



**Report Title:** Acute Oral Toxicity (LD50) Study in Albino Rats

**Test Type:** Acute Oral Toxicity (LD50)

**Conducting Laboratory and Location:** International Research and Development Corporation

**Test Substance(s):** #T7119 - 2% Shampoo at pH 7.5. Undiluted material used for dosing.

**Species:** Rat

**# of Animals:** 20 male, 20 female

**Test Conditions:** Dosed orally with 10.71, 15.00, 21.00, and 29.40 g/kg.

**Results:** Combined: LD<sub>50</sub>>16.16 g/kg. See related studies 191-081, 191-082

**Study #:** 191-080

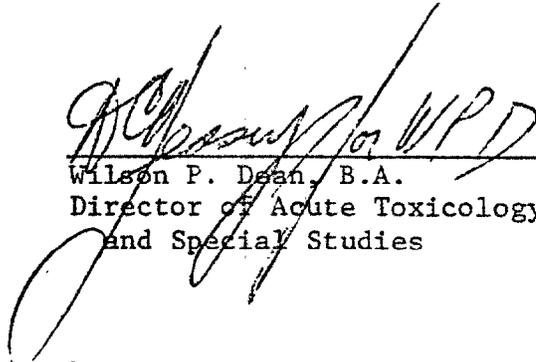
**Report Date:** 11/9/77

**Accession #:** 19195

International Research and Development Corporation

TG 134

SPONSOR: Procter and Gamble Company  
TEST MATERIAL: T-7119  
STUDY NUMBER: 191-080  
SUBJECT: Acute Oral Toxicity (LD<sub>50</sub>)  
Study in Albino Rats.

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

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

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Date: November 9, 1977

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I. SYNOPSIS

The median effective dose and 95% confidence limits of T-7119 were found to be 16156 (13847 - 18780) mg/kg.

II. TEST MATERIAL

The test material was received from The Procter and Gamble Company, Cincinnati, Ohio on August 4, 1977. It was identified as "T-7119" and was received as a pale yellow viscous liquid.

III. METHOD

Twenty male and 20 female rats of the Charles River CD strain (obtained from Charles River Laboratories, Portage, Michigan), weighing 207 to 288 grams (pre-fasting body weight), were used in this study. The rats were housed by sex in groups of 5 rats per cage in metal metabolism 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 13 days prior to study initiation. Water and Purina Laboratory Chow were available ad libitum except for an overnight period of 18½ to 19¼ hours preceding oral administration during which food, but not water was withheld.

The test material was administered orally, as received, undiluted, at the following dosage levels to male and female rats: 10714, 15000, 21000, 29400 mg/kg.

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

10714 mg/kg level - 10.67 ml/kg.  
15000 mg/kg level - 14.94 ml/kg.  
21000 mg/kg level - 20.92 ml/kg.  
29400 mg/kg level - 29.28 ml/kg.

Observations for pharmacotoxic signs and mortality were made at ¼, ½, 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 7 and 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.

IV. RESULTS

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

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
10714																	0/5	0/5	0/10
15000			1	3			1										1/5	4/5	5/10
21000	1	1	3	3													4/5	4/5	8/10
29400	3	4	1		1										1		5/5	5/5	10/10

Median Effective Dose and 95% Confidence Limits

Combined Male and Female: 16156 (13847 - 18780) mg/kg.

Statistical Reference

Computations were performed by Mr. R. Bruce, Statistician, 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 during the 14-day observation period except for one male (#66196) at the 10714 mg/kg dosage level which showed a body weight loss from day 7 to day 14 and one female (#66201) at the 10714 mg/kg dosage level which exhibited a body weight loss from day 0 to day 7.

D. NECROPSY FINDINGS:

The necropsy findings on the following page were obtained as indicated:

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Gross Necropsy Observations:

Gross Necropsy Observations	Dosage Level (mg/kg)							
	Number Showing Sign/Number Died							
	10714		15000		21000		29400	
	Male	Female	Male	Female	Male	Female	Male	Female
A. Rats which died during the study period.								
Discharge from nose							1/5	
Lungs, congested			1/1	2/4	3/4	4/4	1/5	
Focal hemorrhage of lungs				2/4		1/4		
Stomach distended with material			1/1	2/4	3/4	4/4	4/5	5/5
Gular mucosa of stomach, hyperemia				3/4	2/4	3/4	3/5	2/5
Focal hemorrhage				1/4	2/4	3/4		
Small intestine filled with fluid					1/4	1/4	3/5	4/5
Cecum filled with fecal material					1/4	1/4	1/5	2/5
Hydrometra, Uterus								1/5
Stained anogenital region				1/4				1/5

Gross Necropsy Observations:

Gross Necropsy Observations	Dosage Level (mg/kg)							
	Number Showing Sign/Number Necropsied							
	10714		15000		21000		29400	
	Male	Female	Male	Female	Male	Female	Male	Female
B. Rats which were necropsied at the end of the observation period.								
No gross lesions	2/5		2/4	1/1	1/1	1/1		
Thickening of fore-stomach mucosa	3/5	5/5						
Ulcerations of fore-stomach mucosa			1/4					
Local erosion of fore-stomach mucosa			1/4					

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APPENDIX I

IRDC # A-325

LD50 - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg bw 10.714 P&G Code T-7119

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: 10 ml of sample weighed 10.04 g at 24 °C, S.G. = 1.004 g/ml.

Individual Animal Data

		1	2	3	4	5	1	2	3	4	5
Date	Animal #	66193	66194	66195	66196	66197	66198	66199	66200	66201	66202
	Sex	♂	♂	♂	♂	♂	♀	♀	♀	♀	♀
8/30/77	Prefasted Wt. g	283	272	272	272	270	240	231	227	221	221
8/31/77	Fasted Wt. g	265	263	258	261	256	228	218	212	213	212
8/31/77	Dose/Rat ml	2.86	2.81	2.75	2.78	2.73	2.43	2.33	2.26	2.27	2.21
	Time of Death										
9/14/77	14 Day Wt. g	390	368	351	306	<del>347</del>	277	264	267	249	240
	7 Day Wt. g	315	322	308	314	315	257	241	255	207	230

Avg. prefasted weight 252.8 g

Avg. prefasted weight of survivors 252.8 g

Avg. 14 day weight of survivors 306.5 g

Total Dead: Male 0 Female 0

Animals Received: 8/2/77

$$\frac{10.714 \text{ g/kg}}{1.004 \text{ g/ml}} = 10.67 \text{ ml/kg}$$

Worker's Signature Gene Harris

Date 8/30/77

Corroborating Witness G. Rowing

Date 8/31/77

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APPENDIX 1

IRDC # A-325

LD50 - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg bw 15.000 P&G Code T-7119

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: 10 ml of sample weighed 10.04 g at 24 °C, S.G. = 1.004 g/ml.

Individual Animal Data

		1	2	3	4	5	1	2	3	4	5
Date	Animal #	66203	66204	66205	66206	66207	66208	66209	66210	66211	66212
	Sex	♂	♂	♂	♂	♂	♀	♀	♀	♀	♀
8/30/77	Prefasted Wt. g	282	285	287	271	288	221	213	210	210	222
8/31/77	Fasted Wt. g	267	270	270	255	270	206	195	190	191	202
8/31/77	Dose/Rat ml	3.99	4.03	4.03	3.81	4.03	3.08	2.91	2.84	2.85	3.02
	Time of Death		DAY 1 9/1/77				DAY 1 9/1/77	DAY 3 9/1/77	DAY 1 9/1/77	DAY 1 9/1/77	
9/14/77	14 Day Wt. g	328		366	319	315					247
	7 day wt. g	282		318	269	295					217

Avg. prefasted weight 249.0 g  
Avg. prefasted weight of survivors 270.2 g  
Avg. 14 day weight of survivors 313.2 g  
Total Dead: Male 1 Female 4  
Animals Received: 8/2/77

$$\frac{15.000 \text{ g/kg}}{1.004} = 14.94 \text{ ml/kg}$$

Worker's Signature Gene Harris  
Corroborating Witness G. Reung

Date 8/31/77  
Date 8/31/77

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APPENDIX 1

IRDC # A-325

LD50 - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg bw 21.000 P&G Code T-7119  
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: 10 ml of sample weighed 10.04 g at 24 °C, S.G. = 1.004 g/ml.

Individual Animal Data

		1	2	3	4	5	1	2	3	4	5
Date	Animal #	66213	66214	66215	66216	66217	66218	66219	66220	66221	66222
	Sex	♂	♂	♂	♂	♂	♀	♀	♀	♀	♀
8/30/77	Prefasted Wt. g	273	284	285	272	210	210	209	212	209	215
8/31/77	Fasted Wt. g	258	270	268	262	192	191	190	195	191	196
8/31/77	Dose/Rat ml	5.40	5.65	5.61	5.48	4.02	4.00	3.97	4.05	4.00	4.17
	Time of Death	4hours	DATA	DATA	DATA		DATA	4hours	4hours	DATA	DATA
9/14/77	14 Day Wt. g					299		234			

7 Day WT. g  
Avg. prefasted weight 237.7 g  
Avg. prefasted weight of survivors 209.5 g  
Avg. 14 day weight of survivors 266.5 g  
Total Dead: Male 4 Female 4  
Animals Received: 8/18/77

240  
299<sup>3</sup>  
234  
21.000 g/kg = 20.92 ml/kg  
1.004 g/ml

Worker's Signature Lene Harris  
Corroborating Witness G. Rung

Date 8/31/77  
Date 8/31/77

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APPENDIX 1

IRDC = A-325

LD50 - RECORD OF INDIVIDUAL DOSE LEVEL

Dose level g/kg bw 29.400 P&G Code T-7119
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: 10 ml of sample weighed 10.04 g at 24 °C, S.G. = 1.004 g/ml.

Individual Animal Data

Table with columns for Date, Animal #, Sex, Prefasted Wt. g, Fasted Wt. g, Dose/Rat ml, Time of Death, and 14 Day Wt. g. Rows include animal numbers 66223-66231 and their respective data points.

7 Day Wt. g

Avg. prefasted weight 219.6 g
Avg. prefasted weight of survivors g
Avg. 14 day weight of survivors g
Total Dead: Male 5 Female 5
Animals Received: 0/12/77

29.400 g/kg / 1.004 g/ml = 29.28 ml/kg

Worker's Signature Gene Harris
Corroborating Witness G. Rowig

Date 8/31/77
Date 8/31/77

ACUTE ORAL TOXICITY OBSERVATION DATA

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

P&G Code T-7119

Dose Level g/kg 10.714

Dose Time 10:40

Dose Date 8/31/77

SYMPTOMS: Time	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																				
Motor activity decrease	8(3)	8(3)	8(3)	9(4)	9(5)	0	4(0)				1(0)	0								
Respiratory rate increase		1																		
Respiratory rate decrease																				
Fine body tremors																				
Coarse body tremors																				
Blanching <sup>RESPIRATORY</sup> <sub>CONSTRICTION</sub>		1																	1(0)	
Cyanosis																				
Gasping																				
Abdominal Gripping																				
Diarrhea		1(1)	1(1)	3(2)	2(1)	0	0													
Pilo Erection																				
Other:																				
salivation	1(2)	4(1)	6(2)	3(0)	0		0													
ataxia	5(2)	7(3)	7(3)	6(1)	4(0)	0	2(0)													
salivation		4(1)	3(2)	3(3)	4(4)	0	0													
UPPER 10% stomach abdomen																				
Worker's Initials	SR	SR	SP	SP	SP	GL	JM	AP	AP	AP	JM	SP	AL	JM	PK	GH	WMM	JM	WMM	

Special Notes: (Including Necropsy Observations)

ACUTE ORAL TOXICITY OBSERVATION DATA

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

P&G Code T-7119 Dose Level g/kg 15.000 Dose Time 10.50 Dose Date 8/31/77

SYMPTOMS:	Time	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																											
Motor activity decrease		8(4)	10(6)	10(5)	10(5)	10(5)	6(2)	4(2)						2(0)	0												
Respiratory rate increase			1																								
Respiratory rate decrease																											
Fine body tremors																											
Coarse body tremors																											
Bleaching			1																								
Cyanosis																											
Gasping																											
Abdominal Gripping																											
Diarrhea			3(1)	5(1)	5(1)	3(0)	0	0																			
Pilo Erection																											
Other:																											
urination stained Abdomen		2(1)	3(2)	4(3)	8(5)	8(5)	3(1)	3(1)																			
ataxia		6(2)	7(3)	8(4)	8(4)	7(3)	1(1)	5(2)	1(1)																		
salivation		10(5)	10(5)	10(5)	8(4)	4(2)	0	0																			
limb force decrease			1(1)	1(1)	1(1)	2(2)	0	1(1)																			
DEATH							4(2)		1(1)																		
Worker's Initials		JP	JP	SP	JP	JP	B	JM	DP	DP	DP	JM	SP	BC	JM	RU	GH	W	W	W	W	W	W	W	W	W	W

Special Notes: (Including Necropsy Observations)

ACUTE ORAL TOXICITY OBSERVATION DATA

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

P&G Code T-7119

Dose Level g/kg 21.000

Dose Time 10:55

Dose Date 8/31/77

SYMPTOMS: Time	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																				
Motor activity decrease	9(5)	10(5)	10(5)	10(5)	9(4)	2(1)	2(1)		1(0)	1(0)	1(0)	0	5	1(0)						
Respiratory rate increase		1																		
Respiratory rate decrease																				
Fine body tremors																				
Coarse body tremors																				
Bleaching		1																		
Cyanosis																				
Gasping																				
Abdominal Gripping																				
Diarrhea		4(1)	9(3)	7(2)	3(0)	2(1)	1(1)	1(1)							1(1)					
Pilo Erection																			2(1)	2(1)
Other:																				
anIMATION strained abdomen	1(1)	2(1)	5(4)	9(5)	6(4)	2(1)	1(1)	1(1)	1(1)		1(1)	0								
ataxia	9(4)	10(5)	10(5)	10(5)	6(3)	2(1)	2(1)	1(1)												
salivation	9(5)	10(5)	10(5)	9(5)	2(1)		0													
limb tone decrease			1(0)	1(0)	1(0)	2(1)	0													
prostration					1(0)		0													
Death					2(1)	6(3)														
Worker's Initials	SP	JP	SP	SP	SP	BE	JM	DP	DP	DP	SM	JP	BL	JM	RS	EA	WAM	JM	JM	JM

Special Notes: (Including Necropsy Observations)



INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

191-079, (080)

Lab Project No. 081, 082 Sheet 2 Date 8/31/77 Authorized by  W. Dear

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<u>Dr. Griffith</u>	<u>Mr. Pangburn</u>	<u>_____</u>	<u>Mrs. Schwartz</u>	<u>Mr. Thompson</u>
			<u>Miss Morseth</u>	<u>Dr. Thorstenson</u>

<u>Compound</u>	<u>Identification Number</u>	<u>IRDC No.</u>
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

TITLE: ACUTE TOXICITY STUDIES IN RATS AND RABBITS

All test materials, for each of the 4 studies referenced above, will be dosed undiluted.

INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

Lab Project No. 191-080 Sheet 1 Date 8/5/77 Authorized by J. Jessup Dr. Jess

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				Miss Morseth	<u>    </u>	Dr. Thorstenson	<u>    </u>

<u>Compound</u>	<u>Identification Number</u>	<u>IRDC No.</u>
T-7119		A-325

TITLE: ACUTE TOXICITY STUDIES IN RATS AND RABBITS

Conduct in accordance with the attached protocol.

Procter & Gamble  
Standard Procedure / for Toxicological Evaluation

Acute Oral Toxicity - Rats

Date:

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, Charles River Caesarean-derived, 190-270 g, conditioned to the environment for a minimum of 7 days. Maintain the animals according to standards outlined in the Guide For the Care and Use of Laboratory Animals, DHEW No. (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.

Acute Oral Toxicity - Rats (P&C Procedure) (cont'd)

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 as calculated by the Probit Method\*. File the final report within 3 weeks after completion of the experiment.

Principal Investigator: M. J. Winrow

Date 7/28/77

APPENDIX I

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

Dose level g/kg bw \_\_\_\_\_ P&G 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  
\_\_\_\_\_ % (w/w) \_\_\_\_\_ (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 \_\_\_\_\_

