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Document Control Officer
Chemical Information Division
Office of Toxic Substances (WH-557)
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

Gentlemen:

Subject: Section 8(e) Toxic Substances Control Act (TSCA)
Perfluoroalkane Carboxylic Acids and Corresponding
Ammonium Carboxylates

Please find attached 3M Report entitled "Oral Rangefinder Study of T-2998C2C in Pregnant Rats", dated March 12, 1981. Preliminary information from this study has indicated that oral dosing of the subject ammonium carboxylate mixture produces the described teratogenic effects. This Report and the findings described in the article published in the August 1980 American Industrial Hygiene Journal and referenced as part of 8EHQ-1180-0374C, leads us to submit this information pursuant to Section 8(e) of TSCA and EPA's statement of interpretation published in the FEDERAL REGISTER, March 16, 1978.

Perfluoroalkane ammonium carboxylates is a generic chemical name for a mixture of homologs which can be expressed by the general formula $C_nF_{2n+1}COO^-NH_4^+$. Each of these homologs was reported on the TSCA Inventory.

As previously stated in our November 19 submission, our employee records and epidemiology data indicate that to date no human health problems have been observed nor disease patterns detected which are attributable or related to fluorochemical exposure. This mixture of homologous ammonium carboxylates and the corresponding homologous carboxylic acids are currently commercially available and used as follows:

3M Brand Fluorochemical Acid FC-26	Emulsifier additive in chemical specialty products (international market only)

FLUORAD® Brand Fluorochemical Surfactant FC-126 (ammonium carboxylates)	Additive used in chemical specialty products
FLUORAD® Brand Fluorochemical Surfactant FC-143 (ammonium carboxylates)	Emulsifier used in chemical processing and as an additive in chemical specialty products

At our Chemolite production facility, located at Highway 61 and Washington County Road 19, St. Paul, MN 55133, the subject chemicals are manufactured from of locally-produced perfluoroalkane carboxylic acids and of the same acid imported from our European plant in Antwerp, Belgium. Chemical reaction occurs in a closed system. Approximately 36 employees are intermittently exposed to the subject chemicals during production at the Chemolite facility. Approximately of perfluoroalkane carboxylates are exported annually.

We plan to inform, by April 1, those customers and 3M employees who have, through uses and/or processing, potential significant exposure to the subject chemicals. At that time, we will summarize these findings and outline our recommendations for handling and using these products. We are by copy of this letter advising NIOSH of these new preliminary teratogenic findings. As additional information becomes available to us, we plan to advise these customers and employees accordingly.

In view of the attached preliminary findings and in line with our ongoing testing and monitoring program on fluorochemicals, the following program is planned for the ammonium carboxylate mixture:

(1) A teratogenicity study in rats.

(2) A subsequent teratogenicity study in rabbits.

(3) Continual industrial hygiene program to improve and refine manufacturing and packaging processes which have been developed to further reduce the exposure to plant employees.

Since certain of the information provided herein is considered confidential business information, we are providing a sanitized version of this report for the public file. In addition, we have deleted from the confidential submission inconsequential information such as the names of 3M employees for the purpose of protecting their privacy.

Should additional correspondence be necessary on this matter, please contact:

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Manager, Regulatory Affairs Department
Commercial Chemicals Division
3M
3M Center, 223-6S-04
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Telephone: 612/733-7062

Yours very truly,

G. L. Hegg

George L. Hegg
Group Vice President
Chemicals, Film & Allied Products

GLH:sua

Attachments

cc: Acting Director, NIOSH
Park Lawn Building
5600 Fishers Lane
Rockville, MD 20857

Report Number: M-601

Date: March 12, 1980

Oral Rangefinder Study of T-2998CoC in Pregnant Rats

Experiment No.: 0680RR0016

Conducted At: St. Paul, Minnesota

Dosing Period: January 20, 1980 to January 29, 1980

Study Director:

2/24/81
Date

2/24/81
Date

2/25/81
Date

Introduction

This oral rangefinder study[A] was conducted to determine the upper dose level of T-2990C00[B] for a subsequent oral teratology study in rats. The study was sponsored by 3M Commercial Chemical Division, St. Paul, Minnesota and was conducted by the Safety Evaluation Laboratory, St. Paul, Minnesota. The study was conducted in accordance with the Safety Evaluation Laboratory's Standard Operating Procedures for such studies. The storage location for the raw data and a copy of the final report is maintained in the Safety Evaluation Laboratory's record archives.

Methods

Thirty-six time-mated Sprague-Dawley derived female rats from Charles River Breeding Laboratory were used in the study. The animals were indiscriminately removed from the shipping boxes by Animal Lab personnel and placed in the rack of cages from the left to right starting at the top and working down. Later the Study Director assigned dose groups by vertical rows. The rats were housed individually in hanging stainless steel cages with wire mesh floors and fronts in a temperature and humidity controlled room. Purina Laboratory Chow and water were available ad libitum. The lights were on a 12 hour light/dark cycle.

The animals were observed daily from day 3 through day 20 of gestation for abnormal clinical signs. Body weights were recorded on days 3, 6, 9, 12, 15 and 20 of gestation and the rats dosed accordingly using a constant dose volume of 5 ml/kg of body weight. T-2990C00 was suspended in corn oil and administered daily by oral intubation at doses of 150, 100, 75, 50 or 25 mg/kg/day to groups of 6 rats on days 6 through 15 of gestation. A control group of 6 rats received only corn oil by oral intubation on the same days. On day 20 of gestation the rats were killed by cervical dislocation and each uterus, including its contents, was examined immediately to determine if the animal was pregnant. Because two previous teratology studies (Experiment Nos: 0S00TR0008 and 0S00TR0010) with chemically related compounds resulted in fetuses with teratogenic changes in the lens of the eye, a few fetuses were also taken at day 20 of gestation and examined for eye abnormalities.

Blood samples from three rats in each dose group were taken before the first dose and at day 20 of gestation. Liver specimens were also taken from the same rats on day 20 of gestation. The plasma samples and liver specimens were frozen and submitted to the sponsor.

Results and Discussion

The oral administration of T-2990C00 at 150, 100, 75, 50 or 25 mg/kg/day to rats during the period of organogenesis (days 6 through 15 of gestation) did not result in any deaths. A toxic effect of reduced body weight gain occurred between days 6 and 9 of gestation in the 150 mg/kg/day dose group (Table 1).

The two nonpregnant 150 mg/kg/day rats had a more severe effect on body

weight on day 9 of the study than the pregnant high dose dams (Appendix I). They lost a considerable amount of weight and one was observed to have urinary incontinence on days 11, 12 and 13. The pregnant dams of the 100, 75, 50 and 25 mg/kg/day dose groups did not have abnormal clinical signs and gained weight at comparable levels to the 0 mg/kg/day group.

Four fetuses were examined from each of four dams in the 150 and 25 mg/kg/day dose groups for eye changes. All of the readable fetuses sectioned had eye changes consisting of one or more of the following: large lens clefts, dark streak running one-half to three-quarters of the way through the lens or disorganized lens fibers (Table 2). The lens abnormalities occurred in the same location as those observed in the two previous teratology studies (Experiment Nos: 0580TR0008 and 0580TR0010) on chemically related compounds. The abnormalities in this study appeared more pronounced than in the previous studies. In the previous studies, the teratogenic effect was a developmental eye abnormality which appeared to be an arrest in development of the primary lens fibers forming the embryonal lens nucleus, followed by secondary aberrations of the secondary lens fiber of the fetal nucleus. The same general morphological changes occurred in this rangefinder study with T-2998CoC.

Conclusion

The objective of determining an upper dose level for an oral rat teratology study was met in this study. The above results suggest that the 150 mg/kg/day dose level would be an appropriate high dose in a rat teratology study because of the toxic effect of reduced body weight gain. In addition to the toxic effect of reduced body weight gain, the teratogenic effect of lens abnormality was observed and is likely to be reproduced in a teratology study.

Table 1

Oral Rangefinder Study of T-2998CoC in Pregnant Rats
Mean Body Weight Gains of Pregnant Rats
With Standard Deviations (g)

	Day				
	6	9	12	15	20
Control	30 4.2	18 7.4	21 7.5	29 1.6	76 10.7
150 mg/kg/day	21 5.5	5 17.8	25 a 6.8	12 13.8	84 12.1
100 mg/kg/day	29 4.1	15 5.1	17 4.4	19 12.6	84 12.5
75 mg/kg/day	27 6.6	11 10.0	21 2.7	19 10.5	74 12.6
50 mg/kg/day	30 6.5	16 2.7	22 5.6	27 7.3	72 10.0
25 mg/kg/day	24 7.6	16 6.0	24 6.9	29 9.2	82 5.8

a Significantly higher than the control (Dunnett's t test $p < 0.05$)

Table 2

Oral Rangefinder Study of T-2998000 in Pregnant Rats
Ratios of Fetuses with Eye Changes to Fetuses Examined[a]

High Dose Group (150 mg/kg/day)	Low Dose Group (25 mg/kg/day)
16/16	15/15[b]

[a] Four fetuses examined from each of four dams
[b] One fetus not examined because eye architecture destroyed in sectioning

Appendix 2

Oral Range-Finder Study of T-2000CoC in Pregnant Rats

Individual Body Weights (g) and Mean Body Weights
with Standard Deviation for Pregnant Rats

	Day 1	6	9	12	15	20
0 MG/KG/DAY						
NIR	216	194	224	244	269	297	382
NIR	217	186	214	226	262	297	370
NIR	219	192	217	227	253	282	365
NIR	212	207	239	250	258	285	360
NIR	246	190	231	257	280	311	369
MEAN		195	225	242	264	292	367
STAN. DEV		7.7	10.3	11.5	10.5	11.5	6.2
NON PREGNANT ANIMALS							
NIR	220	190	212	221	215	225	222

	Day 1	6	9	12	15	20
150 MG/KG/DAY						
OIR	221	202	222	216	257	287	367
OIR	224	192	218	217	257	261	344
OIR	225	177	191	222	244	242	314
OIR	247	206	232	226	262	278	375
MEAN		195	216	220	255	267	391
STAN. DEV		12.9	17.5	4.6	7.7	19.4	24.2
NON PREGNANT ANIMALS							
OIR	222	207	229	199	200	212	246
OIR	223	181	205	181	196	215	271

Appendix I (Continued)

Oral Rangefinder Study of T-2998CoC in Pregnant Rats

Individual Body Weights (g) and Mean Body Weights
with Standard Deviation for Pregnant Rats

		Day					
		3	6	9	12	15	20
100 MG/KG/DAY							
P1R	326	164	193	210	229	253	327
P1R	327	214	240	248	268	265	331
P1R	328	262	286	302	317	349	452
P1R	329	200	235	245	256	268	353
P1R	330	185	218	234	248	268	363
P1R	348	189	219	240	263	290	371
MEAN		202	232	247	264	282	366
STAN. DEV		33.6	31.3	30.4	29.6	34.9	45.5

		Day					
		3	6	9	12	15	20
75 MG/KG/DAY							
Q1R	331	192	221	243	265	268	346
Q1R	332	198	212	228	249	271	346
Q1R	333	172	203	215	235	263	346
Q1R	334	211	243	236	261	270	326
Q1R	335	193	216	225	244	268	331
Q1R	349	200	231	248	265	293	383
MEAN		194	221	233	253	272	346
STAN. DEV		12.9	14.1	12.2	12.4	10.6	20.6

Appendix I (Concluded)

Oral Rangefinder Study of T-2998CoC in Pregnant Rats

Individual Body Weights (g) and Mean Body Weights
with Standard Deviation for Pregnant Rats

		Day					
		3	6	9	12	15	20
50 MG/KG/DAY							
R1R	336	193	219	236	253	276	350
R1R	337	177	201	213	235	259	330
R1R	338	226	251	262	283	314	397
R1R	339	170	198	218	237	254	308
R1R	340	187	226	245	267	304	378
R1R	350	192	229	243	276	308	382
MEAN		191	221	236	259	286	359
STAN DEV		19.4	19.6	18.2	20.1	26.2	33.0

		Day					
		3	6	9	12	15	20
25 MG/KG/DAY							
S1R	342	216	239	266	283	304	388
S1R	343	207	234	249	279	304	383
S1R	344	185	200	227	253	292	369
S1R	345	200	219	233	249	270	348
S1R	351	205	233	238	268	307	398
MEAN		203	227	243	266	295	377
STAN DEV		11.4	12.8	15.4	15.2	15.3	19.4

NON PREGNANT ANIMALS

S1R	341	187	203	219	220	228	238