Slight increase in # of casts in kidney sections in some dogs (unrelated to dosages and of doubtful significance).

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(4) Comment:

-effects of 2,4,5-T not as severe as those of 2,4-D in acute studies.

-delayed death in chronic studies with 2,4-D may indicate a cumulative effect of 2,4-D.

-signs observed in dying animals in acute study differed from those in chronic study.

(5) Summary: 2,4-D acute oral LD_{50} in dogs = 100 mg/kg, doses at this level or higher produced a definite myotonia with anorexia and weight loss.

2,4,5-T acute oral LD_{50} in dogs = 100 mg/kg or higher; such doses produced only signs of a mild spasticity.

Death during the repeated administration of 2,4-D or 2,4,5-T was not related to pathological changes in the liver, kidney, or other organs examined.

C. "Summary of Toxicological Information on 2,4-D and 2,4,5-T Type Herbicides and an Evaluation of the Hazards to livestock associated with their use", (Rowe and Hymas, 1954).

(1) Early in 1950, Grigsby and Farwell published results of experiments with 2,4-D and 2,4,5-T involving domestic livestock, concluded "it seems that the farm use of these materials for pasture weed control is a reasonably safe procedure."

(2) Commercial Herbicides - formulations of active ingredients appearing as a salt (water-soluble) or an ester (soluble in oil); most formulations also contain a dispersant, a solvent, a wetting agent, perhaps a diluent (usually considered inert ingredients though they may affect herbicidal effectiveness).

(3) Oral Administration of Single Doses:

(a) test materials administered primarily by intubation.

(b) aqueous, or olive oil or corn oil, solutions used

(c) LD_{50}'s:

	2,4,5-T	2,4-D
rats =	500 mg/kg	375 mg/kg
mice =	389 mg/kg	368 mg/kg
guinea pigs =	381 mg/kg	469 mg/kg
chicks =	310 mg/kg	541 mg/kg
dogs =	100 mg/kg	100 mg/kg

DOW 1 151722

(d) toxic symptons of LD_{50}'s include loss of appetite, weight loss, depression, roughness of coat, general tenseness, muscular weakness; post mortem findings - stomach irritation, minor liver and kidney injury, lung congestion.

(4) Oral Administration of Repeated Doses of 2,4-D:

(a) Rats - fed 2,4-D 5 times/week by intubation, in olive oil solutions. Dosages were 0.0, 3.0, 10.0, 30.0, 100.0, 300 mg/kg.

Results - no adverse effects at control, 3, 10, 30 mg/kg levels; 100 mg/kg group - gastrointestinal irritation, swelling in liver, depressed growth rate; 300 mg/kg group failed rapidly & died, severe gastro-irritation observed.

(b) Another Rat Study - fed 2,4-D for 113 days at levels of 0, 100, 300, 1000, 3000 and 10,000 ppm.

Results - no adverse effects in control, 100 and 300 ppm groups; 1000 ppm group suffered depressed growth rate, excessive mortality, slightly increased liver weights, liver swelling; 3000 and 10,000 ppm groups were destroyed after 12 days since they were not eating and were losing weight; examination revealed increased liver and kidney weight, l. and k. pathological changes.

(c) Chicks - fed 2,4-D for 7 days at levels of 0,500, 1,000 and 3000 ppm.

Results - only adverse effects in 3000 ppm group - reduction in food intake and retarded growth rate (no histopathological exams made).

16033

(5) Oral Administration to Steers - (experiments performed to see if extrapolation of data on small animals to larger animals is justified).

(a) "Esteron Brush Killer" used (formulation of esters of 2,4-D and 2,4,5-T); administrations made by intubation.

-experiment #1: 291 kg steer given single dose of 1000 mg/kg - no toxic symptoms.

-experiment #2: 295 kg steer given 1000 mg/kg esteron for 3 days.

results: general depression, decreased food and water intake, decreased rumen motility; animal died on 3rd day after last dose (death was undramatic). Necropsy revealed dry rumen contents with strong smell of esteron, abomasum was impacted, intestinal contents entirely fluid, congested mesenteric vessels, spleen dark and shrunken.

-experiment #3: 295 kg steer given 500 mg/kg for 2 days.

results: on 3rd day, animal was off feed, rumen motility ceased. On 4th day, steer appeared perfectly normal, no discernible after-effects.

-experiment #4: 336 kg steer given 500 mg/kg for 3 days.

results: no toxic symptoms observed, animal remained on full feed.

-experiment #5: 250 kg steer given 100 mg/kg for 15 days.

results: outward appearance normal. Killed 48 hrs after last dose for study. Duodenal hemorrhage, abomasum irritation, hemorrhagic necrosis of liver, fatty degeneration, slight edema and congestion in kidneys were found.

(b) "Kuron" used in another experiment: 250 kg steer given 100 mg/kg Kuron for 15 days.

results: outward appearance normal. Killed 48 hours after last dose for examination. Very slight edema in kidney, but this is frequently observed in untreated animals; its significance is questionable.

(6) Discussion:

(a) Dogs more susceptible to 2,4-D and 2,4,5-T than other species studied; chicks appear tolerant.

(b) "Inert" ingredients in commercial formulations have no effect on toxicity of active materials.

(c) 2,4-D and 2,4,5-T can be tolerated without adverse effects in doses only slightly smaller than those which cause toxic effects when given only once - these materials have a low degree of chronicity, therefore.

(d) There is a similarity in susceptibility of cattle and small lab animals to these herbicides.

(e) If esteron were applied at the normal rate of no more than 47 mg/sq. ft. (or 2 qts. per acre) a 350 kg (770 lb.) animal would have to consume all forage on 744 sq. ft. to acquire a 100 mg/kg dose of herbicide, a level at which ill effects would not be expected.

(f) ". . . there is little, if any, direct hazard to livestock or wild-life foraging areas treated with herbicides of the type described herein. This has been confirmed by the extensive use of these materials over a number of years without any proved cases of adverse effects."

(g) Spraying of certain plants with 2,4-D can increase their nitrite content to hazardous levels, but some of these plants were sprayed accidentally, and others are not ordinarily eaten by livestock. Toxic amounts of these materials can be obtained if animals have access to spray tanks or other containers of the material.

DOW A 1517241

16035

D. "Results of Toxicological Tests on (2,4,5-T)", Dow, August 1950. (data submitted to FDA Hearing on residue tolerances).

(1) Because of similarities between 2,4-D and 2,4,5-T, residue tolerances for both should be same - 20 ppm "would provide a wide margin of safety."

(2) 10% solution of 2,4,5-T in propylene glycol introduced into rabbit eye caused pain and irritation immediately, severe conjunctivitis and moderate corneal damage apparent 5 hours later, continued for 2 days before healing began.

(3) 10% solution of 2,4,5-T in butyl carbitol acetate applied to rabbit ear and abdomen caused slight irritation.

(4) 2,4,5-T is moderate in acute oral toxicity for the four species, rat, mouse, cavie, and chick (rat more resistant, chick most susceptible).

(5) Handling hazards and precautions:

-swallowing, although unlikely, could cause serious ill effects; induce vomiting.

-avoid contact with eyes and skin, don't wear clothing or shoes contaminated with material.

-no inhalation studies to date, but doubtful that toxic concentrations would be inhaled due to irritation it will produce in upper respiratory passages.

E. "Toxicity tests in NuAmine D/T", Report to Diamond Alkali Company by Hazleton labs, February 1962.

(1) NuAmine D/T = 1,3 - propylene diamine esters of 2,4-D and 2,4,5-T.

(2) Acute Oral Administration - NuAmine D/T given to Sprague-Dawley rats (6 groups of 5 each) by stomach tube, either in water emulsion or undiluted dosages of 10, 31.6, 100, 316, 1000 or 3160 micrograms/kg body weight. Concentrations of material varied from 1%, 10%, or 100%. Observation period of 14 days following dosing.

MRID 1 151725

(a) Mortality: After 24 hrs., 2 in 1000 microgram/kg group, and all (5/5) in 3160 microgram/kg group died. On day 12, another in 1000 microgram group died, and another on day 14. These were only deaths recorded.

(b) Other Effects:

-10,31.6, and 100 micrograms/kg groups: normal appearance and behavior, increase in body weight, no pathological findings.

-316 microg./kg: 4/5 seemed normal, 1 was depresse on days 12-14. Slight increase in average body weight. 2/5 showed congestion and hemorrhage of lungs.

-1000 microg./kg: 4/5 normal at first, 1 showed depression, ataxia, and labored respiration after 4 hrs. 2 died after 24 hrs., survivors showed depression and labored respiration. After 48 hrs., all survivors appeared normal; at 2nd week, all showed unthriftiness, depression, labored respiration and ataxia. 2 more died on days 12&14.

Autopsies showed lung, adrenal congestion, kidney and stomach hemorrhage, hematuria, intestinal inflamation, discoloration and/or reduced size in kidneys spleen and liver, stomach inflammation, congestion of fat around tests.

-3160 micrograms/kg: appeared normal following intubation; depression and ataxia after 1 hr.; prostration, ptosis, salivation, labored respiration, poor reflexes after 4 hours; 1 death at 5 hours, survivors showed hematuria. Total mortality by 24 hours.

Autopsies revealed congestion of lungs, adrenals, liver and spleen; kidney and stomach mucosa hemorrhage; intestinal inflammation; bloody fluid in stomach and urinary bladder.

(3) Acute Eye Application - NuAmine D/T applied to eyes of 3 albino rabbits (left eye only, right served as control).

DOW # 151720

16037

Single application of 0.05 ml of undiluted test material made into conjunctival sac. Periodic observations for 1 week. Food (Purina rabbit pellets) and water ad lib.

(a) Results: Animals seemed normal throughout study, slight decrease in body weights in some.

Eyes showed erythema, film over cornea, slight vascularization of sclera and nictitating membrane, lacrimation, edema of lids (obscuring eye and preventing thorough exam after a few hours), exudation, corneal opacity, and corneal lesion (1 animal).

(4) Acute Dermal Application - albino rabbits used; single application of 50% volume/volume aqueous emulsion of NuAmine D/T at dose of 0.1 mg/kg body weight, and single application of undiluted test material at doses of 0.1, 0.5, 2.0 ml/kg. Test material applied to abdominal skin. "Purina Rabbit Pellets" and water ad lib.

(a) Results: 3 deaths at 2 ml/kg level, no deaths at any other level. Estimated acute dermal LD_{50} of NuAmine D/T for albino rabbits = 1.2 ml/kg.

1. 50% emulsion: application(0.1 ml/kg) produced no signs of systemic toxicity, no pathological findings. 24 hours after application - moderate erythema and edema. At fourth and fifth days, erythema and edema subsided, but animals showed slight or moderate atonia and desquamation. By 12th day, almost all signs of irritation gone.

2. Undiluted:

-0.1 ml/kg - normal appearance and behavior. Autopsy showed kidney congestion, mottled and blanched livers.

-0.5 ml/kg - normal appearance and behavior. Autopsy showed kidney congestion, and granular appearance of liver.

MRID 41517727

-2.0 ml/kg - 3 deaths at this level, on 4th, 5th, and 7th days of observation. 24 hrs. post application, 3 animals showed depression and labored respiration, 4th seemed normal. Toxic signs gradually became more severe: depressed reflexes and coordination, labored respiration, ptosis, ataxia, coma phonation, salivation. Autopsies showed congestion or hemorrhage of lungs and kidney; bloody urine in 1 bladder, bright yellow urine in another; liver damage (blanching and discoloration) and toughened liver surface; spongy brain tissue with excessive fluid in skull; extremely congested or hemorrhagic appearance of skull cap and bone marrow. One survivor was sacrificed, showed congestion of kidneys. Subcutaneous edema, damage to all layers of the skin.

Dermal effects - 24 hrs. after application, skin at all dosage levels showed edema and blanched areas surrounded by moderate erythema. In 3 animals that died at highest dosage, dermal irritation was relatively unchanged at time of death. Survivors in all levels - edema subsided after 3-5 days, scab formations or marked desquamation, atonia, coriaceousness, and fissuring developed to end of observation.

(5) Repeated Dermal Applications - albino rabbits given 1 ml/kg NuAmine D/T in varying strengths (4, 12, 20 oz./gal. aqueous emulsions) 5 days a week for 4 weeks.

Results: each group showed moderate degree of dermal irritation - erythema, edema, atonia, desquamation. Several in 20 oz./gal. group showed fissuring. One animal in each of the test groups died, all showed systemic toxicity - depression, labored respiration, sprawling of limbs, weakness, weight loss. Moribund animals also showed prostration, poor coordination, depressed reflexes, clonic convulsions. Abnormal blood and/or urine findings in each group, severe liver, kidney and skin damage in 4 and 20 oz./gal. groups.

E-1 "Microscopic examination of bone marrow sections" from NuAmine D/T study, Hazleton Labs report to Diamond Alkali Co., 12/16/65. - supplement to report of 2/23/62; tests on bone marrow taken from rabbits receiving repeated dermal applications of NuAmine-D/T.

16039

Results: No distinctive effect on bone marrow at 2 concentrations (4 and 12 oz./gal.). Higher concentration (20 oz./gal.) group showed somewhat atrophied adipose tissue. A possible effect - megakaryocytes (in 20 oz./gal. group) underwent degenerative changes, more so than in controls.

MRID 151729

F. "Results of 90-day Dietary Feeding Studies of Dowanol 97B (ester of 2,4,5-T) in Rats", Dow, 11/27/61

(1) Dowanol 97B ester of 2,4,5-T is an agricultural herbicide (amber liquid)

(2) experimental procedure: 5 groups of 20 m & f rats were maintained for 90 days on diets containing 0.0(control), 0.3, 0.1, 0.03, and 0.01% of the ester. Food (ground Famo Laboratory Chow) and water ad lib.

(3) Results:

0.03 and 0.01% levels: no evidence of adverse effects; increase in average weight of spleen in males, increase in body weight of females - believed due merely to chance.

0.3% level: growth retardation in males, liver and kidney/body weight ratio increased in males. M and F livers were large and light in color, some swelling and necrosis. Some swelling in male kidneys; female kidneys appeared greenish, some swelling and necrosis. Increase in serum alkaline-phosphatase determinations in males.

0.1% level: livers (m and f) showed some swelling and necrosis, females showed hypercellularity of glomerular tuft, swelling of renal tubular epithelium. Increase in average male kidney weight.

(4) Conclusions: the Dowanol 97B ester of 2,4,5-T is moderate in repeated oral toxicity in 90 day feedings. Levels of 0.03% and below were tolerated without evidence of adverse effect. Male and female rats showed some injurious effects (liver & kidney pathology) at levels of 0.1% and above.

Long-term dietary studies (2 years, with rats and dogs) may be required if ester is found in significant amounts as residue in food.

G. "The Toxicologic Effects of Certain Fungicides and Herbicides on Sheep and Cattle", Palmer and Radeleff, 1964

(1) "In contrast to insecticides, organic fungicides and herbicides (with only a few exceptions) have generally been considered to provide comfortable margins of safety for grazing livestock when the compounds are used according to directions."

16040

(2) Sheep and cattle maintained on grain concentrates with hay supplements.

(3) Commercially available formulations used, as fluid dilutions or in gelatin capsules; number of doses varies.

DOW 1517730

Results:

(1) Fungicides -

a) "Captan": sheep are regularly poisoned by doses of 250 mg./kg or higher; reduction to 50 or 100 mg/kg permits animals to eliminate most of material without being harmed. Cattle more tolerant of Captan than sheep. Depression and anorexia, tendency to stay away from group were only toxic signs in sheep; in one heifer, diarrhea and abortion observed. At necropsy, hepatic and renal changes noted but not remarkable.

b) "Zineb": Single doses of 500 mg/kg. tolerated by sheep and cattle. 90 daily doses of 100 or 250 mg./kg. did not poison sheep. In single poisoned sheep (15 doses of 500 mg./kg.), anorexia and bright yellow diarrhea observed. Necropsy showed congestion of the lungs, hepatitis, and nephritis.

c) "Ceresan M": Sheep fed 1, 1.5, or 2 lbs. of treated grain per day. Lethal to all, at doses of 1 lb./day x 33 doses, 1.5 lb./day x 22 doses, or 2 lb./day x 6 doses. Signs of poisoning included anorexia, diarrhea, weight loss, nasal discharge, stilted gait and lameness. Necropsy showed lesions characteristic for mercurial poisoning. (Ceresan contains mercury).

(2) Herbicides -

a) 2,4-D: administered as alkanolamine salt and as propylene glycol butyl ether ester to sheep and cattle. Very little difference in toxicity of 2 derivatives. "Remarkable tolerance" of 481 daily doses of 100 mg./kg. by sheep indicates little probability of acute poisoning in normal applications of the compounds. Toxic signs in sheep - anorexia, depression, weight loss; in cattle - muscular weakness, ataxia, dry, cracked muzzle, ulceration of nasal mucous membrane. Necropsy - lesions varied, usually liver and kidney degeneration; rumen stasis with bright, undigested ingesta; hemorrhages in heart and excess of pericardial fluid.

16041

b) 2, 4, 5-T: administered as triethylamine salt and as propylene glycol butyl ether ester to sheep and cattle. Salt appeared least toxic (sheep tolerated 481 doses of 100 mg./kg.) while esters were lethal at 369 doses of 100 mg./kg. Esters were lethal to sheep and cattle after 7 doses of 250 mg./kg. 2, 4, 5-T somewhat more toxic to sheep and cattle than 2, 4-D, "although poisoning under ordinary circumstances of use would be most unlikely."

c) 2, 4, 5-TP (2 - (2, 4, 5-trichlorophenoxy) - propionic acid) administered as butyl ether esters of propionic acid derivative to sheep and cattle. Markedly more toxic than 2,4-D or 2, 4, 5-T (sheep succumbed to 11 doses of 100 mg./kg., cattle to 29 such doses). Signs of poisoning: anorexia & progressive weight loss. Necropsy showed degeneration of liver and kidneys, hemorrhages on heart surface, congestion of visceral blood vessels, swelling of lymph glands, rumen atony with large quantities of ingesta.

(3) Benzoic Acid Compounds - dimethylamine salts of 2, 3, 6-trichloro- (Trysben) and 2-methoxy - 3,6-dichloro enzoic acids (Banvel D) tested. Both compounds slightly more toxic than phenoxyacetic acids studies. Trysben at dosage of 250 mg./kg. x 10 doses was lethal to the one sheep, but the cow was unaffected; at 500 mg./kg. x 2 doses, the compound produced mild poisoning in one other cow. Banvel D in doses of 250 mg./kg. x 10 doses did not affect a sheep, but killed another sheep at 500 mg./kg. x 2 doses. A cow was not affected by 5 doses of 250mg/kg. Signs of poisoning: salivation, trembling, depression, tympanites. Necropsy showed congested lungs, hemorrhages on heart, pericardium and larger blood vessels, undigested feed in rumen, edema in respiratory system, inflamed kidneys, liver engorged with blood.

(4) Triazines - (Propazine, Simazine, and Atrazine): administered to sheep and cattle; Atrazine was lethal at all doses tested (50 mg./kg. x 199 doses, 100 mg. x 16, 250 x 2) for sheep, and lethal to the cow tested at 250 mg./kg. x 2 doses. At the 250 mg./kg. level in sheep, Simazine was more toxic than Propazine; at 50 mg./kg. Simazine was more toxic than Atrazine. Signs of poisoning (Propazine) anorexia and depression. Signs of poisoning (Atrazine and Simazine): muscular spasms and fasciculation, stiff gait, increased respiratory rates. Necropsy in sheep and cattle given Atrazine showed degeneration and discoloration of the adrenal glands; congestion of lungs, liver and kidneys; presence of undigested food in rumens.

DOW 1 1511731

16042

(5) Miscellaneous compounds:

a) Dalapon (2, 2-dichloropropionic acid) - sodium salt is of a low order of toxicity (500 mg./kg. x 10 doses not toxic to sheep or cattle, one sheep tolerated 481 doses of 100 mg./kg.) No poisonous signs.

b) MCP Amine (2-methyl (4-chloro-o-toloxyacetic acid) - alkanolamine salts poisoned one sheep lethally at 383 doses of 100 mg./kg.; a cow was poisoned by 8 doses of 500 mg./kg. but survived. Signs of poisoning in cattle: anorexia, chronic tympanites; in sheep, anorexia, depression and ataxia before death.

c) Fenuron (3-phenol-1,1-dimethyl urea) - appeared more toxic than most herbicides discussed, but high dosages still required to produce poisoning (e.g., 250-500 mg./kg. x 2-10 doses). Toxic signs: depression, anorexia, complete incoordination (heifer - abortion); slow recovery. Necropsy: lung congestion, heart hemorrhages.

d) Bandane (polychlorodicyclo pentadiene isomers) - sheep poisoned by 3 doses of 250 mg./kg. but survived, while same dosage was lethal for cattle. Toxic signs in sheep: salivation, anorexia, tympanites, dyspnea and depression. Toxic signs in cattle: tense muscles, muscular spasms. (Even when dosing stopped, signs progressed, duplicating tetanus). Death preceded by convulsions. Necropsy: hemorrhages of cerebrum and medulla oblongata, hemorrhage of right psoas muscle, skeletal fat replaced by gelatinous material, lung congestion.

(6) Discussion: studies offer no "reason to alter the already generally accepted concept of the hazards presented by these herbicides." Further study needed re toxic signs.

(7) Conclusions: feeding Ceresan M (13-38 mg./kg.) on treated grain by mistake can easily poison sheep; other materials studied are safe when used as recommended.

H. "Commercial Fishery Investigations", Philip A. Butler - Acute and Chronic Toxicity Studies, 1964

(1) purpose of project: to learn how to protect and preserve marine environment from possibly adverse effects of agricultural chemicals; discovery of pesticides that may be useful in improving fish harvests

DOW 1 151732

(2) "The need for this research does not imply that the widespread use of pesticide formulations automatically constitutes a serious threat to marine life."

(3) "Even the most harmless of chemicals, including water, is toxic when present in sufficient quantity."

(4) different forms of marine life may react quite differently to the same chemical

(5) four bioassay groups (phytoplankton metabolism, oyster shell growth, shrimp survival, fish survival) tested for sensitivity to four pesticides (dyrene, methyl parathion, phosdrin, phosphamidon). Phosdrin and phosphamidon produced the least reaction; dyrene had some effect on all 4 groups, especially fish survival; shrimp survival was very sensitive to methyl parathion.

(6) phytoplankton - microscopic sea plants, essential link in conversion of solar energy into food for more complex marine animals. Using decrease in growth, or decrease in carbon fixation as a standard, toxicities of pesticides may be compared.

(7) crustacea - shrimp is most valuable fishery; most pesticides kill terrestial members of shrimp's phylum (arthropod). Some pesticides paralyze shrimp and other crustaceans, rather than kill; toxic criteria for this group is effective concentration causing paralysis or death to half the samples within a stated period (EC_{50})

(8) mollusks - clams and oysters store high concentrations of chemicals that exist in only trace amounts in the surrounding sea water. Mollusks, however, are able to close their valves and protect themselves from toxic substances in the environment. Thus, tests must be conducted at sublethal concentrations; growth is an objective index to measure, using EC_{50} measure of effect.

(9) fish - younger specimens usually most quickly affected by pesticides.

(10) 2, 4, 5-T (polyglycol butyl ether ester):

- EC_{50} for oyster shell growth = 0.14 mg./liter (96 hrs.), 1 week recovery period.

I. "Commercial Fisheries Investigations," Philip A. Butler - Laboratory Studies and Toxicology

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16044

(1) phytoplankton - majority of chemicals tested caused significant decrease in productivity at 1 ppm, although at lower concentrations an increase in productivity rate was frequently observed (probably because pesticide was toxic to animal part of natural phytoplankton community). Herbicides and DDT very toxic to some plant species.

(2) crustacea - post-larvae of brown shrimp and blue crabs are quite sensitive to chlorinated hydrocarbon insecticides. All shrimp and most crab tests conducted in sea water with acetone stock solution of pesticide (constant flow systems, in which test solutions are renewed continually, have advantage of insuring sufficient oxygen and desired concentration of pesticide). After exposure to lethal or near lethal concentrations, crabs and shrimps often moribund for hours.

(3) mollusks - oyster and clam tested, constant flow system with acetone-stock solutions of pesticides. Oyster closes its shell when sufficiently irritated by contaminated water - does not feed while closed and therefore does not grow; therefore relative chemical toxicity is indicated by changes in growth rate (shell growth). Controls used to compare growth rates. Chlorinated hydrocarbon insecticides were most toxic pesticides to oysters - most inhibited shell growth at well below 1 ppm; other pesticides (organophosphorus and carbamate insecticides) had little or no effect on oyster growth - they decomposed in water. Metabolism increased at summer temperatures; therefore, at higher temperatures some chlorinated hydrocarbon insecticides killed oysters at concentrations which at lower winter temperatures only stopped growth. 1-4 week recovery period for reduced growth rate; data indicates that "a single field application which might temporarily affect oyster growth would probably not have a lasting effect." Chronic, rather than acute, exposure to pollutants is more likely.

Chemicals tested included aldrin, dieldrin, DDT, toxaphene, malathion and acetone (acetone used as a solvent in program, so tested for possible toxicity). In general, no decrease in growth rate; treated groups sometimes grew slightly better than controls. Oysters did not acquire tolerance to pesticides.

-EC_{50} for decrease in shell growth:
2,4,5-T acid (temps. of 16°, 30°C) - no decrease at 2 ppm
2,4-D acid (temps: 9°, 30°C) - no decrease at 2 ppm

DOW 1 1517734

16045

(4) fish - juvenile white mullet & longnose killifish used as test animals in running sea water aquaria. 24 and 48 hr. median tolerated limit values (TLm) obtained. Chronic low-level pollution studies important, since many marine fish pass their early growth stages in estuaries.

3 groups of Spot (leiostomus xanthurus) exposed 3 mos. to sublethal concentrations of dieldrin (0.1, 0.01, 0.001 ppb), in running sea water. High mortalities, 30-37%, but also in controls. No differences in mean lengths, though some experimental fish had axial skeletal distortions, not in controls.

Survivors exposed to 2 ppb dieldrin to determine if earlier low-level exposure had created any resistance: 80% of experimental fish survived 24-hr. exposure, while previously unexposed fish all died.

-2,4,5-T acid tested on longnose killifish showed no effect at 50 ppm (24 and 48 hrs. TLm) with 19° C water temperature.

-Esteron 99 (formulation): TLm for 50% mortality in mullet - 1.5 ppm (24 and 48 hrs.) at 20°C; in killifish = 3.5 ppm (24 hrs.) and 3.0 ppm (48 hrs.) at 19°C.

(5) Future considerations: "... to determine which pesticides now considered necessary may be expected to cause the least damage to marine resources. . . careful selection of the control agent and method of application can lessen the current pesticide hazards."

J. "Commercial Fishery Investigations", P.A. Butler - Acute Toxicity, 1965

(1) Crustacea - shrimp - most valuable commercial fishery resource, spend part of life span in estuaries susceptible to pesticide pollution. Since they are rather closely related to insects, insecticides are particularly toxic to them - either kill quickly or paralyze them so they lose sense of balance. Tests conducted 24, 48 hrs. in flowing seawater.

Results: 2,4,5-T acid had no effect on brown shrimp mortality or equilibrium at 1 ppm after 24, 48 hrs. (avg. water temp. = 28°C)

2,4,5-T polyglycol butyl ether ester tested on brown shrimp in 28°C water caused 10% mortality (or loss of equilibrium) at 1 ppm after 24 hrs., and 20% mortality at 1 ppm after 48 hrs.

DOW 1151735

18046

Veon 245 tested on brown shrimp in 28°C water had no effect on mortality or equilibrium after 24 hr. and 48 hr. exposure at 1 ppm level.

(2) Fish - younger specimens most quickly affected, therefore juveniles used in tests. Sea water used.

Results:

-2,4,5-T polyglycol butyl ether ester tested on Spot in 16°C water temp.; had 24 and 48 hr. EC_{50} of 0.32 ppm for mortality.

-Veon 245, also tested on Spot, in 27°C, had no effect after 24 and 48-hr. concentrations at 1 ppm.

DOW 1151736

K. "Recommendations for Minimizing Dangers of Pest Control and Pesticides to Fish and Wildlife", John L. Georgs, June, 1963

(1) be sure there is real need for pesticide use

(2) discuss possible hazards with biologists prior to use

(3) avoid treatment of any significant portion of range of a rare species or one with specialized habits - consult with conservation officials

(4) treat minimum necessary area; avoid direct treatment of streams, etc., consider danger of runoff contamination

(5) judge danger of chemical both by its toxicity and its disappearance rate

(6) use method of application which will minimize contact with wildlife. Emulsions are more toxic to water environments than oil solutions or suspensions. Granules often concentrate the effect of the toxicant in one stratum.

(7) no double-dosing

(8) avoid main spring migration, nesting periods of birds, etc. when choosing time of treatment - consider possibility of using repellants or scare devices to move mobile wildlife from area.

(9) physical or biological control methods have advantage over chemical methods - more specific, reduce pests without loss of beneficial population.

(10) susceptibility to different pesticides varies greatly among animals

16047

(11) DDT susceptibility: 0.1 - 5 lbs./acre -

heavy kill effect on crustaceans and fish, moderate kill to amphibians and reptiles, some kill to birds, no effect on mammals until 5 lbs./acre level

(12) table with toxicities of other chemicals as compared to DDT: 2,4,5-T derivatives (DDT=1):

rats - LD_{50} of 0.4 (single oral dose)

bobwhites - 0.2 chronic toxicity LD_{50} (10-100 days)

pheasants - 0.1 - " " LD_{50} "

mallards - 0.2 " " LD_{50} "

bluegills - LD_{50} of 0.1 (96 hr. test)

(13) disposal of pesticides always difficult procedure - unopened containers should be returned to wholesaler or sold; disposal of opened containers:

- burned in a h o t flame (liquid organic chemicals)
- addition of lime (wettable powders)
- dumping into sanitary landfill-type dump, containerized if soluble
- empty containers - burned or dumped - do not clean equipment at creeks or waterways

MRID 151737

16048

1743

DoW 1151350

18.209

Lauren —

John says you
do not have the
English translation.
Agnes

16049

18.209 — 73-11-27

TT-66-10329

DOW 1151350H

CLINICAL AND EXPERIMENTAL INVESTIGATIONS CONCERNING THE ETIOLOGY OF CHLORACNE

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by K.H. Schulz

Arch.klin. exp. Derm., 206 (1957)
589 - 596

Pages 9
Photocopy 1.10
Microfilm

A number of workers in a chemical factory at Hamburg developed certain dermatological symptoms between the middle of 1954 and spring 1955. On the basis of anamneses and diagnoses, these symptoms were attributed to chloracne. Altogether 31 people were affected, whose individual clinical pictures will not be discussed in the present article. The clinical picture corresponded to that frequently obtained in occupations necessitating contact with perchlorinated naphthalenes and diphenyls. The symptoms comprised numerous comedones, pustules, some furuncles and retention cysts, all affecting invariably the face, neck, and the nape (see Fig. 1), and in some cases also the back, chest, genitals, and the limbs.

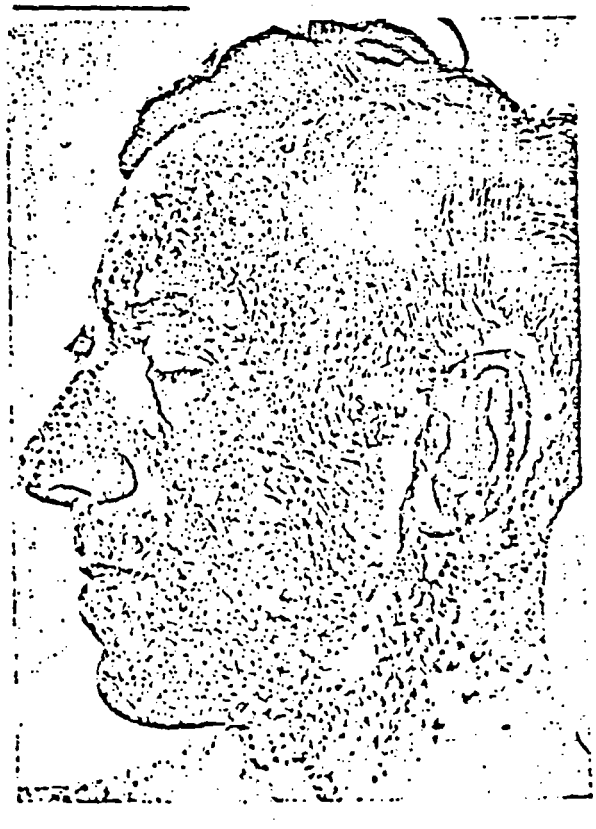

Fig. 1:
Chloracne arising from contact with technical trichlorophenol (chemical worker, aged 35)

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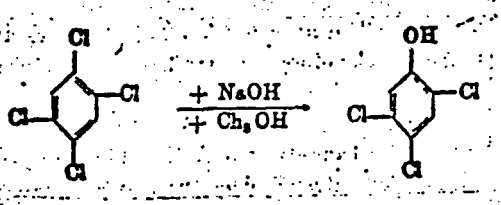
In addition to dermatological symptoms, several patients presented chronic conjunctivitis and blepharitis. General subjective complaints, such as loss of appetite, debility, and nausea were often expressed. Fortunately, however, objectively detectable affections of the liver, kidneys, central nervous system, and the hemopoietic apparatus, were always absent.

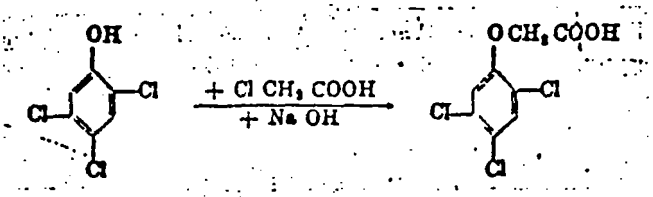
All the patients had worked in the 'Trichlorophenol Section' of the factory, manufacturing 2,4,5-trichlorophenoxyacetic acid, which is a widely used, highly active herbicide, prepared from α-hexachlorocyclohexane in a multistage process whose last two steps, being the most important ones in the present context, are as follows:

1. Preparation of trichlorophenol by the alkaline hydrolysis of tetrachlorobenzene, carried out at 170°C in the presence of sodium hydroxide and methanol:



Tetrachlorobenzene — 2,4,5-trichlorophenol

2. Preparation of the final product by the addition of chloroacetic acid and sodium hydroxide to the trichlorophenol:



2,4,5-trichlorophenol — 2,4,5-trichlorophenoxyacetic acid

It was soon found that only those workers were affected who were engaged in the preparation and the further processing of trichlorophenol.

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It should be mentioned in this connection that cases of chloracne have been found among personnel engaged in the manufacture of trichlorophenol in chemical works not only in Hamburg, but also in Southern and in Western Germany, these cases being occasionally accompanied by severe afflictions of the liver.

Trichlorophenol itself was first assumed to be the original cause of intoxication. According to previous reports[1], contact with highly chlorinated phenols, e.g. pentachlorophenol, causes chloracne. This assumption, however, soon had to be abandoned, for the following two reasons:

1. Work with trichlorophenol had proceeded for two years without resulting in any harmful effect. The complaints first arose after a change in the preparation of trichlorophenol, whose details can no longer be neglected.

2. The results of the animal experiments clearly disprove the causative function of pure 2,4,5-trichlorophenol.

Animal experiments

The animal experiments were carried out on rabbits' ears, on which Hofmann and Neumann[4], Braun[2], and Landes[6] and others used highly chlorinated naphthalenes and induced symptoms very similar to those of chloracne in human subjects. In each animal, the inside of one ear was painted daily with the substances to be tested for their chloracne-inducing activity, whilst the other ear, serving as a control, was treated with the solvent only. The duration of the experiments varied between 3 and 8 weeks.

The chemical plant mentioned above supplied the technical 2,4,5-trichlorophenol (95% pure), which was employed in 2% and 5% solutions in polyglycol and resulted in the following symptoms: inflammation of the ears, accompanied by the reddening of the surface and moderate swelling,

developed in about 5 to 7 days; a few days later the picture changed - the diffuse inflammation had subsided and new symptoms appeared, which closely resembled those of chloracne in man. Follicles, filled with hyperkeratotic material, projected out of the plane of the skin, so that the surface of the latter assumed a sandpapery appearance (see Fig. 2). In contrast, ears treated with the solvent alone developed no symptoms.

DOW 151353

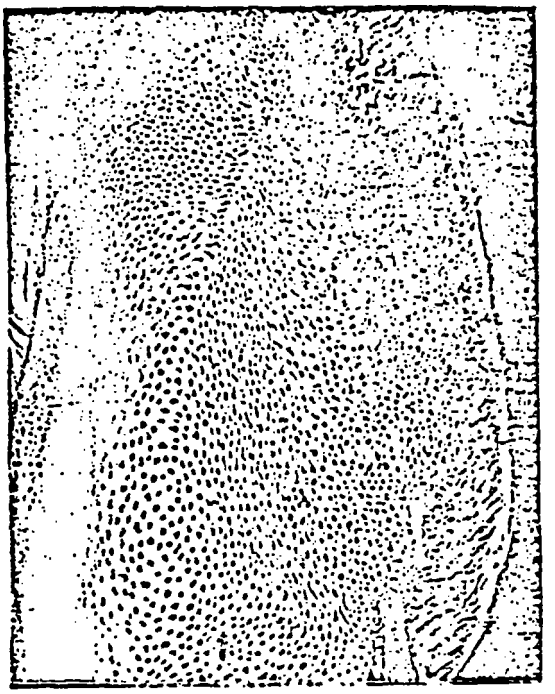

Fig. 2:

Rabbit's ear after a 3-week treatment with a 3% solution of technical trichlorophenol in polyglycol (follicular hyperkeratosis, follicular distension)

From the histological point of view, an acanthotic thickening of the epidermis was observed, together with edema and moderate cell infiltration in the cutis. The follicles were strong and their epithelia, distended almost infundibularly and filled with keratotic material, were extended.

Unlike technical trichlorophenol, chemically pure, twice-distilled trichlorophenol did not induce these symptoms even after an 8-week application. Experiments using the distillation residue gave once more the same positive results. The results are shown in Table 1 below.

16053

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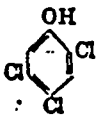
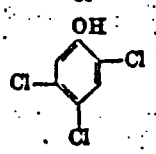
Table 1. Results of animal experiments carried out with a view to determining the etiology of chloracne (by painting rabbits' ears)

Substance	Structural formula	Concentration %	Results	
			Ear	Hepatic toxicity
2,4,5-Trichlorophenol (technical grade)		5	++	slight
2,4,5-Trichlorophenol (chemically pure)		5-10	ϕ	ϕ
1,2,4,5-Tetrachlorobenzene		5-10	ϕ	ϕ
Distillation residue of trichlorophenol	-	1-5	++	slight

ϕ = None

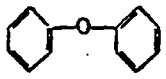
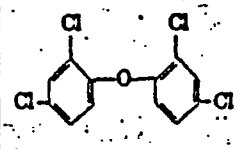
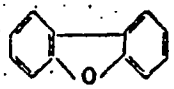
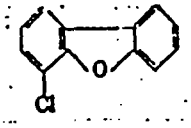
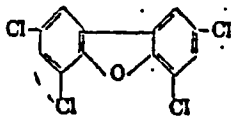
It emerges from these results that the substance causing chloracne is not trichlorophenol itself, but arises in all probability as a by-product in the alkaline hydrolysis of tetrachlorobenzene into trichlorophenol.

Further investigations* aimed at gaining more information of the nature of the substances causing chloracne. Since, owing to extraneous circumstances, the residue could not be separated, synthetic compounds were used in these experiments. Naturally, such compounds were selected that were likely to be formed in the industrial production of trichlorophenol from tetrachlorobenzene. The results are listed in Table 2.

* Carried out in collaboration with Dr. Sorge, Head of the Trichlorophenol Section.

DOW 1151355

Table 2: Results of animal experiments carried out with a view to determining the etiology of chloracne (by painting rabbits' ears)

Substance	Structural formula	Concentration %	Results		Remarks
			Ear	Hepatic toxicity	
Diphenyl ether		5-10	ϕ	ϕ	
Mono-, di-, tri-, and tetrachlorinated diphenyl ethers		5-10	ϕ	slight	
Diphenylene oxide (dibenzofuran)		5-10	ϕ	ϕ	
Monochlorinated dibenzofuran		5-10	ϕ	ϕ	
Tri- and tetra chlorinated dibenzofuran		0.1-5	(+)	very strong	Positions of the Cl atoms are uncertain

ϕ = none

Experiments with diphenyl ethers showed that neither the unsubstituted nor any of the mono-, tri-*, and tetrachlorinated ethers was capable of producing symptoms of chloracne in the rabbits' ears.

Since their formation under the relevant reaction conditions is possible, the chlorine derivatives of dibenzofuran (diphenylene oxide) were next tested. Dibenzofuran differs from diphenyl ether in the presence of a furan structure by ring closure taking place between two benzene rings. The unsubstituted and the monochlorinated compounds were found to be

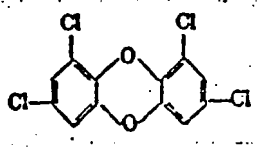
* Translator's note: Sic. Dichlorodiphenyl ether is omitted.

DOW 1151356

inactive in the animal experiments. The tri- and the tetrachlorinated dibenzofurans, on the other hand, exhibited a strong hepatic toxicity. Daily painting of the ears (over an area having a diameter of about 3 cm) with 0.1 and 0.5% solutions led to death in 2 to 3 weeks. Autopsy revealed an appreciable engorgement of the liver and distended necrotic tissues, occasionally imbibed through hemorrhages. A single peroral application of a dose of 1 mg/kg led to severe hepatic conditions, which could be studied with the aid of the Hofmann-Oettel[5] modification of the bromosulfthalein reaction. The symptoms described above appeared also on the ears of the animals, but to a smaller extent, as in the experiments with the distillation residue. Therefore the question still remains whether tri- and tetrachlorinated dibenzofurans were the true cause of the cases of chloracne under consideration.

Although the question may be posed whether the highly chlorinated naphthalenes and diphenyls, whose chloracne-inducing activity has long been known, could be regarded as the cause in the present case as well, from a chemical viewpoint it is hardly probable that these compounds can be formed under the reaction conditions in question.

Clinical observation led a step nearer to elucidating the nature of the cause. A chemical laboratory assistant has recently developed severe chloracne. This patient had been engaged in the laboratory preparation of highly chlorinated diphenylene dioxides in a laboratory outside Hamburg, where, after about 10-14 days, he developed chloracne in conjunction with facial dermatitis. Since the patient worked with chemically pure compounds, it must be assumed that highly chlorinated diphenylene dioxides are capable of evoking symptoms of chloracne in man.



Tetrachlorodiphenylene dioxide
(positions of the Cl atoms are uncertain)

These compounds may have a causative function in the chloracne cases

DOW 1513571

found in the chemical plant as well, since, from a chemical viewpoint, chlorinated diphenylene dioxides may be formed in the hydrolysis of tetrachlorobenzene into trichlorophenol.

Animal experiments with chlorinated diphenylene dioxides are in progress, and the results obtained so far indicate that tetrachlorodiphenylene dioxide has a high hepatic toxicity in rabbits.

Although the proof is still incomplete and the distillation residue of the technical trichlorophenol has not been investigated, it is hoped that a contribution has been made to the etiology of chloracne, particularly with the aid of the highly chlorinated diphenylene dioxides. Further investigations are aimed at the final elucidation of this problem.

Discussion

A. Szakall (Hamburg): Comedones on the zygomatic arch of patients wearing spectacles are probably ascribable to the chafing of the surface cells of the horny layer, followed by cell proliferation with increased horny formation. The inner surface of the spectacle frame in contact with the skin becomes rough* in use, and gives rise to friction. Pinkus [J. invest. derm., 19, 431 (1952)] has shown that a weakening of the horny layer leads to cell proliferation, with increased horn formation. The removal of four surface cell-layers is sufficient to result in cell proliferation.

P. Keller (Aix-la-Chapelle): Is it possible that the formation of large comedones around the eyes in patients wearing spectacles is due to a chlorine content of the synthetic material of the frame ? These comedones were found in a tank officer around that eye only, which he used with the periscope, and the formation of the comedones persisted for years afterwards.

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* Translator's note: Sic.

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O. Braun-Falco (Mainz): With respect to Prof. Keller's remarks concerning the follicular 'spectacles hyperkeratosis', this is believed to have a physical cause (e.g. the pressure of the frame), and resembles in this connection the comedones appearing after x-ray contact irradiation.

References:

1. E.W. Baader and H.J. Bauer, Industrial Intoxication due to pentachlorophenol. Industr. Med. a. Surg. 20, 286-290 (1951).
2. W. Braun, Chlorakne, Monographien zur Zeitschrift Berufsdermatosen (Chloracne, Monographs of the Journal of Occupational Dermatosis) vol. 1. Aulendorf: printed by Editio Cantor.
3. H. Grimmer, Occupational acne caused by chlorinated aromatic hydrocarbons, Zbl. Arbeitsmed. u. Arbeitsschutz, 5, 76-83 (1955).
4. H. Th. Hofmann, and W. Newmann, Animal experimental investigations of the dermatological effect of chlorinated naphthalenes, Zbl. Arbeitsmed. u. Arbeitsschutz 2, 169-173 (1952).
5. H.Th. Hofmann, and H. Oettel, The use of the bromosulfthalein reaction as a simple micromethod in the study of the hepatic function, Arztl. Wschr. 1954, 965-967.
6. E. Landes, Discussion, Bemerk. Dermat. Wschr. 130, 1191 (1954).

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DDM 1151359

CLINICAL AND EXPERIMENTAL INVESTIGATIONS CONCERNING THE ETIOLOGY OF CHLORACNE

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by K.H. Schulz

Arch.klin. exp. Derm., 206 (1957)
589 - 596

Pages 9
Photocopy 1.10
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A number of workers in a chemical factory at Hamburg developed certain dermatological symptoms between the middle of 1954 and spring 1955. On the basis of anamneses and diagnoses, these symptoms were attributed to chloracne. Altogether 31 people were affected, whose individual clinical pictures will not be discussed in the present article. The clinical picture corresponded to that frequently obtained in occupations necessitating contact with perchlorinated naphthalenes and diphenyls. The symptoms comprised numerous comedones, pustules, some furuncles and retention cysts, all affecting invariably the face, neck, and the nape (see Fig. 1), and in some cases also the back, chest, genitals, and the limbs.

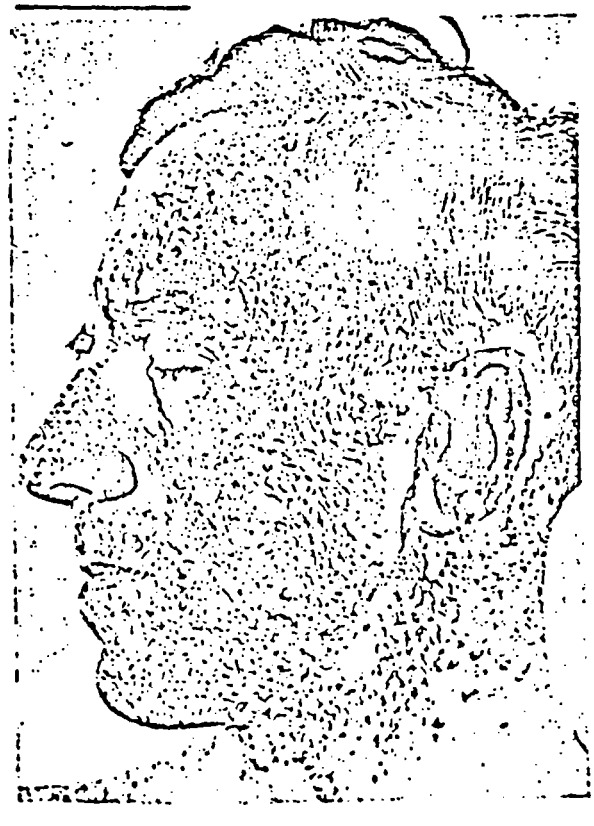

Fig. 1:
Chloracne arising from contact with technical trichlorophenol (chemical worker, aged 35)

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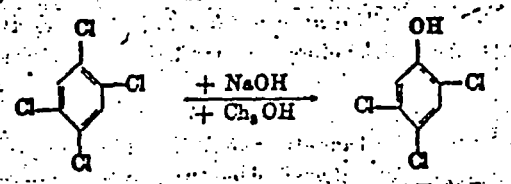
In addition to dermatological symptoms, several patients presented chronic conjunctivitis and blepharitis. General subjective complaints, such as loss of appetite, debility, and nausea were often expressed. Fortunately, however, objectively detectable affections of the liver, kidneys, central nervous system, and the hemopoietic apparatus, were always absent.

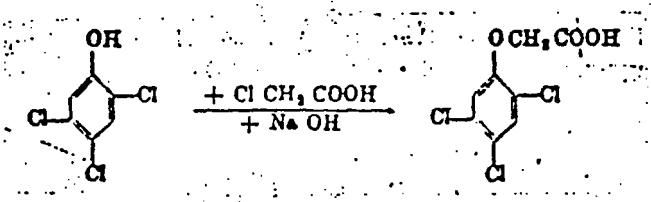
All the patients had worked in the 'Trichlorophenol Section' of the factory, manufacturing 2,4,5-trichlorophenoxyacetic acid, which is a widely used, highly active herbicide, prepared from α-hexachlorocyclohexane in a multistage process whose last two steps, being the most important ones in the present context, are as follows:

1. Preparation of trichlorophenol by the alkaline hydrolysis of tetrachlorobenzene, carried out at 170°C in the presence of sodium hydroxide and methanol:



Tetrachlorobenzene — 2,4,5-trichlorophenol

2. Preparation of the final product by the addition of chloroacetic acid and sodium hydroxide to the trichlorophenol:



2,4,5-trichlorophenol — 2,4,5-trichlorophenoxyacetic acid

It was soon found that only those workers were affected who were engaged in the preparation and the further processing of trichlorophenol.

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It should be mentioned in this connection that cases of chloracne have been found among personnel engaged in the manufacture of trichlorophenol in chemical works not only in Hamburg, but also in Southern and in Western Germany, these cases being occasionally accompanied by severe afflictions of the liver.

Trichlorophenol itself was first assumed to be the original cause of intoxication. According to previous reports[1], contact with highly chlorinated phenols, e.g. pentachlorophenol, causes chloracne. This assumption, however, soon had to be abandoned, for the following two reasons:

1. Work with trichlorophenol had proceeded for two years without resulting in any harmful effect. The complaints first arose after a change in the preparation of trichlorophenol, whose details can no longer be neglected.

2. The results of the animal experiments clearly disprove the causative function of pure 2,4,5-trichlorophenol.

Animal experiments

The animal experiments were carried out on rabbits' ears, on which Hofmann and Neumann[4], Braun[2], and Landes[6] and others used highly chlorinated naphthalenes and induced symptoms very similar to those of chloracne in human subjects. In each animal, the inside of one ear was painted daily with the substances to be tested for their chloracne-inducing activity, whilst the other ear, serving as a control, was treated with the solvent only. The duration of the experiments varied between 3 and 8 weeks.

The chemical plant mentioned above supplied the technical 2,4,5-trichlorophenol (95% pure), which was employed in 2% and 5% solutions in polyglycol and resulted in the following symptoms: inflammation of the ears, accompanied by the reddening of the surface and moderate swelling,

developed in about 5 to 7 days; a few days later the picture changed - the diffuse inflammation had subsided and new symptoms appeared, which closely resembled those of chloracne in man. Follicles, filled with hyperkeratotic material, projected out of the plane of the skin, so that the surface of the latter assumed a sandpapery appearance (see Fig. 2). In contrast, ears treated with the solvent alone developed no symptoms.

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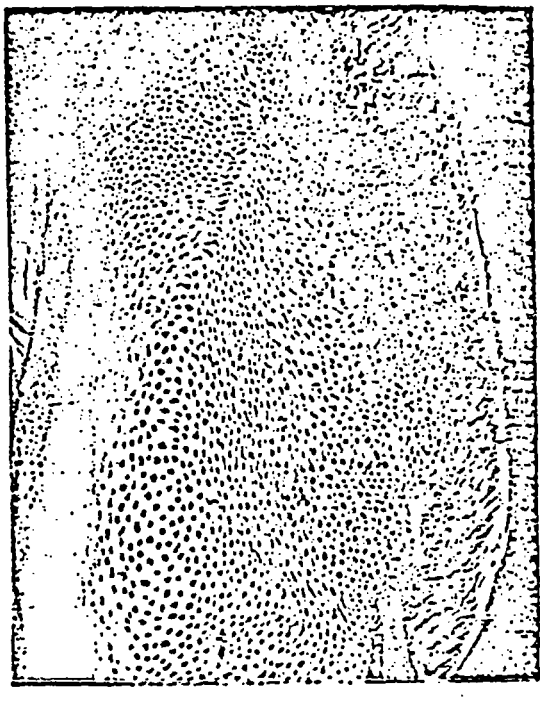

Fig. 2:
Rabbit's ear after a 3-week treatment with a 3% solution of technical trichlorophenol in polyglycol (follicular hyperkeratosis, follicular distension)

From the histological point of view, an acanthotic thickening of the epidermis was observed, together with edema and moderate cell infiltration in the cutis. The follicles were strong and their epithelia, distended almost infundibularly and filled with keratotic material, were extended.

Unlike technical trichlorophenol, chemically pure, twice-distilled trichlorophenol did not induce these symptoms even after an 8-week application. Experiments using the distillation residue gave once more the same positive results. The results are shown in Table 1 below.

1606

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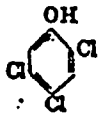
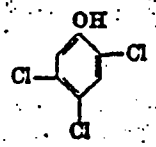
Table 1. Results of animal experiments carried out with a view to determining the etiology of chloracne (by painting rabbits' ears)

Substance	Structural formula	Concentration %	Results	
			Ear	Hepatic toxicity
2,4,5-Trichlorophenol (technical grade)		5	++	slight
2,4,5-Trichlorophenol (chemically pure)		5-10	ϕ	ϕ
1,2,4,5-Tetrachlorobenzene		5-10	ϕ	ϕ
Distillation residue of trichlorophenol	-	1-5	++	slight

ϕ = None

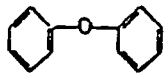
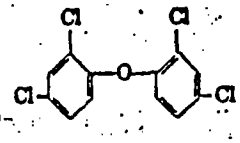
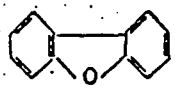
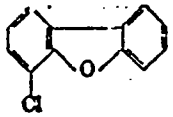
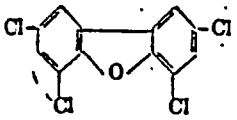
It emerges from these results that the substance causing chloracne is not trichlorophenol itself, but arises in all probability as a by-product in the alkaline hydrolysis of tetrachlorobenzene into trichlorophenol.

Further investigations* aimed at gaining more information of the nature of the substances causing chloracne. Since, owing to extraneous circumstances, the residue could not be separated, synthetic compounds were used in these experiments. Naturally, such compounds were selected that were likely to be formed in the industrial production of trichlorophenol from tetrachlorobenzene. The results are listed in Table 2.

* Carried out in collaboration with Dr. Sorge, Head of the Trichlorophenol Section.

DOW 1151364

Table 2: Results of animal experiments carried out with a view to determining the etiology of chloracne (by painting rabbits' ears)

Substance	Structural formula	Concentration %	Results		Remarks
			Ear	Hepatic toxicity	
Diphenyl ether		5-10	ϕ	ϕ	
Mono-, di-, tri-, and tetrachlorinated diphenyl ethers		5-10	ϕ	slight	
Diphenylene oxide (dibenzofuran)		5-10	ϕ	ϕ	
Monochlorinated dibenzofuran		5-10	ϕ	ϕ	
Tri- and tetra chlorinated dibenzofuran		0.1-5	(+)	very strong	Positions of the Cl atoms are uncertain

ϕ = none

Experiments with diphenyl ethers showed that neither the unsubstituted nor any of the mono-, tri-*, and tetrachlorinated ethers was capable of producing symptoms of chloracne in the rabbits' ears.

Since their formation under the relevant reaction conditions is possible, the chlorine derivatives of dibenzofuran (diphenylene oxide) were next tested. Dibenzofuran differs from diphenyl ether in the presence of a furan structure by ring closure taking place between two benzene rings. The unsubstituted and the monochlorinated compounds were found to be

* Translator's note: Bis. Dichlorodiphenyl ether is omitted.

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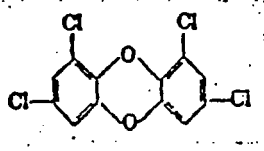
inactive in the animal experiments. The tri- and the tetrachlorinated dibenzofurans, on the other hand, exhibited a strong hepatic toxicity. Daily painting of the ears (over an area having a diameter of about 3 cm) with 0.1 and 0.5% solutions led to death in 2 to 3 weeks. Autopsy revealed an appreciable engorgement of the liver and distended necrotic tissues, occasionally imbibed through hemorrhages. A single peroral application of a dose of 1 mg/kg led to severe hepatic conditions, which could be studied with the aid of the Hofmann-Oettel[5] modification of the bromosulfthalein reaction. The symptoms described above appeared also on the ears of the animals, but to a smaller extent, as in the experiments with the distillation residue. Therefore the question still remains whether tri- and tetrachlorinated dibenzofurans were the true cause of the cases of chloracne under consideration.

Although the question may be posed whether the highly chlorinated naphthalenes and diphenyls, whose chloracne-inducing activity has long been known, could be regarded as the cause in the present case as well, from a chemical viewpoint it is hardly probable that these compounds can be formed under the reaction conditions in question.

Clinical observation led a step nearer to elucidating the nature of the cause. A chemical laboratory assistant has recently developed severe chloracne. This patient had been engaged in the laboratory preparation of highly chlorinated diphenylene dioxides in a laboratory outside Hamburg, where, after about 10-14 days, he developed chloracne in conjunction with facial dermatitis. Since the patient worked with chemically pure compounds, it must be assumed that highly chlorinated diphenylene dioxides are capable of evoking symptoms of chloracne in man.



Tetrachlorodiphenylene dioxide
(positions of the Cl atoms are uncertain)

These compounds may have a causative function in the chloracne cases

DOW 1 51369

found in the chemical plant as well, since, from a chemical viewpoint, chlorinated diphenylene dioxides may be formed in the hydrolysis of tetrachlorobenzene into trichlorophenol.

Animal experiments with chlorinated diphenylene dioxides are in progress, and the results obtained so far indicate that tetrachlorodiphenylene dioxide has a high hepatic toxicity in rabbits.

Although the proof is still incomplete and the distillation residue of the technical trichlorophenol has not been investigated, it is hoped that a contribution has been made to the etiology of chloracne, particularly with the aid of the highly chlorinated diphenylene dioxides. Further investigations are aimed at the final elucidation of this problem.

Discussion

A. Szakall (Hamburg): Comedones on the zygomatic arch of patients wearing spectacles are probably ascribable to the chafing of the surface cells of the horny layer, followed by cell proliferation with increased horny formation. The inner surface of the spectacle frame in contact with the skin becomes rough* in use, and gives rise to friction. Pinkus [J. invest. derm., 19, 431 (1952)] has shown that a weakening of the horny layer leads to cell proliferation, with increased horn formation. The removal of four surface cell-layers is sufficient to result in cell proliferation.

P. Keller (Aix-la-Chapelle): Is it possible that the formation of large comedones around the eyes in patients wearing spectacles is due to a chlorine content of the synthetic material of the frame? These comedones were found in a tank officer around that eye only, which he used with the periscope, and the formation of the comedones persisted for years afterwards.

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* Translator's note: Sic.

DOW 1151367

O. Braun-Falco (Mainz) : With respect to Prof. Keller's remarks concerning the follicular 'spectacles hyperkeratosis', this is believed to have a physical cause (e.g. the pressure of the frame), and resembles in this connection the comedones appearing after x-ray contact irradiation.

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16067

v. Mc Namara — Archiv für klinische und experimentelle Dermatologie, 206, pp. 589-596 (1957).

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DOW 1151368

Durchschnitt wesentlich höher als bei der Psoriasis, doch nur wenig über den Werten des konstitutionellen Ekzems lagen. Besonders auffällig und der Nachprüfung auf breiterer Basis wert erscheint mir die Feststellung, daß der Pemphigus (14 Fälle) trotz besonders hoher Durchschnitts-Eosinophilie nur zu $^1/_7$, die Dermatitis herpetiformis (12 Fälle) dagegen fast in der Hälfte der Fälle negative Thorn-Teste hatte. Das Verhalten des Pemphigus ist um so bemerkenswerter, als es sich ja bei ihm um eine schwere Erkrankung handelt und außerdem sehr hohe ACTH- bzw. Cortison-Dosen angewendet werden können, ohne daß, wie bei anderen Dermatosen, auf eine derartig forcierte Hormontherapie verstärkte Rückfälle folgen.

Ich fasse zusammen: Ein negativer Ausfall des Thorn-Tests braucht durchaus nicht Ausdruck einer primären oder sekundären Rinden-Funktionsstörung zu sein. Er bedarf auf jeden Fall der Überprüfung mit Hilfe des peroralen Cortison-Tests, der über die Ansprechbarkeit der Peripherie Auskunft gibt. Die intravenöse Modifikation des Eosinophilen-Tests nach THORN ist ein zuverlässiges, auch in größerem Umfange anwendbares und daher empfehlenswertes Verfahren. Es ergab sich, daß im dermatologischen Krankengut der Thorn-Test relativ oft negativ ausfällt und die Höhe der Eosinophilen-Ausgangswerte allem Anschein nach nicht oder doch nicht allein dafür maßgebend ist. Der sich aus dieser Feststellung ergebende Fragenkomplex bedarf weiterer eingehender Bearbeitung.

Dioxin

68. K. H. Schulz-Hamburg: Klinische und experimentelle Untersuchungen zur Ätiologie der Chloracne. Mit 2 Textabbildungen.

In einem Hamburger chemischen Werk traten in der Zeit von Mitte 1954 bis Frühjahr 1955 bei einer Anzahl von Arbeitern Hautveränderungen auf, die nach Anamnese und Befund als sogenannte Chloracne anzusprechen waren. Insgesamt waren 31 Personen erkrankt. Auf das klinische Bild soll hier nicht im einzelnen eingegangen werden. Es entsprach weitgehend den nach beruflichem Kontakt mit perchlorierten Naphthalinen und Diphenylen häufiger beobachteten Krankheitsbildern. Die Erscheinungen setzten sich aus zahlreichen Comedonen, Pusteln, einzelnen Furunkeln und Retentionscysten zusammen und erstreckten sich in allen Fällen auf Gesicht, Hals, Nacken. Bei mehreren Kranken waren auch Rücken, Brust, Genitalien sowie die Extremitäten befallen (Abb. 1).

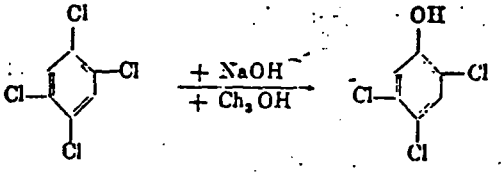
Neben den Veränderungen der Haut wiesen mehrere Patienten chronische Conjunctivitiden und Blepharitiden auf. Subjektive Allgemeinbeschwerden, wie Appetitlosigkeit, Mattigkeit, Übelkeit waren mehrfach zu eruieren. Objektiv nachweisbare Schädigungen von Leber,

16068

Nieren, Zentralnervensystem und des blutbildenden Apparates wurden erfreulicherweise aber in keinem Falle festgestellt.

Die Kranken arbeiteten alle im sogenannten Trichlorphenolbetrieb des Werkes, in dem ein viel verwendetes, hochwirksames Unkrautvertilgungsmittel, die Trichlorphenoxyessigsäure, hergestellt wurde. Der Herstellungsgang dieses Produktes geht vonm α-Hexachlorcyclohexan aus und durchläuft mehrere Stufen. Die beiden letzten, für uns wichtigsten Phasen sind:

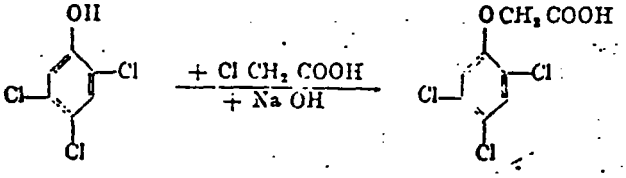
1. die Herstellung von Trichlorphenol durch alkalische Verseifung von Tetrachlorbenzol bei Temperaturen von 170°C in Gegenwart von Natronlauge und Methanol



Tetrachlorbenzol 2, 4, 5-Trichlorphenol

und

2. die Gewinnung des Endproduktes aus Trichlorphenol unter Zugabe von Monochloressigsäure und Natronlauge:



2, 4, 5 Trichlorphenol 2, 4, 5-Trichlorphenoxyessigsäure

Es zeigte sich nun bald, daß nur diejenigen Arbeiter erkrankt waren, die bei der Herstellung und Weiterverarbeitung des Trichlorphenols beschäftigt waren.

An dieser Stelle sei erwähnt, daß auch in chemischen Fabriken außerhalb Hamburgs in Süd- und Westdeutschland bei der Gewinnung von Trichlorphenol Erkrankungen an Chloracne, die zum Teil mit schweren Leberschäden kombiniert waren, aufgetreten sind.

Unsere Vermutung ging zunächst dahin, daß das Trichorphenol selbst die ursächliche Noxe darstellt, zumal in der Literatur Mitteilungen existieren, wonach der Umgang mit höher chlorierten Phenolen, z. B. Pentachlorphenol, zu Erkrankungen an Chloracne geführt hätte (Baader u. Bauer u. a.). Diese Annahme mußten wir aber bald fallen lassen, und zwar aus folgenden Gründen:

1. Mit Trichlorphenol war schon etwa 2 Jahre lang gearbeitet worden, ohne daß Gesundheitsschäden beobachtet werden waren. Erst nachdem

DOW 1151370

eine im einzelnen nicht mehr zu übersehende Verfahrensumstellung bei der Herstellung von Trichlorphenol vorgenommen worden war, stellten sich die Erkrankungen ein.

2. Die Ergebnisse von Tierversuchen sprachen eindeutig gegen die ursächliche Bedeutung von reinem 2, 4, 5-Trichlorphenol.

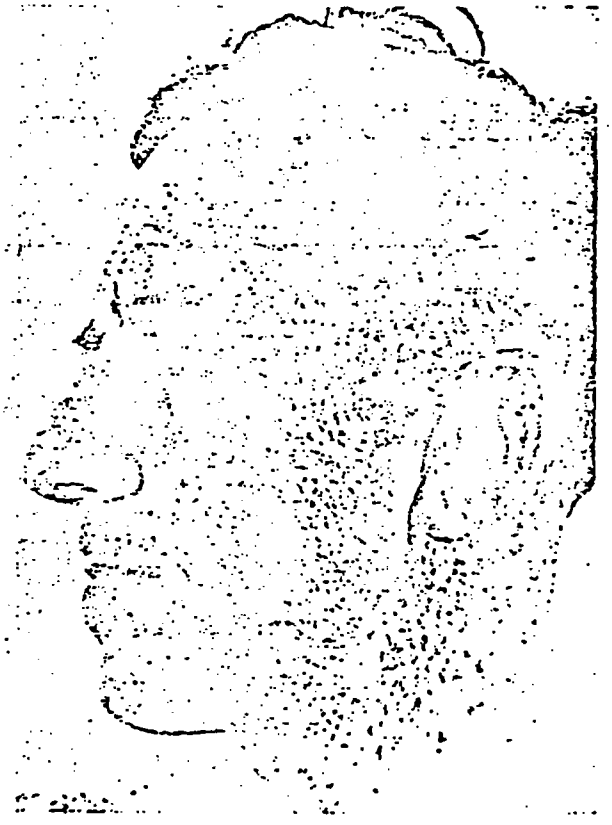


Abb. 1. Chloracne bei 35jähr. Chemiearbeiter, nach Umgang mit techn. Trichlorphenol entstanden

Tierexperimente

Zu den tierexperimentellen Untersuchungen benutzten wir das Kaninchenohr, an dem HOFMANN u. NEUMANN, BRAUN, LANDES u. a. mit hochchlorierten Naphthalinen Veränderungen erzeugen konnten, die denen der menschlichen Chloracne weitgehend ähneln. Die Innenseite eines Ohres wurde mit den auf chloracneerzeugende Wirkung zu untersuchenden Substanzen täglich gepinselt, das zweite Ohr zur Kontrolle nur mit dem Lösungsmittel behandelt. Die Versuchsdauer betrug 3—8 Wochen.

16070

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Mit dem von dem chemischen Werk zur Verfügung gestellten Trichlorphenol, das als technisches Produkt zu etwa 95% reines 2, 4, 5-Trichlorphenol enthält und in 2% sowie 5% Lösung in Polyglykol verwendet wurde, traten folgende Veränderungen auf: Etwa 5—7 Tage nach Beginn der Pinselungen entwickelte sich zunächst eine mit flächenhafter

Abb. 2. Kaninchenohr nach 3wöchiger Behandlung mit 3% techn. Trichlorphenol in Polyglykol (Follikuläre Hyperkeratosen, Follikelschwellung)

Rötung und mäßiger Schwellung einhergehende Entzündung des Ohres. Einige Tage später änderte sich das Bild: Die diffuse Entzündung bildete sich zurück, und es traten nun Veränderungen auf, die mit denen der menschlichen Chloracne sehr verwandt sind: erweiterte, mit Hyperkeratosen angefüllte Follikel, die über das Hautniveau hervorragten, so daß die Oberfläche ein reibeisenartiges Aussehen annahm. Das nur mit dem Lösungsmittel behandelte Ohr wies demgegenüber keine Veränderungen auf.

Histologisch fanden sich eine acanthotische Verdickung der Epidermis sowie ein Ödem und mäßige Zellinfiltration in der Cutis. Die Follikel waren stark, fast trichterförmig erweitert und von keratotischen Massen angefüllt, das Follikelepithel verbreitert.

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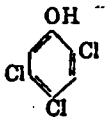
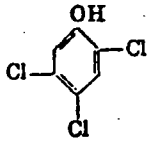
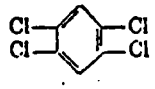
Im Gegensatz zum technischen Trichlorphenol ließen sich nun mit chemisch reinem, doppelt destilliertem Trichlorphenol diese Veränderungen auch nach 8wöchiger Pinselung nicht hervorrufen. Die Versuche mit dem Destillationsrückstand zeigten wieder die gleichen positiven Ergebnisse. In der nun folgenden Tabelle sind die Resultate wiedergegeben.

Tabelle 1. *Tierexperimentelle Untersuchungen zur Ätiologie der Chloracne* (Pinselung von Kaninchenohren)

Substanz	Strukturformel	Prüfkonzentration %	Ergebnisse	
			Ohr	Lebertoxizität
2,4,5-Trichlorphenol (techn. Produkt)		5	++	schwach
2,4,5-Trichlorphenol (chemisch rein)		5—10	ø	ø
Tetrachlorbenzol (symmetr. chemisch rein)		5—10	ø	ø
Destillationsrückstand von Trichlorphenol	—	1— 5	++	schwach

Aus diesen Befunden geht hervor, daß der chloracneauslösende Faktor nicht im Trichlorphenol selbst zu suchen ist, sondern als Nebenprodukt bei der alkalischen Verseifung von Tetrachlorbenzol zu Trichlorphenol entstanden sein mußte.

Ziel der weiteren Untersuchungen, die in Zusammenarbeit mit Herrn Dr. SORGE, dem Leiter des Trichlorphenolbetriebes, durchgeführt wurden, war es nun, über die Natur der zur Chloracne führenden Substanzen Näheres zu erfahren. Da die Isolierung aus dem Rückstand aus äußeren Gründen bisher noch nicht möglich war, versuchten wir, auf dem Umweg über synthetisierte Verbindungen dem Ziel näher zu kommen. Es wurden naturgemäß solche Substanzen herangezogen, für die Wahrscheinlichkeit besteht, daß sie sich bei der technischen Herstellung von Trichlorphenol aus Tetrachlorbenzol bilden. Die Ergebnisse finden sich in der Tab. 2.

Zunächst wurden chlorierte *Diphenyläther* untersucht. Dabei zeigte sich, daß weder der unsubstituierte Diphenyläther noch die 1, 3 und

DOW 1151372

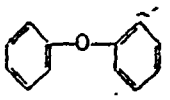
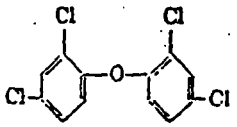
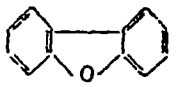
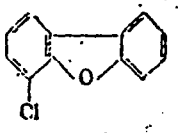
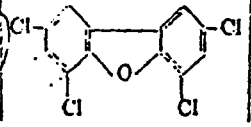
16072

DOW 1151373

4fach chlorierten Verbindungen in der Lage waren, am Kaninchenohr irgendwelche Erscheinungen im Sinne einer Chloracne hervorzurufen.

Von Interesse schienen uns weiterhin Chlorierungsprodukte des *Dibenzofurans* (= Diphenylenoxyd) zu sein, deren Entstehung unter den genannten Reaktionsbedingungen ebenfalls möglich ist. Vom Diphenyläther unterscheidet sich Dibenzofuran dadurch, daß hier zwischen zwei

Tabelle 2. *Tierexperimentelle Untersuchungen zur Ätiologie der Chloracne* (Pinselung von Kaninchenohren)

Substanz	Strukturformel	Prüfkonzentration %	Ergebnisse: Ohr	Ergebnisse: Lebertoxicität	Bemerkungen
Diphenyläther		5—10	ø	ø	
Mono- bis tetrachlorierte Diphenyläther		5—10	ø	schwach	
Diphenylenoxyd (Dibenzofuran)		5—10	ø	ø	
Monochloriertes Diphenylenoxyd		5—10	ø	ø	
Tri- und tetrachlorierte Diphenylenoxyde		0,1— 5	(+)	sehr stark	Stellung der Cl-Atome nicht sicher

Benzolringen ein Ringschluß zum Furan erfolgt ist. Die unsubstituierten und einfach chlorierten Substanzen waren im Tierversuch unwirksam. Dagegen zeigten die tri- und tetrachlorierten Dibenzofurane eine starke hepatotoxische Wirkung. Die tägliche Pinselung eines fünfmarkstückgroßen Ohrbezirkes mit 0,5%ig und 0,1%igen führte innerhalb von 2 bis 3 Wochen zum Tod der Tiere. Autoptisch fanden sich an der Leber ausgedehnte, z. T. hämorrhagisch imbibierte Nekrosen und erhebliche Verfettung. Eine einmalig peroral applizierte Dosis von 1 mg/kg führte zu einem schweren Leberschaden, die sich mit der von Hofmann u. Oettel angegebenen Modifikation des Bromthaleintestes gut verfolgen ließ. An den Ohren der Tiere traten auch die oben beschriebenen Erscheinungen

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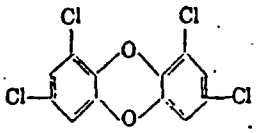
DOW 1513774

auf, jedoch waren diese geringer ausgeprägt als in den Versuchen mit dem Destillationsrückstand, so daß es noch fraglich bleibt, ob die 3- und 4fach chlorierten Dibenziofurane die eigentliche Ursache bei unseren Chloracnefällen darstellen.

Man könnte sich fragen, ob nicht höher chlorierte Naphthaline und Diphenyle, deren chloracneerzeugende Wirkung seit langem immer beschrieben worden ist, auch bei unseren Fällen als Ursache in Frage kommen. Es ist vom chemischen Standpunkt aber sehr wenig wahrscheinlich, daß sich diese Verbindungen unter diesen Reaktionsbedingungen bilden können.

Einen Schritt weiter bei der Klärung der Ursache kamen wir durch eine klinische Beobachtung. Vor kurzem kam ein chemisch technischer Assistent mit einer schweren Chloracne zu uns. In einem chemischen Labor außerhalb Hamburgs war er mit der laboratoriumsmäßigen Herstellung von mehrfach chlorierten Diphenylendioxyden beschäftigt. Etwa 10—14 Tage nach Beginn dieser Tätigkeit entwickelte sich die Erkrankung im Anschluß an eine Gesichtsdermatitis. Da der Patient mit chemisch reinen Verbindungen gearbeitet hatte, kann angenommen werden, daß mehrfach chlorierte *Diphenylendioxyde* in der Lage sind beim Menschen das Krankheitsbild einer Chloracne hervorzurufen.



Tetrachlordiphenylendioxyd

Stellung der Cl-Atome nicht sicher.

Auch für die in der chemischen Fabrik aufgetretenen Erkrankungen kommen diese Verbindungen ursächlich in Frage, denn nach Ansicht der Chemiker ist durchaus damit zu rechnen, daß sich chlorierte Diphenylendioxyde bei der Verseifung von Tetrachlorbenzol zu Trichlorphenol bilden.

Die Tierversuche mit chlorierten Diphenylendioxyden stehen erst am Anfang. Nach den bisherigen Befunden scheint dem aus dieser Reihe untersuchten Tetrachlordiphenylendioxyd beim Kaninchen eine große Lebertoxicität eigen zu sein.

Wenn auch die Beweiskette noch nicht vollständig ist und insbesondere der Nachweis im Destillationsrückstand des verwendeten technischen Trichlorphenols noch fehlt, so glauben wir doch, mit den höher chlorierten Diphenylendioxyden Verbindungen in den Händen zu haben, die mit der eigentlichen Noxe zu mindest nahe verwandt sind. Weiteren Untersuchungen wird es vorbehalten sein, hier endgültig Klarheit zu schaffen.

16074

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Aussprache

A. Szakall-Hamburg: Comedonen bei Brillenträgern über den Jochbögen sind wohl durch Abschabung der obersten Zellagen der Hornschicht und anschließende Zellproliferation mit vermehrter Hornbildung zu erklären. Die Bügel der Hornbrillen werden im Gebrauch an der die Haut berührenden Innenfläche rauh, wodurch die Reibwirkung entsteht. Daß eine Verdünnung der Hornschicht zu Zellproliferation mit vermehrter Hornbildung führt, konnte Pinkus (J. Invest. Dermatology 19, 431, 1952) zeigen. Es genügt, nur 4 oberflächliche Zellagen der Hornschicht abzuziehen, um Zellproliferation im Rete zu erzielen.

Ph. Keller-Aachen: Keller fragt, ob die häufig bei Brillenträgern zu beobachtenden enormen Comedonenbildungen, die lediglich in der Augenumgebung gehäuft vorkommen, auf einen Chlorgehalt der Brillengestelle aus Kunststoffen zurückzuführen sind.

Er hat diese Comedonen bei einem Panzeroffizier nur einseitig an dem Auge beobachtet, mit dem dieser durch das Periskop blickte; die Bildung der Comedonen persistierte noch jahrelang später.

O. Braun-Falco-Mainz zu Prof. Kellers Bemerkungen über die follikuläre „Brillenhyperkeratose": glaubt, daß diese follikulären Keratosen *physikalisch* (z. B. Druck des Brillengestelles) bedingt sind und erinnert in diesem Zusammenhang an die Comedonenreaktion nach Röntgennahbestrahlung.

69. B. Knick-Mainz: Cortisonprobleme im Grenzgebiet von innerer Medizin und Dermatologie.

Bei internen Erkrankungen reagiert die Haut als Gesamtorgan gewöhnlich in außerordentlich starkem Maße mit, so auf extreme Streß-Situationen, Infektionsbelastungen, endogene und exogene Noxen. An ihr als Substrat sind in besonderem Maße Grundsymptome der ursächlichen Erkrankung, Krankheitsverlauf und Ansprechen auf die durchgeführte Therapie zu verfolgen. Dies gilt gleichermaßen für Systemerkrankungen mit Hautmanifestationen, wie z. B. das Boecksche Sarkoid die Lymphogranulomatose, Lupus erythematodes und die klassischen Kollagenosen.

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Clinical Picture and Etiology of Chloracne

By K. H. Scultz, University Dermatology Clinic, Hamburg-Eppendorf

Chloracne is the name for forms of occupational acne which develop as a result of intoxication with certain chlorinated aromatic compounds. The name dates back to Herxheimer who described the first case in 1899 and still assumed that in analogy to bromine and iodine, the acneiform eruptions are the result of free chlorine as the etiological toxin. This view proved to be incorrect. The proposed designation "perna disease" of Wauer, Teleky and others based on the finding that this clinical picture occurred more frequently under the influence of *per*chlorinated naphthalenes also does not go to the heart of the matter, since other chlorinated aromatics in addition to chlorinated naphthalenes are also etiologically important.

The *clinical picture of symptoms* primarily affects the skin. Beyond this, internal organs may be affected and nervous system and emotional disorders may appear.

The skin symptoms are in the regions of the follicles. Comedones, resulting from a follicular hyperkeratosis, predominate and frequently are so numerous that hardly a single follicle remains untouched and the affected region of the skin obtains a dirty-gray appearance. In addition, at the peak of the disease, fairly large sebaceous cysts, inflammatory nodules, pustules and furuncles appear and in some of the patients, large spots or patches of pigmentation appear in regions exposed to light. Preferential sites are the face as well as the exposed areas of the throat and neck. Frequently, the external ear, especially, the ear lobes, are involved where small cysts can be easily palpated. In more pronounced forms, changes can also be found on the back, chest and extremities and in males, on the genitalia. Hands and feet usually are not involved. It is not rare that the symptoms of acne are preceded by a dermatitis with erythema and edema. In this phase of the condition, photosensitivity frequently exists which evidently contributes to the development of dermatitis and the mentioned pigmentations (S. Braun, Grimmer).

Generally, a *differential diagnosis* is not particularly difficult. The primary problem is to define the condition compared to other forms of occupational acne and acne vulgaris, which is generally possible with consideration of the clinical aspect, localization and especially the patient's history. Acneiform dermatoses caused by tars, pitch and mineral oils are found primarily on the extremities and trunk, while the face is more rarely involved. The predominance of inflammatory changes, such as folliculitis and furuncles in oil and tar acne and of comedones in chloracne are other characteristic features. Drug-caused acneiform exanthemas due to iodine, bromine or cortisone also have a picture differing from chloracne.

The *course* is eminently chronic. In spite of intensive local and general therapy, recidivism may occur even years after the elimination of the causal toxins. Healing frequently takes place with extensive pitted, permanently disfiguring cicatrization (Schmidt and Boslet).

The skin is not the only indicative region of intoxication with chloracne-causing substances. Damage of internal organs is not rare, with the *liver* being in the foreground. Several authors have reported on grave damage of hepatic parenchyma accompanied by icterus and functional disorders, including a number of fatal cases of acute atrophy of the liver (see reviews of W. Braun and A. Risse-Sundermann). The pronounced liver-toxocity of chloracne-causing substances was also confirmed in animal experiments (Bennett, Drinker and Warren; Hofmann, Oettel; Schulz).

In addition to liver damage, changes in the kidneys, pancreas, gastrointestinal tract and myocardium can also be observed, although much more rarely.

Nervous system and psychological disorders were found primarily among workers occupied in the production and processing of chlorinated phenols (Truhant et al.). General fatigue, weakness of the legs, headache, attacks of vertigo, paresthesias, muscle pain, tendency to orthostatic collapse, local paresis and disturbed sensibility, anomalies in reflexes as well as an autonomic syndrome with lowered drive, depression, reduced power of recall and concen-

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tration, disturbed sleep, irritability, loss of appetite, reduced libido and impotence have been reported as the most frequent neurological and psychopathological symptoms of intoxication which become manifest often only several months after it occurs (Bauer, Schulz and Spiegelberg). With regard to the question of distinguishing the latter from psychoneurotic obsessions (wish for compensation), reference is made to the discussions of Spiegelberg.

Etiology.—When we review the literature, we find that periods of greater incidence of chloracne have existed in the last 60 years, which can be correlated with industrial development. W. Braun has described these relationships in his monograph.

The first cases were observed near the turn of the century when chlorine and hydrochloric acid began to be produced by the electrolytic route. At that time, the condition occurs primarily among workers having the assignment to clean the so-called hydrochloric acid towers, but only when tar was used as the protective coating of the walls. Although the causal toxin could not be determined at the time, it can be assumed on the basis of our present knowledge that the reaction products of chlorine and aromatic components of the tar must be considered as etiological factors of this condition.

The next period of increased chloracne frqucy coincides with the introduction of so-called halogenated waxes. These are mixtures of highly chlorinated naphthalenes and diphenyls with a waxy consistency and a number of valuable properties. They are water-repellent, nonflammable, resistant to acids, are a good dielectric and are not pest-promoting. The halogenated waxes developed during the first world war at that time were used primarily for the manufacture of gas masks. Numerous cases of chloracne occurred in the manufacturing plants.

In the middle twenties, these halogenated waxes were used in the mining industry as a water-repellent and nonflammable insulation for detonators. The high incidence of diseases observed in detonator manufacturing plants has been described by Teleky.

The next massive occurrence is related with the rise of the electrical and radio industry. Chlorinated naphthalenes and diphenyls were in more widespread use for the insulation of wires and condensors at the start of the thirties. Several hundred cases including one fatality with liver atrophy became known especially in the United States.

With the entry of the United States in the second world war, the field of application of these materials expanded also into ship building; this had the following reason: It was found that the halogenated waxes were in the position to insulate ships from the dangerous weapon of German magnetic mines. Consequently, large quantities of these materials were used in American shipyards for the impregnation of ship hulls. Mass incidences of chloracne with several fatalities were the results.

In spite of all negative experiences, the use of chlorinated naphthalene waxes did not stop after the last war. Chloracne cases of greater or lesser frequency were repeatedly observed in the electrotechnical and cable industry (Braun, Grimmer, Risse-Sundermann). From the pathogenic aspect, it is of interest to note an observation of Herzberg of 7 patients who developed intestinal symptoms and acneiform dermatoses following the use of industrial chlorinated greases for frying.

The question of the relationships between chemical structure and acne-producing effects of chlorinated naphthalenes is the subject of several experimental studies. Teleky as well as Drinker and Warren arrived at the conclusion about thirty years ago that the toxicity of the molecules increases with an increasing number of chlorine atoms on the ring. Later experiments conducted by Schley and Kligman with human subjects and with the use of several chlorinated naphthalenes showed that penta- and hexachloronaphthalenes produced the strongest effects; compounds with 1 to 3 as well as 7 and 8 chlorine atoms were far less toxic of inactive. We confirmed this finding in animal experiments using rabbit ears (Schulz 1965).

In the last 10–15 years, halogenated waxes have become less important as etiological factors of chloracne. Evidently, this is related with the fact that they are no longer as important industrially and have been replaced by synthetics of the most diverse nature in most fields of application.

In the fifties, the incidence of chloracne was observed in entirely different sectors of industry i.e. in the *production and processing of chlorinated phenols.* Reports of group involvements have been published from at least three

16077

Industrial plants in Western Germany. Baader and Bauer as well as Brinkman described 17 workers of a plant in Nordrhein-Westfalen who developed the typical skin symptoms as well as damage of the internal organs and central nervous system disorders in the production of pentachlorophenol.

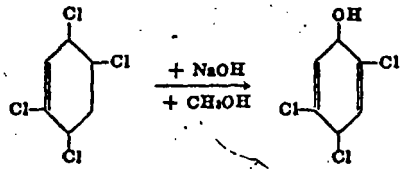
A larger number (about 60 cases) of similar disorders were recorded several years later in the region of southwest Germany among workers occupied in the production of of trichlorophenol (Hergt, Oettel, Hofmann). Approximately at the same time, 31 workers in a Hamburg plant became ill after working with industrial 2,4,5-trichlorophenol, an intermediate of the synthesis of trichlorophenoxyacetic acid, a weed killer.

Siliar high incidences of the disease occurred a few years ago in chemical plants of the Netherlands and the U.S. during analogous production processes.

The high frequency of cases in Hamburg led to studies of the etiology. They were conducted by us together with Dr. Sorge, the former manager of the chlorophenol plant.

Rabbit ears were used as the biological substrate on which symptoms corresponding to human chloracne can be produced by local painting as demonstrated by Hofmann and Neumann with chloronaphthalenes. The results, which have been reported earlier (Schulz 1957; Kimmig and Schulz 1957), can be briefly summarized as follows:

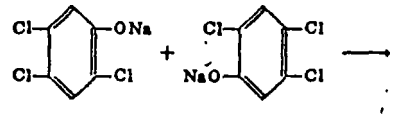
First, it was found that it was not possible to produce changes in the rabbit ear in the form of chloracne with the use of the chemically pure compound in contrast to the technical grade of 2,4,5-trichlorophenol used in the plant. Pure 1,2,4,5-tetrachlorobenzene also was inactive. The toxic factor therefore must have formed as a byproduct during the alkaline hydrolysis of tetrachlorobenzene into trichlorophenol.



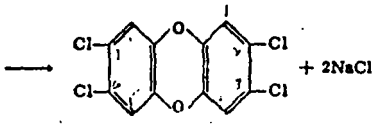
1,2,4-tetrachlorobenzene 2,4,5-trichlorophenol

Alkaline hydrolysis of 1,2,4,5-tetrachlorobenzene into 2,4,5-trichlorophenol.

Since the isolation of well-defined compounds from the distillation residue of trichlorophenol was unsuccessful, a number of especially synthesized substances were investigated which might have formed as a byproduct of the cited saponification process on the basis of theoretical considerations. The majority of investigated compounds proved to be inactive. Only dibenzofurans with 3 and 4 chlorine atoms (diphenylene oxides) and 2,3,6,7-tetrachlorodibenzodioxine (tetrachlorodiphenylene dioxide) led to the characteristic changes on the rabbit ear already in low concentrations. Moreover, it was demonstrated that 2,3,6,7-tetrachlorodibenzodioxine had formed by the following reaction route in the industrial process of alkaline hydrolysis of 1,2,4,5-tetrachlorodibenzene.



Sodium salt of 2,4,5-trichlorophenol



2,3,6,7-tetrachlorodibenzodioxine
(2,3,6,7-tetrachlorodiphenylene dioxide)

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Under the conditions of a salt fusion in a solvent-free state, 2 molecules of sodium trichlorophenolate form 1 molecule 2,3,6,7-tetrachlorodibenzodioxine with the elimination of 2 molecules of NaCL. Dr. Sorge synthesized the compound and in addition, isolated it from the distillation residue of industrial trichlorophenol.

Animal experiments conducted with tetrachlorodibenzofuran and 2,3,6,7-tetrachlorodibenzodioxine showed an extremely high toxicity of these compounds. Even concentrations of 0.001–0.005% of tetrachlorodibenzodioxine led to severe reactions on the rabbit ear after local application. On human skin in a self-experiment, two applications of 10 γ of the substance produced the symptoms characteristic of chloracne. On the rabbit ear, tetrachlorodibenzofuran showed an activity which was about 10 to 20 times less pronounced. Moreover, the unexpectedly high hepatotoxic action is worthy of note, particularly after tetrachlorodibenzodioxine. Single oral doses of 20–50 γ/kg body weight regularly produced lethal liver necrosis, while doses of 10 γ/kg were lethal for about 50% of the rabbits.

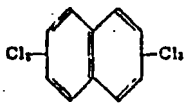
On the basis of these chemical and toxicological findings, it is justified to conclude that 2,3,6,7-tetrachlorodibenzodioxine played an important role in the etiology of the cases of chloracne which occurred during the industrial production of trichlorophenol. It cannot be ruled out, however, that other, as yet unknown chlorinated aromatics of highly toxic properties may form during the industrial process under certain conditions. The results of the study are an example that materials which form only in small amounts as byproducts of large-scale syntheses can be of importance in occupational medicine. If such toxic byproducts can be uncovered and their mechanism of formation can be elucidated, this will create an important prerequisite for successful prophylaxis. In our special case, the plant succeeded in avoiding the formation of highly toxic byproducts by modifying the production process.

Our animal experiments were extended to other chlorinated aromatics to which other authors ascribed a chloracne-causing action on the basis of clinical observations. (Reviews of these compounds in the monograph of W. Braun.) Neither benzenes and phenols with 1 to 6 chlorine atoms nor chlorinated diphenylethers produced an effect in animal experiments. It seems indicated to assume. therefore, that neglected toxic byproducts were of decisive etiological importance in these cases rather than the main products.

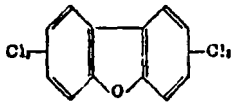
In connection with the acne produced by chloronaphthalenes, the question arose whether toxic byproducts rather than the chloronaphthalenes themselves might not be considered as the true toxins (Oettel). In the production of industrial naphthalene by fractional distillation of tar, the presence of other aromatic compounds deriving from the tar apparently cannot be ruled out. In the following chlorination process, such substances might then also undergo CL-substitution. These question prompted us to carry out animal experiments on rabbit ears using chemically pure chloronaphthalenes of different degrees of chlorination specially synthesized for this purpose.*

In agreement with the findings of Shelley and Kligman, we found that naphthalenes containing 5-6 chlorine atoms have a chloracne-producing effect. The necessary concentrations, however, were about 100 times higher than those of tetrachlorodibenzofuran (diphenylene oxide) about about 1000 times higher than for 2,3,6,7-tetrachlorodibenzodioxine (tetrachlorodiphenylene dioxide).

On the basis of the present state of the art, therefore, the chloracne-producing activity of the following compounds appears to be sufficiently demonstrated or at least highly probable:



Naphthalenes containing 5–6 chlorine atoms:



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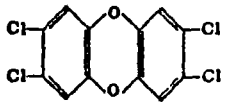
Dibenzofurans (diphenylene oxides) with higher degrees of chlorination:



2,3,6,7,-tetrachlorodibenzodioxine:

In conclusion, it should be noted that the toxicodermatosis represented by chloracne results from intoxication with certain chlorinated aromatics. The causally responsible compounds partly involve highly toxic substances which can cause damage in various internal organs, especially the liver and nervous system, in addition to the skin. Since the skin does not always represent the only manifestation site, it is recommended that thorough internal and neurological as well as psychiatric examinations be made in cases of suspected chloracne.

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*I am indebted to Prof. Dr. Zelle, Fa. C. H. Boehringer Sohn, Ingelheim, for the synthesis of the compounds.

Report on Methodology for Chlorinated Aromatics in Fats, Oils, and Fatty Acids

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ABSTRACT

The official, first action electron capture GLC (EC-GLC) method for chick edema factor (polychlorodibenzo-p-dioxins) have been reviewed. This general procedure, which underwent collaborative study in 1967, has undergone several minor modifications which result in better recoveries of polychlorodibenzo-p-dioxins and increased specificity in interpretation of the gas chromatographic results. The EC-GLC method can be used as a screening test, or where a typical pattern of GLC peaks is obtained as a preliminary test, but confirmatory tests are needed to demonstrate structure and toxicity of polychlorodibenzo-p-dioxins. Preliminary work with combined GLC-Mass Spectrometry indicated that this technique might provide a suitable test, if adequate sample cleanup can be accomplished. A chicken embryo assay has been developed to the point where toxicity can be observed in three to five days after injection of eggs.

A preliminary procedure has been developed for isolation and gas chromatography of chlorophenols in fats and fatty acids. Polychlorophenols have been found to be precursors of chlorodibenzo-p-dioxins. The use of a non-specific microbiological test for chlorophenols employing the *Bacillus megaterium* was evaluated. Chlorophenols were found to produce uniformly graded growth inhibition of the test organism in the range 1–100 μg.

The widespread use of toxic organochlorine compounds in agriculture and industry requires development of sensitive methods for their detection in a wide variety of commodities. In addition, it is equally important that methods be developed to detect toxic breakdown or conversion products of organochlorine compounds. One of the most urgent needs in the fat and oil industry is for a rapid and specific method for polychlorodibenzo-p-dioxins (chick edema factors) in fats, oils, and fatty acids. The official, first action, microcoulometric and electron capture methods for chick edema factors (CEF) are essentially screening procedures (1,2,3). Both methods, at present, require a rather time consuming three-week chick bioassay (4) for confirmation.

The purpose of this report is to review the current status of chemical and biological methods for chlorophenols and chlorinated dibenzo-p-dioxins in fats, oils, and fatty acids.

CEF consists of a mixture of chlorinated dibenzo-p-dioxins which occur occasionally as a trace contaminant in fats. Recently, a communication (5) from this laboratory reported the results of a preliminary study which demonstrated the possibility that CEF could arise from residues of pentachlorophenol and 2,3,4,6-tetrachlorophenol in fats and fatty acids. Chlorophenols and their salts, when heated, undergo condensation reactions and form chlorinated derivatives of dibenzo-p-dioxin. The following equation illustrates this condensation reaction.

Technical grades of pentachlorophenol contain ca 10% of 2,3,4,6-tetrachlorophenol which also undergoes thermal condensation reactions and forms hexachloro derivatives of dibenzo-p-dioxins. The condensation of 2,3,4,6-tetrachlorophenol with pentachlorophenol forms two heptachloro derivatives of dibenzo-p-dioxin.

An electron capture GLC method has been developed for pentachlorophenol and 2,3,4,6-tetrachlorophenol in fats, oils, and fatty acids (6). However, recov-

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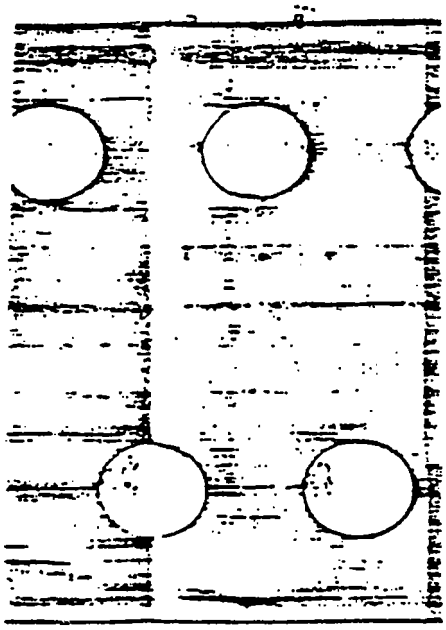

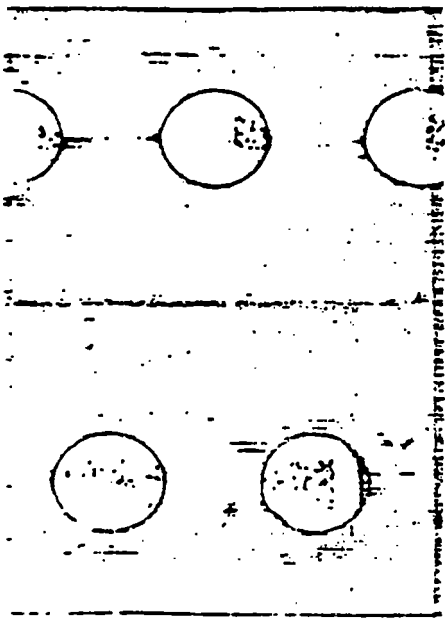

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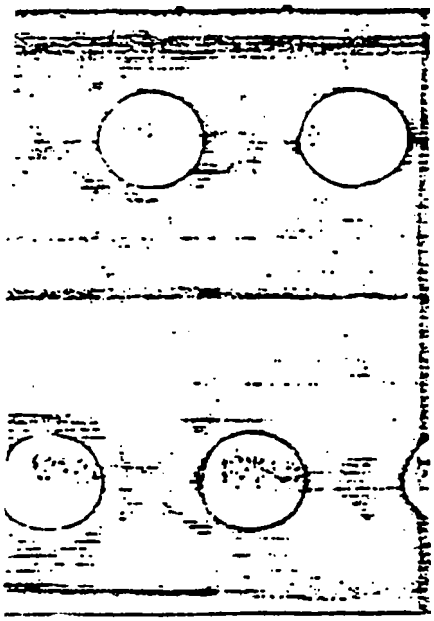

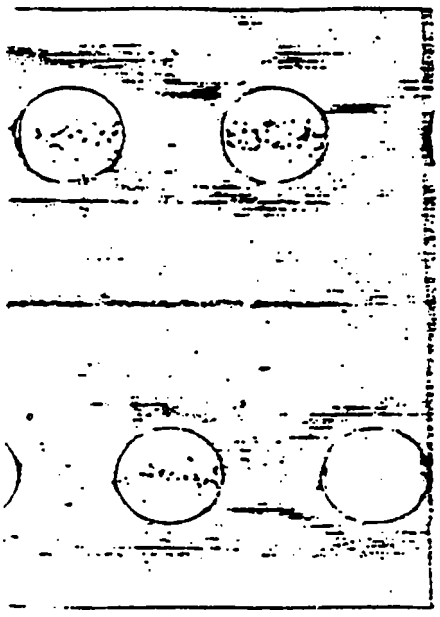

OCCUPATIONAL CHLORACNE

MARCUS M. KEY, M.D.* and DONALD J. BIRMINGHAM, M.D.**

The story of chloracne illustrates one of the problems in occupational health of an old chemical causing trouble in a new application. Actually, there are a number of chemicals that are chloracnegens. Most of these have in common a similar chemical configuration, namely, they are 2 ring chlorinated compounds, naphthylenes and diphenyls being the usual ring structures.

The Public Health Service's Division of Occupational Health has been interested in chloracne since the middle 1930's when workers who made synthetic waxes developed an acne-like eruption and liver damage from exposure to chlorinated diphenyls (Schwartz, 1936). The acne occurred not only on the face and neck but also on covered parts such as shoulders and belt line where contaminated clothing rubbed. The contaminated clothing was also responsible for chloracne in the wife and child of one of the workers. In addition, some of the workers with chloracne developed acute yellow atrophy of the liver, presumably from inhalation or percutaneous absorption or both.

Chloracne was first observed by Herxheimer in Germany in 1899 among workers manufacturing chlorine electrolytically with carbon electrodes (Carozzi, 1930). American experience with chloracne dates back to 1912 when manufacture of synthetic waxes began, but there were no published reports until Schwartz's in 1936 (Schwartz et al., 1957). The subsequent experience of the Public Health Service with outbreaks of chloracne is summarized in Table I. In addition to chloracne and liver damage, hyperpigmentation, hirsutism, porphyria, fatigue, and irritability have been noted occasionally.

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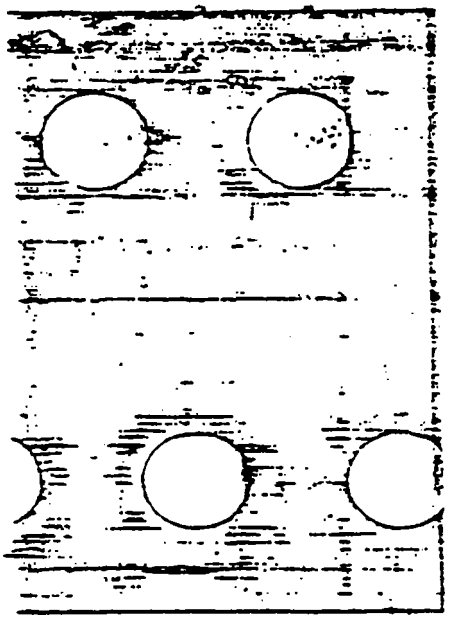

TABLE I. CHLORACNE OUTBREAKS

OPERATION	MATERIAL	CHLORACNEGEN
manufacture of synthetic waxes (Schwartz, 1936)	synthetic waxes	chlorinated naphthalene chlorinated diphenyls
cable stripping (Schwartz, 1943)	Halowax insulation	chlorinated naphthalene
metal cutting (Schwartz & Barlow, 1942)	chlorinated cutting oil	chloronaphthalenes
hydrochloric acid manufacture (Schwartz et al., 1957)	reaction product of coal tar and salt	unidentified
2,4,5-T manufacture (Bleiberg et al., 1964)	2,4,5-T herbicide	contaminant
electroplating	masking wax	chlorinated naphthalene
decoration of bent glass (Birmingham, 1964)	plasticizer in glass enamel	chlorinated di- and triphenyls
barge tank repair (McLean, 1964)	hydrochloric acid and rubber	unidentified
weed killing (Goldstein, 1962)	2,4,5-T herbicide	contaminant
bottle making	mold lubricant	unidentified

Outbreaks of chloracne in chemical plants manufacturing 2,4,5-T herbicide (Bleiberg et al., 1964; Dugois and Colomb, 1956; Kimmig and Schuz, 1957) and recent reports to the Division of Occupational Health of chloracne among herbicide users, has prompted us to attempt to identify the chloracnegenic contaminant(s) in commercial 2,4,5-T. Several investigators have previously worked on this problem and have ascertained that pure 2,4,5-T is not chloracnegenic and that on a theoretic basis, the contaminant may be a chlorinated dibenzo p-dioxin (Kimmig and Schuz, 1957; Jones and Krizek, 1962). The usual laboratory indicator is the rabbit ear canal in which chloracne can be produced in two to three weeks (Hofmann and Neumann, 1952; Rambrick, 1957). The histopathology is distinctive and similar to that of human chloracne--metaplasia of sebaceous glands and replacement by keratin plugs and cysts. Using the rabbit ear canal as an indicator we have shown that three different brands of 2,4,5-T herbicide are chloracnegenic and the pure 2,4,5-T is not.

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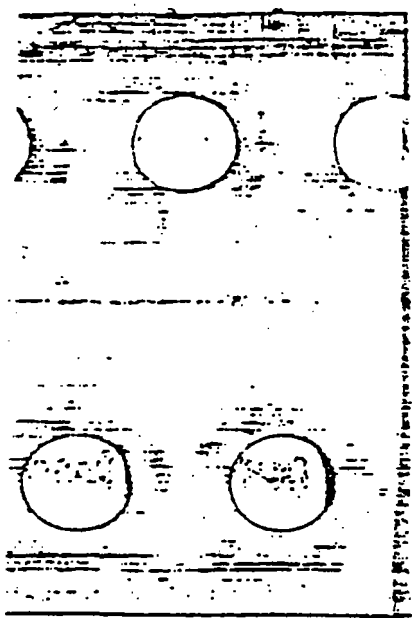

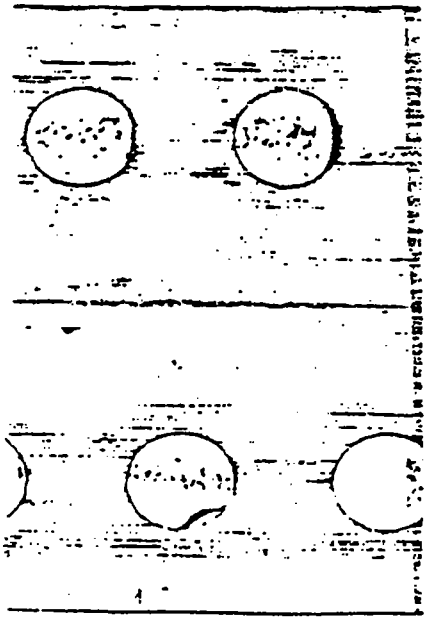

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16085

DOW 1131842

The Preparation of Trichlorophenoxy Acetic Acid Avoiding the Formation of Chlorakne Exciters

Our synthesis of 2,4,5 trichlorophenoxy acetic acid runs in the following stages:

1. Trichlorobenzene $\xrightarrow{Cl_2}$ tetrachlorobenzene
2. Tetrachlorobenzene $\xrightarrow{NaOH}$ trichlorophenol sodium
   a. Autoclave reaction
   b. Evaporation of CH_3OH
   c. Water vapor distillation of anisole
   d. Isolation of trichlorophenol by acidification and subsequent distillation
3. Trichlorophenol $\xrightarrow{NaOH,\ CH_2ClCOONa}$ 2,4,5-trichlorophenoxy-
4. acetic acid sodium
4. Additional working up to pure crystalline 2,4,5 T-acid

In our experience the chlorakne exciting effect on impurities may be traced back to by-products that can be formed by the usual conventional process only if trichlorophenol sodium or other alkali salts is prepared from trichlorophenol, purified, and worked up further, and if there are thereby reaction conditions that are similar to or exactly the same as those of a salt melt.

From this point of view with regard to the formation of chlorakne exciter for the individual steps in the method, the following are valid:

For 1 and 4. These steps are not at all dangerous.

For 2. The chlorakne exciter may be formed at this step.

For 2a. In order to prevent this in the autoclave reaction it is necessary to avoid the superheating of the autoclave contents (highest temperature 150°C) and in addition care must be taken to assure that the work is done at the greatest possible dilution with methanol.

For 2b. In the methanol distillation the water that is formed should be kept back in the distillation vessel so that the dangerous dry heating of trichlorophenol sodium will be avoided. The sump temperature should not exceed 100°C.

For 2c. The water vapor distillation for driving off the trichloroanisole must be done in such a way that there will be the smallest possible (or no) change in theconcentration of the sodium trichlorophenol solution. If necessary water must be added.

For 2d. In the distillation of the crude phenol it is necessary to see that no sodium trichlorophenol and no table salt enter the distillation vessel and are heated with the phenol.

For 3. In this step it is also possible for the chlorakne exciter to be formed. In order to prevent this the condensation of sodium trichlorophenol with chloroacetic acid sodium should never be conducted in an anhydrous medium. A concentration above 40% should be avoided in all cases.

In short, the following may be said about the properties of the chlorakne exciter; as a neutral substance it is volatile with water vapor so that it may become enriched in sept 2c in the trichloroanisole that is distilling off. Therefore it is best to avoid the addition of more trichloroanisole and to destroy it by burning.

Since the chlorakne exciter shows clear evidence of sublimation even at a temperature of over 100°C, in spite of its high melting point, the reaction product from steps 2 and 3 should be worked up in completely closed apparatuses and care must be taken that the working area be sufficiently ventilated.

——— Signed: Weyland

DOW 1131843

C. H. Boehringer Sohn
22b Ingelheim am Rhein
Germany

Dow Chemical Company
1714 Eastman Rd.
Midland, Michigan
USA

Attention Leonard Rickin

February 11, 1957

Our ref: Dr. Wey/B

Re: The chlorakne. Preparation of Trichlorphenol

Gentlemen!

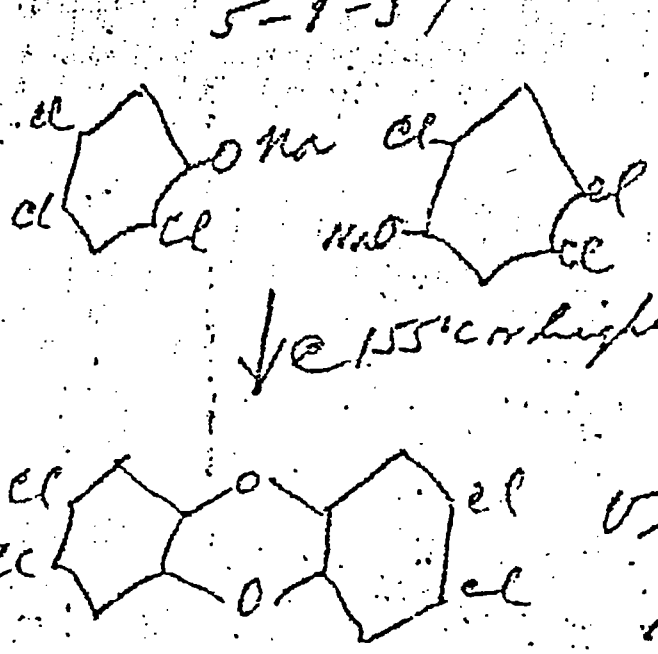
We hereby refer to our 1955 correspondence on the above subject. At that time you were kind enough to share your experience with us.

Since our own work on avoiding chlorakne exciters has come to a type of conclusion, we should like to make the results available to you and are accomplishing that by attaching a short description.

We hope that we have been able to give you, by means of this explanation, a contribution to the assurance of the synthesis of trichlorophenoxy acetic acid and assume that the contribution will also be of interest to you.

Sincerely

attch.



DOW 1131841

Vol. I - Hart Hearings 1751

EFFECTS OF 2,4,5-T ON MAN AND THE ENVIRONMENT

UOM T 130285

HEARINGS

BEFORE THE

SUBCOMMITTEE ON ENERGY, NATURAL RESOURCES, AND THE ENVIRONMENT

OF THE

COMMITTEE ON COMMERCE

UNITED STATES SENATE

NINETY-FIRST CONGRES

SECOND SESSION

ON

EFFECTS OF 2,4,5-T ON MAN AND THE ENVIRONMENT

APRIL 7 AND 15, 1970

Serial 91-60

Printed for the use of the Committee on Commerce

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45-362 WASHINGTON : 1970

Bauer et al. 1961 Chloracne article (introduced by J. Verrett)

pp. 241-249

16089

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OCCUPATIONAL INTOXICATION OCCURRING IN THE PRODUCTION OF CHLOROPHENOL COMPOUNDS BY H. BAUER, K. H. SHULZ AND U. SPIEGELBERG, HAMBURG

MAY 20, 1961

INTRODUCTION, GENERAL

In the last few years, professional work in the production of chlorinated phenols has been the cause of group outbreaks of acne in at least three West

16090

German chemical works, the acne persisting over a long period and being associated with other effects on the health.

Diseases in a group of 17 workers from a company in North Rhine/Westphalia were reported by BAADER and BAUER, as well as by BRINKMANN in 1950/51. The workers in that company were engaged in the production of pentachlorophenol. Apart from comedone acne with various degrees of secondary pustular infection and boils, most of the workers, whilst still in the first stages of the skin diseases, also experienced pain and weakness in the lower limbs, mild paraesthesia, heart complaints and indeterminate psychovegetative disturbances. Subsequent examination of the records of 17 cases[1] revealed the following findings:

All 17 were suffering from an acne, 4 of these being very severe, 8 fairly severe, and 5 moderately severe to mild. In almost all cases there were extensive pustular infections and boils, 4 with bursitis on the elbow.

Other disturbances amongst the workers included 11 cases of bronchitis, 5 of myocardiac damage, 2 of cirrhosis of the liver (one of which proved fatal), 9 of neuritis symptoms (severe pains in the lower extremities in 7 patients, sensibility disturbances in 4 cases, mild paresis without atrophy in 2 patients, and 2 cases of weakening of the Achilles' reflex). Seven workers complained of physical conditions such as continuous fatigue, depression, lack of vitality, nervousness, slight headaches, disturbed sleep, and decrease in libido and potency.

A larger number (about 60 cases, Prof. Hergt) of similar conditions occurred in two Mid-Rhenish companies amongst workers who had been engaged for long periods, generally several years, in the production of trichlorophenol (saponification of 1,2,4,5,-tetrachlorobenzene to 2,4,5-trichlorophenol by treatment with methanolic caustic soda solution). These trichlorophenol workers, like those in a third group of affected persons from the Hamburg region who will subsequently be dealt with in more detail, suffered from further disturbances to health, these often not occurring until a fairly long time after occupational exposure had ceased. In the course of a discussion on a paper by SPIEGELBERG, who referred briefly to our Hamburg cases in a lecture at the 1960 North-West German Neurologists' and Psychiatrists' Congress in Lüneberg on psychopathological delayed and chronic damage following occupational intoxication. Janzarik described largely identical disturbances amongst workers from the Mid-Rhenish companies.

The third group comprised 31 workers in a Hamburg company. Those of this group who were affected were engaged in the trichlorophenol department of the company, in which the herbicide 2,4,5,-trichlorophenoxyacetic acid was manufactured from technical 2,4,5-trichlorophenol by heating trichlorophenol together with caustic soda solution and monochloroacetic acid in autoclaves. After completion of this esterification process, the end product was purified by double recrystallization. The task of the workers consisted first of all in charging the autoclaves, for which purpose the trichlorophenol in flake form had to be removed by shovel from open barrels. In this operation, a fine dust formed and dispersed throughout the room.

Other operations were concerned with filling and controlling centrifuges and regulating feed and outlet pipes. Since it was the workers most exposed to contact with trichlorophenol who suffered from the severest skin conditions, it was logical from the outset to suspect the causal noxa to be present in the trichlorophenol. The extent to which this assumption was valid is discussed later in this paper in connexion with etilogy.

SOME CLINICAL OBSERVATIONS

Of the 31 workers of this Hamburg company, 9 are still receiving medical attention 5 years after the termination of occupational exposure, this being due to residues of their acne, chronic neuromuscular weakness of the leg musculation, vaso-vegetative lability and, most especially, marked psychopathological disturbances. Details of the established complaints and damage to health are given in the table. The development of the skin conditions in the patients followed, by and large, a uniform pattern. Numerous comedones formed, first on the face, especially on the cheeks above the malar bones, fore-

[1] Our thanks are due to the Berufsgenossenschaft der Chemischen Industrie for placing their records and other documents at our disposal, and also for their understanding in the sometimes lengthy clinical examinations.

DOW 1 130287

16091

head, temples, chin and ears, after which folliculitis, pustules, boils and retention cysts occurred as a result of secondary infections. As the disease progressed, these symptoms spread in the majority of patients, especially to the sides of the neck, back of the neck, upper half of the back, chest, forearms, genitals and thighs. Numerous boils formed, particularly on the back of the neck and on the back. The efflorescences were generally located so closely together that scarcely any follicles remained unchanged.

In certain workers who had apparently been more strongly exposed, the development of these acne-like symptoms preceded a dermatitis associated with erythema and swelling, this extending to the region of the eyes, the cheeks and the forehead. At about the same time, blepharoconjunctivitis occurred in several patients, this, like the skin symptoms, becoming chronic in some cases.

As the table of findings shows, spots or, in certain cases, patches of pigmentation occurred in the faces of some patients, these giving the skin a dirty, greyish-brown appearance.

The overall clinical picture was identical to the symptoms occurring after working with chlorinated naphthalenes, diphenylenes and other aromatics as first described by HERXHEIMER (1899) and subsequently by several other authors (BETTMANN, HOLTZMANN, TELEKY, HERZBERG, BRAUN, GRIMMER, etc.). (For further details, see W. BRAUN and A. RISSE-SUNDERMANN (1959)). Although not a completely exact description, the designations "chloracne" and "perna disease" have become the most popular for these forms of occupational intoxication.

TABLE OF FINDINGS

Skin and mucous membranes: Dermatitis of the face in initial stage; comedones, retention cysts, nodules, pustules, boils; patches of pigmentation; blepharoconjunctivitis.

Internal organs: Loss of appetite; abdominal complaints; loss of weight; reduction in general condition; altered acidity of the gastric juice; gastritis; damage to liver; pulmonary emphysema, dyspnea; myocardiac damage; blood pressure; edema; pathological urine finding (renal damage).

Nervous system.—Neurological: Muscular pains; weakness in legs; (general) fatigue; increased sleep requirements; paresthesia; headaches; attacks of giddiness; orthostatic collapse tendency; paresis (implicit); coordination disturbances; hypaesthesia; reflex irregularities; vegetative hyperexcitability; EEG finding [1]; EMG finding.[2]

Nervous system.—Psychopathological: Decrease in initiative and interests; hyperaesthetic-emotional traits; pronounced fluctuations in intensity; disturbances in memory and concentration; disturbances in libido and potency; alcohol intolerance; depressions; decrease in impulsion; affective disturbances in the restricted sense of the term; experimental weakness in mental capacity; organic Rohrschach psychogram; individual neurotic traits.

n. = normal, abn. = abnormal, p. = pathological, n.s.p. = not definitely pathological, v.mU. = premature fatigue in the electromyographic series stimulus test.

The course of the dermatological manifestations proved to be extremely obstinate in our cases. The therapeutic measures employed (drainage of the comedones, external keratolytic and antibacterial measures, as well as the internal administration of antibiotics in severe cases) could not prevent the reformation of comedones, retention cysts and boils in the first year or two, although there was no further contact with the causal noxae. Only after a long time did the tendency to relapses cease. A residual condition now to be found, particularly amongst the serious cases is closely arranged pitted scars which have a disfiguring effect, especially where localization occurs in the face (pseudo-atrophodermia vermiculata).

All affected workers reported pronounced fatigue and weakness in the legs, often with pain, especially in the region of the proximal leg musculation. These conditions were marked, even in the early stage of the disease, and in some cases even before the development of skin changes. Paraesthesia was reported in the records or in spontaneous information in only 2 of 9 cases.

[1] Our thanks are due to Doz. Dr. BOCHNIK and Dr. BUSCHART for conducting the electro-encephalographic investigations, and to Dr. PUFF and Dr. RUEDAS for the electro-myographic investigations.

DOW 1 130288

16092

OOW 1 130289

Implicit paresis or atrophy, weakening of the reflexes, or absence of muscle expansion reflexes as a sign of toxic polyneuropathy was not established in any of the cases. Two of the patients examined indicated a decrease in sensibility with isolated epicritical disturbances in the lower limbs. No definite signs of neurogenic damage that could have been expected with peripheral nerve lesions were established electro-myographically; premature fatigue, which was recorded in the series stimulus test, requires further confirmation regarding both the method and the raised findings. As these findings show, the neuromuscular disturbances do not fit in with the typical picture of toxic polyneuritis or polyneuropathy.

The electroencephalographic examination produced an abnormal electroencephalogram in 6 cases, with frequency lability and dysrhythmic groups of a partly asymmetrical character. In one of the patients examined, accentuated dysrhythmia and raised cerebral excitability were revealed after photostimulation. The electroencephalographic changes found were uncharacteristic and afforded no diagnostic viewpoints of any real consequence.

Some of the workers examined complained of headaches, attacks of giddiness and orthostatic collapse tendency. In 5 of the 9 patients examined, there were distinct signs of vegetative hyperexcitability, fine tremor of the hands, increased perspiration on the hands and legs, axillary perspiration, raised dermagraphism and suggestions of Chvostek's sign. The blood pressure value measured during out-patient check-ups were all in the normal region, though at the lower limit of the norm in 5 of the 9 patients examined. Orthostatic collapse tendency was not established either during out-patient visits or during in-patient observation by an internist. In 2 cases, myocardiac damage was suspected.

Abdominal complaints such as a feeling of fullness, pressure in the stomach and liver region, and slight pain, were reported by 5 of the 9 patients. There were 4 reports of disturbances in the gastric secretions, 3 of subacidity, one of hyperexcitability and one radiographic finding of gastritis.

Very thorough investigations were conducted as part of repeated out-patient examinations and in-patient observation to ascertain any liver damage.[3] Whilst the liability reactions were uncharacteristic in all cases, the bromphthalein test indicated slight delay in the dyestuff excretion in 2 instances. In 3 cases, the liver biopsy produced pathological findings, these comprising 2 cases of slight perihepatitic changes and in one case a fatty liver with inflammatory symptoms and slight fibrosis of the liver. Owing to the clinical and histological findings, it was suspected that a condition following virus hepatitis existed in this instance. Deposits of ferrous and non-ferrous yellow-brown pigment were established in this case, although these did not correspond to the grey, non-ferrous pigment discovered by KALK and WILDHIRT in chlorophenol intoxication. The excretion of erythrocytes in the urine of one worker whose renal findings were otherwise normal remained unaccounted for.

The psychopathological changes in the chlorophenol workers who were all psychiatrically and psychopathologically examined were especially remarkable. In 6 cases the course could be observed over a 2-year period and there was an opportunity for objective anamnesis investigation and experimental psychological examinations.[4] With a very large degree of agreement, a subjective syndrome of complaints was reported by the patients under investigation, this syndrome extending from the psychoneuropathic complaints in the region of the extremities, cardiovascular and abdominal symptoms to the mental/spiritual sphere, especially in the modes of behaviour associated with the vital forces (BÜRGER-PRINZ). Considered in detail, there were reports of disturbances in the vital senses such as general sense of weakness, feeling of fatigue, indisposition, sense of insecurity, inner restlessness and a feeling of illness. The basic mental mood was reported to be deteriorated and lowered towards behaviour characterized by dissatisfaction or sullenness and irritation. Not infrequently, a mood component of fear and unease was present. Changes in affectivity in the restricted sense of the term were reported by the patients in the form of increased emotional reactions, irritability, tendency to fits of temper and also a certain hebetude.

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[3] Prof. Dr. HORNBOSTEL and Dr. SCHONFELDER. I. Med. Univ.-Klinik. Hamburg-Eppendorf.

[4] Our thanks are due at this point to Dipl. Psychologist W. von SCHUBERT, for conducting the tests (Rorschach psychogram and Hamburg-Wechsler intelligence test for adults).

16083

DOW 1 130290

General loss of strength and reduced inner vitality and impulsion were symptoms noted in each of the cases observed. The probands described reduction in initiative and interests, weak willpower, reduced efficiency, and more rapid exhaustion in physical and mental/spiritual matters.

The subjective and objective anamnestic psychopathological picture is further complicated by a number of additional symptoms that are present with a greater or lesser degree of regularity. Disturbances of the instincts occurred in practically all cases. Thus, probands suffered from a sharp reduction in potency, and most also from decreased libido. The appetite had deteriorated and occasionally there were substantial fluctuations in weight. The sleep and sleep requirements of most probands were distributed in that there was an increase in disturbances to sleep itself and concurrently, but less often, to the process of falling asleep.

In certain cases, a decrease in mental capacity, especially disturbances of the memory and perception, were mentioned. In the majority of instances, alcohol intolerance was noted. Finally, mention should be made of hyperaesthetic traits with hypersensitivity to light and noise. Marked fluctuations of the psychopathological syndromes described were reported in nearly all cases.

Changes were described in the intensity of the symptoms, daily patterns of fluctuation occurring in favour of early morning, late morning or evening hours. In many probands, there were intervals of some days or weeks in which they were practically free from complaints.

For completeness' sake, a further two less common phenomena are described. Two probands stated that the general symptoms and the polyneuropathic symptoms were relieved for a varying length of time by the use of cold media (cold showers and washing with cold water). One proband reported abnormal, constantly changing eating habits, such as a wish for nothing but black bread, milk soup, or three litres of milk daily, there being no desire for food of other types at these times.

Compared with the multifarious polysymptomatic subjective pictures, the objective psychopathological signs can be recorded at less length. In exploratory conversations, the majority of the probands displayed a distinct, slightly depressed and subdued mood, which could be brightened only slightly or not at all. So far as impulsion was concerned, the patients examined gave an impression of lifelessness; their psychomotivity was feeble and fatigued. The impression was rather one of slight cerebral organic impulsion reduction than of inhibition. The affective modes of behaviour were occasionally notable for their reduced reactivity and oscillation capacity, though also because of lability and decompensability. In 2 cases, pronounced hypochondria and, in one case, slight but distinct alienation of the total personality were recorded.

The psychological tests are significant for the discovery of finer intellectual performance shortcomings and psycho-organic disturbances in affectivity. In the majority of the probands tested by the Hamburg-Wechsler intelligence test for adults (HAWIE), there was a significantly raised percentage of degeneration, this providing a certain indication of an acquired decrease in mental capacity. In the Rorschach psychogram, coartation of the experiential type, signs of weakened emotional reactivity, poor concentration, reduction in tempo, sluggishness of the mental processes and a tendency to perservation point to cerebro-organically governed changes.

DISCUSSION

On the basis of the findings in three independent groups of chlorophenol workers, which together included more than 100 affected by diseases, a characteristic clinical picture is provided, the most important features of this being the following disturbances:

1. Following initial dermatitis of the face and symptoms of irritability on the part of the conjunctiva; often together with gradually developing acne primarily in the region of the face, then the back of the neck, shoulders and upper trunk, and in severe cases on the entire body, with comedones, pustules, boils and patches of pigmentation. In several cases with severe irritation of the mucous membranes of the face and the upper respiratory tract; sometimes with continuing blepharoconjunctivitis.

2. In several cases, disturbances connected with the internal organs, especially damage to the liver, with deposits of a nonferrous pigment as a

16094

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characteristic biopsy finding. In some cases, chronic bronchitis and isolated instances of myocardiac damage.

3. In all cases, general fatigue and weakness principally affecting the proximal muscles of the lower limbs, often with pain in the musculation and in some cases paraesthesia and slight hypaesthesia. In isolated cases only, more pronounced disturbances of sensitivity, slight paresis (implicit) and weakening of reflexes.

4. A psychovegetative syndrome with the following disturbances: Subjective: Disturbances of the vital senses, disturbances in the basic mental mood and affectivity, disturbance in impulsion, weakness of memory and concentration, hypermesthetic traits, vegetative dysregulation, tendency to orthostasis, sleep disturbances, much increased sleep requirements, disturbances of the instinct sphere, reduction in libido and potency, and alcohol intolerance.

Objective.—psychopathological: Reduction in impulsion, subdepressive traits of a type characterized by genuine vital moments of depression, disturbances in affectivity in the sense of a certain levelling-out, increased excitability; occasionally hebetude, hypochondria and personality alienation.

Experimental psychological. HAWIE: Increased degeneration percentage; Rorschach psychogram: Cœrtation of the experiential type, signs of weakened emotional reactivity, weakness of concentration, reduction in tempo, sluggishness of mental processes, tendency to perseveration.

The dermatological picture of the chlorophenol intoxication described shows extensive agreement with the disease caused by chlorinated aromatic hydrocarbons as first described by HERXHEIMER and later by several authors (see BRAUN, RISSE-SUNDERMANN). On the basis of the observations that chlorinated naphthalenes were principally responsible, WAUER, and later TELEKY, suggested the designation "perna disease" (*PER*chlorinated *NA*phthalene). TELEKY pointed out that the chloracne already described by HERXHEIMER in 1899 was produced not by pure chlorine but by chlorinated hydrocarbons or the simultaneous action of chlorine and tar. Further observations on perna disease made by MITTELSTADT, FLINN and JARWIK, DRINKER and collaborators, and GREENBURG and collaborators, indicated that not only the skin symptoms but also fatigue, loss of appetite, giddiness, and severe liver damage with acute yellow atrophy of the liver leading to death can result from work with chlorinated naphthalenes. BAADER mentions epidemics at American shipyards during the Second World War. In his description of the cases occurring in America and Great Britain, sometimes with a fatal outcome, TELEKY refers to the report of BROWN, President of the Halowax Co., New York (1937), that only the manufacture of the higher stages of chlorination and the combination with chlorinated diphenyls and other substances led to severe damage to the health and in some cases to fatal acute yellow atrophy of the liver. TELEKY also refers to the animal experiments by C. K. DRINKER and collaborators to support the view that only the higher chlorinated diphenylamines produce serious damage.

The general symptoms in occupational chlorophenol intoxications are apparently more pronounced than those occurring with the lower chlorinated naphthalenes employed earlier. This fact was also observed by TRUHAUT and collaborators amongst workers who had been using pentachlorophenol for wood preservation, as well as KUBOTA in Japan, who mentions multifarious disturbances of the autonomous nervous system and who observed several fatal cases. In all three German groups of chlorophenol intoxication, liver damage was established, the damage that was most pronounced and studied most intensely being that found amongst the cases of disease occurring in two Mid-Rhenish companies (HERGT, KALK and WILDHIRT). In all the groups, several cases of chronic emphysema bronchitis and myocardiac damage were found, although these disturbances did not occur nearly so regularly as the pronounced fatigue and neuromuscular weakness, which we observed in all our patients. The psychosyndrome described was equally regular, this being found not only by us but also by JANZARIK and RICHERT to a completely identical degree amongst the Mid-Rhenish workers.

The psychopathological syndrome could be distinguished with a sufficient degree of certainty by differential diagnostics from endogenic psychosis, especially mild cyclothymic diseases, neurotic personality developments and organic psychosyndromes of different etiology, and somewhat presenile or

16095

OOW 1 130292

cerebrosclerotic processes of degeneration. Phenomonologically, the relationships to the pseudoneurasthenic syndrome, which is described in connexion with a large number of occupational intoxications such as those caused by *lead, carbon monoxide, manganese, thallium, arsenic, carbon disulphide, trichloroethylene*, etc. (for relevant articles, see BORBELY, von HATTINGSBERG MEGGENDORFER, MOESCHLIN, PENTSCHEW, TELEKY)—and especially the relationships to particular endogenic mood conditions—are obvious. Lowering of the vital level, moments of depression, vegetative symptoms, and, not least, fluctuations in intensity can be observed predominantly in endogenic-depressive conditions. On the other hand, alcohol intolerance, hyperaesthetically excitable and polyneuropathic traits influence the differential diagnostic aspect more in the direction of an apparently exogenic condition. The somewhat older psychiatric literature should be borne in mind in this connexion (MEGGENDORFER, STERTZ), this placing the neurasthenic syndrome quite definitely in the pattern of exogenic symptom complexes. Not least, reference should be made to the phenomenological relationship of our observations to the (exogenic) hypernesthetic-emotional conditions of weakness of BONHOFFER, which, from the psychopathological aspect, have significantly been designated by EWALD as no longer het -onomous but homonomous in the sense propounded by KLEIST.

Despite the phenomenological relationships discussed, th · psychopathological delayed syndrome of the chlorophenol workers scarcely co· esponds completely with any of the known clinical pictures. In any case, the (.estion of a special psychic-vegetative delayed intoxication syndrome, which was discussed by SPIEGELBERG in connexion with observations on persons suffering chronic occupational damage from military poison gas, also demands consideration in view of the observations mentioned in this paper.

It has been possible to rule out psychogenic-neurotic moments so far as our subjects are concerned, provided that individual neurotic conditions, i.e. characterogenic and experiential situative data are involved. Two of the nine probands exhibited considerable psychopathic or neurotic structural elements. However, it was easily possible to separate these two probands from the other completely or largely non-neurotic cases. Certain "collective-neurotic" factors have, in our opinion, to be taken into account as an unfortunate but practically unavoidable fact in all group investigations but especially those involving etiological evidence (SPIEGELBERG). Reactions of this type have also been observed in our cases in the sense of a superimposed psychogenic accessory with, as it were, "physiological" but not inadequate, individual-neurotic (complex-determined) idemnification wishes. The psychopathological analysis of the individual case and the comparison of the findings in each instance with such independent collectives of the same etiology afford sufficient protection from authoritative and scientific false assessments. Despite the long course, the prognosis of the psychopathological intoxication results appears favourable. Although technical aspects of the pension situation have not yet been finally clarified, there was, on the whole, a certain subjective improvement in the symptoms, or else they remained static. We have not observed any objective deteriorations, except for the momentary intensity fluctuations. The experience of the Mainz Nerve Clinic (RICHER) and the impressions of works medical staff (KNECHT) suggest a benign course of acute and chronic intoxications, provided no toxic parenchyma damage, as such, influences the prognosis unfavourably.

It seemed appropriate to attribute the toxic action to the high-chlorinated chlorophenols, this view being supported by animal experiments conducted by MACHLE and THOMAS, H. KITZMILLER, a series of other investigators (KEHOE, DEICHMANN, GRUEBLER, BOYD, McGAVACK, TERRANOVA, PICCIONE cited acc. to von OETTINGEN) and also our own animal experiments. KIMMIG and SCHULZ were, however, able to show that the use of non-industrial, analytically pure, high-chlorinated chlorophenols (trichlorophenols, pentachlorophenols) does not lead to the characteristic symptoms of chlorophenol intoxication.

Animal experiments were carried out with a view to discovering the noxae causing the symptoms. The rabbit's ear proved to be a suitable test object since it is possible to produce the changes on this with the substances causing chloracne, these changes closely resembling those of human chloracne (HOFMANN and NEUMANN, BRAUN, LANDES, etc.). Brushing with a

16096

DOW 1130293

substance which is active in this respect leads at first to patches of dermatitis in conjunction with reddening, swelling and flaking; then, some days later, hyperkeratosis linked with the follicles and also small cysts occur, these being easy to record histologically, as well. In addition to the brushing experiments, tests were carried out on rabbits to determine the general toxicity, whilst cats, too, were used for testing a number of substances. In these tests, it was found, in corroboration of findings derived by OETTEL and also HOFMANN from similar cases of intoxication in a large chemical works in southern Germany, that the substances producing chloracne possess marked liver toxicity in rabbits. It was possible to trace effectively the damage to the parenchyma of the liver intra vitam with the micro-modification of the bromsulphthalein test given by HOFMANN and OETTEL. In autopsies, diffuse steatoses and extensive necrosis of the parenchyma of the liver were found. The investigations, which have already been reported (SCHULZ 1956; KIMMIG and SCHULZ 1957) led to the following results:

The effective substances must have occurred in the alkaline hydrolysis of 1,2,4,5-tetrachlorobenzene to 2,4,5-trichlorophenol, this having been carried out technically under pressure at about 180°C in the presence of methanol and caustic soda solution. However, it was not the trichlorophenol itself but the by-products that formed in small quantities in the course of the pressurized phenol process that were regarded as the causal noxae; for it was not possible to produce any of the above-named changes on the rabbit's ear with pure, repeatedly distilled 2,4,5-trichlorophenol or with 1,2,4,5-tetrachlorobenzene, although they did occur with the trichlorophenol used technically.

Since the isolation of defined compounds from the residue occurring in the distillation of technical trichlorophenol was not possible at first, compounds were synthesized by chemical means and given to us for testing on animals where there was a certain likelihood that these substances may occur as by-products in the saponification of tetrachlorobenzene to trichlorophenol. The substances initially available were various chlorination products of the diphenyl ether and the dibenzofuran (diphenylene oxide).

Although the diphenyl ether and its 1× to 4× chlorinated derivatives, and also dibenzofuran and monochlorodibenzofuran were ineffective in experiments on animals, 3× and 4× chlorinated dibenzofurans, even in concentrations as low as 0.05%, produced the symptoms mentioned on the rabbit's ear. Single doses of 0.5 to 1 mg/kg administered orally produced severe liver damage in rabbits, this leading to the death of the animals in most instances.

The clinical observation of a laboratory assistant engaged elsewhere, who fell ill with severe chloracne after exposure to tetrachlorodibenzodioxine, indicated the chlorine derivatives of the dibenzodioxine.

Tetrachlorinated dibenzodioxines, especially 2,3,6,7-tetrachlorodibenzodioxine, were highly effective on the rabbit's ear, even in low concentrations. Three brushed applications with 0.01–0.005% solutions (in polyglycol) were sufficient to cause severe areas of inflammation and follicularly arranged hyperkeratosis. When administered orally, single doses of 0.05–0.1 mg/kg body weight led to severe liver damage and generally the death of the animals.

The assumption that 2,3,6,7-tetrachlorodibenzodioxine is actually of considerable importance in causing the chloracne diseases occurring in the chemical works received further substantial support from the chemical angle. It was possible to prove that this compound is formed from two molecules of sodium trichlorophenolate in association with the cleavage of NaCl under the pressure and temperature conditions prevailing in the autoclave.

It was, moreover, possible to isolate the named tetrachlorodibenzodioxine from the by-product occurring in the technical pressurized phenol process (alkaline saponification from tetrachlorobenzene to trichlorophenol). To prove that 2,3,6,7-tetrachlorodibenzodioxine is capable of producing alterations in the form of chloracne not only on the rabbit's ear but also on human skin, one of us (SCHULZ) carried out a test on his own body. Two brushed applications of a 0.01% solution on a circumscribed skin area of the forearm led within two days to a mild dermatitis, then some days later to a follicular hyperkeratosis and comedones, these also being easy to record histologically. The etiological significance of this substance for the diseases described here seems to us to be sufficiently evidenced by this experiment. However, it is not impossible that other chlorinated aromatic compounds with highly toxic characteristics may occur in this technical process, these possibly not having been so far identified or tested in experiments on animals.

16097

The experimental and clinical findings are an impressive example of the fact that, in works pathology, substances occurring in small quantities as by-products in chemical processes can be of importance. In experiments to discover the origin of frequency occurring occupational intoxications, this viewpoint should not be ignored. If it is possible to prove that impurities attached to the main product should be regarded as the causal noxae of an occupational disease, this constitutes an important prerequisite for successful prophylaxy.

In our own special case, it was possible, by changing the plant chemistry aspect of the manufacturing process, to prevent the formation of the highly toxic, multi-chlorinated dibenzodioxines and dibenzofurans. Since than, 2,4,5-trichlorophenol is again being manufactured in this works and processed into the herbicide 2,4,5-trichlorophenoxyacetic acid, without symptoms of intoxication of any kind occurring amongst the workers.

DOW 1130294

A Technic for Testing Acnegenic Potency in Rabbits, Applied to the Potent Acnegen, 2,3,7,8-Tetrachlorodibenzo-*p*-Dioxin*

E. Linn Jones, M.D. and Helen Krizek, Ph.D.

Follicular hyperkeratosis is an important feature of the occupational disease known as chloracne, which is characterized by the appearance of papules, comedones and cysts after exposure to industrial materials containing highly chlorinated diphenyls, highly chlorinated naphthalenes, and other chlorinated aromatic compounds. A characteristic epithelial hyperplasia and hyperkeratosis can be produced on the inner surface of the rabbit ear by such compounds (1, 2), and a difference in intensity of response has been noted and suggested as a basis for comparative tests (2). Experimental studies heretofore (1–7) have been, however, directed chiefly to the ability or the failure of various materials to produce this effect in experimental animals and in man, and in delineating its gross and its histological features; these studies have used either material of unstated origin, or else mixtures (*e.g.* Halowax, 1014). We have attempted to study the phenomenon of acnegen-induced hyperkeratinization on the rabbit ear in a quantitative fashion by recovering and weighing the keratin formed after applying known amounts of a single, well-characterized chemical compound under controlled conditions. To recover keratin a new technic was developed based on the resistance of this material to digestion by pepsin. As test compound we have chosen 2,3,7,8-tetrachlorodibenzo-*p*-dioxin, which has been reported to be so potent that painting the rabbit ear three times with a 0.05%-0.001% solution was sufficient to produce the acneform response (7). With a compound of such potency, the expected effects could be produced without the necessity of applying the material in an ointment or as a crust, circumstances which would have made very uncertain the quanity actually in contact with the skin.

EXPERIMENTAL

Preliminary gross and histologic observation indicated that 0.3 micrograms applied to the rabbit's ear gave, by gross observation, a minimal follicular plugging whereas 0.02 micrograms caused no observable effect. Accordingly, 0.3 micrograms was chosen as the lowest dose; in addition dose levels of 1.0, 3.0 and 10.0 micrograms were studied.

Seven mature, white, male rabbits were used for each dose level, except in the first studied (0.3 micrograms) for which only six were used. Seven days after wax epilation †, of the inner surface of the ears, 1 ml. acetone solution of the compound was applied to one ear of each of the rabbits, and 1 ml. acetone to the other. Special effort was made to distribute the liquid uniformly over

* From the Section of Dermatology, Department of Medicine, University of Chicago, Chicago 37, Illinois.

This research was supported by the Research and Development Division, Office of the Surgeon General, Department of the Army, under Contract No. DA-49-007-MD-111 and by United States Public Health Service Medical Training Grant No. 2A-5263(C1).

Presented at the Twenty-third Annual Meeting of The Society for Investigative Dermatology, Inc., Chicago, Ill., June 26, 1962.

† With "Improved Zip."

16098

1753-(20)

THE DOW CHEMICAL COMPANY

DOW 1 1298 44

MIDLAND
February 22, 1965

"EXCITER" PROBLEM, MEETING - FEBRUARY 18, 1965

Present: V. K. Rowe
W. P. Falsey
K. C. Barrons
W. L. Corbin
R. C. Hoff
H. R. Hoyle
D. E. Pletcher
W. M. Gill
L. Silverstein
C. E. Otis
G. E. Lynn
F. C. Amstutz
E. C. Staehling

cc: J. D. Doedens

Otis introduced the meeting by indicating that recent information indicates "Exciter" components may be present in Dow 2,4,5-trichlorophenol. Bioproducts is concerned about 2,4,5-T acid, esters, formulations, silvex, ronnel, and Erbon. This meeting is to review status of our knowledge of this subject, potential hazards, possible effect on Dow image, legal implications, and need for possible quarantine. These basic decisions are to be made without consideration of economic impact.

Summarizing past experiences, V. K. Rowe said that Dow had no chloracne problems related to trichlorophenol production for 25 years until process changes were effected in the spring of 1964. Based on research information accumulated over the years, some ideas have been put together regarding the likely compounds which give rise to this problem. The 2,3,5,8-tetrachlorodibenzodioxin has been pretty well established as a possible contaminant. Also, there is some indication of the possible presence of the 2,3,7,9 derivative and two other components designated as "Unknown No. 1" and "Unknown No. 2".

Hoyle said that the rabbit test will detect 4 ppb of the 2,3,7,8-dioxin. VPC will detect 0.2-0.5 ppm of the 2,3,7,8-dioxin in trichlorophenol. Also, VPC will detect about 5.0 ppm of the 2,3,7,8-dioxin in 2,4,5-T acid. (By phone on Feb.19,1965, Hoyle indicated to the writer that it is now felt that VCP will detect 1.0 ppm.)

In samples checked from October, 1964, to the present, no dioxin was found in trichlorophenol samples from 349 bldg. using the animal test. The animal test has indicated some activity in one sample of a filter cake which represented impurities removed in T-acid processing.

16089

DOW 1 129845

Setting of limits of analytical methods and correlation of VPC and animal test data are not complete.

Eighteen applications at 4 ppb in TCP represents the threshold for animal reaction.

Ten exposures at 0.5 ppm in TCP gives a mild reaction.

One exposure at 40 ppm in TCP gave a positive reaction.

It is encouraging to note that exacting tests have indicated no evidence of liver damage in exposed operators. It was agreed that Rowe should move ahead with contact with U.S. Public Health Service and Department of Agriculture representatives as soon as our scientific data is better correlated. Full cooperation will be offered as regards analytical, testing, and toxicological information. Process details are not to be revealed. Also, contacts are to be made with other companies who manufacture trichlorophenol, namely, Diamond, Monsanto, Hercules, and Hooker. Rowe planned to contact his counterpart in Monsanto on February 19, 1965. Where he does not have established contacts, he will suggest that Lew Corbin take care of discussions. Thompson-Hayward do not make trichlorophenol but are aware of and have been in discussion with Dow on this problem.

It was agreed that V. K. Rowe should serve as Dow contact for any inquiries which come to anyone in Dow regarding the "Exciter" problem. Also, Rowe is to serve as a focal point and advise regarding possible hazards which may result from the sale of trichlorophenol derived bioproducts until this situation is fully resolved. Staehling summarized analytical data on process samples of trichlorophenol as follows:

sensitivity → (ppm) 1.0 1.0

Date	Unknown No.1	2,3,7,9 Dioxin	2,3,7,8 Dioxin	Unknown No. 2	Calc'd as Dioxin 1 + 2
1963: June	<1	<1	<1	6	6
Oct.	3	<0.5	<0.5	14	17
1964: Feb.	2	<1	<1	2	4
June	3	<1	6	4	7
Sept.	25	<1	<1	20	45
Nov.	3	<0.5	0.8	5	8
Dec.	3	<0.5	<0.5	3	6
1965: Jan.7	8	<0.5	0.8	9	17
Feb.8	10	<0.5	<0.5	20	30
Feb.15	3	<1.0	<1	10	13

DOW 1 129846

Staehling indicated that there was some evidence that through a process change he could come up with trichlorophenol showing less than 1 ppm of "Unknown No. 1", each of the dioxins, and "Unknown No. 2".

After considerable discussion it was agreed to set a specification of trichlorophenol for bioproducts use to include the designation that none of the dioxins should be present within a sensitivity of 1 ppm and that the specification for the two "Unknowns" should be 10 ppm maximum. This specification should continue until suitable correlation between bio-assay and analytical data are shown to warrant changing the specifications.

Ronnel made from trichlorophenol (sample, 2-8-65) (30 ppm of No. 1 plus No. 2) will be quarantined unless the bio-assay is negative. It was agreed not to use the 2-15 sample of trichlorophenol (13 ppm) for ronnel manufacture.

A pre-shipment sample of Monsanto T-acid showed 10 ppm of the 2,3,7,8-dioxin. Analytical data will be obtained on the shipment received and compared with Dow reference samples before a decision is made whether to use or return the T-acid. (NOTE: Hoyle indicated on Feb. 19, 1965, that this shipment showed 3 to 7 ppm of the dioxin.

It was agreed to meet Feb. 22, 1965, to decide on the disposition of the Monsanto T-acid.

DEP

D. E. Pletcher
Bioproducts Department

DEP/mm

TCDD Toxicity
Non-teratogenic,
Except from 2,4,5-T
Advisory Committee Report
p. 33 et seq.

DOW 1129422

Of TCDD. TCDD has been recognized as a contaminant of commercial preparations of 2,4,5-T for several years; however, there has been no extensive study of its toxicity. According to Johnson[13] the acute LD_{50} for TCDD is 0.022-0.045 mg/kg in the rat and 0.0006 mg/kg in the guinea pig. Because of the high potency of this compound in the guinea pig, these experiments were repeated and confirmed by

Dow Chemical Co. Some information on the toxicity of TCDD is available from a study of TCDD teratogenic effect in the rat (see Section II B, p. 44). No evidence of clinical effect on the dams was found at doses of 0.0005 mg/kg/day, although embryotoxicity appeared in litters of females given 0.000125 mg/kg/day. Some vaginal hemorrhage was caused by 0.002 mg/kg/day and 0.008 mg/kg/day caused pallor and debilitation.

DOW 1 129423

As far as occupational exposure is concerned, it is clear that any danger of 2,4,5-T formulations resides in their TCDD content. The primary manifestation of industrial TCDD intoxication is chloracne, an easily detected, in fact highly disfiguring, dermatitis. It is significant that this condition has not been a problem in factories producing 2,4,5-T with a low content of TCDD, nor among persons who apply the herbicide as a part of their regular occupation. It is therefore highly unlikely that exposure to traces of TCDD will have any effect on persons who use 2,4,5-T formulations occasionally or who merely encounter possible traces of it in the environment.

Data are too limited for a firm conclusion but there is no evidence to suggest that TCDD as a contaminant in 2,4,5-T is likely to be encountered by animal or man in sufficient dosage to cause toxic reactions.

References Cited in Section II A

1. Drill, V. A. and T. Hiratzka, 1953. Toxicity of 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid. A Report on Their Acute and Chronic Toxicity in Dogs. AMA Arch. Indust. Hyg. Occup. Med., 7:61-67.

1805

ICM C. ... T.N. 32 15 (1)

C... K.N. 66651-1

DOW 766318

MATERIAL: 33.3 Isobutyl Hexyn-3-ol

(3 mg/kg) dose .01 % SOLUTION IN: ☐ UNDILUTED ☐ WATER ☒ CORN OIL

ROUTE: ☐ INT ☐ ... ☐ ... ☐ ... ☐ ... ☐ ... ☐ ... ☐ ...

CAGE	CAGE FOOD	...	...	...	...	...	...	...	DATE
						5/21	5/21	5/21	
159-1	10/31/66	5410♂	1.68	[illegible]	.53	1.77 1.76	2.16 2.00	[illegible]	
		5450♂	1.61	[illegible]	1.05	1.74 1.96	2.01 2.25	2.53	
		6470♂	1.66	[illegible]	2.03	1.75 1.90	2.28 2.55	2.75	
		5470♂	1.63	[illegible]	4.11	1.90 1.95	2.16 2.41	2.50	
		5[illegible]♂	1.85	[illegible] .50	4.25	1.78 2.12	2.36 2.50	2.64	
									sac. 11/4/66 BT
159-6		6010♂	1.80	.0316	.57	1.85 1.80	1.83 1.86	1.86	
		6030♂	1.66	.0316	.52	1.71 1.51	1.95 1.20	dead 10/31/66 BT	
		6060♂	1.80	.0316	.57	1.90 dead	10/31/66 BT	extreme pelvic limb	
		6150♂	1.78	.0316	.56	1.91 1.95	1.83 2.00	2.17	
		6180♂	1.90	.0316	1.0	1.95 2.06	2.16 2.30	2.53	sac. 11/4/66 BT
184-1		6760♂	1.65	.063	1.04	1.65 1.68	1.47 1.56	dead 10/31/66 BT	
		6720♂	1.80	.063	1.13	1.92 1.79	1.33 1.43	1.60	
		6740♂	1.62	.063	1.02	1.71 1.94	1.45 1.57	1.72	sac. 11/4/66 BT
		6760♂	1.70	.063	1.07	1.80 dead	10/31/66 BT		[illegible]
		6780♂	1.72	.063	1.08	1.82 1.81	1.80 1.94	2.10	sac. 11/4/66 BT
		Tissues taken on all animals sacrificed							
		on 11/4/66. BT							
OBSERVATION BY						BT	BT BT	BT	

COMMENTS ON BACK OF THIS PAGE

SIGNED Bruce Tinker DATE 11/4/66

FORM C-1099 PRINTED IN U.S.A. 58-62 (FRONT)

16104

METHODOLOGY

Animals subjected to acute oral toxicity studies are fed by single-dose intubation using a calibrated syringe and a suitable rubber catheter. In the case of small rats or mice a blunt hypodermic needle is substituted for the catheter. Materials are administered in the undiluted form or prepared as suspensions or solutions in water or corn oil. All animals are weighed and observed at intervals over a two-week post-feeding period or until any weight loss is stabilized and the animals appear healthy. Pathological observation is made on all animals.

Animal's weight at time of administration to dosing.

DATE

DOW 766319

ITEM GRADE _____ ACCOUNT NO. _____ T NO. [illegible]

CLIENT NO. _____ K NO. 6681-1

MATERIAL 2,3,7,8 - Tetrachlorodibenzo-p-dioxin

(Micrograms/kg) dosage 101

% SOLUTION IN: ☐ UNDILUTED ☐ WATER ☒ CORN OIL

SEXES: ☐ FAT ☐ OILY ☐ [illegible] ☐ [illegible]

AGE: ☐ MALE ☐ FEMALE

☐ WITH FOOD ☐ (OTHER)

CAGE	BIRD NO.	[illegible]	[illegible]	[illegible]	INITIAL WEIGHT (GM.)					DATE
					10/13 1.1	10/21 1.13	11/4			
84-C	10176	[illegible]	0.52	.126	1.57	1.66 1.58	1.25 1.27	1.36	sac.	11/4/66 BT
		6[illegible]	1.64	.126	2.07	1.72 1.68	1.23 1.22	dead	11/2/66	BT X
		6[illegible]	1.73	.126	2.17	1.77 1.61	1.42 1.42	10/24/66	BT	X
		6[illegible]	1.73	.126	2.19	1.78 1.69	1.51 1.42	1.32	sac.	11/4/66 BT
		6[illegible]	1.61	.126	2.07	1.87 1.82	1.72 1.68	1.66		
110-1		677 OF	1.60	.252	4.04	1.63 dead	10/10	Kept	loose	BT
		6710F	1.82	.252	4.59	1.84 1.82	1.80 dead	10/28/66	BT	X
		6[illegible]	1.78	.252	4.49	1.73 1.76	dead	10/26/66	BT	[illegible]
		6[illegible]	1.78	.252	4.49	1.51 1.69	1.40 1.37	dead	10/31/66	BT X
		6[illegible]	1.70	.252	4.28	1.72 1.53	1.34 1.47	1.54	sac.	11/4/66 BT
110-2		6[illegible]	1.70	.50	8.50	1.70 1.55	1.26	dead	10/27/66	BT X
		6[illegible]	1.64	.50	8.20	1.60	dead	10/[illegible]/66	BT	[illegible]
		6850F	1.85	.50	9.40	1.83 1.80	1.62 1.52	1.45	sac.	11/4/66 BT
		6[illegible]	1.75	.50	8.75	1.73 1.65	1.35	dead	10/28/66	BT
		6[illegible]	1.92	.50	9.60	1.88 1.68	1.56 1.46	dead	11/2/66	BT X

Tissues taken on all animals sacrificed on 11/4/66. BT

OBSERVATION BY: BT BT BT BT

COMMENTS ON BACK OF THIS PAGE

SIGNED Bruce Tinker DATE 11/4/66

FORM C-1670 PRINTED IN U.S.A. 10-62 (FRONT)

DOW 766320

16106

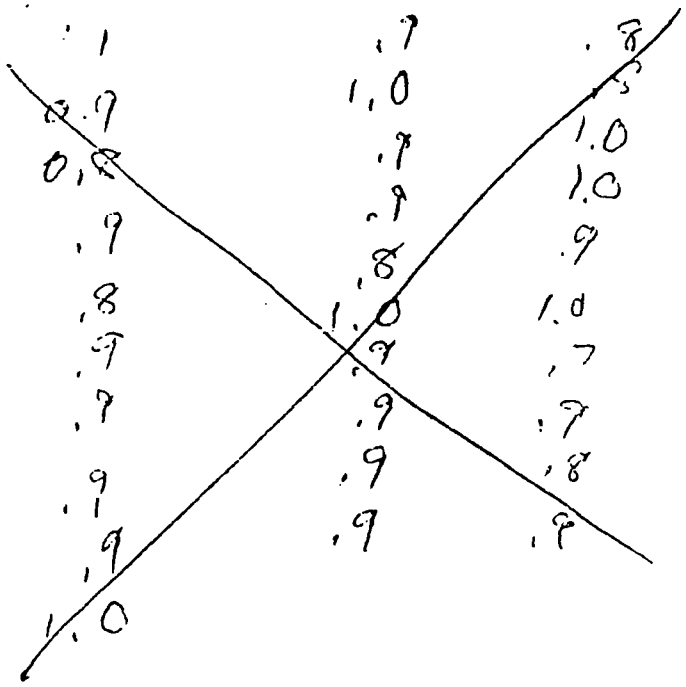
METHODOLOGY

Animals subjected to acute oral toxicity studies are fed by single-dose intubation using a calibrated syringe and a suitable rubber catheter. In the case of small rats or mice a blunt hypodermic needle is substituted for the catheter. Materials are administrated in the undiluted form or prepared as suspensions or solutions in water or corn oil. All animals are weighed and observed at intervals over a two-week post-feeding period or until any weight loss is regained and the animals appear healthy. Pathological observation is made on representative animals.

Animals to be fasted overnight prior to dosing.

DATE	COMMENTS
6/8/66	[illegible]

DOW 766321



DOW 766329

Photographs

110-9	10/21/66	ear (3)
		belly (3)
110-9	10/25/66	whole rabbit from front (3)
		ear close-up (3)

Midterm # and Code #

control (no TCOBD)
TCOBD acute oral

591-01	10/3	10/4	10/21	10/28	11/4
159-1	1.1	1.0	1.1	1.0	0
	~~1.0~~				
	BT	BT	BT	BT	
595-01	10/3	10/4	10/21	10/28	
159-2	0.9	1.0	1.0	0.9	
	~~2.0~~				
	BT	BT	BT	BT	
647-01	10/3	10/4	10/21	10/28	
159-3	0.8	0.9	0.9	1.0	
	BT	BT	BT	BT	

DOW 7663322

597 or 159-4	10/7	10/14	10/21	10/28
	0.9	0.9	1.0	1.1
	BT	BT.	BT	BT
549 or 154-5	10/7	10/14	10/21	10/28
	0.8	0.9	0.8	1.0
	BT	BT	BT	BT

Signed Bruce Tinker Date 11/4/66

.0316 mgm/kg TCDBD

acute oral

DOW #66323

Animal # and Cage #						
601 ♂ 154-6	~~0.7~~ 0.9 BT	10/14 0.9 ~~norm~~ BT	10/21 0.9 norm BT	10/24 norm BT	10/28 1.0 norm.	
605 ♂ 154-7	~~0.7~~ 0.9 BT	10/14 0.9 BT	10/21 0.8 BT	10/24 norm. BT	0.9 norm	Dead ~~10~~ 11/1/66. Chest cavity fille with clear fluid. Liver: modt. to severe necrosis of large areas of liver. Sub/cut edema at sternum. Some fluid in abdominal cavity. BT & SS
606 ♂ 154-8	~~1.0~~ 0.9 BT	~~10/14~~ dead	10/15/66 BT			Extreme fatty liver. SS

15 cc 15 1-9	10/7 0.9 BT	10/14 0.9 BT	10/21 1.0 BT	10/24 norm BT	0.9 norm.
15 cc 15 1-10	10/7 1.6 BT	10/14 1.0 BT	10/21 1.1 BT	10/24 norm BT	1.1

BT

Signed Bruce Tinker Date 11/4/66

.063 mg/kg TCDBD

acute oral

Animal # and Cage #							
670 ♂ 184-1	Wt 10/7 0.9 BT	10/14 0% BT	10/21 0.9 5 hyp. at base of ear BT	10/24 5 hyp. base of ear edema & scabbing BT	10/28 0.9 Base of ear tag-like swellings. Vesicles.	Dead 10/31/66. BT	DOW 466324
672 ♂ 184-2	Wt 10/7 1.0 BT	10/14 1.0 BT	10/21 0.9 BT	10/24 norm BT	10/28 0.9 norm	11/4 0.9 Appears normal.	
674 ♂ 184-3	Wt 10/7 0.9 BT	10/14 0.9 ul green belly BT	10/21 0.8 4 hyp. base of ear BT	10/24 4 hyp. base of ear scab-sev swelling BT	10/28 1.1 Base of ear swollen	0.9 Base of ear sl. swollen. 3 hyperemia.	
676 ♂ 184-4	Wt 10/7 0.9 BT	~~0 hrt~~	Dead	10/14/66	BT	Liver enlarged. Foca hemorrhagic necrosis & diffuse fatty changes. ++++ SS	
678 ♂ 184-5	Wt 10/7 0.8 BT	10/14 0.9 ul green belly BT	10/21 0.9 norm BT	10/24 norm BT	10/28 1.0 BT	1.1 Appears normal. BT	

Signed Bruce Tinker Date 11/4/66

16110

.126 mg/kg TCDBD

acute oral

DOW

766325

Animal # and Cage #						
680 ♂ 184-6	10/7 1.0 BT	10/14 0.9 sl. gran. belly BT	10/21 1.4 Ship base of ear wart-like projections on belly BT	10/24 4 ship base of ear slowly swollen BT scab in ear canal	10/28 2.5 Base of ear & eyelids swollen. many vesicles.	11/4 2.5 Ears scabbed shut. Eyes swollen shut. Loss of hair around head & neck. Insides have scabbed. BT
682 ♂ 184-7	10/7 0.9 BT	10/14 0.9 sl. gran. belly BT	10/21 1.0 same eruptions on belly as above. BT	10/24 4 ship base of ear slowly swollen scab in ear canal. BT	10/28 1.7 same, with vesicles on belly.	Dead 11/2/66. Liver dark, with modest focal necrosis present BT & SS
684 ♂ 184-8	10/7 0.9 BT	10/14 1.0 BT	10/21 0.9 Eruptions on belly	Dead	10/24/66	BT
686 ♂ 184-9	10/7 0.9 BT	10/14 1.0 sl. ship on ear & gran belly BT	10/21 2.4 Eruptions on belly. BT 5 ship on ear	10/24 4 ship base of ear slowly swollen - BT	10/28 2.7 Ears swollen & scabbed shut. Vesicles on belly	11/4 2.6 Animal prostrate. Ears swollen & scabbed shut. Eyes swollen shut. Loss of hair around ears & neck. BT
688 ♂ 184-10	10/7 0.9 BT	10/14 1.0 sl. gran belly BT	10/21 1.0 BT	10/24 norm BT	10/28 norm BT	11/4 Appears normal. BT

Signed Bruce Tinker Date 11/4/66

.252 mg/kg TCDBD

acute oral

DOW 466326

Animal # and Cage #						
6770F 110-1	10/7 0.8 BT	died 10/10/66 BT fatty liver SS				
6710F 110-2	10/7 0.5 BT	10/14 0.9 5 loss on ear BT	10/21 2.0 moult follicultis BT 5 loss + 4 edema	10/24 whole ear severely involved. BT	dead 10/28/66. Lung +++, pneumonia, congestion & edema. Liver ++ One lobe showed necrosis & fibrosis. Kidney ++ degeneration & congestion. Bloody urine. FO	
6730F 110-3	10/7 1.0 BT	10/14 0.9 BT	10/21 1.6 5 loss on ear. Eruptions on belly BT	dead 10/17/66 BT Severe liver necrosis. Peritonitis. SS		

7580 110-4	10/7 10 0 BT	10/14 0.9 al. green belly BT	10/21 1.0 norm. BT	10/24 4 hyp Base of ear somewhat swollen. Many vesicles on belly. BT	10/28 2.5 Base of ear severely swollen & scabbed shut.	Dead 10/31/66. Liver: areas of focal necrosis. ++ Fluid in peritoneal & thoracic cavities
6740 110 5	10/7 0 9 BT	10/14 0.7 al. green belly BT	10/21 2.0 Sl. more exudative Eruptions on belly. BT	10/24 5 hyp Base of ear somewhat swollen. Few vesicles on belly. BT	10/28 1.0 ← same BT	11/4 0.9 Base of ear somewhat swollen. Vesicles subsided. Loss of hair on back of neck. BT

Signed Bruce Tinker Date 11/4/66

16112

Photographs

110-2	10/25/66	close-up of ear (3)
110-6	10/25/66	under chin (3)
		back of neck (2)

DOW 766327

.50 mg/kg TCDBD
acute oral

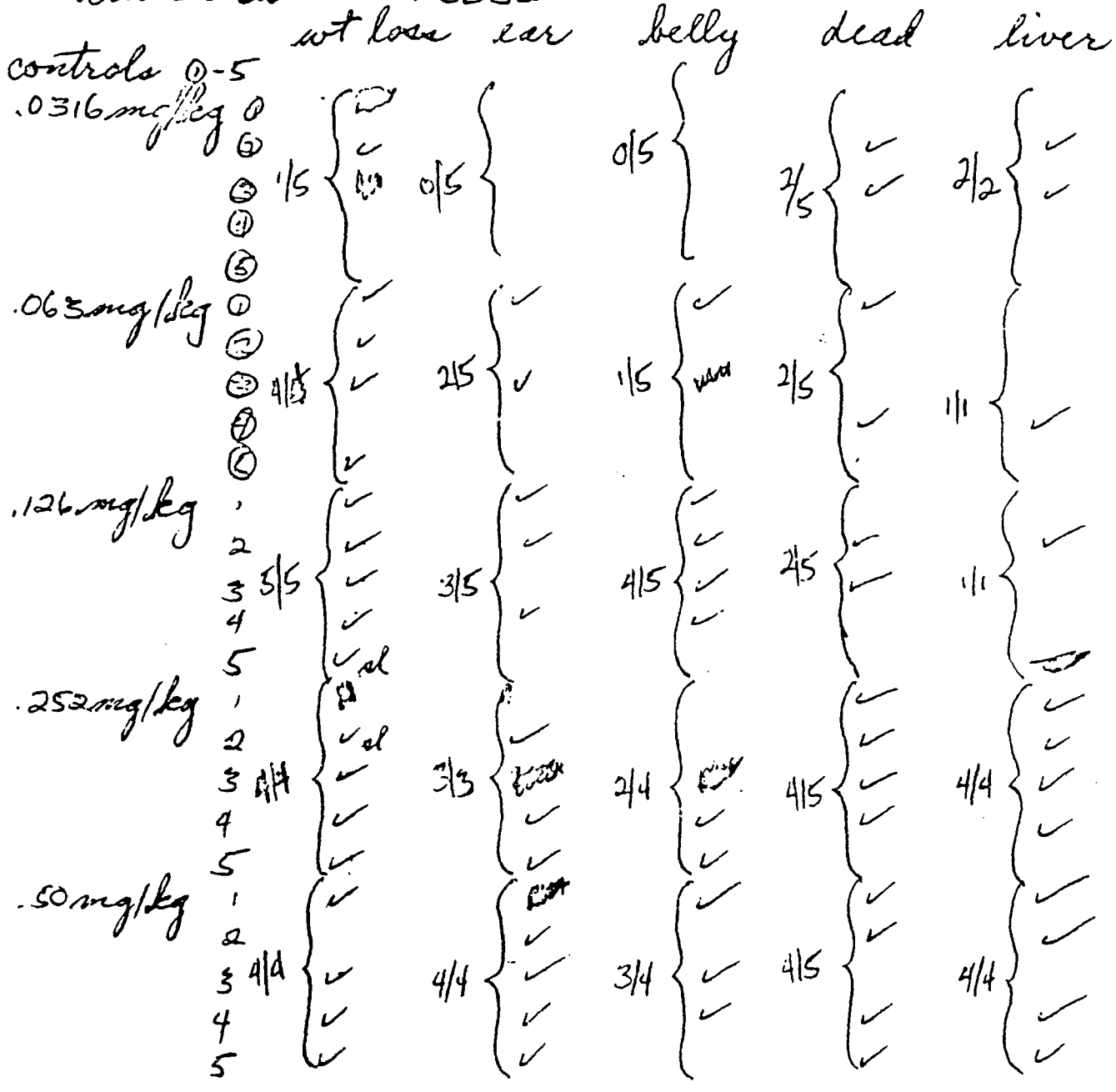
DOW 766328

Animal # and Cage #						
654 ♂ 110-6	10/7 1.0 BT	10/14 1.0 sl. queasy belly BT	10/21 2.0 Slupp on ear Eruptions on belly. BT	10/24 Slupp. Ear base severely swollen. Many & large vesc. on belly. BT		dead 10/27/66 Liver dark with focal areas of necrosis present & moderate fatty change. Moderate lung congestion. SS & BT
683 ♂ 110-7	10/7 0.7 BT	~~10/14~~ died	10/14/66	BT		Liver enlarged. Focal Hemorrhagic necrosis & diffuse fatty changes. ++++ SS
685 ♂ 110-8	10/7 .9 BT	10/14 0.9 sl. queasy belly BT	10/21 1.1 3 lupp on ear BT	10/24 Base of ear swollen. Few vesc. Pussy blood coming out of ear. BT	10/28 0.9 Base of ear & eyelids swollen.	11/4 0.9 Base of ear severely swollen & scabbed over. Eyes swollen shut. Loss of hair behind neck, around ears & eyelids. BT
656 ♂ 10-9	10/7 0.8 BT	10/14 0.9 5 lupp. on ear. sl. queasy belly BT	10/21 2.7 Base of ear severely swollen & has been bleeding. BT	10/24 Base of ear severely swollen & blocked with scab. Many vesicles on belly. BT		Dead 10/28/66. Lung congest & edema. Liver congestion areas of necrosis. Kidney congestion & degeneration with bloody urine. Severe peritonitis. FO
687 ♂ 10 10	10/7 0.9	10/14 0.9 sl. queasy belly BT	10/21 1.0 BT	10/24 4 lupp. Base of ear somewhat swollen. No vesicles BT	10/28 1.0 = same BT	Dead 11/2/66. Liver. Moderate to severe large areas of necrosis.

Signed Bruce Tinker Date 11/4/66

16114

Acute oral TCDBD



DOW 766330

DOW 757112

349 BUILDING

Sodium trichlorophenate from 199 Building is received ~~by~~ at 349 Building where it is neutralized, ~~which effects~~ effecting a ten-fold concentration of the material to provide crude trichlorophenol. This "wet feed" is ~~past~~ passed through a drying column; the "dry oil" is then distilled in two color stills.

The first animal tests run on ~~349~~ daily samples in 1957 indicated activity only in the tar from the color stills. This was mild activity, less than that demonstrated by the caustic insoluble oil at 199 Building Similar samples taken in early 1964 again showed the tar from the color stills to be active. Samples taken in October 1964 showed activity in the wet feed, in the dry oil and again in the tar from the color stills. The product was still not active on animals. Samples taken in November 1964 showed activity again in the wet feed, the dry oil and the product ~~was~~ were inactive. The degree of activity in the crude material was less than that in the October samples.

The contaminated phenate ~~mentioned above,~~ found in 199 Bldg at the end of October 1964 was processed by 349 Building. ~~The activities of two~~ two pipe fitters and an operator at 349 in early November ~~involved~~ cleaning lines and changing valves in lines which had carried the contaminated phenate. The actual exposure that brought on chloracne in the 349 Building personnel is not definitely established but this is the most likely situation which could have caused it.

In early November, Clare Bailey, 349 Building Superintendent, issued a written sheet describing precautions to be taken because of the

potential hazard. This resulted from the 1964 experience and was promulgated on Bailey's initiative as a precautionary measure. About the first of this year, 1965, objections by workmen to working in 349 caused the adoption of full-scale protective measures in that building in regard to the trichlorophenol process. Further complaints caused the extension of such precautions to the entire reactor room, including the bisphenol process. Wipe tests eventually indicated that the bisphenol area was free of contamination. In fact, only limited areas of the trichlorophenol section show contamination. Clean-up and further wipe tests are being delayed until process equipment has been moved to a new location outside the work area of 349 Building. Extensive clean-up will be necessary in the alleyway behind 349 because of contamination from the trichlorophenol tar.

A health supervisor is now stationed at 349 Building and full precautions are being taken on any jobs where exposure is possible. Only three cases of chloracne have shown up at 349 thus far, none since the incident in early November.

Composite samples of finished trichlorophenol from 349 have been run on animals at either a 10% or 1% concentration in Dowanol PM. Under these conditions, no finished product from 349 has shown activity on animals. Quite recently, VPC has succeeded in lowering sensitivity for TCBD in trichlorophenol to about 1 ppm. They have since analyzed some retainer samples and found some with detectable TCBD plus unknowns that appear in the same place as the chlorinated benzofurans. These samples were extracted with chloroform for analysis. The chloroform extracts, when placed on rabbits' ears, are showing activity.

DOW 16118

EVERGREEN 4-6430

INDUSTRIAL TOXICOLOGY LABORATORIES

FORMERLY SMYTH LABORATORIES

INDUSTRIAL TOXICOLOGY, INVESTIGATIONS OF PUBLIC HEALTH, INDUSTRIAL HEALTH, AND BACTERIOLOGICAL PROBLEMS, CLINICAL AND LABORATORY INVESTIGATIONS OF PHARMACEUTICAL PRODUCTS.

34TH STREET BELOW CHESTNUT STREET
PHILADELPHIA 4, PA.

HENRY FIELD SMYTH, M.D., Dr. P.H.
CONSULTANT
JOSEPH STAMBUL, M.D.
INTERNIST
JOSEPH V. KLAUDER, M.D.
DERMATOLOGIST
JEFFERSON H. CLARK, M.D.
PATHOLOGIST
HERMAN A. SHELANSKI, PH. D.
TOXICOLOGIST

HERMAN A. SHELANSKI
DIRECTOR

June 26, 1950

DOW MN073280 255635

Mr. V. K. Rowe
The Dow Chemical Company
Midland, Michigan

Dear Mr. Rowe:

I wish to submit the following report on the patch test study made with the materials listed below.

1. 2,4-Dichlorophenoxyacetic acid (Sample #1)
2. 2,4-Dichlorophenoxyacetic acid (Sample #2)
3. 2,4-Dichlorophenoxyacetic acid, Mixed alkanol amine salts.
4. Mono, Di, and Tripropylene glycol, Butyl Ether (B) 2,4-Dichlorophenoxyacetate.
5. TCX No. 9, Esteron 44
6. TCX No. 10, Esteron 245T
7. 2,3,4,6-Tetrachlorophenol, Sodium Salt.
8. α-Bromo-p-nitroacetophenone

200 unselected human subjects (100 males and 100 females) were studied. The material to be tested was placed in contact with the skin of the back and allowed to remain for a period of 5 days. At the end of this time, the patches were removed and the reactions noted. Three weeks after removal of the first series of patches, the material was again applied to the backs of the same subjects and allowed to remain in contact with the skin for a period of 48 hours. At the end of this time, the patches were removed and the reactions noted. The results obtained are as follows.

1. 2,4-Dichlorophenoxyacetic acid (Sample #1) - 100% as supplied

First Application -
1 male had a 1+ reaction, 99 males had no reaction.
None of the females showed any reaction.

Second Application -
None of the males and none of the females showed any reaction.

2. 2,4-Dichlorophenoxyacetic acid (Sample #2) - 100% as supplied

First Application -
5 males had 1+ reactions, 10 males had 2+ reactions. 85 males had no reaction.

16119

Second Application -
None of the males and none of the females had any reactions.

3. 2,4-Dichlorophenoxyacetic acid, Mixed alkanol amine salts - 10% aqueous
First Application -
3 males had a 1+ reaction, 1 males had a 2+ reaction. 96 males had no reaction.
2 females had 2+ reactions. 98 females had no reaction.

Second Application -
1 male had 2+ reaction. 99 males had no reactions.
None of the females had any reactions.

4. Mono, Di, and Tripropylene glycol, Butyl Ether (B) 2,4-Dichlorophenoxyacetate - 100% as supplied
First Application -
None of the females and none of the males had any reactions.
Second Application -
None of the males and none of the females had any reactions.

5. TCX No. 9, Esteron 44 - 100% as supplied
First Application -
None of the males and none of the females had any reactions.

Second Application -
None of the males and none of the females had any reactions.

6. TCX No.10, Esteron 245T - 100% as supplied
First Application -
None of the males and none of the females had any reactions.

Second Application -
None of the males and none of the females had any reactions.

7. 2,3,4,6-Tetrachlorophenol, Sodium Salt - 1% aqueous
First Application -
3 males had 1+ reactions, 2 males had 2+ reactions. 95 males had no reactions.
5 females had 1+ reactions, 2 females had 2+ reactions. 93 females had no reactions.
Second Application - None of the males or females had any reactions.

8. a-Bromo-p-nitroacetophenone
First Application - ~~0%~~ Butyl Carbitol Acetate 0.1 % (See letter of 9-20-50 from Skeletal. T2 1 9-6-5)
None of the males and none of the females had any reactions.

Second Application - 1% Butyl Carbitol Acetate
2 males had 1+ reactions. 98 males had no reactions.
2 females had 1+ reactions. 98 females had no reactions.
Rechecked later - same results

From the above information, it appears that substances 1, 4, 5, 6, and 8 do not appear to be primary irritants. Substances 2, 3, and 7 have mild primary irritant action if kept in contact with the skin for a prolonged period of time. None of these materials

DOW 7556636

tend to appear to be sensitizers.

Dr. Klauder's report will follow ours.

If there is any further information which we can supply, please do not hesitate to call upon us.

Very truly yours,

INDUSTRIAL TOXICOLOGY
LABORATORIES

Herman A. Shelanski,
Director

HAS/ers
Encl.

DOW 755637

MN073280 DOW 755596

November 2,1962

Mr. George W. Mullins
Resident Claim Manager
Employers Mutuals of Wausau
1717 West End Building
1717 West End Avenue
Nashville 3, Tennessee

Dear Mr. Mullins:

This is in reply to your letter of October 26, 1962, asking us for what information we may have relative to the toxicity of 2,4-D and 2,4,5-T herbicides.

The toxicological information we have on this type of chemical is very well described in our publication entitled, "Summary of Toxicological Information on 2,4-D and 2,4,5-T Type Herbicides and an Evaluation of the Hazards to Livestock Associated with Their Use". This publication gives the basic toxicological information on these materials. A copy of this reprint is enclosed. Also, about 10 years ago, we published an article entitled, "Health Hazards Associated with the Handling and Use of Herbicides". While this deals with materials other than 2,4-D and 2,4,5-T type herbicides, you may find it interesting. A copy of this is also enclosed. Because we have received a number of questions regarding the possible effects of swallowing substantial amounts of the material accidentally, we have prepared a sheet giving the symptoms, possible effects, and suggested treatment for the benefit of poison control centers and physicians. A copy of this is also enclosed, but I do not know whether it will be of any use to you. It is entitled, "2,4-D and Related Type Herbicides, Toxicological Information and Suggestions Regarding Treatment for Persons Swallowing 2,4-D and Related Type Herbicides.

Generally speaking, 2,4-D and 2,4,5-T present very little hazard from the standpoint of the user and practically none to those who might accidentally be exposed to a small amount of spray drift. The claims presented by the lady mentioned in your letter sound to me to be preposterous. Her difficulty must have been caused by something entirely unrelated to 2,4-D or 2,4,5-T. How her drinking water supply could have been contaminated to any measurable degree by drift is inconceivable.

You ask about our experience with people in the plant who have been handling and making these materials for many years. I have

consulted with our Medical Department and they recall no cases of any significant systemic effects. They have, of course, seen an occasional case of transitory dermatitis, eye irritation, respiratory irritation due to dust, and I believe one case of nausea, but they doubt that this was due to these materials. This type of experience is typical of most chemical manufacturing operations.

I trust this information will be helpful to you.

Sincerely yours,

V. K. Rowe
Biochemical Research Laboratory
1701 Building

VKR/jd

Encl.

cc: C. G. Kramer, M.D.
D. G. Kochlinger
V. K. Rowe (2)
T23.14-11-20
Correspondence

DOW 255597

EMPLOYERS MUTUAL LIABILITY INSURANCE COMPANY OF WISCONSIN
EMPLOYERS MUTUAL FIRE INSURANCE COMPANY
HOME OFFICE: WAUSAU, WISCONSIN

1877

Address Reply To
EMPLOYERS MUTUALS OF WAUSAU
1717 WEST END BUILDING
1717 WEST END AVENUE
NASHVILLE 3, TENNESSEE
PHONE ALPINE 5-7477

Dr. V. K. Rowe
Dow Chemical Company
Agricultural Chemicals Dept.
Midland, Michigan

October 26, 1962

MN073280

DOW 755593

Dear Dr. Rowe:

We are the insurers for a number of electric power distributors who use chemical spray for weed and brush control along their right of ways. We are concerned in this particular with the chemical formulation known as 2,4-D and 2,4,5-T.

We have been presented a claim by a lady that some of this chemical sprayed along the right of way in the vicinity of her residence found its way into her drinking water supply by some unexplained means, presumably by drift, resulting in nausea, bronchitis and defective vision. It is further alleged that she breathed some of the "fumes" from this spray.

We understand that you have research papers on this subject which would be of a great benefit to us in defense of this type of claim, and particularly with reference to workers in some of your plants where this chemical is made who have undergone periodic examinations with no ill effects noted.

We would appreciate your kindness in supplying us with whatever material you may have on this subject, and any further personal comments you have to make would be appreciated.

Very truly yours,

GMullins/f

Resident Claim Manager

RECEIVED
OCT 31 1962
Biochem. Res. Lab.

16124

MN073280 DOW 755561

March 31, 1958

Cecil M. Kohn, M.D.
Suite 630
Professional Building
Kansas City, Missouri

Dear Dr. Kohn:

This is in reply to your letter of March 24th inquiring as to whether we have any information concerning the toxicity of 2,4-D to humans. Insofar as I know there has never been a case of death or serious illness due to 2,4-D or related products. There have been a few cases of dermatitis alleged to have been caused by this type of material. In each case where a thorough investigation has been possible it has been found that the causative agent was the oils used as diluents rather than to the 2,4-D or 2,4,5-T type materials. This is consistent with the negative results of sensitization studies conducted on human subjects with 2,4-D and 2,4,5-T derivatives commonly used as herbicides.

I believe the publication from our laboratory entitled, "Summary of Toxicological Information on 2,4-D and 2,4,5-T Type Herbicides and an Evaluation of the Hazards to Livestock Associated with Their Use," contains most of the pertinent references dealing with the toxicity of these materials. We also sponsored some work on dogs and this is reported in an article by Hill entitled, "Toxicity of 2,4-Dichlorophenoxyacetic Acid and 2,4,5-Trichlorophenoxyacetic Acid. A Report on Their Acute and Chronic Toxicity in Dogs." Reprints of both of these articles are enclosed.

The laboratory data we have obtained together with the very broad experience in the use of these materials convinces us that they are among the least hazardous of the chemicals used around the home or farm.

If you have specific questions which you believe we might be able to help you with, please do not hesitate to contact us.

Very truly yours,

V. K. Rowe
Biochemical Research Laboratory
12-634 Building

VKR/ba

Enc.

T 23.14-11-E

cc: V. K. Rowe
W. W. Allen
Clyde Bryant

CABLE ADDRESS DOWCHEMCO
BRANCH SALES OFFICES
NEW YORK CITY
SAN FRANCISCO
PHILADELPHIA
LOS ANGELES
WASHINGTON
SAINT LOUIS
CLEVELAND
HOUSTON
CHICAGO
ATLANTA
SEATTLE
DETROIT
BOSTON

THE DOW CHEMICAL COMPANY
MIDLAND · MICHIGAN

DOW

July 18, 1951

Mr. Charles L. Hovey
Eastern States Farmers' Exchange
West Springfield, Massachusetts

Dear Charlie:

Your letter of July 12 to Clyde Bryant has been referred to me. We know of no recent work at Ohio State University which shows that certain crops may become poisonous when treated with 2,4-D. I believe the report in which you are interested was made by Dr. C. J. Willard of Ohio State University at the December, 1950 Seventh Annual Meeting of the Northcentral Weed Control Conference in Milwaukee. This paper is found in the proceedings of this conference, pages 110 through 112. I am enclosing, herewith, a copy of the portion of the paper which bears particularly on the problem which you have brought up, also a list of the pertinent references.

You are acquainted with the work undertaken at Michigan State with our various herbicides, which showed that there is little, if any, danger in grazing treated pasturage. It is quite apparent from the evidence to date, that the important hazard with regard to the use of herbicides, particularly of the growth control type, is a possible indirect effect as pointed out by Dr. Willard in his article. Since there appears to be some evidence that normally unpalatable vegetation may be made attractive to grazing animals by 2,4-D or 2,4,5-T sprays, it would seem logical to keep animals off the treated area for a certain period of time. If the increased palatability is of a temporary nature and disappears in 72 hours or less, it would be logical to advise keeping stock away from the treated area for three or four days after spraying.

With brush and trees, the evidence is as meager as it is with herbaceous, annual or perennial weeds. It may be possible that animals should be kept away from treated brush of certain species for longer than three to four days. In any event, where cherry is present, there is little question but that the safe policy is to advise keeping cattle out of the treated area until the foliage dies.

DOW MN073280 7554451

July 18, 1951

As to the hazards involved in nitrate poisoning, we have little if any more information than is available in the excerpt from the article by Dr. Willard. It is surprising that there is so little definite information to go on, but studies of this sort are not too easy to undertake.

Up to the present time, we have not put a warning statement on our labels with regard to keeping livestock away from treated areas. However, there is a feeling that we may adopt some sort of a precautionary statement.

Sincerely yours,

THE DOW CHEMICAL COMPANY

Lawrence Southwick
Agricultural Chemicals Section
Technical Service
and Development

jl

DOW 7554452

COPY

COPY

MN073280 DOW 7554443

MISSOURI STATE HIGHWAY DEPARTMENT

Jefferson City, Missouri

April 2, 1951

MATERIALS: Handling Herbicides

Mr. L. L. Coulter
Research and Development
Dow Chemical Company
Midland, Michigan

Dear Sir:

We have recently received a report from our Workmen's Compensation Department to the effect that one of our maintenance men had a leg infection which was caused by contact with the chemicals used in spraying tree stumps. The chemical used was 2,4,5-T mixed with diesel oil (one pint to five gallons). This is the first report of such injury to come to our attention, and we would like to have your opinion as to the relative possibility of skin irritations that might be expected from the ordinary handling of 2,4-D, 2,4,5-T and T.C.A. and your suggestions as to safeguards to use in the handling of these chemicals.

Very truly yours,

(signed)

F. V. Reagel
Engineer of Materials

jg

Indirect Effects of Herbicides

C. J. Willard

Under "Indirect Effects of Herbicides" we have included all effects other than direct damage to the weeds or crop plants to which they are applied. The discussion will concern the newer organic herbicides only. This is an extensive litrerature on the effects of sodium chlorate and arsenicals, which does not need reviewing here.

The indirect effects we have considered are:

1. Effects outside the treated field due to drift or vapors of the herbicides.
2. Unforseen effects on the "balance of nature".
3. Destruction of wild flowers, game cover, etc., in roadside spraying.
4. Poisonous effects of herbicides.
   a. Direct effects
   b. Poisoning from poisonous plants, not usually eaten, but eaten after spraying.
   c. Poisoning from ordinarily harmless plants made poisonous by the effect of sprays on them.
5. Effects on the composition of crops.

DOW 7554434

The first problem, drift of dust, droplets, or vapors to adjacent or not-so-adjacent susceptible plants, has been so widely discussed that I will take time to make just one point about vapors. Any effect of vapors must be more or less a mass action effect. Dr. Alban and I have used experimental amounts of esters around susceptible plants for years, with no effects on them. But those were small plots. If you spray 10 acres with esters and wind moves slowly across this area (Have you noticed how almost every story of vapor damage begins "There was hardly any wind"?) the air may easily pick up a toxic load of vapor.

As weed control men, we must constantly emphasize the hazards involved in using these extremely powerful chemicals, and personally and by precept, see to it that every precaution is taken against damage where no damage is intended. This cannot be said too often, or made too emphatic. Carelessness in application has already resulted in some severely restrictive laws, and others will follow if they seem to be needed.

Several articles have appeared expressing the fear that we "weed men" will run wild and exterminate local flora of all kinds in all places. Killing plants even with modern chemicals, still takes time and material, which cost money. We are not likely to use either when we do not have an economic reason for doing so. In so doing we may kill some plants that we do not intend to kill, simply because they are in bad company.

We should not be, nor [illegible] or oblivious to changes in the balance of nature. We should study these changes and, so far as possible, avoid recommendations that produce unfavorable changes, or suggest ways of overcoming them. For example, repeated roadside spraying may take out legumes and, on many soils, require nitrogen fertilization to maintain a healthy sod.

The complaint about killing wild flowers along roadsides is one to which we must, at least partially, plead guilty, but without apologies. Some of these complaints remind me of the anti-vivisection groups throughout the country, to whom, if one were to judge by either actions, the life of a stray dog is more sacred than the lives of children. We will always have some unreasonable complaints. So far as in us lies, we should be "wise as serpents and harmless as doves". We should listen to these complaints, study them, and then, if the weight of evidence is then on the side of weed control, answer them cooperatively and courteously and go ahead.

DOW 7554435

Dr. E. P. Sylwester has done this beautifully in his roadside spraying campaign in Iowa. He started this in cooperation with the Highway Department in 1948. The unsightly unremoved dead brush along the road started critics talking so vigorously that the campaign was "soft-pedaled" in 1949, resulting in poorer results and greater expense for the Highway Department.

So, this spring, Dr. Sylwester arranged for a printed debate between himself and one of his active opponents in the Sunday Des Moines Register and Tribune, which has a Sunday circulation of nearly half a million. He also defended the roadside spraying program at some 50 meetings throughout the state. As a result, the Iowa roadside spraying program is going ahead full steam, with relatively little criticism. His handling of the program was a model of public relations for all of us.

So far as anything I might say here defending roadside spraying is concerned, I could only say what Dr. Sylwester said, or say it less well. That article has been reprinted several times, most recently in "Down to Earth" (Fall, 1950). I suggest that you get it. It is a trenchant defense of the beauty, safety, and economy of grasscovered roadsides, produced by spraying, as contrasted with the miles of poison ivy, wild carrot, brush, hemp, ragweed, etc., etc., which still corstitute the average roadside.

Poisoning by herbicides is a more serious matter. Fortunately our problems are small compared to those of the entomologists, but we definitely do have problems. In the first place, any new thing gets blamed for anything that happens in its vicinity. When Dr. Sears of our Department made a week's tour of northwestern Ohio in 1947 putting on a few spraying and dusting demonstrations with 2,4-D, two reports of poisoning followed - both later shown to be erroneous, but illustrating the tendency to blame troubles onto anything new. Last summer I investigated a case of alleged sheep poisoning by a

"brush killer" used by an electric coop. Investigation showed that there was no reasonable chance that the spraying was responsible, but the spray truck passed along a little before the sheep took sick, so the two things were linked, both by the farmer and by the veterinarian.

Of the new herbicides, TCA is caustic to the skin and the dinitros are definitely poisonous. The DN's are a serious hazard to the person applying them - death has resulted from long exposure to air contaminated by droplets of DN spray - but so far no complaints of livestock poisoning from DN's have come to our attention, and grazing experimentally sprayed areas with them at four times the recommended doses has given no serious results (8). The same is true of TCA (3).

There have been a few reports of persons who are allergic to or affected by 2,4-D. There is no reason to suppose that at least some of these reports are not true. These are important to the few individuals concerned, and worthy of serious study, but we now have experience enough to say that they are highly exceptional. To help put the matter in proper perspective, in my personal experience I know more people who are poisoned by eggs than I have definitely heard of being unfavorably affected by 2,4-D.

Many tests (8, 11, 12) have shown that stock will consume grass sprayed with 2,4-D and 2,4,5-T readily and without injury under ordinary conditions. These materials have been directly fed to milkcows without injurious effects on the cattle. Most reports also state that there was no effect on the milk - Dr. Grigsby in a letter reporting unpublished work this summer (1950) says that cows fed large quantities of 2,4-D gave milk with a characteristic phenol flavor during the feeding and for 12 hours after the last dose of 2,4-D had been given.

These experiments and the experiences of thousands of farmers with sprayed pastures pretty well dispose of direct 2,4-D toxicity to stock. However, almost all of us have seen sprayed plants eaten that had not been eaten before - all the way from S. M. Raleigh's case of rodents choosing to eat rows of corn treated pre-emergence with 2,4-D to stock eating Canada thistles (C. B. Lee), velvet leaf (J. L. Hutchison), jimson weeds (F. W. Slife), wild parsnip (Geo. Briggs, C. J. Willard), sunflowers (T. F. Yost), docks (Crafts and Harvey), round leaved mallow (N. E. Shafer) and unpalatable weeds in general (Chas. J. Gilbert, H. E. Wood).

Clearly, if any of these weeds were injurous or poisonous, their sudden consumption after spraying could cause sickness or death of the stock. Actual instances are few but suggestive. C. J. Gilbert mentions cases of poisonous range weeds causing death when eaten after spraying. Both Warren Shaw and Oliver Lee report poisoning of cattle from 2,4-D-sprayed wild cherry and if this

DOW 755436

definitely poisonous plant is present in an area to be sprayed, it would certainly be well to keep stock out of it. J. H. Fleetwood reports hearing of a case of swine eating sprayed mature cockle-burs with severe sickness following. Crafts and Harvey (4) make a similar report concerning sprayed thistles eaten by lambs. Virgil Freed mentions several instances of ragwort poisoning livestock after being sprayed with 2,4-D. He writes: "Normally, livestock become poisoned on this plant only when they are forced to graze it by lack of other vegetation, particularly in the late winter and early spring months. However, in the instances mentioned above, it was a case of the animal actually seeking out this plant two or three days after spraying and consuming sufficient quantities to be toxic. Plants that had been treated for a period longer than one to three days did not appear to be palatable to the animal and the initial palatability was attributed to the marked increase in sugar that accompanies application of 2,4-D to these plants. Normally the higher sugar content extends from 24 to 72 hours after spraying, thereafter declining steadily." A wise precaution, therefore, would be to keep stock out of sprayed pastures containing any poisonous weeds for 3 to 4 days to a week.

DOW 7554437

Much the most serious possible 2,4-D poisoning effect that has been reported was due to the accumulation of nitrates in sugar beet leaves that have been sprayed with sub-lethal amounts of 2,4-D. For these data I am almost entirely indebted to an unpublished paper submitted to "Science" by L. M. Stahler and E. Whitehead, which I am abstracting in part.

Nitrate poisoning of stock has been known for some time (1, 2, 5, 7) especially in connection with oat hay. Beet leaves from a Manitoba field damaged by airplane spraying of an adjacent wheat field in 1948 caused the death of several steers. A local veterinarian recognized the symptoms as those of nitrate poisoning. The standard treatment, injection with methylene blue, revived living but recumbent steers within an hour. The leaves were analyzed for nitrate and showed nitrate levels far above those known to be toxic.

In August, 1949, 375 acres of beets on seven farms in North Dakota were sprayed with insecticide contaminated with 2,4-D (15). Through the cooperation of Dr. Helgeson and associates, Dr. Stahler obtained samples of beet leaves from each field and also from three adjacent untreated fields. The leaves from untreated fields averaged 0.22 percent KNO_3; the average of the seven treated fields was 4.5 percent KNO_3, with a range of 1.81 to 8.77 percent. Over 1.5 percent of KNO_3 in the dry matter of forage is considered toxic.

The toxicity of nitrates is not direct, but in the rumen of ruminants, nitrates are reduced to nitrites, which so alter the blood that it cannot carry oxygen from the lungs to the tissues. The blood becomes brown instead of red, giving a gray-tan appearance to the mucous membranes of the nose and mouth. Unless treated

promptly, death may come in a few hours or less.

Pigweed (Amaranthus retroflexus) and lambsquarters (Chenopodium album) are common weeds closely related to beets which Olson and Whitehead (13) at South Dakota have shown to accumulate nitrates in hazardous amounts, even without 2,4-D treatments. J. W. Zahnley writes me of unpublished work by Harold Jones of Kansas State College, showing that lambsquarters, pigweed, and smartweed (Polygonum sp.) treated with 2,4-D were extremely high in nitrate, while those not treated contained very little. This seemed to be due to the 2,4-D checking the assimilation of nitrates into protein, so that nitrate accumulated in the treated plants, but was used up in the untreated ones. It would surely be risky to spray a pasture containing these weeds. Presumably, if they are killed outright, they will not accumulate more nitrate before death, but with the practical irregularities in spraying we cannot be sure that this will occur. Corn, sorghum, proso, sunflower (Helianthus spp.) gumweed (Grindelia spp.) and spiderwort (Tradescantia spp.) have also been indicated (12) as containing lethal quantities of nitrate under some conditions.

Mr. C. D. Floyd, State Apiarist for Minnesota, reports one rather clear case of poisoning of bees pasturing on mustard sprayed after it came in bloom. He was not able to duplicate the result the next year, even by feeding the bees syrup contaminated by supposedly the same 2,4-D formulation used the year before. However, something killed the bees the preceding year (1948). Mr. Floyd said no reports of injury were received in 1950. Apparently the trouble is at least unusual.

There will be many of these problems, real and imaginary, as weed control continues to develop. Our attitude, as good weed control men, must be to consider every complaint, even those which look absurd, cautiously and carefully, neither saying "Impossible" without investigation, or fearfully accepting unproven responsibility.

There have been many reports of 2,4-D increasing the protein content of grain (6, 9, 14). In general, these effects seem physiologically to be like the increased protein obtained in a dry season: that is, the protein elements in the grain are laid down first, and if the grain does not "fill" well, it will be higher in protein than one that does fill. Usually, at least, the protein per acre has not been increased by spraying.

However, many of the effects on the vegetative parts of plants (10, 3) are not so simple and a wide field is open for the study of the effects of 2,4-D and related compounds on forage. The vegetable men know well the greater development of fiber in asparagus, etc., following 2,4-D treatments. In field crops we have no data as yet, but the problem is highly important.

DOW 755438

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Subject: Toxicity of 2,4-D and 2,4,5-T

(1) On page 8 of your paper entitled "The Use of 2,4-D, 2,4,5-T and Other Herbicides for Vegetation Control on Transmission Rights-of-Way" there appears under V item 3, a section entitled "Nonpoisonous". We have looked this section of the paper over and would suggest that this section be replaced by the following including the seven references given:

"3-Toxicity

2,4-D and 2,4,5-T are both low in toxicity to men and animals and are easy to handle and use with safety.

"Mitchell and co-workers (1) report that cattle and sheep were pastured on areas freshly sprayed with 2,4-D without ill effects; that a cow was given daily doses of 5.5 grams of 2,4-D for 106 days without ill effect or contamination of milk; and that a man took 0.5 gram of 2,4-D daily after a meal for 21 days without ill effects.

"Bjorn and Northen (2) report their work with chicks and in conclusion state: 'The question might be raised as to the possibility of chicks being killed by feeding on plants which had been sprayed with 2,4-D. At a spraying rate of 1 lb. of 2,4-D/acre, a chicken weighing 1 kg. would have to consume all of the 2,4-D applied on 72 sq. ft. within a day or two to obtain a lethal dose.'

"The results of studies on several species of laboratory animals reported by Hill and Carlisle (3) and by Bucher (4) indicate that 2,4-D is low in toxicity when taken by mouth for all the species studied.

"The effect of 2,4-D on fish has been reported by Harrisson and [illegible] (5). Lynch et al, in a report of the U.S. Dept. of Interior, Fish and Wildlife Service (February, 1947), conclude that 2,4-D presents no problem in concentrations usually needed for the control of aquatic weeds.

"Eide (6) studied the effects of various insecticides on honeybees and concluded that 2,4-D was "non-toxic" under practical conditions of use.

"The toxicological information available on 2,4-D is much more extensive than that on 2,4,5-T, probably because it is the older of the two products. All the toxicological information available (7), however, indicates that 2,4,5-T is essentially the same as 2,4-D in toxicity to warm blooded animals.

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2,4-D Toxicity I-Toxicity Toward Certain Species of Fish
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(6) Paul M. Eide
Insecticides on Honeybees
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(7) Unpublished Data
Biochemical Research Department
The Dow Chemical Company"

(2) If you have any questions regarding this suggested substitution we would be glad to discuss them with you.

Sincerely yours,

V. K. Rowe
Biochemical Research Department

VKR/mg
cc: L. W. Southwick

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