

MR 279511

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September 24, 2003 SEP 27 AM 9:15



~~CONFIDENTIAL~~

By Hand Delivery

Document Processing Center (7407)
Office of Pollution, Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N. W.
Washington, DC 20460
Attention: Section 8(e) Coordinator

01 SEP 27 AM 9:17

Re: **TSCA Section 8(e) Submissions**

Dear Sir/Madam:

3M Company ("3M") requests that EPA place the attached studies in the TSCA Section 8(e) docket. We have included a master index for these studies identifying the study title, test substance and CAS number. A Confidential Business Information (CBI) version of this index and the studies also is being submitted today pursuant to EPA procedures. 3M has not provided CBI substantiation with this submission, but would be willing to do so at the Agency's request.

3M has concluded that data in these studies may not be, strictly speaking, "corroborative" of previously reported or published information as defined in EPA's reporting guidance or otherwise potentially may warrant 8(e) submission based on EPA's reporting guidance.

3M appreciates EPA's attention to this matter. Please contact the undersigned if you have any questions or require further information regarding this submission.

Very truly yours,

Katherine E. Reed (9.24)

Dr. Katherine E. Reed, Ph.D
Staff Vice President
Environmental Technology and Safety
Services
(651) 778-4331
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2004 DEC 8 PM 4:16



Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
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Primary Eye Irritation Study - Rabbits				
Guinea Pig Contact Dermal Irritation/Sensitization	20% solids (Eihomeen S/12 1.0M with diethyl sulfate 0.94M); 80% water [Eihomeen S/12 = R-N(EI)X(C2H4OH)2 where R=C18 with 1-2 double bonds]		20% (61791-24-0 with 64-67-5); 80% 7732-18-5	
Primary Eye Irritation Study - Rabbits	Butanoic acid, heptaffluoro-, calcium salt		2366-98-5	
Acute Oral Toxicity Screen with T-2712CoC in Albino Rabbits	perfluorohexanoic acid		307-24-4	
Primary Skin Irritation Test with T-2725Ec (Repeat Application) in Albino Rabbits				
Acute Ocular Irritation Test with T-2725Ec in Albino Rabbits				
Sensitization Study with T-2741AC in Albino Guinea Pigs				
Oral Rangelinder Study of T-3140BS in Pregnant Rats	1-[3'-(perfluorooctanesulfonate) anilino amidel]-2-potassium 3,4,5,6-tetrachlorophthalate		57589-85-2	
Oral Rangelinder Study of T-3139BS in Pregnant Rats	80% 1-[3'-(perfluorooctanesulfonate) anilino amidel]-2-potassium 3,4,5,6-tetrachlorophthalate; 5% C7 homolog; 5% C5 homolog; 5% C4 homolog; 5% C6 homolog		80% 57589-85-2; 5% 68541-01-5; 5% 68541-02-6; 5% 68568-54-7; 5% 68815-72-5	
Acute Ocular Irritation Test with T-2997CoC in Albino Rabbits	perfluoroethylcyclohexylsulfonic acid diethanol amine salt		sell of 133201-07-7 and 111-42-2	
Sensitization Study with T-3386 in Albino Guinea Pigs				
In Vitro Microbiological Mutagenicity Assays of 3M Company's Compound T-3411				

COMPANY SANITIZED

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

<p>Acute Oral Toxicity Screen with T-3448 in Albino Rats In Vitro Microbiological Mutagenicity Assays of 3M Company's Compound T-3516</p>	<p>68% poly(oxy-1,2-ethanediyl), alpha-12-ethyl[[heptadecylfluorooctyl)sulfonylamino]ethyl-omega-hydroxy-; 12% polyethylene glycol; 7% water; 4.86% poly(oxy-1,2-ethanediyl), alpha-12-ethyl[[pentadecylfluorohexyl)sulfonylamino]ethyl-omega-hydroxy-; 4% residual organic fluorochemical; 3% heptadecylfluoro-1-octanesulfonic acid; 0.81% poly(oxy-1,2-ethanediyl), alpha-12-ethyl[[undecylfluoropentyl)sulfonylamino]ethyl-omega-hydroxy-; 0.3% 1,4-dioxane; 0.2% n-ethylperfluorooctanesulfonamideethyl alcohol; 0.03% linear n-ethyl perfluorooctanesulfonamide</p>	<p>68% 29117-08-6; 12% 25322-68-3; 7% 7732-18-5; 4.86% 56372-23-7; 4.05% 68298-79-3; 3.24% 68298-81-7; 3% 1763-23-1; 0.81% 68298-80-6; 0.3% 123-91-1; 0.2% 1691-99-2; 0.03% 4151-50-2</p>
<p>Acute Dermal Toxicity Study with T-3451 in Albino Rabbits Acute Oral Toxicity - Method, Summary, Pathology: Primary Dermal Irritation - Method, Summary: Primary Eye Irritation - Maximization - Method, Summary Acute Oral Toxicity - Method, Summary, Pathology: Primary Dermal Irritation - Method, Summary: Primary Eye Irritation - Method, Summary;</p>	<p>C8F17SO2N(CH3)Na</p>	<p>Unknown</p>
<p>Dermal Sensitization Study in Guinea Pigs, Maximization Test - Method, Summary</p>		
<p>4 Hour Acute Aerosol Inhalation Toxicity Study with T-3825 in Rats Primary Eye Irritation/Corrosion Study in Rabbits</p>		
<p>4-Hour Acute Aerosol Inhalation Toxicity Study with T-3825 in Rats</p>		

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

T-3820: Acute Inhalation Toxicity Test				
T-3821: Acute Inhalation Toxicity Test				
T-3845 Acute Inhalation Toxicity Test	heptafluorobutyl chloride		375-16-6	
Evaluation of the Acute Inhalation Toxicity of T-3920 in the Rat				
Primary Eye Irritation Study in Rabbits - Method, Summary	Decanoic acid, nonadecafluoro- ammonium salt		3108-42-7	
Acute Oral Toxicity Study in Rats (OECD Guidelines)	95% ammonium perfluorodecanoate: 5% ammonium perfluorooctanoate		5% 3825-26-1	
Acute Inhalation Toxicity Study with T-4129 in the Rat				
Acute Inhalation Toxicity Study with T-4130 in the Rat				
Acute Oral Toxicity Study in Rats; Acute Dermal Irritation Study in Rabbits; Acute Eye Irritation Study in Rabbits				
Dermal Sensitization Study in Guinea Pigs - Maximization Test				
Mutagenicity Test on T-4413 Mouse Lymphoma Forward Mutation Assay with Duplicate Cultures				
Acute Inhalation Toxicity Study with T-4354 in the Rat				
Primary Dermal Irritation/Corrosion Study in Rabbits				
Acute Inhalation Toxicity Study in the Rat with T-4397				
Primary Eye Irritation/Corrosion Study of T-5261 in Rabbits	lithium tetrafluoroethane-1,2-disulfonimide		Unknown	
Acute Inhalation Toxicity Evaluation on T-5231 in Rats				
4-Hour, Acute Inhalation Toxicity Study with T-5305 in Rats				
4-Hour, Acute Inhalation Toxicity Study (Limit Test) with T-5343.1 in Rats				

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

4-Hour, Acute Inhalation Toxicity Study With T-5306 in Rats			
4-Hour, Acute Inhalation Toxicity Study (Limit Test) with T-5357, 1			
Acute Dermal Toxicity Study of T-4201 in Rabbits	Lithium Bis(Trifluoromethanesulfonyl)imide	90076-65-6	
Subacute 28-Day Oral Toxicity with T-2816 by Daily Gavage in the Rat Followed by a 14 Day Recovery Period			
Subacute 28-Day Oral Toxicity with T-2816 by Daily Gavage in the Rat Followed by a 14-Day Recovery Period			
Acute Inhalation Toxicity Evaluation on T-5187 in Rats			
T-4240 4-Week Oral Toxicity Study in Rats			
Dermal Sensitization Study of T-5473 in Guinea Pigs - Maximization Test			
4-Hour, Acute Inhalation Toxicity Study With T-5698 in Rats			
Acute Inhalation Toxicity Evaluation On T-5708 in Rats			
T-5486 Assessment of Cardiac Sensitization Potential in Dogs	octafluoropropane	76-19-7	
Acute Inhalation Toxicity Evaluation on T-5655 in Rats			
T-4201 4 Week Oral Toxicity Study in Rats with 2-Week Recovery Period	Lithium Bis(Trifluoromethanesulfonyl)imide	90076-65-6	
T-5658: Eye Irritation to the Rabbit			
Acute Inhalation Toxicity Evaluation on T-5715 in Rats			
Acute Inhalation Toxicity Evaluation on T-5716 in Rats			
Acute Inhalation Toxicity Study of T-5724 in Rats			
Acute Inhalation Toxicity Study of T-5725 (Resin Solution) in Rats			

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

Acute Inhalation Toxicity Study (Limit Test) of T-5927 in Rats				
Acute Inhalation Toxicity Study of T-5928 in Rats (LC50)				
Acute Inhalation Toxicity Evaluation on T-5829 in Rats				
Single-Dose Intravenous Pharmacokinetic Study of T-5963 in Rabbits				
Single-Dose Intravenous Pharmacokinetic Study of T-6030 in Rabbits				
5-Daily Dose Dermal Absorption/Toxicity Study of T-6029 and T-6032 in Rabbits	87-93% fluorinated alkyl alkoxylates; 4-10% linear N-ethyl perfluorooctanesulfonamide; 2-4% poly(oxy-1,2-ethanediyl); alpha-[2-(ethyl[(pentadecafluorohexyl)sulfonylamino]ethyl)-omega-methoxy]; 0-4% residual organic fluorochemicals; 0-2% c8 sulfonamide; 0.1-1% 1-heptanesulfonamide, N-ethyl-	87-93% 68958-61-2; 4-10% 4151-50-2; 2-4% 68958-60-1; 0-2% 31506-32-8; 0.1-1% 68957-62-0		
Single-Dose Intravenous Pharmacokinetic Study of T-6061 in Rabbits				
Single-Dose Intravenous Pharmacokinetic Study of T-6065 in Rabbits				
Single Dose Intravenous Pharmacokinetic Study of T-6063 in Rabbits				
Acute Inhalation Toxicity Study of T-6235 in Rats				
Primary Dermal Irritation/Corrosion Study of T-6402 in Rabbits				
Dermal Sensitization Study of T-6402 in Guinea Pigs- Maximization Test (EC Guidelines)				
Acute Eye Irritation/Corrosion Study with T-6318 in the Rabbit	1-Butanesulfonic acid, 1,1,2,2,3,3,4,4,4-nonafluoro-, Sodium Salt	102061-82-5		

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

Primary Skin Irritation / Corrosion Study with T-6567 in the Rabbit (4-Hour Semi-Occlusive Application)			
Assessment of Contact Hypersensitivity to T-6318 in the Albino Guinea Pig (Maximization Test)	1-Butanesulfonic acid, 1,1,2,2,3,3,4,4,4-nonafluoro-, Sodium Salt	102061-82-5	
Single-Dose Intravenous Pharmacokinetic Study of T-6502 in Rabbits			
Single-Dose Intravenous Pharmacokinetic Study of T-6504 in Rabbits			
Single Dose Intravenous Pharmacokinetic Study of T-6506 in Rabbits			
A Study for Effect on Embryofetal Development of the Rat (Inhalation Administration)	20-80% methyl nonafluorobutyl ether; 20-80% methyl nonfluorobutyl ether	20-80% 163702-08-7; 20-80% 163702-07-6	
Bacterial Reverse Mutation Test of T-6695			
5-day Inhalation Toxicity of Perfluorocyclohexene ([]): T-6878) in Rats	70% crude perfluorocyclohexene; 30% perfluoromethylcyclopentene	70% 355-75-9	
5-Daily Dose Dermal Adsorption/Toxicity Study of T-6502 and T-6503 in Rabbits			
Primary Eye Irritation/Corrosion Study of T-6786 in Rabbits	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8	
Primary Dermal Irritation/Corrosion Study of T-6804 in Rabbits	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8	
5-Day Inhalation Toxicity Screen of HFE []	c-C6F11OCH3	4943-08-2	
Primary Eye Irritation/Corrosion Study of T-6804 in a Rabbit (OECD Guidelines)	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8	
Acute Oral Toxicity Study of T-6804 in Rats (OECD Guidelines)	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8	
Dermal Sensitization Study of T-6908 in Guinea Pigs, Mazimization Test (EC Guidelines)			

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

Eye Irritation/Corrosion Study of T-4127 in the Rabbit	N-Me Fos Amide-Triphenylbenzyl Phosphonium Chloride Complex; D-1624	31506-32-8	
Single-Dose Intravenous Pharmacokinetic Study of T-6924 in Rabbits			
Dermal Sensitization Study of T-6924 in Guinea Pigs - Maximization Test (EC Guidelines)			
Dermal Sensitization Study of T-7003 in Guinea Pigs - Maximization Test (EC Guidelines)			
Report of Sera and Liver Data for [] Monoester - Preliminary ADME Study in Rats	N-ethyl heptadecafluoro-N12-(phosphonoxy)ethyl] octanesulfonamide diammonium salt	67969-69-1	
[] Diester-Pharmacokinetic Study in Rats (Study No. T-7043.1, DT-26)	ammonium bis[ethyl(perfluorooctane)sulfonanyl]phosphate	30381-98-7	
Single Dose Intravenous Pharmacokinetic Study with T-7082 in Rabbits			
[] Monoester - Pharmacokinetic Study in Rats (Study No. T-6997.2)	N-ethyl heptadecafluoro-N12-(phosphonoxy)ethyl] octanesulfonamide diammonium salt	67969-69-1	
Determination of PFOS Presence and Concentration in Serum from the Dermal Absorption Studies of T-7106 and T-7107 in Hra:(NZW)SPF Rabbits			
Dermal Sensitization Study of T-7285.5 in Guinea Pigs - Maximization Test (EPA/OECD Guidelines)			
Twenty-eight Day Repeated-Dose Oral Toxicity Study of T-6861 in Rats	Lithium Bis(perfluoroethylsulfonyl)imide	132843-44-8	
Twenty-eight Day Repeated Dose Oral Toxicity Study of T-7005 in Rats			

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

Acute (4-Hour) Inhalation Toxicity of Test Atmospheres Obtained after Heating [] in Rats	[]	[]	[]
Toxicokinetic Study of Perfluorooctanesulfonamidoacetate ([]: T-7071.2) in Rats	perfluorooctanesulfonamido carboxylic acid	2806-24-8	[]
Acute Nose-Only Inhalation Toxicity Study of T-7087, T-7088, T-7089 and T-7090 in Rats (Limit Test)	[]	[]	[]
Acute Ocular Irritation Study of T-7485 Applied to New Zealand White Rabbits	potassium nonafluorobutanesulfonate	29420-49-3	[]
Toxicokinetic Study of Perfluorooctane Sulfonamide (PFOSA: T-7132.2) in Rats	perfluorooctanesulfonamide	754-91-6	[]
Acute Four-Hour Inhalation Study in Rats	Perfluorobutanesulfonyl Fluoride (96-98%) And Perfluorosulfolane (2-4%)	96-98% 375-72-4; 2-4% 42060-64-0	[]
Primary Eye Irritation/Corrosion Study of T-7508.2 in Rabbits	[]	[]	[]
MV31 K-Salz: Test for Primary Dermal Irritation in the Rabbit	[]	[]	[]
Assessment of Acute Oral Toxicity with T-7560 in The Rat (Acute Toxic Class Method)	[]	[]	[]
Acute Eye Irritation/Corrosion Study with T-7560 in the Rabbit	[]	[]	[]
[] Potassium bis-(perfluorobutanesulfonyl)imide (perfluorobutanesulfonyl)imide Repeat Dose ADME Study in Rats	Potassium bis(perfluorobutanesulfonyl)imide	129135-87-1	[]
Toxicity Study by Repeat Dose Inhalation Administration to CD Rats for 4 Weeks	Perfluorobutanesulfonyl Fluoride (96-98%) And Perfluorosulfolane (2-4%)	96-98% 375-72-4; 2-4% 42060-64-0	[]
A Sub-acute(28 Day) Inhalation Toxicity Study, Including a Recovery Study, with T-7479 in Rats	1,1,1,2,2,4,5,5-nonafluoro-4-(trifluoromethyl)-3-pentanone	756-13-8	[]
Xenobiochemical Receptor trans-Activation by Perfluorooctane-based Chemicals	perfluorooctanesulfonamide	754-91-6	[]



Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

	<p>84% 1-octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8- heptadecafluoro-, potassium salt; 5.5% potassium (perfluorohexyl)sulfonate; 4% potassium nonafluorobutanesulfonate; 4% potassium perfluorohexanesulfonate; 2% potassium perfluorooctanesulfonate; 0.5% unknown</p>	<p>84% 2795-39-3; 5.5% 3871-99-6; 4% 29420-49-3; 4% 60270-55-5; 2% 3872-25-1</p>
<p>Acute Inhalation Toxicokinetic Study of Perfluorooctanesulfonyl Fluoride (POSF) T-7098, 4</p>	<p>perfluorooctanesulfonyl fluoride</p>	<p>307-35-7</p>
<p>Five-Day Inhalation Toxicity Study of HFE [] in Male CD Rats</p>	<p>c-C6F11-CF2-O-CH3</p>	<p>181214-67-5</p>
<p>Acute Toxicity Screen of Perfluorocyclohexene (T-6878) in Rats</p>	<p>70% crude perfluorocyclohexene; 30% perfluoromethylcyclopentene</p>	<p>70% 355-75-9</p>
<p>Toxicokinetic Study in Rats [] (T-7056)</p>	<p>[]</p>	<p>[]</p>
<p>Assessment of Acute Oral Toxicity with T-7601, 3 in the Rat (Acute Toxic Class Method)</p>	<p>N-Methyl Perfluorobutylsulfonamide = 95% 1- Butanesulfonamide, 1,1,2,2,3,3,4,4,4- Nonafluoro-n-Methyl; 5% N-Methyl-4-Hydroxy- Perfluorobutylsulfonamide</p>	<p>68298-12-4</p>
<p>Subchronic 90-Day Oral Toxicity Study with T-7320 By Daily Gavage in the Rat Followed by a 28-Day Recovery Period</p>	<p>[]</p>	<p>[]</p>
<p>Protein Binding of Perfluorobutane Sulfonate, Perfluorohexane Sulfonate, Perfluorooctane Sulfonate, and Perfluorodecane to Plasma (Human, Rat, and Monkey), and Various Human-Derived Plasma Protein Fractions</p>	<p>84% 1-octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8- heptadecafluoro-, potassium salt; 5.5% potassium (perfluorohexyl)sulfonate; 4% potassium nonafluorobutanesulfonate; 4% potassium perfluorohexanesulfonate; 2% potassium perfluorooctanesulfonate; 0.5% unknown</p>	<p>84% 2795-39-3; 5.5% 3871-99-6; 4% 29420-49-3; 4% 60270-55-5; 2% 3872-25-1</p>
	<p>potassium nonafluorobutanesulfonate</p>	<p>29420-49-3</p>
	<p>potassium (perfluorohexyl)sulfonate</p>	<p>3871-99-6</p>

Master Index to Studies Submitted Under TSCA 8(e) by 3M Company on September 24, 2004
 (Confidential Business Information Redacted)

	potassium perfluorooctanoate	2395-00-8	
Five Day Inhalation Toxicity Study of [] Monochloride, [] and HFC225cb in Male CD Rats	C4F9-OCH2Cl c-C6F11-CF2-O-CH3 CF2ClCF2CHClF	205367-42-6 (n-isomer) and 221617-86-3 (l-isomer) 181214-67-5 507-55-1	
Toxicokinetic Screen of [] (T-7483) in Rats	C7F15C(O)N(H)CH3 84% 1-octanesulfonic acid, 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluoro-, potassium salt; 5.5% potassium (perfluorohexyl)sulfonate; 4% potassium nonafluorobutanesulfonate; 4% potassium perfluoroheptanesulfonate; 2% potassium perfluoropentanesulfonate; 0.5% unknown	89685-56-3	
Low Level Oral Perfluorooctanesulfonate (PFOS) Dose Toxicokinetic Study in Rats: Serum and Liver PFOS		84% 2795-39-3; 5.5% 3871-99-6; 4% 29420-49-3; 4% 60270-55-5; 2% 3872-25-1	

**ACUTE OCULAR IRRITATION STUDY OF T-7485 APPLIED TO
NEW ZEALAND WHITE RABBITS**

STUDY NUMBER: 132-005

SPONSOR

3M Corporate Toxicology
3M Center, Building 220-2E-02
P.O. Box 33220
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Telephone: 651-737-2678
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SPONSOR'S REPRESENTATIVE

John L. Butenhoff, Ph.D., DABT, CIH
Senior Laboratory Manager

TESTING FACILITY

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FAX: 501-397-2002

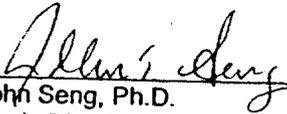
STUDY DATES

Study Initiation: June 8, 2000
Animal Phase Initiation: June 9, 2000
Animal Phase Completion: June 29, 2000
Study Completion: August 9, 2000

GLP COMPLIANCE STATEMENT

Study Number: 132-005

I certify that this study was performed in compliance with the United States Food and Drug Administration (FDA) Good Laboratory Practice Regulations (21 CFR Part 58) and OECD Regulations [C(81)30 (final)] and that the report accurately reflects the raw data.



John Seng, Ph.D.
Study Director
Primedica Redfield

8/5/00

Date

QUALITY ASSURANCE STATEMENT

Study Number: 132-005

This study has been inspected and audited by the Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) regulations promulgated by the U.S. Food and Drug Administration and OECD Regulations. The following is a record of the dates that audits/inspections were performed and reported by the QAU.

DATE OF AUDIT/INSPECTION	TYPE OF AUDIT/INSPECTION	DATES REPORTED TO STUDY DIRECTOR AND MANAGEMENT
06/08/00	Protocol	06/08/00
06/09/00	Dose Administration, Ocular Scoring, and Clinical Observations	06/09/00
07/11/00	In-Life Raw Data, Formulations Raw Data, and Tables	07/12/00
07/19/00	Draft Report	07/19/00
08/09/00	Final Report	08/09/00

The report accurately reflects the original data.

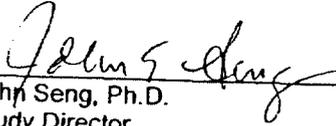
APPROVED BY:

 8/09/00
Julie Tomboli, B.S. Date
Quality Assurance Auditor
Primedica Redfield

TITLE

ACUTE OCULAR IRRITATION STUDY OF T-7485 APPLIED TO
NEW ZEALAND WHITE RABBITS

APPROVED BY:



John Seng, Ph.D. 8/9/00
Study Director Date
Primedica Redfield

TABLE OF CONTENTS

	<u>Page</u>
Cover Page.....	1
GLP Compliance Statement.....	2
Quality Assurance Statement.....	3
Title and Signature Page.....	4
Table of Contents.....	5
Study Abstract.....	6
Objective.....	7
Materials and Methods.....	7
Archival Statement.....	8
Results.....	9
Conclusion.....	9
Appendices.....	10
Appendix 1 - Individual Clinical Observations.....	11
Appendix 2 - Individual Ocular Scores and Ocular Irritation Ratings.....	14
Appendix 3 - Certificate of Analysis.....	20
Appendix 4 - Protocol and Amendment.....	22
Appendix 5 - Protocol Deviations.....	34
Appendix 6 - Key Personnel.....	36

ACUTE OCULAR IRRITATION STUDY OF T-7485 APPLIED TO NEW ZEALAND WHITE RABBITS

STUDY ABSTRACT

The objective of this study was to determine the acute effects of a single ocular application of test material to New Zealand White rabbits.

The rabbits were individually housed in stainless steel cages. Animal identification consisted of uniquely numbered ear markings and cage cards. On Study Day 1, the animals were approximately 16 weeks old.

The animals were acclimated for at least seven days prior to Study Day 1 and were examined by the Staff Veterinarian prior to being released for use on the study. Three females were assigned to the study based on the following study design:

Group Number	Group Designation	Dosage Level (mg)	Number of Animals
			Females
1	Limit Dose	100*	3

*Due to test material adherence to the weigh boats, approximately 80 mg of test material was instilled into each animal's left eye.

The test material (approximately 80 mg) was instilled into the left eye of each animal on Study Day 1. Both eyes were held closed for approximately two seconds. Both eyes were flushed with approximately 5 mL of 0.9% saline after the 24-hour score was recorded.

Observations for mortality and moribundity were recorded twice daily (a.m. and p.m.). Clinical observations were recorded predose, approximately one hour postdose, once daily thereafter, and when a change was noted. Predose clinical observations were all normal while at one hour postdose, excessive lacrimation of the left eye was recorded in all three rabbits. The excessive lacrimation of the left eye persisted throughout the remainder of the study. All animals' eyes were normal when the pretest ophthalmologic examinations were performed.

Maximum average ocular scores for 24- and 72-hours postdose were 30 and 35, respectively. By definition, the findings at 24- and 72-hours will not maintain the categories of non-irritating, practically non-irritating, or minimally irritating. Ocular irritation scores at the 7-day reading were less than 10 (scores were 6, 4, and 30 for the three rabbits) for 67% of the rabbits. Also, the seven-day mean score was 13. By definition, the resulting scores indicate that T-7485 should be rated as a moderate irritant.

In conclusion, instillation of approximately 80 mg of T-7485 produced a moderate irritant rating.

OBJECTIVE

The objective of this study was to determine the acute effects of a single ocular application of test material to New Zealand White rabbits.

MATERIALS AND METHODS

TEST AND CONTROL MATERIALS: The test material and vehicle were identified as follows:

Test Material:	T-7485 (Potassium Perfluorobutane Sulfonate, PFBS)
Lot Number:	2
Date Received:	April 6, 2000
Physical Description:	White Powder
Storage:	Room Temperature
Amount Received:	500 grams

The Sponsor assumed responsibility for characterization (identity, purity, and stability) determinations of the test material. The test material was inventoried when received at Primedica Redfield, and a record of all test material usage was maintained. The Certificate of Analysis for the test material is in Appendix 3.

The test material was used as received.

TEST ANIMALS: Healthy female New Zealand White rabbits were received from Myrtle's Rabbitry, Inc. for use on the study. The animals were individually housed in stainless steel cages. Animal identification consisted of uniquely numbered ear markings and cage cards. On Study Day 1, the animals were approximately 16 weeks old.

Teklad Certified Rabbit Diet #8630 was provided at approximately 125 grams per day, and filtered tap water was provided *ad libitum*. The feed and water were routinely analyzed for contaminants. There were no known contaminants in the feed or water that would be expected to affect the results of the study. The results of these analyses are on file at Primedica Redfield.

Environmental controls were set to maintain temperatures of 16° to 22°C (61° to 72°F) with a relative humidity of 30% to 70%. These parameters were recorded at least once daily. A 12:12 hour light:dark cycle and ten or greater air changes per hour were maintained in the animal room.

GROUP DESIGNATION AND TREATMENT: The animals were acclimated for a minimum of seven days prior to Study Day 1 and were examined by the Staff Veterinarian prior to being released for use on the study. Three females were assigned to the study based on the following study design:

Group Number	Group Designation	Dosage Level (mg)	Number of Animals
			Females
1	Limit Dose	100*	3

*Due to test material adherence to the weigh boats, approximately 80 mg of test material was instilled into each animal's left eye.

The test material (approximately 80 mg) was instilled into the left eye of each animal on Study Day 1. Both eyes were held closed for approximately two seconds. Both eyes were flushed with approximately 5 mL of 0.9% saline after the 24-hour score was recorded.

JUSTIFICATION FOR SPECIES SELECTION, NUMBER OF ANIMALS, ROUTE OF ADMINISTRATION, AND DOSE LEVEL: Rabbits are an animal model for acute toxicity studies of this type. The number of animals assigned to the study represented the minimum required to meet the objective of the study and the OECD guidelines (#405).

In the assessment and evaluation of the toxic characteristics of a substance, determination of the irritant and/or corrosive effects on the eyes is necessary. Dose levels were chosen by the OECD guideline #405.

CLINICAL OBSERVATIONS: Observations for mortality and moribundity were recorded twice daily (a.m. and p.m.). Clinical observations were recorded predose, approximately one hour postdose, once daily thereafter, and when a change was noted.

OPHTHALMOLOGIC EXAMINATIONS: An ophthalmological examination was performed by the Staff Veterinarian prior to dose administration to verify that all animals' eyes were normal.

OCULAR SCORING: Ocular irritation was scored at approximately 1, 24, 48, and 72 hours postdose and daily on Study Days 5 through 21 using the scoring scale found in the protocol (Appendix 4).

STUDY TERMINATION: On Study Day 21, the study was terminated and all animals were euthanized via an overdose of sodium pentobarbital. No necropsies were performed.

STATISTICS: No statistical analyses were performed.

ARCHIVAL STATEMENT

All original data and the original final report will be retained at Primedica Redfield's archives, located at 100 East Boone Street, Redfield, Arkansas, for a period of five years after issuance of the final report. After this time, the Sponsor will be contacted for disposition instructions.

RESULTS

CLINICAL OBSERVATIONS: Observations for mortality and moribundity were recorded twice daily (a.m. and p.m.). Clinical observations were recorded predose, approximately one hour postdose, once daily thereafter, and when a change was noted. The individual clinical observations are in Appendix 1.

Predose clinical observations were all normal, while at one hour postdose, excessive lacrimation of the left eye was recorded in all three rabbits. The excessive lacrimation of the left eye persisted throughout the remainder of the study.

OPHTHALMOLOGIC EXAMINATIONS All animals' eyes were normal when the pretest ophthalmologic examinations were performed.

OCULAR SCORING: Due to test material adherence to sample containers, only approximately 80% of the 100 mg of test material was instilled in the left eye of the rabbits. Ocular irritation was scored at approximately 1, 24, 48, and 72 hours postdose and daily on Study Days 5 through 21 using the scoring scale found in the protocol (Appendix 4). The individual ocular scores are located in Appendix 2.

Maximum average ocular scores for 24- and 72-hours postdose were 30 and 35, respectively. By definition, the findings at 24- and 72-hours will not maintain the categories of non-irritating, practically non-irritating, or minimally irritating. Ocular irritation scores at the 7-day reading were less than 10 (scores were 6, 4, and 30 for the three rabbits) for 67% of the rabbits. Also, the seven-day mean score was 13. By definition, the resulting scores indicate that T-7485 should be rated as a moderate irritant (as defined in Ocular Irritation Ratings, Appendix 2).

CONCLUSION

In conclusion, instillation of approximately 80 mg of T-7485 produced a moderate irritant rating.

APPENDICES

**APPENDIX 1
INDIVIDUAL CLINICAL OBSERVATIONS**

PROTOCOL 132-005: ACUTE OCULAR IRRITATION STUDY OF T-7485 APPLIED TO NEW ZEALAND WHITE RABBITS

APPENDIX 1: TIMED CLINICAL OBSERVATIONS - INDIVIDUAL - FEMALE RABBITS

STUDY DAY 1	DOSE GROUP 1	80 MG
RABBIT #	PREDOSE	1 HOUR POSTDOSE
1674	APPEARS NORMAL	EXCESSIVE LACRIMATION, LEFT EYE
1676	APPEARS NORMAL	EXCESSIVE LACRIMATION, LEFT EYE
1678	APPEARS NORMAL	EXCESSIVE LACRIMATION, LEFT EYE

PROTOCOL 132-005: ACUTE OCULAR IRRITATION STUDY OF T-7485 APPLIED TO NEW ZEALAND WHITE RABBITS

APPENDIX 1: CLINICAL OBSERVATIONS - INDIVIDUAL - FEMALE RABBITS

DOSE GROUP 1	80 MG	RABBIT #	DESCRIPTION
1674	SD(2- 6)		EXCESSIVE LACRIMATION, LEFT EYE
	SD(7- 12)		LACRIMATION, LEFT EYE
	SD(13- 18)		EXCESSIVE LACRIMATION, LEFT EYE
1676	SD(20)		EXCESSIVE LACRIMATION, LEFT EYE
	SD(2- 6)		EXCESSIVE LACRIMATION, LEFT EYE
	SD(7- 12)		LACRIMATION, LEFT EYE
1678	SD(13- 20)		EXCESSIVE LACRIMATION, LEFT EYE
	SD(2- 6)		EXCESSIVE LACRIMATION, LEFT EYE
	SD(7- 12)		LACRIMATION, LEFT EYE
		SD(13- 20)	EXCESSIVE LACRIMATION, LEFT EYE
		SD(21)	LACRIMATION, LEFT EYE

SD = STUDY DAY

**APPENDIX 2
INDIVIDUAL OCULAR SCORES AND OCULAR IRRITATION RATINGS**

**APPENDIX 2
INDIVIDUAL OCULAR SCORES**

Group 1 80 mg T-7485

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	1	1	2	2	4	3
1676	1	1	1	2	1	3
1678	2	3	2	2	2	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	1	1	1	2	3	3
1676	2	2	1	2	2	3
1678	1	1	1	2	2	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	1	2	2	3
1676	2	2	1	2	2	3
1678	2	3	1	2	3	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	1	1	1	3
1676	2	2	1	2	2	3
1678	2	3	1	2	3	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	1	1	2
1676	1	1	1	2	1	2
1678	2	3	1	2	3	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	1	1	2
1676	1	1	0	2	1	2
1678	2	3	1	2	3	3

**APPENDIX 2
INDIVIDUAL OCULAR SCORES**

Group 1 80 mg T-7485

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	1	1	1
1676	0	0	0	1	0	1
1678	1	3	1	2	2	1

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	1	0	1
1676	0	0	0	1	0	1
1678	1	3	1	2	2	1

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	1	0	1
1676	0	0	0	1	0	1
1678	1	3	1	2	2	1

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	1	3	1	2	2	1

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	1	3	1	1	2	1

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	1	3	1	1	2	1

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	2	3	1	1	3	2

APPENDIX 2
INDIVIDUAL OCULAR SCORES

Group 1 80 mg T-7485

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	2	4	1	2	3	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	2	4	1	2	2	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	3	4	1	2	2	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	3	4	1	2	2	3

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	3	4	1	2	3	1

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	0
1676	0	0	0	0	0	1
1678	4	4	2	2	3	1

ANIMAL NUMBER	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
	OPACITY	AREA			CHEMOSIS	DISCHARGE
1674	0	0	0	0	0	1
1676	0	0	0	0	0	1
1678	4	4	2	2	3	1

APPENDIX 2
INDIVIDUAL OCULAR SCORES

Group 1 80 mg T-7485

ANIMAL NUMBER	STUDY DAY 21					
	CORNEA		IRIS	REDNESS	CONJUNCTIVAE	
OPACITY	AREA	CHEMOSIS			DISCHARGE	
1674	0	0	0	0	0	0
1676	0	0	0	0	0	0
1678	4	4	2	2	3	1

**APPENDIX 2
OCULAR IRRITATION RATINGS**

Rating	Maximum Average Score	Definition
Non-Irritating	0.00 - 0.50	To maintain this category, all scores at the 24-hour reading must be zero; otherwise, increase category one level.
Practically Non-Irritating	0.51 - 2.50	To maintain this category, all scores at the 24-hour reading must be zero; otherwise, increase category one level.
Minimally Irritating	2.51 - 15.00	To maintain this category, all scores at the 72-hour reading must be zero; otherwise, increase category one level.
Mildly Irritating	15.01 - 25.00	To maintain this category, all scores at the 7-day reading must be zero; otherwise, increase category one level.
Moderately Irritating	25.01 - 50.00	To maintain this category, scores at the 7-day reading must be less than or equal to 10 for 60% or more of the animals. Also the 7-day mean score must be less than or equal to 20. If the 7-day mean scores are less than or equal to 20, but less than 60% of the animals show scores less than 10, then no animal among those showing scores greater than 10 can exceed a score of 30 if the category is to be maintained; otherwise, increase category one level.
Severely Irritating	50.01 - 80.00	To maintain this category, scores at the 7-day reading must be less than or equal to 30 for 60% or more of the animals. Also the 7-day mean score must be less than or equal to 40. If the 7-day mean scores are less than or equal to 40, but less than 60% of the animals show scores less than 30, then no animal among those showing scores greater than 30 can exceed a score of 60 if the category is to be maintained; otherwise, increase category one level.
Extremely Irritating	80.01 - 110.00	

NOTE: The category of the test material is not to be increased more than one level above its maximum average score.

**APPENDIX 3
CERTIFICATE OF ANALYSIS**

**APPENDIX 4
PROTOCOL AND AMENDMENT**

Primedica Redfield Protocol

Protocol Number: 132-005

ACUTE OCULAR IRRITATION STUDY OF T-7485 APPLIED TO NEW ZEALAND WHITE RABBITS

PROTOCOL NO.: 132-005

OBJECTIVE: Determine the acute effect(s) of a single ocular application of test material to New Zealand White rabbits.

LOCATION OF STUDY AND CONDITIONS OF TESTING:

It is the intention of 3M Corporate Toxicology, through the conduct of this study, to generate animal safety data that may be submitted to regulatory authorities. Primedica Redfield, 100 East Boone Street, Redfield, Arkansas, 72132, is accredited by AAALAC and licensed by the United States Department of Agriculture to conduct research in laboratory animals. All the conditions of testing will conform to the Animal Welfare Act (CFR 9) and its amendments. Primedica Redfield will follow all requirements specified in this approved protocol and all applicable governmental regulations regarding Good Laboratory Practices as well as Primedica Redfield's Standard Operating Procedures. Changes in the protocol may be made by consultation with and approval from 3M Corporate Toxicology followed by written verification of the change. 3M Corporate Toxicology reserves the right to inspect facilities and procedures used for this study by means of announced or unannounced site visits. Primedica Redfield will notify 3M Corporate Toxicology promptly by telephone prior to release of any data for review.

SPONSOR: 3M Corporate Toxicology
3M Center, Building 220-2E-02
P.O. Box 33220
St. Paul, MN 55133-3320
Telephone: 651-737-2678
FAX: 651-733-1773

SPONSOR'S REPRESENTATIVE: John L. Butenhoff, Ph.D, DABT, CIH
Senior Laboratory Manager

TESTING FACILITY: Primedica Redfield
Mail: P.O. Box 308
Deliveries: 100 East Boone St.
Redfield, AR 72132
Telephone: 501-397-2540
FAX: 501-397-2002

PERSONNEL: Study Director: John Seng, Ph.D.
Principle Investigator: Karen Tranter, B.A., LATG
Veterinarian: Allan Manus, D.V.M., M.Sc., ACLAM
Pathologist: TBD

PROPOSED STUDY DATES: Experimental Start Date: June 9, 2000
Experimental Termination Date: TBD
Draft Report Date: July 24, 2000

Primedica Redfield Protocol

Protocol Number: 132-005

1. REGULATORY COMPLIANCE AND QUALITY ASSURANCE

This study will be conducted in accordance with the following Good Laboratory Practice Regulations/Standards/Guidelines:

- 21 CFR 58
- C(81)30 (Final) (OECD)

The Quality Assurance Unit, in accordance with Primedica Redfield's Standard Operating Procedures (SOPs), will audit the protocol, study conduct, and the final report.

2. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE REVIEW

The protocol will be reviewed and approved by Primedica Redfield's Institutional Animal Care and Use Committee (IACUC) for compliance with regulations prior to study initiation.

In the opinion of the Sponsor, indicated by the signature on this protocol, the study does not unnecessarily duplicate any previous work.

3. MATERIALS

TEST MATERIAL

T-7485 (Potassium perfluorobutane sulfonate, PFBS)

IDENTIFICATION

The lot number will be listed in the raw data and final report.

PHYSICAL DESCRIPTION White powder

STORAGE CONDITIONS

The bulk test material will be stored in its original container and will be stored at room temperature. The test material will be used as received.

ANALYTICAL CHEMISTRY

The Sponsor assumes responsibility for characterization (identity, purity, and stability) of the bulk test material (including under test conditions). Information on the composition and method of synthesis of the bulk test material will be held by the Sponsor. The doses, unless otherwise stated, will be calculated assuming the test material to be 100% pure.

INVENTORY

The test material container(s) will be inventoried when received at the testing laboratory, and a record of all test material use will be maintained. The technician dosing the animals will: 1) Record the weight or volume of the test material container immediately before and after dosing; 2) Compute and record the amount used and compare it to the theoretical amount immediately after dosing; 3) Keep the formulated test material use log in the animal study books at all times; 4) The dose used must be within $\pm 10\%$ of theoretical.

Primedica Redfield Protocol

Protocol Number: 132-005

TEST MATERIAL RETENTION

Unused test material may be returned to the Sponsor or designee at the termination of the study, or retained for use on future studies. The Sponsor will be notified in advance of shipping, and a transmittal letter will accompany the shipment. The material will be packed in a suitable container to maintain the conditions specified by the Sponsor during transit plus an adequate margin of safety for any transit delays.

SAFETY PRECAUTIONS

General safety precautions as required by Primedica Redfield's policies and procedures will be followed. The Sponsor's Representative will be notified of any personnel exposures requiring a physician's examination or care.

4. ANIMALS

Species: Rabbits
Strain/Source: New Zealand White, Myrtle's Rabbitry, Thompson Station, Tennessee
Age at Initiation: At least 12 weeks
Number and Sex: Three females (female nulliparous and non-pregnant)
Identification: Indelible ink and color-coded cage card

ANIMAL HUSBANDRY

HOUSING

The animals will be individually housed in stainless steel cages. The cages conform to standards set forth in the Guide for the Care and Use of Laboratory Animals, National Academy Press, Washington, D.C., 1996.

FEED

Teklad Certified Rabbit Diet #8630 will be provided at approximately 125 grams per day. This diet is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Results of the manufacturer's analyses are on file at Primedica Redfield.

WATER

Filtered tap water will be provided *ad libitum*. Samples of the water are analyzed for total dissolved solids, hardness, and specified microbiological content and for environmental contaminants. Results of these analyses are on file at Primedica Redfield.

CONTAMINANTS

There are no known contaminants in the feed or water that would be expected to interfere with this study.

ENVIRONMENT

Environmental controls are set to maintain a temperature of 16° to 22°C (61° to 72°F) with a relative humidity of 30% to 70%. These parameters are recorded at least once daily. A 12:12 hour light:dark cycle is maintained.

Primedica Redfield Protocol

Protocol Number: 132-005

ACCLIMATION

Animals will be acclimated for a minimum of seven days prior to the study start. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test. At the request of the Study Director, excess animals may be used as replacement animals. Animals will be examined by the Staff Veterinarian prior to release of that shipment of animals for use on the study.

JUSTIFICATION FOR SPECIES SELECTION AND NUMBER OF ANIMALS

Rabbits are an animal model for acute toxicity studies of this type. The number of animals assigned to this study represents the minimum required to meet the objective(s) of the study and the OECD guidelines (#405).

5. EXPERIMENTAL METHODOLOGY**STUDY DESIGN**

Group Number	Group Designation	Dosage Level (mg)	Number of Animals
			Females
1	Limit Dose	100	3

FREQUENCY AND DURATION OF ADMINISTRATION

One hundred milligrams of test material will be instilled into the left eye of each animal on Study Day 1. Both eyes will be held shut for approximately two seconds. Both eyes will be flushed with 0.9% saline after the 24 hour score has been recorded (SOP 252.07).

JUSTIFICATION FOR ROUTE OF ADMINISTRATION AND DOSE LEVEL

In the assessment and evaluation of the toxic characteristics of a substance, determination of the irritant and/or corrosive effects on the eyes of mammals. Dose levels were chosen by the OECD guideline #405.

ANTEMORTEM OBSERVATIONS**CLINICAL OBSERVATIONS**

Observations will be performed and recorded twice daily (a.m. and p.m.) for moribundity and mortality.

Clinical observations will be performed, according to Primedica Redfield's SOPs, and recorded predose, approximately one hour postdose, once daily thereafter, and when a change is noted.

OPHTHALMOLOGIC EXAMINATIONS

An ophthalmological examination will be conducted by a staff veterinarian within 24 hours before testing to verify that the eyes are normal.

Primedica Redfield Protocol

Protocol Number: 132-005

OCULAR SCORING

Ocular irritation will be scored at approximately 1, 24, 48, and 72 hours postdose, as defined in Attachment A. If there is no evidence of irritation at 72 hours postdose, the study may be terminated. Extended observation may be necessary if there is persistent corneal involvement or other ocular irritation in order to determine the progress of the lesions and their reversibility or irreversibility.

POSTMORTEM OBSERVATIONS

MORIBUND ANIMALS AND ANIMALS FOUND DEAD

Animals unlikely to survive until the next scheduled observation will be weighed, euthanized, and necropsied. Animals found dead will be weighed and necropsied. In either case, a complete necropsy will be performed as detailed below. Euthanasia of moribund animals will be authorized by the Study Director or Staff Veterinarian with the concurrence of the Study Director.

All animals surviving to the end of the study may be returned to the testing facility's methodology population.

NECROPSY

All animals that die during the study will be subjected to a complete necropsy examination. A complete necropsy is defined as examination of the external surface of the body, all orifices, and the cranial, thoracic, and abdominal cavities, and their contents. Gross lesions will be preserved in a suitable fixative for possible histopathology; all other tissues will be discarded. Histopathology will be provided at additional expense to the Sponsor.

6. *STATISTICAL ANALYSIS*

Statistical analysis will not be required.

7. *REPORT*

An audited draft report will be sent to the Sponsor. Revisions to the initial draft report will be provided to the Sponsor by mail or fax transmission as printed copies of the corrected pages only. Additional revisions or complete copies of the revised draft reports will be provided at additional expense to the Sponsor.

Three copies (one bound, two unbound) of the approved final report will be submitted to the Sponsor approximately two weeks after approval of the draft report. The final report will include all elements required/recommended by the regulations and guidelines.

Primedica Redfield Protocol

Protocol Number: 132-005

The report will include, but is not limited to, those items listed below:

- Descriptive text of the study objective
- Summary
- Test material identification (Certificate of Analysis, stability data, and analytical analysis if any are performed)
- Methods
- Results and conclusions
- Ocular scoring
- A copy of the protocol, all protocol amendments, and all protocol deviations that may affect the integrity of the study

8. MAINTENANCE OF RAW DATA AND RECORDS

Original data or copies thereof, will be available at Primedica Redfield to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data and the original final report will be retained in the archives of the laboratory for at least five years. Wet tissues, slides, and blocks (if generated) will be retained at Primedica Redfield for one year. After one year the storage of the wet tissues, slides, and blocks will be negotiated with the Sponsor. After five years the storage of the paper data will be negotiated with the Sponsor. The Sponsor will be notified prior to disposal of any original study data.

9. QUALITY ASSURANCE REVIEW

This is to certify that this protocol has been reviewed by Quality Assurance.



Val Gartner, B.A.
Quality Assurance Auditor
Primedica Redfield

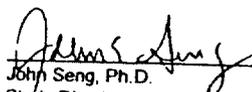
6/8/00
Date

10. APPROVALS



John L. Butenhoff, Ph.D., DABT, CIH
Senior Laboratory Manager
3M Corporate Toxicology

6/14/00
Date



John Seng, Ph.D.
Study Director
Primedica Redfield

6/8/00
Date

Primedica Redfield Protocol

Protocol Number: 132-005

**ATTACHMENT A
OCULAR IRRITATION SCORING SYSTEM**

Primedica Redfield Protocol

Protocol Number: 132-005

ATTACHMENT A
OCULAR IRRITATION SCORING SYSTEM

CORNEA	GRADE
<i>Opacity</i> : degree of density (most dense area used for reading)	
No Ulceration or Opacity	0
Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible	1*
Easily discernible translucent area, details of iris slightly obscured	2*
Nacreous area, no details of iris visible, size of pupil barely discernible	3*
Opaque cornea, iris not discernible through the opacity	4*

IRIS	GRADE
Normal	0
Markedly deepened rugae (folds), congestion, swelling, moderate circumcorneal hyperemia or injection (any of these or any combination of these), iris still reacting to light (sluggish reaction is positive)	1*
No reaction to light, hemorrhage, gross destruction (any or all of these)	2*

CONJUNCTIVAE	GRADE
<i>A. Redness</i> : refers to palpebral and bulbar conjunctivae excluding cornea and iris	
Normal Blood Vessels	0
Some blood vessels definitely hyperemic (injected)	1
Diffuse, crimson color, individual vessels not easily discernible	2*
Diffuse, beefy red	3*
<i>B. Chemosis</i> : swelling of the lids and/or nictitating membrane	
No swelling	0
Any swelling above normal (includes nictitating membrane)	1
Obvious swelling with partial eversion of the lids	2*
Swelling with lids half closed	3*
Swelling with lids more than half closed	4*

The total score for the eye is the sum of all scores obtained for the cornea, iris, and conjunctivae.

* INDICATES A POSITIVE REACTION (Federal Hazardous Substance Act Interpretation)

REFERENCES

¹ Hackett, R.B., and McDonald, T.O., Eye Irritation, *Dermatotoxicology*, Fourth Edition, Marzulli, F.N. and Maibach, H.I.: 749-815, 1991.

Primedica Redfield Protocol

Protocol Number: 132-005

ATTACHMENT A

OCULAR IRRITATION SCORING SYSTEM

CORNEA	VALUE
A. Opacity: degree of density (most dense area used for reading)	
No Ulceration or Opacity	0
Scattered or diffuse areas of opacity (other than slight dulling of normal luster), details of iris clearly visible	1*
Easily discernible translucent area, details of iris slightly obscured	2*
Nacreous area, no details of iris visible, size of pupil barely discernible	3*
Opaque cornea, iris not discernible through the opacity	4*
B. Area Involved: total area exhibiting any opacity regardless of degree	
0% - No Ulceration or Opacity	0
0-25% - One quarter or less, but not zero	1
25-50% - Greater than one quarter, but less than half	2
50-75% - Greater than half, but less than three quarters	3
75-100% - Greater than three quarters up to the whole area	4
C. Fluorescein Staining: appearance of staining	
Cornea not examined	X
No abnormal fluorescein staining	0
Fluorescein staining	1
Area Involved	
<25% - One quarter or less, but not zero	A
25-50% - Greater than one quarter, but less than half	B
50-75% - Greater than half, but less than three quarters	C
75-100% - Greater than three quarters up to the whole area	D

A x B x 5 TOTAL MAXIMUM = 80

IRIS	VALUE
A. Grades	
Normal	0
Markedly deepened rugae (folds), congestion, swelling, moderate circumcorneal hyperemia or injection (any of these or any combination of these), iris still reacting to light (sluggish reaction is positive)	1*
No reaction to light, hemorrhage, gross destruction (any or all of these)	2*

A x 5 TOTAL MAXIMUM = 10

* INDICATES A POSITIVE REACTION (FHSA Interpretation)

Primedica Redfield Protocol

Protocol Number: 132-005

ATTACHMENT A

OCULAR IRRITATION SCORING SYSTEM
(continued)

CONJUNCTIVAE	VALUE
A. Redness: refers to palpebral and bulbar conjunctivae excluding cornea and iris	
Normal Blood Vessels	0
Some blood vessels definitely hyperemic (injected)	1
Diffuse, crimson color, individual vessels not easily discernible	2*
Diffuse, beefy red	3*
B. Chemosis: swelling of the lids and/or nictitating membrane	
No swelling	0
Any swelling above normal (includes nictitating membrane)	1
Obvious swelling with partial eversion of the lids	2*
Swelling with lids half closed	3*
Swelling with lids more than half closed	4*
C. Discharge	
No discharge	0
Any amount different than normal (does not include small amounts often observed in the inner canthus of normal animals)	1
Discharge with moistening of the lids and hairs just adjacent to the lids	2
Discharge with moistening of the lids and hairs, and a considerable area around the eye ..	3
(A + B + C) x 2	TOTAL MAXIMUM = 20

The total score for the eye is the sum of all scores obtained for the cornea, iris, and conjunctivae.

* INDICATES A POSITIVE REACTION (FHSA Interpretation)

Primedica Redfield Protocol Amendment

Protocol Number: 132-005

STUDY NUMBER: 132-005
AMENDMENT: 1
STUDY TITLE: ACUTE OCULAR IRRITATION STUDY OF T-7485 APPLIED TO NEW ZEALAND WHITE RABBITS
DATE ISSUED: July 24, 2000

AMENDMENT # 1

ITEM 1: Page 8, Attachment A

DELETE

REASON: Attachment A contained two different scoring scales. The scale on pages 9 and 10 was used on this study.

APPROVALS:

John L. Butenhoff 7/26/00

John L. Butenhoff, Ph.D., DABT, CIH Date
Senior Laboratory Manager
3M Corporate Toxicology

John Seng 7/24/00
John Seng, Ph.D. Date
Study Director
Primedica Redfield

**APPENDIX 5
PROTOCOL DEVIATIONS**

PROTOCOL DEVIATIONS

There were no protocol deviations that adversely affected the integrity of the study.

**APPENDIX 6
KEY PERSONNEL**

