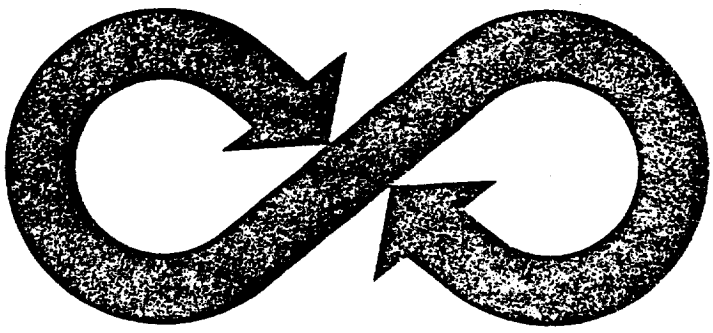

Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO. 78-7185

AN ACUTE INHALATION TOXICITY STUDY OF T-2306 CoC IN THE RAT

Submitted to: 3M Company

Attention: Dr. William C. McCormick

Date: December 31, 1979

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I. GENERAL

A series of one-hour inhalation exposures was performed on rats to determine the median lethal concentration (LC_{50}) of T-2306 CoC dust. The test material, a fine white powder, received from the 3M Company was labeled "3M Company; T-2306 CoC". These studies were initiated on January 24, 1979 and completed on April 6, 1979.

II. EXPERIMENTAL

A. Test Material Delivery

For each exposure, the test material was sieved through a 60-mesh sieve and packed into the large-diameter cylinder of a Wright dust-feed mechanism. Dry air, at flow rates ranging from 12 to 16 liters per minute, was passed through the dust-feed mechanism. The resultant dust-laden air-stream was directed into a 32.2-liter glass exposure chamber housing the test animals. Desired concentrations were achieved by varying the air flow rates and the gear ratios on the dust feed mechanisms. The test material exposures lasted for one hour each.

The packed cylinder, cutting blade, and nozzle were weighed before and after each exposure. The difference in weight represented the amount of material delivered during the exposure. The nominal concentration was determined by dividing the amount of material delivered by the total air flow through the chamber during the exposure.

B. Test Animals

The test animals used in this experiment consisted of groups of five male and five female Sprague-Dawley rats obtained from Charles River Breeding Laboratories, Wilmington, Massachusetts. Pre-exposure weights ranged from 201 to 299 grams. Observations for abnormal signs were recorded

II. EXPERIMENTAL (Cont.)

B. Test Animals (cont.)

prior to the exposure, at 15-minute intervals during the exposure, 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 (Day 0), and on Day 1, Day 2, Day 4, Day 7, and Day 14 (terminus). All animals dying spontaneously were necropsied as soon as possible after death. On Day 14, all survivors were sacrificed (ethyl ether) and gross necropsy examinations were performed. Blood samples were collected at terminus on all animals surviving through Day 14 of each group. The blood samples were drawn aortically, pooled by group and by sex and were sent to the sponsor for analysis.

C. Control Animals

In order to provide control data for this study, a group of five male and five female Sprague-Dawley rats, weighing from 203 to 263 grams were exposed to dry air at a flow rate of 12 liters per minute. All other exposure conditions, observation procedures, necropsy procedures, and blood sampling procedures were performed the same as for the test material exposed animals.

D. LC_{50} Determination

The median lethal concentration and 95% confidence limits were calculated according to the method of Litchfield and Wilcoxon.[1]

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[1]Litchfield, J.T., and F. Wilcoxon J. Pharma. Exp. Therapy 96: 99-115 (1949).

III. RESULTS AND DISCUSSION

A. Exposure Concentrations

During the test material exposures, totals of 44.13, 23.13, 6.77, 13.38, 2.06, 4.67, 0.0, 1.81 and 4.10 grams of the test material were delivered, yielding equivalent nominal exposure concentrations of 45.97, 24.09, 7.05, 13.9, 2.86, 6.49, 0.0, 1.89 and 4.88 milligrams per liter (Groups I-IX, respectively). A summary of exposure conditions and mortality results is given in Table 1.

Results of the Group I exposure (45.97 milligrams per liter) were not easily comparable to the 18.6 milligrams per liter group of Bio/dynamics project 78-7184. A second exposure (Group II) was performed at approximately 20 milligrams per liter. Group I was terminated on Day 2 to allow for collection of blood samples from survivors (see C. High Level Exposures). Group IV (13.9 milligrams per liter) was also terminated (Day 1) as a result of a cylinder blowout during the exposure. Groups I and IV are not used in calculation of the LC_{50} value and Group IV results are not discussed in this report.

B. Control Exposure

No abnormalities were observed in the control animals (Group VII) during the sham exposure or upon removal from the exposure chamber. Dry rales was observed in one of ten animals at three hours post-exposure. The most significant observation recorded during the 14-day in-life period was dry rales (seven of ten rats) which was scattered in occurrence. Exposure, post-exposure, and in-life physical observations are presented in Tables 7 and 15. Body weights, presented along with necropsy observations in Table 23, are considered normal. The most significant abnormal observation upon necropsy was lung discoloration.

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III. RESULTS AND DISCUSSION (Cont.)

C. High Level Exposures

During the Group I (45.97 milligrams per liter) exposure, a dense cloud of test material was visible in the exposure chamber making animal observation difficult. Labored breathing and/or gasping followed by closing of the eyes and reduction of activity were observed in all animals. Excessive salivation and lacrimation and mucoid nasal discharge were observed in some animals. Upon removal from the exposure chamber and during the four hour post-exposure period, red and mucoid nasal discharge, dry rales, and yellow-staining of the ano-genital fur were most frequently observed. These observations are presented in Table 2.

By Day 2, three of five males and two of five females had died spontaneously. It was decided to terminate Group I on Day 2 in order to collect blood samples from the surviving animals. Samples are retained by the sponsor. Prior to their termination, survivors exhibited reduced activity, red nasal discharge, excessive lacrimation, yellow staining of the ano-genital fur and general poor condition. A full list of individual physical observations are given in Table 10. Body weights, presented along with necropsy observations in Table 18, were depressed in all animals prior to death. Abnormal necropsy observations were of lung discoloration and liver discoloration.

In Group II (24.09 milligrams per liter), there was 100% mortality with the last spontaneous death occurring on Day 6. In-chamber observations were similar to those described for Group I. However, the onset was delayed. Post-exposure observations, also similar to those described for Group I, were mainly of red nasal discharge, dry rales, and yellow staining of the ano-genital fur. These observations are presented in

III. RESULTS AND DISCUSSION (Cont.)

C. High Level Exposures (cont.)

Table 3. Observations recorded during the in-life period, presented in Table 11, were mainly of yellow staining of the ano-genital fur, dried red material around the nose, and general poor condition. Weight loss was steady prior to the death of the animals. Individual body weights are presented along with necropsy observations in Table 19. Abnormal necropsy observations include lung, liver, spleen, and kidney discoloration.

D. LC_{50} Exposures

A series of five additional one-hour exposures were used along with the Group II exposure in calculating the LC_{50} value.

In both Groups III and VI (7.05 and 6.49 milligrams per liter, respectively) there was 80% mortality. Observations recorded during each exposure period were similar to those described for the higher level exposure groups. Observations immediately following the exposures were also similar to those described for the higher level groups but were less severe. These observations are presented in Table 4 (Group III) and Table 6 (Group VI).

In both Groups III and VI the last spontaneous deaths occurred on Day 10. Observations of yellow or orange staining of the ano-genital fur, dried red material on the face, and general poor condition were recorded during the in-life periods in both the survivors and those animals dying spontaneously. These observations were more frequent in Group III (7.05 mg/l), the higher level group. Other noteworthy observations recorded during this period were body tremors, convulsions, and breathing described as rapid, labored, or irregular. Other observations recorded during the

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III. RESULTS AND DISCUSSION (Cont.)

D. LC_{50} Exposures (cont.)

in-life periods were scattered in occurrence.

Individual physical observations are presented in Table 12 (Group III) and Table 14 (Group VI).

All animals dying spontaneously experienced weight losses prior to death. Those animals surviving the 14-day in-life period (62F and 63F - Group III, 120F and 122F - Group VI) had not regained their original Day 0 body weight by Day 14. Individual body weights and necropsy observations are presented in Table 20 (Group III) and Table 22 (Group VI). Abnormal necropsy observations for those animals dying spontaneously included lung, liver, and small intestine discoloration and gaseous distention of the small intestines. Surviving animals sacrificed at terminus had lung discoloration (two of four rats) and absence of abdominal body fat (one of four rats).

Groups IX, V, and VIII (4.88, 2.86, and 1.89 milligrams per liter, respectively) had 20%, 10%, and 0% mortality, respectively. In-chamber observations were again similar to those described for the higher level exposure groups but no mucoid nasal discharge was observed. Observations recorded immediately following the exposures were most frequently of excessive salivation, mucoid nasal discharge, and yellow staining of the ano-genital fur. Exposure and post-exposure observations are presented in Table 9 (Group IX), Table 5 (Group V), and Table 8 (Group VIII).

Spontaneous deaths occurred on Days 7 and 10 in Group IX and on Day 12 in Group V. In-life observations common to these groups were mucoid nasal discharge, dry rales, and yellow staining of the ano-genital fur. Other noteworthy signs were soft stool, hypersensitivity to touch,

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III. RESULTS AND DISCUSSION (Cont.)

D. LC_{50} Exposures (cont.)

dried red material on the face, and rapid breathing. Abnormal in-life observations were less frequent in the lower level exposure groups. Individual physical observations are presented in Table 17 (Group IX), Table 13 (Group V) and Table 16 (Group VIII).

Animals dying spontaneously in Group IX (17OM, 18OF) and Group V (103F) lost weight steadily prior to death. Weight gain in the surviving animals was slower than is normally observed. In Group IX one of eight surviving rats did not regain its Day 0 body weight; in Group V four of nine and in Group VIII four of ten. When weight gain was observed in Groups IX and V it usually did not occur before Day 7. In Group VIII weight gain usually did not occur before Day 4. Individual body weights are presented along with necropsy observations in Table 25 (Group IX), Table 21 (Group V) and Table 24 (Group VIII). The most frequent abnormal necropsy observation was lung discoloration.

E. LC_{50} Determination

According to the method of Litchfield and Wilcoxon, the estimated LC_{50} value for a one-hour exposure to T-2306 CoC was determined to be 5.2 milligrams per liter with approximate 95% confidence limits of 4.4 milligrams per liter and 6.4 milligrams per liter.

IV. CONCLUSION

A series of one-hour inhalation exposures to a dust of T-2306 CoC was performed on Sprague-Dawley rats. The nominal exposure concentrations of Groups II, III, V, VI, VII, VIII and IX were 24.09, 7.05, 2.86, 6.49, 0.0, 1.89 and 4.88 milligrams per liter, respectively. Total mortality was produced at the nominal exposure concentration of 24.09 milligrams per liter. Partial mortality was produced at nominal exposure concentrations of 7.05 (80%), 6.49 (80%), 4.88 (20%) and 2.86 (10%) milligrams per liter.

Predominate physical abnormalities observed during the exposure and post-exposure periods were labored breathing, reduced activity, excessive salivation and lacrimation, mucoid and red nasal discharge, yellow staining of the ano-genital fur, dried red material on the facial area, and general poor condition. The most frequent abnormal necropsy observations were of lung and liver discoloration. Lung discoloration was also observed in a high number of control rats and thus may not be treatment-related.

The nominally determined median lethal concentration (LC_{50}) for a one-hour exposure to T-2306 CoC was determined to be 5.2 milligrams per liter with approximate 95% confidence limits of 4.4 milligrams per liter and 6.4 milligrams per liter.

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Table 1
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Summary of Exposure Conditions and Mortality Results

Group	Date Exposed	Nominal Exposure Concentration	Test Material Delivered	Chamber Flow Rate	Length of Exposure	Mortality	Day of Last Spontaneous Death
		mg/l	g	lpm	min.		
I[a]	1-24-79	45.97	44.13	16	60	5/10	2
II	1-25-79	24.09	23.13	16	60	10/10	6
III	3-1-79	7.05	6.77	16	60	8/10	10
IV[b]	3-8-79	13.9	13.38	16	60	0/10	-
V	3-9-79	2.86	2.06	12	60	1/10	12
VI	3-12-79	6.49	4.67	12	60	8/10	10
VII[c]	3-13-79	0.0	0.0	12	60	0/10	-
VIII	3-22-79	1.89	1.81	16	60	0/10	-
IX	3-23-79	4.88	4.10	14	60	2/10	10

[a]Group I terminated Day 2, not used in calculation of LC_{50}.
[b]Group IV terminated Day 1, not used in calculation of LC_{50}.
[c]Control group.

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An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Key to Tables 2-9

[a]Key:

NOA	-	No Observable Abnormalities
A-G	-	Ano-Genital
T	-	Removal from Chamber

Table 2
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Group I - 45.97 mg/l

Time Interval (min. into exposure)	NOA[a]	Reduced Activity	Eyes Closed	Excessive Lacrimation	Excessive Salivation	Labored Breathing	Gasping	Mucoid Nasal Discharge	Red Nasal Discharge	Yellow A-G Fur[a]	Red Material Peri-Ocular	Dry Rales	Moist Rales	Soft Stool
Pretest	10 of 10													
5						10 of 10	10 of 10							
10			10 of 10			10 of 10	10 of 10							
15		10 of 10	10 of 10	some	some	10 of 10	10 of 10							
30		10 of 10	10 of 10	some	some	10 of 10		some						
45		10 of 10	10 of 10		some	10 of 10		some						
60		10 of 10	10 of 10		some	10 of 10		some						
T[a]			4 of 10	3 of 10	4 of 10			2 of 10	8 of 10	9 of 10	2 of 10	5 of 10		
Post-Exposure Period														
120					4 of 10			7 of 10	2 of 10	9 of 10		6 of 10		1 of 10
180								4 of 10	5 of 10	9 of 10	1 of 10	5 of 10		
240	2 of 10							6 of 10	1 of 10	6 of 10		4 of 10		1 of 10
300			1 of 10	6 of 10					6 of 10	8 of 10		2 of 10	4 of 10	1 of 10

Table 3
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Group II - 24.09 mg/l

Time Inteval (min. into exposure)	NOA[a]	Labored Breathing	Excessive Lacrimation	Excessive Salivation	Eyes Closed	Mucoid Nasal Discharge	Reduced Activity	Dry Rales	Moist Rales	Yellow A-G Fur[a]	Red Nasal Discharge
Pretest	10 of 10										
15		most	most	most	most	most					
30		10 of 10		some	10 of 10	some	10 of 10				
45		10 of 10		10 of 10	10 of 10	10 of 10	10 of 10				
60		10 of 10		10 of 10	10 of 10		10 of 10				
T[a]			4 of 10	10 of 10				3 of 10	3 of 10	5 of 10	
Post-Exposure Period											
120			2 of 10	6 of 10				6 of 10		8 of 10	
180			1 of 10	1 of 10				4 of 10	5 of 10	10 of 10	8 of 10
240			1 of 10			1 of 10		3 of 10	2 of 10	10 of 10	8 of 10
300								4 of 10		10 of 10	9 of 10

Table 4
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Group III - 7.05 mg/l

Time Interval (min. into exposure)	NOA[a]	Reduced Activity	Eyes Closed	Excessive Lacrimation	Excessive Salivation	Labored Breathing	Mucoid Nasal Discharge	Yellow A-G Fur[a]	Dry Rales	Red Nasal Discharge
Pretest	10 of 10									
5		10 of 10	10 of 10	some	some					
15		10 of 10	10 of 10	most	most	most				
30		10 of 10	10 of 10	10 of 10	10 of 10	some				
45		10 of 10	10 of 10	10 of 10	10 of 10	some				
60		10 of 10	10 of 10	10 of 10	10 of 10	some	some			
T[a]				2 of 10	5 of 10		6 of 10	8 of 10	4 of 10	
Post-Exposure Period										
120					5 of 10		1 of 10	10 of 10	2 of 10	
180					1 of 10		7 of 10	7 of 10	3 of 10	
240	2 of 10						5 of 10	3 of 10	3 of 10	1 of 10
300	5 of 10							4 of 10	1 of 10	

Table 5
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Group V - 2.86 mg/l

Time Interval (min. into exposure)	NOA[a]	Reduced Activity	Eyes Closed	Excessive Lacrimation	Excessive Salivation	Labored Breathing	Mucoid Nasal Discharge	Yellow A-G Fur[a]	Dry Rales	Soft Stool	Brown A-G Fur[a]
Pretest	10 of 10										
5		10 of 10		10 of 10							
10		10 of 10	10 of 10	10 of 10	10 of 10	some					
15		10 of 10	10 of 10	10 of 10	10 of 10	some					
30		10 of 10	10 of 10	10 of 10	10 of 10	some					
45		10 of 10	10 of 10	10 of 10	10 of 10	some					
60		10 of 10	10 of 10	10 of 10	10 of 10	some					
T[a]	1 of 10			1 of 10	9 of 10		6 of 10	4 of 10	3 of 10	1 of 10	
Post-Exposure Period											
120	3 of 10				2 of 10		1 of 10	5 of 10	2 of 10	1 of 10	
180	5 of 10				1 of 10		2 of 10	1 of 10	1 of 10	1 of 10	
240	8 of 10						1 of 10				1 of 10.
300	5 of 10						3 of 10		2 of 10	2 of 10	

Table 6
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Group VI - 6.49 mg/l

Time Interval (min. into exposure)	NOA[a]	Reduced Activity	Eyes Closed	Excessive Lacrimation	Excessive Salivation	Labored Breathing	Mucoid Nasal Discharge	Yellow A-G Fur[a]	Dry Rales	Moist Rales	Red Nasal Discharge
Pretest	10 of 10										
5		10 of 10	most	some			some				
15		10 of 10	10 of 10		most	most	some				
30		10 of 10	10 of 10	most	most	most	most				
45		10 of 10	10 of 10	most	some	most	most				
60		10 of 10	10 of 10	most	some		most				
T[a]				4 of 10	8 of 10		1 of 10		1 of 10	4 of 10	
Post-Exposure Period											
120 min	4 of 10						2 of 10	3 of 10	3 of 10	1 of 10	1 of 10
180 min	3 of 10			2 of 10	2 of 10		5 of 10				
240 min	3 of 10			3 of 10	1 of 10		7 of 10	2 of 10	2 of 10		
300 min	2 of 10				2 of 10		6 of 10	1 of 10			

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Table 7
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Group VII - 0 mg/l (Control)

Time Interval (min. into exposure)	NOA[a]	Dry Rales
Pretest	10 of 10	
15	10 of 10	
30	10 of 10	
45	10 of 10	
60	10 of 10	
T[a]	10 of 10	
120	10 of 10	
180	10 of 10	
240	9 of 10	1 of 10
300	10 of 10	

Table 8
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Group VIII - 1.89 mg/l

Time Interval (min. into Exposure)	NOA[a]	Reduced Activity	Eyes Closed	Excessive Lacrimation	Excessive Salivation	Labored Breathing	Mucoid Nasal Discharge	Yellow A-G Fur[a]	Dry Rales	Dried Red Material on Face
Pretest	10 of 10									
5		10 of 10		most	10 of 10	most				
15		10 of 10	10 of 10	10 of 10	10 of 10	most 10				
30		10 of 10	10 of 10	10 of 10	most	10 of 10				
45		10 of 10	10 of 10	10 of 10	10 of 10	10 of 10				
60		10 of 10	10 of 10	10 of 10	10 of 10	10 of 10				
T[a]					4 of 10		8 of 10	9 of 10	1 of 10	
Post-Exposure Period										
120	1 of 10				3 of 10		3 of 10	6 of 10	1 of 10	
180	7 of 10					2 of 10			2 of 10	
240	5 of 10				2 of 10		3 of 10		2 of 10	1 of 10
300	6 of 10				3 of 10		2 of 10		2 of 10	

Table 9
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Exposure and Post-Exposure Observations
Group IX - 4.88 mg/l

Time Interval (min. into Exposure)	NOA[a]	Reduced Activity	Eyes Closed	Excessive Lacrimation	Excessive Salivation	Labored Breathing	Mucoid Nasal Discharge	Yellow A-G Fur[a]	Dry Rales
Pretest	10 of 10								
5		10 of 10	most		most	some			
10		10 of 10	10 of 10	some	most	most			
15		10 of 10	10 of 10	10 of 10	most	10 of 10			
30		10 of 10	10 of 10	most	most	most			
45		10 of 10	10 of 10	most	most	most			
60		10 of 10	10 of 10	most	most	most			
T[a]	1 of 10			1 of 10	6 of 10		3 of 10	4 of 10	4 of 10
Post-Exposure Period									
120	1 of 10				4 of 10		3 of 10	8 of 10	2 of 10
180	4 of 10				4 of 10		2 of 10	3 of 10	1 of 10
240	5 of 10				4 of 10			1 of 10	
300	6 of 10				2 of 10			2 of 10	

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An Acute Inhalation Toxicity Study of T-2306 CoC in the Rat

Physical Observations
Key to Tables 10-17

N.O.A.	-	No Observed Abnormalities.
Agr.	-	Agressive Behavior
(+)Act.	-	Increased Activity
(-)Act.	-	Reduced Activity
Exc.Lacr.	-	Excessive Lacrimation
Exc.Sal.	-	Excessive Salivation
A-G	-	Ano-Genital
Poor Cond.	-	Poor condition

Table 10
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Physical Observations[1]
Group I - 45.97 mg/l

An. No.	Sex	Behavior (-) Act.	Respiration Nasal Discharge Red	Respiration Rales Dry	Ocular Exc. Lacr.	Appearance Dried Red Material Around Nose	Appearance Eye(s) Closed	Appearance Yellow Stains A-G Area	Appearance Poor Cond.	Digest Soft Stool	Other Convulsions	Other Body Tremors	Total Number of Days Observed
								1	1				1
10	M	1	1										0
11	M							1	1				1
12	M	1	1					2	1		1		2
13	M		2						1			1	2
14	M	1	1			1							
20	F	1	1			1		1					1
21	F	1	1		1			2					2
22	F	1	1		1	1	1	1					1
23	F	1	1	1	1			2					2
24	F		2	1	1			2		1			2

1A total of 2 observations were reported during the study. Group was terminated on Day 2. Total number of abnormalities observed may exceed 2 since an animal may have been observed with more than one abnormality during any given observation period. Total number of observations may also be less than 2 due to the spontaneous death of an animal.

Table II
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Physical Observations[1]
Group II - 24.09 mg/l

An. No.	Sex	Behavior		Respiration					Ocular	Appearance					Digestion		Other				Total Number of Days Observed
		NOA	(-) Act.	Nasal Discharge Red	Nasal Discharge Muc	Rales Dry	Rales Moist	Labored Breathing	Exc. Lacr.	Red and/or Brown Mat'l. Nasal Area Dry	Red and/or Brown Mat'l. Nasal Area Moist	Stains A-G Area Yellow Red	Stains A-G Area Yellow Orange	Stains A-G Area Yellow Yellow	Poor Cond.	Exc. Sal.	Ataxia	Convulsions	Loss of Righting Reflex	Fur Wet Nasal Area	
30	M			2					1		1			2	1						2
31	M							1	1	3		1		2	2						3
32	M			1	1	1			1	3				3	2		1				3
33	M	1	1	1		1		1		2				4	1	1		1	1		5
34	M		1	1		1		1	2	3			1	2	2		1				4
40	F				1		1		1	1	1			2	1						2
41	F		1		1					2				4	2						4
42	F				1			1		2			1	2	2						3
43	F					1								1							1
44	F		3	2	1	1		2	1	1			1	4	3		1		1	1	5

[1]Total number of observations may exceed total number of days observed (usually 14, unless there were spontaneous deaths) since an animal may have observed with more than one abnormality during an observation period.

Table 12
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Physical Observations[1]
Group III - 7.05 mg/l

An. No.	Sex	N.O.A.	Respiration: Nasal Discharge Red	Respiration: Nasal Discharge Mucoid	Respiration: Rales Dry	Respiration: Rales Moist	Respiration: Breathing Labored	Respiration: Breathing Rapid	Respiration: Breathing Irreg.	Appearance: Dry Red Material Nasal Area	Appearance: Pilo-Erection	Appearance: Stained A-G Orange	Appearance: Stained A-G Yellow	Appearance: Poor Cond.	Digest: Soft Stool	Other: Convul-sions	Other: Body Tremors	Other: Siezure	Total Number of Days Observed
50	M		1	1			1				1		1	2			1	1	3
51	M		1				3					1	4	3					5
52	M						1		1										2
53	M			1			1		1				3	1			1		3
54	M				1		1						7		1	2	2		8
60	F		1		1		2			2			9	5		1	2		9
61	F				1	1	1	2		4			10	2			1		10
62	F	3			1		2	2		2			11	1		1	3		14
63	F			1			1	2		9	1		14	1	1		1		14
64	F	1					2	1		5			2	1					8

[1]Total number of observations may exceed total number of days observed (14, except when there were spontaneous deaths) since an animal may have been observed with more than one abnormality during an observation period.

Table 13
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Physical Observations[1]
Group V - 2.86 mg/l

An. No.	Sex	N.O.A.	Behavior		Respiration					Ocular		Appearance				Digestion		Other			Total Number of Days Observed
			Agr	(+) Act.	Nasal Discharge Mucoid	Rales Dry	Rales Moist	Breathing Labored	Breathing Rapid	Exc. Lacr.	Film Covering Eye(s)	Dried Red Material Nasal Area	Hair loss	Yellow Stains A-G Area	Poor Cond.	Soft Stool	Exc. Sal.	Sensitive to: Touch	Sensitive to: Movement	Cold Extremities	
90	M	11				1										2					14
91	M	8			1	2	1					1				1	1				14
92	M	10				3	1					1				1	1				14
93	M	9			3	1						2				1					14
94	M	5			2	1				1		4					2				14
100	F	4			2	1	2					2	8-abdomen 5-L.hind leg								14
101	F	12			1									1							14
102	F	2				6				1		8	1-B.hind legs	7							14
103	F	1	3	2	2			1	1		1	2		7	1			3	1	1	14
104	F	7				5	1		1			2									14

[1]Total number of observations may exceed total number of days observed since an animal may have been observed with more than one abnormality during an observation period.

Table 14
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Physical Observations[1]
Group VI - 6.49 mg/l

An. No.	Sex	Behavior: N.O.A.	Behavior: Agr	Behavior: (-) Act.	Respiration: Nasal Discharge Red	Respiration: Nasal Discharge Muc	Respiration: Rales Dry	Respiration: Breathing Labored	Respiration: Breathing Rapid	Ocular: Film Covering Eye(s)	Ocular: Exc. Lacr.	Appearance: Dried Red/Brown Material: Nose	Appearance: Dried Red/Brown Material: Mouth	Appearance: Dried Red/Brown Material: Forepaws	Appearance: Stained A-G Area: Orange	Appearance: Stained A-G Area: Yellow	Appearance: Poor Cond.	Digestion: Exc. Sal.	Digestion: Soft Stool	Other: Con-vul-sions	Other: Body Tre-mors	Other: Cold Extre-mities	Other: Sensitive to: Touch	Other: Sensitive to: Sound	Total Number of Days Observed
110	M				1		1					1/0				2			1						2
111	M	1										1/0	2/0						2	1	1				5
112	M				1							2/0	0/1			2			2	1	1				4
113	M	1		1		1		1			1					1	1	1		1	1				4
114	M		1			1		1				2/0	1/0			1		2	2	1					3
120	F						6		2			5/0	9/0	1/0	3	11							3		14
121	F							2		1		7/0	6/0	1/0	3	6				2		1		1	10
122	F	2	1		1	2	1	2	2			3/0				1	1			1	1		3		14
123	F	1				1	1					1/0	1/0			1									3
124	F											2/0	2/0			2			2						3

[1]Total number of observations may exceed total number of days observed (usually 14, except when an animal died spontaneously) since an animal may have been observed with more than one abnormality during an observation period.

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Table 15
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Physical Observations[1]
Group VII - 0 mg/l

An. No.	Sex	N.O.A.	Respiration: Nasal Discharge: Mucoid	Respiration: Rales: Dry	Respiration: Rales: Moist	Appearance: Dried Material Around Nose: Red	Appearance: Dried Material Around Nose: Brown	Other: Hypersensitive to Touch	Total Number of Days Observed
130	M	8		3		2		1	14
131	M	14							14
132	M	11	1	2					14
133	M	12		2					14
134	M	12	1	1		1			14
140	F	12		1	1				14
141	F	13					1		14
142	F	10		3		1			14
143	F	14							14
144	F	10		4					14

[1]A total of 14 observations were reported during the study. Total number of abnormalities observed may exceed 14 since an animal may have been observed with than one abnormality during any given observation period.

Table 16
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Physical Observations[1]
Group VIII - 1.89 mg/l

An. No.	Sex	N.O.A.	Respiration				Appearance				Digest		Other	Total Number of Days Observed
			Nasal Discharge	Rales		Breathing	Dried Red Material		Stained A-G Area		Soft Stool	Exc. Sal.	Sensitive to Touch	
			Mucoid	Dry	Moist	Rapid	Nose	Mouth	Yellow	Brown				
150	M	7	3	2									3	14
151	M	9	2	1			1					1	2	14
152	M	8	1	1				1			1	1	2	14
153	M	13											1	14
154	M	6		4	1					1			2	14
160	F	1	4	7		2	1		5			1	4	14
161	F	8	2	1		2							5	14
162	F	7		3	1	4							1	14
163	F	8		4		1							1	14
164	F	4	1	5		1	1						3	14

[1]Total number of observations may exceed total number of days observed since an animal may have been observed with more than one abnormality during an observation period.

Table 17
Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Physical Observations[1]
Group IX - 4.88 mg/l

			Respiration				Appearance					Digest	Other					
							Dried Red Material			Stained A-G Area								
An. No.	Sex	N.O.A.	Nasal Discharge Mucoid	Rales Dry	Breathing Rapid	Breathing Labored	Nose/ Mouth	Head	Hairloss	Yellow	Orange	Soft Stool	Convul-sions	Body Tremors	Sensitive to Touch	Fur Stained Red	Total Number of Days Observed
170	M	1										2	1	3	2		6
171	M	5	1	2			3/0					1			5		14
172	M		2	5					4-B. fore-paws	1					6		14
173	M	8	2			1									3		14
174	M	5	2				2/1			1	1				8		14
180	F				1					5	3				9		9
181	F	4	2				5/0			6	1				5		14
182	F	6	1	1	1		3/0	1							1	1	14
183	F	6		2					1-abdomen	3					4		14
184	F	7	2	3											6		14

[1]Total number of observations may exceed total number of days observed (usually 14, except when an animal died spontaneously) since an animal may have been observed with more than one abnormality during an observation period.

Table 18
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group I - 45.97 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2[a]	Day 4	Day 7	Day 14	Necropsy Observations*
10	M	214	177	170[b]				B. lungs mottled pink and dark red. Liver mottled purple and brown.
11	M	229	198[b]					B. lungs mottled dark red, pink, and red.
12	M	251	203	195[b]				B. lungs mottled pink and dark red. Liver mottled dark purple and brown with brown area (1 cm x 1 cm) on visceral surface of L. lobe.
13	M	240	197	182				Liver has white areas (approx. 1 cm diameter) on all lobes.
14	M	221	171	172				B. lungs mottled pink and white.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[a]Group I terminated on Day 2.
[b]Spontaneous death.

Table 18 (cont.)
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group I - 45.97 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2[a]	Day 4	Day 7	Day 14	Necropsy Observations*
20	F	202	169	162[b]				B. lungs mottled pink and purple.
21	F	201	172	162				B. lungs mottled white, orange, and pink.
22	F	211	176	167[b]				B. lungs mottled red and dark red. Liver mottled purple and brown.
23	F	204	180	169				B. lungs mottled oange and red with white foci. Liver mottled dark red and purple with brown area (1 cm x 4 cm) on visceral surface of medial lobe.
24	F	201	172	164				B. lungs mottled pink and orange. Entire surface of liver light brown in color.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[a]Group I terminated on Day 2.
[b]Spontaneous death.

Table 19
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group II - 24.09 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
30	M	266	221	198[a]				B. lungs mottled dark red and red. Liver mottled dark red and tan. Upper half of spleen light red, lower half dark red. Small intestines distended with gas.
31	M	248	212	190[a]				B. lungs mottled red and dark red. Liver mottled dark brown, black, and purple. B. kidneys mottled brown and purple. Spleen mottled black and purple. Small intestines yellow and pink in color.
32	M	230	199	183[a]				B. lungs mottled red and dark red. Liver mottled dark brown, purple, and tan. Small intestines yellow and pink in color.
33	M	278	148	227	310[a]			B. lungs mottled orange, red, and dark red. Liver mottled purple, black, and brown on anterior surfaces of all lobes; visceral surfaces mottled tan, red, and brown. Small intestine distended with gas. Absence of abdominal fat around adrenal glands and kidneys.
34	M	227	192	175	157[a]			B. lungs mottled orange and red. Liver mottled brown, purple, and black; white area on visceral surfaces of L. lobe (approx. .5 cm x 2 cm), white area on visceral surface of medial lobe (approx. .2 cm x .7 cm). Abse of abdominal fat around adrenal glands and kidneys.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[b]Spontaneous death.

Table 19 (cont.)
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group II - 24.09 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
40	F	210	188	172[a]				B. lungs bright red in color with scattered tan areas; all lobes slightly distended. Liver abnormally dark red in color with tan areas on dorsal surfaces. Upper half of spleen light red in color, lower half dark red.
41	F	213	195	187	178[a]			B. lungs bright red in color. Liver mottled purple, brown, and black; brown and tan areas on visceral surfaces of medial and left lobes (approx. .3 cm x 1 cm). Absence of abdominal fat around adrenal glands and kidneys.
42	F	217	189	185[a]				B. lungs mottled pink, red, and dark red. Liver mottled purple, brown and black. Spleen black and purple in color.
43	F	218	196	181[a]				B. lungs bright dark red. Liver abnormally dark red-brown in color. Ileum, duodenum, and jejunum distended with gas. Half of spleen appears black in color. Stomach impacted with food.
44	F	224	199	185	168[a]			B. lungs mottled orange, red, and dark red. Liver mottled black, brown, and purple. Small intestines green in color and distended with gas. Absence of abdominal fat covering adrenal glands and kidneys on dorsal body wall.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[b]Spontaneous death.

Table 20
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group III - 7.05 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
50	M	291	251	245[a]				B. lungs mottled orange and red. Liver mottled purple and tan. Small intestines yellow-green in color and distended with gas.
51	M	286	249	237	212[a]			Thymus dark red in color. B. lungs orange-red in color Both surfaces of L. lateral lobe of liver mottled.
52	M	297	262	248[a]				B. lungs mottled dark and light red. Liver mottled dark red and tan. Thoracic cavity contains small amount of fluid.
53	M	288	263	259[a]				Thymus congested. B. lungs mottled red and dark red. Liver congested.
54	M	265	242	237	231	211[a]		B. lungs mottled red and white.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[b]Spontaneous death.

Table 20 (cont.)
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group III - 7.05 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
60	F	220	189	184	174	155[a]		B. lungs mottled orange and dark tan with light tan foci on L. lobe. Liver mottled brown and dark brown. Small intestines dark green in color.
61	F	213	186	177	165	152[a]		B. lungs mottled pink and red. Liver has brown and green areas (.5 cm x 1 cm) on visceral surfaces of L. and R. lobes. Small intestines green-yellow in color and distended with gas. Posterior half of L. kidney dark brown in color. Distal (caudal) tip of spleen black in color. Stomach distended with gas.
62	F	229	208	205	190	192	216	N.O.A.
63	F	214	197	189	178	165	148	Absence of abdominal adipose tissue.
64	F	221	206	203	190	173[a]		B. lungs mottled dark red and dark pink. Liver spotted brown and tan with some purple mottling. Intestines yellow in color.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[a]Spontaneous death.

Table 21
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group V - 2.86 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
90	M	250	233	232	231	253	291	B. lungs have purple foci.
91	M	248	234	230	239	255	302	B. lungs have red foci.
92	M	232	208	193	185	211	252	B. lungs have purple foci.
93	M	225	208	208	221	238	268	N.O.A.
94	M	254	230	218	196	182	242	Red focus on diaphragm surface of L. posterior lobe of left lung.
100	F	213	194	192	190	208	227	N.O.A.
101	F	212	198	195	182	175	211	N.O.A.
102	F	209	197	195	190	189	205	N.O.A.
103	F	210	192	194	172	167[a]		Anterior and middle lobe of R. lung and anterior half of L. lung mottled tan and purple; posterior and post-caval lobe of R. lung and posterior (caudal) half of L. lung bright red in color. Liver has brown area (1 cm x .5 cm) on visceral surface of median lobe. Absence of abdominal body fat covering adrenals and kidneys.
104	F	213	198	193	186	190	204	N.O.A.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[a]Spontaneous death.

Table 22
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group VI - 6.49 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
110	M	274	238	223[a]				B. lungs mottled orange and dark red. Liver mottled dark red and brown; light brown areas on visceral surface of R. lobe (approx. .2 cm x .5 cm). Small intestines yellow-green in color and distended with gas. Absence of abdominal fat covering kidneys and adrenal glands.
111	M	254	220	202	179[a]			B. lungs mottled dark and light red. Jejunum, ileum, and duodenum yellow in color. L. lateral lobe of liver mottled dark red and tan.
112	M	237	215	202	170[a]			Liver mottled dark red and light green.
113	M	234	205	197	168[a]			B. lungs mottled red, tan, and pink with numerous red foci. Liver motttled brown and tan. Anterior half of stomach cream colored. Absence of abdominal body fat.
114	M	281	254	236[a]				B. lungs mottled orange and red. Liver mottled dark red and dark brown. Small intestines yellow-green in color and distended with gas. Absence of abdominal body fat.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[a]Spontaneous death.

Table 22 (cont.)
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group VI - 6.49 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
120	F	214	193	185	176	168	172	B. lungs mottled pink and red. Absence of abdominal fat.
121	F	227	202	192	178	160[a]		B. lungs bright red in color. Liver has alternating patches of brown and dark red.
122	F	220	199	190	176	162	201	B. lungs mottled pink and white. Absence of fat covering adrenals and kidneys.
123	F	218	192	183[a]				B. lungs mottled dark red and orange. Liver mottled dark red and brown. Small intestines yellow-green in color. Absence of abdominal body fat.
124	F	209	182	171[a]				B. lungs mottled orange and red. Liver mottled brown and dark red. Absence of abdominal body fat.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[a]Spontaneous death.

Table 23
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group VII - 0 mg/l (control)

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
130	M	241	238	242	249	257	280	B. lungs mottled pink and grey.
131	M	256	252	268	274	279	311	B. lungs have small grey foci.
132	M	233	238	248	260	249	306	B. lungs mottled light and dark red; nodular green areas on L. lung.
133	M	263	263	274	281	295	329	B. lungs pink with dark red foci.
134	M	218	215	224	231	244	272	B. lungs mottled red and white.
140	F	205	201	208	208	207	220	B. lungs mottled pink and white.
141	F	203	199	204	214	213	214	B. lungs mottled red and pink with red foci.
142	F	216	213	219	215	226	231	B. lungs pink with dark red foci. L. kidney has dilated pelvis.
143	F	208	210	212	213	205	226	N.O.A.
144	F	203	201	204	209	210	219	B. lungs mottled pink and red.

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

Table 24
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group VIII - 1.89 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
150	M	264	240	226	208	210	265	B. lungs have numerous red and white foci.
151	M	276	253	248	248	264	314	N.O.A.
152	M	299	280	270	279	280	312	B. lungs mottled pink and tan with many dark foci.
153	M	286	264	264	270	289	318	B. lungs mottled tan and pink with numerous red foci; few white foci of L. lobe.
154	M	274	248	242	240	251	293	B. lungs mottled pink and grey.
160	F	215	198	186	175	200	211	B. lungs mottled pink and orange.
161	F	212	191	184	192	189	219	B. lungs mottled pink and red; posterior lobe of R. lung has two large white foci.
162	F	230	202	190	178	196	226	B. lungs mottled pink and orange.
163	F	228	208	204	199	206	224	B. lungs mottled pink and tan with small dark foci.
164	F	204	188	179	169	166	195	B. lungs have numerous white foci.

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

Table 25
An Acute Inhalation Toxicity Study
of T-2306 CoC in the Rat

Individual Body Weights and Necropsy Observations
Group IX - 4.88 mg/l

Animal Number	Sex	Body Weights (g) Day 0	Day 1	Day 2	Day 4	Day 7	Day 14	Necropsy Observations*
170	M	228	206	195	171[a]			B. lungs bright red in color. Liver mottled purple and brown.
171	M	255	230	220	194	191	269	B. lungs pink with dark foci.
172	M	257	242	242	240	249	288	B. lungs mottled pink and beige with numerous red foci.
173	M	239	215	204	197	209	264	B. lungs pinkish-red with dark red mottling.
174	M	240	224	220	211	206	246	B. lungs light tan in color with numerous red foci.
180	F	217	193	185	167	147[a]		B. lungs mottled pink and red. Liver has brown areas on visceral surfaces of R. and L. lobes. L. kidney has brown area (.5 cm diameter) on ventral surface. Small intestines yellow-green in color and distended with gas. Absence of abdominal fat pads.
181	F	207	194	196	181	188	215	B. lungs pink with dark red mottling.
182	F	204	189	186	185	174	205	B. lungs mottled pink and white with few red foci.
183	F	213	189	184	169	174	222	B. lungs mottled pink and tan with dark red foci.
184	F	225	195	190	177	b	213	B. lungs mottled light tan and white with few red foci.

* N.O.A. - No observed abnormalities.
Key: R = right; L = left; B = bilateral.
[b]Spontaneous death.
[b]Body weight not recorded.