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**Exhibit
1252**

State of Minnesota v. 3M Co.,
Court File No. 27-CV-10-28862

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1252.0001

Oral Rangefinder Study of T-2998CoC in Pregnant Rats

Experiment No.: 0680RR0018

Conducted At: Riker Laboratories, Inc.
St. Paul, Minnesota

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

Study Director: E. G. Gortner

E. G. Gortner 2/24/81
E. G. Gortner Date
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Introduction

This oral rangefinder study^a was conducted to determine the upper dose level of T-2998CoC^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, Riker Laboratories, Inc., 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 Care 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-2998CoC 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 (Riker Experiment Nos: 0680TR0008 and 0680TR0010) 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-2998CoC 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

^a Riker Experiment No. 0680RR0018
^b FC-143

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 (Riker Experiment Nos: 0680TR0008 and 0680TR0010) 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	20 4.2	18 7.4	21 7.5	29 1.6	76 10.7
150 mg/kg/day	21 5.5	5 17.8	20 ^a 8.8	12 13.8	84 12.1
100 mg/kg/day	22 4.1	15 5.1	17 4.4	19 12.6	84 13.5
75 mg/kg/day	27 6.6	11 10.6	21 2.7	19 10.5	74 12.6
50 mg/kg/day	20 6.5	16 3.7	22 5.6	27 7.3	73 10.0
25 mg/kg/day	24 2.6	16 6.1	24 6.7	29 9.3	82 5.8

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

Table 2

Oral Rangefinder Study of T-2998CoC in Pregnant Rats
Ratios of Fetuses with Eye Changes to Fetuses Examined^a

High Dose Group

(150 mg/kg/day)

16/16

Low Dose Group

(25 mg/kg/day)

15/15^b

^a Four fetuses examined from each of four dams

^b One fetus not examined because eye architecture destroyed in sectioning

Appendix I

5.

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
0 MG/PG/DAY							
N1R	316	194	223	244	269	297	302
N1R	317	186	214	238	262	292	310
N1R	318	192	217	227	253	282	265
N1R	319	207	235	256	258	285	360
N1R	346	190	231	257	280	311	369
MEAN		190	225	243	264	291	309
STAN. DEV.		7.7	10.3	11.5	10.5	11.5	8.2
NON PREGNANT ANIMALS							
N1R	326	184	213	224	215	223	222

		Day					
		3	6	9	12	15	20
150 MG/PG/DAY							
O1R	321	202	222	216	257	287	367
O1R	324	193	218	217	257	261	344
O1R	325	177	191	222	244	243	314
O1R	347	206	232	236	262	278	378
MEAN		190	216	220	255	267	351
STAN. DEV.		12.9	17.5	4.6	7.7	19.4	28.3
NON PREGNANT ANIMALS							
O1R	322	207	228	198	200	219	246
O1R	323	181	200	181	196	215	221

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					
		2	6	9	12	15	20
100 MG/KG/DAY							
P1R	326	164	197	210	229	253	327
P1R	327	214	240	248	268	285	321
P1R	328	262	286	302	317	349	402
P1R	329	200	235	245	256	268	303
P1R	320	185	218	224	248	268	262
P1R	348	189	218	240	263	290	371
MEAN		202	232	247	264	282	366
STAN. DEV		33.6	31.3	30.4	29.6	34.9	40.5

		Day					
		2	6	9	12	15	20
75 MG/KG/DAY							
U1R	331	192	221	243	265	268	346
U1R	332	198	213	228	249	271	346
U1R	333	172	203	215	235	263	346
U1R	334	211	243	236	261	270	328
U1R	335	193	216	225	244	268	321
U1R	349	206	231	248	265	293	383
MEAN		194	221	233	250	272	346
STAN. DEV		12.9	14.1	12.2	12.4	10.6	20.0

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	328
R1R	338	226	251	262	283	314	297
R1R	329	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	208	227	252	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	19.3	19.4

NON PREGNANT ANIMALS

S1R	341	187	203	219	220	228	238
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