psl product safety labs
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PRODUCT

Lot #22L-2

STUDY TITLE

Primary Eye Irritation

DATA REQUIREMENT

40 CFR 158, Guideline #81-4

AUTHOR

Gary Wnorowski, B.A.

STUDY COMPLETED ON

November 3, 1995

PERFORMING LABORATORY

Product Safety Labs
725 Cranbury Road
East Brunswick, New Jersey 08816

LABORATORY PROJECT IDENTIFICATION NUMBER

3871

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Exhibit
2791
State of Minnesota v. 3M Co.,
Court File No. 27-CV-10-28862

3M_MN01062303

2791.0001

STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA 10 (d) (1) (A), (B) or (C).

GOOD LABORATORY PRACTICE STATEMENT

Lot #22L-2

This study meets the requirements of 40 CFR Part 160 with the following exception: The stability, characterization, identity and verification of the test substance concentration as received and tested are the responsibility of the study sponsor.

Study Director:

Gary Wnorowski, B.A.

Nov 3, 1995
Date

Submitter:

1-16-96
Date

Sponsor:

1-16-96
Date

TABLE OF CONTENTS

PRIMARY EYE IRRITATION

PROTOCOL NO.:	P324
AGENCY:	[EPA (FIFRA)]
STUDY NUMBER:	
SPONSOR:	
PRODUCT IDENTIFICATION:	Lot #22L-2
PRODUCT DESCRIPTION:	Light yellow powder
DATE RECEIVED:	June 30, 1995
PSL REFERENCE NO.:	E50630-1R
SPONSOR REFERENCE NO.:	GP95-046
DATE OF PROTOCOL APPROVAL:	July 24, 1995
DATES OF TEST:	July 27 - August 17, 1995
NOTEBOOK NO.:	95-29; pages 217-228

1. PURPOSE:

To provide information on health hazards likely to arise from a single instillation of Lot #22L-2 into the eyes of rabbits. Data from this study may be used as a basis for classification and labeling.

2. SUMMARY:

A Primary Eye Irritation test was conducted with rabbits to determine the potential for Lot #22L-2 to produce irritation and/or corrosion via the ocular route. Based on the results of testing, the test substance is classified as severely irritating to the eye. The classification was raised from moderately to severely irritating due to the presence of a score greater than 30 in all rabbits at the 24 hour evaluation interval (See Table 3).

One-tenth of a gram of the test substance was instilled into the right eye of six healthy rabbits. The left eye remained untreated and served as a control. Ocular irritation was

evaluated by the method of Draize *et al*[1]. The eye scores were further classified by the system of Kay and Calandra (modified)[2].

One hour after test substance instillation, all treated eyes exhibited conjunctival irritation. From 24 to 72 hours corneal opacity and iritis were also evident in all 6 animals. The incidence and severity of corneal opacity and iritis decreased thereafter. Conjunctivitis persisted in all treated eyes through day 10. Pannus was noted in 2 animals between days 7 through 21. Although conjunctivitis and/or corneal opacity persisted in two rabbits through study termination, all other animals were free from ocular irritation by day 21.

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[1] Draize JH, Woodward G, and Calvery HO. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J Pharmacol Exp Ther* 1944; 82:377-390.

[2] Maximum Mean Total Score - Kay JH, and Calandra JC. Interpretation of eye irritation tests. *J Soc Cos Chem* 1962; 13:281-289. See Table 3 for the classification system.

The incidence, severity and reversibility of irritation are detailed below:

Time Post Instillation	Incidence of Irritation		
	Corneal Opacity	Iritis	Conjunctivitis
1 hour	0/6	0/6	6/6
24 hours	6/6	6/6	6/6
48 hours	6/6	6/6	6/6
72 hours	6/6	6/6	6/6
Day 4	4/6	4/6	6/6
Day 7	3/6	1/6	6/6
Day 10	3/6	1/6	6/6
Day 14	3/6	0/6	3/6
Day 17	3/6	0/6	2/6
Day 21	2/6	0/6	1/6

Time Post Instillation	Severity of Irritation: Maximum Mean Total Score (MMTS[1])
1 hour	15.0
24 hours	39.5
48 hours	35.2
72 hours	33.5
Day 4	24.3
Day 7	18.2
Day 10	12.0
Day 14	7.8
Day 17	5.2
Day 21	2.8

[1] Maximum Mean Total Score - Kay JH, and Calandra JC. Interpretation of eye irritation tests. *J Soc Cos Chem* 1962; 13:281-289. See Table 3 for the classification system.

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Lot #22L-2

PRIMARY EYE IRRITATION

We the undersigned declare that the methods, results and data contained in this report faithfully reflect the procedures and raw data used or collected during the study.

Gary Wnorowski, B.A.
Study Director — Nov 3, 1995 — Date

Ralph Shapiro, Ph.D.
Laboratory Director — November 3, 1995 — Date

Jacek Ochalski, D.V.M.
Principal Toxicology Technician — Oct. 30, 1995 — Date

Jasbir Bawa, B.S.
Assistant Toxicology Technician — Oct 30, 1995 — Date

Kenneth Barr
Assistant Toxicology Technician — October 30, 1995 — Date

3. MATERIALS:

A. Test Substance:

The test substance identified as , Lot #22L-2 was received on June 30, 1995 and was further identified with PSL Code Number E50630-1R. The test substance was a light yellow powder and was stored at room temperature. The sample was instilled as received. Documentation of the methods of synthesis, fabrication, or derivation of the test substance is retained by the sponsor.

Characterization of the test substance as provided to Product Safety Labs by the sponsor was (See Appendix B):

Composition: - 93.3%
Related compounds - 4.3%

pH: Not applicable

Solubility: Soluble in acetone, ethanol and methanol

Stability: Stable

Expiration Date: June 28, 1997

B. Animals:

3.B.1 **Number of Animals:** 6

3.B.2 **Sex:** 3 males and 3 females

3.B.3 **Species/Strain:** Rabbit/New Zealand albino

3.B.4 **Age:** Adult

3.B.5 **Source:** Received from Davidson's Mill Farm, South Brunswick, NJ on June 30, July 7 and 14, 1995

4. METHODS:

A. Husbandry:

4.A.1 **Housing:** The animals were singly housed in suspended stainless steel caging with mesh floors which conform to the size recommendations in the Guide for the Care and Use of Laboratory Animals DHEW (NIH) No. 86.23. Litter paper was placed beneath the cage and was changed at least three times per week.

4.A.2 **Animal Room Temperature Range:** 67-71°F

180

4.A.3 Photoperiod: 12 hour light/dark cycle

4.A.4 Acclimation Period: 13, 20 or 27 days

4.A.5 Food: Pelleted Purina Rabbit Chow #5326

4.A.6 Water: Filtered tap water was supplied *ad libitum* by automatic water dispensing system.

4.A.7 Contaminants: There were no known contaminants reasonably expected to be found in the food or water which interfered with the results of this study. Results of the analysis of the food and water are kept on file at Product Safety Labs. The dates of the most recent analyses are presented in Appendix A.

B. Identification:

4.B.1 Cage: Each cage was identified with a cage card indicating at least the study number and identification and sex of the animals.

4.B.2 Animal: A number was allocated to each rabbit on receipt and a stainless steel ear tag bearing this number was attached to the animal. This number, together with the sequential animal number assigned to study 3871, constituted unique identification.

5. PROCEDURE:

A. Preparation and Selection of Animals:

Prior to instillation, both eyes of a number of animals were examined using a fluorescein dye procedure. One drop of 2% ophthalmic fluorescein sodium was instilled into both eyes of each rabbit. The eyes were irrigated with physiological saline (0.9% NaCl) approximately 30 seconds after instillation of the fluorescein. Using a Blak-Ray Lamp (compact 4 watt UV Lamp), the eyes were checked for gross abnormalities according to the "Scale for Scoring Ocular Lesions" (Table 2). Only healthy animals without pre-existing ocular irritation were selected for test.

B. Instillation:

One-tenth of a gram of the test substance was instilled into the conjunctival sac of the right eye of each rabbit by pulling the lower lid away from the eyeball. The upper and lower lids were then gently held together for about 1 second before releasing, to prevent loss of the test substance. The other eye of each rabbit remained untreated with the test substance and served as a control. Elizabethan collars were placed on each rabbit and they were returned to their designated cages.

C. **Ocular Scoring:**

Ocular irritation was evaluated using a high-intensity white light (Mag Lite) in accordance with Draize *et al.* (Table 2)[1] at 1, 24, 48 and 72 hours and 4, 7, 10, 14, 17 and 21 days post-instillation. Twenty-four hours after instillation, the collars were removed. The fluorescein dye evaluation procedure described in Section 5.A was used at 24 hours and as needed to evaluate the extent of corneal damage or to verify reversal of effects. Individual scores were recorded for each animal. In addition to the observation of the cornea, iris and conjunctivae, any other observed lesions were noted. The average score for all rabbits at each scoring period was calculated to aid in data interpretation.

D. **Classification of Eye Scores:**

The average 24-hour score (MMTS) of the rabbits was determined to further classify the test substance by the system of Kay and Calandra (Table 3)[2].

E. **Cage-Side Observations:**

The animals were observed for signs of gross toxicity, behavioral changes and mortality at least once daily during the test period. Observations included gross evaluation of skin and fur, eyes and mucous membranes, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern. Particular attention was directed to observation of tremors, convulsions, salivation, diarrhea and coma.

6. STUDY CONDUCT:

This study was conducted at Product Safety Labs, 725 Cranbury Road, East Brunswick, New Jersey 08816 to comply with Good Laboratory Practices as defined in 40 CFR 160: U.S. EPA Good Laboratory Practice Standards: Pesticide Programs (FIFRA) and in accordance with Pesticide Assessment Guidelines, Subdivision F: Hazard Evaluation: Human and Domestic Animals, Section 81-4.

7. QUALITY ASSURANCE:

The draft final report was audited for agreement with the raw data records and for compliance with the protocol, Product Safety Labs Standard Operating Procedures and appropriate Good Laboratory Practice Standards. Dates of inspections and audits performed during the study, and the dates of reporting of the inspection and audit findings to the Study Director and Facility Management are presented in the Quality Assurance Statement.

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[1] Draize JH, Woodward G, and Calvery HO. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J Pharmacol Exp Ther* 1944; 82:377-390.

[2] Kay JH, and Calandra JC. Interpretation of eye irritation tests. *J Soc Cos Chem* 1962; 13:281-289.

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8. **DEVIATIONS FROM FINAL PROTOCOL:** None

9. **RECORDS TO BE MAINTAINED:**

A copy of this signed report, together with the protocol and all raw data generated at Product Safety Labs, is retained in the Product Safety Labs Archives.

10. **RESULTS:**

All animals appeared active and healthy. Apart from the eye irritation noted below, there were no signs of gross toxicity, adverse pharmacologic effects or abnormal behavior.

One hour after test substance instillation, all treated eyes exhibited conjunctival irritation. From 24 to 72 hours corneal opacity and iritis were also evident in all 6 animals. The incidence and severity of corneal opacity and iritis decreased thereafter. Conjunctivitis persisted in all treated eyes through day 10. Pannus was noted in 2 animals between days 7 through 21. Although conjunctivitis and/or corneal opacity persisted in two rabbits through study termination, all other animals were free from ocular irritation by day 21.

The 24 hour Maximum Mean Total Score of , Lot #22L-2 is 39.5.

A. **Individual Scores for Ocular Irritation:** See Table 1

B. **Scale for Scoring Ocular Lesions:** See Table 2

C. **Classification of Eye Irritation Scores:** See Table 3

11. **CONCLUSION:**

Based on the scoring system used, Lot #22L-2 is classified as severely irritating to the eye when instilled as received. The classification was raised from moderately to severely irritating due to the presence of a score greater than 30 in all rabbits at the 24 hour evaluation interval (See Table 3).

TABLE - 1

INDIVIDUAL SCORES FOR OCULAR IRRITATION

	Rabbit No. 8191									
	Hours				Days					
	1	24	48	72	4	7	10	14	17	21
I. Cornea										
A. Opacity	0	1[1]	1[1]	1[1]	1[1]	0[1]	0	0	0	0
B. Area	4	4	3	3	2	4	4	4	4	4
(AxB)x5	0	20	15	15	10	0	0	0	0	0
II. Iris										
A. Values	0	1	1	1	1	0	0	0	0	0
Ax5	0	5	5	5	5	0	0	0	0	0
III. Conjunctivae										
A. Hyperemia	3	3	3	3	2	0	0	0	0	0
B. Chemosis	2	3	3	3	2	0	0	0	0	0
C. Discharge	3	3	3	3	3	1	1	0	0	0
(A+B+C)x2	16	18	18	18	14	2	2	0	0	0
Total	16	43	38	38	29	2	2	0	0	0

[1] 2% fluorescein sodium used to evaluate the extent of corneal opacity.

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TABLE - 1 (cont.)

INDIVIDUAL SCORES FOR OCULAR IRRITATION

	Rabbit No. 8192									
	Hours				Days					
	1	24	48	72	4	7	10	14	17	21
I. Cornea										
A. Opacity	0	1[1]	1[1]	1[1]	0[1]	0	0	0	0	0
B. Area	4	2	1	1	4	4	4	4	4	4
(AxB)x5	0	10	5	5	0	0	0	0	0	0
II. Iris										
A. Values	0	1	1	1	0	0	0	0	0	0
Ax5	0	5	5	5	0	0	0	0	0	0
III. Conjunctivae										
A. Hyperemia	3	3	3	3	2	0	0	0	0	0
B. Chemosis	2	3	3	3	2	1	0	0	0	0
C. Discharge	3	3	3	3	3	1	1	0	0	0
(A+B+C)x2	16	18	18	18	14	4	2	0	0	0
Total	16	33	28	28	14	4	2	0	0	0

[1] 2% fluorescein sodium used to evaluate the extent of corneal opacity.

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TABLE - 1 (cont.)

INDIVIDUAL SCORES FOR OCULAR IRRITATION

	Rabbit No. 8193									
	Hours				Days					
	1	24	48	72	4	7	10	14	17	21
I. Cornea										
A. Opacity	0	1[1]	1[1]	1[1]	1[1]	2[1]	1[1]	1[1]	1[1]	0[1]
B. Area	4	3	3	2	1	1	1	1	1	4
(AxB)x5	0	15	15	10	5	5	5	5	5	0
II. Iris										
A. Values	0	1	1	1	1	0	0	0	0	0
Ax5	0	5	5	5	5	0	0	0	0	0
III. Conjunctivae										
A. Hyperemia	2	3	3	3	3	2	2	0	0	0
B. Chemosis	2	3	3	3	3	0	2	1	0	0
C. Discharge	2	3	3	3	3	2	1	0	0	0
(A+B+C)x2	12	18	18	18	18	14	10	2	0	0
Total	12	38	38	33	28	24	15	7	5	0

[1] 2% fluorescein sodium used to evaluate the extent of corneal opacity.

TABLE - 1 (cont.)

INDIVIDUAL SCORES FOR OCULAR IRRITATION

	Rabbit No. 8194									
	Hours				Days					
	1	24	48	72	4	7	10	14	17	21
I. Cornea										
A. Opacity	0	1[1]	1[1]	1[1]	0[1]	0	0	0	0	0
B. Area	4	2	1	1	4	4	4	4	4	4
(AxB)x5	0	10	5	5	0	0	0	0	0	0
II. Iris										
A. Values	0	1	1	1	0	0	0	0	0	0
Ax5	0	5	5	5	0	0	0	0	0	0
III. Conjunctivae										
A. Hyperemia	3	3	3	3	1	0	0	0	0	0
B. Chemosis	2	3	2	2	1	0	0	0	0	0
C. Discharge	3	3	3	3	3	1	1	0	0	0
(A+B+C)x2	16	18	16	16	10	2	2	0	0	0
Total	16	33	26	26	10	2	2	0	0	0

[1] 2% fluorescein sodium used to evaluate the extent of corneal opacity.

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TABLE - 1 (cont.)

INDIVIDUAL SCORES FOR OCULAR IRRITATION

	Rabbit No. 8195									
	Hours				Days					
	1	24	48	72	4	7	10	14	17	21
I. Cornea										
A. Opacity	0	1[1]	1[1]	1[1]	1[1]	2[1]	2[1]	2[1,2]	2[1,2]	2[1,2]
B. Area	4	4	3	3	3	3	2	2	1	1
(AxB)x5	0	20	15	15	15	30	20	20	10	10
II. Iris										
A. Values	0	1	1	1	1	1	1	0	0	0
Ax5	0	5	5	5	5	5	5	0	0	0
III. Conjunctivae										
A. Hyperemia	3	3	3	3	3	2	2	1	1	0
B. Chemosis	2	4	3	3	3	3	2	2	1	1
C. Discharge	3	3	3	3	3	2	1	1	0	0
(A+B+C)x2	16	20	18	18	18	14	10	8	4	2
Total	16	45	38	38	38	49	35	28	14	12

[1] 2% fluorescein sodium used to evaluate the extent of corneal opacity.

[2] Pannus present.

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TABLE - 1 (cont.)

INDIVIDUAL SCORES FOR OCULAR IRRITATION

	Rabbit No. 8196									
	Hours				Days					
	1	24	48	72	4	7	10	14	17	21
I. Cornea										
A. Opacity	0	1[1]	1[1]	1[1]	1[1]	2[1,2]	2[1,2]	2[1]	2[1]	1[1,3]
B. Area	4	4	4	3	2	2	1	1	1	1
(AxB)x5	0	20	20	15	10	20	10	10	10	5
II. Iris										
A. Values	0	1	1	1	1	0	0	0	0	0
Ax5	0	5	5	5	5	0	0	0	0	0
III. Conjunctivae										
A. Hyperemia	2	3	3	3	3	2	1	0	0	0
B. Chemosis	2	4	3	3	2	1	1	1	1	0
C. Discharge	3	3	3	3	1	1	1	0	0	0
(A+B+C)x2	14	20	18	18	12	8	6	2	2	0
Total	14	45	43	38	27	28	16	12	12	5

[1] 2% fluorescein sodium used to evaluate the extent of corneal opacity.

[2] Pannus present.

[3] Corneal opacity score determined using white light source.

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TABLE - 2

SCALE FOR SCORING OCULAR LESIONS[1]

1. Cornea
   A. Opacity-degree of density (area most dense taken for reading)
      No Opacity 0
      Scattered or diffuse area, details of iris clearly visible 1
      Easily discernible translucent areas, details of iris slightly obscured 2
      Opalescent areas, no details of iris visible, size of pupil barely discernible 3
      Opaque, iris invisible 4

   B. Area of cornea involved
      One quarter (or less) but not zero 1
      Greater than one quarter, but less than half 2
      Greater than half, but less than three quarters 3
      Greater than three quarters, up to whole area 4

   A X B X 5 Total Maximum = 80

2. Iris
   A Values
      Normal 0
      Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive) 1
      No reaction to light, hemorrhage, gross destruction (any or all of these) 2

   A X 5 Total Maximum = 10

3. Conjunctivae
   A. Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)
      Vessels normal 0
      Vessels definitely injected above normal 1
      More diffuse, deeper crimson red, individual vessels not easily discernible 2
      Diffuse beefy red 3

   B. Chemosis
      No swelling 0
      Any swelling above normal (includes nictitating membrane) 1
      Obvious swelling with partial eversion of lids 2
      Swelling with lids about half-closed 3
      Swelling with lids about half-closed to completely closed 4

   C. Discharge
      No discharge 0
      Any amount different from normal (does not include small amounts observed in inner canthus of normal animals) 1
      Discharge with moistening of the lids and hairs just adjacent to lids 2
      Discharge with moistening of the lids and hairs, and considerable area around the eye 3

   Score (A + B + C) X 2 Total Maximum = 20

Total Maximum Score: 110 represents the sum of all scores obtained for the cornea, iris and conjunctivae.

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[1] Draize JH, Woodward G, and Calvery HO. Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. *J Pharmacol Exp Ther* 1944; 82:377-390.

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TABLE - 3

CLASSIFICATION OF EYE IRRITATION SCORES

MMTS[1]	Classification[2]	Symbol
0.0 - 0.5	Non-irritating	N
0.6 - 2.5	Practically non-irritating	PN
2.6 - 15.0	Minimally irritating	M_1
15.1 - 25.0	Mildly irritating	M_2
25.1 - 50.0	Moderately irritating	M_3
50.1 - 80.0	Severely irritating	S
80.1 - 100.0	Extremely irritating	E
100.1 - 110.0	Maximally irritating	M_x

[1] Maximum Mean Total Score - Kay JH, and Calandra JC. Interpretation of eye irritation tests. *J Soc Cos Chem* 1962; 13:281-289.

[2] If more than 40% of the rabbits tested had total scores >10 or an individual rabbit scored >30, the preliminary classification is raised to the next highest level.

APPENDIX A

Animal feed analysis independently performed on October 7, 1994 for presence of chlorinated insecticides:

Aldrin	DDE
Dieldrin	DDD
Heptachlor	DDT
Heptachlor Epoxide	Endosulfan I & II
Chlordane	Endrin
Methoxychlor	Endrin aldehyde
alpha, beta, delta & gamma BHC	Toxaphene
	Endosulfan Sulfate

and for the presence of organophosphate insecticides:

Malathion	Ethyl Parathion
Methyl Parathion	Ethion
Diazinon	Parathion

LABORATORY: INDUSTRIAL LABORATORIES
1450 East 62nd Street
Denver, CO 80216

STUDY NUMBERS: IL94107971, IL94107972 and IL94107973

Water analysis performed on October 21, 1994 for NJDEPE Safe Drinking Water Act parameters and percent fluoride content.

LABORATORY: NEW JERSEY LABORATORIES
DEPE #12660
A.A. Labs Division
222 Easton Avenue
New Brunswick, NJ 08901

SAMPLE ID: 23119-1

Results of feed and water analysis for possible contaminants: Acceptable; none detected or within regulatory standards.

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APPENDIX B

Chemical Services: Analytical

CERTIFICATE OF ANALYSIS

ES0630-12

ARTICLE IDENTIFICATION

Article Name:

Manufacturer: 3M

Origin of Production: Commercial ____; Pilot Plant ____; Laboratory __X__;

Technical Product __X__; Formulation of Technical Product ____; Analytical Standard ____;

Laboratory Project ID No.: P95-021 Batch No.: 22L-2

PHYSICAL PROPERTIES

Liquid ____; Solid __waxy__; Color: __light yellow__

Recommended Storage Conditions:

Ambient Temperature: __X__
In refrigerator: ____
In deep freezer: ____
Additional Comments: __none__

Expiration Date: 6/28/1997

This article is stable at least __2__ years from date of analysis when stored at recommended conditions.

ARTICLE INGREDIENT IDENTIFICATION

Common Name.

CAS No.: Not available

Structural formula:

Molecular Weight:

Identity by means of:

Chromatographic Retention Time __X__; IR ____; UV ____; MS ____; Other Methods: ____

ANALYTICAL DATA

Content of Active Ingredient/Impurities:

= 93.297 %
Related compounds = 4.290 %
Fluoride ion = 0.036%

Analytical Method Nos.:

TM-1128. by IC
TM-1140, Fluoride by ISE

Date of Analysis:

6/28/95

GLP - COMPLIANCE

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QUALITY ASSURANCE INSPECTIONS

Intervals for QA inspections are randomly selected prior to study initiation by the Quality Assurance Unit. Records of the findings of these inspections are kept on file. The summary below provides verification of statements made in the final report section which addresses Quality Assurance audits.

Inspections were made of:

DATE	PROCEDURE INSPECTED
7/27/95	Test substance preparation
7/27/95	Initiation of dosing
10/2/95	Raw data
10/2/95	Draft report
10/30/95	Final report

Findings reported to: Study Director 7/28, 10/2/95

Management 7/28, 10/30/95

Frank Fielder, B.S.
Quality Assurance Supervisor