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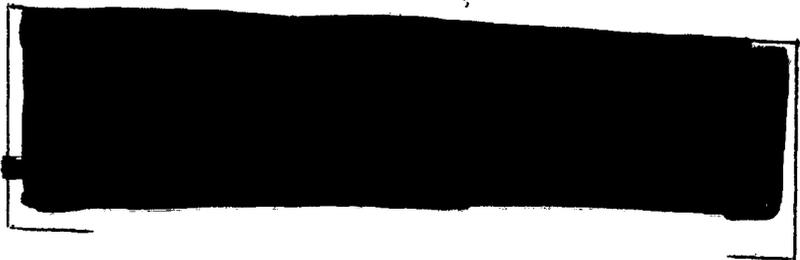
Attn: Section 8(e) Coordinator (CAP Agreement)

Re: Submission of a study pursuant to TSCA Section 8(e) Compliance Audit Program and the CAP Agreement.

Regulatee:



Submitted by:



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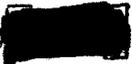
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Composition of Test Material in Toxigenics Study 410-1343

| <u>Chemical</u> | <u>CAS #</u> |
|----------------------------------|--------------|
| Sodium Tripolyphosphate | 7758-29-4 |
| Sodium Carbonate | 497-19-8 |
| Sodium Chloride | 7647-14-5 |
| Potassium Chloride | 7447-40-7 |
| Sodium Dodecyl Benzene Sulfonate | 25155-30-0 |
| Mineral Oil | 8012-95-1 |
| Sodium Dichloroisocyanurate | 51580-86-0 |



Report Title: Acute Oral LD₅₀ Study in Rats using 

Study Summary

The test material was administered by oral gavage to groups of 10 albino rats at the following doses (in Mg/Kg) 1,778, 1,996, 2,239, 2,512 and 2,818.

Prolonged and intermittent lethargy and ataxia were observed in individual surviving animals throughout the 14 day observation period. These observations appear to be consistent with the guidance provided in the TSCA 8(e) Reporting Guide, Acute Toxicity Tests with Non-Lethal Neurobehavioral Findings (pp 31-34).



Document Control Number
OTS0559878 (88-920008813S) (8EHQ-0292-10519S)

TOXIGENICS' STUDY 410-1343

ACUTE ORAL LD₅₀ STUDY IN RATS USING
83-52A

SUBMITTED TO:



SUBMITTED BY:

TOXIGENICS, INC.
1800 EAST PERSHING ROAD
DECATUR, IL 62526

NOVEMBER 30, 1983

TABLE OF CONTENTS

| <u>SECTION</u> | <u>PAGE</u> |
|-----------------------|-------------|
| I. Summary..... | 1 |
| II. Introduction..... | 3 |
| III. Personnel..... | 3 |
| IV. Procedures..... | 4 |
| V. Results..... | 10 |

LIST OF TABLES AND FIGURES

| | |
|---|----|
| Table 1: Summary of Main Study Results - Males..... | 13 |
| Table 2: Summary of Main Study Results - Females..... | 15 |
| Table 3: Litchfield-Wilcoxon LD ₅₀ Determination: Males... | 17 |
| Table 4: Litchfield-Wilcoxon LD ₅₀ Determination: Females. | 18 |
| Figure 1: Dose-Response Curve: Males..... | 19 |
| Figure 2: Dose-Response Curve: Females..... | 20 |

LIST OF APPENDICES

APPENDIX

| | |
|---|-----|
| A. Individual Range-Finding Data | A-1 |
| B. Individual Main Study Body Weight and Test Article Administration Data | B-1 |
| C. Individual Main Study Abnormal Clinical Sign Data | C-1 |
| D. Individual Main Study Mortality and Gross Necropsy Data | D-1 |

I. Summary

The test article, 83-52A, was administered by oral gavage to groups of albino rats to determine the oral LD₅₀ values. The methodology described in the EPA/OPP Guidelines (1982) was used.

The oral LD₅₀ values of the test article were determined to be 2,389 mg/kg of body weight for males and 1,992 mg/kg of body weight for females. The 95% confidence intervals were within 14.2% of the LD₅₀ value for males and within 16.8% of the LD₅₀ value for females.

The following mortalities were observed during main study:

| | Main Study Dose Level (mg/kg) | | | | |
|----------|-------------------------------|--------------|--------------|--------------|--------------|
| | <u>1,778</u> | <u>1,995</u> | <u>2,239</u> | <u>2,512</u> | <u>2,818</u> |
| Males: | 1/5 | 0/5 | 2/5 | 2/5 | 5/5 |
| Females: | 2/5 | 2/5 | 3/5 | 5/5 | |

Main study deaths were observed on days 1, 2, or 3 following dosing except for 3 animals that were found dead on days 9 or 11. Range-finding animals dosed at 2,818 or 5,012 mg/kg were found dead on the day of dosing or on day 1, and range-finding animals dosed at 501, 891, or 1,585 mg/kg survived a 14-day observation period.

Body weight gains were observed for 8 surviving main study animals, and body weight losses or no weight gains were observed on days 7 and/or 14 for 15 surviving main study animals.

Lethargy was observed for all animals and ataxia was observed for all but 2 animals after dosing on day 0. Lethargy and ataxia were observed as late as days 8, 10, or 11 for 3 main study animals found dead and as late as day 14 for one surviving

main study animal. Other abnormal clinical signs observed during the study included: prostration; irregular breathing; salivation; squinting; lacrimation; crusty eyes, nose, and muzzle; piloerection; red stained or yellow/brown stained fur; loose and no stools; abdomen swollen; body cool to touch; emaciation; and moribund. These abnormal clinical signs were observed as early as day 0 and as late as days 8, 10, or 14 for 4 main study animals.

Abnormal necropsy findings were observed for all main study animals except for 6 main study males dosed at either 1,778, 1,995, or 2,512 mg/kg. Abnormalities observed for these animals included: thickened or sloughing stomach mucosa; depressions or discolorations of stomachs; severe dilation or watery contents of stomachs; a projecting mass on one stomach and possible perforation of the wall of one other stomach; discoloration of the small intestine or lung; abnormal fluid in the abdominal cavity or urinary bladder; nodular discolorations on one uterus; an enlarged spleen; exudate in the ocular, nasal, and pelvic regions; and stained fur in the perianal region. No other abnormalities were observed during necropsy of all main study animals.

Report prepared by:

Blair Wingard
Blair Wingard, B.S.

11/30/83
Date

Study Director:

T. Bradford Barnes
T. Bradford Barnes, Ph.D.

11/30/83
Date

ToxiGenics

A Subsidiary of Whittaker Corporation

All work relating to this study was done in conformity with the FDA - Good Laboratory Practice Regulations (21 CFR 58). The study was inspected by a Quality Assurance Specialist on the dates shown below. Management, including the Study Director, was informed of the results of the inspections on the dates shown. The data in the report were compared with the raw data and are in agreement. The report and study file were examined to assure that any problems found during the Quality Assurance audits were corrected, and if necessary, their effect on the study documented.

Phase Inspection: conducted October 13, 1983.

Final Data and Report Audit: conducted November 21, 22, and 23, 1983, reported to Management, including the Study Director, November 28, 1983.

Donald G. MacKellar 12/2/83
Donald G. MacKellar, B.A. Date
Director, Quality Assurance and
Regulatory Affairs

All raw data relating to this study will be stored at ToxiGenics, Inc. Storage will conform to EPA and FDA regulations as per ToxiGenics' SOP's and may include volume reduction by conversion to certified microform.

Date of Report: November 30, 1983

II. Introduction

The following study was conducted using rats to determine the acute oral LD₅₀ of 83-52A using the methodology described in the EPA/OPP Guidelines, 1982. The study was performed at ToxiGenics, Inc., 1800 East Pershing Road, Decatur, IL 62526 from October 13, 1983 to November 8, 1983.

III. Personnel

The following were the Study Director, principal technician, and scientific personnel involved with the study:

Study Director: T. Bradford Barnes, Ph.D.

General Acute Supervisor: Blair Wingard, B.S.

Principal Technician: Gary L. Doyle, B.S.

ToxiGenics

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Director of Pathology: William O. Iverson, D.V.M.,
Diplomate, American College of Veterinary Pathologists
Environmental Pathology Laboratories, Inc. at ToxiGenics
Manager of Veterinary Sciences: Vincent W. Chaffee, D.V.M., Ph.D.
Director of Toxicology: Dale A. Mayhew, Ph.D.
Archivist: Donald G. MacKellar, B.A.

IV. Procedures

A. Test System

Young adult, albino rats were obtained from Charles River Breeding Laboratories, Inc., (Portage, MI facility), 251 Ballardvale Street, Wilmington, MA 01887. The rat is the species preferred in the EPA/OPP Guidelines for acute oral toxicity testing.

Animals were housed individually in stainless steel, wire-bottomed cages that conformed to the size standards specified in DHEW Publication (NIH) 78.23. The cages on each rack were numbered in a standard manner and a list of random numbers was generated by computer program* for the number of animals of each sex received. Upon receipt, each animal was removed from the shipping container and housed in the appropriate randomly selected cage. Each animal was then assigned a sequential animal number unique within ToxiGenics and identified with an ear tag bearing this animal number. The sequential animal number was listed on a cage card that was affixed to the front of the animal's cage.

* Methods adapted from Carnahan, Luther, and Wilkes, Applied Numerical Methods, Wiley, 1969.

The animals were quarantined for at least 8 days after receipt. Veterinary Sciences personnel examined the animals for health status and observed the animals for mortality, morbidity, and abnormal signs at least once each day during quarantine except for one day prior to main study dosing. Only healthy animals were used in this study.

The quarantine and study room (283) was cleaned daily, and the cages were cleaned and sanitized as specified in ToxiGenics' Standard Operating Procedures. Urine and feces fell through the wire mesh floor onto animal caging board. The cage boards were changed at least 2 times a week.

The animal room was well ventilated and air-conditioned, and the temperature and humidity were monitored daily in this room during the quarantine and study periods. The temperature ranged from 68 to 74°F and the relative humidity varied from 35 to 69 percent except for one day when a temperature of 66°F was recorded.

The animal room was lighted from approximately 6:00 a.m. to 6:00 p.m. (12-hour light/12-hour dark cycle) using automatic timers. Range-find dosing was completed at 12:05 p.m., and main study dosing was completed at 11:30 a.m. and 9:45 a.m. on the 2 days of dosing.

Purina Certified Rodent Chow 5002 was fed to the animals ad libitum during the quarantine and study periods except for fasting prior to dosing. Filtered tap water was provided ad libitum through an automatic watering system and was analyzed periodically as specified in ToxiGenics' Standard Operating Procedures.

B. Test Article

The test article, 83-52A, was a granular solid supplied by the Sponsor. Records concerning the test article purity, source, and other data required in 21 CFR, 58.105 are the responsibility of the Sponsor and are not presented in this report.

A small sample of the test article was removed after receipt and stored according to ToxiGenics' Standard Operating Procedures. The test article was stored at room temperature after receipt.

Prior to range-finding, a 50% weight/weight suspension of the test article in deionized water was prepared and mixed. This 50% suspension would not pass through a gavage needle so a 33.3% w/w suspension was prepared by adding additional deionized water. This 33.3% suspension was found to be suitable for dosing.

On the days of range-finding and main study dosing, 33.3% w/w suspensions of the test article in deionized water were prepared and mixed. These suspensions were also stirred during the dosing procedures.

Deionized water was considered to be an appropriate vehicle.

During the study, 84.25 grams of the test article were used for concentration determinations and dosing suspension preparations.

C. Experimental Design

The duration of testing was 14 days for range-finding and 14 days for the main study. The following is an outline of the experiment.

| | Dose Level (mg/kg) | Number of Animals | |
|----------------|--------------------|-------------------|--------|
| | | Male | Female |
| Range-Finding: | 501 | 1 | 1 |
| | 891 | 1 | 1 |
| | 1,585 | 1 | 1 |
| | 2,818 | 1 | 1 |
| | 5,012 | 1 | 1 |
| Main Study: | 1,778 | 5 | 5 |
| | 1,995 | 5 | 5 |
| | 2,239 | 5 | 5 |
| | 2,512 | 5 | 5 |
| | 2,818 | 5 | |

Range-finding dose levels were selected at logarithmically spaced intervals and were designed to cover a range of 500 to 5,000 mg/kg. The logarithmically spaced main study dose levels were based upon range-finding results. Range-finding animals were dosed on October 13, 1983, and the initial main study groups (1,778, 1,995, 2,239, and 2,512 mg/kg) were dosed on October 25, 1983. One additional main study group (2,818 mg/kg-males only) was dosed on November 2, 1983 to more accurately determine the LD₅₀ value for males.

Range-finding and main study animals were fasted overnight. In the morning of the days of dosing, body weights were recorded, doses were calculated, and a measured volume of freshly prepared 33.3% test article suspension was delivered to each animal by

oral gavage in a single dose. Diet was returned to the cage of each surviving animal approximately 4 hours after test article administration.

Animals were observed for mortality and abnormal clinical signs once each hour after dosing on day 0 (to the 4 to 5 hour interval, and also at the 6 to 7 hour interval for main study males dosed at 2,818 mg/kg). Observations for mortality and abnormal clinical signs were done twice daily thereafter for the duration of range-finding or main study testing. These twice daily observations were done in the early morning and late afternoon of days 1 to 13 and in the morning of day 14 after dosing of each group.

Body weights of all range-finding and main study animals were recorded prior to test article administration on the days of dosing (day 0). Body weights were also recorded on days 7 and 14 for surviving range-finding and main study animals, and at the time found dead for other animals.

All surviving range-finding animals were euthanized with carbon dioxide on day 14 and discarded. Range-finding animals were not examined at necropsy.

All surviving main study animals were rendered unconscious by exposure to carbon dioxide and exsanguinated prior to necropsy on day 14. All external surfaces, orifices, and organs; cranial cavity; carcass; external and cut surfaces of the brain; abdominal, thoracic, and pelvic cavities and their viscera; and

cervical tissues and organs of each main study animal (found dead or sacrificed on day 14) were examined at necropsy. Necropsies were conducted under the supervision of a qualified pathologist.

The oral LD₅₀ value, the 95 percent confidence interval, the slope of the dose-response curve, and correction factors for 0 and 100 percent observed responses were calculated for each sex using a computer program employing a method adapted from Litchfield and Wilcoxon⁺. Dose-response curves were prepared by computer program using the calculated LD₅₀ data.

Mean, standard deviation, and standard error of the mean values were calculated for the main study body weight and test article administration data (milliliters administered and calculated milligram values).

⁺ Litchfield, J.T., Jr. and Wilcoxon, F., "A Simplified Method of Evaluating Dose-Effect Experiments", Journal of Pharmacology and Experimental Therapeutics, Vol. 96, 1949, pages 99-113.

V. Results

The main study body weight, abnormal clinical sign, mortality, and gross necropsy data for males and females are summarized in Tables 1 and 2, respectively. Results of the LD₅₀ determinations are presented in Tables 3 and 4, and the dose-response curves are presented in Figures 1 and 2. The individual data for the range-finding and main study phases are presented in Appendices A to D.

The following is a summary of mortalities observed during main study testing:

| <u>Dose Level (mg/kg)</u> | <u>Main Study</u> | |
|---------------------------|---------------------------------|------------------------------|
| | <u>Number Dead/Number Males</u> | <u>Number Tested Females</u> |
| 1,778 | 1/5 | 2/5 |
| 1,995 | 0/5 | 2/5 |
| 2,239 | 2/5 | 3/5 |
| 2,512 | 2/5 | 5/5 |
| 2,818 | 5/5 | |

All main study deaths, except for 3, occurred on days 1, 2, or 3 following dosing. One main study female dosed at 1,778 mg/kg was found dead on day 9, and 2 other main study animals (one male dosed at 2,512 mg/kg and one female dosed at 2,239 mg/kg) were found dead on day 11. Range-finding males and females dosed at 2,818 or 5,012 mg/kg were found dead on the day of dosing or on day 1. Range-finding animals dosed at 501, 891, or 1,585 mg/kg survived a 14-day observation period.

The oral LD₅₀ values were determined to be 2,389 mg/kg for males and 1,992 mg/kg for females. The 95% confidence intervals were within 14.2% of the LD₅₀ value for males and within 16.8% of the LD₅₀ value for females.

Consistent body weight gains were observed on days 7 and 14 for all surviving range-finding animals and for 8 of the 23 surviving main study animals. Body weight losses or no weight gains were observed on days 7 and/or 14 for 15 of the 23 surviving main study animals in male groups dosed at 1,778 to 2,512 mg/kg and in female groups dosed at 1,778 or 2,239 mg/kg. Body weight losses were observed from the days of dosing to the days of death of all found dead range-finding and main study animals.

Lethargy was observed following dosing on day 0 for all range-finding and main study animals and was observed as late as days 8, 10, 11, or 14 for 4 main study animals. Ataxia was observed on day 0 for all animals except for 2 males (501 mg/kg range-finding animal or 2,818 mg/kg main study animal). Ataxia was observed as late as days 8, 11, or 12 for 4 main study animals.

Other abnormal clinical signs observed for main study animals as early as day 0 and as late as day 7 included: prostration, irregular breathing, salivation, squinting, lacrimation, crusty eyes, crusty nose, crusty muzzle, piloerection, red stained and/or yellow/brown stained fur - perianal region, loose stools, no stools, abdomen swollen, body cool to touch, emaciation, and moribund. Emaciation, piloerection, yellow/brown stained fur, body cool to touch, squinting, and abdomen swollen were also observed for some main study animals as late as days 10, 12, or 14. Some of these abnormal clinical signs were also observed for most range-finding animals.

No other abnormal clinical signs were observed during the study.

Abnormal necropsy findings were observed for all main study females; for all main study males dosed at 2,239 or 2,818 mg/kg; and for either 2, 3, or 4 main study males dosed at 1,778, 1,995, or 2,512 mg/kg, respectively. Abnormalities observed during necropsy included: thickened stomach mucosa; sloughing of stomach mucosa; depressions or discoloration of stomachs; severe dilation or watery contents of stomachs; a small projecting mass on one stomach; possible perforation of the wall of one stomach; discoloration of the small intestine; discoloration of the lung; abnormal fluid in the abdominal cavity or urinary bladder; nodular discolorations on one uterus; an enlarged spleen; exudate in the ocular, nasal, or pelvic regions; and stained fur in the perianal region. No other abnormalities were observed during necropsy of all main study animals.

TABLE 1: SUMMARY OF MAIN STUDY RESULTS - MALES
 ACUTE ORAL LD₅₀ STUDY IN RATS
 TEST ARTICLE: 83-52A

| Parameter | Number of Animals Responding/5 Animals Tested | | | |
|--|---|---------------|--------------------|----------------------|
| | 1,778 | 1,995 | 2,239 | 2,512 |
| <u>Body Weights of Survivors (Gain or Loss):</u> | Gain | Gain and Loss | Gain and Loss | Gain and Loss |
| <u>Abnormal Clinical Signs**:</u> | | | | |
| <u>Lethargy</u> | 5 (0-5) [1-3] | 5 (0-5) [1-3] | 5 (0-5) [1-3, 5-6] | 5 (0-5) [1-5, 8-14] |
| <u>Ataxia</u> | 5 (0-5) [1] | 5 (0-5) [1-2] | 5 (0-5) [1-2] | 5 (0-5) [1-4, 10-12] |
| <u>Irregular breathing</u> | 1 [1] | None | None | None |
| <u>Salivation</u> | None | None | None | 2 (0-1, 4-5) |
| <u>Squinting</u> | None | 3 (3-5) | 3 (3-5) | None |
| <u>Lacrimation</u> | 1 [1] | None | 1 [1] | None |
| <u>Crusty eyes</u> | None | 1 [1] | 2 [2] | None |
| <u>Crusty nose</u> | 2 [1-2] | None | None | None |
| <u>Crusty muzzle</u> | None | None | None | 2 (1-5, 6-7) [1] |
| <u>Piloerection</u> | None | None | 1 [1-2] | None |
| <u>Red stained fur - perianal region</u> | 2 (2-5) [1] | None | 1 (4-5) [1] | 3 [1, 3-14] |
| <u>Yellow/brown stained fur - perianal region</u> | None | None | 3 (1-5) [1-2] | 3 (1-5, 6-7) [1] |
| <u>Loose stools</u> | None | None | 2 (1-5) [1] | 3 (1-5, 6-7) |
| <u>No stools</u> | None | None | 4 [2] | None |
| <u>Abdomen swollen</u> | None | None | None | None |
| <u>Emaciated</u> | None | None | None | None |
| <u>Moribund</u> | None | None | 1 [2] | None |
| <u>Found dead</u> | 1 [2] | None | 2 [2] | 5 [1] |
| <u>Incidence of Gross Necropsy Findings:</u> | | | | |
| <u>Number with Abnormal Findings</u> | 2 <1-SS> | 3-SS | 5 <3-SS> | 4 <2-SS> |
| <u>Stomach</u> | | | | |
| - Thickened glandular mucosa | 1-SS | 2-SS | 1-SS | 3 <2-SS> |
| - Thickened non-glandular mucosa | 1 | None | None | None |
| - Sloughing of mucosa | None | None | 2-SS | 2 <1-SS> |
| - Depression, black, glandular | None | None | 1 | None |
| - Discoloration; diffuse; red, black, brown, green, or combination | 1 | None | 2 | 1 |
| - Projecting mass (small) without normal mucosa | None | 1-SS | None | None |
| - Possible perforation of wall | 1 | None | None | None |
| - Severe dilation, filled with food | None | None | None | 1 |
| - Watery contents | None | None | None | None |

**Incidence and duration for the dose level in hours () after dosing and days [] following dosing.
 SS = Incidence of necropsy findings of scheduled sacrifice animals, indicated by < >.

TABLE 1 (continued): SUMMARY OF MAIN STUDY RESULTS -- MALES

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Parameter | Number of Animals Responding/5 Animals Tested | | | |
|---|---|-------|-------|-------|
| | 1,778 | 1,995 | 2,239 | 2,512 |
| | | | | 2,818 |
| Small Intestine | | | | |
| - Discoloration, diffuse, red | 1 | None | None | None |
| Abdominal Cavity | | | | |
| - Fluid, diffuse, red | 1 | None | None | None |
| Lung | | | | |
| - Discoloration, diffuse, red | None | None | None | 2 |
| External Surfaces | | | | |
| - Exudate, diffuse, black, ocular and/or nasal region | None | None | 2 | 1 |
| - Stained fur in perianal region; yellow/brown, red, or brown | None | None | None | 1-SS |
| | | | | 4 |

SS = Incidence of necropsy findings of scheduled sacrifice animals, indicated by < >.

TABLE 2: SUMMARY OF MAIN STUDY RESULTS - FEMALES
 ACUTE ORAL LD₅₀ STUDY IN RATS
 TEST ARTICLE: 83-52A

| Parameter | Number of Animals Responding/5 Animals tested | |
|---|---|----------------|
| | Dose Level (mg/kg): 1,995 | 2,239 |
| Body Weights of Survivors (Gain or Loss): | 1,778 | 2,512 |
| <u>Abnormal Clinical Signs**:</u> | | |
| <u>Lethargy</u> | 5 (0-5) [1-2,8] | 5 (0-5) [1-3] |
| Ataxia | 5 (0-5) [8] | 5 (0-5) [1-2] |
| Prostration | None | 2 [1-2] |
| Irregular breathing | None | 2 [1-2] |
| Squinting | None | 2 [1] |
| Lacrimation | None | 1 (4-5) |
| Crusty eyes | None | 2 [2-3] |
| Crusty nose | 2 [2-3] | None |
| Crusty muzzle | 2 [1] | 2 [1-2] |
| Piloerection | 1 [8] | None |
| Red stained fur - perianal region | 4 (2-5) | None |
| Yellow/brown stained fur - perianal region | 4 (3-5) [1-8] | 4 (1-5) [1-14] |
| Loose stools | 1 [2] | 2 (1-5) |
| No stools | None | 4 [2] |
| Body cool to touch | None | None |
| Abdomen swollen | 1 [7-8] | None |
| Moribund | None | 2 [2] |
| Found dead | 2 [2,9] | 2 [2,3] |
| <u>Incidence of Gross Necropsy Findings:</u> | | |
| <u>Number with Abnormal Findings</u> | 5 <3-SS> | 5 <3-SS> |
| Stomach | | |
| - Thickened glandular mucosa | 4 <3-SS> | 3 <2-SS> |
| - Thickened non-glandular mucosa | 1-SS | 1-SS |
| - Sloughing of mucosa | 1-SS | None |
| - Discoloration; diffuse; combination of red, black, brown, green, or white | 1 | 1 |
| - Severe dilation | 1 | None |
| Small Intestine | | |
| - Discoloration, diffuse, red | None | 1 |
| Lung | | |
| - Discolorations, multiple, focal, red | None | None |
| | | 1 |
| | | 5 |
| | | 2 |
| | | 4 |
| | | None |
| | | 4 |
| | | None |
| | | None |
| | | 1 [1] |
| | | 5 [1,2] |
| | | 5 (0-5) |
| | | 5 (0-5) |
| | | 3 (3-5) [1] |
| | | 1 [1] |
| | | 4 (3-5) [1] |
| | | 1 [1] |
| | | None |
| | | 3 (2-5) |
| | | 4 (1-5) [1] |
| | | 4 (1-5) |
| | | None |
| | | None |
| | | 1 [1] |
| | | 1 [6-11] |
| | | None |
| | | 1 [1] |
| | | 5 [1,2] |
| | | 5 <2-SS> |
| | | 3 <2-SS> |
| | | 1-SS |
| | | 2 <1-SS> |
| | | 2 |
| | | 1 |
| | | 1 |
| | | 1 |
| | | None |
| | | None |

**Incidence and duration for the dose level in hours () after dosing and days [] following dosing.
 SS = Incidence of necropsy findings of scheduled sacrifice animals, indicated by < >.

TABLE 2 (continued): SUMMARY OF MAIN STUDY RESULTS - FEMALES

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Parameter | Number of Animals Responding/5 Animals Tested | | | 2,512 |
|--|---|------------------------------|-------|-------|
| | 1,778 | Dose Level (mg/kg): 1,995 | 2,239 | |
| Uterus | | | | |
| - Nodular discolorations, red-black | 1-SS | None | None | None |
| Urinary Bladder | | | | |
| - Fluid, diffuse, amber | None | None | None | 1 |
| Spleen | | | | |
| - Enlarged, mild | None | None | None | 1 |
| External Surfaces | | | | |
| - Exudate, diffuse, black or red-black, ocular or nasal region | 1 | 2 | 1 | None |
| - Exudate, diffuse, red, pelvic region | None | None | 1 | None |
| - Stained fur in perianal region, yellow/brown | 1 | None | None | None |

SS = Incidence of necropsy findings of scheduled sacrifice animals, indicated by < >.

TABLE 3: LITCHFIELD-WILCOXON LD₅₀ DETERMINATION: MALES
 ACUTE ORAL LD₅₀ STUDY IN RATS
 TEST ARTICLE: 83-52A

| DOSE LEVEL (MG/KG) | OBSERVED DEATHS PROPORTION | DEATHS PERCENT | EXPECTED DEATHS PERCENT | DIFFERENCE |
|--------------------|----------------------------|----------------|-------------------------|------------|
| 1,778.0 | 1/5 | 20.0 | 8.5 | 11.5 |
| 1,995.0 | 0/5 | 0.0(7.8) | 20.1 | -12.3 |
| 2,239.0 | 2/5 | 40.0 | 38.2 | 1.8 |
| 2,512.0 | 2/5 | 40.0 | 59.2 | -19.2 |
| 2,818.0 | 5/5 | 100.0(89.5) | 77.9 | 11.6 |

Total number of animals: 25

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 2.492

Critical Chi Square (P=.05) for 3 degrees of freedom: 7.812

The data are not significantly heterogeneous.

Calculated LD₅₀: 2388.9 mg/kg

95% Confidence Limits: 2091.0 - 2729.2 mg/kg

The confidence limits are within 14.2% of the LD₅₀.

Slope: 10.71 (probits/log dose)

There are 20 animals included in groups with expected deaths between 16% (LD₁₆ = 1926.7 mg/kg) and 84% (LD₈₄ = 2961.9 mg/kg).

TABLE 4: LITCHFIELD-WILCOXON LD₅₀ DETERMINATION: FEMALES
 ACUTE ORAL LD₅₀ STUDY IN RATS
 TEST ARTICLE: 83-52A

| DOSE LEVEL (MG/KG) | OBSERVED DEATHS PROPORTION | EXPECTED DEATHS PERCENT | EXPECTED DEATHS PERCENT | DIFFERENCE |
|--------------------------|-------------------------------|----------------------------|----------------------------|------------|
| 1,778.0 | 2/5 | 40.0 | 30.1 | 9.9 |
| 1,995.0 | 2/5 | 40.0 | 50.3 | -10.3 |
| 2,239.0 | 3/5 | 60.0 | 70.5 | -10.5 |
| 2,512.0 | 5/5 | 100.0 (91.0) | 85.7 | 5.4 |

Total number of animals: 20

Note - The values in parentheses are those used by the Litchfield-Wilcoxon method to compute Chi Square contributions.

Calculated Chi Square: 0.826

Critical Chi Square (P=.05) for 2 degrees of freedom: 6.080

The data are not significantly heterogeneous.

Calculated LD₅₀: 1991.7 mg/kg

95% Confidence Limits: 1704.7 - 2327.0 mg/kg

The confidence limits are within 16.8% of the LD₅₀.

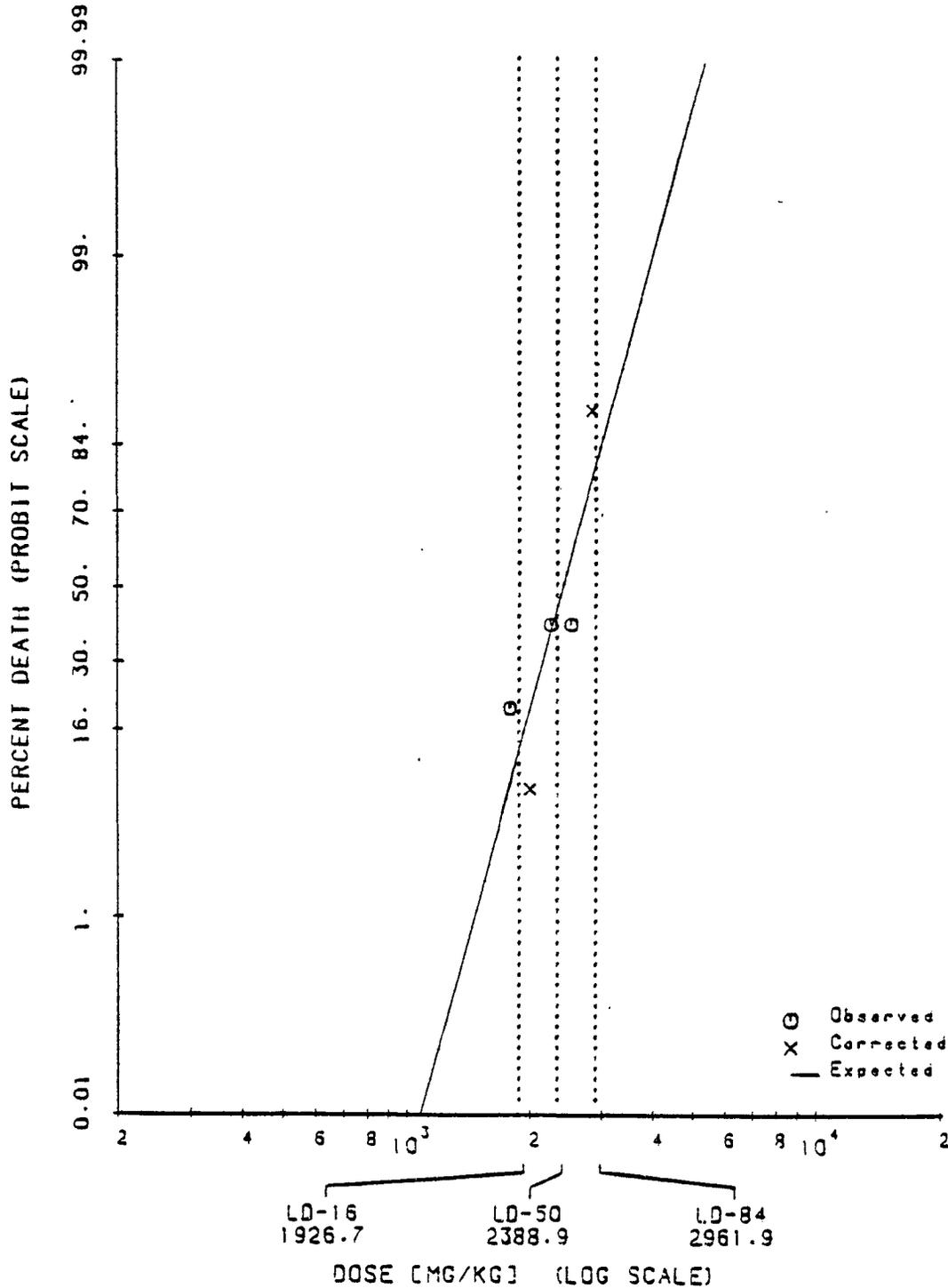
Slope: 10.58 (probits/log dose)

There are 15 animals included in groups with expected deaths between 16% (LD₁₆ = 1602.3 mg/kg) and 84% (LD₈₄ = 2475.7 mg/kg).

FIGURE 1: DOSE-RESPONSE CURVE: MALES

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

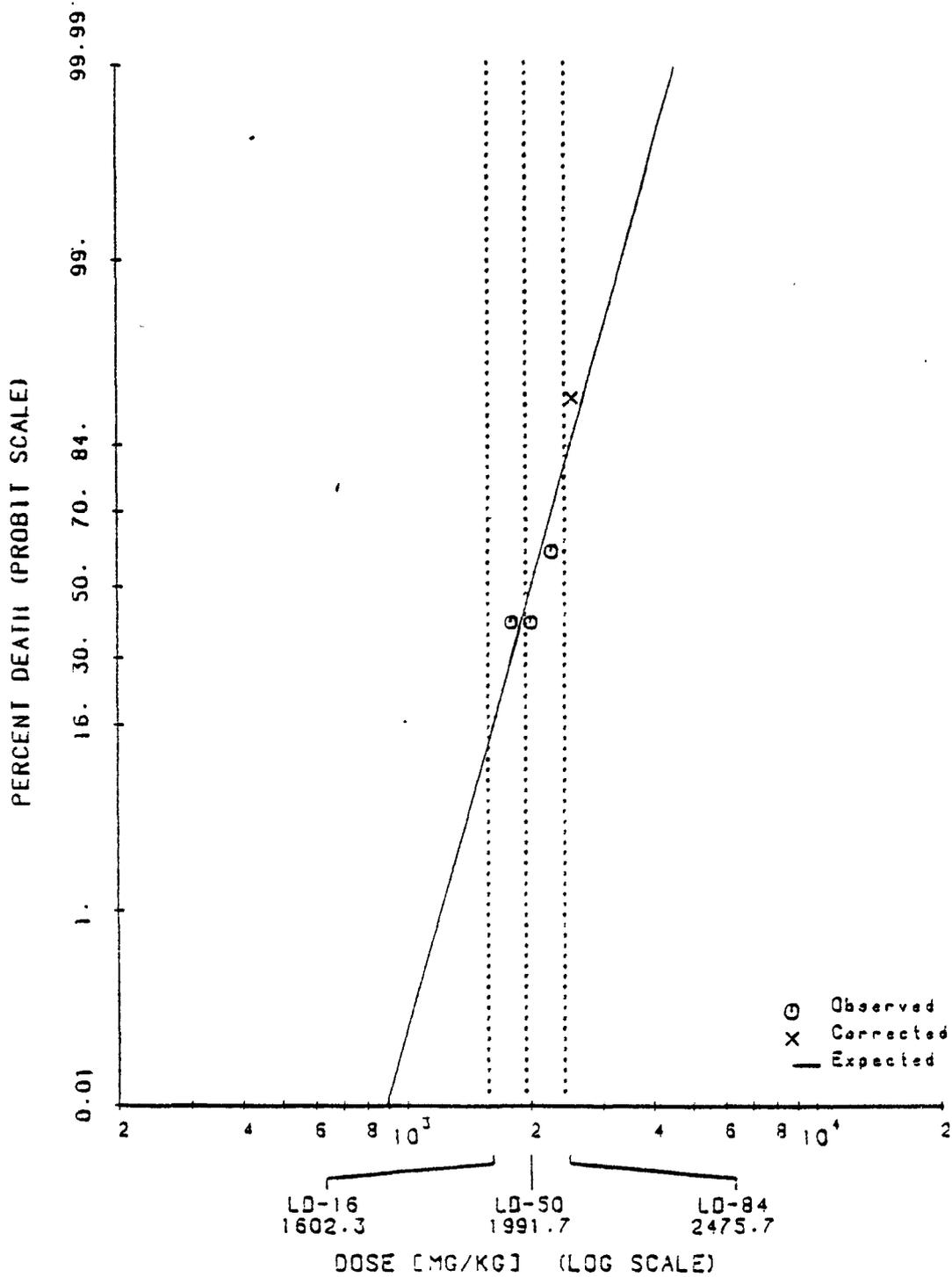


NOTE: The 0% and 100% observed death points were plotted as corrected values computed by the Litchfield-Wilcoxon method [see value in parentheses in the observed deaths (percent) column of Table 3].

FIGURE 2: DOSE-RESPONSE CURVE: FEMALES

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A



NOTE: The 100% observed death point was plotted as a corrected value computed by the Litchfield-Wilcoxon method [see value in parentheses in the observed deaths (percent) column of Table 4].

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APPENDIX A: INDIVIDUAL RANGE-FINDING DATA

INDIVIDUAL BODY WEIGHT AND TEST ARTICLE ADMINISTRATION DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Body Weights (grams) | | | Body Weight Change (grams) | Amount of Test Article Administered | |
|--------------------|---------------|-----|----------------------|---------|-----|----------------------------|-------------------------------------|------|
| | | | Day of Study 0 | 7 | 14 | | (mg) | (ml) |
| 501 | AE9813 | M | 183 | 246 | 280 | 97 | 93 | 0.28 |
| 891 | AE9814 | M | 203 | 264 | 323 | 120 | 180 | 0.54 |
| 1,585 | AE9815 | M | 190 | 238 | 293 | 103 | 300 | 0.90 |
| 2,818 | AE9816 | M | 207 | (1-187) | | [-20] | 599 | 1.8 |
| 5,012 | AE9817 | M | 201 | (0-195) | | [-6] | 999 | 3.0 |
| 501 | AE9890 | F | 191 | 214 | 231 | 40 | 97 | 0.29 |
| 891 | AE9891 | F | 212 | 237 | 258 | 46 | 190 | 0.57 |
| 1,585 | AE9892 | F | 200 | 201 | 222 | 22 | 316 | 0.95 |
| 2,818 | AE9893 | F | 207 | (1-198) | | [-9] | 599 | 1.8 |
| 5,012 | AE9894 | F | 205 | (1-196) | | [-9] | 1,032 | 3.1 |

() = Day found dead and final body weight.

[] = Body weight change of found dead animals.

NOTE: Volumes of the 33.3% test article suspension of 1.0 milliliter or less were rounded to the nearest hundredth milliliter, and volumes of the same suspension over 1.0 milliliter were rounded to the nearest tenth milliliter for administration. The milligrams of the test article are rounded values calculated from the milliliters administered.

APPENDIX A (continued): INDIVIDUAL RANGE-FINDING DATA

INDIVIDUAL MORTALITY AND ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|-----|------------------------------|--|--|
| 501 | AE9813 | M | SS, 14 | Crusty muzzle Lethargy | 0 to 1 hour 1 to 4 hours |
| 891 | AE9814 | M | SS, 14 | Lethargy Ataxia | 0 to 5 hours; day 1-AM 1 to 5 hours |
| 1,585 | AE9815 | M | SS, 14 | Lethargy Ataxia | 0 to 5 hours; day 1 0 to 5 hours |
| 2,818 | AE9816 | M | FD, 1 | Lethargy Ataxia and loose stools Yellow/brown stained fur - perianal region Found dead | 0 to 5 hours 1 to 5 hours 2 to 5 hours Day 1-AM |
| 5,012 | AE9817 | M | FD, 0 | Lethargy Ataxia Squinting Prostration, irregular breathing, loose stools, and yellow/brown stained fur - perianal region Body cool to touch and moribund Found dead | 0 to 2 hours 1 to 2 hours 1 to 4 hours 2 to 4 hours 3 to 4 hours 4 to 5 hours |
| 501 | AE9890 | F | SS, 14 | Ataxia Lethargy | 1 to 4 hours 3 to 4 hours |

FD = Found dead

SS = Scheduled sacrifice

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

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APPENDIX A (continued): INDIVIDUAL RANGE-FINDING DATA

INDIVIDUAL MORTALITY AND ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|-----|------------------------------|---|--|
| 891 | AE9891 | F | SS, 14 | Lethargy and ataxia | 0 to 5 hours |
| 1,585 | AE9892 | F | SS, 14 | Lethargy Ataxia Yellow/brown stained fur - perianal region | 0 to 5 hours; day 1 1 to 5 hours Day 1 |
| 2,818 | AE9893 | F | FD, 1 | Lethargy and ataxia Squinting Loose stools, irregular breathing, and yellow/brown stained fur - perianal region Found dead | 0 to 5 hours 1 to 5 hours 3 to 5 hours Day 1-AM |
| 5,012 | AE9894 | F | FD, 1 | Lethargy and ataxia Loose stools, squinting, lacrimation, and yellow/brown stained fur - perianal region Prostration and irregular breathing Body cool to touch and moribund Found dead | 0 to 2 hours 1 to 5 hours 2 to 5 hours 3 to 5 hours Day 1-AM |

FD = Found dead

SS = Scheduled sacrifice

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX B: INDIVIDUAL MAIN STUDY BODY WEIGHT AND
 TEST ARTICLE ADMINISTRATION DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Body Weights (grams) | | | Body Weight Change (grams) | Amount of Test Article Administered | |
|--------------------|---------------|-----|----------------------|------------|------------|----------------------------|-------------------------------------|------------|
| | | | Day of Study 0 | 7 | 14 | | (mg) | (ml) |
| 1,778 | AE9847 | M | 253 | 267 | 318 | 65 | 466 | 1.4 |
| | AE9848 | M | 241 | (2-217) | | [-24] | 433 | 1.3 |
| | AE9849 | M | 282 | 282 | 343 | 61 | 500 | 1.5 |
| | AE9850 | M | 216 | 204 | 240 | 24 | 400 | 1.2 |
| | AE9851 | M | <u>289</u> | <u>326</u> | <u>378</u> | <u>89</u> | <u>500</u> | <u>1.5</u> |
| | Mean | | 256 | 270 | 320 | 60 | 460 | 1.4 |
| | S.D. | | 30 | 50 | 59 | 27 | 43 | 0.1 |
| S.E. | | 13 | 25 | 29 | 13 | 19 | 0.1 | |
| 1,995 | AE9852 | M | 285 | 311 | 361 | 76 | 566 | 1.7 |
| | AE9853 | M | 257 | 246 | 287 | 30 | 500 | 1.5 |
| | AE9854 | M | 244 | 221 | 224 | -20 | 500 | 1.5 |
| | AE9855 | M | 267 | 242 | 321 | 54 | 533 | 1.6 |
| | AE9856 | M | <u>254</u> | <u>283</u> | <u>339</u> | <u>85</u> | <u>500</u> | <u>1.5</u> |
| | Mean | | 261 | 261 | 306 | 45 | 520 | 1.6 |
| | S.D. | | 16 | 36 | 53 | 42 | 30 | 0.1 |
| S.E. | | 7 | 16 | 24 | 19 | 13 | 0.0 | |
| 2,239 | AE9857 | M | 293 | 310 | 361 | 68 | 666 | 2.0 |
| | AE9858 | M | 247 | (2-198) | | [-49] | 566 | 1.7 |
| | AE9859 | M | 289 | (2-239) | | [-50] | 633 | 1.9 |
| | AE9860 | M | 274 | 262 | 266 | -8 | 599 | 1.8 |
| | AE9861 | M | <u>261</u> | <u>241</u> | <u>266</u> | <u>5</u> | <u>599</u> | <u>1.8</u> |
| | Mean | | 273 | 271 | 298 | 22 | 613 | 1.8 |
| | S.D. | | 19 | 35 | 55 | 41 | 38 | 0.1 |
| S.E. | | 9 | 20 | 32 | 23 | 17 | 0.1 | |

() = Day found dead and final body weight.

[] = Body weight change of found dead animals, not included in body weight change mean values.

NOTE: The volumes of the 33.3% test article suspension were rounded to the nearest tenth milliliter for administration. The milligrams of the test article are rounded values calculated from the milliliters administered.

APPENDIX B (continued): INDIVIDUAL MAIN STUDY BODY WEIGHT AND TEST ARTICLE ADMINISTRATION DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-352A

| Dose Level (mg/kg) | Animal Number | Sex | Body Weights (grams) | | | Body Weight Change (grams) | Amount of Test Article Administered | |
|--------------------|---------------|-----|----------------------|------------|------------|----------------------------|-------------------------------------|------------|
| | | | Day of Study 0 | 7 | 14 | | (mg) | (ml) |
| 2,512 | AE9862 | M | 284 | 298 | 357 | 73 | 699 | 2.1 |
| | AE9863 | M | 259 | 193 | 160 | -99 | 666 | 2.0 |
| | AE9864 | M | 291 | (2-257) | | [-34] | 733 | 2.2 |
| | AE9865 | M | 254 | 217 | (11-205) | [-49] | 633 | 1.9 |
| | AE9866 | M | <u>274</u> | <u>265</u> | <u>336</u> | <u>62</u> | <u>699</u> | <u>2.1</u> |
| | Mean | | 272 | 243 | 284 | 12 | 686 | 2.1 |
| | S.D. | | 16 | 47 | 108 | 96 | 38 | 0.1 |
| S.E. | | 7 | 24 | 62 | 56 | 17 | 0.1 | |
| 2,818 | AE9845 | M | 313 | (1-292) | | [-21] | 866 | 2.6 |
| | AE9846 | M | 326 | (1-304) | | [-22] | 932 | 2.8 |
| | AE9867 | M | 306 | (1-279) | | [-27] | 866 | 2.6 |
| | AE9868 | M | 302 | (1-278) | | [-24] | 866 | 2.6 |
| | AE9869 | M | <u>308</u> | (1-298) | | [-10] | <u>866</u> | <u>2.6</u> |
| | Mean | | 311 | | | | 879 | 2.6 |
| | S.D. | | 9 | | | | 30 | 0.1 |
| S.E. | | 4 | | | | 13 | 0.0 | |
| 1,778 | AE9923 | F | 197 | 184 | (9-186) | [-11] | 366 | 1.1 |
| | AE9924 | F | 222 | (2-201) | | [-21] | 400 | 1.2 |
| | AE9925 | F | 235 | 240 | 267 | 32 | 433 | 1.3 |
| | AE9926 | F | 220 | 210 | 230 | 10 | 400 | 1.2 |
| | AE9927 | F | <u>237</u> | <u>237</u> | <u>233</u> | <u>-4</u> | <u>433</u> | <u>1.3</u> |
| | Mean | | 222 | 218 | 243 | 13 | 406 | 1.2 |
| | S.D. | | 16 | 26 | 21 | 18 | 28 | 0.1 |
| S.E. | | 7 | 13 | 12 | 10 | 13 | 0.0 | |

() = Day found dead and final body weight.

[] = Body weight change of found dead animals, not included in body weight change mean values.

NOTE: The volumes of the 33.3% test article suspension were rounded to the nearest tenth milliliter for administration. The milligrams of the test article are rounded values calculated from the milliliters administered.

APPENDIX B (continued): INDIVIDUAL MAIN STUDY BODY WEIGHT AND TEST ARTICLE ADMINISTRATION DATAACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Body Weights (grams) | | | Body Weight Change (grams) | Amount of Test Article Administered | |
|--------------------|---------------|-----|----------------------|------------------|-------------------|----------------------------|-------------------------------------|------------|
| | | | Day of Study | 7 | 14 | | (mg) | (ml) |
| 1,995 | AE9928 | F | 209 | 181 | 210 | 1 | 433 | 1.3 |
| | AE9929 | F | 212 | 208 | 236 | 24 | 433 | 1.3 |
| | AE9930 | F | 236 | (2-191) | | [-45] | 466 | 1.4 |
| | AE9931 | F | 238 | 237 | 239 | 1 | 466 | 1.4 |
| | AE9932 | F | <u>215</u> | (<u>2-189</u>) | | [-26] | <u>433</u> | <u>1.3</u> |
| | Mean | | 222 | 209 | 228 | 9 | 446 | 1.3 |
| | S.D. | | 14 | 28 | 16 | 13 | 18 | 0.1 |
| S.E. | | 6 | 16 | 9 | 8 | 8 | 0.0 | |
| 2,239 | AE9933 | F | 225 | (1-209) | | [-16] | 500 | 1.5 |
| | AE9934 | F | 216 | (2-196) | | [-20] | 500 | 1.5 |
| | AE9935 | F | 228 | 206 | 216 | -12 | 500 | 1.5 |
| | AE9936 | F | 219 | 238 | 249 | 30 | 500 | 1.5 |
| | AE9937 | F | <u>249</u> | <u>230</u> | (<u>11-207</u>) | [-42] | <u>566</u> | <u>1.7</u> |
| | Mean | | 227 | 225 | 233 | 9 | 513 | 1.5 |
| | S.D. | | 13 | 17 | | | 30 | 0.1 |
| S.E. | | 6 | 10 | | | 13 | 0.0 | |
| 2,512 | AE9938 | F | 226 | (1-222) | | [-4] | 566 | 1.7 |
| | AE9940 | F | 238 | (2-217) | | [-21] | 599 | 1.8 |
| | AE9941 | F | 232 | (1-217) | | [-15] | 599 | 1.8 |
| | AE9942 | F | 212 | (1-207) | | [-5] | 533 | 1.6 |
| | AE9943 | F | <u>228</u> | (<u>1-219</u>) | | [-9] | <u>566</u> | <u>1.7</u> |
| | Mean | | 227 | | | | 573 | 1.7 |
| | S.D. | | 10 | | | | 28 | 0.1 |
| S.E. | | 4 | | | | 12 | 0.0 | |

() = Day found dead and final body weight.

[] = Body weight change of found dead animals, not included in body weight change mean values.

NOTE: The volumes of the 33.3% test article suspension were rounded to the nearest tenth milliliter for administration. The milligrams of the test article are rounded values calculated from the milliliters administered.

APPENDIX C: INDIVIDUAL MAIN STUDY ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|--------|--|--|
| 1,778 | AE9847 | M | Lethargy Ataxia Crusty nose | 1 to 5 hours 3 to 5 hours Days 1 and 2-AM |
| | AE9848 | M | Lethargy Ataxia Red stained fur - perianal region Lacrimation and irregular breathing Found dead | 1 to 5 hours; day 1 2 to 5 hours; day 1 Day 1 Day 1-PM Day 2-AM |
| | AE9849 | M | Ataxia Lethargy Red stained fur - perianal region Crusty nose | 0 to 5 hours 1 to 5 hours; days 1 and 2-AM 2 to 5 hours Days 1-PM and 2-AM |
| | AE9850 | M | Lethargy Ataxia | 0 to 5 hours; days 1 to 3-AM 0 to 5 hours |
| | AE9851 | M | Lethargy Ataxia | 1 to 5 hours 3 to 5 hours |
| | 1,995 | AE9852 | M | Lethargy Ataxia Squinting Crusty eyes |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

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APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|--------------------|--|---|
| 1,995 (cont.) | AE9853 | M | Lethargy | 0 to 5 hours; days 1 to 3 |
| | | | Ataxia | 1 to 5 hours |
| | | | Squinting | 3 to 5 hours |
| | AE9854 | M | Lethargy and ataxia Squinting | 0 to 5 hours 3 to 5 hours |
| | AE9855 | M | Lethargy Ataxia | 0 to 5 hours; days 1 and 2-AM 1 to 5 hours; days 1 and 2-AM |
| AE9856 | M | Lethargy Ataxia | 0 to 5 hours; day 1-AM 0 to 5 hours | |
| 2,239 | AE9857 | M | Lethargy and ataxia | 0 to 5 hours |
| | AE9858 | M | Lethargy and ataxia Squinting Red stained fur - perianal region Yellow/brown stained fur - perianal region Lacrimation Moribund, no stools, and crusty eyes Found dead | 0 to 5 hours; days 1 and 2-AM 4 to 5 hours 4 to 5 hours; day 1 Days 1 and 2-AM Day 1-PM Day 2-AM Day 2-PM |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|-----|--|---|
| 2,239 (cont.) | AE9859 | M | Lethargy and ataxia | 0 to 5 hours; days 1 and 2-AM |
| | | | Loose stools | 1 to 5 hours; day 1 |
| | | | Yellow/brown stained fur - perianal region | 1 to 5 hours; days 1 and 2-AM |
| | | | Squinting | 4 to 5 hours |
| | | | Piloerection | Days 1 and 2-AM |
| | | | No stools and crusty eyes | Day 2-AM |
| | AE9860 | M | Found dead | Day 2-PM |
| | | | Lethargy and ataxia | 0 to 5 hours |
| | | | Loose stools | 1 to 5 hours |
| | AE9861 | M | Yellow/brown stained fur - perianal region | 1 to 5 hours; days 1 and 2 |
| | | | No stools | Day 2-AM |
| | | | Lethargy | 0 to 5 hours; days 1 to 3, 5-PM, and 6-AM |
| Ataxia | | | 0 to 5 hours | |
| 2,512 | AE9862 | M | Squinting | 3 to 5 hours |
| | | | No stools | Day 2-AM |
| | | | Lethargy | 0 to 5 hours; days 1 and 2 |
| | | | Ataxia | 0 to 5 hours |
| | | | Yellow/brown stained fur - perianal region | Days 1 and 2 |
| No stools | Day 2-AM | | | |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|-----|---|--|
| 2,512 (cont.) | AE9863 | M | Lethargy | 0 to 5 hours; days 1 to 5 and 8 to 14-AM |
| | | | Ataxia | 0 to 5 hours; days 1 to 4-AM and 10-PM to 12 |
| | | | Loose stools | 1 to 5 hours; day 1 |
| | | | Yellow/brown stained fur - perianal region | 1 to 5 hours; days 1 to 14-AM |
| | | | Squinting | 3 to 5 hours |
| | | | No stools | Day 2-AM |
| | | | Piloerection | Days 8, 9, and 11 to 14-AM |
| | | | Abdomen appeared swollen | Days 9-PM to 12 |
| | | | Emaciated | Days 13 and 14-AM |
| | AE9864 | M | Lethargy and ataxia | 0 to 5 hours; day 1 |
| | | | Loose stools and yellow/brown stained fur - perianal region | 1 to 5 hours; day 1 |
| | | | Squinting | 3 to 5 hours; day 1-PM |
| | | | Piloerection | Day 1-PM |
| | | | Found dead | Day 2-AM |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|-----|--|--|
| 2,512 (cont.) | AE9865 | M | Lethargy | 0 to 5 hours; days 1, 2-PM to 5, and 8 to 10 |
| | | | Ataxia | 0 to 5 hours |
| | | | Loose stools | 1 to 5 hours; days 2-PM and 4-AM |
| | | | Yellow/brown stained fur - perianal region | 1 to 5 hours; days 1 to 7 |
| | | | Squinting | 3 to 5 hours |
| | | | Abdomen appeared swollen | Days 3-PM to 5, and 8 to 10 |
| | | | Piloerection | Days 3-PM to 10 |
| | | | Found dead | Day 11-AM |
| | AE9866 | M | Lethargy | 0 to 5 hours; day 1 |
| | | | Ataxia | 0 to 5 hours |
| 2,818 | AE9845 | M | Lethargy | 1 to 5 and 6 to 7 hours |
| | | | Ataxia and loose stools | 3 to 5 and 6 to 7 hours |
| | | | Found dead | Day 1-AM |
| | AE9846 | M | Lethargy | 1 to 5 and 6 to 7 hours |
| | | | Ataxia | 3 to 5 and 6 to 7 hours |
| | | | Red stained fur - perianal region | 6 to 7 hours |
| | | | Found dead | Day 1-AM |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed | |
|--------------------|---------------|---|--|--|----------|
| 2,818 (cont.) | AE9867 | M | Salivation | 0 to 1 hour | |
| | | | Lethargy and crusty muzzle | 1 to 5 and 6 to 7 hours; day 1-AM | |
| | | | Red stained fur - perianal region | 3 to 5 and 6 to 7 hours | |
| | | | | Irregular breathing and yellow/brown stained fur - perianal region | Day 1-AM |
| | | | | Found dead | Day 1-PM |
| | AE9868 | M | Lethargy and loose stools | 1 to 5 and 6 to 7 hours | |
| | | | Yellow/brown stained fur - perianal region | 1 to 5 hours | |
| | | | Salivation | 4 to 5 hours | |
| | | | Ataxia, crusty muzzle, and red stained fur - perianal region | 6 to 7 hours | |
| | | | Found dead | Day 1-AM | |
| AE9869 | M | Lethargy | 1 to 5 and 6 to 7 hours | | |
| | | Ataxia | 3 to 5 and 6 to 7 hours | | |
| | | Loose stools and yellow/brown stained fur - perianal region | 4 to 5 and 6 to 7 hours | | |
| | | Found dead | Day 1-AM | | |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

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APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed | | |
|--------------------|-----------------------------------|--------------|--|--|-------------|---------------------|
| 1,778 | AE9923 | F | Ataxia | 1 to 5 hours; day 8-PM | | |
| | | | Lethargy | 2 to 5 hours; days 1, 2, and 8 | | |
| | | | Red stained fur - perianal region | 2 to 5 hours | | |
| | | AE9924 | F | Yellow/brown stained fur - perianal region | Days 1 to 8 | |
| | Abdomen appeared swollen | | | Days 7 and 8 | | |
| | Piloerection | | | Day 8 | | |
| | | AE9825 | F | Found dead | Day 9-AM | |
| | | | | F | Ataxia | 0 to 5 hours |
| | | | | | Lethargy | 2 to 5 hours; day 1 |
| | Red stained fur - perianal region | 2 to 5 hours | | | | |
| | | | Crusty muzzle and yellow/brown stained fur - perianal region | Day 1 | | |
| | | | Found dead | Day 2-AM | | |
| | | | Ataxia | 0 to 5 hours | | |
| | | | Lethargy | 1 to 5 hours; days 1 and 2 | | |
| | | | Red stained fur - perianal region | 4 to 5 hours | | |
| | | | Yellow/brown stained fur - perianal region | Days 1 to 3-AM | | |
| | | | Crusty muzzle | Day 1-PM | | |
| | | | Crusty nose and loose stools | Day 2-AM | | |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

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APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATAACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|-----|--|--|
| 1,778 (cont.) | AE9826 | F | Ataxia Lethargy Yellow/brown stained fur - perianal region | 1 to 5 hours 2 to 5 hours; day 1 3 to 5 hours; days 1 to 5 |
| | AE9827 | F | Crusty nose Lethargy Ataxia Red stained fur - perianal region | Days 2 and 3-AM 0 to 5 hours; day 1-AM 1 to 5 hours 4 to 5 hours |
| 1,995 | AE9928 | F | Lethargy Ataxia Loose stools Yellow/brown stained fur - perianal region | 0 to 5 hours; days 1 to 3 0 to 5 hours; days 1 and 2-AM 1 to 5 hours 1 to 5 hours; days 1 to 14-AM |
| | AE9929 | F | Lacrimation No stools Crusty muzzle Crusty eyes Ataxia Lethargy Yellow/brown stained fur - perianal region | 4 to 5 hours Day 2-AM Day 2 Days 2 and 3-AM 0 to 5 hours; day 2-AM 1 to 5 hours; day 1 1 to 5 hours; days 1 to 3 |
| | | | Loose stools No stools | 1 to 5 hours Day 2-AM |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed | | |
|--|---------------|--|--------------------------------------|------------------------|----------|------------------------|
| 1,995 (cont.) | AE9930 | F | Lethargy | 0 to 5 hours | | |
| | | | Ataxia | 0 to 5 hours; day 1-AM | | |
| | | | Prostration and irregular breathing | Days 1 and 2 | | |
| | | | Crusty muzzle | Days 1 and 2-PM | | |
| | | | Squinting | Day 1-PM | | |
| | | | No stools, crusty eyes, and moribund | Day 2 | | |
| | | | Found dead | Day 3-AM | | |
| | | | AE9931 | F | Lethargy | 0 to 5 hours; day 1-AM |
| | | | | | Ataxia | 0 to 5 hours |
| Yellow/brown stained fur - perianal region | Day 2-AM | | | | | |
| AE9932 | F | Ataxia | 0 to 5 hours; day 1 | | | |
| | | Lethargy | 1 to 5 hours; day 1 | | | |
| | | Irregular breathing and yellow/brown stained fur - perianal region | Days 1 and 2-AM | | | |
| | | Squinting | Day 1-PM | | | |
| | | Prostration, no stools, and moribund | Day 2-AM | | | |
| | | Found dead | Day 2-PM | | | |
| 2,239 | AE9933 | F | Lethargy and ataxia | 0 to 5 hours | | |
| | | | Red stained fur - perianal region | 2 to 5 hours | | |
| | | | Found dead | Day 1-AM | | |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed | |
|--------------------|---------------|--|---|---|----------|
| 2,239 (cont.) | AE9934 | F | Lethargy and ataxia | 0 to 5 hours; day 1-AM | |
| | | | Loose stools and yellow/brown stained fur - perianal region | 1 to 5 hours | |
| | | | Piloerection and red stained fur - perianal region | Day 1 | |
| | | | | Prostration, irregular breathing, and lacrimation | Day 1-PM |
| | | | | Found dead | Day 2-AM |
| | AE9935 | F | Lethargy | 0 to 5 hours; day 1 | |
| | | | Ataxia | 0 to 5 hours | |
| | | | Yellow/brown stained fur - perianal region | Days 1 and 2 | |
| | | | Crusty eyes | Days 1-PM and 2-AM | |
| AE9936 | F | Lethargy | 0 to 5 hours; day 1-AM | | |
| | | Ataxia | 0 to 5 hours | | |
| | | Yellow/brown stained fur - perianal region | Day 1 | | |
| | | Crusty nose | Day 2-AM | | |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|----------|---|---|
| 2,239 (cont.) | AE9937 | F | Lethargy | 0 to 5 hours; days 1 to 7 and 9-PM to 11-AM |
| | | | Ataxia | 0 to 5 hours; day 11-AM |
| | | | Loose stools | 1 to 5 hours |
| | | | Yellow/brown stained fur - perianal region | 1 to 5 hours; days 1 to 5, 10, and 11-AM |
| | | | Squinting | 3 to 5 hours; day 11-AM |
| | | | Crusty eyes | Day 2 |
| | | | Abdomen appeared swollen | Days 6 to 11-AM |
| | | | Piloerection | Days 8 to 11-AM |
| | | | Body cool to touch | Day 11-AM |
| | | | Found dead | Day 11-PM |
| 2,512 | AE9938 | F | Lethargy | 0 to 4 hours |
| | | | Ataxia | 1 to 4 hours |
| | | | Loose stools and yellow/brown stained fur - perianal region | 1 to 5 hours |
| | | | Squinting | 3 to 5 hours |
| | | | Prostration | 4 to 5 hours |
| | Found dead | Day 1-AM | | |
| | AE9940 | F | Lethargy, ataxia, and loose stools | 1 to 5 hours |
| | | | Yellow/brown stained fur - perianal region | 1 to 5 hours; day 1 |
| | | | Squinting | 3 to 5 hours; day 1 |
| | | | Prostration, irregular breathing, and moribund | Day 1 |
| Lacrimation | | | Day 1-PM | |
| Found dead | Day 2-AM | | | |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

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PM = Late afternoon

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APPENDIX C (continued): INDIVIDUAL MAIN STUDY
ABNORMAL CLINICAL SIGN DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Abnormal Clinical Signs | Time Interval Observed |
|--------------------|---------------|-----|--|------------------------|
| 2,512 (cont.) | AE9941 | F | Lethargy | 0 to 3 hours |
| | | | Ataxia | 1 to 3 hours |
| | | | Prostration | 3 to 5 hours |
| | | | Red stained fur - perianal region | 4 to 5 hours |
| | | | Found dead | Day 1-AM |
| | AE9942 | F | Lethargy | 0 to 5 hours |
| | | | Ataxia, loose stools, and yellow/brown stained fur - perianal region | 1 to 5 hours |
| | | | Red stained fur - perianal region | 2 to 5 hours |
| | | | Squinting | 4 to 5 hours |
| | | | Found dead | Day 1-AM |
| | AE9943 | F | Lethargy and ataxia | 0 to 5 hours |
| | | | Loose stools and yellow/brown stained fur - perianal region | 1 to 5 hours |
| | | | Red stained fur - perianal region | 2 to 5 hours |
| | | | Squinting | 4 to 5 hours |
| | | | Found dead | Day 1-AM |

NOTE: Hour intervals indicate the time abnormal clinical signs were observed following dosing on day 0. Day indicates the time abnormal clinical signs were observed on the days following dosing. If an abnormal clinical sign was observed in the early morning and late afternoon of a day, no AM and PM designations are presented.

AM = Early morning

PM = Late afternoon

APPENDIX D: INDIVIDUAL MAIN STUDY MORTALITY AND GROSS
 NECROPSY DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Organ(s) | Abnormality Observed |
|--------------------|---------------|-----|------------------------------|--------------|---|
| 1,778 | AE9847 | M | SS, 14 | Stomach (GL) | Thickening of mucosa Discoloration, diffuse, black-red-green, ca. 75 to 100% involved Possible perforation in stomach wall, ca. 0.2 cm. Stomach (NG) Thickened, diffuse, moderate Small Intestine Discoloration, diffuse, red, ca. 50 to 75% involved Abdominal Cavity Fluid, diffuse, red, possibly blood, ca. 2.0 to 4.0 ml. |
| | AE9848 | M | FD, 2 | Stomach (GL) | |
| | AE9849 | M | SS, 14 | | |
| | AE9850 | M | SS, 14 | | |
| | AE9851 | M | SS, 14 | | |
| | AE9852 | M | SS, 14 | | |
| | AE9853 | M | SS, 14 | | |
| | AE9854 | M | SS, 14 | Stomach (GL) | |
| | AE9855 | M | SS, 14 | Stomach (GL) | |
| | AE9856 | M | SS, 14 | | |
| 2,239 | AE9857 | M | SS, 14 | Stomach (GL) | Thickening of mucosa Discoloration, diffuse, green-brown, firm, rough, ca. 75 to 100% involved External Surface (ocular region) Exudate, diffuse, black, bilateral, mild |
| | AE9858 | M | FD, 2 | Stomach (GL) | |

FD = Found dead
 ca. = approximately

SS = Scheduled sacrifice
 GL = Glandular portion
 NG = Non-glandular portion

APPENDIX D (continued): INDIVIDUAL MAIN STUDY MORTALITY
 AND GROSS NECROPSY DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Organ(s) | Abnormality Observed |
|--------------------|---------------|-----|------------------------------|---|--|
| 2,239 (cont.) | AE9859 | M | FD, 2 | Stomach (GL) | Depression, black, ca. 0.1 cm. Discoloration, diffuse, red-black, ca. 75 to 100% involved |
| | | | | External Surface (ocular region) | Exudate, diffuse, black, bilateral, crusted, moderate |
| | AE9860 | M | SS, 14 | Stomach (GL) | Sloughing of mucosa |
| | AE9861 | M | SS, 14 | Stomach (GL) | Sloughing of mucosa |
| 2,512 | AE9862 | M | SS, 14 | | None |
| | AE9863 | M | SS, 14 | Skin (perianal region) | Discoloration, yellow-brown stained fur |
| | | | | Stomach (GL) | Thickened appearance |
| | | | | Stomach (NG) | Sloughing of mucosa |
| | AE9864 | M | FD, 2 | External Surface (ocular and nasal regions) | Exudate, diffuse, black, bilateral, crusted, mild |
| | | | | Stomach (GL) | Thickened, diffuse, green-red, moderate, ca. 75 to 100% involved |
| | | | | Stomach (NG) | Thickened, diffuse, moderate, ca. 75 to 100% involved |
| | AE9865 | M | FD, 11 | Stomach | Dilated, severe, filled with food |
| | | | | Stomach (GL) | Discoloration, diffuse, red, ca. 75 to 100% involved |
| | | | Stomach (GL and NG) | Apparent mucosal sloughing | |

FD = Found dead
 ca. = approximately

SS = Scheduled sacrifice
 GL = Glandular portion
 NG = Non-glandular portion

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APPENDIX D (continued): INDIVIDUAL MAIN STUDY MORTALITY
AND GROSS NECROPSY DATAACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Organ(s) | Abnormality Observed |
|--------------------|---------------|-----|------------------------------|------------------------|---|
| 2,512 (cont.) | AE9866 | M | SS, 14 | Stomach (GL) | Thickening of mucosa |
| 2,818 | AE9845 | M | FD, 1 | Skin (Perianal region) | Discoloration, yellow-brown stained fur |
| | | | | Lung | Discoloration, diffuse, red, severe |
| | | | | Stomach | Watery contents, ca. 2 ml. |
| | | | | Stomach (GL) | Discoloration of mucosa, diffuse, severe, red |
| | AE9846 | M | FD, 1 | Skin (Perianal region) | Discoloration, red stained fur |
| | | | | Stomach | Watery contents, ca. 2 ml. |
| | | | | Stomach (GL) | Discoloration, diffuse, black, severe |
| | | | | | Thickened, diffuse, moderate |
| | AE9867 | M | FD, 1 | Lung | Discoloration, diffuse, red, severe |
| | | | | Stomach | Watery contents, ca. 2 ml. |
| | | | | Stomach (GL) | Discoloration of mucosa, diffuse, black, severe |
| | AE9868 | M | FD, 1 | Skin (Perianal region) | Discoloration, brown stained fur |
| | | | | Stomach | Watery contents, ca. 2 ml. |
| | | | | Stomach (GL) | Discoloration of mucosal surface, red, moderate |

FD = Found dead
ca. = approximately

SS = Scheduled sacrifice
GL = Glandular portion

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APPENDIX D (continued): INDIVIDUAL MAIN STUDY MORTALITY
AND GROSS NECROPSY DATAACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Organ(s) | Abnormality Observed |
|--------------------|---------------|-----|------------------------------|---------------------------------|--|
| 2,818 (cont.) | AE9869 | M | FD, 1 | Skin (Perianal region) | Discoloration, brown stained fur |
| | | | | Stomach | Watery contents, ca. 2 ml. |
| | | | | Stomach (GL) | Discoloration of mucosa, black |
| 1,778 | AE9923 | F | FD, 9 | Skin (Perianal region) | Discoloration, yellow-brown stained fur |
| | | | | Stomach | Severe dilatation, impacted with food |
| | | | | Stomach (GL) | Discoloration, diffuse, black, moderate |
| | AE9924 | F | FD, 2 | External Surface (nasal region) | Exudate, diffuse, red-black, crusted, mild |
| | | | | Stomach (GL) | Thickened, diffuse, green-brown, moderate, ca. 75 to 100% involved |
| | AE9925 | F | SS, 14 | Stomach (GL) | Thickened, diffuse, moderate |
| | AE9926 | F | SS, 14 | Stomach (GL) | Thickening of mucosa |
| | AE9927 | F | SS, 14 | Stomach (GL) | Thickened, diffuse, moderate |
| | | | | Stomach (NG) | Thickened, diffuse, mild |
| | | | | Uterus | Apparent mucosal sloughing Discolorations, multiple, red-black, nodular |

FD = Found dead
ca. = approximately

SS = Scheduled sacrifice
GL = Glandular portion
NG = Non-glandular portion

APPENDIX D (continued): INDIVIDUAL MAIN STUDY MORTALITY
AND GROSS NECROPSY DATAACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Organ(s) | Abnormality Observed | |
|--------------------|---------------|--------|------------------------------|----------------------------------|--|--|
| 1,995 | AE9928 | F | SS, 14 | Stomach | Thickened, diffuse, moderate - GL, mild - NG | |
| | AE9929 | F | SS, 14 | Stomach (GL) | Thickening of mucosa | |
| | AE9930 | F | FD, 3 | External Surface (ocular region) | Exudate, diffuse, black, bilateral, mild, crusted | |
| | | | | Stomach (GL) | Thickened, diffuse, green-brown-black, moderate, ca. 75 to 100% involved | |
| | | | | Stomach (NG) | Thickened, diffuse, clear, edematous, moderate, ca. 75 to 100% involved | |
| | AE9931 | F | SS, 14 | Stomach | Thickened, diffuse, moderate - GL, edematous and moderate - NG | |
| | AE9932 | F | FD, 2 | External Surface (ocular region) | Exudate, diffuse, black, bilateral, crusted, mild | |
| | | | | Stomach (GL) | Discoloration, diffuse, black-green, ca. 75 to 100% involved | |
| | 2,239 | AE9933 | F | FD, 1 | External Surface (oral region) | Exudate, diffuse, red, mild |
| | | | | | Stomach (GL) | Discoloration, diffuse, black-red, ca. 75 to 100% involved |

FD = Found dead
ca. = approximately

SS = Scheduled sacrifice
GL = Glandular portion
NG = Non-glandular portion

APPENDIX D (continued): INDIVIDUAL MAIN STUDY MORTALITY
AND GROSS NECROPSY DATAACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Organ(s) | Abnormality Observed |
|--------------------|---------------|-----|------------------------------|--|--|
| 2,239 (cont.) | AE9934 | F | FD, 2 | External Surface (pelvic and nasal regions) | Exudate, diffuse, red, crusted, moderate |
| | | | | Stomach (GL) | Thickened, diffuse, brown-green-red, moderate, ca. 75 to 100% involved |
| | | | | Small Intestine | Discoloration, diffuse, red, ca. 5 to 15% involved |
| | AE9935 | F | SS, 14 | Stomach | Thickened, diffuse, moderate - GL, edematous and mild - NG |
| | | | | Stomach (NG) | Apparent mucosal sloughing |
| | AE9936 | F | SS, 14 | Stomach (GL) | Thickened mucosa |
| | AE9937 | F | FD, 11 | Stomach | Dilated, severe |
| | | | Stomach (GL) | Apparent mucosal sloughing (GL and NG) | |
| | | | Stomach (GL) | Discoloration, diffuse, red-black, ca. 75 to 100% involved | |
| 2,512 | AE9938 | F | FD, 1 | Stomach (GL) | Thickened, diffuse, moderate |
| | | | | Stomach (NG) | Discoloration, diffuse, green-red-white, ca. 75 to 100% involved |
| | AE9940 | F | FD, 2 | Stomach (GL) | Thickened, diffuse, clear, edematous, ca. 75 to 100% involved |
| | | | Stomach (GL) | Thickened, diffuse, green-brown-red, moderate, ca. 75 to 100% involved | |

FD = Found dead
ca. = approximately

SS = Scheduled sacrifice
GL = Glandular portion
NG = Non-glandular portion

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APPENDIX D (continued): INDIVIDUAL MAIN STUDY MORTALITY
AND GROSS NECROPSY DATA

ACUTE ORAL LD₅₀ STUDY IN RATS

TEST ARTICLE: 83-52A

| Dose Level (mg/kg) | Animal Number | Sex | Animal Fate and Day of Death | Organ(s) | Abnormality Observed | |
|--------------------|---------------|-----|------------------------------|--------------|--|---|
| 2,512 (cont.) | AE9941 | F | FD, 1 | Lung | Discolorations, multiple (more than 5), focal, red, ca. 0.1 to 0.3 cm. | |
| | | | | Spleen | Enlarged, mild | |
| | | | | Stomach (GL) | Discoloration, diffuse, green-red, ca. 75 to 100% involved | |
| | | | | | Stomach (NG) | Thickened, diffuse, clear, edematous, ca. 75 to 100% involved |
| | | | | | Urinary Bladder | Fluid, diffuse, amber, moderate |
| | AE9942 | F | FD, 1 | Stomach (GL) | Discoloration, diffuse, green-red, ca. 75 to 100% involved | |
| | | | | Stomach (NG) | Thickened, diffuse, clear, edematous, ca. 75 to 100% involved | |
| | AE9943 | F | FD, 1 | Stomach (GL) | Discoloration, diffuse, green-red, ca. 75 to 100% involved | |
| | | | | Stomach (NG) | Thickened, diffuse, edematous, ca. 75 to 100% involved | |

FD = Found dead
ca. = approximately

GL = Glandular portion
NG = Non-glandular portion