(7-3-98)

DATA EVALUATION RECORD

Amine Oxide

Study Type: Acute Pack (§81-1, -2, -4, -5, and -6)

Work Assignment No. 3-27 (D244072)

Prepared for

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U.S. Environmental Protection Agency
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Disclaimer

This Data Evaluation Record may have been altered by the Antimicrobial Division subsequent to signing by Dynamac Corporation personnel.

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DATA EVALUATION RECORD

STUDY TYPE: Acute Oral Toxicity - Rat
OPPTS Number: 870.1100 OPP Guideline Number: §81-1

DP BARCODE: D244072 SUBMISSION CODE: S538885
P.C. CODE: 000439
EPA REG. NO.: 003573-LO

TEST MATERIAL (PURITY): P0434 (27.72% amine oxide)

SYNONYMS: None specified

CITATION: Cardin, C., et al. (1978) Acute oral LD50 toxicity study of P0434 in rats. Springborn Institute for Bioresearch, Inc., Spencerville, OH. Laboratory Project Number 3029.234. October 9, 1978. MRID 44475201. Unpublished.

SPONSOR: The Procter & Gamble Company, Cincinnati, OH.

EXECUTIVE SUMMARY: In an acute oral toxicity study (MRID 44475201), groups of five young adult Sprague Dawley rats/sex were given single oral doses of P0434 (27.72% amine oxide, from MRID # 44475203) at 2,000, 2,800, 3,900, 5,400 (>limit dose), or 7,600 mg/kg. The test substance was administered as received. An additional five animals/sex received distilled water and served as controls. Animals were observed for clinical signs of toxicity and mortality for up to 14 days postdosing.

Oral LD_{50} Males > 5,400 mg/kg (observed)
Females ≈ 3,900 mg/kg (observed)
Combined = 4,800 (4,100-5,600) mg/kg (95% C.I.)

P0434 is classified as **TOXICITY CATEGORY III** based on the observed LD_{50} value in female animals.

Mortality occurred in 19/30 animals tested at ≥3,900 mg/kg within 4 days of administration. Clinical effects included decreased motor activity, excessive salivation, diarrhea, rattling respiration, nasal and/or ocular hemorrhaging, and blanching. Effects subsided from surviving animals from all dose groups by

day 6. No treatment-related effect on overall body weight was observed. Necropsy of decedent animals revealed abnormal contents (often with blood) of the stomach and/or intestines, irritated stomachs and intestines, and discolored lungs. Discolored lungs were also observed upon necropsy of animals sacrificed after 14 days.

This study is classified **acceptable (§81-1)** and satisfies the guideline requirement for an acute oral study in the rat.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided. This study, however, precedes GLP compliance and current Subdivision F guideline requirements. A signed and dated Quality Assurance statement was not provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: P0434
   Description: Clear liquid
   Lot/Batch #: Not specified (received 09/28/78)
   Composition: % Amine oxide not specified
   Specific gravity: 0.94 g/mL (at room temperature)
   CAS #: Not provided

   The test material was mixed thoroughly before administration.

2. Vehicle: None employed

3. Test animals: Species: Rat
   Strain: Harlan (SD)(CD)
   Age: Not specified (young adult, based on weight)
   Weight: 190-268 g males; 190-242 g females
   Source: Harlan Industries, Inc. (location not specified)
   Acclimation period: ≥4 Days
   Diet: Purina Rat Chow, amounts not specified
   Water: Tap water, ad libitum
   Housing: One animal per cage
   Environmental conditions:
   Temperature: 71-72 _F
   Humidity: 52-72%
   Air changes: Not specified
   Photoperiod: 12-Hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: September 12 - October 10, 1978

2. Animal assignment and treatment: Animals were assigned to the groups listed in Table 1; rationale for dose selection was not specified. Following an 18- to 20-hour fasting period, young adult rats were given a single oral dose of neat P0434 or distilled water (control) by gavage. The rats were observed for signs of toxicity and/or mortality at 15 and 30 minutes, 1, 2, and 4 hours, and once daily thereafter for up to 14 days. Body weights were recorded on days -1 (prior to fasting), 0 (prior to dosing), and 14 (if applicable). At 14 days, the surviving animals were sacrificed, and all animals (upon death) were necropsied and examined for gross pathological changes.

TABLE 1. Doses, mortality/animals treated

Dose, mg/kg	Males	Females	Combined
Control[a]	0/5	0/5	0/10
2,000	0/5	0/5	0/10
2,800	0/5	0/5	0/10
3,900	1/5	3/5	4/10
5,400[b]	0/5	5/5	5/10
7,600	5/5	5/5	10/10

[a] Distilled water at 20,000 mg/kg
[b] >Limit dose

3. Statistics: The acute oral LD_{50} value (with 95% C.I.) for combined sexes was calculated using the method of Weil [Weil, C., Biometrics, pp. 249-263 (1952)]. Data from the 2,000-mg/kg group were not used in the calculations. The LD_{50} values for separate sexes were not determined.

II. **RESULTS AND DISCUSSION:**

A. Mortality: Mortality data are presented in Table 1. Mortality occurred in 19/30 animals tested at $\geq$3,900 mg/kg within 4 days of administration.

Oral LD_{50} Males > 5,400 mg/kg (observed)

Females ≈ 3,900 mg/kg (observed)
Combined = 4,800 (4,100-5,600) mg/kg (95% C.I.)

B. Clinical observations: Clinical effects generally observed in all test groups included decreased motor activity (50/50)[1], excessive salivation (50/50), and diarrhea (11/50). Additional effects observed in animals from the ≥5,400 mg/kg dose groups included rattling respiration (6/20), nasal hemorrhaging (5/20), ocular hemorrhaging (4/20), and blanching (2/20). Effects subsided from surviving animals from all dose groups by day 6. No abnormal effects were observed in control animals.

C. Body Weight: No treatment-related effect on body weight was observed upon comparison of overall (0-14 days) gains. Control animals gained averages of 51% for males and 32% for females. In comparison, surviving test animals gained averages of 54-59% for males and 27-30% for females.

D. Necropsy: Necropsy of decedent animals revealed abnormal contents (often with blood) of the stomach and/or intestines (18/19); irritated stomachs (17/19); irritated intestines (12/19); red lungs (5/19), once with bright red spots; liver-colored or tan lungs (4/19); and petechiae of the lungs (1/19). Necropsy of animals sacrificed after 14 days revealed red lungs (24/31), petechiae of the lungs (5/31), and/or liver-colored areas of the lung (3/31).

E. Deficiencies: Although LD_{50} values for each sex were not calculated, it was possible to approximate the levels based on the data generated. As a result, this deficiency is considered minor.

A Quality Assurance statement was not provided, and clinical effects were presented in summary format. These deficiencies, however, are considered minor and should have no effect on the results of the study.

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[1] Since data were not presented on an individual basis, these values represent the sum of the maximum number of animals exhibiting effect.

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DATA EVALUATION RECORD

STUDY TYPE: Acute Dermal Toxicity - Rabbit
OPPTS Number: 870.1200 OPP Guideline Number: §81-2

DP BARCODE: D244072 SUBMISSION CODE: S538885
P.C. CODE: 000439
EPA REG. NO.: 003573-LO

TEST MATERIAL (PURITY): P0434 (27.72% amine oxide)

SYNONYMS: None specified

CITATION: Cardin, C., et al. (1978) Acute percutaneous toxicity study of P0434 in rabbits. Springborn Institute for Bioresearch, Inc., Spencerville, OH. Laboratory Project Number 3029.232. October 12, 1978. MRID 44475202. Unpublished.

SPONSOR: The Procter & Gamble Company, Cincinnati, OH.

EXECUTIVE SUMMARY: In an acute dermal toxicity study (MRID 44475202), three young adult New Zealand White rabbits/sex were dermally exposed to P0434 (% amine oxide not specified) at approximately 1,880 mg/kg (< limit dose) for 24 hours. The test substance was applied as received to three intact and three abraded sites (one per animal); however, the actual size of the application area was not specified. Animals were observed for dermal irritation and mortality for up to 14 days postdosing.

Dermal LD_{50} Males = >1,880 mg/kg (observed)
Females = >1,880 mg/kg (observed)

P0434 is classified as **TOXICITY CATEGORY II** based on the observed LD_{50} values in both sexes.

All animals survived the 14-day observation period; however, clinical signs of toxicity were not recorded. Overall moderate and persistent dermal irritation was observed at 6/6 treatment sites, and was comparable between intact and abraded skin. Irritation included erythema, atonia, desquamation, fissuring, eschar formation, and exfoliation. Body weight data were not provided. Necropsy after 14 days revealed slightly irritated

stomachs, petechiae on the lungs, dark red spots on lungs, and/or tan-colored lungs.

In this study, 1) only three animals/sex were used, 2) the test material was applied at less than the limit dose, 3) the exact size of the application areas were not specified, 4) clinical effects were not recorded, 5) body weight data were not provided, and 6) the test article was not properly characterized. Also, the Agency does not condone the use of abraded skin in dermal toxicity studies. Despite these obvious deficiencies, there was no mortality observed in this study at a dose approximating a limit dose, and using the present dataset would preclude use of additional animals. Therefore, this study is classified **acceptable (§81-2)** and satisfies the guideline requirement for an acute dermal study in the rabbit.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided. This study, however, precedes GLP compliance and current Subdivision F guideline requirements. A signed and dated Quality Assurance statement was not provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: P0434
   Description: Clear liquid
   Lot/Batch #: Not specified (received 09/23/78)
   Composition: % Amine oxide not specified
   Specific gravity: Not specified
   CAS #: Not provided

   The test material was mixed thoroughly before administration.

2. Vehicle: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Not specified (young adult, based on weight)
   Weight: 2.28-2.42 kg males, 2.13-2.42 kg females
   Source: Kings Wheel (location not specified)
   Acclimation period: ≥7 Days
   Diet: Purina Lab Rabbit Chow, amounts not specified
   Water: Tap water, ad libitum
   Housing: One animal per cage
   Environmental conditions:
   Temperature: 67-72 °F
   Humidity: 69-72%

Air changes: Not specified
Photoperiod: 12-Hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: September 5-19, 1978

2. Animal assignment and treatment: Animals were assigned to the two test groups noted in Table 1. Fur from the back areas of three young adult New Zealand White rabbits/sex was clipped from the shoulder to rump just prior to dermal administration of neat P0434 at 2.0 mL/kg; this is equivalent to approximately 1,880 mg/kg based on a specific gravity of 0.94 g/mL (from MRID 44475201). Half of the sites were abraded with the clipper head prior to administration. The test material was spread over the entire clipped area using a calibrated syringe; however, the actual size of the application area was not specified. The test sites were covered with 8-ply gauze and dental dam which was secured with Elastoplast tape, and the animals were fitted with Newmann harnesses. Following a 24-hour exposure period, the harnesses and coverings were removed, and the test sites were washed with water-moistened paper towels. The rabbits were observed for dermal irritation and mortality once daily following patch removal for 14 days. Body weights were recorded at days 0 (prior to dosing) and 14. At 14 days, all animals were necropsied and examined for gross pathological changes.

TABLE 1. Doses, mortality/animals treated

Dose, mL/kg	Males	Females	Combined
Intact Skin			
2.0	0/2	0/1	0/3
Abraded Skin			
2.0	0/1	0/2	0/3

3. Statistics: Not applicable to this study.

II. **RESULTS AND DISCUSSION:**

A. Mortality: All animals survived the 14-day observation period.

Dermal LD_{50} Males = >1,880 mg/kg (observed)
Females = >1,880 mg/kg (observed)

B. Clinical observations: Clinical signs of toxicity were not recorded.

Overall moderate and persistent dermal irritation was observed at 6/6 treatment sites, and was comparable between intact and abraded skin. At the three intact sites, slight to severe erythema (scores of 1-3) was observed at 1-14 days, slight to marked atonia (scores of 1-3) was observed at 2-14 days, slight desquamation (scores of 1) was observed at 7-14 days, slight to moderate fissuring (scores of 1-2) was observed at 4-14 days, eschar formation was evident at 3-14 days, and exfoliation was observed at 6-14 days. At the three abraded sites, slight to severe erythema (scores of 1-3) was observed at 1-14 days, slight to marked atonia (scores of 1-3) was observed at 2-14 days, slight to moderate desquamation (scores of 1-2) was observed at 7-14 days, slight to moderate fissuring (scores of 1-2) was observed at 5-11 days, eschar formation was evident at 3-14 days, and exfoliation was observed at 7-14 days. No edema was observed during the study.

C. Body Weight: Data were collected, but not provided.

D. Necropsy: Necropsy after 14 days revealed slightly irritated stomachs (6/6), petechiae on the lungs (2/6), dark red spots on lungs (1/6), and tan-colored lungs (1/6).

E. Deficiencies: The following deficiencies were noted in this study:

- Only three animals/sex were used
- The test material was applied at 2.0 mL/kg (approximately equivalent to 1,880 mg/kg), which is less than the limit dose of 2,000 mg/kg
- The exact size of the application areas were not specified
- Aside from dermal irritation, clinical effects were not recorded
- Body weight data were not provided

- the Agency does not condone the use of abraded skin in dermal toxicity studies.

Despite these obvious deficiencies, there was no mortality observed in this study at a dose approximating

a limit dose, and using the present dataset would preclude use of additional animals. Therefore, this study does is classified **acceptable (§81-2)** and satisfies the guideline requirement for an acute dermal study in the rabbit.

A signed and dated Quality Assurance statement was not provided. This deficiency, however, is considered minor and should have no impact on the results of the study.

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DATA EVALUATION RECORD

STUDY TYPE: Primary Eye Irritation - Rabbit
OPPTS Number: 870.2400 OPP Guideline Number: §81-4

DP BARCODE: D244072 SUBMISSION CODE: S538885
P.C. CODE: 000439
EPA REG. NO.: 003573-LO

TEST MATERIAL (PURITY): P7271 (% amine oxide not specified)

SYNONYMS: None specified

CITATION: Dean, W., and D. Jessup (1978) Primary eye irritation study in the albino rabbit. International Research and Development Corporation (location not specified). Laboratory Study Number 191-187. April 17, 1978. MRID 44434904. Unpublished.

SPONSOR: The Procter & Gamble Company, Cincinnati, OH.

EXECUTIVE SUMMARY: In a primary eye irritation study (MRID 44434904), 0.1 mL of P7271 (% amine oxide not specified) was instilled into the conjunctival sac of the right eye of six young adult New Zealand White rabbits. Three of the treated eyes were rinsed after 4 seconds with lukewarm water. An additional three animals were treated with 0.1 mL of a 10% P7271 aqueous solution. The animals were observed for up to 35 days following treatment, and eye irritation was scored by the Draize method.

In all eyes treated with 100% P7271 and not rinsed, severe and persistent ocular irritation was observed. Irritation was characterized by corneal opacity through 35 days, iridial effects through 28 days, and positive conjunctival effects through 14 days. Additional effects observed during the study included conjunctival blanching and peeling of the corneal epithelial in 3/3 eyes between 1 hour and 35 days, vascularization of the corneal surface in 3/3 eyes between 7 and 35 days, granulation scar tissue with neovascularization in 2/3 eyes between 14 and 35 days, pannus in 2/3 eyes at 7 days, phlyctena in 1/3 eyes at 28 days, and bulbar conjunctivae extending over corneal surface in 1/3 eyes at 35 days.

Similar effects were observed in the treated (100%) and rinsed eyes. Irritation was characterized by corneal opacity through 35 days, iridial effects through 7 days, and positive conjunctival effects through 14 days. Additional effects included peeling of

the corneal epithelial in 3/3 eyes between 1 hour and 35 days, conjunctival blanching in 3/3 eyes between 1 hour and 7 days, pannus in 3/3 eyes between 7 and 21 days, vascularization of the corneal surface in 2/3 eyes between 14 and 21 days, and granulation scar tissue with neovascularization in 1/3 eyes at 14 days.

In eyes treated with 10% P7271, ocular irritation included corneal opacity through 4 days, iridial changes through 2 days, and positive conjunctival irritation through 3 days. Additional effects included peeling of the corneal epithelial in 3/3 eyes between 1 and 4 days, conjunctival blanching in 3/3 eyes between 1 hour and 1 day, and pannus in 1/3 eyes at 7 days.

In this study, **P7271 is a corrosive ocular irritant**, and is classified as **TOXICITY CATEGORY I** for primary eye irritation based on the degree of irritation observed at 21 days in unwashed eyes treated with 100% P7271.

This study is classified **unacceptable (§81-4)** and does not satisfy the guideline requirements for a primary eye irritation study in the rabbit. Test article characterization must be provided in order for this study to be acceptable.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided. This study, however, precedes GLP compliance and current Subdivision F guideline requirements. A signed and dated Quality Assurance statement was not provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: P7271
   Description: Clear viscous liquid
   Lot/Batch #: PSC 77.021(a)
   Composition: % Amine oxide not specified
   pH: Not specified
   CAS #: Not provided

2. Vehicle and/or positive control: For Group III animals, distilled water was used to dilute the test material.

3. Test animals: Species: Rabbit
Strain: New Zealand White
Age: Not specified (young adult, based on weight)
Weight: 2.08-2.60 kg (combined sexes)
Source: Kuiper's Rabbit Ranch, Gary, IN
Acclimation period: ≥7 Days
Diet: Purina Rabbit Chow, ad libitum
Water: Tap water, ad libitum
Housing: Individual
Environmental conditions: Not specified

B. STUDY DESIGN and METHODS:

1. In-life dates: Between November 15, 1977 and April 17, 1978 (not further specified)

2. Animal assignment and treatment: Animals were assigned to the test groups noted in Table 1. A 0.1-mL aliquot of 100 or 10% P7271 was instilled into the conjunctival sac of the right eye of nine young adult New Zealand White rabbits (five male and four female). The upper and lower lids were held together for 1 second before releasing to prevent loss of the material. Approximately 4 seconds after instillation, 3/9 treated eyes (Group II) were flushed with 20 mL of lukewarm water. The left eye of each animal served as an untreated control. The animals were observed for ocular irritation at 1 hour and 1, 2, 3, 4, 7, and 14 days following instillation; animals treated at 100% (Groups I and II) were also observed at 21, 28, and 35 days. At the 3-day, 7-day, and subsequent observations, fluorescein dye was used to confirm the presence or absence of corneal ulceration. Eye irritation was scored by a detailed Draize scale (half numbers were included).

TABLE 1. Dose Groups

Group	Number/Sex	Concentration (%)	Wash
I	2M, 1F	100	No
II	1M, 2F	100	Yes
III	2M, 1F	10[a]	No

[a] Distilled water vehicle

II. RESULTS AND DISCUSSION:

A. Clinical observations: The incidence of positive ocular irritation for treated (100%) unwashed eyes (Group I) is summarized in Table 2. Severe and persistent ocular irritation was observed in all eyes. At 1 day, all treated eyes exhibited scattered or diffuse corneal opacity (scores of 1) affecting up to 100% of the total area (scores of 3-4), iridial changes (scores of 1), moderate to severe conjunctival redness (scores of 2-3), slight to severe conjunctival chemosis (scores of 2.5-4), and moderate to severe conjunctival discharge (scores of 2-3). At 7 days, all treated eyes exhibited translucent to opalescent corneal opacity (scores of 2-3) affecting up to 70% of the total area based on fluorescein retention, iridial changes (scores of 1-2), moderate conjunctival redness (scores of 2), very slight to moderate conjunctival chemosis (scores of 1-2.5), and very slight to slight conjunctival discharge (scores of 0.5-1). At 21 days, scattered/diffuse to complete opacity (scores of 1-4) affecting up to 30% of the total area based on fluorescein retention persisted in 3/3 eyes, iridial changes (score of 2) persisted in 1/3 eyes, very slight to slight conjunctival redness (scores of 0.5-1) persisted in 3/3 eyes, very slight to slight conjunctival chemosis (scores of 1-1.5) persisted in 2/3 eyes, and slight or severe conjunctival discharge (scores of 1 or 3) was observed in 2/3 eyes. Corneal opacity persisted in all treated eyes through 35 days; iridial effects subsided from 2/3 eyes by 21 days and from all eyes by 35 days; and positive conjunctival irritation subsided from all eyes by 21 days. Additional effects observed during the study included conjunctival blanching and peeling of the corneal epithelial in 3/3 eyes between 1 hour and 35 days, vascularization of the corneal surface in 3/3 eyes between 7 and 35 days, granulation scar tissue with neovascularization in 2/3 eyes between 14 and 35 days, pannus in 2/3 eyes at 7 days, phlyctena in 1/3 eyes at 28 days, and bulbar conjunctivae extending over corneal surface in 1/3 eyes at 35 days. In this study, P7271 is a corrosive ocular irritant.

TABLE 2. Incidence of Positive Ocular Effects in Treated (100%) Unwashed Eyes (Group I)

Observations	Number "Positive"/Number Tested									
	Hr	Days								
	1	1	2	3	4	7	14	21	28	35
Corneal Opacity	---	3/3	3/3	3/3	3/3	3/3	3/3	3/3	3/3	3/3
Iritis	3/3	3/3	3/3	3/3	3/3	3/3	2/3	1/3	1/3	---
Conjunctivae										
Redness	2/3	3/3	3/3	3/3	3/3	3/3	1/3	---	---	---
Chemosis	3/3	3/3	3/3	3/3	3/3	2/3	1/3	---	---	---
Discharge[a]	1/3	3/3	2/3	2/3	---	---	---	1/3	1/3	---

--- No positive observations.
[a] Discharge is not included in evaluating a positive reaction; however, scores of ≥2 are reported.

The incidence of positive ocular irritation for treated (100%) washed eyes (Group II) is summarized in Table 3. Although less severe and less persistent, significant ocular irritation was observed in all eyes. At 1 day, scattered or diffuse corneal opacity (scores of 1) affecting up to 50% of the total area (scores of 2) was observed in 2/3 eyes, iridial changes (scores of 1) were observed in 3/3 eyes, moderate conjunctival redness (scores of 1.5-2) was observed in 3/3 eyes, slight conjunctival chemosis (scores of 2) was observed in 3/3 eyes, and slight to moderate conjunctival discharge (scores of 1-2) was observed in 3/3 eyes. At 7 days, scattered/diffuse to translucent corneal opacity (scores of 1-2) affecting up to 50% of the total area based on fluorescein retention was observed in 3/3 eyes, iridial changes (scores of 1) persisted in 1/3 eyes, very slight to moderate conjunctival redness (scores of 0.5-2) persisted in 3/3 eyes, very slight to moderate conjunctival chemosis (scores of 0.5-2) persisted in 3/3 eyes, and slight to moderate conjunctival discharge (scores of 1-2) persisted in 2/3 eyes. At 21 days, scattered/diffuse to translucent corneal opacity (scores of 1-2) affecting up to 10% of the total area based on fluorescein retention persisted in 2/3 eyes, slight conjunctival redness (scores of 1) persisted in 2/3 eyes, and very slight conjunctival chemosis (scores of 0.5) persisted in 2/3 eyes. A single rabbit died prior to the 28-day reading. The study author reported that the death was from pneumonia and not compound-related. Corneal

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opacity persisted in ½ remaining animals through 35 days. Iridial effects subsided from all treated eyes by 14 days, and positive conjunctival irritation subsided from all eyes by 21 days. Additional effects observed during the study included peeling of the corneal epithelial in 3/3 eyes between 1 hour and 35 days, conjunctival blanching in 3/3 eyes between 1 hour and 7 days, pannus in 3/3 eyes between 7 and 21 days, vascularization of the corneal surface in 2/3 eyes between 14 and 21 days, and granulation scar tissue with neovascularization in 1/3 eyes at 14 days.

TABLE 3. Incidence of Positive Ocular Effects in Treated (100%) Washed Eyes (Group II)

Observations	Number "Positive"/Number Tested									
	Hr	Days								
	1	1	2	3	4	7	14	21	28[b]	35
Corneal Opacity	---	2/3	3/3	3/3	3/3	3/3	2/3	2/3	1/2	1/2
Iritis	3/3	3/3	3/3	3/3	3/3	1/3	---	---	---	---
Conjunctivae										
Redness	1/3	1/3	---	2/3	2/3	2/3	1/3	---	---	---
Chemosis	3/3	3/3	---	1/3	1/3	1/3	1/3	---	---	---
Discharge[a]	---	1/3	---	1/3	---	1/3	---	---	---	---

--- No positive observations.
[a] Discharge is not included in evaluating a positive reaction; however, scores of ≥2 are reported.
[b] One rabbit died of pneumonia.

The incidence of positive ocular irritation for treated (10%) unwashed eyes (Group III) is summarized in Table 4. Irritation was most severe 2 days following instillation and included scattered or diffuse corneal opacity (score of 1) affecting up to 75% of the total area (scores of 1-3) in 2/3 eyes, iridial changes (scores of 1) in 3/3 eyes, slight to moderate conjunctival redness (scores of 1.5-2) in 3/3 eyes, very slight conjunctival chemosis (scores of 0.5-1.5) in 3/3 eyes, and very slight to slight conjunctival discharge (scores of 0.5-1) in 2/3 eyes. Corneal opacity subsided from both affected eyes by 7 days; iridial changes subsided from all eyes by 3 days; and positive conjunctival effects subsided from all eyes by 4 days. Additional effects observed during the study included peeling of the corneal epithelial in 3/3 eyes between 1 and 4 days, conjunctival blanching in 3/3

eyes between 1 hour and 1 day, and pannus in 1/3 eyes at 7 days.

TABLE 4. Incidence of Positive Ocular Effects in Treated (10%) Unwashed Eyes (Group III)

Observations	Number "Positive"/Number Tested						
	Hr	Days					
	1	1	2	3	4	7	14
Corneal Opacity	---	1/3	2/3	2/3	2/3	---	---
Iritis	1/3	3/3	3/3	---	---	---	---
Conjunctivae							
Redness	1/3	1/3	1/3	1/3	---	---	---
Chemosis	1/3	1/3	---	---	---	---	---
Discharge[a]	---	---	---	---	---	---	---

--- No positive observations.
[a] Discharge is not included in evaluating a positive reaction; however, scores of ≥2 are reported.

B. Deficiencies: Only three animals were used to evaluate the ocular irritancy of P7271 at full strength and without immediate rinsing. Although this does not fulfill guideline requirements, it is obvious from the data that the test material is corrosive to the eye and additional data are not required.

The following were not provided: individual observations (aside from ocular) for the entire day of dosing and daily thereafter; a signed and dated Quality Assurance statement; and the environmental conditions for the animals during the study. These deficiencies, however, are considered minor and should have no significant impact on the results of the study.

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DATA EVALUATION RECORD

STUDY TYPE: Primary Dermal Irritation - Rabbit
OPPTS Number: 870.2500 OPP Guideline Number: §81-5

DP BARCODE: D244072 SUBMISSION CODE:S538885
P.C. CODE: 000439
EPA REG. NO.: 003573-LO

TEST MATERIAL (PURITY): P7271 (% amine oxide not specified)

SYNONYMS: None specified

CITATION: Dean, W., and D. Jessup (1978) Primary skin irritation study in the albino rabbit. International Research and Development Corporation (location not specified). Laboratory Study Number 191-186. February 15, 1978. MRID 44434905. Unpublished.

SPONSOR: The Procter & Gamble Company, Cincinnati, OH.

EXECUTIVE SUMMARY: In a primary dermal irritation study (MRID 44434905), three young adult New Zealand White rabbits were dermally exposed to 0.4 mL of P7271 (% amine oxide not specified) for 24 hours (worst-case scenario). The test substance was applied as received to one intact and one abraded site per animal (approximately 4 cm^2/site). Animals were observed for dermal irritation 30 minutes and 48 hours following patch removal; irritation was scored by the Draize scale.

Thirty minutes following patch removal, well-defined to moderate/severe erythema and severe edema were observed at 3/3 intact sites and blanching was observed at 2/3 sites. Forty-eight hours following patch removal, well-defined to severe erythema and severe edema persisted at 3/3 sites, and blanching persisted at 2/3 sites. Additional observations were not conducted. Results following application to abraded skin were similar.

Based on the limited data obtained in this study, **P7271 appears to be a severe dermal irritant; however an accurate TOXICITY CATEGORY could not be assigned.**

Since 1) only three animals were used, 2) the exposure period was 24 hours, and 3) the observation period lasted only 48 hours following patch removal, this study does not satisfy the guideline requirement for a primary dermal irritation study in

the rabbit and is classified **unacceptable (§81-5)**. A new study, conducted under current guidelines, should be submitted.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided. This study, however, precedes GLP compliance and current Subdivision F guideline requirements. A signed and dated Quality Assurance statement was not provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Material: P7271
   Description: Clear viscous liquid
   Lot/Batch #: Not specified
   Composition: % Amine oxide not specified
   pH: Not specified
   CAS #: Not provided

2. Vehicle: None employed

3. Test animals: Species: Rabbit
   Strain: New Zealand White
   Age: Not specified (young adult, based on weight)
   Weight: 2.54-2.72 kg (combined sexes)
   Source: Kuiper's Rabbit Ranch, Gary, IN
   Acclimation period: 12 Days
   Diet: Purina Rabbit Chow, ad libitum
   Water: Tap water, ad libitum
   Housing: Individual
   Environmental conditions: Not specified

B. STUDY DESIGN and METHODS:

1. In-life dates: Between November 14, 1977 and February 15, 1978 (not further specified)

2. Animal assignment and treatment: Fur from the backs of three young adult New Zealand White rabbits (two male and one female) was clipped just prior to dermal administration with 0.4 mL of P7271. The test substance was applied as received to one intact and one abraded[1] site per animal using Parke-Davis Readi-Bandages (approximately 4 cm^2 each). The patches were secured with Elastoplast tape, and each animal was fitted with a collar. Following a 24-hour exposure

[1] Abrasion (using the clipper head) penetrated the stratum corneum, but did not cause bleeding.

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period (worst-case scenario), the coverings and collars were removed, and residual test material was removed from the skin with a damp cloth. The rabbits were observed for dermal irritation 24 and 72 hours following the initiation of exposure (30 minutes and 48 hours, respectively, following patch removal). Erythema and edema were scored separately using the Draize scale.

II. RESULTS AND DISCUSSION:

A. Clinical observations: Well-defined to moderate/severe erythema (scores of 2-3) and severe edema (scores of 4) were observed at 3/3 intact sites 30 minutes following patch removal (at 24 hours). Forty-eight hours following patch removal (at 72 hours), well-defined to severe erythema (scores of 2-4) and severe edema (scores of 4) persisted at 3/3 sites. Blanching was also observed at 2/3 sites after 24 and 72 hours. No additional observations were conducted. Based on the limited data obtained in this study, P7271 appears to be a severe dermal irritant.

Results from application to abraded skin were similar. Well-defined to moderate/severe erythema (scores of 2-3), severe edema (scores of 4), and blanching were observed at 3/3 abraded sites at 30 minutes. After 48 hours, well-defined to severe erythema (scores of 2-4), severe edema (scores of 4), and blanching persisted at 3/3 sites.

B. Deficiencies: The following major deficiencies were noted in this study:

- Only three animals were used
- The exposure period was 24 hours
- The observation period lasted only 48 hours following patch removal

In combination, these deficiencies prevent an accurate assessment of the dermal irritancy of P7271. As a result, this study does not fulfill guideline requirements and is deemed unacceptable. A new study, conducted under current guidelines, should be submitted. Please note that if the test compound is considered corrosive or has a pH of ≤ 2 or ≥ 11.5, the guideline may be waived.

In addition, the following were not provided: individual observations (aside from dermal) for the entire day of

dosing and daily thereafter; a signed and dated Quality Assurance statement; and the environmental conditions for the animals during the study. These deficiencies, however, are considered minor and should have no significant impact on the results of the study.

EPA Reviewer: Tim McMahon, Ph.D. _____
Antimicrobial Division (7510W)

EPA Work Assignment Manager: Tim McMahon _____
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DATA EVALUATION RECORD

STUDY TYPE: Dermal Sensitization - Guinea pig
OPPTS Number: 870.2600 OPP Guideline Number: §81-6

DP BARCODE: D244072 SUBMISSION CODE:S538885
P.C. CODE: 000439
EPA REG. NO.: 003573-LO

TEST MATERIAL (PURITY): P7270 and P7294 (% amine oxide in each test compound not specified)

SYNONYMS: None specified

CITATION: Wyatt, J., and M. Vinegar (1978) Delayed contact hypersensitivity studies in guinea pigs of P7270 and P7294. Hill Top - Toxicology, Miamiville, OH. Laboratory Study Number 77-986-21. January 25, 1978. MRID 44434906. Unpublished.

SPONSOR: The Procter & Gamble Company, Cincinnati, OH.

EXECUTIVE SUMMARY: In a dermal sensitization study (MRID 44434906) conducted with P7270 and P7294 (% amine oxide in each test compound not specified), 30 young adult Hartley albino guinea pigs per compound were tested using methods based on those derived by Buehler.

Twenty-four and 48 hours following the single challenge with 2% P7294 to previously-induced animals, slight patchy erythema was observed at 5/20 (average score of 0.125) and 4/20 sites (0.10), respectively. In comparison, 24 or 48 hours following challenge to controls, slight patchy erythema was observed at 1/10 sites (0.05). Based on the results of this study, **P7294 appears to be a very slight dermal sensitizer. This conclusion is in contrast with the study author's, who reported that challenge with P7294 produced no positive repsonses. Therefore, data from this portion of the study are equivocal.**

Twenty-four and 48 hours following the single challenge with 2% P7270 to previously-induced animals, slight patchy erythema was observed at 7/20 (0.175) and 2/20 sites (0.05), respectively. In comparison, 24 and 48 hours following challenge to controls, slight patchy erythema was observed at 2/10 (0.10) and 1/10 sites (0.05), respectively. Based on the results of this study, **P7270 does not appear to be a dermal sensitizer**; however, positive control data were not provided to validate the test methods and

species employed.

Since positive control data were not provided, this study does not satisfy the guideline requirement for a dermal sensitization study in the guinea pig and is classified **unacceptable (§81-6)**. The portion of this study conducted with P7270 may be upgraded to acceptable status if positive control data obtained within 6 months of the definitive study using the Buehler method are provided. Since equivocal results were obtained for the P7294 portion of this study, additional investigations may be required. It is recommended that the registrantconduct a new study with appropriately characterized test material.

COMPLIANCE: Signed and dated GLP and Data Confidentiality statements were provided. This study, however, precedes GLP compliance and current Subdivision F guideline requirements. A signed and dated Quality Assurance statement was not provided.

I. MATERIALS AND METHODS

A. MATERIALS:

1. Test Materials:

P7270
Description: Clear liquid
Lot/Batch #: Not specified
Purity: % Amine oxide not specified
CAS #: Not provided

P7294
Description: Clear gel
Lot/Batch #: Not specified
Purity: % Amine oxide not specified
CAS #: Not provided

P7294 (10% solution)
Description: Slightly foamy clear liquid
Lot/Batch #: Not specified
Purity: % Amine oxide not specified
CAS #: Not provided

P7294 (25% solution)
Description: Slightly foamy clear liquid
Lot/Batch #: Not specified
Purity: % Amine oxide not specified
CAS #: Not provided

P7294 (50% solution)
Description: Slightly foamy clear liquid
Lot/Batch #: Not specified

Purity: % Amine oxide not specified
CAS #: Not provided

2. Vehicle and positive control: Distilled water was used to dilute the test compounds in the laboratory; however, the solvent used in the original dilutions (sent from the sponsor) was not specified.

Positive control data were not generated or provided.

3. Test animals: Species: Guinea pig
Strain: Hartley albino
Age: Not specified
Weight: Not specified
Source: Williams Kentucky Cavies (P7294) or Sweetwater Farm, Inc. (P7270)
Acclimation period: ≥4 Days
Diet: Purina Guinea Pig Chow, ad libitum
Water: During acclimation: medicated water containing 4% sulfaethoxypyridazine; thereafter, tap water, ad libitum
Housing: Individual
Environmental conditions: Not specified
Temperature: 22 ± 2°C
Humidity: Approximately 50%
Air changes: Approximately 10/Hour
Photoperiod: 12-Hour light/dark cycle

B. STUDY DESIGN and METHODS:

1. In-life dates: Between November 4, 1977 and January 25, 1978 (not further specified)

2. Animal assignment and treatment: The study was conducted using methods derived by Buehler [Buehler, E., Arch. Dermatol., 91:171-175 (1965)]. To determine the highest non-irritating concentration, supplemental experiments were conducted concurrently with the definitive induction phase. Sixteen animals received 0.4 mL applications of either P7294 or P7270 at 100% or at 1, 2, 5, 10, 25, or 50% dilutions in distilled water (when diluted in the laboratory). Based on the results, the challenge portions of the definitive experiment were conducted with 2% of each test compound.

Treatment groups consisted of 30 animals per compound (20 test and ten control). For the P7270 study, 15 animals/sex were used and for the P7294 study, 6 males and 24 females were used.

For the induction phase, fur on the backs of 20 Hartley albino guinea pigs was clipped 1 day prior to dermal administration with 0.4 g of P7294 (100%) or 0.4 mL of P7270 (100%). A Parke-Davis Readi Bandage coverlet with a 20- x 20-mm Webril swatch moistened with appropriate test compound was placed on the upper left quandrant of the animal. The guinea pigs were then placed in restrainers and rubber dental dam was placed over each animal's back and secured to the restrainer with clips. Following a 6-hour exposure period, the coverings were removed, and the animals were returned to their cages; removal of residual test material was not described. Application of the test materials was repeated once weekly (at unspecified intervals) for 2 consecutive weeks (three total applications).

Two weeks following the final induction treatment, all test and control animals received a single challenge exposure with 0.4 mL of 2% P7294 or 2% P7270. Application was to the untreated lower left quadrant as previously described. Animals from the P7294 group, however, were left in the restrainers for 8.75 hours instead of 6 hours. Approximately 3 to 5 hours prior to the first challenge reading, all sites were depilated with Neet. The guinea pigs were observed for dermal irritation 24 and 48 hours following the challenge treatment. Skin reactions were scored according to the following scale:

0 - No reaction
± - Slight patchy erythema
1 - Slight confluent or moderate patchy erythema
2 - Moderate erythema
3 - Severe erythema, with or without edema

II. RESULTS AND DISCUSSION:

A. Induction reactions and duration: Induction reactions were not recorded.

B. Challenge reactions and duration: Twenty-four and 48 hours following the single challenge with 2% P7294 to previously-induced animals, slight patchy erythema (scores of ±) was observed at 5/20 and 4/20 sites, respectively. This correspondes to average values

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(assuming ± = 0.5) of 0.125 and 0.10, respectively. In comparison, 24 or 48 hours following challenge to controls, slight patchy erythema was observed at 1/10 sites, which correspondes to averages of 0.05. Based on the results of this study, P7294 appears to be a very slight dermal sensitizer. This conclusion is in contrast with the study author's, who reported that challenge with P7294 produced no positive repsonses. Therefore, data from this portion of the study are equivocal.

Twenty-four and 48 hours following the single challenge with 2% P7270 to previously-induced animals, slight patchy erythema (scores of ±) was observed at 7/20 and 2/20 sites, respectively. This correspondes to average values of 0.175 and 0.05, respectively. In comparison, 24 and 48 hours following challenge to controls, slight patchy erythema was observed at 2/10 and 1/10 sites, respectively, which correspondes to averages of 0.10 and 0.05, respectively. Based on the results of this study, P7270 does not appear to be a dermal sensitizer.

C. Positive control: No data were generated.

D. Deficiencies: Since positive control data were not generated or provided, the methods and species employed in this study were not validated. As a result, this study does not fulfill guideline requirements and is classified **unacceptable**. The portion of this study conducted with P7270 may be upgraded to acceptable status if positive control data obtained within 6 months of the definitive study using the Buehler method are provided. Since equivocal results were obtained for the P7294 portion of this study, additional investigations may be required. It is recommended that the registrantconduct a new study with appropriately characterized test material.

In addition to the above, the following data were not provided: dermal irritation during the induction phase of the experiment; individual clincal observations and body weights; a signed and dated Quality Assurance statement; and the environmental conditions for the animals during the study. These deficiencies, however, are considered minor and should have no significant impact on the results of the study.