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Submitting Organization	PROCTER & GAMBLE CO		
Contractor			
Document Title	INITIAL SUBMISSION: ACUTE PERCUTANEOUS TOXICITY OF [] IN RABBITS WITH COVER LETTER DATED 082492 (SANITIZED)		
Chemical Category	CONFIDENTIAL		

8EHO-92-10098

Procter & Gamble COMPANY SANITIZED

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

Public Display Copy

August 24, 1992

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8EHO-92-10098, INIT
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02 AUG 31 11:00 AM '92

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 materials identified in the attached report as P1906 and P1907 are confidential mixtures. The compositions of the mixtures are appended as Attachment 1. The report is titled "Acute Percutaneous Toxicity". Any correspondence relating to this submission should reference study # 1348-32390.

This submission provides data on the acute percutaneous toxicity of a mixture of P1906 and P1907 mixed in a 5.5 to 1 ratio and dosed at 2 ml/kg. This mixture resulted in severe skin irritation, the death of 3/6 rabbits treated, and the occurrence of slightly fatty livers in the three animals which died on test. Surviving animals had no significant findings other than skin effects at necropsy.

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:

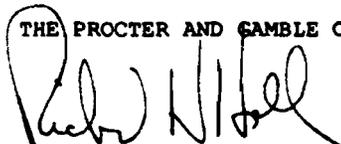
1. Confidentiality of the chemical constituents and their percentages should be maintained indefinitely. There are no plans for this information to be otherwise disclosed, and this technology has significant commercial value.
2. To our knowledge, there have been no government confidentiality determinations made for this mixture.

~~Procter & Gamble~~

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.
 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

Procter&Gamble

Attachment I

Public Display Copy

The mixture identified as P1906 is:

Alkyl benzene sulfonic acid

Sodium alkyl ethoxy sulfate

Alkyl ethoxylate

Fatty acid

Citric acid

Substituted amine

Mono ethanol amine

Propylene glycol

Ethanol

Substituted stilbene

Fragrance

Boric Acid

Calcium salt

Substituted amine

Enzyme

57 - 55 - 6 (SM#10410CU 3/2/11)

Procter&Gamble

Attachment I (cont.)

Public Display Copy

The mixture identified as P1907 is:

Derivatized organic acid

Magnesium sulfate

Sodium sulfate

Alkyl benzene sulfonic acid

Organic acid

Water

1348-32390

THE PROCTER & GAMBLE COMPANY
Miami Valley Laboratories
P.O. Box 39175
Cincinnati, Ohio 45247

ACUTE PERCUTANEOUS TOXICITY

805-0087

ETS 3201

P1906
P1907

April 4, 1983

MS-0007

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Protocol.....	Attached



THE PROCTER & GAMBLE COMPANY

MIAMI VALLEY LABORATORIES

P. O. BOX 39175
CINCINNATI, OHIO 45247

The following study was reviewed by the Quality Assurance Unit:

LABORATORY: The Procter & Gamble Company
MVF - Miami Valley Laboratories
P.O. Box 39175
Cincinnati, Ohio 45247

STUDY NUMBER: MS-0007

DIVISIONAL REQUEST DOCUMENT: SIS 1281

TSID: P1906, P1907

TYPE OF STUDY: Acute Percutaneous Toxicity

PORTION(S) OF STUDY REVIEWED:	REVIEWED BY:	DATE(S) OF REVIEW:	DATE(S) FINDINGS REPORTED TO STUDY DIRECTOR:
Test Substance Handling	L. K. Klahn	1/14/85	1/14/85

The protocol was reviewed for compliance to the GLP regulations.

Significant audit findings (if any) were reported to the Study Director and Facility Management immediately. All audit findings are reported to Management on a periodic basis.

The final study report was reviewed for inaccuracies and procedural compliance. The results reflect the raw data of the study.

T. E. Gulman / JER 4/4/85
Quality Assurance Unit Coordinator

SUMMARY AND CONCLUSIONS

The acute dermal LD50 of a combination of P1907 and P1906 (1:5.5 ratio) was found to be 2.0 ml/kg. This test substance mixture resulted in the death of 3 of 6 animals. Relatively severe dermal responses were noted on all animals which resulted in the development of eschar on the surviving animals. The extent of dermal irritation was not considered to be the direct cause of death.

Postmortem examination of 3 animals that died prematurely revealed severe dermal treatment area skin erythema and evidence of fatty livers, but no evidence to suggest a probable cause of death. Remaining animals were necropsied according to schedule, and although dermal treatment area skin alterations consistent with the final in-life observation were present, no evidence of any other alterations was observed. The significance of the fatty alteration in livers of animals that died prematurely could not be determined within the confines of the present study.

OBJECTIVES AND BACKGROUND

The purpose of this study was to evaluate and characterize the gross dermal and systemic effect produced by P1907 and P1906 (1:5.5 ratio) when applied to the backs of rabbits at a dose level of 2 ml/kg.

STUDY IDENTIFICATION

STUDY DIRECTOR: G. A. Wines

DIVISIONAL TOXICOLOGIST: E. V. Miller

SPONSORING DIVISION: Packaged Soap & Detergent Division

TESTING FACILITY: The Procter & Gamble Company
Miami Valley Laboratories
Biological Testing Facility

DIVISIONAL REQUEST DOCUMENT

NUMBERS: NIS 1201

STUDY NUMBER: 905-0007

STUDY NUMBER: ED-7771

DATES: 1/10/65 - 1/24/65

MATERIALS AND METHODS (PROTOCOL ATTACHED)

TEST SUBSTANCE

TEST SUBSTANCE

IDENTIFICATION: P1906, P1907

CONCENTRATION OF TEST

SUBSTANCE TESTED: One (1) part P1907 and 5.5 parts P1906 (Undilute)

TEST SUBSTANCE STORAGE

CONDITION: Room Temperature and Humidity

CONTROL SUBSTANCE: None

ANALYSIS OF TEST

SUBSTANCE/CARRIER

MIXTURE: Not required, see Protocol Page 3

TEST SYSTEM**SPECIES, STRAIN AND SOURCE**

OF ANIMALS: Rabbit, New Zealand Albino, Hazelton Research Animals

INITIAL ANIMAL WEIGHT RANGE: 2807-3983g

ANIMAL RESTRAINT: Harness

GROUP AND TREATMENT:NUMBER OF ANIMALS

<u>GROUP</u>	<u>MALE</u>	<u>FEMALE</u>	<u>TREATMENT</u>
1	4626, 4633, 4646	4595, 4597, 4617	1 part P1907 + 5.5 parts 1906, undilute, 2 ml/kg (Intact skin)

IN-LIFE

The study was conducted according to the attached protocol. There were no known deviations.

ANATOMIC PATHOLOGY

Three animals were found dead on January 13, 1985 and postmortem examinations were performed on these animals on January 14, 1985 (4646, 4597, 4617). P. H. Long, D.V.M., of the Pathology Section performed these necropsies.

Scheduled postmortem examinations were performed on the three remaining animals (4626, 4633, 4595) on January 24, 1985. The following pathology personnel were in attendance:

E. L. Kanerva - Pathologist Designate
W. E. Wyder - Necropsy Coordinator
D. M. Barnett - Prosector

No tissues were taken at either sacrifice for histologic processing.

RESULTS AND DISCUSSIONIN-LIFE

The acute dermal LD₅₀ of a mixture of P1906 and P1907 was found to be approximately 2.0 ml/kg. The test substance mixture produced severe erythema (6 animals) and slight edema (4 of 6 animals) on the test sites following the 24 hour exposure period.

The abdominal area of all animals was moist when the wrappings were removed. This eventually led to denuded (all survivors) and raw (1 survivor) skin in this area. Stenias developed on 5 of 6 animals within 3-4 days. Three animals died on days 4-5. Signs of anorexia were observed for all animals that died plus one survivor. General signs of morbidity and depression were also observed for 4 of 6 animals. Test site skin eschar leading to exfoliation was noted on all survivors. Except for skin, all gross signs of toxicity subsided by day 7 although one animal showed a significant body weight loss over the course of the study (In-Life Table 1).

Individual animal skin and health data sheets are attached as In-Life Appendices 1 and 2, respectively.

Anatomic Pathology

Postmortem examinations of 3 animals that died prematurely were conducted on 1/14/55. Examination of each animal revealed severe dorsal treatment area skin erythema, evidence of a fatty liver (generally mild), little or no food in the stomach, and evidence of postmortem change. In addition, one animal had pulmonary congestion. The probable cause of the premature death of these animals could not be determined.

The remaining animals were necropsied according to schedule. Gross examination of these animals revealed dorsal treatment area skin alterations that were consistent in degree and nature with the final in-life observations. There was, however, no evidence of any other alterations. The significance of the fatty alteration in livers of animals that died prematurely could not be determined within the confines of the present study.

D. Williams
Study Director

P. P. ...
Anatomic Pathologist
Designate

W. H. ...
Anatomic Pathologist

In-Life Table 1
805-0007

INDIVIDUAL ANIMAL BODY WEIGHTS

<u>ANIMAL #/ SEX</u>	<u>INITIAL (g)</u>	<u>FINAL (g)</u>	<u>CHANGE (g)</u>
4595 F	2807	2945	138
4626 W	3214	3331	117
4633 W	3009	2765	-244
4597 F	3403	♦	♦
4646 W	2928	♦	♦
4617 F	3283	♦	♦

♦ Premature death

PROTOCOL NO. C10 (Cont'd)

Acute Percutaneous Toxicity

Issue Date: May 1, 1964

Site Preparation:

Clip an area on the back of each animal from shoulder to rump, approximately 15 cm wide, with a small animal clipper. The skin of all animals is left intact.

Dose Preparation:

Test Group(s) (Check appropriate boxes)

Dose undiluted as follows: 2 ml/kg. 2 g/kg

Dose as a freshly prepared _____ (w/v) solution/suspension as follows: 2 ml/kg. 2 g/kg
Vehicle: _____

Dose as a freshly prepared _____ (w/v) solution/suspension as follows: 2 ml/kg. 2 g/kg
Vehicle: _____

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 _____.

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 _____.

PROTOCOL NO. CV8 (Cont'd)Acute Percutaneous Toxicity

Issue Date: May 1, 1984

Dosing Instructions:

Spread the test substance over the clipped area. Cover with a layer of 8-ply gauze, rubber dam and several wrappings of 3-inch Elastoplast tape or equivalent wrapping material. Restrain the animal to prevent it from removing the wrappings. Dry or powdered substances are placed directly onto the gauze. The gauze containing the dry test material is placed upon a layer of rubber dam and wrapping tape. Place the animal on his back over the test substance and secure the wrapping tape around the trunk. Repeat this procedure for the remaining animals.

[] See Options on page 4

Observations:

After 24 hours, remove the animal from restraints, uncover the test sites, remove the test substance with wet disposable gauze, paper towel, or equivalent. Observe daily for next 90 days for signs of skin irritation using the attached scale (Appendix 1). Observe twice daily for mortality following the Test Facility's Standard Operating Procedures. There should be at least 4 hours between observations, or the maximum possible elapsed time on weekends or holidays. On the 14th day, count, weigh, and sacrifice the surviving animals.

Necropsy:

Necropsy animals that died or were sacrificed during study and examine grossly for any abnormalities. Perform the necropsy following the Test Facility's Standard Operating Procedures. Record all gross necropsy findings.

[X] See Options on page 5

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.

Options:

[] Shave the skin of _____ males and _____ females to make a total of _____ animals/group (including shaved and intact skin). Shave according to the Test Facility's Standard Operating Procedure so as to penetrate the hairy layer of the epidermis without causing bleeding.

PROTOCOL NO. 610 (Cont'd)

Acute Percutaneous Toxicity

Issue Date: May 1, 1984

Options (Cont'd):

- 170 Perform a gross necropsy on all animals surviving at the conclusion of the 14-day observation period according to the Test Facility's Standard Operating Procedures. Record all gross necropsy findings.

Report:

Report should include how study was conducted, dates of study initiation and termination, and the individual animal observations including deaths, if any, degree of skin irritation as a function of time, body weights, signs of gross systemic effects and necropsy observations. If no deaths are observed at the 2 ml/kg or 2 gm/kg dose level, the LD₅₀ value is reported as greater than 2 ml (liquids) or 2 gm (solids or semi-solids) per kg of body weight. If deaths were observed at the 2 ml/kg or 2 gm/kg dose level, additional dose levels may be requested to produce a sufficient number of deaths to calculate an LD₅₀ value. If additional dose levels are not requested, the LD₅₀ value will not be reported. This report shall conform to all requirements outlined in Section 58.105, Subpart A, Code of Federal Regulations.

Sponsor: Kenneth W. Mills
 Divisional Toxicologist

Date Approved by Sponsor's Divisional Toxicologist 12/17/84

Proposed Starting Date 1-10-85

Defined as Treatment Date

Proposed Completion Date: 1-24-85

Defined as Gross Necropsy Date)
) to be completed)
) by the Test)
) Facility)

Study Director: B. A. [unclear]

Date: 1/6/85

Study Cost: \$950

PROTOCOL - APPENDIX 1

SCALE FOR EVALUATING SKIN REACTIONS

Erythema

- 0 - None
- 1 - Slight (barely perceptible)
- 2 - Moderate (well defined)
- 3 - Severe (best red)

Edema

- 0 - None
- 1 - Slight (barely perceptible to well defined by definite raising)
- 2 - Moderate (raised approximately 1 mm)
- 3 - Severe (raised more than 1 mm)

Stasis (not including eschar area)

- 0 - Normal
- 1 - Slight (impairment of elasticity)
- 2 - Moderate (slow return to normal)
- 3 - Marked (no elasticity)

Desquamation (not including eschar area)

- 0 - None
- 1 - Slight (slight scaling)
- 2 - Moderate (scabs and flakes)
- 3 - Marked (pronounced flaking with denuded areas)

Fissuring

- 0 - None
- 1 - Slight (definite cracks in epidermis)
- 2 - Moderate (cracks in dermis)
- 3 - Marked (cracks with bleeding)

Eschar

- N - No
- Y - Yes

Exfoliation (sloughing of the eschar tissue)

- N - No
- Y - Yes

CERTIFICATE OF AUTHENTICITY

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