

Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO. 78-7187

AN ACUTE INHALATION TOXICITY STUDY
OF T-2308 CoC IN THE RAT

Submitted to: 3M Company
St. Paul, Minnesota 55101

Attention: Frank Griffith, Ph.D.

Date: April 12, 1979

**Exhibit
2801**

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

3MA00234875

2801.0001

78-7187

I. GENERAL

An experiment was performed to assess the acute inhalation toxicity of T-2308 CoC in rats. The test material, received from the 3M Company, was labeled "3M Company; T-2308 CoC" and was in the form of a fine, white powder.

II. EXPERIMENTAL

The test material was packed into a Wright dust-feed mechanism, operating at a gear ratio of 1:6. Dry air, at a flow rate of 15.0 liters per minute, was directed through the dust-feed mechanism. The resultant dust was directed, undiluted, into a 32.2-liter glass exposure chamber containing the test animals. The exposure lasted for one hour.

The cylinder containing the test material was weighed before and after the exposure period. The weight loss was equal to the total amount of material delivered. This, divided by the total volume of air passed through the chamber during the exposure, gave the nominal exposure concentration.

The test animals consisted of five male and five female Sprague-Dawley rats obtained from Charles River Breeding Laboratories, Wilmington, Massachusetts. On the day of exposure (Day 0 - October 4, 1978) the pre-exposure weights ranged from 212 to 299 grams. The basic health of the animals was checked and found acceptable by a pretest examination. The test animals were observed for abnormalities at 15-minute intervals during the exposure period, upon removal from the exposure chamber, hourly for four hours post-exposure, and daily thereafter for 14 days. Individual body weights were recorded prior to exposure on Day 0 and on Day 1, Day 2, Day 4, Day 7 and Day 14 (terminus). Animals dying during the post-exposure period

78-7187

II. EXPERIMENTAL (cont.)

were weighed and necropsied as soon as possible after death. On Day 14, all surviving animals were sacrificed (ethyl ether) and gross necropsy examinations were performed.

III. RESULTS AND DISCUSSION

During the exposure period, 22.26 grams of the test material was delivered in a total volume of 900 liters of air, yielding a nominal exposure concentration of 24.7 milligrams per liter.

Throughout the one-hour exposure period, the test animals exhibited labored breathing, gasping, closing of the eyes, excessive lacrimation, mucoid nasal discharge, excessive salivation, and inactivity. Abnormal signs observed in the test animals upon removal from the exposure chamber were dry rales (seven of ten rats), moist rales (two of ten rats), labored breathing (seven of ten rats), excessive lacrimation (five of ten rats), red nasal discharge (two of ten rats), mucoid nasal discharge (four of ten rats), and yellow staining of the ano-genital fur (five of ten rats).

At one hour post-exposure abnormal signs observed in the test animals were the same as those noted upon removal from the chamber. During the three remaining hours of the four-hour post-exposure interval, dry rales was observed continuously in six of ten animals and moist rales was seen in two of ten rats. Sporadic observations of dry and moist rales were also observed in two animals each during this period. Labored breathing was noted in six of ten animals, a film over both eyes was seen in five of ten animals, and yellow staining of the ano-genital fur was noted in six of ten animals.

78-7187

III. RESULTS AND DISCUSSION (cont.)

A total of five rats (four male, one female) died between Day 5 and Day 8 of the 14-day observation period. Abnormalities noted in these rats prior to death were labored breathing (five of five rats), mucoid nasal discharge (three of five rats), red nasal discharge (one of five rats), dry rales (four of five rats), moist rales (four of five rats), yellow staining of the ano-genital fur (five of five rats), piloerection (four of five rats), hind limb weakness (two of five rats), poor condition (two of five rats), decreased activity (two of five rats), and aggressive behavior (two of five rats). General hypothermia was noted in one of five rats and hypothermic extremities was seen in one of five rats. One rat (no. 10) was noted to have tonic and clonic convulsions prior to death, as well as loss of righting reflex.

At the necropsy examinations of these animals, abnormalities noted were lung discoloration in four of five animals and liver discoloration in three of five animals. Intestinal distention with gas was also noted in two of the animals. In the males that died, steady weight losses were seen prior to death. In the female, a large weight loss was seen on Day 1, followed by small regains prior to death. The necropsy observations and body weight data for these animals are presented in Table 1.

Abnormal signs observed in the five surviving rats were similar to those seen in the rats that died during the first four to six days of the observation period. Labored breathing was noted in five of five rats, however this sign was gone by Day 2 in three rats and only one rat continued to have

78-7187

III. RESULTS AND DISCUSSION (cont.)

labored breathing through Day 14. Gasping was observed once each in two rats on Day 2 and Day 12. Mucoïd nasal discharge (noted in four of five rats) was gone in all rats by Day 6 and red nasal discharge was observed once in one rat on Day 1. Dry rales was seen in five of five rats and persisted in three rats through Day 14. Moist rales was noted in four of five animals and continued in only one rat beyond Day 2 of the observation period. Yellow staining of the ano-genital fur was noted in four of five animals but this sign had also abated by Day 4. Excessive lacrimation was observed once each in two of five rats. Soft stool was also observed in two of five rats on Day 2. Rapid breathing was observed in one rat (no. 24) on Day 11. A slight hair loss under the chin was observed in one rat from Day 8 to Day 14. First observed on Day 7, piloerection was noted in three of five rats, however only the surviving male showed this sign continuously.

The surviving five rats were necropsied on Day 14 and lung discoloration was noted in one animal, distention of the small intestines with gas was noted in one animal, and distention of the stomach with gas was noted in two animals. The male rat, which survived, showed steady weight loss through Day 7 followed by regain on Day 14, but the Day 14 body weight was considerably lower than the rat's pre-exposure weight. In the surviving females weight losses were seen through Day 2 or Day 4, followed by abnormally slow regains through Day 14, except in female no. 22, where a large weight loss was noted between Days 7 and 14. Individual body weights and necropsy observations are presented for all animals in Table 1.

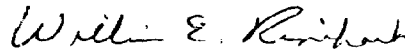
78-7187

IV. CONCLUSION

A one-hour inhalation exposure to a maximum-attainable dust of T-2308 CoC, at a nominal concentration of 24.7 milligrams per liter, produced definite signs of toxicity (respiratory and ocular irritation) and 50% mortality in Sprague-Dawley rats. Necropsy observations and body weight data on the surviving animals indicated that the toxic effects described had not completely reversed at 14 days post-exposure.



Jeffrey W. Thackara, B.S.
Manager, Inhalation Toxicology



William E. Rinehart, Sc.D.
Vice President, Science

Report Preparation: Lynn L. Ficarra, B.A.

/mes

Table 1
An Acute Inhalation Toxicity Study
of T-2308 CoC in the Rat

Individual Body Weights and Necropsy Observations

Animal Number	Sex	Body Weights (g)							Necropsy Observations*
		Day 0	Day 1	Day 2	Day 4	Day 7	Day 14		
10	M	234	197	191	169	Dead ^a		B. Lungs mottled deep red and bright red. Liver dark red in color. Intestine and stomach distended with gas.	
11	M	266	226	223	214	211	246	N.O.A.	
12	M	233	199	183	180	Dead ^a		N.O.A.	
13	M	299	268	266	235	Dead ^b		B. Lungs mottled light and dark red. Liver mottled light and dark red.	
14	M	260	222	218	211	199	Dead ^c	B. Lungs mottled dark red and tan. Liver blackish red with grey patches. Small intestine distended with gas.	
20	F	227	192	195	199	207	231	Stomach distended with gas.	
21	F	239	211	212	218	Dead ^a		B. Lungs dark red with black foci.	
22	F	222	196	191	199	215	166	Stomach and intestines distended with gas.	
23	F	228	189	177	180	194	228	B. Lungs mottled pink and tan with scattered red foci.	
24	F	212	184	179	186	202	223	N.O.A.	

* N.O.A. - no observed abnormalities.

Key: R = right; L = left; B = bilateral.

^a Found dead on Day 5.

^b Found dead on Day 7.

^c Found dead on Day 8.