

Attachments to Letter to C. Auer dated May 18, 2000
Studies and Other Information on Certain
Perfluorooctane Sulfonate-Related Compounds

AR226-0963

ORIGINAL

Section No CBI

2. FOSA	Perfluorooctanesulfonamide
---------	----------------------------

8-EHQ-0800-373

Acute Toxicity

- 1) Acute Oral Toxicity Screen with T-3421 in Albino Rats, Safety Evaluation Laboratory, Riker laboratories, Inc., Project No. 0883AR0287, 3M Reference No. T-3421 (KTZ-15), January 17, 1984
- 2) Acute Ocular Irritation Test with T-3421 in Albino Rabbits, Safety Evaluation Laboratory, Riker laboratories, Inc., Project No. 0883EB286, 3M Reference No. T-3421 (KTZ-15), August 24, 1983
- 3) Primary Skin Irritation Test with T-3421 in Albino Rabbits, Safety Evaluation Laboratory, Riker laboratories, Inc., Project No. 0883AR0288, 3M Reference No. T-3421 (KTZ-15), August 9, 1983

Studies in Progress

- 1) Protocol, Feces Method Development Metabolism Study for Perfluorooctanesulfonate Derivatives [N-EtFOSE, PFOS, and FOSA], 3M Strategic Toxicology Laboratory, Study Nos., T-636.17; T-6295.21; T-7132.3; ST-41, In-Life Start Date November 22, 1999, In-Life End Date November 24, 1999
- 2) Protocol, Pharmacokinetic Study of Perfluorooctane Sulfonamide [FOSA] in Rats, 3M Strategic Toxicology Laboratory, Study Nos., T132.2; ST-39, In-Life Start Date October 4, 1999, In-Life End Date November 2, 1999
- 3) Protocol, Cell Proliferation Study with N-Ethyl Perfluorooctanesulfonamido Ethanol (N-EtFOSE; 3M T-6316.11), Perfluorooctane Sulfonic Acid Potassium Salt (PFOS; 3M T-6295.16), and N-Ethyl Perfluorooctanesulfonamide (PFOSA 3M T-7091.1) in Rats, Pathology Associates International, Study No. 1132-100

EPA-OTS



0008118001

000109

RECEIVED
00 AUG 21 AM 9:20

Acute Oral Toxicity Screen
with T-3421
in Albino Rats

BEST COPY AVAILABLE

Experiment No.:

0883AR0287

Conducted At:

Safety Evaluation Laboratory
Riker Laboratories, Inc.
St. Paul, Minnesota

Dates Conducted:

August 2, 1983 to September 7, 1983

Conducted By:

D. M. Markoe, Jr. 12/30/83
D. M. Markoe, Jr., BS Date
Toxicologist
Study Director

Reviewed By:

Karen D. O'Malley 1/12/84
K. D. O'Malley, BS Date
Senior Toxicologist
Acute Toxicology

K. L. Ebbens 1/17/84
K. L. Ebbens, BS Date
Supervisor, Toxicology Testing

dc:

M. T. Case
~~M. D. Griffith~~
W. C. McCormick

600110

Summary

The acute oral toxicity screen with T-3421 was conducted from August 2, 1983 to September 7, 1983 at Riker Laboratories, Inc., St. Paul, Minnesota using male and female albino rats ranging in body weight from 191-258 grams. The test article was administered by gastric intubation at dosage levels of 5,000, 2,000, 500 and 200 mg/kg body weight with mortalities of 10/10, 10/10, 10/10 and 2/10 noted respectively from one hour to six days post dose administration. The untoward behavioral reactions which occurred during the 14 day observation period generally consisted of hypoactivity, lethargy, prostration, diarrhea and unkempt appearance with the onset occurring from 1-30 minutes to day four post dose administration. Clonic convulsions were noted in two animals prior to death, transient alopecia was noted in two animals while dyspnea and salivation were noted in one animal during the study. All reactions subsided by day eleven or death precluded recovery. Body weight gains were noted in animals which survived the study period. Necropsies performed at termination of the study revealed no visible lesions while hyperemic or hemorrhagic lungs and/or hemorrhagic intestinal tract generally were noted in the animals which died during the conduct of the study. The acute oral LD50 of T-3421 is greater than 200 mg/kg and less than 500 mg/kg in male and female albino rats.

Introduction

The objective of this study was to determine the acute oral LD50 of T-3421 in albino rats. This study was conducted in accordance with the Food and Drug Administration's Good Laboratory Practice Regulation of 1978. The raw data generated by the Study Director and the final report are stored in the conducting laboratory's archives.

600111

Method and Results

Young albino rats^a were used in this test. All animals were held under quarantine for several days prior to testing with only animals which appeared to be in good health and suitable as test animals at the initiation of the study used. The rats were housed in stock cages in temperature and humidity controlled rooms and permitted a standard laboratory diet^b plus water ad libitum except during the 16 hour period immediately prior to gastric intubation when food was withheld.

Five male and five female rats were administered the test material at preselected dosage levels. The doses were administered at a constant volume of 10 ml/kg directly into the stomachs of the rats using a hypodermic syringe equipped with an intubation needle.

After gastric administration of the test material, the rats were returned to their cages and observed for the following 14 days. Initial, seven day and final body weights, mortalities (Table 1) and adverse reactions (Table 2) were recorded. A necropsy was conducted on all animals that died during the study as well as those euthanatized at the end of the 14 day observation period (Table 1). The protocol, principal personnel involved in the study, composition characteristics and Quality Assurance statement are contained in Appendices I - IV.

^a King Labs, Oregon, WI

^b Ralston Purina Laboratory Chow, Ralston Purina, St. Louis, MO

TABLE 1
ACUTE ORAL TOXICITY STUDY - ALBINO RATS
 with T-3421
 Mortality, Necropsy and Body Weight Data

BEST COPY AVAILABLE

Dose ^a (mg/kg)	Sex	Animal Number	Individual Body Weights (g)			Number Dead Number Tested	Percent Dead
			Test Day Number:				
			0	7	14		
5000	M	3R3553	208	(Day 6)	-	5/5	100
		3R3554	210	(Day 2)	-		
		3R3555	197	(Day 6)	-		
		3R3556	219	(1 Hour)	-		
		3R3557	214	(Day 6)	-		
5000	F	3R3573	191	(1 Hour)	-	5/5	100
		3R3574	207	(1 Hour)	-		
		3R3575	207	(1 Hour)	-		
		3R3576	192	(1 Hour)	-		
		3R3577	209	(Day 1)	-		
2000	M	3R3558	195	(Day 6)	-	5/5	100
		3R3559	207	(Day 6)	-		
		3R3560	209	(Day 6)	-		
		3R3561	217	(Day 6)	-		
		3R3562	207	(Day 2)	-		
2000	F	3R3578	199	(Day 6)	-	5/5	100
		3R3579	218	(1 Hour)	-		
		3R3580	201	(1 Hour)	-		
		3R3581	205	(Day 1)	-		
		3R3582	203	(1 Hour)	-		
500	M	3R4070	210	(Day 3)	-	5/5	100
		3R4071	212	(Day 4)	-		
		3R4072	213	(Day 6)	-		
		3R4073	217	(Day 5)	-		
		3R4074	216	(Day 4)	-		
500	F	3R4106	204	(Day 6)	-	5/5	100
		3R4107	200	(Day 4)	-		
		3R4108	205	(Day 5)	-		
		3R4109	221	(Day 3)	-		
		3R4110	198	(Day 4)	-		

000113

BEST COPY AVAILABLE

TABLE 1 (concluded)

ACUTE ORAL TOXICITY STUDY - ALBINO RATS

with T-3421

Mortality, Necropsy and Body Weight Data

Dose ^a (mg/kg)	Sex	Animal Number	Individual Body Weights (g)			<u>Number Dead</u> <u>Number Tested</u>	Percent Dead
			Test Day Number:				
			0	7	14		
200	M	3R4075	251	(Day 6)	-	1/5	20
		3R4076	236	274	297		
		3R4077	253	303	336		
		3R4078	258	302	345		
		3R4079	248	249	297		
200	F	3R4111	220	230	243	1/5	20
		3R4112	212	242	242		
		3R4113	217	236	236		
		3R4114	238	253	257		
		3R4115	225	(Day 5)	-		

Note: Figures in parenthesis indicate time of death

^a Test article administered as a suspension in water.
The approximate oral LD50 is greater than 200 mg/kg and less than 500 mg/kg in fasted male and female albino rats.

Necropsy

Necropsy of the animals which survived the observation period revealed no visible lesions while necropsy of those animals which died during the conduct of the study generally had hyperemic or hemorrhagic lungs. Hemorrhagic small intestine was noted at the 500 mg/kg dose level and one animal from the 200 mg/kg dose group. One incidence of mottled liver was noted at the 5,000 mg/kg level.

000114

TABLE 2

ACUTE ORAL TOXICITY SCREEN - ALBINO RATS

with T-3421

Summary of Reactions

Dose mg/kg	Reactions Sex	Observation Periods																
		Minutes			Number Affected/Number Dosed													
					Days													
		1-30	60	120	1	2	3	4	5	6	7	8	9	10	11	12	13	14
5000	M																	
	Hypoactivity		2/5	0/4		3/3	3/3	-	-	*								
	Lethargy	2/5	3/5	4/4	4/4	0/3												
	Salivation	1/5	0/5															
	Dyspnea		1/5	0/4														
	Diarrhea				4/4	3/3	3/3	-	-	*								
	Unkempt Appearance					3/3	3/3	-	-	*								
5000	F																	
	Hypoactivity	1/5	0/3															
	Lethargy	4/5	1/3	0/1	*													
	Prostration		2/3	1/1														
2000	M																	
	Hypoactivity		2/5	2/5	5/5	4/4	4/4	-	-	*								
	Lethargy	3/5	3/5	1/5	0/5													
	Prostration			2/5	0/5													
	Diarrhea				5/5	4/4	4/4	-	-	*								
	Unkempt					4/4	4/4	-	-	*								
	Appearance																	
2000	F																	
	Hypoactivity	2/5	1/2	0/2	1/1	1/1	1/1	-	-	*								
	Lethargy	3/5	1/2	0/2														
	Prostration			2/2	0/1													
	Diarrhea				1/1	1/1	1/1	-	-	*								
	Unkempt					1/1	1/1	-	-	*								
	Appearance																	

00011

000115

TABLE 2 (concluded)

ACUTE ORAL TOXICITY SCREEN - ALBINO RATS

with T-3421

Summary of Reactions

BEST COPY AVAILABLE

Dose mg/kg	Reactions	Sex	Observation Periods																
			Minutes			Number Affected/Number Dosed													
						Days													
			1-30	60	120	1	2	3	4	5	6	7	8	9	10	11	12	13	14
500	Hypoactivity Convulsions (clonic)	M							2/3 1/3	1/1 0/1	*								
500	Hypoactivity Ataxia							1/4	3/3 0/3	2/2	*								
200	Convulsions (clonic)	M								1/5	0/4								
200	Alopecia	F											2/4	2/4	-	2/4	0/4		

Key:

Blank indicates no significant reactions

- observations inadvertently missed over weekend

* Total Death

000116

BEST COPY AVAILABLE

Riker Experiment No.: 0613470277

APPENDIX I
PROTOCOL

7.

TEST: Acute Oral Toxicity Scan

SPONSOR: 3M Commercial Chemical Division

CONDUCTED BY: Safety Evaluation Laboratory, Riker Laboratories, Inc., St. Paul, Minnesota

TEST ARTICLE: T-5401

CONTROL ARTICLE: NONE

PROPOSED STARTING/COMPLETION DATE OF TEST: 6/88 - 9/88

TEST SYSTEM: ALBINO RATS, SD

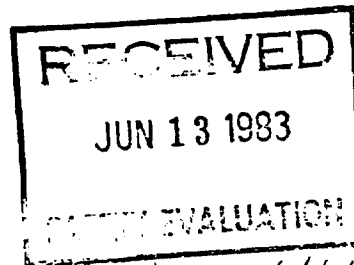
SOURCE: KING LINES, OREGON, WI

Sex: 1:1
Number: 100
Weight Range: 250 - 300 gm
100/100

OBJECTIVE: The objective of this test will be to characterize the acute oral toxicity of the test article in albino RATS. Rats were selected as a test system for reproducibility of response, historical use, ease in handling and general availability.

METHOD: The animals will be housed in stainless steel suspended wire mesh cages in temperature and humidity controlled rooms during both the quarantine and test periods, with food^a and water offered *ad libitum*^b. Each animal will be identified by color coding, according to the laboratory's standard operating procedure, which will correspond to the animal numbers on a card affixed to the outside of the cage. A single dosage of 5,000 mg/kg will be administered each animal, however, if this dosage level does not adequately characterize the toxicity of the test article, additional animals will be administered the test article at supplemental dosage levels. Any additional dosage levels will be documented and filed with this protocol. The test article will be administered to the animals in the form received from the sponsor. After administration of the test article, the animals will be returned to their cages and observed for any untoward behavioral reactions for the following 14 days. Initial and final body weights will be recorded. A gross necropsy which will include, but not be limited to heart, lungs, liver, kidneys and general gastrointestinal tract will be conducted on all animals which die during the conduct of the test as well as the animals surviving the test period. Any gross abnormalities which are observed during the conduct of the necropsy will be recorded with specific mention to the organ and/or site observed. The acute median lethal dose (LD₅₀) of the test article will be calculated, if possible, using a probit analysis method at the end of the observation period. All raw data generated by the study director and the final report will be stored in the Riker Laboratories' Archive, St. Paul, Minnesota.

- ^a Purina Laboratory Chow, Ralston Purina, St. Louis, Missouri
^b Food will be withheld for a 16-20 hour period prior to dosing.



W. C. Mc Cormick
Sponsor

6-8-88
Date

D. C. Mc Cormick
Study Director

Date

600117

APPENDIX I (concluded)
Deviations and/or Amendments to Protocol

1. Weekend observation for August 6 and 7 were inadvertently missed and on
September 3rd.

D. M. Markoe, Jr. 10/5/83
Study Director Date

2. Due to a delay in study conduct the proposed completion date should be amended
to 1/84.

D. M. Markoe, Jr. 12/29/83
Study Director Date

- 3.
- Study Director Date

- 4.
- Study Director Date

- 5.
- Study Director Date

APPENDIX II

Principal Participating Personnel Involved in the Study

<u>Name</u>	<u>Function</u>
D. M. Markoe, Jr., BS	Toxicologist Study Director
K. L. Ebbens, BS	Supervisor Toxicology Testing
K. D. O'Malley, BS	Senior Toxicologist Acute Toxicology
G. C. Pecore	Supervisor Animal Laboratory

BEST COPY AVAILABLE

APPENDIX III

Test and/or Control Article Characterization

for
KTZ-15 (CC 834-4)
 T-3421

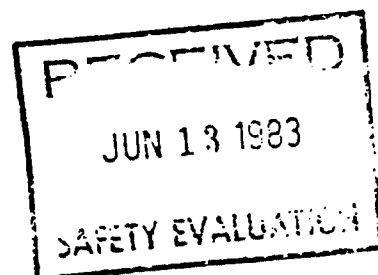
1. The identity strength, uniformity, composition, purity or other pertinent characterizations of the test and/or control substances have been determined and documented as of 25 May 83 *J. H. Miller*
2. The method of synthesis or origin of the test and control substances, including their amount and the method of bioassay (if applicable) is documented.
 yes ☒ no ☐

3. The stability of the test and/or control substances have been determined or will be determined as of 25 June 83 *accord of Test*

The above information and documentation are located in the sponsor's records.

D. Rucker 5/25/83
 Sponsor Date

cc L.D. Wenter 236-2B
W.C. McCormick 220-2E
 W.H. Pearson 223-65E
 D. Parby 236-1



000120

BEST COPY AVAILABLEAPPENDIX IVQUALITY ASSURANCE STATEMENT

Acute Toxicology Laboratory Studies

Study No.: 0783AR6287

This short term study was audited by Compliance Audit, and the final report examined against the raw data on January 25, 1984. The results of the audit were reported to the study director and to management on January 25, 1984.

In addition to the data audit, different significant phases for studies underway in the Acute Toxicology Laboratory are inspected weekly on a recurring cycle, and the facilities are examined by Compliance Audit on a three month schedule.

Cyale E. Van Puchstein
Compliance Audit

January 25, 1984
Date

000121