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International Research and Development Corporation

SPONSOR:

3M Company

AR 226-0955

TEST MATERIAL:

Fluorad® Fluorochemical Surfactant FC-95

SUBJECT:

Acute Oral Toxicity (LD₅₀)
Study in Rats.

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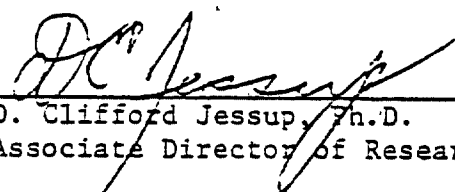
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T A B L E O F C O N T E N T S

	<u>Page</u>
I. Synopsis	1
II. Test Material	2
III. Method	3
IV. Results	4
A. Mortality and LD ₅₀ Values	4
B. Pharmacotoxic Signs	4
C. Body Weights	5
D. Necropsy Findings	6

Table No.

1. Pharmacotoxic Signs	7-8
2. Summary of Gross Necropsy Observations	9

I. SYNOPSIS

Based upon the data obtained, the acute oral LD₅₀ values and 95% confidence limits were calculated to be as follows:

Male Rats: 233 (160 - 339) mg/kg,

Female Rats: 271 (200 - 369) mg/kg,

Combined Male and Female Rats: 251 (199 - 318) mg/kg.

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Page 2

II. TEST MATERIAL

The test material was received from the 3M Company, St. Paul, Minnesota on October 24, 1977. It was identified as "Fluorad[®] Fluorochemical Surfactant FC-95, 3M Stock No. 98-0207-0103-7, Lot 640, Net wt. 5 lbs. 2.2 kg." and was received as a white powder.

III. METHOD

Twenty male and 20 female rats of the Charles River CD strain (obtained from The Charles River Breeding Laboratories, Inc., Portage, Michigan), weighing from 172 to 212 grams, were used for this study. The rats were housed by sex in groups of 5 rats per cage, in hanging wire-mesh cages in temperature and humidity controlled quarters. They were maintained in accordance with the recommendations contained in H.E.W. Publication No. 74-23 (N.I.H.) entitled "Guide for the Care and Use of Laboratory Animals". Water and Purina Laboratory Chow were available ad libitum, except for an overnight period immediately preceding oral administration during which food, but not water, was withheld.

The test material was suspended in a 20% acetone/80% corn oil mixture and administered orally by gavage at the following dosage levels to male and female rats: 100, 215, 464 and 1000 mg/kg.

Five rats of each sex were used at each dosage level. Volumes of 10 ml/kg of body weight were administered at all dosage levels.

All rats were observed for mortality and pharmacotoxic signs during the first four hours after dosing, at 24 hours and daily thereafter for a total of 14 days. Body weights were recorded immediately prior to dosing (control weight) and at 7 and 14 days. All rats which died on study were subjected to gross necropsy examination as were all survivors at the end of the 14 day study period.

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Page 4

IV. RESULTS

A. MORTALITY AND LD₅₀ VALUES:

Dose - Mortality Data

Dosage Level mg/kg			Number of Deaths														Total Mortalities		
	Hrs		Days																
	0-4		1	2	3	4	5	6	7-14										
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Male	Female	Total		
100															0/5	0/5	0/10		
215									2					1	2/5	1/5	3/10		
464					1	1	1		2	1				1	5/5	5/5	10/10		
1000			1	1	2		1	1				1	2	1	5/5	5/5	10/10		

The Acute Oral LD₅₀ Values and 95% Confidence Limits:

Male Rats: 233 (160 - 339) mg/kg,

Female Rats: 271 (200 - 369) mg/kg,

Combined Male and Female Rats: 251 (199 - 318) mg/kg.

Slope:

Male Rats: 1.00,

Female Rats: 1.00,

Combined Male and Female Rats: 1.00.

Statistical References:

¹Weil, C. S. 1952. Tables for Convenient Calculation of Median Effective Dose and Instruction in Their Use. Biometrics, 8: 249-263.

²Thompson, W. R. and Weil, C. S. 1952. On the Construction of Tables for Moving Average Interpolation. Biometrics, 8: 51-54.

³Eby, R. 1957. Statistical Tables for Dose Evaluation, Report No. 5711. Miles-Ames Research Laboratory, Elkhart, Indiana.

B. PHARMACOTOXIC SIGNS:

The following pharmacotoxic signs were observed during the 14 day observation period: (see Table 1):

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Page 5

C. BODY WEIGHTS:

The following body weights were obtained during the 14 day observations periods:

<u>Dosage Level (mg/kg)</u>	<u>Individual Rat Number</u>	<u>Sex</u>	<u>Control Weight (grams)</u>	<u>7 Day Weight (grams)</u>	<u>14 Day Weight (grams)</u>
100	76838	Male	172	224	272
	76839	Male	212	250	291
	76840	Male	201	218	282
	76841	Male	179	200	270
	76842	Male	188	235	276
	76818	Female	181	195	218
	76819	Female	179	175	200
	76820	Female	191	190	241
	76821	Female	180	210	220
	76822	Female	184	178	203
	76843	Male	182	170	230
	76844	Male	177	Died	Died
215	76845	Male	188	160	244
	76846	Male	198	190	218
	76847	Male	201	Died	Died
	76823	Female	189	152	214
	76824	Female	188	145	201
	76825	Female	177	150	200
	76826	Female	198	180	Died
	76827	Female	179	132	192
	76848	Male	175	Died	Died
	76849	Male	193	Died	Died
	76850	Male	183	Died	Died
	76851	Male	187	140	Died
464	76852	Male	178	Died	Died
	76828	Female	209	Died	Died
	76829	Female	189	Died	Died
	76830	Female	183	130	Died
	76831	Female	183	Died	Died
	76832	Female	178	Died	Died
	76853	Male	178	Died	Died
	76854	Male	180	Died	Died
	76855	Male	190	Died	Died
	76856	Male	193	Died	Died
	76857	Male	197	Died	Died

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Page 6

<u>Dosage Level (mg/kg)</u>	<u>Individual Rat Number</u>	<u>Sex</u>	<u>Control Weight (grams)</u>	<u>7 Day Weight (grams)</u>	<u>14 Day Weight (grams)</u>
1000	76833	Female	185	Died	Died
	76834	Female	193	Died	Died
	76835	Female	191	Died	Died
	76836	Female	183	Died	Died
	76837	Female	195	Died	Died

D. NECROPSY FINDINGS:

Gross necropsy observations were noted as indicated in Table 2.

NUMBER OF RATS SHOWING PHARMACOTOXIC
SIGNS AND TIME [HOUR] (DAY) OBSERVED

TABLE - 1.

COMPOUND - Fluorad[®] Fluorochemical Surfactant FC-95:

MALES

OBSERVATION	100 mg/kg	215 mg/kg	464 mg/kg	1000 mg/kg	
Normal	3(3-11), 5(12-14)	3(3-7), 2(8), 3(9), 2(10), 3(11-14)			
Diarrhea			1(2)		
Hypoactivity	5[1,2½,4], 5(1-2), 2(3-7), 1(8-9)	5[1,2½,4], 5(1-2) 2(3-4)	5[1,2½,4], 5(1-2), 4(3), 3(4), 1(5-7)	5[1,2½,4], 4(1), 2(2-3), 1(4-5)	
Decreased Limb Tone	1[2,4], 3(2)	3[2½], 4[4], 3(2) 1(3-4)	3[2½,4], 5(2), 1(7)	1[1], 5[2½,4], 1(1-2) 1(5)	
Ataxia	1[2½,4], 2(1), 3(2)	3[2½,4], 3(2), 1(3-4)	3[2½], 4[4], 4(1), 5(2), 1(3-4)	1[1], 5[2½,4], 4(1), 1(2)	
Corneal Opacity	5(2), 2(3-11)	2(2)	1(2)		
High Carriage		1(8), 1(10)			
Death		2(5)	1(3), 1(4), 2(5), 1(8)	1(1), 2(2), 1(4), 1(6)	

Study No.: 137-083

NUMBER OF RATS SHOWING PHARMACOTOXIC
SIGNS AND TIME [HOUR] (DAY) OBSERVED

TABLE - 1.(Cont.)

COMPOUND - Fluorad[®] Fluorochemical Surfactant FC-95:

FEMALES

OBSERVATION	100 mg/kg	215 mg/kg	464 mg/kg	1000 mg/kg	
Normal	3(3), 4(4-5), 3(6) 4(7-11), 5(12-14)	2(1-2), 5(3-7), 2(8) 2(8), 4(9), 2(10), 3(11-13), 4(14)	2(3-4)	1(3-4)	
Ptosis				1(6)	
Piloerection				1(6)	
Hypoactivity	5[1,2½,4], 5(1-2), 1(3-9)	5[1,2½,4], 3(1-2), 1(8)	5[1,2½,4], 5(1-2) 2(3-4), 3(5-6), 1(7)	5[1,2½,4], 4(1-2) 2(3-4), 3(5), 1(6)	
Decreased Limb Tone	2[2,4], 2(1), 3(2)	2[2½], 3[4], 2(2)	4[2½,4], 3(2), 1(7)	4[2½], 5[4], 1(1-4), 1(6)	
Ataxia	2[2½,4], 2(1), 3(2)	2[2½], 3[4], 2(2)	4[2½,4], 2(1), 3(2)	4[2½], 5[4], 1(1-4) 1(6)	
Prostration				1(6)	
Tremors				1(2)	
Corneal Opacity	2(2), 1(3-11)				
High Carriage		2(8), 2(10), 1(11-13)			
Death		1(9)	1(3), 1(5), 2(7), 1(8)	1(1), 1(3), 2(6), 1(7)	

Study No.: 137-083

TABLE 2.

Summary of Gross Necropsy Observations.

Site Lesion	Deaths						Terminal Sacrifice			
	215 mg/kg		464 mg/kg		1000 mg/kg		100 mg/kg		215 mg/kg	
	M	F	M	F	M	F	M	F	M	F
Number necropsied	2	1	5	5	5	5	5	5	3	4
No gross lesions			1				5	1	3	2
External										
yellow stained urogenital region				2		2				
partially cannibalized	2	1								
broken left front leg		1								
red stain around mouth			1							
white stain around mouth				1	1	1				
Stomach										
distension			3		3	1	1			
mucosa, thickened							2			1
mucosa, hyperemia							2			
fluid filled	1	1	1		1	1				1
glandular mucosa, hyperemia	1	1	3	4	3	5				
glandular mucosa, thickened	2		1	2		1				
glandular mucosa, erosion		1								
glandular mucosa, dark red foci			1			1				
glandular mucosa, ulcerations						1				
Lungs										
congestion	1	1	4	2	3	3				1
edema						1				
Intestines										
fluid filled						2				
contains transparent red mucoid-like material	1									