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RHÔNE-POULENC INC.
CN 7500, CRANBURY, NJ 08512-7500
TELEPHONE: (609) 395-8300

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September 4, 1992

**CERTIFIED MAIL
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Document Processing Center (TS-790)
Attn: Section 8(e) Coordinator (CAP Agreement)
Office of Toxic Substances
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID NO.: 8ECAP - 0004

RP CAP REPORT NO.: RPS - 0197

Dear Sir/Madam:

On behalf of Rhône-Poulenc Inc. (RPI, CN5266, Princeton, NJ 08543-5266) and its subsidiaries, the attached report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA (8ECAP - 0004).

The enclosed report provides information on the following chemical substance:

Chemical Identity:	Trimethylolpropane triacrylate (TMPTA) (Coded as C-254 in report)
CAS Registry No:	15625-89-5
CAS Registry Name:	2-Propenoic acid, 2-ethyl-2-[[[(1-oxo-2-propenyl)oxy]methyl]-1,3-propanediyl ester

REC'D
2/7/95

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The title of the enclosed report is:

An Acute Intraperitoneal Toxicity Study in Rats

The following is a summary of the adverse effects observed in this report.

The test material produced neurologic signs in most or all of the animals at the 100, 300, and 500 mg/kg dose levels. These included ataxia, flaccid limb and body tone, and impaired righting and visual placing reflexes. Also noted in a few animals were impaired toe pinch, corneal, pupillary, and startle reflexes, and (in single animals) convulsions and spastic gait. The single survivor at 100 mg/kg and the two survivors at 300 mg/kg did not exhibit any of these signs. At 30 mg/kg, one animal exhibited an abnormal righting reflex at 24 hours only. The intraperitoneal LD50 was 90 mg/kg for both sexes combined.

RPI does not claim any portion of the information in this submission to be TSCA confidential business information (TSCA CBI).

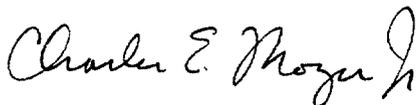
RPI has not previously submitted any TSCA Section 8(e) notices or premanufacture notification on the subject chemical substance.

RPI has submitted other studies on this material under the CAP agreement; see RP CAP Report Nos. RPS-0198 and RPS-0270.

On August 15, 1985, Celanese submitted to EPA all available toxicity data on the multifunctional acrylates. However, RPI does not have a detailed list in our records of the reports that were submitted. Therefore, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

Further questions regarding this submission may be directed to Dr. Glenn S. Simon, Director of Toxicology at (919)549-2222 (Rhône-Poulenc, P.O. Box 12014, 2 T.W. Alexander Drive, Research Triangle Park, NC 27709).

Sincerely,



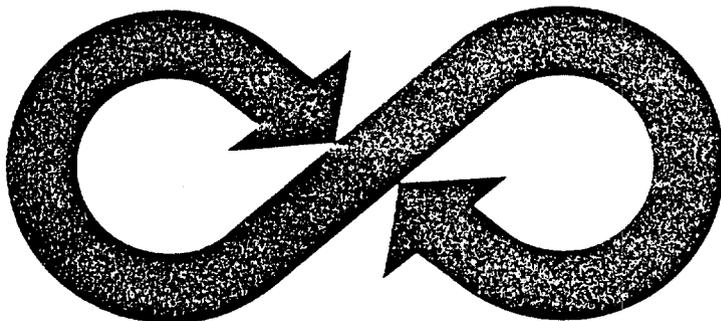
Charles E. Moyer, Jr., Ph.D.
Director, Product Safety
(609)860-3589

CEMjr/mm
Enclosures

ACRYLATES-MULTIFUNCTIONAL-TMP

C-254

CAP ID No. S-LT-PCW-0146
Reviewed for Sec. 8 (e)
Compliance Program
On 10/23/91 By PCW



Bio/dynamics Inc.

Division of Biology and Safety Evaluation

PROJECT NO. 6818-81

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

Test Material: C-254

Submitted to: Celanese Corporation
New York, New York

Date: July 22, 1982

I. INTRODUCTION

An acute intraperitoneal toxicity study in rats with C-254 was conducted for the Celanese Corporation at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey 08873. The purpose of this study was to evaluate the acute toxicity of the test material when administered by intraperitoneal injection to rats; to determine the intraperitoneal LD₅₀ of the material; and to determine whether neurologic effects could be produced with acute administration.

This report has been reviewed by the Quality Assurance Unit of Bio/dynamics, Inc. to assure its conformance with the protocol and the raw data.

II. DATES OF STUDY:Range finding:

Animal Receipt:	October 13, 1981
Initiation (Dosing):	October 28, 1981
Termination:	November 4, 1981

Animal Receipt:	October 20, 1981
Initiation (Dosing):	November 6, 1981
Termination:	November 7, 1981

LD₅₀ Determination:

Animal Receipt:	November 17, 1981
Initiation (Dosing):	December 1, 1981
Termination:	December 15, 1981

Additional Doses for
LD₅₀ Determination:

Animal Receipt:	November 24, 1981
Initiation (Dosing):	December 14, 1981
Termination:	December 28, 1981

III. STUDY PERSONNEL:

Study Director: Carol S. Auletta, B.A., D.A.B.T.
Supervisor: Donna L. Blaszcak, B.S.
Technician-In-Charge: Nancy Minczeski, B.A.
Study Monitor: Carol Loder, B.S.
(Report Preparation)

IV. MATERIALS:

A. Test Animals: Albino Rats

Strain: Sprague-Dawley CD^R

Reason for Selection: Standard laboratory animal

Supplier: Charles River Breeding Laboratories, Inc.
Wilmington, Massachusetts 01887

Number: Range-finding: Eighteen (one/sex/dose level)
LD₅₀ Determination: Sixty (five/sex/dose level)

Age: Young Adults

Weight: Males: 256 - 300 grams
(pretest) Females: 240 - 255 grams

Equilibration Period: 14 - 20 days

Observations: All animals were checked for viability twice daily. Prior to assignment to study all animals received a physical examination to ascertain suitability for study.

Husbandry:

Housing: Group-housed (six/cage) during equilibration. Individually housed during study.

Cages: Suspended, stainless steel cages with wire mesh bottoms.

IV. MATERIALS (cont.):

Environmental Conditions: Temperature: 68-76°F is considered an acceptable temperature range for rats; room temperature was monitored twice daily and maintained within this range to the maximum extent possible.

Humidity: monitored daily

Light Cycle: 12 hours light, 12 hours dark

Food: Purina Laboratory Chow, ad libitum

Water: Automatic watering system, ad libitum
Municipal water supply (Elizabethtown Water Company)

Identification: Each animal was identified with a metal ear tag bearing a unique number prior to testing.

Selection: All animal numbers from each shipment of animals were placed in random order, using a random numbers table. A separate list was generated for males and females. Animals for study were selected by following these lists. Any animals considered unsuitable because of poor health or outlying body weight were excluded and the succeeding number was used.

B. Test Material: C-254

Description: Liquid

Date of Receipt: September 28, 1981

Received From: Celanese Corporation

Storage: Room temperature

V. METHODS:A. Test Design:

Doses for the preliminary range-finding screen were administered as follows:

<u>Number of Animals</u>		<u>Dose Level</u>	<u>Dose Volume</u>	<u>Conc.</u>
<u>M</u>	<u>F</u>	(mg/kg) (C-254)	(ml/kg C-254 in Corn Oil)	(% w/w C-254 in Corn Oil)
1	1	27.3	0.32	9.1
1	1	91	1.1	9.1
1	1	273	3.2	9.1
1	1	910	10.6	9.1
1	1	2730	31.8	9.1
1	1	835	5.2	16.7
1	1	2505	15.6	16.7
1	1	4175	25.9	16.7
1	1	8350	51.8	16.7

Based on mortality observed at these dose levels; doses for the LD₅₀ determination were administered as follows:

<u>Number of Animals</u>		<u>Dose Level</u>	<u>Dose Volume</u>	<u>Conc.</u>
<u>M</u>	<u>F</u>	(mg/kg) (C-254)	(ml/kg C-254 in Corn Oil)	(% w/w C-254 in Corn Oil)
5	5	30	0.21	1.0
5	5	100	0.72	1.0
5	5	300	2.1	1.0
5	5	500	3.4	1.0
5	5	1000	7.0	1.0
5	5	2500	17.3	1.0

B. Preparation of Test and Control Material:

Vehicle: Corn Oil

Procedure: Appropriate amounts of the test material were weighed and placed in an appropriate container and vehicle was added to achieve the total desired weight.

Control Material (corn oil) was administered as received, no mixture was required.

V. METHODS (cont.):C. Administration of Test and Control Material:

The test and control material were administered by intraperitoneal injection using a syringe of appropriate size, fitted with a 21 gauge needle.

D. Duration of Study:

Range-finding: 7 days

LD₅₀ Determination: 14 days

E. Experimental Evaluation:

Range finding: Animals were observed for viability twice daily for fourteen days and deaths were recorded.

LD₅₀ Determination:

Viability Checks: Twice Daily

Observations for Pharmacologic and Toxicologic Signs:

Approximately 1, 2 and 4 hours after dosing and daily thereafter for fourteen days.

Neurologic Examination:

Approximately 1, 2, 4 and 24 hours after dosing.

Body Weights:

Pretest (weights used for calculation of doses)

Day of Dosing (just prior to dosing)

Days 7 and 14

Terminal: Any animals which did not survive for 14 days were weighed at the time of death or at the time they were found dead.

V. METHODS (cont.):F. Postmortem Examination:

No postmortem examinations were made on animals used for range-finding screens. The following was done for all other animals: Gross postmortem examinations were performed on all animals which died or were found dead during the study. All animals surviving at termination of the observation period (Day 14) were killed by carbon dioxide inhalation and examined grossly. All abnormalities were recorded but no tissues were saved.

G. Reference - LD₅₀ Calculation:

Miller, Lloyd C. and M.L. Tainter., Estimation of the ED₅₀ and Its Error by Means of Logarithmic-Probit Graph Paper, Proc. Soc. Exp. Biol. Med. 57: 261-264 (1944).

VI. RESULTS AND DISCUSSION:A. Mortality:

Dose levels and mortality for preliminary range-finding studies were as follows:

<u>Dose Level</u> (mg/kg)	<u>Mortality</u>
27.3	0/2
91	0/2
273	0/2
835	2/2
910	1/2
2505	2/2
2730	1/2
4175	2/2
8350	2/2

Based on results of this study, several doses were administered for LD₅₀ determination. Four doses which produced an appropriate range of mortality were selected for presentation in this report. (Data from other dose levels will be maintained in the study file). Dose levels, mortality data and the estimated LD₅₀ with 95% confidence limits were as follows:

<u>Dose Level</u> (mg/kg)	<u>Mortality</u>			<u>Time to Death</u>
	<u>Males</u>	<u>Females</u>	<u>Total</u>	
30	0/5	0/5	0/10	-
100	4/5	5/5	9/10	1-2 Days
300	3/5	5/5	8/10	4-6.5 Hr
500	5/5	5/5	10/10	3.5-6 Hr
LD ₅₀ (mg/kg):	120	55	90	
95% Confidence Limits (mg/kg):	20-220	a	54-126	

^aDue to the distribution of mortality, confidence limits can not be calculated.

VI. RESULTS AND DISCUSSION (cont.):B. Body Weights (Table I)

Two of the five males which received 30 mg/kg exhibited weight losses at Day 7 and two others exhibited gains at Day 7 which were lower than those of control animals. All males in this group gained weight between Days 7 and 14, but overall gains were generally lower than those seen in control animals. Weight gains of females in this group were comparable to those of control females. Weight gains in the three surviving males in the 100 and 300 mg/kg groups were comparable to (100 mg/kg) or slightly lower than (300 mg/kg) control gains.

C. Neurologic Signs (Table II)

Signs seen prior to death in most or all animals in the 100, 300 and 500 mg/kg dose groups included ataxia, flaccid limb and body tone, pelvic elevation, and impaired righting and visual placing reflexes. Also noted in a few animals were impaired toe pinch, corneal, pupillary and startle reflexes and (in single animals) convulsions and a spastic gait. The single survivor in the 100 mg/kg group and the two survivors in the 300 mg/kg group showed no abnormalities. One of the ten animals, all of which survived, in the 30 mg/kg group exhibited an abnormal righting reflex at 24 hours only; no other unusual neurologic signs were noted in this group.

D. Pharmacologic and Toxicologic Signs

Signs seen on the day of dosing in most animals in the 100, 300 and 500 mg/kg groups included decreased activity and respiration rates and apparent severe abdominal discomfort (contortions and writhing). The latter observations are consistent with the lesions described below, which were seen upon postmortem examination. Transient soft stool and fecal staining were seen in survivors in these groups. The only unusual signs at the 30 mg/kg dose level were decreased

VI. RESULTS AND DISCUSSION (cont.):

activity and respiration rates in 3 of the 10 animals at 24 hours. All survivors were free of unusual signs from Day 3 through termination of the study (Day 14).

E. Postmortem Examination (Table IV)

Animals which died and those which were killed after 14 days exhibited a large number of postmortem abnormalities, most notably in the abdominal viscera. Most of these appeared to represent irritation and/or infectious sequelae resulting from intraperitoneal injection of the vehicle and/or test material.

Carol S. Auletta 7/20/82
Carol S. Auletta, B.A., D.A.B.T. Date
Study Director

GMBurke, Sc.D 7/23/82
for Geoffrey K. Hogan, Ph.D., D.A.B.T. Date
Vice-President of Toxicology

Craig Lamb 7/23/82
Craig Lamb, B.A. Date
Manager, Quality Assurance

TABLE I
AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS
TEST MATERIAL: C-254
BODY WEIGHTS (GRAMS) AND TIME FOUND DEAD

-10-
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Dose Level mg/kg	Animal No. & Sex	Pretest Weights		Interim Deaths		Survivors				
		Pre- test	Day of Dosing	Terminal Weight	Time Found Dead ^a	Chg ^b	Day 7	Chg ^b	Day 14	Chg ^b
Control (11/17/81)	5002 M	276	288				324	48	363	87
	4989 M	293	313				327	34	366	73
	5034 M	263	277				302	39	332	69
	4994 M	268	282				306	38	337	69
	5010 M	293	312				339	46	368	75
	5087 F	237	244				253	16	257	20
	5098 F	244	250				257	13	266	22
	5086 F	245	260				268	23	269	24
	5080 F	241	256				253	12	251	10
	5113 F	246	246				262	16	268	22
	Control (11/24/81)	5169 M	300	318				351	51	388
5196 M		286	298				328	42	353	67
5159 M		283	297				324	41	350	67
5192 M		273	281				306	33	333	60
5145 M		277	289				316	39	343	66
5220 F		231	239				239	8	252	21
5222 F		233	239				245	12	247	14
5243 F		247	256				264	17	280	33
5212 F		243	254				258	15	262	19
5264 F		249	256				266	17	285	36
30		5136 M	277	284				270	-7	313
	5160 M	283	294				327	44	362	79
	5176 M	291	307				312	21	353	62
	5185 M	290	298				318	28	348	58
	5194 M	289	297				274	-15	329	40
	5225 F	244	250				264	20	277	33
	5233 F	239	244				260	21	275	36
	5231 F	237	242				249	12	267	30
	5249 F	235	241				249	14	257	22
	5247 F	232	239				256	24	271	39
	100	5208 M	284	291	302	23.5 Hr				
5204 M		288	301				326	38	357	69
5210 M		300	312	328	23.5 Hr					
5180 M		296	313	301	23.5 Hr					
5181 M		300	315	314	23.5 Hr					
5257 F		233	241	258	Day 2	25				
5258 F		231	243	258	Day 1	27				
5268 F		245	253	255	23.5 Hr					
5274 F		235	242	237	Day 2	2				
5279 F		245	250	257	Day 2	12				
300	5031 M	261	272				278	17	321	60
	4985 M	274	292	284	4.0 Hr					
	4992 M	257	276				288	31	314	57
	5005 M	256	276	266	6.5 Hr					
	5030 M	260	268	260	6.5 Hr					
	5122 F	250	255	244	6.5 Hr					
	5094 F	255	265	257	6.5 Hr					
	5112 F	248	258	251	6.5 Hr					
	5058 F	250	263	254	6.5 Hr					
	5078 F	254	266	256	6.5 Hr					
500	4977 M	272	289	279	3.5 Hr					
	4975 M	274	291	281	3.5 Hr					
	5051 M	256	267	260	3.5 Hr					
	4976 M	274	290	276	6.0 Hr					
	5018 M	280	290	283	4.0 Hr					
	5056 F	245	261	251	3.5 Hr					
	5066 F	255	268	261	6.0 Hr					
	5108 F	240	247	240	4.0 Hr					
	5115 F	251	261	254	4.0 Hr					
	5074 F	241	251	244	4.0 Hr					

^aSee Table III for type of death.

^bChange from prefasted weight (grams). Weight changes were not calculated for animals that died on the day of dosing or overnight after dosing (i.e., animals found dead at the 24 hour observation).

TABLE III

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-254

SUMMARY OF PHARMACOLOGIC AND TOXICOLOGIC SIGNS^a

Observations	Dose (mg/kg)	Animals Found Dead					Survivors					Time Last Observed
		Interval: Day:					Interval: Day:					
		Hr:					Hr:					
		1	2	4	24	2	1	2	4	24	2	
Controls (11/17/81 & 11/24/81)												
No observable abnormalities												
Hypopnea	30	-	-	-	-	-	-	-	-	-/1	-	24 Hr
Hypoactivity		-	-	-	-	-	-	-	-	2/1	-	24 Hr
Hypopnea	100	-	2/-	2/-	-/4	-	-	-	-	-	-	
Ocular Discharge		-	-	-	-/1	-	-	-	-	-	-	
Fecal Staining		-	-	-	-	-	1/-	1/-	1/-	1/-	-	24 Hr
Soft Stool		-	-	-	-	-	1/-	1/-	1/-	-	-	4 Hr
Hypothermia		-	-	-	-/3	-	-	-	-	-	-	
Hypoactivity		3/2	3/4	4/4	-/4	-	-	-	-	-	-	
Abdominal Writhing		2/3	4/5	1/4	-	-	-	1/-	-	-	-	2 Hr
Death ^d		-	-	-	4/1	-/4	-	-	-	-	-	
Total Number of Animals		4/5	4/5	4/5	-/4	-	1/-	1/-	1/-	1/-	1/-	
Hypopnea	300	1/5	3/5	2/5	-	-	-	-	-	-	-	
Dyspnea		-	-	2/-	-	-	-	-	-	-	-	
Ocular Discharge		-	-/1	-/2	-	-	-	-	-	-	-	
Fecal Staining		-	-	-	-	-	2/-	2/-	2/-	2/-	-	24 Hr
Unthrifty Coat		-	-	-	-	-	-	-	-	-	2/-	Day 2
Soft Stool		-	-	-	-	-	2/-	2/-	2/-	2/-	-	24 Hr
Hypothermia		-	-	1/1	-	-	-	-	-	-	-	
Hypoactivity		3/5	3/5	-/5	-	-	-	-	1/-	-	-	4 Hr
Prostration		-	-	2/-	-	-	-	-	-	-	-	
Abdominal Writhing and Rolling-Over Movements		3/5	3/5	-/3	-	-	2/-	2/-	-	-	-	2 Hr
Death ^d		-	-	1/-	2/5	-	-	-	-	-	-	
Total Number of Animals		3/5	3/5	2/5	-	-	2/-	2/-	2/-	2/-	2/-	
Hypopnea	500	5/5	5/5	1/1	-	-	No survivors					
Ocular Discharge		-/1	-/1	-	-	-						
Hypothermia		-	-	1/1	-	-						
Hypoactivity		5/5	5/5	-/1	-	-						
Prostration		-	-	1/-	-	-						
Abdominal Writhing and Rolling-Over Movements		5/5	5/5	-	-	-						
Death ^d		-	-	4/4	1/1	-						
Total Number of Animals		5/5	5/5	1/1	-	-						

^aNumbers represent number of males and females out of 5 per sex, exhibiting sign during interval.

^bAnimals found dead - see Table I for time of death.

^cSurvivors - sacrificed at termination of the study (Day 14).

^dDeath of an animal was noted only at the time which it occurred.

TABLE II (cont.)

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-254

SUMMARY OF NEUROLOGIC SIGNS^a

Interval: Day:	Hr:	Animals Which Died				Survivors			
		1	2	4	24	1	2	4	24
<u>Observations*</u>	<u>Dose</u> (mg/kg)								
Pelvic Elevation	500	1/5	1/3	-	-	(No survivors)			
Ataxia		4/5	5/5	-/1	-				
Body Tone-Flaccid		4/4	5/5	1/1	-				
Limb Tone-Flaccid		1/-	3/3	1/1	-				
-Rigid		-/1	-	-	-				
Abnormal Toe Pinch		-	-	1/-	-				
Abnormal Righting									
Reflex		5/5	5/5	1/1	-				
Abnormal Visual									
Placing Reflex		3/3	5/4	1/1	-				
Abnormal Corneal Reflex		-	-	1/-	-				
Abnormal Startle Reflex		-	-	1/1	-				
Death ^b		-	-	4/4	1/1				
Total Number of Animals		5/5	5/5	1/1					

^aNumbers represent number of males and females, out of 5 per sex, which exhibited signs at given interval.

^bDeath of an animal was noted at the time which it occurred.

-: Indicates observation not present.

*A glossary of neurologic terminology is presented in Appendix A.

TABLE IV

AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-254

NECROPSY OBSERVATIONS
SURVIVORS^a

Necropsy Observations	Controls (11/17/81)		Controls (11/24/81)		30 mg/kg		100 mg/kg		300 mg/kg	
	Males		Females		Males		Females		Males	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
AMU	5	5	5	5	5	5	5	5	5	5
IM	0	0	1	1	1	1	2	2	0	0
MB	0	0	1	1	3	3	6	6	3	3
AE	0	8	3	9	1	8	9	8	1	8
LR	2	9	4	0	7	8	6	0	3	9
Lungs: dark red foci mottled pale red pale red mottled dark red	X X X X	X X X X	X X X X	X X X X	X X X X	X X X X	X X X X	X X X X	X X X X	X X X X
Liver: adhered to body cavity wall white membranous covering										
Large Intestine: contained green substance distended										
Spleen: white membranous covering white patch small adhered to body cavity or stomach										
Adrenals: pale red										
Viscera and/or Mesenteries: white foci										
Body Cavity: white fluid dark red fluid										

^aSurvivors=animals were sacrificed at termination of the study (Day 14).
X=Observation present; N.O.A.=No observable abnormalities.

TABLE IV (cont.)
AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-254
NECROPSY OBSERVATIONS
ANIMALS FOUND DEAD^a

	100 mg/kg				300 mg/kg				500 mg/kg			
	Males		Females		Males		Females		Males		Females	
	A	N	M	F	A	N	M	F	A	N	M	F
Necropsy Observations	5	5	5	5	5	5	5	5	4	4	4	5
Ocular Discharge	2	2	2	2	1	0	1	0	9	9	0	9
Nasal Discharge	0	1	8	8	5	5	0	2	8	7	5	1
Lungs:	8	0	0	1	7	8	8	4	9	7	5	1
dark red foci	X	X	X	X	X	X	X	X	X	X	X	X
pale red	X	X	X	X	X	X	X	X	X	X	X	X
bright red	X	X	X	X	X	X	X	X	X	X	X	X
mottled dark red	X	X	X	X	X	X	X	X	X	X	X	X
mottled bright red	X	X	X	X	X	X	X	X	X	X	X	X
mottled pale red	X	X	X	X	X	X	X	X	X	X	X	X
mottled tan	X	X	X	X	X	X	X	X	X	X	X	X
Liver:												
mottled dark red												
postmortem changes												
Stomach:												
black foci												
mucosa-mottled dark red or red thickened												
wrinkled brown substance												
green fluid												
Small Intestine:												
yellow/green/white fluid												
red/red-green fluid												
brown/brown-green fluid												

^aAnimals found dead: see Table I for time of death.
X=Observation present; N.O.A.=No observable abnormalities.

TABLE IV (cont.)
AN ACUTE INTRAPERITONEAL TOXICITY STUDY IN RATS

TEST MATERIAL: C-254

NECROPSY OBSERVATIONS

ANIMALS FOUND DEAD^a

	100 mg/kg		300 mg/kg		500 mg/kg		
	Males		Males		Males		
	Females	Females	Females	Females	Females	Females	
<u>Necropsy Observations</u>	A 5 2 0 8 0 0 1	M 5 2 2 5 7 8 4 9	A 4 9 8 5 5 0	M 5 0 3 2 4 2 8 8	A 4 9 7 7 5 1 6 8	M 5 0 0 1 5 6 6 8 5 4	N.O.A.
<u>Large Intestine:</u> contents hard green-brown fluid	X	X X X	X X X	X X X	X X X	X X X	N.O.A.
<u>Adrenals:</u> dark red/red	X X X X X X X	X X X X X X X	X X X X X X X	X X X X X X X	X X X X X X X	X X X X X X X	N.O.A.
<u>Testes (right and/or left):</u> found in body cavity	X X X						N.O.A.
<u>Body Cavity:</u> yellow fluid with oily suspension orange fluid walls red	X X X X X X X	X X X X X X X	X X X X X X X	X X X X X X X	X X X X X X X	X X X X X X X	N.O.A.
<u>Uterus:</u> distended clear fluid grey		X X X X X X X					N.O.A.

^aAnimals found dead: see Table I for time of death.
X=Observation present; N.O.A.=No observable abnormalities.

APPENDIX A

AN ACUTE INTRAPERITONAL TOXICITY STUDY IN RATS

GLOSSARY - NEUROLOGIC EVALUATIONS

The following is a description of selected terminology and procedures used to assess neurologic function in the rat.

1. Central Nervous System:

- a. Tremors - Involuntary, purposeless, oscillatory movements which result from alternate contraction of opposing muscle groups.
- b. Twitches - Brief, coarse, involuntary muscle contractions which cause the animal to abruptly jerk or twitch its limbs and/or body. They are frequently a precursor to convulsions.

c. Convulsions - These are identified by type:

- 1) Clonic-Type Convulsions - Convulsions with alternated contraction and relaxation of the voluntary muscles. Some examples:

A coordinated, unsymmetrical convulsion with natural, purposeful-like movements, e.g., "running".

Repetitive symmetrical jerks or twitches of the limbs, often accompanied by mild clonus or leading to a severe convulsion.

Clonus of the jaws only.

A seizure where the animal repeatedly "pops" into the air.

A terminal clonic convulsion resulting from respiratory failure.

- 2) Tonic-Type Convulsions

Persistent contraction and spasm of a set of voluntary muscles. Typically a sustained extension of the hindlimbs, usually preceded by tonic flexion.

A seizure in which the head, body and limbs are rigidly extended and arched backwards or forward.

3) Miscellaneous - Type Convulsions

- a) Rock and Roll - A convulsion in which the animal is prostrate on its back and rocks from side to side in a seeming effort to right itself, occasionally rolling over (overshooting) and continuing to rock again.
- b) Sitting-Up - A convulsion in which the animal sits upright on its hindlimbs during the seizure; a sitting-up seizure in which the forelimbs are held together or crossed in an attitude resembling prayer.

2. Behavior (Bizarre or stereotyped behaviors):

- a. Head Flicking - head shaking or backward flip of head.
- b. Head Searching - a stereotyped, repetitive turning of the head from side to side, as though searching the environment.
- c. Hallucinatory-Like - behavior in which the animal appears to be responding to objects not present, e.g., visual tracking or fear-withdrawal.
- d. Compulsive Biting - usually of the grid floor.
- e. Compulsive Licking - usually of the cage walls.
- f. Self-Destructive Biting - usually biting of toes with bleeding.
- g. Prancing Forelimbs - Restless shifting from one forelimb to the other, with slight turning of the body from side to side.

3. Posture:

This reflects both the behavioral and neurologic state of the animal, since tail and pelvic elevation are usually increased by excitation or rigidity and decreased by stupor or flaccidity. It is evaluated, in the main, during forward movement of the animal.

- a. Pelvic Elevation - The elevation of the abdomen from the surface during forward movement of the animal. It primarily reflects the limb position-its extension or flexion. A crouched posture or abnormal head position may also be present.
- b. Tail Elevation - This is observed during the forward movement of the animal; the tail tends to be lower when the animal is at rest.
- c. Limb Rotation - Any abnormal rotation of the hindlimbs from a vertical stance.

4. Gait:

- a. Ataxia/Waddling - This results from an inability of the truncal, pelvic and limb muscles to move in unison, so that the animal tends to excessively sway, rock or lurch to the side as it proceeds forward and is variously unable to walk a straight line. Lateral wobbling movements of the pelvis are due to weakness of the gluteal muscles.
- b. Circling - Tendency to move in circles around and along objects, or in an open environment.
- c. Other:
 - 1) Steppage - Due to paralysis of the muscles of dorsiflexion of the foot or toes, the animal drags its forelimbs in walking, walks on its knuckles, or lifts its forelimbs unusually high to avoid dragging its toes over the ground (spino-muscular involvement).
 - 2) Spastic - Shuffling gait with legs rigidly extended and not lifted during movement. When severe, the animal may walk on tip-toe (cortico-spinal involvement).
 - 3) Dysmetric - Incoordinate movement with a coarse tremor due to overshooting goal and oscillating back and forth trying to reach it (cerebellar or posterior column involvement).
 - 4) Duck-Walk - An involvement of the hindlimbs in which the animal walks with adducted thighs, laterally extended legs and on tip-toe, causing it to assume a crouched posture (produced by narcotic analgesics).
 - 5) Scissor - The forelimbs cross over in extension (in front of one another) due to marked spasticity and adductor hyper-tonicity, and the animal moves on the balls of its feet (cortico-spinal impairment).

5. Muscle Tone:

This reflects both the behavioral and neurologic state of the animal, increasing with apprehension or excitement and decreasing with relaxation. It is scored in terms of the relative presence of muscle resiliency (resistance to compression) or flaccidity (softness with continuing cavity deformation after compression).

- a. Body Tone - This is determined by compressing the sides of the animal between the lower thorax and pelvis several times at approximately one second intervals, using the thumb and index finger.
- b. Limb Tone - The animal is restrained in supine position and the tip of the index finger gently pushed against the plantar surface of each hindpaw several times to determine its resistance to passive flexion.

6. Reflexes:

- a. Toe Pinch - A leg withdrawal response (ipsilateral flexor reflex) after light compression of the lateral surface of the mid-digit of each foot with a forceps.
- b. Pupil - Normally the pupil will constrict on sudden exposure to intense light. Persistent constriction or no response to light are considered abnormal. c.
- Righting - The animal is placed on its back, and allowed to right itself. Sluggish or incomplete righting is considered abnormal.
- d. Visual Placing - The animal is lifted vertically, by mid-tail, approximately 15 cm. above an inverted cage, and then lowered to elicit the visual placing response, usually characterized by an extension of both fore-and-hindlimbs before contact.
- e. Corneal - The blink or eye-closure response of each eye to light tactile stimulation of the cornea.
- f. Startle - A sudden body jerking movement of the animal in response to a finger snap.



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 0503 INFO REQUESTED (VOL ACTIONS)
 0504 INFO REQUESTED (REPORTING RATIONALE)
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CHEMICAL NAME: _____

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUR/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PRODCOMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0299 OTHER	01 02 04
0211 CHR. TOX (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0240 METAB/PHARMACO (HUMAN)	01 02 04		

TRIAQE DATA: NON-CBI INVENTORY
 YES
 NO

CAS SR NO 15625-89-5

ONGOING REVIEW: YES (DROP/REFER)
 YES (DROP/REFER)
 NO (CONTINUE)

IMPLIMINI REF:R

SPECIES: RAT

TOXICOLOGICAL CONCERN: MED
 LOW
 HIGH

USE: _____

PRODUCTION: _____

15625-89-5

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12095A

~~M~~ NP

evidenced by ~~a~~

Acute intraperitoneal toxicity in rats is ~~of moderate concern based on~~ an LD₅₀ of 120 mg/kg in males and 55 mg/kg in females (combined LD₅₀ is 90 mg/kg). Sprague-Dawley rats (5/sex/dose) received intraperitoneal injections of the compound in corn oil. Deaths were as follows: 0/10 at 30 mg/kg, 9/10 (4/5 males, 5/5 females) at 100 mg/kg, 8/10 (3/5 males, 5/5 females) at 300 mg/kg, and 10/10 at 500 mg/kg; deaths in controls were not reported. Signs of neurotoxicity prior to death at 100 mg/kg included tremors (3/10), ataxia (6/10), flaccid limb (2/10) and body tone (6/10), and impaired righting and placing reflexes (7/10). At 300 and 500 mg/kg, additional neurotoxicological signs included convulsions, pelvic elevation, and other abnormal reflexes. At 30 mg/kg, 1/10 rats exhibited an abnormal righting reflex at 24 hours only. Histopathology included abnormalities in the lungs (dark red foci and mottling), and reddish color in the stomach mucosa and adrenals, and fluid in the body cavity.