

ORIGINAL

**TSCA NON-CONFIDENTIAL BUSINESS INFORMATION**

DOCUMENT DESCRIPTION	DOCUMENT CONTROL NUMBER	DATE RECEIVED
8EHQ-92-10394	<b>89110000207</b>	3/22/11

COMMENTS: COMMUN S (DECLASS)

**DOES NOT CONTAIN CBI**

334120



**The Procter & Gamble Company**  
NA Regulatory & Technical Relations  
One Procter & Gamble Plaza (C-6)  
Cincinnati, OH 45202  
www.pg.com

U.S. EPA  
Office of Pollution Prevention and Toxics  
Document Control Office (7407M)  
1200 Pennsylvania Ave., NW  
Washington, DC 20460  
Attn: TSCA Declassification Coordinator

11 MAR 22 AM 6:03  
RECEIVED  
APR 1 2010

**Re: Declassification Activity-Health and Safety Filing  
8EHQ-0892-10394 (EPA DCN 88920008688)**

Dear Sir/Madam:

The Procter & Gamble Company (P&G) provides this submission to amend the Public Display Version of our submission pursuant to the TSCA Section 8(e) Compliance Audit Program (CAP) under terms of CAP Agreement # 8ECAP-0003.

This amended submission is composed of the following:

- (a) new information provided in this cover letter and its attachment(s); and
- (b) the unaltered original submission which directly follows.

Any CBI substantiation which appears in the original submission is no longer applicable as the information which was originally claimed CBI is disclosed in this revised submission.

Should you have any questions concerning this amended submission, please contact me at (513) 983-2531 or [froelicher.jm@pg.com](mailto:froelicher.jm@pg.com).

Sincerely,

THE PROCTER & GAMBLE COMPANY

Julie Froelicher  
NA Regulatory & Technical Relations Manager  
The Procter & Gamble Company  
One Procter & Gamble Plaza  
Cincinnati, OH 45202  
(513) 983-2531  
[froelicher.jm@pg.com](mailto:froelicher.jm@pg.com)



**Attachment 1**  
**Public Display Version**

**Chemical Identity**

**CAS RN**

Water

Isopropanol

Pine oil

Ammonium hydroxide

Potassium hydroxide

Fatty acids, C8-18 and C18-unsatd.

67701-05-7

Benzenesulfonic acid, 2,5-dichloro-4-[4,5-dihydro-3-methyl-5-oxo-4-[(4-sulfophenyl)azo]-1H-pyrazol-1-yl]-, disodium salt

6359-98-4

9,10-Anthracenedione, 1,2-dihydroxy-

72-48-0

Benzenesulfonic acid, 2,2'-(1,2-ethenediyl)bis-[5-[[4-[bis(2-hydroxyethyl)amino]-6-(phenylamino)-1,3,5-triazin-2-yl]amino]-,disodium salt

4193-55-9

Fragrance

8EHQ-0892-103945  
COMPANY SANITIZED

# Procter & Gamble

The Procter & Gamble Company  
Ivorydale Technical Center  
5299 Spring Grove Avenue, Cincinnati, Ohio 45217-1087

92 AUG 01 PM 1:17

## Public Display Copy

August 19, 1992

Document Processing Center (TS-790)  
Office of Toxic Substances  
Environmental Protection Agency  
401 M St. S.W.  
Washington, D.C. 20460

8EHQ-92-10394 INT.  
88920008688

Attn: Section 8(e) Coordinator (CAP Agreement)

This submission is being made pursuant to the TSCA Section 8(e) Compliance Audit Program and the terms of CAP Agreement # 8ECAP-0003. This report discharges our Company obligation to report the attached data under TSCA Section 8(e). The filing of these studies does not indicate that we agree that "substantial risk" exists. We are following the agency's guidance and the terms of the CAP agreement, but we expressly disclaim that the filings reflect a decision that these materials pose any significant human or environmental safety risks.

The material identified in the attached report as B7188 is a confidential mixture. The composition of the mixture is appended as Attachment 1. The report is titled "Acute Oral Toxicity (LD50) Study in Rats". Any correspondence relating to this submission should reference study # 939-20028.

The attached study report indicates oral administration of the test material resulted in pharmacotoxic signs including ataxia and decreased motor activity following oral administration of 3160, 4640, 6810, 10000, and 14700 mg/kg of the test material. Decreased respiratory rate, decreased limb tone, and prostration were observed in all but the low dose group. Aggressive hostility was observed in the 6810 and 10000 mg/kg groups, and absent placing reflex in the 4640, 6810, and 10000 mg/kg groups. The acute oral LD50 is calculated to be 6408 mg/kg.

We do not believe findings in this report reasonably support a conclusion of substantial risk to human health or the environment. Nevertheless, we are submitting this report to discharge any potential liability under TSCA Section 8(e).

To our knowledge, this report has not been the subject of a prior submission to EPA under the provisions of TSCA.

The specific chemical constituents and percentage composition of this mixture is claimed as confidential business information. A sanitized version of this submission containing generic chemical names has been included as part of this submission. Answers to the seven questions required to substantiate this claim of confidentiality are provided below:

1. Confidentiality of the chemical constituents and their percentages should be maintained indefinitely. There are no plans for this information to be otherwise disclosed, and this technology has significant commercial value.
2. To our knowledge, there have been no government confidentiality determinations made for this mixture.
3. The specific chemical identity and exact proportions of the constituents of this mixture have not been disclosed outside the Company. There are no plans to disclose publicly the exact composition of this mixture at any time in the future.

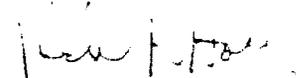
0 0 0 3

*Procter & Gamble*

4. Measures for protection of the compositional information include "need to know" internal restriction within the Company. An internal code is used to protect the identity of the material. Information is maintained in locked files. Employees leaving the Company are contractually bound not to disclose Company secrets.
  5. The exact composition of this mixture has not appeared in advertising or promotional literature, MSD sheets, any publications or any other media available to the general public or competitors.
  6. Disclosure of the information claimed as CBI would result in substantial harm to the Company's competitive position. This formula provides an important commercial opportunity for a competitor. Knowledge of the exact composition of this mixture could enable a competitor to duplicate the formula without R&D cost, thus providing an unfair competitive disadvantage to the Procter & Gamble Company. Development of this formula required many technically trained personnel, hundreds of hours of research and development, and significant capital investment valued in aggregate at . . . . Any competitor would normally be required to make a similar investment to duplicate the formula. Disclosure of this information would allow a competitor to duplicate the formula without incurring significant R&D costs, thus doing substantial harm to our competitive position.
  7. The information we have identified as confidential is not health or safety data.
- Any questions concerning this submission, may be directed to me at (513) 627-5551.

Sincerely,

THE PROCTER AND GAMBLE COMPANY



Richard H. Hall, Ph.D.  
Manager  
Regulatory & Government Affairs  
The Procter & Gamble Company

**Public Display Copy**

**Water**

**Isopropanol**

**Pine oil**

**Fatty acid**

**Ammonium hydroxide**

**Potassium hydroxide**

**Colorant**

**Substituted stilbene**

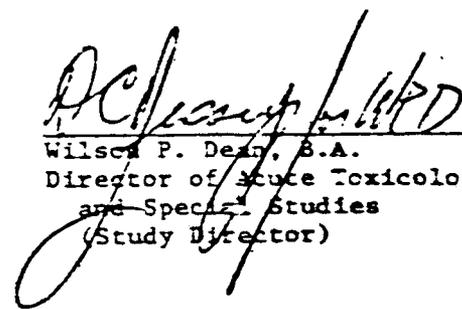
**Fragrance**

939-20028

International Research and Development Corporation

SPONSOR: The Procter and Gamble Company  
TEST MATERIAL: B7188  
SUBJECT: Acute Oral Toxicity (LD<sub>50</sub>)  
Study in Rats.

RECEIVED BY  
MAR 27 1978  
N. E. GILMAN

  
Wilson P. Dean, B.A.  
Director of Acute Toxicology  
and Special Studies  
(Study Director)

Approved by: D. Clifford Jessup, Ph.D.  
Associate Director of Research

Date: March 22, 1978

*International Research and Development Corporation*

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Appendix 1

LD<sub>50</sub> - Record of Individual Dose Level

Appendix 2

Acute Oral Toxicity Observation Data

I. SYNOPSIS

The acute oral LD<sub>50</sub> and 95% confidence limits of combined male and female rats were found to be:

6408 (5144 - 7928) mg/kg.

II. TEST MATERIAL

The test material was received from The Procter and Gamble Company, Cincinnati, Ohio, on October 25, 1977. It was identified as "Sample Code B7188, Submitter code B7188, Request Ltr. #ESBTS 473" and was received as a yellow liquid.

III. METHOD

Twenty-five male and 25 female rats of the Charles River CD strain (obtained from Charles River Breeding Laboratories, Inc., Portage, Michigan) weighing from 200 to 286 (pre-fasting body weight) were used for this study. The rats were housed by sex in groups of 5 rats per cage in hanging wire-mesh cages in temperature and humidity controlled quarters. They were maintained in accordance with the recommendations contained in H.E.W. Publication No. 74-23 (N.I.H.) entitled "Guide for the Care and Use of Laboratory Animals". The rats were conditioned for a minimum of 14 days prior to study initiation. Water and Purina Laboratory Chow were available ad libitum, except for an overnight period of 18½ to 20 hours immediately preceding oral administration during which food, but not water, was withheld.

The test material was administered orally by gavage, as received, undiluted, at the following dosage levels to male and female rats: 3160, 4640, 6810, 10000 and 14700 mg/kg.

Five rats of each sex were used at each dosage level. Volumes administered were as follows:

3160 mg/kg level - 3.31 ml/kg.  
4640 mg/kg level - 4.86 ml/kg.  
6810 mg/kg level - 7.14 ml/kg.  
10000 mg/kg level - 10.48 ml/kg.  
14700 mg/kg level - 15.41 ml/kg.

Observations for pharmacotoxic signs and mortality were made at 1/4, 1/2, 1, 2, 4 and 24 hours and daily thereafter for a total of 14 days. Body weights were recorded prior to fasting, immediately preceding dosing and at 14 days. All rats which died on study were subjected to gross necropsy examination as were all survivors at the end of the 14 day observation period.

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IV. RESULTS

A. MORTALITY AND LD<sub>50</sub> VALUES:

Dose - Mortality Data

Dosage Level mg/kg	Number of Deaths														Total Mortalities			
	Hrs.		Days												Male	Female	Total	
	0-4		1	2	3	4	5	6	7-14									
	M	F	M	F	M	F	M	F	M	F	M	F	M	F				
3160				2												0/5	2/5	2/10
4640																0/5	0/5	0/10
6810			1	1	2	1										1/5	4/5	5/10
10000			3	5		1										4/5	5/5	9/10
14700	5	5														5/5	5/5	10/10

Acute Oral LD<sub>50</sub> and 95% Confidence Limits

Combined Male and Female Rats: 6408 (5144 - 7928) mg/kg.

Statistical Reference

Computations were performed by Mr. R. Bruce, Statistician, The Procter and Gamble Company, using the computer program BLISS 17, written by D. J. Finney, University of Edinburgh, Scotland.

B. PHARMACOTOXIC SIGNS:

See attached Appendix 2.

C. BODY WEIGHTS:

All surviving rats exhibited normal body weight gains with the exception of the male rat (#76972) at the 10000 mg/kg dosage level which exhibited a less than normal body weight gain.

D. NECROPSY FINDINGS:

Necropsy observations were noted as indicated on pages 5 and 7.

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1. Rats which died during the study period:

Gross Necropsy  
Observations:

	Dosage Level ng/kg									
	Number Exhibiting Sign/Number Necropsied									
	3160		4640		6810		10000		14700	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Lungs, congestion		2/2			1/1	4/4	3/4	2/5	3/5	3/5
Stomach, fluid filled					1/1	3/4	3/4	5/5	5/5	5/5
Stomach, distension						2/4	2/4	2/5		
Stomach, mucosa, thickened					1/1		2/4	1/5		
Stomach, mucosa, hyperemia					1/1	1/4	2/4	4/5	3/5	4/5
Small intestines, fluid filled					1/1	1/4	1/4	3/5	5/5	4/5
Liver, mottled coloration					1/1		1/4	1/5		
Urinary bladder, distension					1/1					
Stomach, glandular mucosa, dark red foci						1/4	1/4			
Matted feces around anogenital region		1/2								
Dry red material around nose		1/2						1/5		

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Gross Necropsy Observations:	Dosage Level mg/kg									
	Number Exhibiting Sign/Number Necropsied									
	3160		4640		6810		10000		14700	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Stomach, contains bright red or pink oily material		1/2					1/4			
Red stain around mouth					1/1					
Intestines contain light red oily material						1/4	1/4	1/5		
Liver, pale coloration						1/4	1/4			
White stain around mouth								1/5		

*International Research and Development Corporation*

Revised Page 7

2. Rats which were sacrificed following 14 days of observation:

Gross Necropsy Observations:	Dosage Level mg/kg							
	Number Exhibiting Sign/Number Necropsied							
	3160		4640		6810		10000	
	Male	Female	Male	Female	Male	Female	Male	Female
No gross lesions	4/5		2/5		1/4	1/1		
Lungs, congestion				4/5			1/1	
Stomach, fluid filled	1/5							
Stomach, mucosa, thick- ened		1/3			2/4			
Kidneys, pale coloration			2/5		2/4		1/1	
Kidneys, mottled coloration		3/3	1/5	1/5				
Liver, pale coloration			1/5		1/4			

  
 Wilson P. Dean, B.A.  
 Director of Acute Toxicology  
 and Special Studies

191-VA

APPENDIX 1

ERDC =

LD50 - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg by 3.160 750 Code B-7188  
Number of animals dosed Male 5 Female 5

All data are based on sample as received.

Sample Preparation: \_\_\_\_\_ g of sample, was mixed with \_\_\_\_\_ (g) (ml) solvent \_\_\_\_\_ to make a dosing solution of \_\_\_\_\_ (w/w) \_\_\_\_\_ (v/v).

Specific Gravity: 1.0 ml of sample weighed 0.54 g at 23 °C, S.G. = 0.954 g/ml.

		Individual Animal Data									
		1	2	3	4	5	1	2	3	4	5
Date	Animal #	76940	76941	76942	76943	76944	76945	76946	76947	76948	76949
	Sex	♂	♂	♂	♂	♂	♀	♀	♀	♀	♀
12/27/77	Prefasted Wt. g	286	220	250	268	230	220	203	210	217	248
12/28/77	Fasted Wt. g	250	209	230	255	210	209	191	198	205	232
12/28/77	Dose/24h ml	.83	.69	.76	.84	.70	.69	.63	.66	.68	.77
	Time of Death						DAY 2				DAY 2
	14 Day Wt. g	378	204	297	230	300		272	272		315
	Final Wt. g	340	251	240	252	293	X	238	234	X	270

Avg. prefasted weight 235.2 DP 2/24/78  
Avg. prefasted weight of survivors 239.4 DP 2/24/78  
Avg. 14 day weight of survivors 304.8 DP 2/24/78  
Total Dead: Male 0 Female 2  
Animals Received: 1 R 12/14/77

$$\frac{3.169 \text{ lbs}}{0.954 \text{ g/ml}} = 3.31 \text{ ml/kg}$$

Worker's Signature Charles R Evans Date 12/28/77  
Corroborating Witness [Signature] Date 12/28/77  
Worker's Signature [Signature] Date 5/29/79  
Corroborating Witness [Signature] Date 5/29/79

191-1129

APPENDIX 1

= RDC =

LD50 - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg by 4.640 PSG Code R-7128  
Number of animals dosed Male 5 Female 5

All data are based on sample as received.

Sample Preparation: \_\_\_\_\_ g of sample was mixed with \_\_\_\_\_ (g) (ml) solvent \_\_\_\_\_ to make a dosing solution of \_\_\_\_\_ (w/w) \_\_\_\_\_ (v/v).

Specific Gravity: 1.0 ml of sample weighed 9.54 g at 23 °C, S.G. = 0.954 g/ml.

Since 2.00 <sup>4-177</sup> Individual Animal Data

Date	Animal #	1	2	3	4	5	1	2	3	4	5
	Sex	♂	♂	♂	♂	♂	♀	♀	♀	♀	♀
12/27/77	Prefasted Wt. g	212	218	250	213	236	238	216	235	203	2
12/28/77	Fasted Wt. g	202	205	235	204	225	229	205	223	191	2
12/28/77	Dose/Eat ml	1.0	1.0	1.1	1.0	1.1	1.1	1.0	1.1	0.9	1
	Time of Death		<del>Day 1</del>							<del>Day 1</del>	
	14 Day Wt. g	287	313	295	296	302	296	250	296	215	2
	7 Day Wt. g	250	265	240	250	310	270	220	250	253	2

Avg. prefasted weight 226.4 <sup>DP 2/24/78</sup> g  
Avg. prefasted weight of survivors 226.4 <sup>DP 2/24/78</sup> g  
Avg. 14 day weight of survivors 292.2 <sup>DP 2/24/78</sup> g  
Total Dead: Male 0 Female 0  
Animals Received: CR 12/14/77

$$\frac{4.64 \text{ g/kg}}{0.954 \text{ g/ml}} = 4.86 \text{ ml/kg}$$

Worker's Signature Charles R Evans  
Corroborating Witness M. L. Thompson  
Worker's Signature [Signature]  
Corroborating Witness [Signature]

Date 12/28/77  
Date 12/28/77  
Date 3/29/78  
Date 3/29/78

191-1.9

APPENDIX 1

TRDC =

LD50 - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg by 6.81 P&G Code R-7188  
Number of animals dosed Male 5 Female 5

All data are based on sample as received.

Sample Preparation: \_\_\_\_\_ g of sample was mixed with \_\_\_\_\_ (g) (ml) solvent \_\_\_\_\_ to make a dosing solution of \_\_\_\_\_ (w/w) \_\_\_\_\_ (w/v).

Specific Gravity: 1.0 ml of sample weighed 9.54 g at 23 °C, S.G. = 0.954 g/ml.

200 6/4/77 Individual Animal Data

Date	Animal #	1					2				3			4	
		76960	76961	76962	76963	76964	76965	76966	76967	76968	76969	76970	76971	76972	
	Sex	♂	♂	♂	♂	♂	♀	♀	♀	♀	♀				
12/27/77	Prefasted Wt. g	251	234	221	235	239	219	200	210	215					
12/28/77	Fasted Wt. g	235	222	212	222	225	208	191	198	204					
12/28/77	Dose/Est ml	1.7	1.6	1.5	1.6	1.6	1.5	1.4	1.4	1.5					
	Time of Death		<del>1</del>				<del>3</del>	<del>2</del>				<del>2</del>			
SG 14/78	14 Day Wt. g	322		290	309	352			262						
	7 Day w + 4	275	X	255	270	272	X	X	228	X					

Avg. prefasted weight 225.2 DP 2/24/78

Avg. prefasted weight of survivors 231.2 DP 2/24/78

Avg. 14 day weight of survivors 307.8 DP 2/24/78

Total Dead: Male 1 Female 4

Animals Received: CR 12/14/77

$$\frac{6.81 \text{ g/kg}}{0.954 \text{ g/ml}} = 7.14 \text{ ml/kg}$$

Worker's Signature Charles R Evans

Date 12/28/77

Corroborating Witness [Signature]

Date 12/28/77

Worker's Signature [Signature]

Date 12/28/77

Corroborating Witness [Signature]

Date 12/28/77

LD50 - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg by 10.0 P&G Code B-7188  
Number of animals dosed Male 5 Female 5

All data are based on sample as received.

Sample Preparation: \_\_\_\_\_ g of sample was mixed with \_\_\_\_\_ (g) (ml) solvent \_\_\_\_\_ to make a dosing solution of \_\_\_\_\_ (w/w) \_\_\_\_\_ (w/v).

Specific Gravity: 1.0 ml of sample weighed 9.54 g at 23 °C, S.G. = 0.954 g/ml.

		Individual Animal Data									
		1	2	3	4	5	1	2	3	4	5
Date	Animal #	76970	76971	76972	76973	76974	76975	76976	76977	76978	76979
	Sex	♂	♂	♂	♂	♂	♀	♀	♀	♀	♀
12/27/77	Prefasted Wt. g	230	237	228	235	214	203	225	237	226	205
12/28/77	Fasted Wt. g	210	212	213	225	200	190	213	223	217	191
12/28/77	Dose/Fac ml	2.2	2.2	2.2	2.4	2.1	2.0	2.2	2.3	2.3	2.0
	Time of Death	X <sub>1</sub>	X <sub>1</sub>	X <sub>1</sub>	X <sub>3</sub>	X <sub>1</sub>	X <sub>2</sub>	X <sub>1</sub>	X <sub>2</sub>	X <sub>1</sub>	X <sub>2</sub>
SS WTS	14 Day Wt. g			250							

Avg. prefasted weight 224.0 g DP 2/24/78  
Avg. prefasted weight of survivors 228.0 g DP 2/24/78  
Avg. 14 day weight of survivors 250.0 g DP 2/24/78  
Total Dead: Male 4 Female 5  
Animals Received: 12/14/77

$$\frac{10.0 \text{ g/kg}}{0.954 \text{ g/ml}} = 10.48 \text{ ml/kg}$$

Worker's Signature Charles R Evans  
Corroborating Witness [Signature]  
Worker's Signature [Signature]  
Corroborating Witness [Signature]

Date 12/28/77  
Date 12/28/77  
Date 3/29/78  
Date 3/29/78

171-167

APPENDIX 2

EPSC - A-5273

Dose - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg by 14.7 F50 Code B-7188  
Number of animals dosed Male 5 Female 5

All data are based on sample as received.

Sample Preparation: \_\_\_\_\_ g of sample was mixed with \_\_\_\_\_ (g) (ml) solvent \_\_\_\_\_ to make a dosing solution of \_\_\_\_\_ = \_\_\_\_\_ (v/v) \_\_\_\_\_ (v/v).

Specific Gravity: 10 ml of sample weighed 9.54 g at 23 °C, S.G. = 0.954 g/ml.

Individual Animal Data

Strained 4:00

Date	Animal #	1					2				
		1	2	3	4	5	1	2	3	4	5
	Sex	♂	♂	♂	♂	♂	♀	♀	♀	♀	♀
12/29/77	Prefasted Wt. g	235	218	251	225	210	204	214	225	205	222
12/29/77	Fasted Wt. g	222	206	241	212	200	193	201	195	194	210
12/29/77	Dose/Eat ml	34	32	37	32	31	30	31	30	30	33
	Time of Death	2HR	1HR	1HR	2HR	1HR	2HR	2HR	10.2	1HR	1HR
	14 Day Wt. g										

Avg. prefasted weight 219.4 g <sup>DP 2/24/78</sup>  
Avg. prefasted weight of survivors \_\_\_\_\_ g  
Avg. 14 day weight of survivors \_\_\_\_\_ g  
Total Dead: Male 5 Female 5  
Animals Received: C.R. 12/14/77

$\frac{14.791\text{kg}}{0.9549\text{ml}} = 15.41 \text{ ml/kg}$

Worker's Signature [Signature]  
Corroborating Witness \_\_\_\_\_  
Worker's Signature [Signature]  
Corroborating Witness \_\_\_\_\_

Date 12/29/77  
Date 12/29/77  
Date 3/29/78  
Date 3/29/78



ACUTE ORAL TOXICITY OBSERVATION DATA

No. of Males/Females Affected - Blank Square = Normal

P&G Code B-7188

Dose Level g/kg 4640

Dose Time 8:50

Dose Date 12/28/77

Symptoms	Hours				Days															
	1/4	1/2	1	2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Prior activity increase																				
Prior activity decrease																				
Respiratory rate increase		5/5	5/5	5/5	5/5															
Respiratory rate decrease		0/1	2/4	2/1	2/1															
Fine body tremors																				
Coarse body tremors																				
Bleaching																				
Cyanosis																				
Gaspings																				
Facetial Gripping																				
Diarrhea																				
Pilo erection																				
Other A signs																				
reduced limb tone																				
inadeq Reflex absent																				
incoordination																				
Worker's Initials																				

11/11/77  
11/12/77  
11/13/77  
11/14/77  
11/15/77  
11/16/77  
11/17/77  
11/18/77  
11/19/77  
11/20/77  
11/21/77  
11/22/77  
11/23/77  
11/24/77  
11/25/77  
11/26/77  
11/27/77  
11/28/77  
11/29/77  
11/30/77

Special Notes: (Including Necropsy Observations)

Dead!  
Normal

APPENDIX 2

ACUTE ORAL TOXICITY OBSERVATION DATA

No. of Males/Females Affected - Blank Square = Normal

P&G Code 15-0158 Dose Level g/kg 6 & 10 Dose Time 9:00 Dose Date 12/28

SYMPTOM	Hours				Days															
	1/4	1/2	1	2	4	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Motor activity increase	5/5	5/5	5/5	5/5	5/5		4/3	4/1												
Motor activity decrease																				
Respiratory rate increase																				
Respiratory rate decrease	5/5	5/5	5/5	5/5	5/5		4/3	0/1												
Fine body tremors																				
Coarse body tremors																				
Bleaching of mucous membranes																				
Cyanosis of mucous membranes																				
Gaspings																				
Abnormal Griping																				
Diarrhea																				
Pilo Erection																				
Other: <u>ATA VIA</u>	5/5	5/5	5/5	5/5	4/5		1/3	1/0												
<u>DECREASED URINE TOXIC</u>	5/5	5/5	5/5	5/5	5/5		4/3	0/1												
<u>SECRETION</u>	1/0																			
<u>HAIR REFLEX ABSENT</u>	5/5	5/5	5/5	5/5	4/4		1/3													
<u>HAIR REFLEX ABSENT</u>					3/4			0/2												
<u>HAIR REFLEX ABSENT</u>							3/1													
<u>HAIR REFLEX ABSENT</u>							1/2													
<u>HAIR REFLEX ABSENT</u>							1/2													
Worker's Initials																				

Special Notes: (Including Necropsy Observations)

ACUTE ORAL TOXICITY OBSERVATION DATA

No. of Males/Females Affected - Blank Square = Normal

P/G Code 15-2158

Dose Level 10.000 g/kg

Dose Time 9:15

Dose Date 12/28/52

26

Symptoms	Hours				Days														
	1/4	1/2	1	2	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Prior activity increase																			
Prior activity decrease																			
Respiratory rate increase	5/5	5/5	5/5	5/5	2/0	2/0								1/0	1/0	1/0			
Respiratory rate decrease																			
Fine body tremors	5/5	5/5	5/5	5/5	2/0	2/0		1/0											
Coarse body tremors																			
Bleaching																			
Cyanosis																			
Gesping																			
Abnormal Gripping																			
Diarrhea																			
Pilo Erection																			
Uterus	5/5	5/5	5/5	5/5	2/0	2/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0
Uterine Cervix	5/5	5/5	5/5	5/5	2/0	2/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0
Rectum	1/1	1/1	1/1	1/1	2/0	2/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0
Prostration																			
Mortality																			
Neutral																			
Dead					3/5	2/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0	1/0
Worker's Initials					CS			GH	WS										

Special Notes: (Including Necropsy Observations)



INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

Lab Project No. 191-169 Sheet 1 Date 12/12/77 Authorized by  J. Dean

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<u>Compound</u>	<u>Identification Number</u>	<u>IRDC No.</u>
B-7188	_____	A-527B
_____	_____	_____
_____	_____	_____
_____	_____	_____

TITLE: ACUTE ORAL TOXICITY STUDY IN RATS

Conduct in accordance with the attached protocol and the following special instructions:

1. Initially conduct a dose range study at the following dosage levels: 100, 1000, 5000; 10,000 and 20,000 mg/kg. using 2 rats/dosage level.
2. Use the undiluted test material.

Acute Oral Toxicity - Rats

Date: March 31, 1977

Issue #2

## Purpose:

To measure the acute oral toxicity of a substance in order that it might be compared to more familiar materials.

## Animals:

Rats, Sprague-Dawley derived (caesarean-derived), 190-270 g, conditioned to the environment for a minimum of 4 days. Obtain animals from Charles River, Laboratory Supply or Harlan. Maintain the animals according to standards outlined in the Guide For the Care and Use of Laboratory Animals, DHEW: (NIH-74-23), 1974.

## Procedure:

Place 10 animals in each group, divided equally by sex. Determine prefasted and fasted body weights. Fast the animals for 18-20 hours before administering the test material.

Dissolve or suspend the test material in an appropriate vehicle at the required concentrations and record quantities mixed. Deliver the test material into the stomach of the animal from a syringe fitted with a size 8 catheter as a stomach tube or from a syringe fitted with a 13-gauge animal-feeding needle.

Choose 4 dosage levels, with the lowest being approximately the highest no-death dosage level observed in range-finding studies, or being estimated from prior results with similar compounds. Unless otherwise specified, choose higher dosage levels according to a geometric progression of 1.4 (i.e. the second dose equals the first dose x  $[1.4]^2$ , the third dose equals the first dose x  $[1.4]^3$ , etc.). Administer each dosage level to one group of 10 animals. Adjust the dose for each animal according to fasted weight to give the specified quantities of material per unit of body weight. Administer additional dose levels, as needed, so that the total number of dead is sufficient to calculate an LD<sub>50</sub> value. Immediately after dosing, return the animal to ad libitum feeding. Record all of the above information on the "LD<sub>50</sub> Record of Individual Dose Level" sheet (Appendix I).

## Observations:

Observe the animals and their behavior at intervals of 15, 30, 60, 120 and 240 minutes after dosing and daily thereafter for 14 days. Use the "Toxicity Observation Data" sheet (Appendix 2) to record symptoms and number of animals involved. Unusual observations or symptoms not listed on the "Toxicity Observation Data" sheet should be noted where appropriate (under "Symptoms" or "Special Notes"). Necropsy all animals that die during the course of the study. At 14 days, weigh all surviving animals and record weights. Necropsy surviving animals and examine them grossly for abnormalities.

**Report:**

Report all data recorded on the Record of Individual Dose Level and the Acute Oral Toxicity Observation Data sheets. Report the LD<sub>50</sub> and 95% confidence limits of the test material, preferably calculated by the Probit Method\*. If necessary, other calculation methods may be used to fit the death/dose response. The method used should be specified. File the final report within 3 weeks after completion of the experiment.

PRINCIPAL INVESTIGATOR: J. H. Benedict

DATE: 10/6/77

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\* D. J. Finney, *Statistical Method in Biological Assay*, Third Edition, 1971.

LD<sub>50</sub> - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg by \_\_\_\_\_ P&C Code \_\_\_\_\_

Number of animals dosed Male \_\_\_\_\_ Female \_\_\_\_\_

All data are based on sample as received.

Sample Preparation: \_\_\_\_\_ g of sample was mixed with \_\_\_\_\_ (g) (ml) solvent \_\_\_\_\_ to make a dosing solution of \_\_\_\_\_ % (v/v) \_\_\_\_\_ (w/v).

Specific Gravity: \_\_\_\_\_ ml of sample weighed \_\_\_\_\_ g at \_\_\_\_\_ °C.  
S.G. = \_\_\_\_\_ g/ml.

Individual Animal Data

Date	Animal #									
	Sex									
	Prefasted Wt. g									
	Fasted Wt. g									
	Dose/Rat ml									
	Time of Death									
	14 Day Wt. g									

Avg. prefasted weight \_\_\_\_\_ g  
 Avg. prefasted weight of survivors \_\_\_\_\_ g  
 Avg. 14 day weight of survivors \_\_\_\_\_ g  
 Total Dead: Male \_\_\_\_\_ Female \_\_\_\_\_

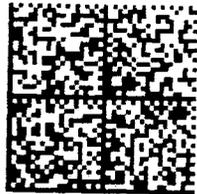
Worker's Signature \_\_\_\_\_

Date \_\_\_\_\_

Corroborating Witness \_\_\_\_\_

Date \_\_\_\_\_





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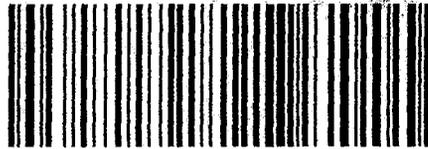
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