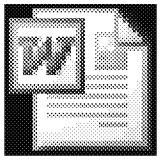
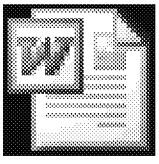
Message

From: GARNETT, RICHARD P [AG/5040] [/O=MONSANTO/OU=EA-5041-01/CN=RECIPIENTS/CN=107838]
Sent: 8/20/2008 2:50:57 PM
To: SERYAPIN, ALEXANDER [AG/5276] [/O=MONSANTO/OU=EA-5040-01/CN=RECIPIENTS/CN=193435]; KAEMPFE, TERRY A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=129103]
CC: VELCEV, MARIN [AG/6170] [/O=MONSANTO/OU=EA-5040-01/CN=RECIPIENTS/CN=1724]; BELVAUX, XAVIER [AG/5040] [/O=MONSANTO/OU=EA-5041-01/CN=RECIPIENTS/CN=234727]; SALTMIRAS, DAVID A [AG/1000] [/O=MONSANTO/OU=NA-1000-01/CN=RECIPIENTS/CN=DASALT]
Subject: RE: MON 78273 for Russia
Attachments: Acute Nose-Only Inhalation Toxicity Study In Rats With MON 78623.pdf; TI summary_acute inhalation_K salt.doc; inhalation risk MON 78273.doc

Sacha,
MON 78623 is the technical K salt of glyphosate, 58% K salt of glyphosate dissolved in water. In the manufacturing process K salt is not isolated. Attached is a copy of the full MON 78623 inhalation study, laboratory study no. 3044.969, Monsanto study no. SB-2003-116 .



Under EU regulations there is no requirement for an inhalation study on the formulated product where it can be demonstrated that the risk of exposure through inhalation is very low. Here is our argumentation which has been successful in all EU MS for all formulations. The inhalation protocol requires a very artificial situation where an aerosol is generated, to achieve an airborne load which is impossible in practice. Therefore our view is that such studies are not relevant to the use of and risk from Roundup products, and merely waste laboratory animals (which is illegal in the EU). Surfactants are typically inhalation toxic if presented as an aerosol, so it would not be surprising if inhalation studies of products containing surfactants were positive.



However, there is a study on a similar formulation which you may be able to use if these arguments fail. The study is on MON 78270,
MON 78270 contains the same concentration of glyphosate as the K salt, and the same surfactant at the same concentration. MON 78270 differs from MON 78273 by the presence of 0.27% citric acid. Citric acid does not have specific properties which would require additional toxicological testing. Thus, except for the skin sensitisation study, the studies conducted with MON 78270 have been used to assess the toxicological profile of MON 78273.

This study shows (not surprisingly) that MON 78270 would be classified in the EU:

T Toxic; R23 Toxic by inhalation
LC50 inhalation, rat, aerosols : 0,25 < LC50 ≤ 1 mg/litre/4h

Terry,
Could you comment, please, having been deeply involved in all the discussions on K salt inhalation studies a few years ago.

Thanks and regards

Richard

-----Original Message-----
From: SERYAPIN, ALEXANDER [AG/5276]
Sent: 13 August 2008 07:27
To: GARNETT, RICHARD P [AG/5040]
Cc: VELCEV, MARIN [AG/6170]
Subject: MON 78273 for Russia

Richard,

As we discuss last time I need have follow documents:

- acute inhalation toxicity for glyphosate potassium salt;
- acute inhalation toxicity for formulation, otherwise I should order this research in Moscow (the same problem will be with Zanussi).

I need the toxicological, ecological and technical information on Zanussi. It is necessary for preparation of the application.

Best regards
Sasha

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS WITH MON 78623

FINAL REPORT

Data Guidelines

EPA-OPPTS, OECD, EEC, JMAFF

Author

Kimberly L. Bonnette, M.S., LATG

Study Completed on

February 6, 2004

Performing Laboratory

Charles River Laboratories, Inc. (CRL)
Discovery and Development Services
[redacted]

Study No.

3044.969

Monsanto Study No.

SB-2003-116

Submitted to:

Monsanto Company
800 N. Lindbergh Blvd.
St. Louis, MO 63167

1. 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).

"We submitted this material to the United States Environmental Protection Agency specifically under provisions contained in FIFRA as amended, and thereby consent to the use and disclosure of this material by EPA according to FIFRA. Some pages of this report may be stamped with the following: CONTAINS TRADE SECRET OR OTHERWISE CONFIDENTIAL INFORMATION OF MONSANTO COMPANY. This claim of confidentiality is not meant to convey supplemental claims of confidentiality regarding data subject to disclosure under sections 10 (d) and (e) of FIFRA. In submitting this material to the EPA according to method and format requirements contained in PR Notice 86-5, we do not waive any protection rights involving this material that would have been claimed by the company if this material had not been submitted to the EPA."

COMPANY: _____

COMPANY AGENT: _____

_____ _____

TITLE DATE

2. COMPLIANCE STATEMENT

This study was conducted in compliance with the Good Laboratory Practice Standards as described by the EPA (40 CFR Parts 160 and 170), the OECD [ENV/MC/CHEM(98)17] and the Japanese Ministry of Agriculture, Forestry and Fisheries (11 Nousan No. 6283).

K L Bonnette

Date 2/6/04

Kimberly L. Bonnette, M.S., LATG
Study Director/Author
CRL

_____

Date _____

Sponsor/Submitter
Monsanto Company

3. QUALITY ASSURANCE STATEMENT

This study has been inspected by the Quality Assurance Unit to assure conformance with the Good Laboratory Practice (GLP) regulations promulgated by EPA (40 CFR Parts 160 and 170), OECD [ENV/MC/CHEM(98)17] and JMAFF (11 Nousan No. 6283). Reports were submitted in accordance with Standard Operating Procedures as follows:

QA INSPECTION DATES

Dates of Inspection	Phase(s) Inspected	Date Findings Submitted: Study Director	Date Findings Submitted: Study Director Management
10/23/03	Protocol Review	01/29/04	01/29/04
10/29/03	Dose Preparation	01/29/04	01/29/04
12/03/03	Animal Receipt	12/03/03	12/03/03
01/29/04	Data Audit	01/29/04	01/29/04
01/29/04	Draft Report Review	01/29/04	01/29/04
01/29/04	Analytical Chemistry Review	01/29/04	01/29/04
01/29/04	Analytical Chemistry Report Review	01/29/04	01/29/04
02/06/04	Final Report Review	02/06/04	02/06/04

The final report has been reviewed to assure that it accurately describes the materials and methods, and the reported results accurately reflect the raw data.

Rebecca A. Young
Quality Assurance Team Leader

Date 2/6/04

4. TABLE OF CONTENTS

5. SUMMARY

The four-hour nose-only inhalation toxicity of MON 78623 was evaluated in Sprague Dawley rats. Two limit tests were performed in which one group of five male and five female rats each received a four-hour nose-only inhalation exposure to a time-weighted average aerosol concentration (analytically determined) of 2.21 or 5.27 mg/L. For the first exposure (2.21 mg/L) the mass median aerodynamic diameter and geometric standard deviation of the sampled particles were 2.9 μ and 2.18, respectively. The percentage of particles ≤ 4.0 μ was determined to be 67%. Since there was no mortality, a second limit test was conducted at a greater target concentration. For the second exposure (5.27 mg/L) the mass median aerodynamic diameter and geometric standard deviation of the sampled particles were 3.8 μ and 2.20, respectively. The percentage of particles ≤ 4.0 μ was determined to be 53%. Following each exposure, the limit test rats were observed daily and weighed weekly. A gross necropsy examination was performed on all limit test animals at the time of scheduled euthanasia (day 14).

No mortality occurred for the 2.21 mg/L dose level. The most notable clinical abnormalities observed during the study included transient incidences of congested breathing and dark material around the facial area. Body weight gain was noted for all animals during the test period. No gross internal findings were observed at necropsy on study day 14.

No mortality occurred for the 5.27 mg/L dose level. The most notable clinical abnormalities observed during the study included transient incidences of congested breathing and few feces. Slight body weight loss was noted for two females during the day 0 to 7 body weight interval and for one female during the day 7 to 14 body weight interval. Body weight gain was noted for all other animals during the test period and all animals exceeded their initial body weight at study termination. No gross internal findings were observed at necropsy.

Under the conditions of this test, the acute inhalation LC50 of MON 78623 was estimated to be greater than 5.27 mg/L in the rat.

6. INTRODUCTION

This study was performed to assess the short-term toxicity of MON 78623 in Sprague Dawley rats when administered by a four-hour nose-only inhalation exposure. This study was intended to provide information on the potential health hazards of the test article with respect to inhalation exposure. Data from this study may serve as a basis for classification and/or labeling of the test article. This study was performed at CRL-Ohio Division, 553 North Broadway, Spencerville, Ohio. The protocol was signed by the Study Director on October 22, 2003 (GLP initiation date). The in-life phase of the study was initiated with test article administration on October 29, 2003 (day 0), and concluded with necropsy on December 29, 2003.

7. MATERIALS AND METHODS

7.1. Experimental Protocol

This study was performed in general conformance with the US EPA, Health Effects Test Guidelines, OPPTS 870.1300, Acute Inhalation Toxicity, August 1998; the OECD Guidelines for the Testing of Chemicals, Section 4: Health Effects, Subsection 403, May 12, 1981; the EEC Part B: Methods for the Determination of Toxicity, B.2, No. L 383 A/117, December 29, 1992; and the JMAFF Agchem Test Guideline, 12 Nohsan No. 8147, 24 November 2000, Revised 26 June 2001, Acute Inhalation Toxicity (2-1-3).

7.2. Test Article

The test article was received from the Sponsor and identified as follows:

Sponsor's ID	Assigned CRL ID	Physical Description	Receipt Dates	Expiration Date
MON 78623 Lot No. GLP-0306-14124-F	S03.018.3044	Clear colorless liquid (pipet); light amber liquid (bulk)	10/20/03 11/25/03	06/04[a]
Purity: 47.2% glyphosate (a.e.), [57.8% potassium salt of glyphosate]				

[a] Last assay – 06/03.

The test article was stored at room temperature. The Sponsor was responsible for any necessary evaluations related to identity, strength, purity, composition, stability and method of synthesis of the test material according to 40 CFR 160.105, 40 CFR 792.105, ENV/MC/CHEM(98)17 and 11 Nousan No. 6283.

7.3. Retention Sample

An approximate 1 mL retention sample was taken and stored at the testing facility at room temperature.

7.4. Test Article Disposition

The remaining test article was returned to the Sponsor following completion of all studies with the test article.

7.5. Method of Test Article Preparation

The test article was utilized as received from the Sponsor and dispensed fresh on the day of dosing. The test article was stirred continuously during the exposure.

7.6. Animals and Animal Husbandry

7.6.1. Description, Identification and Housing

Young adult, Hsd: Sprague Dawley® SD® rats were received on October 22, 2003 and December 3, 2003, from Harlan Sprague Dawley Inc., Indianapolis, Indiana. Upon receipt, metal ear tags displaying unique identification numbers were used to individually identify the animals. Cage cards displaying at least the study number, animal number and sex were affixed to each cage. The animals were housed individually in suspended stainless steel cages. All housing and care were based on the standards recommended by the Guide for the Care and Use of Laboratory Animals [1].

7.6.2. Environment

The animal room temperature and relative humidity ranges were 67-74°F (19-23°C) and 31-65%, respectively. Environmental control equipment was monitored and adjusted as necessary to minimize fluctuations in the animal room environment. Light timers were set to maintain a 12-hour light/12-hour dark cycle and room ventilation was set to produce 10-15 air changes/hour. The animal room temperature and relative humidity were recorded a minimum of once daily.

7.6.3. Food

PMI Certified Rodent Chow #5002 (PMI Nutrition International) was provided *ad libitum* to the animals throughout the study (except during the time that the animals were acclimated to the exposure tubes and maintained in the inhalation room for the exposure procedure). The lot number and expiration date of each batch of diet used during the study were recorded. The feed was analyzed and certified by the supplier for nutritional components and environmental contaminants. Dietary limitations for various environmental contaminants, including heavy metals, pesticides, polychlorinated biphenyls and total aflatoxin are set by the manufacturer. Within these limits, contaminants which may have been present were not expected to compromise the purpose of this study. Results of the dietary analyses (Certificates of Analysis) are provided by the manufacturer for each lot of diet. These are maintained by the testing facility.

7.6.4. Water

Municipal tap water treated by reverse osmosis was available *ad libitum* throughout the study (except during the time that the animals were acclimated to the exposure tubes and maintained in the inhalation room for the exposure procedure). The purified water was supplied by an automatic watering system. Monitoring of the drinking water for contaminants is conducted by the testing facility and the records are available for inspection. Within generally accepted limits, contaminants which may have been present were not expected to compromise the purpose of this study. The water meets the standards specified under the EPA National Drinking Water Regulations (40 CFR Part 141).

7.6.5. Acclimation

Upon receipt, the animals were removed randomly from the shipping cartons, examined by qualified personnel, identified with metal ear tags and then acclimated to the laboratory conditions for a minimum of five days. The animals were observed daily for overt physical or behavioral abnormalities, general health/moribundity and mortality.

7.6.6. Animal Selection

The animals chosen for study use were randomly selected from healthy stock animals using a computerized random numbers table to avoid potential bias. All animals received a detailed pretest observation prior to dosing. Only healthy animals were chosen for study use. Females were nulliparous and nonpregnant. The male animals were approximately 8 to 9 weeks of age and weighed 276-312 grams on the day of exposure. The female animals were approximately 8 to 9 weeks of age and weighed 182-210 grams on the day of exposure.

8. EXPERIMENTAL PROCEDURES

8.1. Preliminary Procedures

8.1.1. Test Article Volatility Determination

The volatility of the test article relative to a distilled water standard was determined prior to experimental initiation. This procedure was performed in order to determine if the test article had sufficiently low volatility to allow for an accurate gravimetric determination of the aerosol concentration. A known quantity of the test article was placed on a preweighed filter disk and was allowed to evaporate for a total of ten minutes. The test article weight was determined each minute and the amount of evaporation of the test article was then determined. The results of this volatility trial indicated that the test article evaporation rate (0.44 mg/minute) was slightly lower than the testing facility determined distilled water evaporation rate (0.55 mg/minute) and therefore was considered to not be volatile.

8.1.2. Preliminary Aerosol Generation Trials

Prior to experimental initiation, preliminary aerosol generation trials were conducted. These trials were performed in order to determine the most efficient means of generating an aerosol

of the appropriate concentration while utilizing equipment that would reduce the aerodynamic particle size. Based on the initial trial work, a concentration ≥ 2.0 mg/L was to be targeted for the first exposure. However, since there was no mortality at the first target level, at the Sponsor's request, a ≥ 5.0 mg/L dose level was also targeted for the second exposure. Data obtained during the preliminary aerosol generation trials are presented in Appendix 1.

8.2. Limit Test

8.2.1. Aerosol Generation Equipment

The test aerosol was generated with a Master Flex Pump and Pump Head (7523-30 and 77200-60) and a Pistol Spraying System. Conditioned high pressure external air was used in generating the test atmosphere. The aerosol was blown through a 5L Elutriator, the Multi-Stage 10L nose-only inhalation chamber and then vented from the chamber to an air treatment system which consisted of a prefilter, a HEPA filter, a charcoal bed and a water scrubbing tower (see Figure 1).

8.2.2. Dosing

On day 0, the animals chosen for the limit test were weighed, placed in a nose-only exposure tube and allowed to acclimate to the exposure tube for at least one hour. Animals that appeared to have been acclimated to the exposure tube (i.e., minimal struggling and no inversion) were considered to be acceptable. Animals that did not appear to acclimate to the exposure tube were not acceptable. All animals were removed from the exposure tubes and returned to their cages.

The acceptable animals were then placed in exposure tubes and the tubes inserted into the Multi-Stage 10L nose-only inhalation chamber and the test article aerosolized at the following levels:

Analytical Exposure Level (mg/L)	No. of Animals	
	Male	Female
2.36	5	5
5.27	5	5

Each aerosol exposure consisted of a 3-minute T99 equilibration period, a 240-minute exposure period and a 3-minute de-equilibration period equal to the T99 equilibration period. After each aerosol exposure, animals were removed from the exposure tubes and residual test article was removed from the animal's exterior surfaces (where practical) by wiping the haircoat with a towel. The animals were then returned to *ad libitum* feed and water. The following parameters were measured during the exposure.

8.2.2.1. Chamber Air Flow

Air flow readings were recorded at the initiation of the T99 equilibration period, at approximately 30-minute intervals during each aerosol exposure and at the conclusion of the de-equilibration period.

8.2.2.2. Aerosol Concentration

The aerosol concentration was measured at the beginning of each aerosol exposure (after equilibration), at approximate 30-minute intervals during the aerosol exposure, and at the conclusion of each aerosol exposure (before de-equilibration). Samples of the test article aerosol were collected in the inhalation chamber by gravimetric technique. Both gravimetric and analytical aerosol concentrations were determined. A 5 L sample of the aerosol was drawn from the breathing zone of the animals in the chamber through a preweighed glass fiber filter. For the analytical concentration, the gravimetrically obtained samples were analyzed by liquid chromatography for the non-volatile glyphosate component of the test article. These analyses were performed in order to determine the analytical (actual) concentrations of the aerosol in the chamber for each sampling period. The average time weighted analytical concentration of the test atmosphere was then calculated for each exposure. Chemistry methods and results are detailed in the Analytical Chemistry Report in Appendix 2.

Note: Gravimetric concentrations were determined as a marker in order to make adjustments during the actual exposure since the chemistry methodology could not be conducted during the exposure. Since the aerosol concentration was based on analytical chemistry data, the gravimetric data is not presented and will remain in the raw data only.

8.2.2.3. Chamber Temperature and Humidity

The chamber temperature and humidity were measured electronically and recorded at approximate 30-minute intervals during each aerosol exposure using a Vaisala HMI 41 Thermohygrometer.

8.2.2.4. Aerosol Aerodynamic Particle-Size Distribution

The aerosol aerodynamic particle-size distribution was determined three times during each aerosol exposure using the ITP 7 Stage Cascade Impactor. Each stage of the impactor was fitted with a preweighed glass fiber filter. Five liters per minute of the chamber air were

drawn through the impactor and the change in weight of each filter was then determined and recorded. The mean particle-size distribution was subsequently determined using an Excel computer adaptation of the manual method. The Mass Median Aerodynamic Diameter, Geometric Standard Deviation and percentage of particles ≤ 4.0 µ were then determined.

8.2.2.5. Chamber Oxygen

Chamber oxygen content was measured and recorded at approximate 30-minute intervals during each aerosol exposure using a GC-501 Oxygen Detector.

8.2.3. Clinical Observations

The limit test animals were observed for clinical abnormalities during each aerosol exposure (no positive clinical observations were noted during either exposure), two times on study day 0 (post-exposure) and daily thereafter (days 1-14). Clinical observations included but were not limited to changes in the skin and fur, eyes and mucous membranes, respiratory system, circulatory system, autonomic and central nervous systems, including tremors and convulsions, changes in the level of activity, gait and posture, reactivity to handling or sensory stimuli, altered strength and stereotypies or bizarre behavior. A general health/mortality check was performed twice daily (in the morning and in the afternoon).

8.2.4. Body Weights

Individual body weights were obtained for the limit test animals prior to exposure on day 0 and for all animals on days 7 and 14.

8.2.5. Gross Necropsy

All animals were euthanized by carbon dioxide inhalation at study termination (day 14) and were necropsied. Body cavities (cranial, thoracic, abdominal and pelvic) were opened and examined. No tissues were retained.

8.3. Protocol Deviations

No protocol deviations occurred during this study.

9. DATA ACQUISITION AND ELECTRONIC RECORDS

Electronic data were recorded on a Compaq Alpha Server DS10 utilizing the Toxicology Analysis System Customized, Acute Toxicology Module, Version 1.0.0 or higher. The testing facility study number assigned to this study is 3044.969. The computer study number used to collect data for the study phases was 3044969. The tables within the report display the applicable computer study number.

10. ANALYSIS OF DATA

Data from the limit test were analyzed and an LC50 value estimated as follows:

<50% Mortality: LC50 was estimated as greater than the administered dose.
=50% Mortality: LC50 was estimated as equal to the administered dose.
>50% Mortality: LC50 was estimated as less than the administered dose.

Body weight means and standard deviations were calculated separately for males and females. The aerodynamic particle-size distribution of the test article aerosol was plotted using an Excel computer adaptation of the three cycle logarithmic probability paper as per the ITP Cascade Impactor instruction manual. The Mass Median Aerodynamic Diameter, Geometric Standard Deviation and particles $\leq$ 4.0 µ were determined based on the distribution.

11. MAINTENANCE OF RAW DATA AND RECORDS

The following records were transferred to the testing facility archives for a period of seven years from issuance of the final report.

-Protocol, protocol amendments and protocol deviations
-Study-related correspondence
-Test article receipt, utilization and preparation data
-Animal husbandry data
-In-life and pathology data
-Final report

The Sponsor will be contacted prior to final disposition of these items.

12. RESULTS

12.1. Aerosol Generation and Chamber Environmental Data

12.1.1. Aerosol Generation Data

Summary Data: Table 1
Individual Data: Appendix 3

For the first exposure (2.21 mg/L) the mass median aerodynamic diameter and geometric standard deviation of the sampled particles were 2.9 µ and 2.18, respectively. The percentage of particles $\leq$ 4.0 µ was determined to be 67%. Since there was no mortality, a second limit test was conducted at a greater target concentration. For the second exposure (5.27 mg/L) the mass median aerodynamic diameter and geometric standard deviation of the sampled particles were 3.8 µ and 2.20, respectively. The percentage of particles $\leq$ 4.0 µ was determined to be 53%.

12.1.2. Chamber Environmental Data

Summary Data: Table 1
Individual Data: Appendix 3

For the first exposure the chamber temperature and relative humidity for the aerosol exposure ranged from 71.2-73.1°F and 52.2-60.1%, respectively. For the second exposure the chamber temperature and relative humidity for the aerosol exposure ranged from 70.4-71.5°F and 65.7-67.9%, respectively. Oxygen content was maintained at 20.9% throughout each exposure.

12.2. Limit Test Data

12.2.1. Mortality

Individual Data: Table 2

No mortality occurred for the 2.21 mg/L and 5.27 mg/L dose levels.

12.2.2. Clinical Observations

Individual Data: Table 2

The most notable clinical abnormalities observed for the 2.21 mg/L dose level included transient incidences of congested breathing and dark material around the facial area.

The most notable clinical abnormalities observed for the 5.27 mg/L dose level included transient incidences of congested breathing and few feces.

12.2.3. Body Weight Data

Individual Data: Table 3

Body weight gain was noted for all animals for the 2.21 mg/L dose level.

For the 5.27 mg/L dose level, slight body weight loss was noted for two females during the day 0 to 7 body weight interval and for one female during the day 7 to 14 body weight interval. Body weight gain was noted for all other animals and all animals exceeded their initial body weight at study termination.

12.2.4. Gross Necropsy

Individual Data: Table 4

No gross internal findings were observed at necropsy for the 2.21 mg/L and 5.27 mg/L dose levels on study day 14.

13. CONCLUSION

Under the conditions of this test, the acute inhalation LC50 of MON 78623 was estimated to be greater than 5.27 mg/L in the rat.

Kimberly L. Bonnette, M.S., LATG
Study Director

Date 2/6/04

14. REPORT REVIEW

Rusty E. Rush, M.S., LAT, DABT
Director, Toxicology

Date 2-6-04

15. REFERENCE

1. Guide for the Care and Use of Laboratory Animals, DHHS Publication No. (NIH) 96-03, 1996.

16. TABLES

Table 1. Summary of Aerosol Generation and Chamber Environmental Data

TABLE 1

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS

SUMMARY OF AEROSOL GENERATION AND CHAMBER ENVIRONMENTAL DATA

	EXPOSURE LEVEL (MG/L)	
	2.21	5.27
CHAMBER AND EXPOSURE DATA		
CHAMBER VOLUME (L):	10	10
ELUTRIATOR VOLUME (L):	5	5
INITIAL CHAMBER AIR FLOW RATE (L/MIN):	25	24
CALCULATED AIR CHANGES PER HOUR:	100.00	95.24
T99 EQUILIBRATION PERIOD (MIN):	3	3
EXPOSURE TIME (MIN):	240	240
DE-EQUILIBRATION PERIOD (MIN):	3	3
AEROSOL CONCENTRATIONS		
CALCULATED NOMINAL CONCENTRATION (MG/L):	297.94	1460.22
TIME-WEIGHTED MEAN ANALYTICAL CONCENTRATION (MG/L):	2.21	5.27
AEROSOL PARTICLE-SIZE ANALYSIS		
MASS MEDIAN AERODYNAMIC DIAMETER (μ):	2.9	3.8
GEOMETRIC STANDARD DEVIATION:	± 2.18	± 2.20
PERCENTAGE OF PARTICLES ≤ 4.0 μ (%):	67	53
CHAMBER ENVIRONMENTAL DATA		
TEMPERATURE RANGE (°F):	71.2-73.1	70.4-71.5
HUMIDITY RANGE (%):	52.2-60.1	65.7-67.9
OXYGEN CONTENT (%):	20.9	20.9

Table 2. Individual Clinical Observations

TABLE 2

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

MALES 2.21 MG/L

MALE#	OBSERVATIONS	DAY OF STUDY 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
A8540	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P	P													
A8542	SCHEDULED EUTHANASIA															P
	DARK MATERIAL AROUND EYE(S)				P											
A8543	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P	P													
A8544	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P	P													
	DARK MATERIAL AROUND EYE(S)	P														
A8545	SCHEDULED EUTHANASIA															P

GRADE CODE: 1=SLIGHT 2=MODERATE 3=SEVERE P=PRESENT L=LEFT R=RIGHT B=BILATERAL

TABLE 2

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

MALES 5.27 MG/L

MALE#	OBSERVATIONS	DAY OF STUDY 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
A8729	SCHEDULED EUTHANASIA															P
A8726	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
A8730	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P	P	P												
A8731	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
A8735	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														

GRADE CODE: 1=SLIGHT 2=MODERATE 3=SEVERE P=PRESENT L=LEFT R=RIGHT B=BILATERAL

TABLE 2

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

FEMALES 2.21 MG/L

FEMALE#	OBSERVATIONS	DAY OF STUDY 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
A8551	SCHEDULED EUTHANASIA															P
	DARK MATERIAL AROUND EYE(S)	P														
A8555	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P	P													
A8557	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
A8558	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
	DARK MATERIAL AROUND EYE(S)	P														
	DARK MATERIAL AROUND NOSE	P														
A8559	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
	DARK MATERIAL AROUND EYE(S)	P							P							

GRADE CODE: 1=SLIGHT 2=MODERATE 3=SEVERE P=PRESENT L=LEFT R=RIGHT B=BILATERAL

TABLE 2

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL CLINICAL OBSERVATIONS
(POSITIVE FINDINGS)

FEMALES 5.27 MG/L

FEMALE#	OBSERVATIONS	DAY OF STUDY 0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
A8750	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
A8748	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
	FEW FECES		P													
A8749	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
A8752	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														
	FEW FECES		P													
A8753	SCHEDULED EUTHANASIA															P
	CONGESTED BREATHING	P														

GRADE CODE: 1=SLIGHT 2=MODERATE 3=SEVERE P=PRESENT L=LEFT R=RIGHT B=BILATERAL

Table 3. Individual Body Weights

TABLE 3

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES 2.21 MG/L

	DAY OF STUDY			
ANIMAL#	0	7	14	AT DEATH (DAY)
A8540	294	310	335	
A8542	312	337	364	
A8543	292	303	338	
A8544	288	292	327	
A8545	305	323	356	
MEAN	298	313	344	
S.D.	10.0	17.5	15.6	
N	5	5	5	

TABLE 3

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

MALES 5.27 MG/L

	DAY OF STUDY		
ANIMAL#	0	7	14 AT DEATH (DAY)
A8729	277	302	319
A8726	290	325	350
A8730	276	306	324
A8731	295	322	345
A8735	280	302	319
MEAN	284	311	331
S.D.	8.4	11.2	14.9
N	5	5	5

TABLE 3

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES 2.21 MG/L

	DAY OF STUDY		
ANIMAL#	0	7	14 AT DEATH (DAY)
A8551	194	212	234
A8555	185	193	209
A8557	182	200	213
A8558	188	196	214
A8559	184	202	216
MEAN	187	201	217
S.D.	4.7	7.3	9.5
N	5	5	5

TABLE 3

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL BODY WEIGHTS (GRAMS)

FEMALES 5.27 MG/L

	DAY OF STUDY		
ANIMAL#	0	7	14 AT DEATH (DAY)
A8750	206	219	222
A8748	199	197	204
A8749	210	226	220
A8752	201	195	206
A8753	187	198	211
MEAN	201	207	213
S.D.	8.7	14.4	8.1
N	5	5	5

Table 4. Individual Gross Necropsy Observations

TABLE 4

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL GROSS NECROPSY OBSERVATIONS

MALES 2.21 MG/L

ANIMAL#	DAY OF DEATH	STUDY DAY	OBSERVATION	FATE
A8540	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8542	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8543	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8544	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8545	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA

TABLE 4

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL GROSS NECROPSY OBSERVATIONS

MALES 5.27 MG/L

ANIMAL#	DAY OF DEATH	STUDY DAY	OBSERVATION	FATE
A8729	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8726	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8730	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8731	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8735	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA

TABLE 4

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

INDIVIDUAL GROSS NECROPSY OBSERVATIONS

FEMALES 2.21 MG/L

ANIMAL#	DAY OF DEATH	STUDY DAY	OBSERVATION	FATE
A8551	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8555	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8557	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8558	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8559	12-NOV-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA

TABLE 4

AN ACUTE NOSE-ONLY TOXICITY STUDY IN RATS

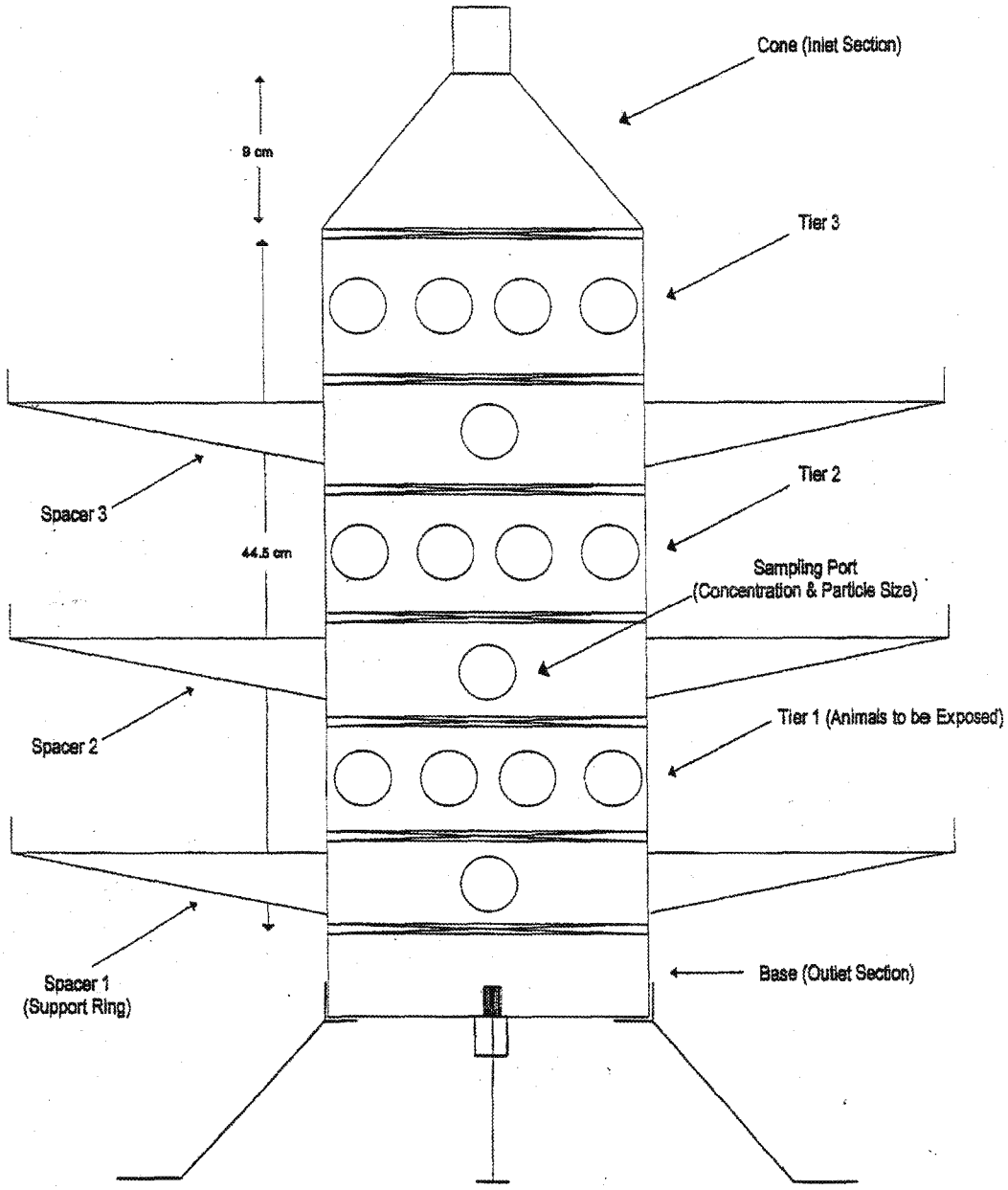
INDIVIDUAL GROSS NECROPSY OBSERVATIONS

FEMALES 5.27 MG/L

ANIMAL#	DAY OF DEATH	STUDY DAY	OBSERVATION	FATE
A8750	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8748	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8749	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8752	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA
A8753	29-DEC-03	14	ALL TISSUES WITHIN NORMAL LIMITS	SCHEDULED EUTHANASIA

17. FIGURE

Figure 1. Multi-Stage 10L Nose-Only Inhalation Chamber



MULTI-STAGE 10 L NOSE-ONLY INHALATION CHAMBER

18. APPENDICES

Appendix 1. Preliminary Aerosol Generation Trials

1. PRELIMINARY AEROSOL GENERATION TRIALS

Prior to experimental initiation, preliminary aerosol generation trials were conducted. These trials were performed to determine the appropriate means of generating the aerosol exposure atmosphere of the test article at the targeted ≥2.0 mg/L analytical concentration initially and aerodynamic particle size (1-4 microns Mass Median Aerodynamic Diameter). The type of equipment used during each trial procedure is presented in the table that follows.

A gravimetric concentration of approximately ≥2.0 mg/L was targeted initially by varying the pump speed from 2.0-6.5 mL/minute (Trial Nos. 1-7, 21-32). These trials indicated that the gravimetric concentration was proportional to the analytical concentration and, therefore, could be utilized as a "real time" estimate for the analytical concentration. The particle size (2.5 μ) obtained during Trial No. 2 (targeting a concentration of 2.0 mg/L) was acceptable. Since these trials indicated that the equipment was acceptable to produce the appropriate target concentration/particle size, the initial exposure (≥2.0 mg/L concentration) was conducted with this equipment using a pump speed of 5 mL/min.

A higher analytical concentration of 5.0 mg/L or maximum attainable concentration was also (Trials 8-20 and 33) explored. The particle size (3.2 μ) obtained during Trial No. 13 (targeting a concentration of 5.0 mg/L) was acceptable. These trials indicated that an additional increase in pump speed beyond 20 mL/minute did not necessarily increase the chamber concentration resulting in a maximum attainable analytical concentration of 5.0-5.9 mg/L. Therefore, this equipment was utilized at a 19 mL/min pump speed for the second exposure targeting an analytical concentration of ≥ 5.0 mg/L.

TRIAL TABLE 1

PRELIMINARY AEROSOL GENERATION TRIALS

TRIAL NO.	EQUIPMENT USED	INPUT AIR (PSI)	TEST ARTICLE CONCENTRATION (%)	MAXIMUM ATTAINABLE CONCENTRATIONS (MG/L)	
				GRAVIMETRIC	ANALYTICAL
1	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 2.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.06	--
2	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR ITP 7 STAGE CASCADE IMPACTOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 4.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	2.48	3.088
3	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 4.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	2.74	3.204
4	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 4.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	2.32	2.737
5	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 4.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	3.18	--

NOTE: TARGETING ≥ 2.00 MG/L GRAVIMETRIC CONCENTRATION FOR TRIALS 1-5.

TRIAL TABLE 1

PRELIMINARY AEROSOL GENERATION TRIALS

TRIAL NO.	EQUIPMENT USED	INPUT AIR (PSI)	TEST ARTICLE CONCENTRATION (%)	MAXIMUM ATTAINABLE CONCENTRATIONS (MG/L)	
				GRAVIMETRIC	ANALYTICAL
6	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 3.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	2.78	--
7	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 3.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	2.60	3.045
8	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 8.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.46	--
9	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 10.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.82	--
10	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 11.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	3.08	--

NOTE: TARGETING ≥ 2.00 MG/L GRAVIMETRIC CONCENTRATION FOR TRIALS 6-7.
TARGETING ≥ 5.00 MG/L GRAVIMETRIC CONCENTRATION FOR TRIALS 8-10.

TRIAL TABLE 1

PRELIMINARY AEROSOL GENERATION TRIALS

TRIAL NO.	EQUIPMENT USED	INPUT AIR (PSI)	TEST ARTICLE CONCENTRATION (%)	MAXIMUM ATTAINABLE CONCENTRATIONS (MG/L)	
				GRAVIMETRIC	ANALYTICAL
11	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 11.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.72	5.211
12	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 12.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.74	5.695
13	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR ITP 7 STAGE CASCADE IMPACTOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 15.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.88	4.655
14	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 20.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	5.04	5.387
15	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 20.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.82	--

NOTE: TARGETING $\geq$ 4.50 MG/L GRAVIMETIC CONCENTRATION FOR A $\geq$ 5.00 MG/L ANALYTICAL CONCENTRATION FOR TRIALS 11-15.

TRIAL TABLE 1

PRELIMINARY AEROSOL GENERATION TRIALS

TRIAL NO.	EQUIPMENT USED	INPUT AIR (PSI)	TEST ARTICLE CONCENTRATION (%)	MAXIMUM ATTAINABLE CONCENTRATIONS (MG/L)	
				GRAVIMETRIC	ANALYTICAL
16	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 21 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.68	--
17	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 22 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.84	5.751
18	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 23 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.66	--
19	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 20 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	5.16	5.720
20	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 20 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	5.14	5.874

NOTE: TARGETING $\geq$ 4.50 MG/L GRAVIMETRIC CONCENTRATION FOR A $\geq$ 5.00 ANALYTICAL CONCENTRATION FOR TRIALS 16-20.

TRIAL TABLE 1

PRELIMINARY AEROSOL GENERATION TRIALS

TRIAL NO.	EQUIPMENT USED	INPUT AIR (PSI)	TEST ARTICLE CONCENTRATION (%)	MAXIMUM ATTAINABLE CONCENTRATIONS (MG/L)	
				GRAVIMETRIC	ANALYTICAL
21	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 2.2 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	0.88	--
22	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 3.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	0.94	--
23	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 4.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.34	--
24	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 4.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.42	--
25	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 5.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.30	--

NOTE: TARGETING ≥ 2.00 MG/L GRAVIMETRIC CONCENTRATION FOR TRIALS 21-25.

TRIAL TABLE 1

PRELIMINARY AEROSOL GENERATION TRIALS

TRIAL NO.	EQUIPMENT USED	INPUT AIR (PSI)	TEST ARTICLE CONCENTRATION (%)	MAXIMUM ATTAINABLE CONCENTRATIONS (MG/L)	
				GRAVIMETRIC	ANALYTICAL
26	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 6.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.66	--
27	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 6.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	2.40	--
28	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 5.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.80	2.184
29	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 5.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	2.04	--
30	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 4.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.32	--

NOTE: TARGETING ≥ 1.50 MG/L GRAVIMETRIC CONCENTRATION FOR A ≥ 2.00 MG/L ANALYTICAL CONCENTRATION FOR TRIALS 26-30.

TRIAL TABLE 1

PRELIMINARY AEROSOL GENERATION TRIALS

TRIAL NO.	EQUIPMENT USED	INPUT AIR (PSI)	TEST ARTICLE CONCENTRATION (%)	MAXIMUM ATTAINABLE CONCENTRATIONS (MG/L)	
				GRAVIMETRIC	ANALYTICAL
31	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 5.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.58	--
32	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 5.5 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	1.64	--
33	ONE MULTI-STAGE 10L NOSE-ONLY CHAMBER 5L ELUTRIATOR MASTER FLEX PUMP AND PUMP HEADS 7523-30 AND 77200-60 PISTOL SPRAYING SYSTEM 19.0 ML/MIN PUMP SPEED 16 GAUGE TUBING SIZE	30	100	4.94	5.585

NOTE: TARGETING ≥ 1.50 MG/L GRAVIMETRIC CONCENTRATION FOR TRIALS 31-32.
TARGETING ≥ 4.50 MG/L GRAVIMETRIC CONCENTRATION FOR TRIAL 33.

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA
Trial 2

Stage	Effective Cutoff Diameter	Filter Weights (mg) Pre-sample	Post-sample	Difference Weights	% of Total	Cumulative % <ECD
1	10.00	100.2	100.4	0.2	2.0	98.0
2	6.11	100.9	101.9	1.0	9.9	88.1
3	3.70	102.7	104.6	1.9	18.8	69.3
4	2.22	101.6	104.7	3.1	30.7	38.6
5	1.39	101.6	103.1	1.5	14.9	23.8
6	0.79	99.9	101.9	2.0	19.8	4.0
7	0.50	101.3	101.4	0.1	1.0	3.0
Filter	-	100.9	101.2	0.3	3.0	
		Total of Difference Weights:		10.1		

Mass Median Aerodynamic Diameter = 2.5 microns
Geometric Standard Deviation = 2.08
Percentage ≤ 4.0 microns = 75 %

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA
Trial 13

Stage	Effective Cutoff Diameter	Filter Weights (mg) Pre-sample	Post-sample	Difference Weights	% of Total	Cumulative % <ECD
1	10.00	101.9	102.9	1.0	5.2	94.8
2	6.11	101.3	103.5	2.2	11.5	83.2
3	3.70	100.7	106.5	5.8	30.4	52.9
4	2.22	101.2	107.4	6.2	32.5	20.4
5	1.39	100.1	102.2	2.1	11.0	9.4
6	0.79	99.6	100.8	1.2	6.3	3.1
7	0.50	100.9	101.1	0.2	1.0	2.1
Filter	-	99.9	100.3	0.4	2.1	
		Total of Difference Weights:		19.1		

Mass Median Aerodynamic Diameter = 3.2 microns
Geometric Standard Deviation = 2.13
Percentage ≤ 4.0 microns = 61 %

Appendix 2. Analytical Chemistry Report

Study No. 3044.969
Monsanto Study No. SB-2003-116

1. MON 78623 ANALYSIS

The analytical method provided by the Sponsor, Monsanto Company, for the analysis of the glyphosate component of MON 78623 was validated prior to the analytical chamber concentration analyses performed at Springborn Laboratories. This method was utilized to determine the inhalation chamber concentration during the Acute Nose -Only Inhalation Toxicity Study.

1.1. Experimental System

1.1.1. HPLC System

Pump:	Waters 600E System Controller
Injector:	Waters WISP 717
Detector:	Waters 2487
Data System:	HP 3396B Integrator
Precolumn:	Phenomenex, SecurityGuard, C18, 4.0 x 3.0 mm ID
Column:	Phenomenex, Synergi, Hydro-RP, 4µ, 80Å, 250 x 4.6 mm ID
Mobile Phase:	A: 0.05 M HCO_2NH_4, pH 3.6/5% Acetonitrile B: 100% HPLC Acetonitrile
Gradient:	100% A, hold for 6 minutes; linear change to 25% A/75% B over 1 minute; hold for 5 minutes; linear change to 100% A over 1 minute; hold at 100% A for 15 minutes
Injection Volume:	10 µL
Flow Rate:	1.0 mL/min
Detection:	500nm; 0.4000 AUFS

1.1.2. Apparatus

Balance:	Mettler AG 245, accuracy of 0.0001 gram; Denver Instrument P602, accuracy of 0.01 gram
Glassware:	Assorted volumetric glassware
Filters:	Whatman Puradisc 25PP, 0.45 µm; Pall Extrathick 25mm glass fiber; Nylon-66 0.2 µm
Shaker:	Labline, Multi-Wrist Shaker
Oven:	Boekel, Model 107905
Pipet:	Mettler-Toledo 100-1000 µL, 500-5000 µL
pH Meter:	Corning 320

Study No. 3044.969
Monsanto Study No. SB-2003-116

1.1.3. Solutions and Reagents

1.1.3.1. Reagents

Water, Millipore, Milli-Q Gradient A10
Acetonitrile, Fisher, HPLC grade, Lot # 030938 (Exp. Date 10/08)
Acetonitrile, Fisher, HPLC grade, Lot # 031009 (Exp. Date 11/08)
NBD-Chloride, Aldrich, 98%, Lot # 10926TO (Exp. Date 8/2/07)
NBD-Chloride, Aldrich, 98%, Lot # 10429MA (Exp. Date 7/10/08)
Hydrochloric Acid, Fisher, Certified A.C.S. Plus, Lot # 031667 (Exp. Date 9/08)
Potassium Tetraborate Tetrahydrate, Aldrich, 99%, 15325DI (Exp. Date 11/05)
Ammonium Formate, Fisher, Certified, Lot # 990125 (Exp. Date 3/04)
Formic Acid, Fisher, Laboratory Grade, 90%, Lot # 003630 (Exp. Date 11/05)
Methanol, Fisher, HPLC Grade, Lot # 030817 (Exp. Date 7/08)
Methanol, Fisher, HPLC Grade, Lot # 030719 (Exp. Date 6/08)

1.1.3.2. Solutions

0.37 M Borate Solution: Prepared by dissolving approximately 11.44 g of potassium tetraborate tetrahydrate in 100 mL of water. The resulting solution was mixed thoroughly and is stable for 6 months post-preparation at room temperature.

1.2 N HCl: Prepared by diluting 10 mL of HCl in 90 mL of water. The resulting solution was mixed thoroughly and is stable for 6 months post-preparation at room temperature.

25 mM NBD-Cl: Prepared by dissolving 2.50 g of NBD-Cl in 500 mL of methanol. The resulting solution was mixed thoroughly and is stable for 6 months post-preparation at room temperature.

Mobile Phase A: For Exposures 1 and 2, the mobile phase was prepared by dissolving 2.3648-2.3653 g of ammonium formate in 1425 mL of water. The pH of the resulting solution was adjusted to 3.60-3.62 with formic acid. Then, 75 mL of acetonitrile was added. For trial work, the mobile phase was prepared by dissolving 1.5770 g of ammonium formate in 950 mL of water. The pH of the resulting solution was adjusted to 3.60 with formic acid. Then, 50 mL of acetonitrile was added. Each resulting solution was mixed thoroughly, filtered through a 0.2 µm Nylon-66 filter, and degassed by helium sparging prior to and during analysis.

Mobile Phase B: 100% acetonitrile used as received.

Diluent: 100% water used as received.

Stock Standard Solution (Trial Work): Prepared by dissolving 300.2 mg of MON 78623 in a 25 mL flask with water.

Standard Solutions (Trial Work): Prepared by serially diluting the stock standard solution with water. Then a further dilution of 1:25 was performed and the final concentrations of the solutions were in the range of approximately 0.04804 to 0.2402 mg/mL. These solutions were then filtered through Whatman Puradisc 25PP 0.45 µm filters prior to derivatization.

Chamber Concentration Solutions (Trial Work): Prepared by placing the weighed glass fiber filter used for gravimetric concentration determination in a capped container with 10 mL of water. The solutions were then agitated mechanically for 10 minutes and filtered through Whatman Puradisc 25PP 0.45 µm filters. The sample solutions were then diluted at a ratio of 1:25 with water prior to derivatization.

Stock Standard Solution (Exposure #1): Prepared by dissolving 127.4 mg of MON 78623 in a 25 mL flask with water.

Standard Solutions (Exposure #1): Prepared by serially diluting the stock standard solution with water. Then a further dilution of 1:25 was performed and the final concentrations of the solutions were in the range of approximately 0.02038 to 0.08152 mg/mL. These solutions were then filtered through Whatman Puradisc 25PP 0.45 µm filters prior to derivatization.

Chamber Concentration Solutions (Exposure #1): Prepared by placing the weighed glass fiber filter used for gravimetric concentration determination in a capped container with 10 mL of water. The solutions were then agitated mechanically for 10 minutes and filtered through Whatman Puradisc 25PP 0.45 µm filters. The sample solutions were then diluted at a ratio of 1:25 with water prior to derivatization.

Stock Standard Solution (Exposure #2): Prepared by dissolving 293.8 mg of MON 78623 in a 25 mL flask with water.

Standard Solutions (Exposure #2): Prepared by serially diluting the stock standard solution with water. Then a further dilution of 1:25 was performed and the final concentrations of the solutions were in the range of approximately 0.04700 to 0.1880 mg/mL. These solutions were then filtered through Whatman Puradisc 25PP 0.45 µm filters prior to derivatization.

Chamber Concentration Solutions (Exposure #2): Prepared by placing the weighed glass fiber filter used for gravimetric concentration determination in a capped container with 10 mL of water. The solutions were then agitated mechanically for 10 minutes and filtered through Whatman Puradisc 25PP 0.45 µm filters. The sample solutions were then diluted at a ratio of 1:25 with water prior to derivatization.

Precolumn Derivatization: In order to analyze the glyphosate component, a precolumn derivatization was performed by adding 1.2 mL of the appropriate control, standard, or sample

solution to a labeled scintillation vial. Both 0.8 mL of the borate solution and 2.4 mL of the NBD-Cl solution were added to each vial. The vials were then capped and shaken by hand prior to being heated in an oven at 80° C for 30 minutes. After removal from the oven the vials were allowed to cool for 10 minutes followed by the addition of 0.9 mL of the HCl solution. After the vials were again shaken by hand, they were allowed to stand for 10 minutes in order for incipient precipitation to occur. These solutions were then transferred to labeled injection vials.

1.2. Analytical Procedures

1.2.1. Standard Curve Analysis

The peak areas of the glyphosate component of each standard were determined, measured, and plotted as a function of concentration to generate a standard curve. The actual values used for the calculations are shown in Chemistry Tables 1, 2 and 3.

1.2.2. Sample Analysis

The peak areas of the glyphosate component of each sample were measured and the concentration was determined by linear fit to the standard curve. The actual values used for the calculations are shown in Chemistry Tables 1, 2 and 3.

1.2.3. System Suitability

System suitability injections were performed following the last sample injection. At least six consecutive injections of Standard 2 (or 3) were performed to demonstrate reproducibility. The percent relative standard deviations of the peak area response and peak retention time response were calculated for the consecutive injections. The first injection of Standard 2 (or 3) in the replicate injections was back calculated into the standard curve. Single injections of Standard 2 (or 3) were also performed between samples such that no more than six consecutive sample injections were performed during the analysis. These single standard injections were also back calculated into the standard curve.

1.3. Results and Conclusions

1.3.1. System Suitability

For Trial Work, Standard 3 was used to calculate the system suitability. The percent relative standard deviation for the peak areas was 1.45%, and the percent relative standard deviation for the retention times was 0.67%. Recovery values were within 2.0% of the nominal concentration. For Exposure #1, Standard 2 was used to calculate the system suitability. The percent relative standard deviation for the peak areas was 0.73%, and the percent relative standard deviation for the retention times was 0.35%. Recovery values were within 6.4% of the nominal concentration. For exposure #2, Standard 2 was used to calculate the system suitability. The percent relative

standard deviation for the peak areas was 0.69%, and the percent relative standard deviation for the retention times was 0.41%. Recovery values were within 2.4% of the nominal concentration.

1.3.2. Analytical Chamber Concentration

The actual sample results of the trial work are shown in Chemistry Table 1, the actual sample results for Exposure #1 are shown in Chemistry Table 2, and the actual sample results for Exposure #2 are shown in Chemistry Table 3.

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Study No. 3044.969
Monsanto Study No. SB-2003-116

CHEMISTRY TABLE 1

STANDARD CURVE AND SAMPLE ANALYSIS VALUES FOR TRIAL WORK

Sample No.	Theoretical Conc. (mg/L)	Peak Area	Analytical Chamber Conc. (mg/L)
Std 1	2.402	93065	NA
Std 2	4.804	195427	NA
Std 3	7.206	302939	NA
Std 4	9.608	401603	NA
Std 5	12.01	481482	NA
Trial # 2	NA	126393	3.088
Trial # 3	NA	131113	3.204
Trial # 4	NA	112023	2.737
Trial # 7	NA	124623	3.045
Trial # 11	NA	213269	5.211
Trial # 12	NA	233068	5.695
Trial # 13	NA	231423	5.655
Trial # 14	NA	220441	5.387
Trial # 17	NA	235347	5.751
Trial # 19	NA	234082	5.720
Trial # 20	NA	240375	5.874

NA – Not Applicable
Correlation coefficient = 0.999

CHEMISTRY TABLE 2

STANDARD CURVE AND SAMPLE ANALYSIS VALUES FOR EXPOSURE #1

Sample No.	Theoretical Conc. (mg/L)	Peak Area	Analytical Chamber Conc. (mg/L)
Std 1	1.019	44681	NA
Std 2	2.038	87802	NA
Std 3	3.058	137928	NA
Std 4	4.076	181458	NA
Trial # 28	NA	99340	2.246
# 1	NA	71421	1.628
# 2	NA	93955	2.127
# 3	NA	55919	1.285
# 4	NA	100207	2.265
# 5	NA	90714	2.055
# 6	NA	113208	2.553
# 7	NA	119717	2.697
# 8	NA	118352	2.667
# 9	NA	54331	1.250
# 10	NA	98253	2.222
# 11	NA	113836	2.567
# 12	NA	144981	3.256
# 1A	NA	69403	1.584
# 7A	NA	117090	2.639

NA – Not Applicable
Correlation coefficient = 0.9996

CHEMISTRY TABLE 3

STANDARD CURVE AND SAMPLE ANALYSIS VALUES FOR EXPOSURE #2

Sample No.	Theoretical Conc. (mg/L)	Peak Area	Analytical Chamber Conc. (mg/L)
Std 1	2.350	97872	NA
Std 2	4.700	199099	NA
Std 3	7.050	307277	NA
Std 4	9.400	414257	NA
Trial # 33	NA	241594	5.585
# 1	NA	210624	4.897
# 2	NA	221328	5.135
# 3	NA	229771	5.323
# 4	NA	238064	5.507
# 5	NA	232663	5.387
# 6	NA	219538	5.095
# 7	NA	235508	5.450
# 8	NA	226813	5.257
# 9	NA	225345	5.224
# 10	NA	206250	4.780

NA – Not Applicable
Correlation coefficient = 0.9999

Appendix 3. Individual Aerosol Generation and Chamber Environmental Data

Analytical Exposure 2.21 mg/L

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
CHAMBER ENVIRONMENTAL DATA
EXPOSURE: 2.21 MG/L

TIME (MIN.)	TEMPERATURE (°F)	RELATIVE HUMIDITY (%)	OXYGEN CONTENT (%)
0	71.2	60.1	20.9
30	72.4	57.2	20.9
60	72.8	55.8	20.9
90	72.4	56.2	20.9
120	72.7	55.8	20.9
150	73.1	56.1	20.9
180	72.8	55.7	20.9
210	72.7	55.7	20.9
240	72.9	52.2	20.9

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
TIME WEIGHTED ANALYTICAL CONCENTRATION
ANALYTICAL EXPOSURE: 2.21 MG/L

Sample No.	Sample Time (min.)	Aerosol Concentration (mg/L)	Mean Concentration Per Interval (mg/L)	Interval Length (min.)	Time Weighted Concentration Per Interval
1	0	1.63			
			1.88	30.00	56.40
2	30	2.13			
			1.71	30.00	51.30
3	60	1.29			
			1.78	16.00	28.48
4	76	2.27			
			2.17	14.00	30.31
5	90	2.06			
			2.31	15.00	34.58
6	105	2.55			
			2.63	15.00	39.38
7	120	2.70			
			2.69	30.00	80.55
8	150	2.67			
			1.96	30.00	58.80
9	180	1.25			
			1.74	14.00	24.29
10	194	2.22			
			2.40	16.00	38.32
11	210	2.57			
			2.92	30.00	87.45
12	240	3.26			
TOTAL				240.00	529.85
TIME WEIGHTED MEAN ANALYTICAL CONCENTRATION (MG/L)					2.21

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA
SAMPLE NO.: A
ANALYTICAL EXPOSURE: 2.21 MG/L

Stage	Effective Cutoff Diameter	Filter Weights (mg) Pre-sample	Post-sample	Difference Weights	% of Total	Cumulative % <ECD
1	10.00	99.3	99.9	0.6	7.2	92.8
2	6.11	101.8	102.5	0.7	8.4	84.3
3	3.70	101.3	102.5	1.2	14.5	69.9
4	2.22	101.3	104.5	3.2	38.6	31.3
5	1.39	100.5	102.2	1.7	20.5	10.8
6	0.79	100.2	100.9	0.7	8.4	2.4
7	0.50	100.8	100.9	0.1	1.2	1.2
Filter	-	101.5	101.6	0.1	1.2	
		Total of Difference Weights:		8.3		

Mass Median Aerodynamic Diameter = 3.0 microns
Geometric Standard Deviation = 2.08
Percentage ≤ 4.0 microns = 64 %

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA
SAMPLE NO.: B
ANALYTICAL EXPOSURE: 2.21 MG/L

Stage	Effective Cutoff Diameter	Filter Weights (mg) Pre-sample	Filter Weights (mg) Post-sample	Difference Weights	% of Total	Cumulative % <ECD
1	10.00	100.9	101.7	0.8	7.1	92.9
2	6.11	100.5	101.9	1.4	12.5	80.4
3	3.70	101.7	104.0	2.3	20.5	59.8
4	2.22	101.6	105.0	3.4	30.4	29.5
5	1.39	98.9	100.8	1.9	17.0	12.5
6	0.79	99.3	100.0	0.7	6.3	6.3
7	0.50	99.5	100.0	0.5	4.5	1.8
Filter	-	101.2	101.4	0.2	1.8	
		Total of Difference Weights:		11.2		

Mass Median Aerodynamic Diameter = 3.1 microns
Geometric Standard Deviation = 2.28
Percentage ≤ 4.0 microns = 62 %

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA
SAMPLE NO.: C
ANALYTICAL EXPOSURE: 2.21 MG/L

Stage	Effective Cutoff Diameter	Filter Weights (mg) Pre-sample	Filter Weights (mg) Post-sample	Difference Weights	% of Total	Cumulative % <ECD
1	10.00	100.9	101.4	0.5	5.4	94.6
2	6.11	100.9	101.3	0.4	4.3	90.3
3	3.70	100.7	101.9	1.2	12.9	77.4
4	2.22	100.8	104.6	3.8	40.9	36.6
5	1.39	101.9	103.6	1.7	18.3	18.3
6	0.79	101.5	102.6	1.1	11.8	6.5
7	0.50	102.3	102.6	0.3	3.2	3.2
Filter	-	100.8	101.1	0.3	3.2	
		Total of Difference Weights:		9.3		

Mass Median Aerodynamic Diameter = 2.5 microns
Geometric Standard Deviation = 2.18
Percentage ≤ 4.0 microns = 73 %

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA

ANALYTICAL EXPOSURE: 2.21 MG/L

Stage	Effective Cutoff Diameter	Cumulative % less than indicated size			
		Sample A	Sample B	Sample C	
1	10.00	92.8	92.9	94.6	
2	6.11	84.3	80.4	90.3	
3	3.70	69.9	59.8	77.4	
4	2.22	31.3	29.5	36.6	
5	1.39	10.8	12.5	18.3	
6	0.79	2.4	6.3	6.5	
7	0.50	1.2	1.8	3.2	
					Mean
Mass Median Aerodynamic Diameter		3.0	3.1	2.5	2.9
Geometric Standard Deviation		2.08	2.28	2.18	2.18
Percentage ≤ 4.0 microns		64	62	73	67

Analytical Exposure 5.27 mg/L

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
CHAMBER ENVIRONMENTAL DATA
EXPOSURE: 5.27 MG/L

TIME (MIN.)	TEMPERATURE (°F)	RELATIVE HUMIDITY (%)	OXYGEN CONTENT (%)
0	70.4	67.2	20.9
30	70.5	67.5	20.9
60	70.7	66.4	20.9
90	71.0	67.9	20.9
120	71.1	66.8	20.9
150	71.3	67.2	20.9
180	71.5	65.7	20.9
210	71.4	66.2	20.9
240	71.3	66.1	20.9

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
TIME WEIGHTED ANALYTICAL CONCENTRATION
ANALYTICAL EXPOSURE: 5.27 MG/L

Sample No.	Sample Time (min.)	Aerosol Concentration (mg/L)	Mean Concentration Per Interval (mg/L)	Interval Length (min.)	Time Weighted Concentration Per Interval
1	0	4.90			
			5.02	10.00	50.20
2	10	5.14			
			5.23	20.00	104.60
3	30	5.32			
			5.42	30.00	162.45
4	60	5.51			
			5.45	30.00	163.46
5	90	5.39			
			5.24	30.00	157.31
6	120	5.10			
			5.28	30.00	158.25
7	150	5.45			
			5.36	30.00	160.65
8	180	5.26			
			5.24	30.00	157.20
9	210	5.22			
			5.01	30.00	150.30
10	240	4.80			
TOTAL				240.00	1264.41
TIME WEIGHTED MEAN ANALYTICAL CONCENTRATION (MG/L)					5.27

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA
SAMPLE NO. A
ANALYTICAL EXPOSURE: 5.27 MG/L

Stage	Effective Cutoff Diameter	Filter Weights (mg) Pre-sample	Post-sample	Difference Weights	% of Total	Cumulative % <ECD
1	10.00	100.5	102.3	1.8	9.9	90.1
2	6.11	101.4	103.9	2.5	13.8	76.2
3	3.70	101.0	105.8	4.8	26.5	49.7
4	2.22	100.4	105.8	5.4	29.8	19.9
5	1.39	100.3	102.4	2.1	11.6	8.3
6	0.79	101.0	101.7	0.7	3.9	4.4
7	0.50	100.9	101.3	0.4	2.2	2.2
Filter	-	100.2	100.6	0.4	2.2	
		Total of Difference Weights:		18.1		

Mass Median Aerodynamic Diameter = 3.6 microns
Geometric Standard Deviation = 2.34
Percentage ≤ 4.0 microns = 55 %

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA
SAMPLE NO.: B
ANALYTICAL EXPOSURE: 5.27 MG/L

Stage	Effective Cutoff Diameter	Filter Weights (mg) Pre-sample	Filter Weights (mg) Post-sample	Difference Weights	% of Total	Cumulative % <ECD
1	10.00	100.8	102.6	1.8	10.2	89.8
2	6.11	100.6	103.1	2.5	14.2	75.6
3	3.70	102.0	106.7	4.7	26.7	48.9
4	2.22	101.1	106.4	5.3	30.1	18.8
5	1.39	100.6	102.7	2.1	11.9	6.8
6	0.79	101.6	102.5	0.9	5.1	1.7
7	0.50	101.1	101.3	0.2	1.1	0.6
Filter	-	100.5	100.6	0.1	0.6	
		Total of Difference Weights:		17.6		

Mass Median Aerodynamic Diameter = 3.9 microns
Geometric Standard Deviation = 2.13
Percentage ≤ 4.0 microns = 52 %

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA
SAMPLE NO.: C
ANALYTICAL EXPOSURE: 5.27 MG/L

Stage	Effective Cutoff Diameter	Filter Weights (mg) Pre-sample	Filter Weights (mg) Post-sample	Difference Weights	% of Total	Cumulative % <ECD
1	10.00	100.9	102.9	2.0	10.9	89.1
2	6.11	100.2	102.7	2.5	13.7	75.4
3	3.70	99.7	104.9	5.2	28.4	47.0
4	2.22	101.3	106.3	5.0	27.3	19.7
5	1.39	101.2	103.2	2.0	10.9	8.7
6	0.79	100.7	102.0	1.3	7.1	1.6
7	0.50	101.4	101.6	0.2	1.1	0.5
Filter	-	100.0	100.1	0.1	0.5	
		Total of Difference Weights:		18.3		

Mass Median Aerodynamic Diameter = 3.9 microns
Geometric Standard Deviation = 2.15
Percentage ≤ 4.0 microns = 52 %

AN ACUTE NOSE-ONLY INHALATION TOXICITY STUDY IN RATS
AERODYNAMIC PARTICLE SIZE DATA

ANALYTICAL EXPOSURE: 5.27 MG/L

	Effective Cutoff	Cumulative % less than indicated size			
Stage	Diameter	Sample A	Sample B	Sample C	
1	10.00	90.1	89.8	89.1	
2	6.11	76.2	75.6	75.4	
3	3.70	49.7	48.9	47.0	
4	2.22	19.9	18.8	19.7	
5	1.39	8.3	6.8	8.7	
6	0.79	4.4	1.7	1.6	
7	0.50	2.2	0.6	0.5	
					Mean
Mass Median Aerodynamic Diameter		3.6	3.9	3.9	3.8
Geometric Standard Deviation		2.34	2.13	2.15	2.20
Percentage ≤ 4.0 microns		55	52	52	53

Appendix 4. CRL Personnel Responsibilities

CRL PERSONNEL RESPONSIBILITIES

Kimberly L. Bonnette, M.S., LATG	Study Director/Director, Acute Toxicology
Dawn D. Rodabaugh, B.S.	Alternate Contact/Toxicologist
Joseph C. Siglin, Ph.D., DABT	General Manager
Rusty E. Rush, M.S., LAT, DABT	Director, Toxicology
Jason W. Smedley, B.S.	Assistant Toxicologist
Pamela S. Smith, ALAT	Study Supervisor, Acute Toxicology
Kevin V. Weitzel, A.S.	Primary Technician/Inhalation Team Leader
Delores P. Knippen	Supervisor, Pharmacy
Steven H. Magness, B.S., LATG	Senior Supervisor, Pathology
Anita M. Bosau, RQAP-GLP	Senior Director, Compliance Assurance
Cheryl A. Bellamy	Senior Supervisor, Report Writing
Deanna M. Talerico, RQAP-GLP	Senior Supervisor, Quality Assurance
J. Dale Thurman, D.V.M., M.S., DACVP	Senior Director, Pathology
M. Gardener Clemons, B.A.	Manager, Analytical Chemistry and Pharmacy
Kathy M. Gasser	Archivist