

ORIGINAL

TSCA NON-CONFIDENTIAL BUSINESS INFORMATION

DOCUMENT DESCRIPTION	DOCUMENT CONTROL NUMBER	DATE RECEIVED
8EHQ- 92-10141	89110000205	3/22/11

COMMENTS: COMMUN S (DECLASS)

DOES NOT CONTAIN CBI

334118



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

8EHQ-0311-10141B
DCN: 89110000205

11 MAR 22 AM 6:03
RECEIVED
03/21/2012

**Re: Declassification Activity-Health and Safety Filing
8EHQ-0892-10141 (EPA DCN 88920008442)**

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Any CBI substantiation which appears in the original submission is no longer applicable as the information which was originally claimed CBI is disclosed in this revised submission.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

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



Attachment 1
Public Display Version

Chemical Identity

CAS RN

Benzenesulfonic acid, C10-16-alkyl derivatives

68584-22-5

Potassium hydroxide

Potassium pyrophosphate

Isopropanol

Pine oil

Cyclohexene, 1-methyl-4-(1-methylethenyl)-, (R)-

5989-27-5

Cyclohexene, 1-methyl-4-(1-methylethylidene)-

586-62-9

Cyclohexene, 1-methyl-4-(1-methylethenyl)-

138-86-3

1-Naphthalenesulfonic acid, 3-[(2,4-dimethyl-5-sulfophenyl)azo]-4-hydroxy-, disodium salt

4548-53-2

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

Water

Procter & Gamble

BEHQ-0892-10141₃

COMPANY SANITIZED

92 AUG 31 PM 1:18

Public Display Copy

August 20, 1992

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

BEHQ-92-10141₃ INIT
8872000E44Z

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 # BECAP-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 B0429-01 is a confidential mixture. The composition of the mixture is appended as Attachment 1. The report is titled "Acute Oral Toxicity (LD₅₀ Value in Rats)". Any correspondence relating to this submission should reference study # 1105-26478.

The attached study report indicates oral administration of the test material resulted in pharmacotoxic signs including ataxia, high carriage, hypoactivity, and piloerection following oral administration of 5000, 5750, 6613, 7604, and 8745 mg/kg of the test material. Tremors were observed in the 7604 and 8745 mg/kg groups, and impaired righting reflex was observed in the 8745 mg/kg group. The acute oral LD₅₀ is calculated to be 7.0 g/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.

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

Alkyl benzene sulfonic acid

Potassium hydroxide

Potassium pyrophosphate

Isopropanol

Pine oil

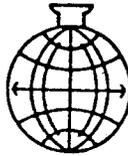
Mixed terpenes

Colorant

Water

0 0 . 0 5

1105-26478



International Research
and Development Corporation

MATTAWAN, MICHIGAN, U.S.A. 49071 TELEPHONE (616) 668-1336

SPONSOR: The Procter and Gamble Company

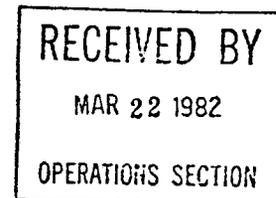
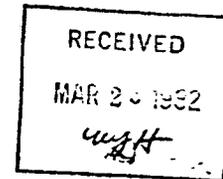
SUBJECT: Acute Oral Toxicity (LD₅₀ Value in Rats)

DRD NO.: BSBS 734S

TSIN: B0429-01

REPORT NO.: 191-722

DATE OF SUBMISSION: March 16, 1982



191-722

"credence through research"

International Research and Development Corporation

Results (Cont.)

Pharmacotoxic Signs (Appendix A):

The major pharmacotoxic signs observed in all dosage levels were: ataxia, high carriage, hypoactivity, piloerection and possible respiratory congestion.

Body Weights (Appendix B):

No remarkable changes or differences were observed in the body weights during the study period.

Pathology (Appendix C):

Treatment related changes were seen at 6613 mg/kg and higher dose levels, in the gastrointestinal tract of animals that died during the study. The changes consisted of mucosal hyperemia of gastrointestinal tract with or without a reddish mucoid fluid content. No macroscopic changes were evident in survivors that were sacrificed at the termination of the study period.

Prepared By:

Daniel Rajasekaran
Daniel Rajasekaran, D.V.M., M.V.Sc. (Path),
F.R.V.C.S. (Path) Sweden
Staff Pathologist

Date

3/15/82

Reviewed By:

Ward R. Richter
Ward R. Richter, D.V.M., A.C.V.P.
Director, Pathology Division

Date

3-16-82

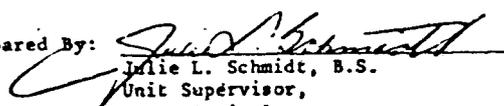
International Research and Development Corporation

Technical Supervisory Staff,
Acute Toxicology and Special Studies:

Paul Moxon, B.S.
Unit Supervisor

Adelsteinn Olafsson, B.S.
Group Supervisor

Prepared By:


Julie L. Schmidt, B.S.
Unit Supervisor,
Acute Toxicology
and Special Studies

7-4-82
Date

Reviewed By:


Dale E. Johnson, Pharm.D., Ph.D.
Associate Director,
Toxicology Division

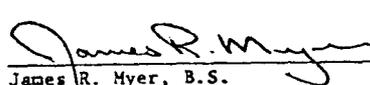
3/12/82
Date

STUDY DIRECTOR STATEMENT

The methods used in IRDC Study Number 191-722 followed the experimental criteria specified in the protocol.

To the best of my knowledge, there were no significant deviations from the Good Laboratory Practice Regulations which affected the quality or integrity of this study. This study was conducted in conformance with the Good Laboratory Practice Regulations. This report accurately reflects the raw data obtained during the performance of this study.

All data including the final study report are stored in the International Research and Development Corporation Archives.


James R. Myer, B.S.
Study Director

3/12/82
Date

191-722

"credence through research"

APPENDIX A
Individual Pharmacotoxic Signs

191-722

90429-01

Individual Pharmacotoxic Signs
3750 mg/kg

Pharmacotoxic Sign	99627		99634		99641		99646		99647		99648		99667		99668		99670		99678		Total Incidence
	Day First Appeared	Day of Clearance																			
Clear wet stain around mouth	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	4
ataxia	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	4
Mucoid diarrhea	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	5
High carriage	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Piloerection	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Possible respiratory congestion	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Wet yellow stained anogenital area	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Dry yellow stained anogenital area	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Hairless anogenital region	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3
Hypersensitive to touch	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Dry reddish brown stain around nose, mouth, ventral surface	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Hypocoactivity	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Dry reddish-brown stain around mouth	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0
Wet yellow stain around mouth	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	3
Wet reddish brown stain - ventral surface	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Dry reddish-brown stain - ventral surface	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Hairless abdomen	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Day of Death																					0

- e - 1/2 hour after dosing, Day 0
- h - 1 hour after dosing, Day 0
- c - 2 1/2 hours after dosing, Day 0
- d - 4 hours after dosing, Day 0
- f - Sign reappeared on Day 1 and cleared on Day 2
- g - Sign did not clear prior to death
- h - Sign reappeared at 4 hours and did not clear prior to death
- i - Sign reappeared on Day 1 and did not clear prior to death
- j - Sign did not clear prior to study termination

Individual Pharmacotoxic Signs
601) mg/kg

Sex	Animal Number	99624			99632			99635			99637			99639			99641			99643			99645			Total Incidence
		Day First Appeared	Day of Clearance																							
Pharmacotoxic Sign																										
Hypersensitive to touch																										
High carriage																										
Wet yellow stained anogenital area																										
Piloerection																										
Possible respiratory congestion																										
Ataxia																										
Wet clear stain around mouth																										
Hypomotility																										
Dry yellow stained anogenital region																										
Discolored shiners																										
Dry reddish-brown stain around mouth and nose																										
Dry yellow stained ventral surface																										
Mucoid diarrhea																										
Hairloss anogenital area																										
Hairloss on face																										
Decreased limb tone																										
Clear wet stain under mouth																										
Clear dry stain under mouth																										
Bradypnea																										
Wet reddish-brown stain around nose and mouth																										
Day of Death																										

a - 1/2 hour after dosing, Day 0
 b - 1 hour after dosing, Day 0
 c - 2 1/2 hours after dosing, Day 0
 d - 4 hours after dosing, Day 0
 e - Sign reappeared after dosing, Day 0
 f - Sign reappeared at 4 hours and cleared on Day 3
 g - Sign reappeared at 4 hours and did not clear prior to death
 h - Sign did not clear prior to death

Individual Pharmacotoxic Signs
8745 mg/kg

Sex	Animal Number	Male		Female		Male		Female		Total Incidence
		Day First Appeared	Day of Clearance							
	Pharmacotoxic Sign	Day First Appeared	Day of Clearance							
	Ataxia	0	1	0	1	0	1	0	1	3
	Piloerection	0	1	0	1	0	1	0	1	3
	Hypocativity	0	1	0	1	0	1	0	1	3
	Possible respiratory congestion	0	1	0	1	0	1	0	1	3
	Wet yellow stained anogenital area	1	3	1	3	1	3	1	3	3
	Pilois	2	3 ^r	0						
	Dry yellow stained anogenital region	3	1	3	1	3	1	3	1	0
	Penetration of penis and crusty material around eyes	6	11	6	11	6	11	6	11	0
	High ear/legs									3
	Wet clear stain around mouth									1
	Decreased limb tone									2
	Bradypnea									0
	Clear discharge - both eyes									0
	Body tremors									1
	Impaired righting reflex									1
	Body hypothermic to touch									1
	Day of Death									4

a - 1/2 hour after dosing, Day 0
 b - 1 hour after dosing, Day 0
 c - 2 1/2 hours after dosing, Day 0
 d - 4 hours after dosing, Day 0
 e - Sign did not clear prior to death
 f - Sign did not clear prior to study termination
 g - Sign reappeared on Day 6 and cleared on Day 10
 h - Sign reappeared on Day 10 and did not clear prior to study termination

APPENDIX B
Body Weights

191-722

ACUTE TOXICITY (LD₅₀) RECORD

TEST COMPOUND B0129-01 STUDY NO. 141-722
 IRDC NO. 7500
 DOSE VOLUME ml/kg: Letter to dose volume calculation given SPECIES Rat SEX F
 ROUTE OF ADMINISTRATION Oral DATE ANIMALS RECEIVED 12/14/51 SOURCE Charles River
 TIME OF FASTING^a 0 FASTING TECHNICIAN 0 DATE 0
 TIME OF DOSING 0 DOSING TECHNICIAN 0 DATE 0

7 cc / ml/kg	ANIMAL NUMBER	44658	44659	44661	44662	44664	TECHNICIAN	DATE
		PREFASTED WEIGHT (g)	235	238	216	225	235	*
	INITIAL BODY WEIGHT (g)	214	216	201	212	218	*	
	ACTUAL DOSE (ml)	1.5	1.5	1.4	1.5	1.5	ML	12/14
	DOSE ADMINISTRATION	✓	✓	✓	✓	5	0	0
DOSAGE	DAY 14 BODY WEIGHT (g)	231					RH	1/2
	DAY BODY WEIGHT (g)							
	DAY BODY WEIGHT (g)							
	DAY BODY WEIGHT (g)							
DOSAGE	ANIMAL NUMBER							
	PREFASTED WEIGHT (g)							
	INITIAL BODY WEIGHT (g)							
	ACTUAL DOSE (ml)							
	DOSE ADMINISTRATION							
	DAY BODY WEIGHT (g)							
	DAY BODY WEIGHT (g)							
DOSAGE	ANIMAL NUMBER							
	PREFASTED BODY WEIGHT (g)							
	INITIAL BODY WEIGHT (g)							
	ACTUAL DOSE (ml)							
	DOSE ADMINISTRATION							
	DAY BODY WEIGHT (g)							
	DAY BODY WEIGHT (g)							

NA - Not Applicable a - food removed J - Dose indicated was administered

PREFASTED BODY WEIGHTS DAY 14 BODY WEIGHT DAY BODY WEIGHT
 BALANCE NO. 4 BALANCE NO. 11/28 BALANCE NO. 11/28
 INITIAL BODY WEIGHTS DAY BODY WEIGHT DAY BODY WEIGHT
 BALANCE NO. 7 BALANCE NO. 11/28 BALANCE NO. 11/28

IR36-61-4 + Refer to fasted/prefasted body weight sheet for 12/14/51.
 0 Refer to first LD₅₀ sheet for 12/14/51.
 0 calculation of LD₅₀ dated at 12/14/51 using 12/14/51

ACUTE TOXICITY (LD₅₀) RECORD

TEST COMPOUND BC424-c1 STUDY NO. 191-722
 IRDC NO. 7502
 DOSE VOLUME ml/kg: Refer to dose volume calculation sheet SPECIES Rat SEX F
 ROUTE OF ADMINISTRATION Oral DATE ANIMALS RECEIVED 12/14/51 SOURCE Charles River
 TIME OF FASTING^a 0 FASTING TECHNICIAN R DATE 0
 TIME OF DOSING 0 DOSING TECHNICIAN 0 DATE 0

5000 mg/kg		44657	44666	44671	44672	44675	TECHNICIAN	DATE
ANIMAL NUMBER								
PREFASTED WEIGHT (g)		218	241	227	208	226	†	
INITIAL BODY WEIGHT (g)		202	225	205	190	215	‡	
ACTUAL DOSE (ml)		0.53	1.0	0.94	0.87	0.99	ML	12/20
DOSE ADMINISTRATION		✓	✓	✓	✓	0	ML	12/29
DAY 14 BODY WEIGHT (g)		237	261	238	218	271	DN	1/12
DAY BODY WEIGHT (g)								
DAY BODY WEIGHT (g)								
DAY BODY WEIGHT (g)								
575.0 mg/kg		44663	44667	44668	44670	44678	TECHNICIAN	DATE
ANIMAL NUMBER								
PREFASTED WEIGHT (g)		226	228	206	236	211	†	
INITIAL BODY WEIGHT (g)		208	210	188	217	199	‡	
ACTUAL DOSE (ml)		1.1	1.1	1.0	1.2	1.1	ML	12/29
DOSE ADMINISTRATION		✓	✓	✓	✓	✓	ML	12/29
DAY 14 BODY WEIGHT (g)		230	230	230	230	230	DN	1/12
DAY BODY WEIGHT (g)								
DAY BODY WEIGHT (g)								
DAY BODY WEIGHT (g)								
66.75 mg/kg		44655	44659	44665	44673	44676	TECHNICIAN	DATE
ANIMAL NUMBER								
PREFASTED BODY WEIGHT (g)		204	202	221	235	210	‡	12/24
INITIAL BODY WEIGHT (g)		191	188	205	214	193	‡	
ACTUAL DOSE (ml)		1.2	1.1	1.3	1.3	1.2	ML	12/29
DOSE ADMINISTRATION		✓	✓	✓	✓	✓	ML	12/29
DAY 14 BODY WEIGHT (g)		211	211	211	223	223	DN	1/12
DAY BODY WEIGHT (g)								
DAY BODY WEIGHT (g)								
DAY BODY WEIGHT (g)								

NA - Not Applicable a - food removed J - Dose indicated was administered

PREFASTED BODY WEIGHTS DAY 14 BODY WEIGHT DAY BODY WEIGHT
 BALANCE NO. BALANCE NO. 1046 BALANCE NO. 1.8

INITIAL BODY WEIGHTS DAY BODY WEIGHT DAY BODY WEIGHT
 BALANCE NO. BALANCE NO. 1.8 BALANCE NO. 1.11

IR36-61-4 * Prior to fasted/prefasted body weight sheet me 12/14/51
 † Refer to last LD₅₀ record sheet me 12/14/51
 ‡ Simultaneously not recorded at time of dosing me 12/14/51

ACUTE TOXICITY (LD₅₀) RECORD

TEST COMPOUND BC-24-C1 STUDY NO. 141-722
 IRDC NO. 7500
 DOSE VOLUME ml/kg: Ch. to dose volume calculation sheet SPECIES Rat SEX M
 ROUTE OF ADMINISTRATION oral DATE ANIMALS RECEIVED 12/14/61 SOURCE Charles River
 TIME OF FASTING^a 0 FASTING TECHNICIAN 0 DATE 0
 TIME OF DOSING 0 DOSING TECHNICIAN 0 DATE 0

mg/kg	ANIMAL NUMBER					TECHNICIAN	DATE
		49625	99629	99634	99640	99644	
mg/kg	PREFASTED WEIGHT (g)						
		267	261	263	265	271	
mg/kg	INITIAL BODY WEIGHT (g)						
		245	254	238	243	250	
mg/kg	ACTUAL DOSE (ml)						
		1.7	1.8	1.7	1.7	1.8	me
mg/kg	DOSE ADMINISTRATION						
		✓	✓	✓	✓	✓	me
mg/kg	DAY 1 BODY WEIGHT (g)						
		321	323	292	330		me
mg/kg	DAY BODY WEIGHT (g)						
mg/kg	DAY BODY WEIGHT (g)						
mg/kg	DAY BODY WEIGHT (g)						
mg/kg	ANIMAL NUMBER						
mg/kg	PREFASTED BODY WEIGHT (g)						
mg/kg	INITIAL BODY WEIGHT (g)						
mg/kg	ACTUAL DOSE (ml)						
mg/kg	DOSE ADMINISTRATION						
mg/kg	DAY BODY WEIGHT (g)						
mg/kg	DAY BODY WEIGHT (g)						
mg/kg	DAY BODY WEIGHT (g)						
mg/kg	DAY BODY WEIGHT (g)						

NA - Not Applicable a - food removed J - Dose indicated was administered

PREFASTED BODY WEIGHTS DAY 14 BODY WEIGHT DAY BODY WEIGHT
 BALANCE NO. + BALANCE NO. 240 BALANCE NO. NA
 INITIAL BODY WEIGHTS DAY BODY WEIGHT DAY BODY WEIGHT
 BALANCE NO. + BALANCE NO. NA BALANCE NO. NA

IR36-61-4 * Refer to fasted/prefasted body weight sheet me 12/20/61
 0 Refer to first LD50 record sheet me 12/20/61

ACUTE TOXICITY (LD₅₀) RECORD

TEST COMPOUND D-29-01 STUDY NO. 141-722
 IRDC NO. 7500
 DOSE VOLUME ml/kg: Refer to dose volume calculation sheet SPECIES Rat SEX M
 ROUTE OF ADMINISTRATION oral DATE ANIMALS RECEIVED 11/17/81 SOURCE Charles River
 TIME OF FASTING* 16:00 FASTING TECHNICIAN ML DATE 12/29/81
 TIME OF DOSING 10:45 DOSING TECHNICIAN ML DATE 12/29/81

DOSE	M/L/KG	ANIMAL NUMBER					TECHNICIAN	DATE
		99626	99627	99631	99636	99643		
5000		PREFASTED WEIGHT (g)	271	283	274	265	252	*
		INITIAL BODY WEIGHT (g)	247	258	248	242	226	*
		ACTUAL DOSE (ml)	1.1	1.2	1.1	1.1	1.0	ML 12/29
		DOSE ADMINISTRATION	✓	✓	✓	✓	⊖	ML 12/29
		DAY 14 BODY WEIGHT (g)	299	362	321	313	308	Q/V 1/12
5250		PREFASTED WEIGHT (g)	299	258	266	281	255	*
		INITIAL BODY WEIGHT (g)	271	244	245	260	229	*
		ACTUAL DOSE (ml)	1.4	1.3	1.3	1.4	1.2	ML 12/29
		DOSE ADMINISTRATION	✓	✓	✓	✓	✓	ML 12/29
		DAY 14 BODY WEIGHT (g)	371	293	321	330	258	Q/V 1/12
6613		PREFASTED BODY WEIGHT (g)	270	268	286	278	273	*
		INITIAL BODY WEIGHT (g)	243	244	257	254	254	*
		ACTUAL DOSE (ml)	1.5	1.5	1.6	1.5	1.5	ML 12/29
		DOSE ADMINISTRATION	✓	✓	✓	✓	✓	ML 12/29
		DAY 14 BODY WEIGHT (g)	321	302	347	332	331	Q/V 1/12

NA - Not Applicable a - food removed ✓ - Dose indicated was administered

PREFASTED BODY WEIGHTS DAY 14 BODY WEIGHT DAY BODY WEIGHT
 BALANCE NO. + BALANCE NO. CHCO BALANCE NO. 10/1
 INITIAL BODY WEIGHTS DAY BODY WEIGHT DAY BODY WEIGHT
 BALANCE NO. * BALANCE NO. 1/1 BALANCE NO. 1/1

IR36-61-4 * Refer to Initial/Instal Body Weight sheet ML 12/29/81
 Specializing
 2-20-81

ACUTE TOXICITY (LD₅₀) RECORD

TEST COMPOUND B0429-01 STUDY NO. 191-722
 IRDC NO. 7500
 DOSE VOLUME ml/kg: 500 mg dose calculated SPECIES Rat SEX m/f
 ROUTE OF ADMINISTRATION Oral DATE ANIMALS RECEIVED 01/17/01 SOURCE Charles Burr
 TIME OF FASTING^a 1600 FASTING TECHNICIAN JP DATE 1/4/02
 TIME OF DOSING 1030 DOSING TECHNICIAN AD DATE 1/5/02

DOSAGE mg/kg	ANIMAL NUMBER	99686	99703	99705	99706	99714	TECHNICIAN	DATE	
		PREFASTED WEIGHT (g)	293	294	283	297			282
	INITIAL BODY WEIGHT (g)	266	259	250	273	258	Ⓢ		
	ACTUAL DOSE (ml)	2.2	2.1	2.1	2.2	2.1	AD	1/5	
	DOSE ADMINISTRATION	✓	✓	✓	✓	✓	AD	1/5	
	DAY 14 BODY WEIGHT (g)	304	[faded]				AD	1/6	
	DAY BODY WEIGHT (g)								
	DAY BODY WEIGHT (g)								
	DAY BODY WEIGHT (g)								
DOSAGE mg/kg	ANIMAL NUMBER	99763	99765	99774	99776	99782	TECHNICIAN	DATE	
		PREFASTED WEIGHT (g)	244	242	236	239			232
	INITIAL BODY WEIGHT (g)	223	229	216	216	213	Ⓢ		
	ACTUAL DOSE (ml)	1.8	1.9	1.7	1.7	1.7	AD	1/5	
	DOSE ADMINISTRATION	✓	✓	✓	✓	✓	AD	1/5	
	DAY 14 BODY WEIGHT (g)	[faded]							
	DAY BODY WEIGHT (g)								
	DAY BODY WEIGHT (g)								
	DAY BODY WEIGHT (g)								
DOSAGE mg/kg	ANIMAL NUMBER	[faded]						TECHNICIAN	DATE
		PREFASTED BODY WEIGHT (g)	[faded]						
	INITIAL BODY WEIGHT (g)	[faded]							
	ACTUAL DOSE (ml)	[faded]							
	DOSE ADMINISTRATION	[faded]							
	DAY 14 BODY WEIGHT (g)	[faded]							
	DAY BODY WEIGHT (g)	[faded]							
	DAY BODY WEIGHT (g)	[faded]							
	DAY BODY WEIGHT (g)	[faded]							

NA - Not Applicable a - food removed J - Dose indicated was administered

PREFASTED BODY WEIGHTS DAY 14 BODY WEIGHT DAY 14 BODY WEIGHT
 BALANCE NO. 65 BALANCE NO. 6224 1/11/02 BALANCE NO. 1A
 INITIAL BODY WEIGHTS DAY 14 BODY WEIGHT DAY 14 BODY WEIGHT
 BALANCE NO. 65 BALANCE NO. N4 BALANCE NO. 1A

IR36-61-4 @ 2:10 to Body Weight Record 1/15/02

Dose Volume Calculation

191-722

The dose volumes for IRDC 7500 were calculated using the following general formula:

$$\frac{\text{dose level g/kg}}{\text{specific gravity g/ml}} = \text{dose volume ml/kg}$$

$$5000 \text{ mg/kg} \quad \frac{5.0 \text{ g/kg}}{1.078 \text{ g/ml}} = 4.6 \text{ ml/kg}$$

$$5750 \text{ mg/kg} \quad \frac{5.750 \text{ g/kg}}{1.078 \text{ g/ml}} = 5.3 \text{ ml/kg}$$

$$6613 \text{ mg/kg} \quad \frac{6.613 \text{ g/kg}}{1.078 \text{ g/ml}} = 6.1 \text{ ml/kg}$$

$$7604 \text{ mg/kg} \quad \frac{7.604 \text{ g/kg}}{1.078 \text{ g/ml}} = 7.1 \text{ ml/kg}$$

ML 12/27/81

S- 12/27/81

Dose Volume Calculation

191-722

The dose volume for IRDC 7500 will be calculated by using the following formula:

$$\text{Dose Volume} = \frac{\text{Dose level } \mu\text{g}}{\text{specific gravity } \mu\text{ml}} = \text{ml/kg}$$

The specific gravity will be used from the determination of 12/18/81.

specific gravity of IRDC 7500 is 1.078 g/ml at 24°C.

$$5745 \mu\text{g/kg} \quad \frac{8.745 \mu\text{g}}{1.078 \mu\text{ml}} = 8.1 \text{ ml/kg}$$

KD 11/5/82

P- 1/5/82

Test Article Preparation

The test article IRDC 7500 was prepared for dosing in an identical manner as on 12/29/81. Refer to Test Article Preparation of 12/29/81 for specific details.

KD 11/5/82

P- 1/5/82

Dosing Procedure

The test article IRDC 7500 was dosed in an identical manner as on 12/29/81. Refer to Dosing Procedure of 12/29/81 for specific details.

KD 1/5/82

P- 1/5/82

APPENDIX C
Individual Macroscopic Observations

191-722

INDIVIDUAL MACROSCOPIC OBSERVATIONS
Died on Study, Males

80429-01

SITE

- OBSERVATION

7604 mg/kg

8745 mg/kg

ANIMALS EXAMINED

99640

99703, 99705,

99706, 99714

ANIMALS WITHIN NORMAL LIMITS

GASTROINTESTINAL TRACT

- Mucosa, hyperemic, diffuse, mild

STOMACH

- Material, red mucoid contents

- Nonglandular mucosa, hyperemic, diffuse, mild

99705, 99706

99640

99640

INDIVIDUAL MACROSCOPIC OBSERVATIONS
Died on Study, Females

B0429-01

SITE	5750 mg/kg	6613 mg/kg	7604 mg/kg	8745 mg/kg
- OBSERVATION				
ANIMALS EXAMINED	99663, 99667, 99668, 99670	99659, 99665, 99673	99658, 99660, 99661, 99669	99763, 99765, 99774, 99778, 99782
ANIMALS WITHIN NORMAL LIMITS	99663, 99667, 99668, 99670	99659		
EXTERNAL				
- Stain, dry, yellow, anogenital area			99669	
GASTROINTESTINAL TRACT				
- Mucosa, hyperemic, diffuse, mild				99763
- Mucosa, hyperemic, multifocal, mild				99774
INTESTINE				
- Material filled, dark red mucoid			99669	
- Mucosa, hyperemia, moderate			99669	
SMALL INTESTINE				
- Hyperemic, multifocal, mild		99665, 99673	99658	
- Mucosa, hyperemic, diffuse, mild			99660	99778
STOMACH				
- Material, red mucoid contents				
- Liquid filled, brown			99661	
- Mucosa, hyperemic, diffuse, mild			99669	
- Mucosa, hyperemic, diffuse, moderate				99778
- Glandular mucosa, hyperemia, moderate			99669	99765
- Glandular mucosa, hyperemic, diffuse, mild			99658	
- Glandular mucosa, hyperemic, diffuse, moderate			99661	
- Nonglandular mucosa, hyperemic, diffuse, mild				99782

INDIVIDUAL MACROSCOPIC OBSERVATIONS
Terminal Sacrifice, Males

BO429-01

SITE	5000 mg/kg	5750 mg/kg	6613 mg/kg	7604 mg/kg	8745 mg/kg
- OBSERVATION					
ANIMALS EXAMINED	99626, 99631, 99633, 99636, 99643	99627, 99634, 99641, 99646, 99647	99624, 99632, 99635, 99637, 99642	99625, 99638, 99639, 99644	99688
ANIMALS WITHIN NORMAL LIMITS	99626, 99631, 99633, 99636, 99643	99627, 99634, 99641, 99646, 99647	99624, 99632, 99635, 99637, 99642	99625, 99638, 99639, 99644	99688

B0429-01

INDIVIDUAL MACROSCOPIC OBSERVATIONS
Terminal Sacrifice, Females

SITE	5000 mg/kg	5750 mg/kg	6613 mg/kg	7604 mg/kg
- OBSERVATION				
ANIMALS EXAMINED	99657, 99666, 99671, 99672, 99675	99678	99655, 99676	99662
ANIMALS WITHIN NORMAL LIMITS	99657, 99666, 99671, 99672, 99675	99678	99655, 99676	99662

INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION
PROTOCOL REVISION OR CLARIFICATION

Protocol Sheet No. 1

Study No. 191-722

Title: ACUTE ORAL TOXICITY (LD₅₀ VALUE IN RATS)

ITEM	JUSTIFICATION
1	Study initiation
2	Clarification of IRDC Quality Assurance procedures
3	Clarification of submission to regulatory agency

ITEM	PROTOCOL REVISION OR CLARIFICATION
1	Conduct study in accordance with the attached protocol
2	This study is subject to IRDC Quality Assurance Department standard operating procedures, with the exception that the final report will not be reviewed by the IRDC Quality Assurance Department.
3	This study will not be submitted to a regulatory agency

Study Director James R. Myer, B.S.

Signature James R. Myer

12/17/81
Date

PROTOCOL NO. C1

Acute Oral Toxicity (LD₅₀ Value in Rats)

Issue Date: September 1, 1981
Supersedes Issue Dated: September 15, 1980

Test Substance Identification Number (TSIN) # B0429-01

Divisional Request Document Number (DRD) # BSBTS 734S

Sponsor: The Procter & Gamble Company
Cincinnati, Ohio

Testing Facility: International Research and Study # 191-722
(To be filled in by Development Corporation (To be filled in by
Operations Section) Mattawan, Michigan 49071 Testing Facility)

Purpose: To establish the acute oral toxicity and/or the LD₅₀ value of a test substance in the rat so that it may be compared with more familiar substances.

Justification for Selection of Test System:

The rat is the animal classically used due to its small size, ready availability, and the large amount of background data.

Route of Administration of Test Substance and Reason for Choice:

By gavage. This is a method for administering a known quantity of test substance and has been the route of choice historically.

Diet and/or Water Analyses Required:

None (no known contaminants expected which would interfere with this study)

Records to be Maintained:

All records that would be required to reconstruct the study and demonstrate adherence to protocol.

PROTOCOL NO. C1 (Cont'd)

Acute Oral Toxicity (LD₅₀ Value in Rats)

Issue Date: September 1, 1981

<u>Test Substance(s)</u>	<u>DRD</u>	<u>Description</u>		<u>Expiration</u>
<u>ISIN #</u>	<u>Number</u>	<u>Color</u>	<u>Physical Form</u>	<u>Date</u>
B0429-01	BSBTS 734S	amber	liquid	N/K

Storage Conditions: (Check one)

Room temperature Refrigerator Freezer
 Other

Hazards: (Check one)

None known. Take ordinary precautions in handling.
 As follows: Ignitable liquid, flash point > 100°F. Avoid sparks and open flames.

Special Instructions: (Check one)

None
 As follows:

Animals: A sufficient number of rats, Sprague-Dawley (CD), 190-300 grams prefasted weight, so that each test group will contain five (5) males and five (5) females.

Animal Care: Follow the approved Standard Operating Procedures of the Test Facility.

Environmental Conditions: Follow the approved Standard Operating Procedures of the Test Facility.

Animal Identification: Follow the approved Standard Operating Procedures of the Test Facility.

PROTOCOL NO. C1 (Cont'd)

Acute Oral Toxicity (LD₅₀ Value in Rats)

Issue Date: September 1, 1981

Estimated LD₅₀ value of the undiluted test substance: 5 g/kg
(If unknown, conduct a range-finding experiment following the Standard Operating Procedures of the Test Facility.)

Group Assignment: Determine prefasted body weights and select animals weighing 190-300 grams for study.

If the range finding experiment or Sponsor's estimate indicates the LD₅₀ value to be >20 g/kg of test substance, administer a single dose of 20 g/kg to ten (10) animals (5 males and 5 females). If the dose volume required to administer 20 g/kg exceeds 25 ml/kg, contact the Sponsor's Divisional Toxicologist for further instructions. If the mortality of these animals indicates that the LD₅₀ value would be >20 g/kg, report an estimated LD₅₀ value of >20 g/kg.

If the range finding experiment indicates an LD₅₀ value of less than 20 g/kg, choose four (4) dosage levels, based upon the range finding experiment. When feasible, choose dosage levels following a geometric progression of 1.4. If high dose levels require dose volumes which exceed 25 ml/kg, contact Sponsor's Divisional Toxicologist for further instructions. Place ten (10) animals in each group, divided by sex (5 males, 5 females). Assign animals to groups following the Standard Operating Procedures of the Test Facility.

If Sponsor's estimate indicates an LD₅₀ value of less than 20 g/kg, five (5) dosage levels may be used, if necessary (to better bracket the estimate), in lieu of running the range finding experiment.

Dose Preparation: Test Group(s): (Check appropriate box)

- Dose test substance undiluted
 Dose as a freshly prepared _____% (w/w) solution/suspension of test substance in _____
 Dose as a freshly prepared _____% (w/v) solution/suspension of test substance in _____
 Dose per Special Instructions (see page 2)

Control Group

A control group should be ; should not be included in this study. If included, the control substance _____ should be tested concurrently with the test substance at a dosage level of _____.

PROTOCOL NO. C1 (Cont'd)

Acute Oral Toxicity (LD₅₀ Value in Rats)

Issue Date: September 1, 1981

Dose Preparation
(Cont'd):

Test Group(s) (Cont'd)

Note

A concentration analysis of the test substance - vehicle mixture(s) will ; will not be required.

If a concentration analysis is required:

- Prepare a sufficient quantity of the test substance - vehicle mixture(s) so that a portion can be returned to the Sponsor's Divisional Toxicologist. Store solution/mixture at room temperature; refrigerator; freezer; other _____

Shipping Instructions

Send approximately _____ ml. Send frozen; under ambient conditions; other _____

- Analyze the test substance - vehicle mixture(s) for test substance concentration using the analytical method in Appendix _____.

Dosing Instructions:

Deprive the animals of food for 18-20 hours ~~before~~ administering the test substance. Determine ~~fasted~~ body weights. Calculate the dose for each animal according to fasted body weight to give the specified quantities of test substance per unit of body weight.*

If additional dosage levels are required to establish a death-to-dose response that will allow the LD₅₀ value to be calculated, the Sponsor should be contacted prior to further work.

*Determine density, if required, to calculate dose levels for all test substances dosed undiluted or solutions prepared for dosing on a weight to weight (w/w) basis.

PROTOCOL NO. C1 (Cont'd)

Acute Oral Toxicity (LD₅₀ Value in Rats)

Issue Date: September 1, 1981

Dosing Instructions
(Cont'd):

The test substance, at the concentration specified under "Dose Preparation", will be gavaged following the Test Facility's Standard Operating Procedures. Record all information necessary to document animal weights and volume of test substance administered to each animal.

Immediately after dosing, return the animal to ad libitum feeding.

Observations:

Option A
LD₅₀ Only

[] Observe all animals for mortality at frequent intervals during the first 4 hours after dosing (at least once during the first 30 minutes) and daily thereafter for the next 14 days. Record time of death. On day 14 discard survivors following the Test Facility's Standard Operating Procedures.

Option B
LD₅₀
+ Symptoms

[] Observe all animals for mortality and pharmacotoxic symptoms at frequent intervals during the first 4 hours after dosing (at least once during the first 30 minutes) and daily thereafter for the next 14 days. Record all pharmacotoxic symptoms and time of death. On day 14 weigh and discard survivors following the Test Facility's Standard Operating Procedures.

Option C
LD₅₀
+ Symptoms
+ Necropsy

[X] Observe all animals for mortality and pharmacotoxic symptoms at frequent intervals during the first 4 hours after dosing (at least once during the first 30 minutes) and daily thereafter for the next 14 days. Record all pharmacotoxic symptoms and time of death. Perform a gross necropsy on all animals that die following the Test Facility's Standard Operating Procedures. On day 14 weigh and perform a gross necropsy on the surviving animals. Record all findings. Discard animals following the Test Facility's Standard Operating Procedures.

Protocol Changes:

If it becomes necessary to change the approved protocol, verbal agreement to make this change should be made between the Study Director and the Sponsor. As soon as practical, this change and the reasons for it should be put in writing and signed by both the Study Director and the Sponsor's Divisional Toxicologist. This document is then attached to the protocol as an addendum.

PROTOCOL NO. C1 (Cont'd)

Acute Oral Toxicity (LD₅₀ Value in Rats)

Issue Date: September 1, 1981

Report:

Report dates of study initiation and termination. Report individual dose levels, body weights, mortality, pharmacotoxic signs, gross necropsy results, etc., where appropriate. Report the LD₅₀ value and 95% confidence limits of the test substance preferably calculated by the Probit Method* by the use of the computer program BLISS17**. Other calculation methods may be used. The method used should be specified in the final report. This report shall conform to all requirements outlined in Section 58.185, Subpart J, Good Laboratory Practices Regulations.

Sponsor: James H. Benedict *James H. Benedict*
Divisional Toxicologist

Date Approved by Sponsor's Divisional Toxicologist *Nov. 4, 1981*

Proposed Starting Date: 12/29/81

Defined as day of dosing

Proposed Completion Date: 1/12/82

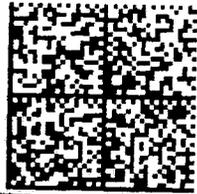
Defined as day of last observation)To be completed
by the Test Facility

Study Director: *James R. Myer*
James R. Myer, B.S.
Date: December 17, 1981

Study Cost: _____

*D. J. Finney, Probit Analysis, 3rd Ed., Cambridge Univ. Press 1971, pp. 50-90.

**Fortran version of BLISS17 program, written by D. J. Finney.



neopost

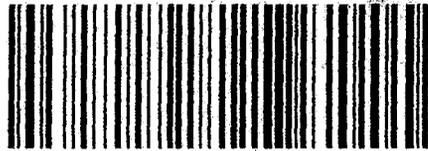
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