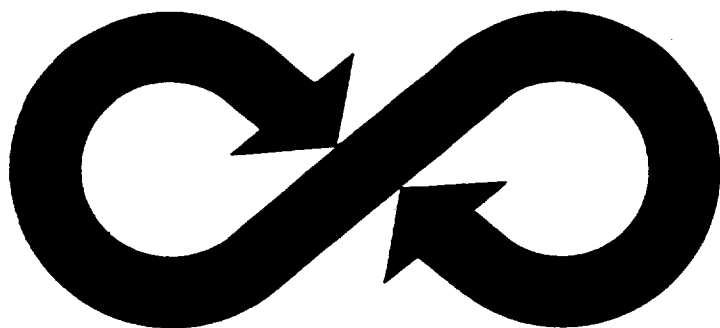




Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO. 78-7186

AN ACUTE INHALATION TOXICITY STUDY
OF T-2307 CoC IN THE RAT

Submitted to: Minnesota Mining and Manufacturing
Company
St. Paul, Minnesota 55101

Attention: James E. Long, Sc.D.

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78-7186

I. GENERAL

An experiment was performed to assess the acute inhalation toxicity of a dust of T-2307 CoC in Sprague-Dawley rats. The test material, received from the Minnesota Mining and Manufacturing Company, was labeled "3M Company, T2307CoC," and was in the form of a fine, yellow-orange powder.

II. EXPERIMENTAL

Two test material exposures were performed. For the first exposure, the test material was placed in a 500-milliliter, three-neck flask, fitted with a stir bar. For the second exposure, the test material was sieved through a 60-mesh sieve and placed in a 1000-milliliter, three-neck flask, fitted with a stir bar. The flasks were placed on a magnetic stir plate to provide constant agitation of the test material during the exposure periods. Dry air, at the flow rate of 10 liters per minute, was passed through the test material, and the resulting dust-laden airstream was directed into a 26.5-liter glass exposure chamber containing the test animals. The exposures lasted for one hour. The flasks containing the test material were weighed before and after the respective exposure periods. The differences in weight were equal to the amounts of material consumed during the exposures. The nominal concentrations were calculated by dividing the weight lost by the total air flow through the chambers during the exposures.

78-7186

II. EXPERIMENTAL (cont.)

The test animals consisted of two groups of five male and five female Sprague-Dawley rats obtained from Charles River Breeding Laboratories, Wilmington, Massachusetts. On the days of exposure (Day 0 - 10/4/78 and 10/12/78), the pre-exposure weights ranged from 200 to 297 grams. The basic health status of the test animals was established by a pre-exposure examination. The animals were observed for abnormalities at 15-minute intervals during the exposure period, upon removal from the 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 (Group I only), Day 3 (Group II only), Day 4, Day 7 and Day 14 (terminus). On Day 14, all survivors were sacrificed (ethyl ether) and gross necropsy examinations were performed. All animals dying spontaneously were examined by gross necropsy as soon as possible after death.

III. RESULTS AND DISCUSSION

During the first exposure period (Group I), a total of 39.98 grams of the test material was delivered in a total volume of 600 liters of dry air, yielding a nominal exposure concentration of 66.63 milligrams per liter. During the second exposure period (Group II), 13.33 grams of the test material was delivered in the same volume of dry air, yielding a nominal exposure concentration of 22.22 milligrams per liter.

78-7186

III. RESULTS AND DISCUSSION (cont.)

After 32 minutes of the Group I exposure, the chamber atmosphere remained static for a short period of time (less than five minutes) while the delivery flask was refilled with test material.

Abnormalities noted in the Group I animals throughout the exposure period were mucoid nasal discharge, excessive lacrimation, and excessive salivation. Squinting or closing of the eyes was observed from 30 minutes of exposure through exposure termination. Chromodacryorrhea was observed in one animal at exposure termination. Signs observed in the Group I animals upon their removal from the exposure chamber were excessive lacrimation (eight of ten rats), excessive salivation (one of ten rats), chromodacryorrhea (two of ten rats), mucoid nasal discharge (three of ten rats), and dry rales (one of ten rats). These signs were also observed sporadically during the four hourly post-exposure observation intervals. Seven of ten rats from Group I died during the 14-day observation period. Pre-death signs in these animals were mucoid nasal discharge (five of seven rats), red nasal discharge (five of seven rats), dry rales (one of seven rats), excessive lacrimation (one of seven rats), excessive salivation (one of seven rats), labored breathing (five of seven rats), yellow staining of the ano-genital fur (seven of seven rats), brown staining of the ano-genital fur (one of seven rats), reduced activity (seven of seven rats), poor general condition (seven of seven rats), spasms (one of seven rats), coldness of the body (two of seven rats), brown nasal discharge (one of seven rats), hair loss (one of seven rats), and rapid breathing (one of seven rats). Signs observed in the three surviving animals during the 14-day in-life period were red nasal discharge (two of three rats), mucoid nasal discharge (three of three rats).

78-7186

III. RESULTS AND DISCUSSION (cont.)

excessive lacrimation (two of three rats), dry rales (one of three rats), labored breathing (three of three rats), yellow staining of the ano-genital fur (three of three rats), brown staining of the ano-genital fur (two of three rats), reduced activity (three of three rats), poor condition (three of three rats), spasms (one of three rats), loss of righting reflex (one of three rats), rapid breathing (one of three rats), and pilo erection (one of three rats).

Individual body weights and necropsy observations of the Group I animals are presented in Table I. Animals dying during the study lost weight steadily prior to death. Two of three surviving rats also exhibited steady weight losses. One male rat (#14), however, was gaining weight by termination of the study. Necropsy observations of the Group I animals were liver discoloration (nine of ten rats), lung discoloration (six of ten rats), adrenal discoloration (one of ten rats), adrenal enlargement (two of ten rats), gaseous distention of the stomach (three of ten rats), gaseous distention of the intestines (one of ten rats), stomach discoloration (one of ten rats), and intestinal discoloration (two of ten rats).

Abnormalities noted in the Group II (22.22 mg/l) rats during the exposure period were excessive lacrimation, excessive salivation, squinting or closing of the eyes, mucoid or red nasal discharge, and/or labored breathing. Upon removal of the animals from the exposure chamber, dry rales (three of ten rats), mucoid nasal discharge (two of ten rats), excessive salivation (one of ten rats), excessive lacrimation (two of ten rats), and yellow staining of the ano-genital fur (nine of ten rats) were observed. These signs were also observed in the rats

78-7186

III. RESULTS AND DISCUSSION (cont.)

during the four hourly post-exposure intervals. Other signs observed sporadically during those intervals were labored breathing and reduced activity. Observations made during the 14-day in-life period were dry rales (seven of ten rats), mucoid nasal discharge (seven of ten rats), rapid breathing (two of ten rats), yellow staining of the ano-genital fur (eight of ten rats), brown staining of the ano-genital fur (two of ten rats), orange staining of the ano-genital fur (two of ten rats), reduced activity (two of ten rats), pilo erection (one of ten rats), hair loss (one of ten rats), coldness of the body (two of ten rats), and generally poor condition (ten of ten rats). Individual body weights and necropsy observations of the Group II animals are presented in Table II. All Group II rats experienced weight loss following exposure to the test material. Though weight gains were retarded, all male rats exceeded their Day 0 body weights by termination of the study. None of the female rats recovered their original weights by Day 14, though three of five females were gaining weight by the end of the study. Necropsy observations of these animals revealed lung discoloration in eight of ten rats.

78-7186

IV. CONCLUSION

A pair of exposures were performed on Sprague-Dawley rats to determine the acute inhalation toxicity of different concentrations of a dust of T-2307 CoC. The first exposure (Group I) yielded a nominal test material exposure concentration of 66.63 milligrams per liter. Seven of ten animals of this group were dead by Day 10 of the study. The second exposure (Group II) yielded a nominal exposure test material concentration of 22.22 milligrams per liter. There was no mortality in the second group. However, all animals exposed to the test material in this study displayed a definite response to their exposure to the dust of T-2307 CoC. In-life observations showed the animals to be in poor condition following the exposure and post-exposure weight gains were markedly depressed. Necropsy examination of the Group I animals revealed liver discoloration in nine of ten rats, marked lung discoloration in six of ten rats and adrenal enlargement in two of ten rats. The main findings on necropsy of Group II animals after 14 days was lung discoloration in eight of ten rats. These findings, especially in Group I, would appear to be indicative of a residual effect of the test material exposure.



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Table I
An Acute Inhalation Toxicity Study
of T-2307 CoC in the Rat
Individual Body Weights and Necropsy Observations
Group I - 66.63 mg/l

Animal Number	Sex	Body Weights (g)						Necropsy Observations*
		Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	
10	M	248	221	207	195	Dead ^b		B. lungs red in color. Liver mottled tan and red. Stomach distended with gas.
11	M	270	242	226	209	Dead ^a		B. lungs red in color. Liver mottled tan and red.
12	M	297	273	260	241	245	216	All lobes of liver mottled tan and red.
13	M	269	251	247	228	197	Dead ^c	B. lungs red in color. All lobes of liver mottled red and grey.
14	M	297	271	267	257	202	236	All lobes of liver mottled red and tan.
20	F	208	198	194	173	149	Dead ^c	B. lungs red in color. All lobes of liver black-red with tan and grey patches. B. adrenal enlarged in appearance and red in color.
21	F	206	194	187	185	183	179	N.O.A.
22	F	234	207	199	184	172	Dead ^d	R. lobe of liver mottled red and tan. B. adrenals enlarged (1.5 x normal size) in appearance.
23	F	228	215	208	183	163	Dead ^e	B. lungs red in color. All lobes of liver abnormally dark red in color. Stomach distended with gas. Small intestines yellow in color, distended with gas.
24	F	238	220	205	194	175	Dead ^e	B. lungs red in color. All lobes of liver abnormally dark red in color. Stomach pale yellow in color, distended with gas. Small intestines yellow in color.

* N.O.A. - no observed abnormalities.
Key: R = right; L = left; B = bilateral.

^a Spontaneous death Day 6.

^b Spontaneous death Day 7.

^c Spontaneous death Day 8.

^d Spontaneous death Day 9.

^e Spontaneous death Day 10.

Table II
An Acute Inhalation Toxicity Study
of T-2307 CoC in the Rat
Individual Body Weights and Necropsy Observations
Group II - 22.22 mg/l

Animal Number	Sex	Body Weights (g)						Necropsy Observations*
		Day 0	Day 1	Day 3	Day 4	Day 7	Day 14	
30	M	281	253	265	256	250	291	Scattered red foci on B. lungs.
31	M	288	266	255	258	272	301	B. lungs mottled pink and red with scattered grey foci.
32	M	266	238	234	237	246	272	B. lungs mottled tan and red with scattered grey foci.
33	M	276	267	262	260	265	282	B. lungs mottled pink and tan with scattered grey foci.
34	M	282	275	277	274	284	314	Scattered red and grey foci on B. lungs.
40	F	214	207	200	194	189	202	Scattered red foci on B. lungs.
41	F	206	179	175	175	177	169	B. lungs mottled pink and red.
42	F	200	196	196	188	188	187	N.O.A.
43	F	224	219	222	210	220	220	N.O.A.
44	F	207	182	179	175	164	195	B. lungs mottled pink and tan.

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

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