FYI-0902-01424

American Chemistry Council *Good Chemistry Makes It Possible*

July 25, 2002

MR 62337

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Stephen L. Johnson
Assistant Administrator
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7101M Fe
~~Ariel Rose Building~~
1200 Pennsylvania Avenue N
Washington, DC 20460

FYI-02-001424

Dear Mr Johnson:

The American Chemistry Council (Council) makes available to the public and appropriate government agencies final reports of environmental, health, and safety research that it manages. In keeping with this policy, the following two final reports that the Council's Brominated Flame Retardant Industry Panel (BFRIP) recently conducted are enclosed:

- Tetrabromobisphenol A (TBBPA): An Activated Sludge, Respiration Inhibition Test;
- Tetrabromobisphenol A (TBBPA): A Toxicity Test to Determine the Effects of the Test Substance on Seedling Emergence of Six Species of Plants.

In addition, a copy of the report, "Hexabromocyclododecane (HBCD): A 90-Day Oral (Gavage) Toxicity Study of HBCD in Rats, completed December 14, 2000," was sent to your office on January 3, 2002. For completeness a copy of the recently completed addendum to that report is also enclosed.

These reports do not include confidential information.

If you have any questions, please contact Wendy K. Sherman, the BFRIP Manager, at 703/741-5639 or via email at wendy.sherman@americanchemistry.com.

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Sincerely yours,

Susan A. Lewis

Susan A. Lewis, Ph.D.
Managing Director, CHEMSTAR

Contain NO CBI

Enclosures (3)

85020000013

AMENDMENT TO THE FINAL REPORT

STUDY TITLE

A 90-DAY ORAL (GAVAGE) TOXICITY STUDY OF HBCD IN RATS

STUDY DIRECTOR

Christopher P. Chengelis, Ph.D., D.A.B.T.

DATE

July 11, 2002

PERFORMING LABORATORY

WIL Research Laboratories, Inc.
1407 George Road
Ashland, Ohio 44805-9281

LABORATORY STUDY NUMBER

WIL-186012

SPONSOR

Chemical Manufacturers Association
Brominated Flame Retardant Industry Panel (BFRIP)
1300 Wilson Blvd.
Arlington, VA 22209

WIL-186012
CMA-BFRIP

A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

COMPLIANCE STATEMENT

This amendment to the final report, designated WIL-186012, was conducted in compliance with the United States Environmental Protection Agency (EPA) Good Laboratory Practice Regulations (40 CFR Part 792), the Organisation for Economic Cooperation and Development (OECD) Principles of Good Laboratory Practice [C (97) 186/Final], the standard operating procedures of WIL Research Laboratories, Inc., and the protocol as approved by the sponsor.

Christopher P. Chengelis, Ph.D., D.A.B.T.
Director, Toxicology
Study Director

11 July 02
Date

A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

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A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

REASON FOR AMENDMENT

Additional histopathological examination of the kidneys for the male rats in the control and high dose recovery groups and serum samples from the satellite groups for study days 2, 55 and 89 were conducted after issuance of the final report. Discussion of these results has been added.

The changes to this report had no impact on the scientific validity or interpretation of the results of this study.

Page 1 (Volume 1 Cover Page)

Change: Changed the number of volumes for the report and the total number of pages.

Reason for Change: Addition of histopathological examination, historical control data and serum analysis necessitated another volume.

Page 15 (Index of Tables)

Change: Added Tables 138, 139, 140, 141, 142 and 143 to Volume 5.

Reason for Change: Addition of serum hormone and histopathology tables.

Page 16 (Index of Appendices)

Change: Addition of Appendix M "Amendment to the Final Report" to Volume 5.

Reason for Change: Added Appendix M for new data.

Page 16A (Index of Attachments)

Change: Addition of historical control data, serum analysis and Protocol Amendments V and VI.

Reason for Change: Addition of new data.

Page 381 (Volume 2 Cover Page)

Change: Changed the number of volumes for the report and the total number of pages.

Reason for Change: Addition of histopathological examination, historical control data and serum analysis necessitated another volume.

Page 748 (Volume 3 Cover Page)

Change: Changed the number of volumes for the report and the total number of pages.

Reason for Change: Addition of histopathological examination, historical control data and serum analysis necessitated another volume.

Page 1120 (Volume 4 Cover Page)

Change: Changed the number of volumes for the report and the total number of pages.

Reason for Change: Addition of histopathological examination, historical control data and serum analysis necessitated another volume.

The signature below certifies that the revised pages (1, 15, 16, 16A, 381, 748 and 1120) have been reviewed and approved by the study director.

Christopher P. Chengelis, Ph.D., D.A.B.T.
Director, Toxicology
Study Director

11 July 02
Date

WIL-186012
CMA-BFRIP

A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

AMENDMENT SUBMISSION

Amendment Prepared By:

Robert A. Wally
for: Misty R. Lance, B.A.
Study Analyst
11 July 2002
Date

Robert A. Wally
Robert A. Wally, B.S.
Group Supervisor, Study Analysis and Reports
11 July 2002
Date

Amendment Reviewed By:

Lewis E. Kaufman, M.S.
Senior Operations Manager, Study Analysis and Reports
7/11/02
Date

Ann Radovsky
Ann E. Radovsky, D.V.M., Ph.D., D.A.C.V.P., D.A.B.T.
Staff Pathologist
7/11/02
Date

Approved and Released By:

Christopher P. Chengelis, Ph.D., D.A.B.T.
Director, Toxicology
Study Director
11 July 02
Date

WIL-186012
CMA-BFRIP

A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

QUALITY ASSURANCE UNIT STATEMENT

Date(s) of Inspection(s)	Phase Inspected	Date(s) Findings Reported to Study Director	Date(s) Findings Reported to Management
*3/5/01	Study Records (P-2)	3/5/01	4/30/01
5/10/02	Study Records (H-1,2)	5/10/02	6/28/02
5/10/02	Study Records (P-1,2)	5/10/02	6/28/02
6/6,9,10/02	Amendment to the Final Report	6/10/02	7/10/02
7/7/02	Revised Amendment to the Final Report	7/8/02	7/10/02

* = Inadvertently omitted from the final report

This amendment to the final report was inspected in accordance with the United States EPA/TSCA Good Laboratory Practice Regulations, the OECD Principles of Good Laboratory Practice, the standard operating procedures of WIL Research Laboratories, Inc., and the protocol. Quality Assurance findings, derived from the inspections of the raw data and the report amendment, are documented and have been reported to the study director. A status report is submitted to management monthly.

This amendment accurately reflects the data generated during the study. The methods and procedures used in the study were those specified in the protocol, its amendments and the standard operating procedures of WIL Research Laboratories, Inc.

The raw data and the amendment to the final report will be stored in the Archives at WIL Research Laboratories, Inc.

Amendment Audited and Released By:

Deborah L Little
Deborah L. Little, B.S., RQAP-GLP
Manager II, Quality Assurance

7/11/2002
Date

A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

REVISED PAGES

FINAL REPORT

Volume 1 of 5
(Text and Summary Tables 1-68)

STUDY TITLE

A 90-DAY ORAL (GAVAGE) TOXICITY STUDY OF HBCD IN RATS

STUDY DIRECTOR

Christopher P. Chengelis, Ph.D., D.A.B.T.

STUDY INITIATED ON

March 2, 2000

STUDY COMPLETION DATE

December 14, 2001

PERFORMING LABORATORY

WIL Research Laboratories, Inc.
1407 George Road
Ashland, Ohio 44805-9281

LABORATORY STUDY NUMBER

WIL-186012

SPONSOR

Chemical Manufacturers Association
Brominated Flame Retardant Industry Panel (BFRIP)
1300 Wilson Blvd.
Arlington, VA 22209

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A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

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A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

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FINAL REPORT

Volume 2 of 5
(Individual Tables 69-93)

STUDY TITLE

A 90-DAY ORAL (GAVAGE) TOXICITY STUDY OF HBCD IN RATS

STUDY DIRECTOR

Christopher P. Chengelis, Ph.D., D.A.B.T.

STUDY INITIATED ON

March 2, 2000

STUDY COMPLETION DATE

December 14, 2001

PERFORMING LABORATORY

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LABORATORY STUDY NUMBER

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FINAL REPORT

Volume 3 of 5
(Individual Tables 94-121)

STUDY TITLE

A 90-DAY ORAL (GAVAGE) TOXICITY STUDY OF HBCD IN RATS

STUDY DIRECTOR

Christopher P. Chengelis, Ph.D., D.A.B.T.

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FINAL REPORT

Volume 4 of 5
(Individual Tables 122-137 And Appendices A-L)

STUDY TITLE

A 90-DAY ORAL (GAVAGE) TOXICITY STUDY OF HBCD IN RATS

STUDY DIRECTOR

Christopher P. Chengelis, Ph.D., D.A.B.T.

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A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

AMENDMENT

WIL-186012
CMA-BFRIP

FINAL REPORT

Volume 5 of 5
(Appendix M)

STUDY TITLE

A 90-DAY ORAL (GAVAGE) TOXICITY STUDY OF HBCD IN RATS

STUDY DIRECTOR

Christopher P. Chengelis, Ph.D., D.A.B.T.

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A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

APPENDIX M

Amendment to the Final Report

I. INTRODUCTION

Detectable levels of HBCD were found in the adipose tissue of the satellite control (Group 5) animals. This prompted a further evaluation of the results to affirm that the Group 1 control animals served appropriately as the control group for comparison with test article-treated animals (Groups 2, 3 and 4).

Standard operating procedures are in place at WIL Research Laboratories, Inc. to prevent possible cross dosing of animals, and a thorough review of the procedures and the study records did not identify a source of contamination.

There were four types of evaluations performed. The first was comparison of control (Group 1) animals to strain- and age-matched control animals from previous studies conducted at WIL Research Laboratories, Inc., under similar experimental conditions, (i.e., historical control data). The second evaluation was additional microscopic evaluation of kidneys in male recovery animals (Groups 1 and 4 at study week 17). The third was analysis of serum of selected animals from satellite Groups 5 and 6 for HBCD content. The fourth evaluation was an individual assessment of clinical chemistry and organ weight data from those control (Group 1) animals with histopathologic findings of hepatocellular vacuolation or thyroid follicular cell hypertrophy.

In addition to the aforementioned evaluation of the Group 1 control animals, the thyroid hormone data from all groups were also re-assessed. During the review of the study, some questions pertaining to the statistical analysis of the thyroid hormone data arose. In the original report, values regarded as "UR" (under instrument range) were excluded from the calculations of means and standard deviations, which were statistically analyzed as described in the protocol using parametric statistical techniques. In the re-evaluation of the serum hormone data, the "UR's" were considered to be zero and statistical analysis was performed as follows. Serum hormone data were subjected to the Kruskal-Wallis nonparametric ANOVA test[1] to determine intergroup differences. If the ANOVA revealed

statistical significance ($p<0.05$), the Mann-Whitney U-test[1] was used to compare the test article-treated groups to the control group.

II. RESULTS

A. HISTORICAL CONTROL COMPARISON

The historical control data contained herein are more closely age-matched to the animals used on this study (17 to 21 weeks of age through the study week 13 necropsy and 22 to 25 weeks of age through the study week 17 necropsy) than the historical control that was included in the original report. The data presented here replaces that presented in the originally released final report.

This historical control data is a compilation from 16 different 13-week oral studies with Charles River IGS animals, which were fasted overnight prior to necropsy. The age range was selected such that only the clinical pathology data collected in conjunction with a week 13 or week 17 necropsy are included for comparison with the week 13 or week 17 data collected on the subject study.

Parameters selected for comparison of historical and study controls included body weight, absolute and relative organ weights (liver, thyroid, prostate), and clinical chemistry (albumin, total serum protein, globulin, gamma glutamyltransferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and chloride). Body weight data are included because they are normally collected on subchronic studies and are well-accepted indicators of the health of the animals. The clinical chemistry parameters and organ weights selected for more in depth examination (summarized in the table below) were those showing differences between control (Group 1) and test article-treated (Groups 2, 3 or 4) animals. Special attention was given to indicators of liver enzyme induction or hepatic and thyroid histopathology.

The results of these analyses are as follows:

1. The mean final body weights of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
2. The mean liver weights (absolute and relative to final body weights) of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
3. The mean prostate weights (absolute and relative to final body weights) of the HBCD study Group 1 males represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
4. The mean thyroid weights (absolute and relative to final body weights) of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
5. The mean serum albumin values of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
6. The mean globulin values of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
7. The mean total serum protein levels of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
8. The mean serum chloride levels of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).

9. The mean serum ALT values of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
10. The mean serum AST values of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).
11. The mean serum GGT values of the HBCD study Group 1 males and females represent the values expected when compared to the WIL age- and strain-matched historical control values (Text Table 1).

Text Table 1: Comparison of Final Mean Body Weights and Selected Organ and Serum Chemistry Results: HBCD 90-Day Study Control (Group 1) Data and WIL Age/Strain-Matched Historical Control Data.

	Males		Females	
Parameter	**HBCD 90-Day Control Group (WIL-186012)**	**WIL Historical Control**	**HBCD 90-Day Control Group (WIL-186012)**	**WIL Historical Control**
Serum Chemistry Data (Mean ± 1 Standard Deviation)				
Albumin (g/dL)	4.3 ± 0.1	4.3 ± 0.3	5.2 ± 0.6	4.9 ± 0.6
Globulin (g/dL)	2.6 ± 0.27	2.6 ± 0.4	2.1 ± 0.2	2.4 ± 0.4
Total Protein (g/dL)	7.0 ± 0.3	6.9 ± 0.4	7.3 ± 0.5	7.2 ± 0.5
Chloride (mEq/ml)	99 ± 3.2	100 ± 4.7	101 ± 2.2	101 ± 4.5
ALT (U/L)	40 ± 13	37 ± 9.1	28 ± 5	40 ± 30
AST (U/L)	89 ± 22	86 ± 18	83 ± 18	107 ± 142
GGT (U/L)	0 ± 0.0	0.2 ± 0.91	0 ± 0.0	0.2 ± 0.5
Body and Organ Weight Data (Mean ± 1 Standard Deviation)				
Final Body Weight - Fasted (g)[a]	529 ± 37	514 ± 51	281 ± 24	281 ± 28
Final Body Weight - Unfasted (g)[a]	547 ± 38	541 ± 25	297 ± 27	299 ± 15
Liver (g)	14.3 ± 1.2	14.1 ± 2.13	8.12 ± 0.9	8.0 ± 0.97
Liver ROW	2.71 ± 0.12	2.73 ± 0.26	2.89 ± 0.21	2.84 ± 0.29
Prostate (g)	0.95 ± 0.19	1.03 ± 0.29	NA	NA
Prostate ROW	0.18 ± 0.03	0.20 ± 0.06	NA	NA
Thyroid (g)	0.023 ± 0.005	0.027 ± 0.006	0.017 ± 0.003	0.022 ± 0.006
Thyroid ROW	0.005 ± 0.001	0.005 ± 0.001	0.006 ± 0.001	0.008 ± 0.002

ROW = organ weight relative to final body weight
NA = Not Applicable
a = Fasted body weights collected at necropsy (presented on organ weight tables); unfasted body weights collected at week 13 (presented on body weight tables).

Therefore, the selected parameters for the HBCD 90-day study control (Group 1) male and female animals are consistent with the age- and strain-matched historical control data generated by WIL Research Laboratories, Inc. for these parameters. The values from the HBCD 90-day study control (Group 1) animals are within the normal range for this age and strain of rats. Clinical chemistry parameters and organ weights from WIL-186012 are consistent with and not substantially different from those recorded in previous studies.

B. GROSS LESION COMPARISON

The impact of possibly ingested test material by HBCD 90-day study control (Group 1) animals on the development of gross lesions after 13 weeks of treatment was assessed at both the week 13 and week 17 necropsies for those macroscopic findings that were noted either in **a]** animals of the control *and* high dose groups only (Groups 1 and 4, respectively), **b]** animals of the control, mid *and* high dose groups only (Groups 1, 3 and 4, respectively) **and/or c]** animals of the control *and* all three treatment groups (Groups 1, 2, 3, and 4). Gross lesions meeting these conditions were found in the kidney (depressed areas) and lung (dark red areas).

At week 13, no control group males had depressed area(s) in the kidneys. One control group female and two high dose females had depressed area(s) in the kidneys. Also, one control group male (no. 43332) and one high dose group male (no. 43372) were noted to have dark red lungs.

Control group female no. 43467 had "several pinpoint to 1 mm in diameter depressed area(s) in the cortex of the right kidney" (refer to page 1029 of the original report). It was stated in the report that "gross depressed areas have histologically normal tissue" and hence, this gross lesion did not correlate with the renal microscopic findings, which were "basophilic tubules" (grade 1), "papillary tubular mineralization" (grade 1) and "subacute inflammation" (grade 1), and were not associated with the depressed areas.

High dose group female no. 43440 had "few pinpoint depressed area(s) in the cortex of the left kidney" (refer to page 1059 of the original report). It was stated in the report that histopathology correlated this gross lesion with underlying "focal subacute inflammation" (grade 1).

High dose group female no. 43477 had "one less than 1 mm in diameter depressed area(s) in the cortex of the left kidney" (refer to page 1067 of the original report). It was stated in the report that "gross depressed areas have histologically normal tissue" and hence, this gross lesion did not correlate with microscopic findings in other parts of the kidney, which were "subacute inflammation" (grade 1) and "pelvic mineralization" (grade 1).

At the study week 17 recovery necropsy, there were no "depressed area(s)" found in the renal cortex in any control group female rats. Depressed area(s) in the kidneys were found in one control group male and one high dose group male. Also, there were two control group males, one mid dose group male and one high dose group male that had dark red areas in the lungs. No control group females were noted with this finding. There was no histopathological correlate for the dark red discoloration of the lungs for these males. Since the study pathologist does not diagnose vascular congestion, the red discoloration observed grossly may have been due to blood within the vasculature. The depressed areas in the kidneys of female rats and the dark red discoloration in the male rats were regarded to have developed spontaneously and unrelated to the administration of the test article.

Control group male no. 43308 had "two less than 1 mm in diameter depressed area(s) in the cortex of the right kidney" (refer to page 1081 of the original report). Histopathology was not performed for this lesion until the extended evaluation was performed (see Section II.C.). This male was also noted with "one 2 mm in diameter dark red area(s) in the right diaphragmatic lobe of the lungs" (refer to page 1081 of the original report). It was stated in the

report that histopathologically there was "no correlate to gross red areas" and that "no significant changes were observed" and hence, this gross lesion did not correlate with the microscopic finding in the lungs which was "vascular mineralization" (grade 1).

Control group male no. 43289 had a "few irregularly shaped dark red area(s) in all lobes of the lungs" (refer to page 1079 of the original report). It was stated in the report that histopathologically, there was "no correlate to gross red areas" and that "no significant changes were observed" in the lungs.

Mid dose group male no. 43290 had "multiple irregularly shaped dark red area(s) in all lobes of the lungs" (refer to page 1089 of the original report). It was stated in the report that histopathologically there was "no correlate to gross red areas" and that "no significant changes were observed" in the lungs.

High dose group male no. 43280 had "one 1 mm in diameter depressed area(s) in the cortex of the right kidney" (refer to page 1097 of the original report). Histopathology was not performed for this lesion.

High dose group male no. 43281 had "multiple irregularly shaped dark red area(s) in all lobes of the lungs" (refer to page 1098 of the original report). It was stated in the report that histopathologically, there was "no correlate to gross red areas" and hence this gross lesion did not correlate with microscopic findings in the lungs which were "vascular mineralization" (grade 1) and "alveolar histiocytosis" (grade 1).

After a treatment period of 13 weeks, followed by four weeks of recovery, "depressed area(s)" in the renal cortex and "dark red area(s)" in the lungs of male rats were assessed to not represent a test article-related alteration. Since the study pathologist does not diagnose vascular congestion, the dark red areas in the lungs that were observed grossly might have been due to blood within the vasculature.

Thus, the pattern of gross kidney and lung lesions followed no particular pattern with regard to time of occurrence, group or histologic correlate. They were regarded to have developed spontaneously and unrelated to the administration of the test article. Coupled with the historical data correlation discussed earlier, this analysis lends further evidence to the conclusions that the control group was appropriate for its intended use.

C. MICROSCOPIC EVALUATION OF THE KIDNEYS

Following issuance of the final report, kidneys from the control and high dose male groups at the recovery necropsy (study week 17) were evaluated histologically (refer to Tables 139 and 143). There were no alterations observed other than those typical spontaneous lesions commonly found in animals of this age and strain.

D. INDIVIDUAL ASSESSMENT OF GROUP 1 CONTROL ANIMALS

The impact of possibly ingested test material by control (Group 1) animals on the development of test article-related microscopic findings was assessed for those microscopic findings that were noted either in **a]** animals of the control *and* high dose groups only (Groups 1 and 4, respectively), **b]** animals of the control, mid *and* high dose groups only (Groups 1, 3 and 4, respectively) **and/or c]** animals of the control *and* all three treatment groups (Groups 1, 2, 3, and 4). Control and high dose group animals in the study week 17 recovery group were similarly evaluated. Microscopic findings fulfilling these criteria were hepatocellular vacuolation and thyroid follicular cell hypertrophy.

Two of 10 Group 1 control males had minimal/mild hepatocellular vacuolation, and 1 of 10 Group 1 control males had minimal thyroid follicular cell hypertrophy. In Group 1 control females, three animals had minimal hepatocellular vacuolation. After the completion of the recovery period, three of five Group 1 control males were reported as having minimal hepatocellular vacuolation. None was reported for females. Minimal thyroid follicular cell

hypertrophy was noted in two of five males and in none of the females at the recovery evaluation.

These control (Group 1) animals' individual final body weights, liver and thyroid weights, and ALT, AST and GGT levels were compiled in Text Table 2. Each rat's data was compared to strain- and age-matched historical control data generated at WIL Research Laboratories (Text Tables 3 and 4). Each of the control (Group 1) rats with microscopic evidence of hepatocellular vacuolation or thyroid follicular cell hypertrophy had final body weights, absolute liver and thyroid weights, and ALT, AST and GGT levels that were within the historical range of age- and strain-matched animals with the exception of AST for male no. 43326 at the week 17 necropsy (Text Table 4). However; the AST value for this animal (152 U/L) was similar to the mean + 3 S.D. in the WIL historical control data for 22-25 week old males (149 U/L) and was within the observed range in the WIL historical control data for 17-21 week old males (53 to 155 U/L).

Text Table 2: Clinical Pathology Parameters and Organ Weight Data from Control (Group 1) Rats with Hepatocellular Vacuolation and/or Thyroid Follicular Cell Hypertrophy.

Animal Number	Necropsy Week/ Gender	Histopathology (Grade)		Absolute Organ Weight (g)		Serum Chemistry (U/L)		
		Hepatocellular Vacuolation	Follicular Cell Hypertrophy	Liver Weight	Thyroid Weight	ALT	AST	GGT
43368	13/M	Mild	-	16.13	0.0254	32	75	0
43379	13/M	Minimal	-	14.94	0.0262	43	81	0
43349	13/M	-	Minimal	13.77	0.0215	29	76	0
43433	13/F	Minimal	-	8.79	0.0210	23	72	0
43438	13/F	Minimal	-	6.88	0.0150	30	88	0
43474	13/F	Minimal	-	6.68	0.0151	34	113	0
43289	17/M	Minimal	Minimal	15.04	0.0273	39	128	0
43308	17/M	Minimal	-	14.92	0.0243	39	116	0
43326	17/M	Minimal	Minimal	13.17	0.0317	54	152	0

M = Males
F = Females
ALT = alanine aminotransferase
AST = aspartate aminotransferase
GGT = gamma glutamyltransferase

Text Table 3: Comparison of Individual Control (Group 1) Animals' Final Body Weights, and Absolute Liver and Thyroid Weights to the WIL Research Laboratories Historical Control Range.

HBCD 90-Day Animal Number (Gender)	Final (Fasted) Body Weight (g)		Absolute Organ Weight (g)			
			Liver		Thyroid	
	HBCD 90-Day	WIL Historical Control Range* (Mean ±2 S.D.)	HBCD 90-Day	WIL Historical Control Range* (Mean ±2 S.D.)	HBCD 90-Day	WIL Historical Control Range* (Mean ±2 S.D.)
Week 13 Necropsy						
43368 (M)	607	412 - 616	16.13	9.8 - 18.3	0.0254	0.0149 - 0.0388
43379 (M)	533	412 - 616	14.94	9.8 - 18.3	0.0262	0.0149 - 0.0388
43349 (M)	541	412 - 616	13.77	9.8 - 18.3	0.0215	0.0149 - 0.0388
43433 (F)	290	225 - 337	8.79	6.0 - 9.9	0.0210	0.0099 - 0.0334
43438 (F)	278	225 - 337	6.88	6.0 - 9.9	0.0150	0.0099 - 0.0334
43474 (F)	229	225 - 337	6.68	6.0 - 9.9	0.0151	0.0099 - 0.0334
Week 17 Necropsy						
43289 (M)	561	451 - 687	15.04	10.9 - 19.5	0.0273	0.0135 - 0.0436
43308 (M)	554	451 - 687	14.92	10.9 - 19.5	0.0243	0.0135 - 0.0436
43326 (M)	509	451 - 687	13.17	10.9 - 19.5	0.0317	0.0135 - 0.0436

*Excludes values exceeding the mean +/- 5 S.D.

Text Table 4: Comparison of Individual Control (Group 1) Animals' Serum ALT, AST and GGT Values to the WIL Research Laboratories Historical Control Range.

HBCD 90-Day Animal Number (Gender)	Serum Chemistries (U/L)					
	ALT		AST		GGT	
	HBCD 90-Day	WIL Historical Control Range* (Mean ±2 S.D.)	HBCD 90-Day	WIL Historical Control Range* (Mean ±2 S.D.)	HBCD 90-Day	WIL Historical Control Range* (Mean ±2 S.D.)
Week 13 Necropsy						
43368 (M)	32	19 - 56	75	49 - 122	0	0 - 2
43379 (M)	43	19 - 56	81	49 - 122	0	0 - 2
43349 (M)	29	19 - 56	76	49 - 122	0	0 - 2
43433 (F)	23	0 - 80	72	0 - 206	0	0 - 1.3
43438 (F)	30	0 - 80	88	0 - 206	0	0 - 1.3
43474 (F)	34	0 - 80	113	0 - 206	0	0 - 1.3
Week 17 Necropsy						
43289 (M)	39	20 - 65	128	51 - 129	0	0 - 0
43308 (M)	39	20 - 65	116	51 - 129	0	0 - 0
43326 (M)	54	20 - 65	152	51 - 129	0	0 - 0

*Excludes values exceeding the mean +/- 5 S.D.

Historical control histopathology data were not used as a comparison to this study because historical control pathology data are inappropriate due to the lack of standardization in reporting non-neoplastic findings. In the experience of the

pathologist of record and consistent with the literature, hepatocellular vacuolation is a common spontaneous alteration. Oil red O stains demonstrated that the hepatocellular vacuoles contained lipid. Lipid vacuoles in hepatocytes can be found in normal animals[2,3] and this lipid accumulation is generally reversible[3]. Lipid vacuoles in hepatocytes in control group animals are presumed to be due to nutritional, metabolic, and/or hormonal factors[4] and do not necessarily impair hepatic function or cause hepatic injury[5]. Levels of the hepatic enzymes ALT, AST, and GGT in individual control group animals diagnosed with hepatocellular vacuolation in the present study were within the range of historical control data.

Hypertrophy of thyroid follicular cell epithelium can also occur in control group animals since activity of the thyroid gland normally varies between individuals[6]. Hypertrophy of thyroid follicular cell epithelium in control animals may be due to mild physiologic stimulation[7]. In this study, the contro groups had a higher incidence of thyroid follicular cell hypertrophy at stud week 17 than at study week 13. There is no indication that either of thes alterations (liver or thyroid) were anything other than spontaneous, particular in light of the normal clinical pathology and organ weight data in these animals. This finding is consistent with the use of Group 1 control animals as true controls.

E. SERUM ANALYSIS: DETERMINATION OF HBCD LEVELS IN SELECTED GROUP 5 AND 6 ANIMALS

Detectable levels of HBCD were found in the adipose tissue of the satellit control (Group 5) animals. This prompted analysis of frozen sera from selecte Group 5 animals, collected concurrently from these animals along with th adipose tissue, for HBCD content. For comparison, HBCD levels in the sera o selected Group 6 animals (e.g. those treated with 1000 mg HBCD/kg) were als determined.

Selection of sera for analysis was based on the HBCD level in the adipose tissue; animals with the highest HBCD adipose content were selected for sera analysis. The limit of quantitation was 5 ppb (5 ng/mL). The results of this analysis are presented in detail in Volume 5, Attachment B. In brief, none of the three HBCD diastereomers present in the test article were detected in the sera of satellite control (Group 5) animals at the quantitation limit of 5 ppb, which was the lowest limit that could be achieved.

The appropriateness of a quantitation limit of 5 ppb in the sera of the satellite (Group 5) control was assessed based on the following calculation. Measurable amounts of HBCD were found in the serum (study days 2, 55 and 89) of the rats treated at 1000 mg/kg. The ratio of HBCD in serum to that in fat is expected to be fairly consistent. Thus, the satellite (Group 6) test sera:adipose ratio can be used to estimate the anticipated serum levels in the Group 5 control as indicated by the following formula:

$$\frac{[S_6]}{[F_6]} \times [F_5] = [S_5]$$

S_5 = Mean serum levels of HBCD in Group 5
S_6 = Estimated mean serum levels of HBCD in Group 6
F_5 = Mean fat levels of HBCD in Group 5
F_6 = Mean fat levels of HBCD in Group 6

The estimates are summarized in Text Table 5. These estimates suggest that given the levels present in fat, the gamma isomer should have been detectable in the serum of animal no. 43367 on day 55 and animal no. 43375 on day 89. None was detected.

Text Table 5: Projected Concentrations of HBCD (ng/ml) in Control (Group 5) Animals

		Alpha			Beta			Gamma		
Animal No.	Group	Alpha Levels in Fat (ng/g)	Mean Ratio from Gr. 6 ($x10^3$)	Projected Concentration in Serum (ng/mL)	Beta Levels in Fat (ng/g)	Mean Ratio from Gr. 6 ($x10^3$)	Projected Concentration in Serum (ng/mL)	Gamma Levels in Fat (ng/g)	Mean Ratio from Gr. 6 ($x10^3$)	Projected Concentration in Serum (ng/mL)
Day 2										
43301	5 (Control)	<75	0.0020188	-	<75	0.0006133	-	439	0.002164	0.9500
43317	5 (Control)	<75	0.0020188	-	<75	0.0006133	-	176	0.002164	0.3809
43408	5 (Control)	<75	0.0020188	-	<75	0.0006133	-	196	0.002164	0.424
43415	5 (Control)	<75	0.0020188	-	<75	0.0006133	-	172	0.002164	0.3722
Day 55										
43367	5 (Control)	5810	0.0002968	1.724	474	0.0002947	0.1397	15,500	0.0003286	5.093
43370	5 (Control)	3740	0.0002968	1.110	187	0.0002947	0.05511	8320	0.0003286	2.734
43469	5 (Control)	2440	0.0002968	0.724	213	0.0002947	0.06277	11600	0.0003286	3.812
43470	5 (Control)	2640	0.0002968	0.7836	237	0.0002947	0.06984	8370	0.0003286	2.750
Day 89										
43375	5 (Control)	3140	0.0003148	0.9885	244	0.0002422	0.0591	9600	0.0004919	4.722
43387	5 (Control)	1840	0.0003148	0.5792	84	0.0002422	0.02034	4280	0.0004919	2.105
43472	5 (Control)	2840	0.0003148	0.894	97.8	0.0002422	0.02369	7250	0.0004919	3.566
43473	5 (Control)	2460	0.0003148	0.7744	99.1	0.0002422	0.024	7230	0.0004919	3.556

F. SERUM HORMONE STATISTICAL EVALUATION

The additional nonparametric statistical evaluation of the serum hormone data revealed that there were statistically significant ($p<0.05$ or $p<0.01$) differences between the test article-treated groups and the control group (refer to tables 138, 140, 141 and 142). In both males and females, there was a trend towards increasing TSH levels with increased dosage. The "UR" values were arbitrarily set to zero for the purposes of performing nonparametric statistics. The resulting means should be regarded only as estimates. No clear dose response was seen. Measured TSH levels in the rat are known to be highly variable, as was seen in this study. For this reason, some investigators do not recommend measurement of serum TSH levels to detect endocrine effects[8, 9].

The findings with T_4 were consistent with the original report in that there were statistically significant decreases in T_4 levels with increased dosage.

III. CONCLUSION

The extensive re-evaluation of the Group 1 (control group) data and the comparisons to historical control data were prompted by the results of the test article fat analyses. The presence of test article in the satellite control (Group 5) fat could suggest dosing irregularities. As mentioned, WIL Research Laboratories, Inc., has procedures in place to guard against such dosing problems. In addition, the ratios of the isomers (alpha, beta and gamma) of HBCD can be considered a fingerprint for the neat test article. The fingerprint for the Group 5 fat (gamma>alpha>beta) was more similar to neat material than the HBCD found in the Group 6 fat. A different ratio (alpha>gamma>beta) was found in the Group 6 (satellite HBCD-treated group) fat samples. Coupled with the findings that no test article was identified as being present in the control formulations or in the Group 5 serum samples, the data on the isomeric ratios suggest that the fat may have been contaminated by neat chemical after collection.

The relevant parameters selected to evaluate the control (Group 1) animals of this HBCD 90-day study are consistent with the age- and strain-matched historical control data generated in the test laboratory. Relevant parameters included final body weights, absolute and relative organ weights (liver, thyroid and prostate), and clinical chemistry values (albumin, total serum protein, globulin, gamma glutamyltransferase [GGT], alanine aminotransferase [ALT], aspartate aminotransferase [AST] and chloride). Furthermore, gross lesions in control (Group 1) animals were consistent with spontaneous alterations seen in this age and strain of rat. Finally, assessment of individual clinical chemistry and organ weight data from those control (Group 1) animals with hepatocellular vacuolation or thyroid follicular cell hypertrophy indicate that these histopathologic changes were spontaneous. All evidence demonstrates that the HBCD study Group 1 controls served conclusively as controls in this study.

The revised statistical analysis of the serum hormone data revealed that ther were increases in TSH levels. This finding is consistent, however, with the othe findings (i.e., other than TSH) included in the original final report and does nc change the conclusions offered in that document. The test article caused increase in liver weight due to centrilobular hypertrophy, resulting in increased metabolisn and clearance of T_4, which in turn caused increases in TSH levels. The increases in TSH will cause the thyroid follicular hypertrophy reported here, albeit not to the extent necessary to cause increases in thyroid weight. As mentioned in the original final report, this mechanism for thyroidal change is well established in rodents and is considered adaptive, not adverse, in nature. The no-observed-adverse-effect level (NOAEL) offered in the final report remains 1000 mg/kg.

IV. REFERENCES

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A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

Tables 138 - 143

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 138
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
SUMMARY OF SERUM HORMONE VALUES

ANALYSIS	GROUP:	----- M A L E ----- 0 MG/KG/DAY	100 MG/KG/DAY	300 MG/KG/DAY	1000 MG/KG/DAY
TSH (ng/ml)					
WEEK 3	MEAN	1.53	4.53	2.50	2.85
	S.D.	1.513	4.328	2.476	1.932
	N	5	5	5	5
WEEK 13	MEAN	0.23	2.63*	2.65**	3.88**
	S.D.	0.372	3.675	2.098	2.981
	N	10	10	10	9
WEEK 17	MEAN	1.50	0.37	0.64	1.27
	S.D.	0.915	0.448	0.583	0.780
	N	5	5	5	5
TOTAL T3 (ng/dL)					
WEEK 3	MEAN	70.28	90.28	65.40	75.16
	S.D.	8.474	21.783	14.954	16.259
	N	5	5	5	5
WEEK 13	MEAN	64.36	58.78	58.96	64.23
	S.D.	9.554	13.007	13.172	9.549
	N	10	10	10	9
WEEK 17	MEAN	64.46	78.68	71.56	82.44
	S.D.	16.745	13.310	10.472	23.868
	N	5	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

* = Significantly different from the control group at 0.05 using Mann-Whitney U test
** = Significantly different from the control group at 0.01 using Mann-Whitney U test

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 138
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
SUMMARY OF SERUM HORMONE VALUES

ANALYSIS	GROUP:	----- M A L E ----- 0 MG/KG/DAY	100 MG/KG/DAY	300 MG/KG/DAY	1000 MG/KG/DAY
TOTAL T4 (uG/dL)					
WEEK 3	MEAN	7.84	7.42	7.02	6.32
	S.D.	2.429	1.165	1.698	1.354
	N	5	5	5	5
WEEK 13	MEAN	7.87	6.34**	6.28**	4.97**
	S.D.	1.223	1.222	1.033	0.755
	N	10	10	10	9
WEEK 17	MEAN	6.42	6.56	7.04	5.50
	S.D.	1.139	1.305	1.307	0.354
	N	5	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

** = Significantly different from the control group at 0.01 using Mann-Whitney U test

TABLE 138
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
SUMMARY OF SERUM HORMONE VALUES

ANALYSIS	GROUP:	-----F E M A L E ----- 0 MG/KG/DAY	100 MG/KG/DAY	300 MG/KG/DAY	1000 MG/KG/DAY
TSH (ng/ml)					
WEEK 3	MEAN	0.22	0.78	1.49	1.46
	S.D.	0.483	0.809	2.329	0.867
	N	5	5	5	5
WEEK 13	MEAN	0.23	1.14*	3.56**	2.43**
	S.D.	0.319	1.148	5.010	1.735
	N	10	10	10	10
WEEK 17	MEAN	0.38	0.37	0.26	0.47
	S.D.	0.438	0.137	0.121	0.222
	N	5	5	5	5
TOTAL T3 (ng/dL)					
WEEK 3	MEAN	76.28	71.40	77.24	80.94
	S.D.	14.358	11.807	4.895	11.968
	N	5	5	5	5
WEEK 13	MEAN	73.40	70.78	67.02	70.31
	S.D.	14.967	19.176	17.215	16.783
	N	10	10	10	9
WEEK 17	MEAN	73.54	73.00	77.74	86.36
	S.D.	8.486	9.605	24.400	26.527
	N	5	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

* = Significantly different from the control group at 0.05 using Mann-Whitney U test
** = Significantly different from the control group at 0.01 using Mann-Whitney U test

TABLE 138
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
SUMMARY OF SERUM HORMONE VALUES

ANALYSIS	GROUP:	0 MG/KG/DAY	-----F E M A L E ----- 100 MG/KG/DAY	300 MG/KG/DAY	1000 MG/KG/DAY
TOTAL T4 (uG/dL)					
WEEK 3	MEAN	5.95	6.06	5.76	5.62
	S.D.	1.462	1.210	1.305	0.817
	N	4	5	5	5
WEEK 13	MEAN	5.43	4.96	4.53*	4.31**
	S.D.	0.860	0.624	0.876	0.762
	N	10	10	10	9
WEEK 17	MEAN	3.20	3.64	3.64	4.00
	S.D.	1.049	0.581	0.467	0.970
	N	5	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

* = Significantly different from the control group at 0.05 using Mann-Whitney U test
** = Significantly different from the control group at 0.01 using Mann-Whitney U test

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PROJECT NO.:WIL-186012
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TABLE 139 (WEEK 17 RECOVERY NECROPSY - KIDNEY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
SUMMARY OF MICROSCOPIC FINDINGS

	----- MALE -----			
GROUP:	1	2	3	4
NUMBER OF ANIMALS IN DOSE GROUP	15	15	15	15
NUMBER OF ANIMALS EXAMINED WEEK 17	5	0	0	5
KIDNEYS				
TOTAL NUMBER EXAMINED	5	0	0	5
EXAMINED, UNREMARKABLE	0	0	0	1
-INFLAMMATION, SUBACUTE	5	0	0	3
MINIMAL	5	NONE	NONE	3
-BASOPHILIC TUBULES	4	0	0	2
MINIMAL	3	NONE	NONE	2
MILD	1	NONE	NONE	NONE
-MINERALIZATION, PAPILLARY TUBULAR	0	0	0	1
MINIMAL	NONE	NONE	NONE	1
-HYPERPLASIA, BOWMAN'S CAPSULE	1	0	0	0
MINIMAL	1	NONE	NONE	NONE
-DILATATION, TUBULAR	1	0	0	0
MINIMAL	1	NONE	NONE	NONE

1- 0 MG/KG/DAY 2- 100 MG/KG/DAY 3- 300 MG/KG/DAY 4- 1000 MG/KG/DAY

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TABLE 140 (WEEK 3 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 0 MG/KG/DAY		MALES	
43365	0.67	57.30	6.10
43368	1.60	72.70	12.00
43369	0.00-A	77.60	7.90
43379	3.99	66.70	6.90
43391	1.37	77.10	6.30
MEAN	1.53	70.28	7.84
S.D.	1.513	8.474	2.429
N	5	5	5

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 140 (WEEK 3 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 100 MG/KG/DAY		MALES	
43371	12.17	74.30	7.80
43380	2.59	123.00	9.30
43382	3.09	79.90	6.80
43384	3.29	72.20	6.50
43386	1.50	102.00	6.70
MEAN	4.53	90.28	7.42
S.D.	4.328	21.783	1.165
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 140 (WEEK 3 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 300 MG/KG/DAY		MALES	
43363	0.00-A	50.10	5.20
43383	0.00-A	89.50	8.80
43385	3.07	68.10	8.00
43388	3.76	61.40	7.90
43392	5.68	57.90	5.20
MEAN	2.50	65.40	7.02
S.D.	2.476	14.954	1.698
N	5	5	5

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 140 (WEEK 3 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 1000 MG/KG/DAY		MALES	
43362	1.84	56.50	6.30
43372	4.90	97.00	6.30
43373	0.86	78.00	6.60
43377	1.71	62.00	8.10
43397	4.96	82.30	4.30
MEAN	2.85	75.16	6.32
S.D.	1.932	16.259	1.354
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 140 (WEEK 3 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 0 MG/KG/DAY		FEMALES	
43467	0.00-A	92.70	7.90
43474	0.00-A	77.50	5.50
43483	1.08	78.40	6.00
43497	0.00-A	53.10	4.40
43501	0.00-A	79.70	QNS
MEAN	0.22	76.28	5.95
S.D.	0.483	14.358	1.462
N	5	5	4

QNS = QUANTITY NOT SUFFICIENT, A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 140 (WEEK 3 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 100 MG/KG/DAY		FEMALES	
43486	0.84	59.90	6.60
43489	0.00-A	58.30	6.70
43502	1.89	77.60	6.60
43511	1.19	75.80	6.50
43515	0.00-A	85.40	3.90
MEAN	0.78	71.40	6.06
S.D.	0.809	11.807	1.210
N	5	5	5

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 140 (WEEK 3 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 300 MG/KG/DAY	FEMALES		
43496	5.62	75.20	6.80
43508	0.00-A	72.60	7.30
43513	0.63	82.30	5.70
43516	0.84	82.70	4.80
43517	0.37	73.40	4.20
MEAN	1.49	77.24	5.76
S.D.	2.329	4.895	1.305
N	5	5	5

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 140 (WEEK 3 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 1000 MG/KG/DAY	FEMALES		
43479	2.31	94.60	5.70
43481	0.00-A	67.60	5.00
43484	1.65	69.30	4.60
43492	1.57	88.70	6.50
43503	1.78	84.50	6.30
MEAN	1.46	80.94	5.62
S.D.	0.867	11.968	0.817
N	5	5	5

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 141 (WEEK 13 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 0 MG/KG/DAY		MALES	
43332	0.00-A	76.40	7.10
43334	0.98	70.00	6.60
43336	0.10	67.50	7.80
43339	0.00-A	63.40	7.10
43349	0.00-A	41.50	6.60
43365	0.86	60.90	6.80
43368	0.00-A	61.80	9.60
43369	0.18	73.40	9.70
43379	0.20	66.70	8.40
43391	0.00-A	62.00	9.00
MEAN	0.23	64.36	7.87
S.D.	0.372	9.553	1.223
N	10	10	10

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 141 (WEEK 13 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 100 MG/KG/DAY	MALES		
43342	0.00-A	48.50	4.00
43350	2.66	44.40	6.80
43351	0.37	72.80	6.50
43354	3.84	68.20	5.30
43364	11.91	68.70	6.00
43371	4.86	53.50	6.80
43380	1.67	74.10	6.70
43382	0.38	42.40	6.00
43384	0.61	45.50	8.80
43386	0.00-A	69.70	6.50
MEAN	2.63	58.78	6.34
S.D.	3.675	13.007	1.222
N	10	10	10

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 141 (WEEK 13 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 300 MG/KG/DAY		MALES	
43323	4.59	59.30	7.30
43331	4.12	86.30	7.90
43341	3.20	46.00	5.90
43355	0.49	59.70	6.50
43361	5.95	74.40	6.90
43363	1.49	55.40	5.00
43383	0.32	40.90	5.80
43385	1.11	61.00	5.90
43388	0.52	53.20	7.00
43392	4.69	53.40	4.60
MEAN	2.65	58.96	6.28
S.D.	2.098	13.172	1.033
N	10	10	10

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 141 (WEEK 13 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 1000 MG/KG/DAY		MALES	
43297	4.47	67.60	4.30
43325	1.58	54.40	5.20
43328	6.93	48.60	4.30
43346	1.17	62.10	5.00
43362	3.69	69.30	4.50
43372	8.62	59.40	5.80
43373	1.15	75.50	6.50
43377	0.61	63.00	4.60
43397	6.74	78.20	4.50
MEAN	3.88	64.23	4.97
S.D.	2.981	9.549	0.755
N	9	9	9

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 141 (WEEK 13 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 0 MG/KG/DAY		FEMALES	
43433	0.85	107.00	5.80
43435	0.00-A	66.80	5.40
43436	0.00-A	64.10	6.20
43438	0.73	65.20	6.60
43449	0.34	88.90	4.60
43467	0.21	69.40	5.30
43474	0.17	60.40	4.70
43483	0.00-A	82.90	5.00
43497	0.00-A	61.40	6.60
43501	0.00-A	67.90	4.10
MEAN	0.23	73.40	5.43
S.D.	0.319	14.967	0.860
N	10	10	10

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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SPONSOR:CMA-BFRIP

TABLE 141 (WEEK 13 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 100 MG/KG/DAY FEMALES			
43420	0.48	72.70	5.00
43439	0.00-A	74.90	5.10
43458	0.00-A	103.00	4.80
43462	0.90	104.00	5.90
43468	1.05	67.60	5.10
43486	2.63	59.50	5.20
43489	1.03	68.40	4.60
43502	3.65	52.50	4.10
43511	0.70	54.70	5.80
43515	0.94	50.50	4.00
MEAN	1.14	70.78	4.96
S.D.	1.148	19.176	0.624
N	10	10	10

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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TABLE 141 (WEEK 13 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 300 MG/KG/DAY		FEMALES	
43463	0.54	38.30	3.40
43475	6.16	57.20	5.30
43478	0.89	62.50	4.50
43491	1.79	53.10	6.00
43495	1.45	68.10	5.50
43496	7.66	74.30	4.90
43508	0.00-A	100.00	4.40
43513	0.41	86.30	3.90
43516	15.77	62.80	3.70
43517	0.95	67.60	3.70
MEAN	3.56	67.02	4.53
S.D.	5.010	17.215	0.876
N	10	10	10

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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SPONSOR:CMA-BFRIP

TABLE 141 (WEEK 13 EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 1000 MG/KG/DAY	FEMALES		
43440	2.09	QNS	QNS
43456	2.83	75.40	3.50
43460	1.49	91.70	4.00
43466	6.87	53.00	4.30
43477	0.96	83.70	4.20
43479	3.21	42.00	3.90
43481	2.66	81.30	4.40
43484	1.09	53.20	3.60
43492	1.79	77.90	4.90
43503	1.34	74.60	6.00
MEAN	2.43	70.31	4.31
S.D.	1.735	16.783	0.762
N	10	9	9

QNS = QUANTITY NOT SUFFICIENT

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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TABLE 142 (WEEK 17 RECOVERY EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 0 MG/KG/DAY		MALES	
43289	1.48	80.60	6.10
43295	1.23	69.30	6.80
43308	3.07	78.20	7.10
43316	0.92	42.30	4.60
43326	0.81	51.90	7.50
MEAN	1.50	64.46	6.42
S.D.	0.915	16.745	1.139
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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SPONSOR:CMA-BFRIP

TABLE 142 (WEEK 17 RECOVERY EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 100 MG/KG/DAY	MALES		
43285	0.00-A	101.00	7.20
43293	0.14	78.70	7.60
43311	0.23	67.90	7.70
43320	0.35	76.60	5.30
43340	1.14	69.20	5.00
MEAN	0.37	78.68	6.56
S.D.	0.448	13.310	1.305
N	5	5	5

A = VALUE BELOW INSTRUMENT RANGE; 0.00 USED FOR STATISTICAL ANALYSIS

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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TABLE 142 (WEEK 17 RECOVERY EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 300 MG/KG/DAY		MALES	
43290	0.28	71.00	5.80
43307	1.66	89.10	6.60
43309	0.26	68.40	8.00
43318	0.46	68.20	8.80
43322	0.53	61.10	6.00
MEAN	0.64	71.56	7.04
S.D.	0.583	10.472	1.307
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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TABLE 142 (WEEK 17 RECOVERY EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 1000 MG/KG/DAY	MALES		
43277	2.47	72.60	5.30
43278	1.44	120.00	5.20
43280	1.02	74.60	5.40
43281	0.34	88.50	5.50
43282	1.08	56.50	6.10
MEAN	1.27	82.44	5.50
S.D.	0.780	23.868	0.354
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

PROJECT NO.:WIL-186012
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TABLE 142 (WEEK 17 RECOVERY EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 0 MG/KG/DAY		FEMALES	
43398	1.15	83.40	3.50
43405	0.07	64.40	3.10
43409	0.14	68.30	1.80
43423	0.27	81.70	2.90
43432	0.29	69.90	4.70
MEAN	0.38	73.54	3.20
S.D.	0.438	8.486	1.049
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 142 (WEEK 17 RECOVERY EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 100 MG/KG/DAY	FEMALES		
43400	0.17	73.10	3.90
43407	0.54	81.60	3.50
43413	0.39	83.50	4.50
43416	0.32	63.90	3.00
43419	0.43	62.90	3.30
MEAN	0.37	73.00	3.64
S.D.	0.137	9.605	0.581
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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TABLE 142 (WEEK 17 RECOVERY EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 300 MG/KG/DAY		FEMALES	
43402	0.47	66.80	3.00
43426	0.20	77.70	3.90
43442	0.17	118.00	4.10
43446	0.24	52.80	3.90
43461	0.21	73.40	3.30
MEAN	0.26	77.74	3.64
S.D.	0.121	24.400	0.467
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

TABLE 142 (WEEK 17 RECOVERY EVALUATION)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL SERUM HORMONE VALUES

ANIMAL	TSH	TOTAL T3	TOTAL T4
	ng/ml	ng/dL	uG/dL
GROUP: 1000 MG/KG/DAY	FEMALES		
43401	0.63	75.70	2.70
43410	0.68	85.30	5.30
43421	0.20	128.00	4.50
43429	0.27	87.50	3.80
43430	0.59	55.30	3.70
MEAN	0.47	86.36	4.00
S.D.	0.222	26.527	0.970
N	5	5	5

uG/dL = MICROGRAMS/DECILITER, ng/ml = NANOGRAMS/MILLILITER, ng/dL = NANOGRAMS/DECILITER

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TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43289 GROUP 1: 0 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.99	0.355
LIVER	15.04	2.681
KIDNEYS	3.61	0.643
HEART	1.84	0.328
SPLEEN	0.62	0.111
PROSTATE	1.03	0.184
RT TESTIS	1.73	0.308
LT TESTIS	1.71	0.305
RT EPIDIDYMIS	0.75	0.134
LT EPIDIDYMIS	0.78	0.139
RT CAUDA EPID	0.3544	0.063
LT CAUDA EPID	0.3636	0.065
THYMUS GLAND	0.2074	0.037
ADRENAL GLANDS	0.0540	0.010
THYROIDS/PARA	0.0273	0.005
FINAL BODY WT(G)	561.	

		GRADE
KIDNEYS	MICRO: INFLAMMATION, SUBACUTE	1
	HYPERPLASIA, BOWMAN'S CAPSULE	1
LIVER	MICRO: INFLAMMATION, SUBACUTE	1
	VACUOLATION, HEPATOCELLULAR	1
LUNGS	GROSS: DARK RED AREA(S)	P
	FEW, IRREGULARLY SHAPED, ALL LOBES	
LUNGS	MICRO: NO SIGNIFICANT CHANGES OBSERVED	
	NO CORRELATE TO GROSS RED AREAS	
THYROID GLANDS	MICRO: HYPERTROPHY, FOLLICULAR CELL	1
	ONE THYROID EXAMINED; OTHER NOT PRESENT; RECUT EVALUATED	
NO SIGNIFICANT CHANGES OBSERVED		

GROSS:

ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
CECUM	COLON	DUODENUM	ESOPHAGUS
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
KIDNEYS	LIVER	LYMPH NODE, MES	NERVE,SCIATIC
PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS	RECTUM
PITUITARY	PROSTATE	SAL. GLAND MAND	SEMINAL VESICLES
SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STOMACH	LYMPH NODE, MAND	THYMUS GLAND	THYROID GLANDS
RT TESTIS	LT TESTIS	TRACHEA	VAS DEFERENS
URINARY BLADDER			

MICRO:LUNGS PROSTATE

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43295 GROUP 1: 0 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.98	0.345
LIVER	15.58	2.714
KIDNEYS	4.06	0.707
HEART	1.61	0.280
SPLEEN	0.65	0.113
PROSTATE	1.29	0.225
RT TESTIS	1.70	0.296
LT TESTIS	1.71	0.298
RT EPIDIDYMIS	0.74	0.129
LT EPIDIDYMIS	0.72	0.125
RT CAUDA EPID	0.3007	0.052
LT CAUDA EPID	0.3127	0.054
THYMUS GLAND	0.3309	0.058
ADRENAL GLANDS	0.0636	0.011
THYROIDS/PARA	0.0313	0.005
FINAL BODY WT(G)	574.	

KIDNEYS
LIVER
NO SIGNIFICANT
CHANGES OBSERVED

		GRADE
MICRO:	INFLAMMATION, SUBACUTE	1
	BASOPHILIC TUBULES	1
MICRO:	INFLAMMATION, SUBACUTE	1

GROSS:

ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
CECUM	COLON	DUODENUM	ESOPHAGUS
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND
THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA
VAS DEFERENS	URINARY BLADDER		

MICRO:

LUNGS	PROSTATE	THYROID GLANDS

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43308 GROUP 1: 0 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.91	0.345
LIVER	14.92	2.693
KIDNEYS	3.53	0.637
HEART	1.69	0.305
SPLEEN	0.69	0.125
PROSTATE	1.49	0.269
RT TESTIS	1.42	0.256
LT TESTIS	1.35	0.244
RT EPIDIDYMIS	0.74	0.134
LT EPIDIDYMIS	0.71	0.128
RT CAUDA EPID	0.3278	0.059
LT CAUDA EPID	0.3340	0.060
THYMUS GLAND	0.2840	0.051
ADRENAL GLANDS	0.0569	0.010
THYROIDS/PARA	0.0243	0.004
FINAL BODY WT(G)	554.	

		GRADE
KIDNEYS	GROSS: DEPRESSED AREA(S)	P
	TWO, LESS THAN 1 MM IN DIAMETER, IN CORTEX, RIGHT	
KIDNEYS	MICRO: INFLAMMATION, SUBACUTE	1
	BASOPHILIC TUBULES	1
	NO CORRELATE TO GROSS DEPRESSED AREA	
LIVER	MICRO: VACUOLATION, HEPATOCELLULAR	1
	INFLAMMATION, SUBACUTE	1
LUNGS	GROSS: DARK RED AREA(S)	P
	ONE, 2 MM IN DIAMETER, RIGHT DIAPHRAGMATIC LOBE	
LUNGS	MICRO: MINERALIZATION, VASCULAR	1
	NO CORRELATE TO GROSS RED AREAS	
PROSTATE	MICRO: INFLAMMATION, CHRONIC ACTIVE	1

NO SIGNIFICANT CHANGES OBSERVED

GROSS:

ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
CECUM	COLON	DUODENUM	ESOPHAGUS
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
LIVER	LYMPH NODE, MES	NERVE,SCIATIC	PANCREAS
RT EPIDIDYMIS	LT EPIDIDYMIS	RECTUM	PITUITARY
PROSTATE	SAL. GLAND MAND	SEMINAL VESICLES	SKELETAL MUSCLE
SKIN	SPINAL CORD	SPLEEN	STOMACH
LYMPH NODE, MAND	THYMUS GLAND	THYROID GLANDS	RT TESTIS
LT TESTIS	TRACHEA	VAS DEFERENS	URINARY BLADDER

MICRO:THYROID GLANDS

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43316 GROUP 1: 0 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.17	0.425
LIVER	13.22	2.587
KIDNEYS	3.30	0.646
HEART	1.46	0.286
SPLEEN	0.70	0.137
PROSTATE	0.99	0.194
RT TESTIS	1.74	0.341
LT TESTIS	1.65	0.323
RT EPIDIDYMIS	0.71	0.139
LT EPIDIDYMIS	0.73	0.143
RT CAUDA EPID	0.2863	0.056
LT CAUDA EPID	0.2963	0.058
THYMUS GLAND	0.4229	0.083
ADRENAL GLANDS	0.0823	0.016
THYROIDS/PARA	0.0294	0.006
FINAL BODY WT(G)	511.	

KIDNEYS
LUNGS
NO SIGNIFICANT
CHANGES OBSERVED

MICRO: INFLAMMATION, SUBACUTE 1
BASOPHILIC TUBULES 1
MICRO: INFLAMMATION, SUBACUTE 1
MICRO: MINERALIZATION, VASCULAR 1

GROSS:	ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
	CECUM	COLON	DUODENUM	ESOPHAGUS
	EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
	KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
	NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
	RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
	SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND
	THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA
	VAS DEFERENS	URINARY BLADDER		
MICRO:	PROSTATE	THYROID GLANDS		

ANIMAL NO. 43316 GROUP 1: 0 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

GRADE

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43326 GROUP 1: 0 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.80	0.354
LIVER	13.17	2.587
KIDNEYS	2.80	0.550
HEART	1.61	0.316
SPLEEN	0.56	0.110
PROSTATE	1.27	0.250
RT TESTIS	1.54	0.303
LT TESTIS	1.40	0.275
RT EPIDIDYMIS	0.62	0.122
LT EPIDIDYMIS	0.53	0.104
RT CAUDA EPID	0.2418	0.048
LT CAUDA EPID	0.2355	0.046
THYMUS GLAND	0.2999	0.059
ADRENAL GLANDS	0.0714	0.014
THYROIDS/PARA	0.0317	0.006
FINAL BODY WT(G)	509.	

GENERAL COMMENT

KIDNEYS

LIVER

LUNGS

PROSTATE

THYROID GLANDS

NO SIGNIFICANT CHANGES OBSERVED

		GRADE
GROSS:	MECHANICAL TRAUMA	P
	PROXIMAL TAIL BROKEN	
MICRO:	BASOPHILIC TUBULES	2
	INFLAMMATION, SUBACUTE	1
	DILATATION, TUBULAR	1
MICRO:	INFLAMMATION, SUBACUTE	1
	VACUOLATION, HEPATOCELLULAR	1
MICRO:	MINERALIZATION, VASCULAR	1
	INFLAMMATION, CHRONIC	1
	HISTIOCYTOSIS, ALVEOLAR	1
MICRO:	INFLAMMATION, CHRONIC ACTIVE	1
MICRO:	CYST, ULTIMOBRANCHIAL	1
	HYPERTROPHY, FOLLICULAR CELL	1

GROSS: ADRENAL GLANDS, AORTA, BRAIN, CECUM, COLON, DUODENUM, ESOPHAGUS, EYES/OPTIC N., HEART, ILEUM, JEJUNUM, KIDNEYS, LIVER, LUNGS, LYMPH NODE, MES, NERVE,SCIATIC, PANCREAS, PITUITARY, RT EPIDIDYMIS, LT EPIDIDYMIS, RECTUM, PROSTATE, SAL. GLAND MAND, SEMINAL VESICLES, SKELETAL MUSCLE, SKIN, SPINAL CORD, SPLEEN, STOMACH, LYMPH NODE, MAND, THYMUS GLAND, THYROID GLANDS, RT TESTIS, LT TESTIS, TRACHEA, VAS DEFERENS, URINARY BLADDER, STERNEBRAE

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43285 GROUP 2: 100 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.11	0.351
LIVER	17.35	2.887
KIDNEYS	3.87	0.644
HEART	1.72	0.286
SPLEEN	0.78	0.130
PROSTATE	0.68	0.113
RT TESTIS	1.70	0.283
LT TESTIS	1.76	0.293
RT EPIDIDYMIS	0.73	0.121
LT EPIDIDYMIS	0.74	0.123
RT CAUDA EPID	0.3264	0.054
LT CAUDA EPID	0.3583	0.060
THYMUS GLAND	0.2941	0.049
ADRENAL GLANDS	0.0686	0.011
THYROIDS/PARA	0.0416	0.007
FINAL BODY WT(G)	601.	

LIVER
THYROID GLANDS
NO SIGNIFICANT
CHANGES OBSERVED

		GRADE
MICRO:	INFLAMMATION, SUBACUTE	1
MICRO:	CYST, ULTIMOBRANCHIAL	2

GROSS:	ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
	CECUM	COLON	DUODENUM	ESOPHAGUS
	EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
	KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
	NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
	RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
	SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND
	THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA
	VAS DEFERENS	URINARY BLADDER		
MICRO:	LUNGS	PROSTATE		

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43293 GROUP 2: 100 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.13	0.373
LIVER	17.06	2.988
KIDNEYS	4.35	0.762
HEART	1.80	0.315
SPLEEN	0.79	0.138
PROSTATE	0.89	0.156
RT TESTIS	1.53	0.268
LT TESTIS	1.58	0.277
RT EPIDIDYMIS	0.72	0.126
LT EPIDIDYMIS	0.81	0.142
RT CAUDA EPID	0.3224	0.056
LT CAUDA EPID	0.4092	0.072
THYMUS GLAND	0.2672	0.047
ADRENAL GLANDS	0.0609	0.011
THYROIDS/PARA	0.0273	0.005
FINAL BODY WT(G)	571.	

LIVER
PROSTATE
NO SIGNIFICANT
CHANGES OBSERVED

MICRO: INFLAMMATION, SUBACUTE				1
MICRO: HYPERTROPHY, EPITHELIAL				1
GROSS: ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN	
CECUM	COLON	DUODENUM	ESOPHAGUS	
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM	
KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS	
NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS	
RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND	
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	
SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND	
THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA	
VAS DEFERENS	URINARY BLADDER			
MICRO: LUNGS	THYROID GLANDS			

GRADE

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43311 GROUP 2: 100 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.14	0.451
LIVER	14.10	2.968
KIDNEYS	3.55	0.747
HEART	1.56	0.328
SPLEEN	0.83	0.175
PROSTATE	0.93	0.196
RT TESTIS	1.68	0.354
LT TESTIS	1.69	0.356
RT EPIDIDYMIS	0.83	0.175
LT EPIDIDYMIS	0.77	0.162
RT CAUDA EPID	0.3558	0.075
LT CAUDA EPID	0.3440	0.072
THYMUS GLAND	0.2363	0.050
ADRENAL GLANDS	0.0688	0.014
THYROIDS/PARA	0.0291	0.006
FINAL BODY WT(G)	475.	

LIVER
NO SIGNIFICANT
CHANGES OBSERVED

GRADE
1

MICRO: INFLAMMATION, SUBACUTE

GROSS:ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
CECUM	COLON	DUODENUM	ESOPHAGUS
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND
THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA
VAS DEFERENS	URINARY BLADDER		
MICRO:LUNGS	PROSTATE	THYROID GLANDS	

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43320 GROUP 2: 100 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.95	0.412
LIVER	13.09	2.767
KIDNEYS	3.54	0.748
HEART	1.47	0.311
SPLEEN	0.68	0.144
PROSTATE	1.00	0.211
RT TESTIS	1.42	0.300
LT TESTIS	1.42	0.300
RT EPIDIDYMIS	0.60	0.127
LT EPIDIDYMIS	0.62	0.131
RT CAUDA EPID	0.2486	0.053
LT CAUDA EPID	0.2944	0.062
THYMUS GLAND	0.1383	0.029
ADRENAL GLANDS	0.0526	0.011
THYROIDS/PARA	0.0303	0.006
FINAL BODY WT(G)	473.	

LIVER
THYROID GLANDS
NO SIGNIFICANT
CHANGES OBSERVED

				GRADE
MICRO: INFLAMMATION, SUBACUTE				1
MICRO: CYST, ULTIMOBRANCHIAL				2
GROSS:ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN	
CECUM	COLON	DUODENUM	ESOPHAGUS	
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM	
KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS	
NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS	
RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND	
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD	
SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND	
THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA	
VAS DEFERENS	URINARY BLADDER			
MICRO:LUNGS	PROSTATE			

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43340 GROUP 2: 100 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.01	0.533
LIVER	12.00	3.183
KIDNEYS	2.86	0.759
HEART	1.47	0.390
SPLEEN	0.65	0.172
PROSTATE	0.74	0.196
RT TESTIS	0.20	0.053
LT TESTIS	1.04	0.276
RT EPIDIDYMIS	0.06	0.016
LT EPIDIDYMIS	0.53	0.141
LT CAUDA EPID	0.2047	0.054
THYMUS GLAND	0.1939	0.051
ADRENAL GLANDS	0.0716	0.019
THYROIDS/PARA	0.0252	0.007
FINAL BODY WT(G)	377.	

GENERAL COMMENT	GRADE
LIVER	
SEMINAL VESICLES	
RT TESTIS	
COAGULATING GL	
NO SIGNIFICANT CHANGES OBSERVED	

				GRADE
GROSS:	ORGAN NOT POSITIVELY IDENTIFIED RIGHT EPIDIDYMIS			P
MICRO:	INFLAMMATION, SUBACUTE			1
GROSS:	SMALL RIGHT			P
GROSS:	SMALL			P
GROSS:	SMALL RIGHT			P
GROSS:	ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
	CECUM	COLON	DUODENUM	ESOPHAGUS
	EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
	KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
	NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
	RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
	STOMACH	LYMPH NODE, MAND	THYMUS GLAND	THYROID GLANDS
	LT TESTIS	TRACHEA	VAS DEFERENS	URINARY BLADDER
MICRO:	LUNGS	PROSTATE	THYROID GLANDS	

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

ANIMAL NO. 43290 GROUP 3: 300 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.	GENERAL COMMENT	GRADE
BRAIN	2.01	0.423		
LIVER	13.03	2.743	LIVER	
KIDNEYS	3.32	0.699	LUNGS	
HEART	1.46	0.307		
SPLEEN	0.70	0.147	LUNGS	
PROSTATE	0.50	0.105		
RT TESTIS	1.47	0.309	THYROID GLANDS	
LT TESTIS	1.52	0.320	TEETH	
RT EPIDIDYMIS	0.69	0.145		
LT EPIDIDYMIS	0.69	0.145	TEETH	
RT CAUDA EPID	0.2892	0.061		
LT CAUDA EPID	0.3178	0.067	NO SIGNIFICANT	
THYMUS GLAND	0.2907	0.061	CHANGES OBSERVED	
ADRENAL GLANDS	0.0650	0.014		
THYROIDS/PARA	0.0350	0.007		
FINAL BODY WT(G)	475.			

GROSS: ORGAN DAMAGED AT NECROPSY — P
ADRENAL GLAND, RIGHT
MICRO: INFLAMMATION, SUBACUTE — 1
GROSS: DARK RED AREA(S) — P
MULTIPLE, IRREGULARLY SHAPED, ALL LOBES
MICRO: NO SIGNIFICANT CHANGES OBSERVED
NO CORRELATE TO GROSS RED AREAS
MICRO: CYST, ULTIMOBRANCHIAL — 2
GROSS: MALALIGNED — P
UPPER INCISOR, BILATERAL
GROSS: BROKEN — P
UPPER INCISOR, BILATERAL

GROSS:	ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
	CECUM	COLON	DUODENUM	ESOPHAGUS
	EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
	KIDNEYS	LIVER	LYMPH NODE, MES	NERVE,SCIATIC
	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS	RECTUM
	PITUITARY	PROSTATE	SAL. GLAND MAND	SEMINAL VESICLES
	SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
	STOMACH	LYMPH NODE, MAND	THYMUS GLAND	THYROID GLANDS
	RT TESTIS	LT TESTIS	TRACHEA	VAS DEFERENS
	URINARY BLADDER			
MICRO:	LUNGS	PROSTATE		

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43307 GROUP 3: 300 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.02	0.374
LIVER	16.69	3.091
KIDNEYS	4.19	0.776
HEART	1.70	0.315
SPLEEN	0.70	0.130
PROSTATE	1.20	0.222
RT TESTIS	1.59	0.294
LT TESTIS	1.62	0.300
RT EPIDIDYMIS	0.66	0.122
LT EPIDIDYMIS	0.70	0.130
RT CAUDA EPID	0.2854	0.053
LT CAUDA EPID	0.3102	0.057
THYMUS GLAND	0.3679	0.068
ADRENAL GLANDS	0.0536	0.010
THYROIDS/PARA	0.0288	0.005
FINAL BODY WT(G)	540.	

		GRADE
LIVER	MICRO: VACUOLATION, HEPATOCELLULAR	1
	INFLAMMATION, SUBACUTE	1
LUNGS	MICRO: HISTIOCYTOSIS, ALVEOLAR	2
	MINERALIZATION, VASCULAR	1
PROSTATE	MICRO: INFLAMMATION, SUBACUTE	1
THYROID GLANDS	MICRO: HYPERTROPHY, FOLLICULAR CELL	1
	CYST, ULTIMOBRANCHIAL	2

NO SIGNIFICANT CHANGES OBSERVED

GROSS:

ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
CECUM	COLON	DUODENUM	ESOPHAGUS
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND
THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA
VAS DEFERENS	URINARY BLADDER		

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43309 GROUP 3: 300 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.05	0.341
LIVER	17.85	2.970
KIDNEYS	4.75	0.790
HEART	1.84	0.306
SPLEEN	0.90	0.150
PROSTATE	1.25	0.208
RT TESTIS	1.91	0.318
LT TESTIS	1.98	0.329
RT EPIDIDYMIS	0.84	0.140
LT EPIDIDYMIS	0.80	0.133
RT CAUDA EPID	0.4189	0.070
LT CAUDA EPID	0.4033	0.067
THYMUS GLAND	0.3740	0.062
ADRENAL GLANDS	0.0560	0.009
THYROIDS/PARA	0.0319	0.005
FINAL BODY WT(G)	601.	

LIVER
LUNGS
NO SIGNIFICANT CHANGES OBSERVED

				GRADE
MICRO:	INFLAMMATION, SUBACUTE			1
	VACUOLATION, HEPATOCELLULAR			1
MICRO:	INFLAMMATION, CHRONIC			1
	HISTIOCYTOSIS, ALVEOLAR			1

GROSS:	ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
	CECUM	COLON	DUODENUM	ESOPHAGUS
	EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
	KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
	NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
	RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
	SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND
	THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA
	VAS DEFERENS	URINARY BLADDER		
MICRO:	PROSTATE	THYROID GLANDS		

ANIMAL NO. 43309 GROUP 3: 300 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

GRADE

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43318 GROUP 3: 300 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.99	0.341
LIVER	16.16	2.772
KIDNEYS	4.00	0.686
HEART	1.79	0.307
SPLEEN	0.91	0.156
PROSTATE	1.39	0.238
RT TESTIS	1.56	0.268
LT TESTIS	1.52	0.261
RT EPIDIDYMIS	0.74	0.127
LT EPIDIDYMIS	0.62	0.106
RT CAUDA EPID	0.2988	0.051
LT CAUDA EPID	0.2614	0.045
THYMUS GLAND	0.1868	0.032
ADRENAL GLANDS	0.0485	0.008
THYROIDS/PARA	0.0206	0.004
FINAL BODY WT(G)	583.	

KIDNEYS
NO SIGNIFICANT
CHANGES OBSERVED

		GRADE
GROSS:	WHITE AREA(S) IRREGULARLY SHAPED, BILATERAL	P
MICRO:	INFLAMMATION, SUBACUTE	1
MICRO:	MINERALIZATION, VASCULAR	1
MICRO:	HYPERTROPHY, FOLLICULAR CELL	1

GROSS: ADRENAL GLANDS, AORTA, BRAIN, CECUM, COLON, DUODENUM, ESOPHAGUS, EYES/OPTIC N., HEART, ILEUM, JEJUNUM, LIVER, LYMPH NODE, MES, LUNGS, NERVE,SCIATIC, PANCREAS, RT EPIDIDYMIS, LT EPIDIDYMIS, RECTUM, PITUITARY, PROSTATE, SAL. GLAND MAND, SEMINAL VESICLES, SKELETAL MUSCLE, SKIN, SPINAL CORD, SPLEEN, STOMACH, LYMPH NODE, MAND, THYMUS GLAND, THYROID GLANDS, RT TESTIS, LT TESTIS, TRACHEA, VAS DEFERENS, URINARY BLADDER

MICRO: PROSTATE

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43322 GROUP 3: 300 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.18	0.447
LIVER	14.58	2.988
KIDNEYS	3.47	0.711
HEART	1.62	0.332
SPLEEN	0.86	0.176
PROSTATE	0.99	0.203
RT TESTIS	1.67	0.342
LT TESTIS	1.64	0.336
RT EPIDIDYMIS	0.73	0.150
LT EPIDIDYMIS	0.78	0.160
RT CAUDA EPID	0.3295	0.068
LT CAUDA EPID	0.3805	0.078
THYMUS GLAND	0.2866	0.059
ADRENAL GLANDS	0.0613	0.013
THYROIDS/PARA	0.0242	0.005
FINAL BODY WT(G)	488.	

LIVER
LUNGS
PROSTATE
THYROID GLANDS

NO SIGNIFICANT CHANGES OBSERVED

				GRADE
MICRO:	INFLAMMATION, SUBACUTE			1
MICRO:	INFLAMMATION, SUBACUTE			1
MICRO:	INFLAMMATION, ACUTE			1
MICRO:	INFLAMMATION, SUBACUTE			1
	HYPERTROPHY, FOLLICULAR CELL			1
	SMALL FOLLICLES; RELATIVELY TALLER EPITHELIUM; DECREASED COLLOID			

GROSS:	ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
	CECUM	COLON	DUODENUM	ESOPHAGUS
	EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
	KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
	NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
	RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
	SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
	SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND
	THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA
	VAS DEFERENS	URINARY BLADDER		

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43277 GROUP 4: 1000 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.92	0.389
LIVER	13.53	2.744
KIDNEYS	3.24	0.657
HEART	1.54	0.312
SPLEEN	0.54	0.110
PROSTATE	1.29	0.262
RT TESTIS	1.50	0.304
LT TESTIS	1.56	0.316
RT EPIDIDYMIS	0.70	0.142
LT EPIDIDYMIS	0.69	0.140
RT CAUDA EPID	0.3075	0.062
LT CAUDA EPID	0.2863	0.058
THYMUS GLAND	0.2603	0.053
ADRENAL GLANDS	0.0419	0.008
THYROIDS/PARA	0.0338	0.007
FINAL BODY WT(G)	493.	

LIVER
MICRO: INFLAMMATION, SUBACUTE — GRADE 1
VACUOLATION, HEPATOCELLULAR — GRADE 1

LUNGS
MICRO: INFLAMMATION, GRANULOMATOUS — GRADE 1

NO SIGNIFICANT CHANGES OBSERVED

GROSS:

ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
CECUM	COLON	DUODENUM	ESOPHAGUS
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
KIDNEYS	LIVER	LYMPH NODE, MES	LUNGS
NERVE,SCIATIC	PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS
RECTUM	PITUITARY	PROSTATE	SAL. GLAND MAND
SEMINAL VESICLES	SKELETAL MUSCLE	SKIN	SPINAL CORD
SPLEEN	STOMACH	LYMPH NODE, MAND	THYMUS GLAND
THYROID GLANDS	RT TESTIS	LT TESTIS	TRACHEA
VAS DEFERENS	URINARY BLADDER		

MICRO: KIDNEYS, PROSTATE, THYROID GLANDS

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

PROJECT NO.:WIL-186012
SPONSOR:CMA-BFRIP

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43278 GROUP 4: 1000 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.91	0.399
LIVER	12.42	2.593
KIDNEYS	3.38	0.706
HEART	1.74	0.363
SPLEEN	0.53	0.111
PROSTATE	1.38	0.288
RT TESTIS	1.46	0.305
LT TESTIS	1.45	0.303
RT EPIDIDYMIS	0.72	0.150
LT EPIDIDYMIS	0.67	0.140
RT CAUDA EPID	0.2935	0.061
LT CAUDA EPID	0.2933	0.061
THYMUS GLAND	0.1742	0.036
ADRENAL GLANDS	0.0467	0.010
THYROIDS/PARA	0.0247	0.005
FINAL BODY WT(G)	479.	

KIDNEYS
LIVER
LUNGS

SKIN

THYROID GLANDS
NO SIGNIFICANT
CHANGES OBSERVED

		GRADE
MICRO:	BASOPHILIC TUBULES	1
MICRO:	INFLAMMATION, SUBACUTE	1
MICRO:	MINERALIZATION, VASCULAR	1
	HISTIOCYTOSIS, ALVEOLAR	1
GROSS:	MASS	P
	4 X 3 X 2 MM, TAN, BUCCAL, MASS #1	
MICRO:	HYPERTROPHY, FOLLICULAR CELL	1

GROSS: ADRENAL GLANDS, AORTA, BRAIN, CECUM, COLON, DUODENUM, ESOPHAGUS, EYES/OPTIC N., HEART, ILEUM, JEJUNUM, KIDNEYS, LIVER, LUNGS, LYMPH NODE, MES, NERVE,SCIATIC, PANCREAS, RT EPIDIDYMIS, LT EPIDIDYMIS, RECTUM, PITUITARY, PROSTATE, SAL. GLAND MAND, SEMINAL VESICLES, SKELETAL MUSCLE, SPINAL CORD, SPLEEN, STOMACH, LYMPH NODE, MAND, THYMUS GLAND, THYROID GLANDS, RT TESTIS, LT TESTIS, TRACHEA, VAS DEFERENS, URINARY BLADDER, STERNEBRAE

MICRO: PROSTATE

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

ANIMAL NO. 43280 GROUP 4: 1000 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.95	0.326
LIVER	17.86	2.987
KIDNEYS	4.27	0.714
HEART	1.79	0.299
SPLEEN	0.78	0.130
PROSTATE	1.07	0.179
RT TESTIS	1.71	0.286
LT TESTIS	1.75	0.293
RT EPIDIDYMIS	0.74	0.124
LT EPIDIDYMIS	0.73	0.122
RT CAUDA EPID	0.2703	0.045
LT CAUDA EPID	0.3037	0.051
THYMUS GLAND	0.3340	0.056
ADRENAL GLANDS	0.0598	0.010
THYROIDS/PARA	0.0214	0.004
FINAL BODY WT(G)	598.	

KIDNEYS NO SIGNIFICANT CHANGES OBSERVED

		GRADE
GROSS:	DEPRESSED AREA(S)	P
	ONE, 1 MM IN DIAMETER, IN CORTEX, RIGHT	
MICRO:	BASOPHILIC TUBULES	1
	NO CORRELATE TO GROSS DEPRESSED AREA	
	INFLAMMATION, SUBACUTE	1
MICRO:	INFLAMMATION, SUBACUTE	1
MICRO:	INFLAMMATION, GRANULOMATOUS	1
MICRO:	INFLAMMATION, SUBACUTE	1
MICRO:	HYPERTROPHY, FOLLICULAR CELL	1

GROSS:

ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
CECUM	COLON	DUODENUM	ESOPHAGUS
EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
LIVER	LYMPH NODE, MES	LUNGS	NERVE,SCIATIC
PANCREAS	RT EPIDIDYMIS	LT EPIDIDYMIS	RECTUM
PITUITARY	PROSTATE	SAL. GLAND MAND	SEMINAL VESICLES
SKELETAL MUSCLE	SKIN	SPINAL CORD	SPLEEN
STOMACH	LYMPH NODE, MAND	THYMUS GLAND	THYROID GLANDS
RT TESTIS	LT TESTIS	TRACHEA	VAS DEFERENS
URINARY BLADDER			

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

TABLE 143 (WEEK 17 RECOVERY NECROPSY) (MALES ONLY)
A 90-DAY ORAL TOXICITY STUDY OF HBCD IN RATS
INDIVIDUAL MACROSCOPIC AND MICROSCOPIC FINDINGS

ANIMAL NO. 43281 GROUP 4: 1000 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	2.18	0.425
LIVER	15.41	3.004
KIDNEYS	3.91	0.762
HEART	1.60	0.312
SPLEEN	0.77	0.150
PROSTATE	1.00	0.195
RT TESTIS	1.46	0.285
LT TESTIS	1.46	0.285
RT EPIDIDYMIS	0.65	0.127
LT EPIDIDYMIS	0.72	0.140
RT CAUDA EPID	0.3376	0.066
LT CAUDA EPID	0.3677	0.072
THYMUS GLAND	0.3296	0.064
ADRENAL GLANDS	0.0782	0.015
THYROIDS/PARA	0.0331	0.006
FINAL BODY WT(G)	513.	

KIDNEYS
LIVER
LUNGS

LUNGS

PROSTATE

NO SIGNIFICANT
CHANGES OBSERVED

		GRADE
MICRO:	INFLAMMATION, SUBACUTE	1
MICRO:	INFLAMMATION, SUBACUTE	1
GROSS:	DARK RED AREA(S)	P
	MULTIPLE, IRREGULARLY SHAPED, ALL LOBES	
MICRO:	MINERALIZATION, VASCULAR	1
	NO CORRELATE TO GROSS RED AREAS	
	HISTIOCYTOSIS, ALVEOLAR	1
MICRO:	INFLAMMATION, SUBACUTE	1

GROSS: ADRENAL GLANDS, AORTA, BRAIN, CECUM, COLON, DUODENUM, ESOPHAGUS, EYES/OPTIC N., HEART, ILEUM, JEJUNUM, KIDNEYS, LIVER, LYMPH NODE, MES, NERVE,SCIATIC, PANCREAS, RT EPIDIDYMIS, LT EPIDIDYMIS, RECTUM, PITUITARY, PROSTATE, SAL. GLAND MAND, SEMINAL VESICLES, SKELETAL MUSCLE, SKIN, SPINAL CORD, SPLEEN, STOMACH, LYMPH NODE, MAND, THYMUS GLAND, THYROID GLANDS, RT TESTIS, LT TESTIS, TRACHEA, VAS DEFERENS, URINARY BLADDER

MICRO: THYROID GLANDS

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

ANIMAL NO. 43282 GROUP 4: 1000 MG/KG/DAY MALE SCHEDULED EUTH 08/23/00 DATE OF DEATH: 08/23/00 STUDY DAY: 119

ORGAN WEIGHT	ABS.(G)	REL.
BRAIN	1.88	0.472
LIVER	11.23	2.822
KIDNEYS	3.29	0.827
HEART	1.25	0.314
SPLEEN	0.66	0.166
PROSTATE	0.66	0.166
RT TESTIS	1.70	0.427
LT TESTIS	1.64	0.412
RT EPIDIDYMIS	0.66	0.166
LT EPIDIDYMIS	0.65	0.163
RT CAUDA EPID	0.2282	0.057
LT CAUDA EPID	0.2886	0.073
THYMUS GLAND	0.2606	0.065
ADRENAL GLANDS	0.0456	0.011
THYROIDS/PARA	0.0271	0.007
FINAL BODY WT(G)	398.	

KIDNEYS NO SIGNIFICANT CHANGES OBSERVED

LUNGS NO SIGNIFICANT CHANGES OBSERVED

THYROID GLANDS NO SIGNIFICANT CHANGES OBSERVED

				GRADE
GROSS:	DARK RED AREA(S)			P
	MULTIPLE, IRREGULARLY SHAPED, IN CORTEX, BILATERAL			
MICRO:	MINERALIZATION, PAPILLARY TUBULAR			1
	INFLAMMATION, SUBACUTE			1
	GROSS RED AREAS DUE TO CONGESTION			
GROSS:	WHITE AREA(S)			P
	MULTIPLE, IRREGULARLY SHAPED, ALL LOBES			
MICRO:	MINERALIZATION, VASCULAR			1
	INFLAMMATION, GRANULOMATOUS			1
	CORRELATES WITH GROSS WHITE AREAS			
MICRO:	HYPERTROPHY, FOLLICULAR CELL			1

GROSS:	ADRENAL GLANDS	AORTA	STERNEBRAE	BRAIN
	CECUM	COLON	DUODENUM	ESOPHAGUS
	EYES/OPTIC N.	HEART	ILEUM	JEJUNUM
	LIVER	LYMPH NODE, MES	NERVE,SCIATIC	PANCREAS
	RT EPIDIDYMIS	LT EPIDIDYMIS	RECTUM	PITUITARY
	PROSTATE	SAL. GLAND MAND	SEMINAL VESICLES	SKELETAL MUSCLE
	SKIN	SPINAL CORD	SPLEEN	STOMACH
	LYMPH NODE, MAND	THYMUS GLAND	THYROID GLANDS	RT TESTIS
	LT TESTIS	TRACHEA	VAS DEFERENS	URINARY BLADDER
MICRO:	PROSTATE			

GROSS GRADE CODE: 1-SLIGHT, 2-MODERATE, 3-MARKED, P-PRESENT
MICRO GRADE CODE: 1-MINIMAL, 2-MILD, 3-MODERATE, 4-SEVERE, P-PRESENT

PGRHv4.31
05/21/2002
R:06/18/2002

WIL-186012
CMA-BFRIP

A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

ATTACHMENT A

Historical Control Data (WIL Research Laboratories, Inc.)

WIL Research Laboratories, Inc.

Improving human health and protecting the environment through scientific research services.®

Historical Control Data from 13-Week Studies Excluding WIL-186012

Crl:CD®(SD)IGS BR rats

WIL Research Laboratories, Inc.
Historical Control Data
Crl:CD®(SD)IGS rats from 13-week studies

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Females (all data) 1623

Females (excluding +/- 5 S.D.) 1628

Hematology Data (Recovery Necropsy) 1633

Males (all data) 1634

Males (excluding +/- 5 S.D.) 1639

Females (all data) 1644

Females (excluding +/- 5 S.D.) 1649

Serum Chemistry Data (Scheduled Necropsy) 1653

Males (all data) 1654

Males (excluding +/- 5 S.D.) 1659

Females (all data) 1664

Females (excluding +/- 5 S.D.) 1669

Serum Chemistry Data (Recovery Necropsy) 1674

Males (all data) 1675

Males (excluding +/- 5 S.D.) 1680

Females (all data) 1684

Females (excluding +/- 5 S.D.) 1689

Organ Weight Data (Scheduled Necropsy) **1694**
Males (all data) 1695
Males (excluding +/- 5 S.D.) 1703
Females (all data) 1711
Females (excluding +/- 5 S.D.) 1717

Organ Weight Data (Recovery Necropsy) **1723**
Males (all data) 1724
Males (excluding +/- 5 S.D.) 1732
Females (all data) 1740
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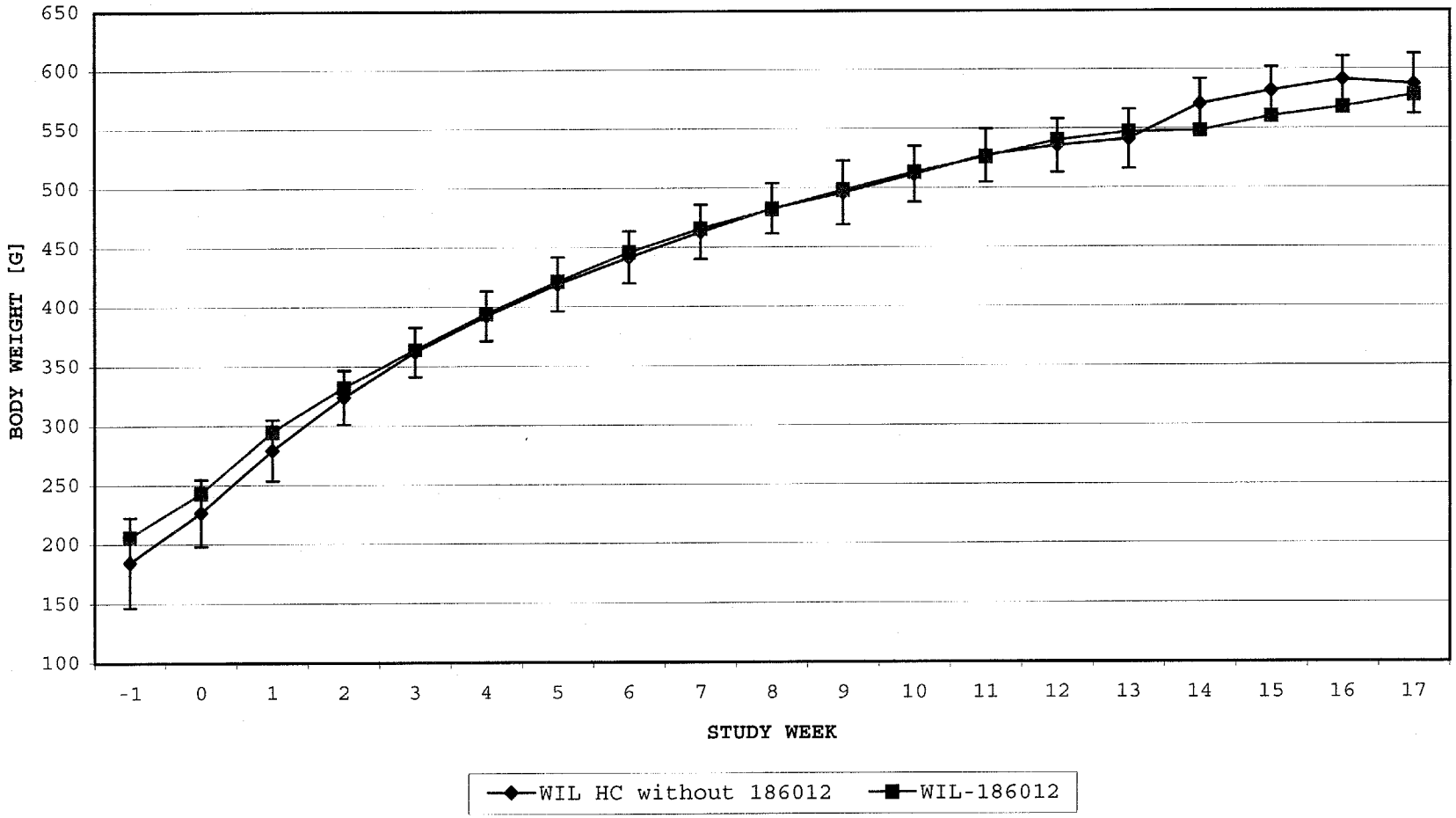
WIL Research Laboratories, Inc.
Historical Control Data
Crl:CD®(SD)IGS rats from 13-week studies

BODY WEIGHT DATA

WIL HISTORICAL CONTROL DATA

WIL Research Laboratories, Inc.

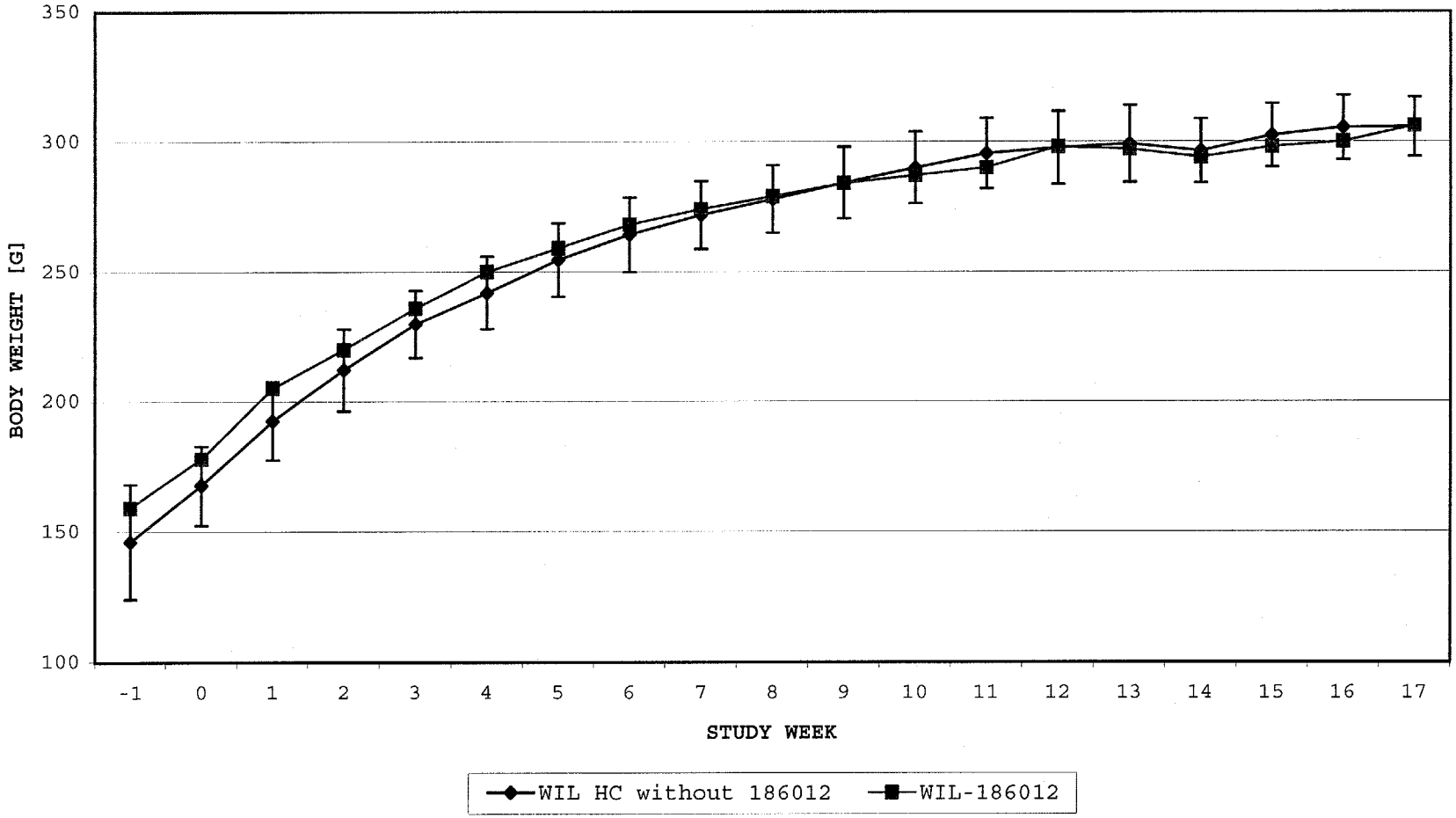
Figure 1
Male Absolute Body Weights [G]
from 13-Week Studies
WIL Historical Control Data



NOTE: Graph represents mean of means for each control group in historical control data (16 total). Error bars represent +/- 1 S.D.

WIL Research Laboratories, Inc.

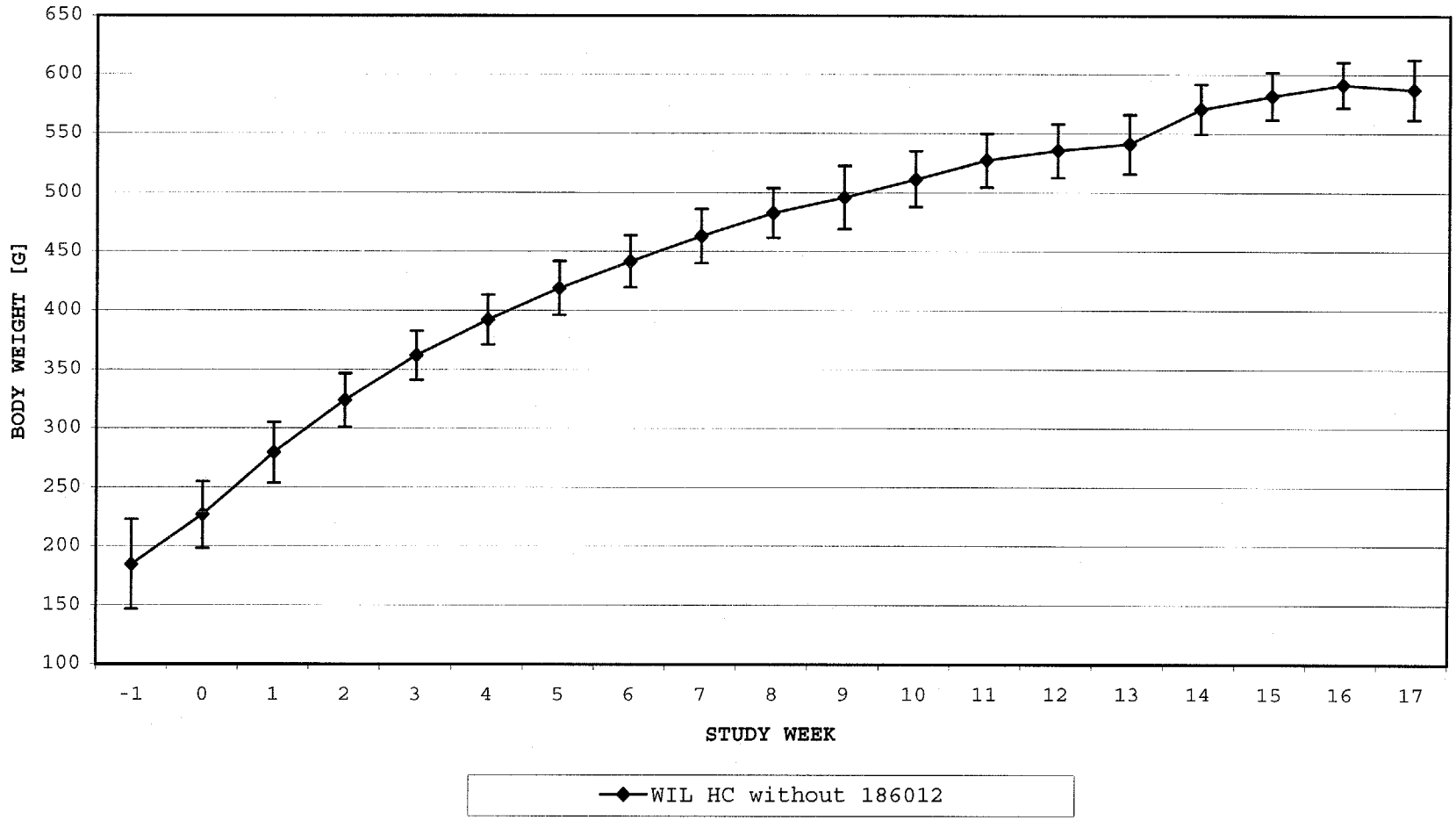
Figure 2
Female Absolute Body Weights [G]
from 13-Week Studies
WIL Historical Control Data



NOTE: Graph represents mean of means for each control group in historical control data (16 total). Error bars represent +/- 1 S.D.

WIL Research Laboratories, Inc.

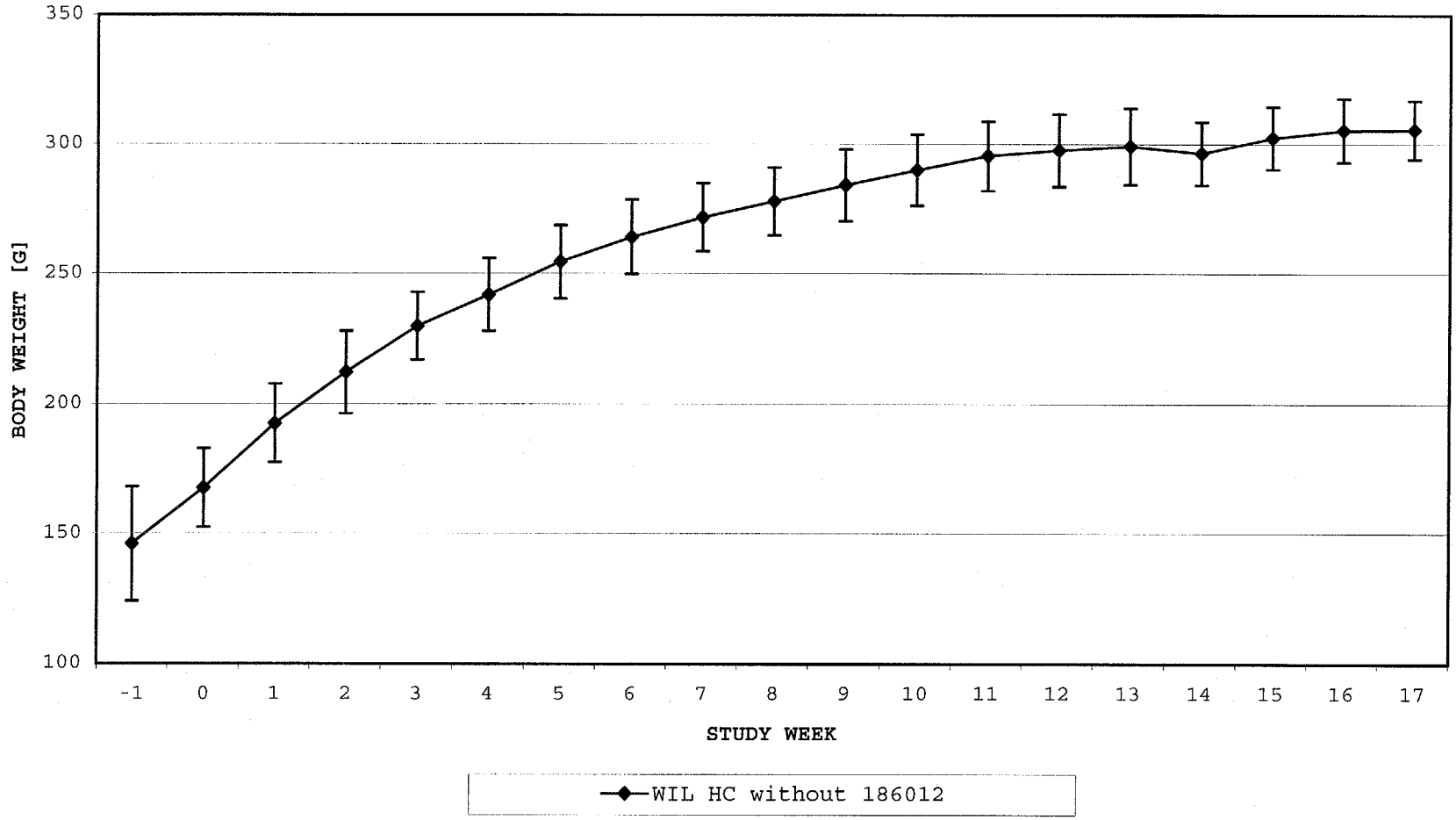
Figure 3
Male Absolute Body Weights [G]
from 13-Week Studies
WIL Historical Control Data



NOTE: Graph represents mean of means for each control group in historical control data (16 total). Error bars represent +/- 1 S.D.

WIL Research Laboratories, Inc.

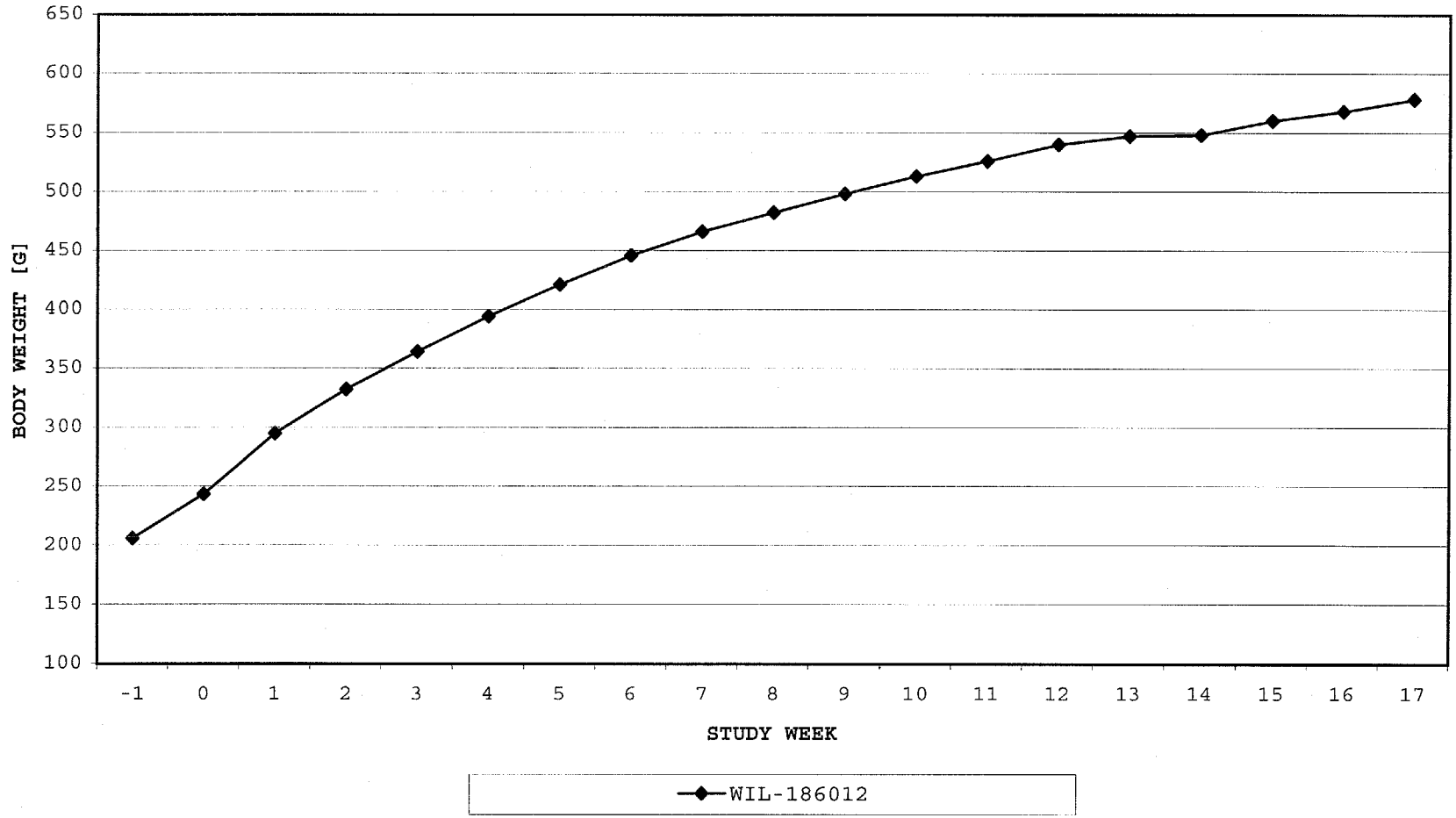
Figure 4
Female Absolute Body Weights [G]
from 13-Week Studies
WIL Historical Control Data



NOTE: Graph represents mean of means for each control group in historical control data (16 total). Error bars represent +/- 1 S.D.

WIL Research Laboratories, Inc.

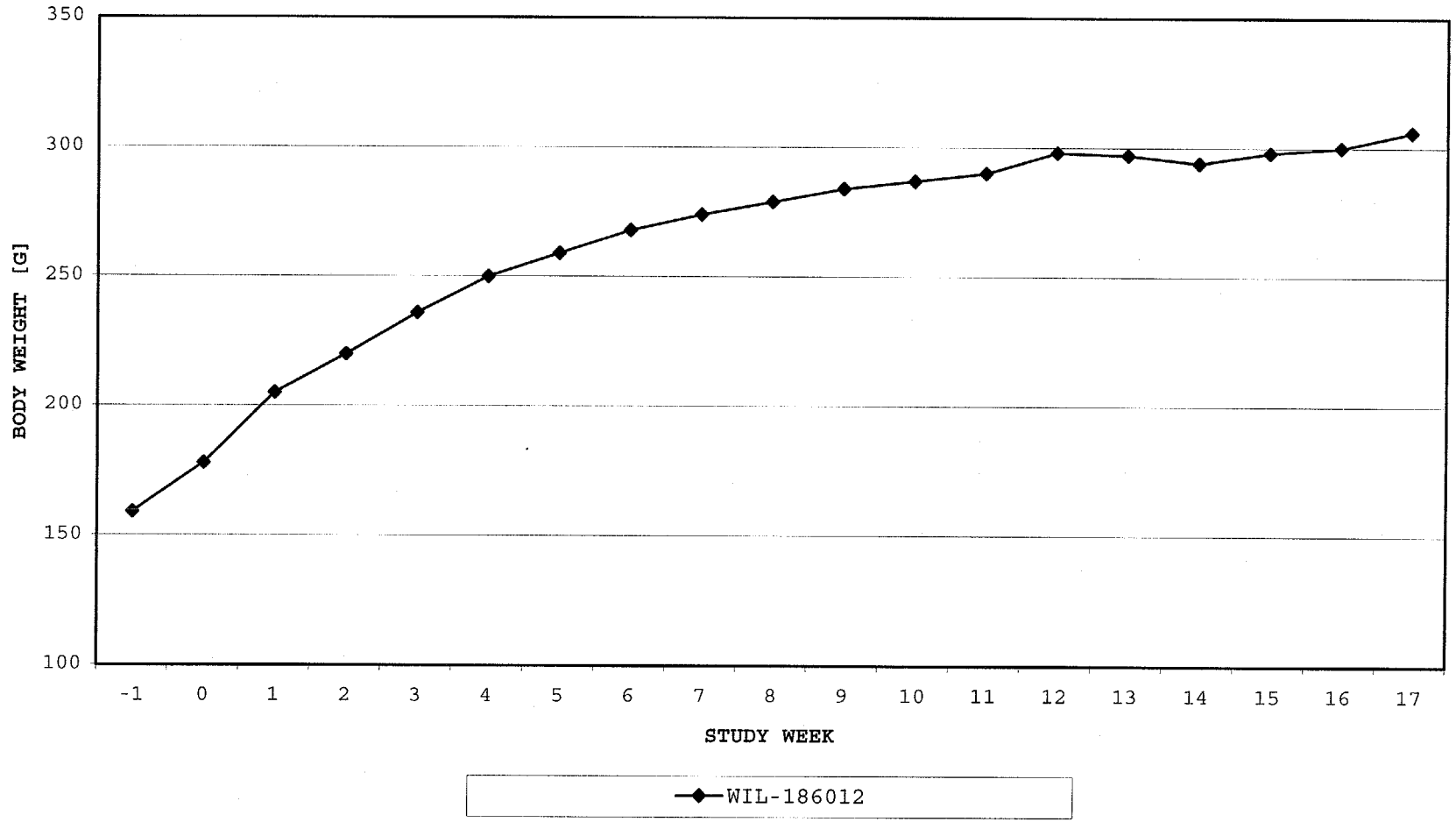
Figure 5
Male Absolute Body Weights [G]
from WIL-186012



NOTE: Graph represents mean of means for each control group in historical control data (16 total). Error bars represent +/- 1 S.D.

WIL Research Laboratories, Inc.

Figure 6
Female Absolute Body Weights [G]
from WIL-186012



NOTE: Graph represents mean of means for each control group in historical control data (16 total). Error bars represent +/- 1 S.D.

WIL Research Laboratories, Inc.

Table 1
Body Weights [G] From 13-Week Studies
WIL Historical Control Data Without WIL-186012

Males

GRAND MEAN OF STUDIES

WEEK	MEAN	MINIMUM	MAXIMUM	S.D.	2 S.D.	NO. OF STUDIES
-2	145	98	231	44.8	89.7	16
-1	185	146	273	37.9	75.9	16
0	227	196	309	28.3	56.7	16
1	279	242	356	25.6	51.2	16
2	324	278	385	22.8	45.6	16
3	362	316	411	21.0	41.9	16
4	392	342	436	21.0	42.1	16
5	419	357	459	22.8	45.5	16
6	442	382	478	22.1	44.2	16
7	463	406	493	23.0	45.9	16
8	483	427	510	21.0	42.0	16
9	496	413	532	26.8	53.7	16
10	511	442	545	23.4	46.9	16
11	527	467	564	22.5	45.1	16
12	535	479	576	22.7	45.4	16
13	541	487	585	25.1	50.3	16
14	571	546	600	21.2	42.5	5
15	582	554	602	20.0	39.9	5
16	591	569	613	19.3	38.6	5
17	587	560	617	25.4	50.7	5

WIL Research Laboratories, Inc.

Table 1
Body Weights [G] From 13-Week Studies
WIL Historical Control Data Without WIL-186012

GRAND MEAN OF STUDIES

Females

WEEK	MEAN	MINIMUM	MAXIMUM	S.D.	2 S.D.	NO. OF STUDIES
-2	123	84	171	28.2	56.3	16
-1	146	116	189	22.0	44.1	16
0	168	151	207	15.2	30.4	16
1	193	173	230	15.1	30.1	16
2	212	182	243	15.8	31.5	16
3	230	208	251	13.0	25.9	16
4	242	219	261	14.0	28.0	16
5	255	226	278	14.1	28.2	16
6	264	238	287	14.3	28.6	16
7	272	251	289	13.1	26.1	16
8	278	256	296	13.1	26.1	16
9	284	257	303	13.8	27.6	16
10	290	261	310	13.8	27.5	16
11	295	264	311	13.5	27.0	16
12	298	275	316	14.0	28.1	16
13	299	273	324	14.8	29.7	16
14	296	287	316	12.3	24.6	5
15	302	293	322	12.2	24.4	5
16	305	294	324	12.4	24.8	5
17	306	291	321	11.4	22.9	5

WIL Research Laboratories, Inc.
Historical Control Data
Crl:CD®(SD)IGS rats from 13-week studies

HEMATOLOGY DATA

SCHEDULED NECROPSY

Abbreviation Key:

Abs = Absolute

fL = femtoliters

g/dL = grams/deciliter

mil/uL = millions/microliter

thous/uL = thousands/microliter

uug = picograms

% = percent

In the Report Header, **Report Type** is designated by **ALL DATA** or **Excluding +/- 5 S.D.** depending upon the data set.

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

APTT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	21.4	4.10	198	29.6 / 13.2	33.7 / 9.1	10.7 / 39.2

BASOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	0	0.1	210	0 / 0.0	0 / 0.0	0 / 1

BASOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.0	0.02	210	0.0 / 0.0	0.1 / 0.0	0.0 / 0.2

EOSINOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1	0.9	210	3 / 0.0	4 / 0.0	0 / 5

EOSINOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.1	0.13	210	0.4 / 0.0	0.5 / 0.0	0.0 / 0.7

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

HEMATOCRIT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	43.6	2.94	210	49.5 / 37.7	52.4 / 34.7	30.2 / 51.1

HEMOGLOBIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	15.2	0.76	210	16.8 / 13.7	17.5 / 13.0	11.1 / 17.0

LYMPHOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	77	7.8	210	93 / 61	100 / 54	42 / 94

LYMPHOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	9.3	2.82	210	15.0 / 3.7	17.8 / 0.9	4.3 / 19.7

MCH

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
uug	18.2	0.65	210	19.5 / 16.9	20.2 / 16.3	16.7 / 20.5

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

MCHC

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	35.0	1.24	210	37.5 / 32.6	38.8 / 31.3	32.5 / 37.7

MCV

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
fL	52.0	1.85	210	55.7 / 48.3	57.5 / 46.4	47.0 / 56.9

MONOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	7	3.9	210	15 / 0.0	19 / 0.0	0 / 24

MONOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.8	0.54	210	1.9 / 0.0	2.5 / 0.0	0.0 / 3.1

NEUTROPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	15	6.1	210	27 / 3	33 / 0.0	2 / 51

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

NEUTROPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1.8	1.19	210	4.2 / 0.0	5.4 / 0.0	0.2 / 14.0

PLATELET

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1251	263.5	210	1778 / 724	2042 / 461	529 / 2593

PROTIME

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	14.3	2.04	198	18.4 / 10.2	20.4 / 8.2	11.2 / 33.3

RED CELLS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mil/uL	8.38	0.538	210	9.46 / 7.31	10.00 / 6.77	5.89 / 10.00

RETICULOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1.9	1.99	80	5.8 / 0.0	7.8 / 0.0	0.0 / 9.4

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

WHITE CELL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	12.1	3.54	210	19.2 / 5.0	22.7 / 1.5	5.3 / 27.5

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Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

APTT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	21.4	4.10	198	29.6 / 13.2	33.7 / 9.1	10.7 / 39.2

BASOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	0	0.0	206	0 / 0	0 / 0	0 / 0

BASOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.0	0.00	206	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0

EOSINOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1	0.9	210	3 / 0.0	4 / 0.0	0 / 5

EOSINOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.1	0.13	210	0.4 / 0.0	0.5 / 0.0	0.0 / 0.7

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

HEMATOCRIT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	43.6	2.94	210	49.5 / 37.7	52.4 / 34.7	30.2 / 51.1

HEMOGLOBIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	15.3	0.71	209	16.7 / 13.8	17.4 / 13.1	13.0 / 17.0

LYMPHOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	77	7.8	210	93 / 61	100 / 54	42 / 94

LYMPHOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	9.3	2.82	210	15.0 / 3.7	17.8 / 0.9	4.3 / 19.7

MCH

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
uug	18.2	0.65	210	19.5 / 16.9	20.2 / 16.3	16.7 / 20.5

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

MCHC

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	35.0	1.24	210	37.5 / 32.6	38.8 / 31.3	32.5 / 37.7

MCV

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
fL	52.0	1.85	210	55.7 / 48.3	57.5 / 46.4	47.0 / 56.9

MONOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	7	3.9	210	15 / 0.0	19 / 0.0	0 / 24

MONOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.8	0.54	210	1.9 / 0.0	2.5 / 0.0	0.0 / 3.1

NEUTROPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	15	5.6	209	26 / 4	32 / 0.0	2 / 38

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

NEUTROPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1.8	0.84	209	3.4 / 0.1	4.3 / 0.0	0.2 / 6.0

PLATELET

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1245	247.1	209	1739 / 751	1986 / 503	529 / 2313

PROTIME

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	14.2	1.53	197	17.3 / 11.2	18.8 / 9.6	11.2 / 22.8

RED CELLS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mil/uL	8.38	0.538	210	9.46 / 7.31	10.00 / 6.77	5.89 / 10.00

RETICULOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1.9	1.99	80	5.8 / 0.0	7.8 / 0.0	0.0 / 9.4

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

WHITE CELL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	12.1	3.54	210	19.2 / 5.0	22.7 / 1.5	5.3 / 27.5

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Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

APTT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	18.0	3.64	197	25.3 / 10.7	28.9 / 7.1	9.7 / 32.2

BASOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	0	0.1	209	0 / 0.0	0 / 0.0	0 / 1

BASOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.0	0.01	209	0.0 / 0.0	0.0 / 0.0	0.0 / 0.1

EOSINOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1	1.0	209	3 / 0.0	4 / 0.0	0 / 4

EOSINOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.1	0.11	209	0.3 / 0.0	0.4 / 0.0	0.0 / 0.8

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

HEMATOCRIT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	41.5	2.98	209	47.5 / 35.6	50.5 / 32.6	33.2 / 50.9

HEMOGLOBIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	14.6	0.83	209	16.3 / 12.9	17.1 / 12.1	11.9 / 17.0

LYMPHOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	79	9.6	209	98 / 60	108 / 50	0 / 93

LYMPHOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	7.2	2.96	209	13.1 / 1.3	16.1 / 0.0	0.0 / 18.9

MCH

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
uug	18.9	0.68	209	20.3 / 17.6	21.0 / 16.9	15.3 / 21.7

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

MCHC

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	35.2	1.17	209	37.5 / 32.9	38.7 / 31.7	32.6 / 37.9

MCV

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
fL	53.8	2.06	209	57.9 / 49.7	60.0 / 47.6	45.9 / 60.0

MONOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	6	5.5	209	17 / 0.0	23 / 0.0	0 / 70

MONOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.6	0.47	209	1.5 / 0.0	2.0 / 0.0	0.0 / 4.6

NEUTROPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	14	6.6	209	27 / 0	34 / 0.0	3 / 41

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

NEUTROPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1.2	0.74	209	2.7 / 0.0	3.4 / 0.0	0.3 / 6.3

PLATELET

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1189	330.4	209	1850 / 528	2180 / 198	280 / 2884

PROTIME

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	13.5	1.15	197	15.8 / 11.2	17.0 / 10.0	11.4 / 19.7

RED CELLS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mil/uL	7.72	0.497	209	8.71 / 6.72	9.21 / 6.23	6.11 / 9.17

RETICULOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1.8	1.91	78	5.7 / 0.0	7.6 / 0.0	0.0 / 9.1

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

WHITE CELL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	9.1	3.46	209	16.0 / 2.2	19.5 / 0.0	2.1 / 23.3

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Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

APTT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	18.0	3.64	197	25.3 / 10.7	28.9 / 7.1	9.7 / 32.2

BASOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	0	0.0	208	0 / 0	0 / 0	0 / 0

BASOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.0	0.00	208	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0

EOSINOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1	1.0	209	3 / 0.0	4 / 0.0	0 / 4

EOSINOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.1	0.10	208	0.3 / 0.0	0.4 / 0.0	0.0 / 0.5

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

HEMATOCRIT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	41.5	2.98	209	47.5 / 35.6	50.5 / 32.6	33.2 / 50.9

HEMOGLOBIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	14.6	0.83	209	16.3 / 12.9	17.1 / 12.1	11.9 / 17.0

LYMPHOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	79	7.9	208	95 / 63	103 / 56	52 / 93

LYMPHOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	7.2	2.96	209	13.1 / 1.3	16.1 / 0.0	0.0 / 18.9

MCH

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
uug	19.0	0.64	208	20.2 / 17.7	20.9 / 17.0	17.3 / 21.7

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

MCHC

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	35.2	1.17	209	37.5 / 32.9	38.7 / 31.7	32.6 / 37.9

MCV

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
fL	53.8	2.06	209	57.9 / 49.7	60.0 / 47.6	45.9 / 60.0

MONOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	6	3.3	208	13 / 0.0	16 / 0.0	0 / 18

MONOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.6	0.38	208	1.3 / 0.0	1.7 / 0.0	0.0 / 2.4

NEUTROPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	14	6.6	209	27 / 0	34 / 0.0	3 / 41

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

NEUTROPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1.1	0.58	207	2.3 / 0.0	2.9 / 0.0	0.3 / 3.6

PLATELET

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1181	309.4	208	1800 / 562	2109 / 253	280 / 2304

PROTIME

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	13.5	1.07	196	15.6 / 11.3	16.7 / 10.3	11.4 / 18.9

RED CELLS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mil/uL	7.72	0.497	209	8.71 / 6.72	9.21 / 6.23	6.11 / 9.17

RETICULOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1.8	1.91	78	5.7 / 0.0	7.6 / 0.0	0.0 / 9.1

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

WHITE CELL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	9.1	3.46	209	16.0 / 2.2	19.5 / 0.0	2.1 / 23.3

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WIL Research Laboratories, Inc.
Historical Control Data
Crl:CD®(SD)IGS rats from 13-week studies

HEMATOLOGY DATA
RECOVERY NECROPSY

Abbreviation Key:

Abs = Absolute

fL = femtoliters

g/dL = grams/deciliter

mil/uL = millions/microliter

thous/uL = thousands/microliter

uug = picograms

% = percent

In the Report Header, **Report Type** is designated by **ALL DATA** or **Excluding +/- 5 S.D.** depending upon the data set.

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

APTT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	24.3	6.27	35	36.8 / 11.7	43.1 / 5.5	15.6 / 37.6

BASOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	0	0.2	35	0 / 0.0	1 / 0.0	0 / 1

BASOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.0	0.02	35	0.0 / 0.0	0.1 / 0.0	0.0 / 0.1

EOSINOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	2	0.9	35	3 / 0.0	4 / 0.0	0 / 3

EOSINOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.2	0.15	35	0.5 / 0.0	0.6 / 0.0	0.0 / 0.6

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

HEMATOCRIT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	44.4	2.42	35	49.2 / 39.5	51.7 / 37.1	39.0 / 50.9

HEMOGLOBIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	15.5	0.66	35	16.8 / 14.1	17.5 / 13.5	13.9 / 16.7

LYMPHOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	74	9.1	35	92 / 55	101 / 46	44 / 90

LYMPHOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	9.5	2.90	35	15.3 / 3.7	18.2 / 0.9	5.8 / 16.4

MCH

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
uug	18.1	0.72	35	19.5 / 16.6	20.2 / 15.9	16.5 / 19.7

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

MCHC

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	34.9	1.35	35	37.6 / 32.2	38.9 / 30.9	32.6 / 37.2

MCV

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
fL	51.9	2.40	35	56.7 / 47.0	59.1 / 44.6	47.9 / 56.9

MONOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	9	4.6	35	18 / 0.0	23 / 0.0	0 / 19

MONOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1.1	0.62	35	2.4 / 0.0	3.0 / 0.0	0.0 / 2.3

NEUTROPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	16	7.1	35	30 / 1	37 / 0.0	7 / 48

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

NEUTROPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	2.0	1.02	35	4.0 / 0.0	5.1 / 0.0	1.0 / 6.9

PLATELET

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1247	301.1	35	1849 / 645	2150 / 344	810 / 2116

PROTIME

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	14.9	2.24	35	19.4 / 10.4	21.6 / 8.2	12.9 / 20.8

RED CELLS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mil/uL	8.57	0.437	35	9.44 / 7.69	9.88 / 7.26	7.72 / 9.58

RETICULOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1.5	0.70	5	2.9 / 0.1	3.6 / 0.0	0.5 / 2.3

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

WHITE CELL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	12.9	2.98	35	18.8 / 6.9	21.8 / 3.9	7.7 / 19.3

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Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

APTT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	24.3	6.27	35	36.8 / 11.7	43.1 / 5.5	15.6 / 37.6

BASOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	0	0.0	34	0 / 0	0 / 0	0 / 0

BASOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.0	0.00	34	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0

EOSINOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	2	0.9	35	3 / 0.0	4 / 0.0	0 / 3

EOSINOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.2	0.15	35	0.5 / 0.0	0.6 / 0.0	0.0 / 0.6

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

HEMATOCRIT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	44.4	2.42	35	49.2 / 39.5	51.7 / 37.1	39.0 / 50.9

HEMOGLOBIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	15.5	0.66	35	16.8 / 14.1	17.5 / 13.5	13.9 / 16.7

LYMPHOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	74	9.1	35	92 / 55	101 / 46	44 / 90

LYMPHOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	9.5	2.90	35	15.3 / 3.7	18.2 / 0.9	5.8 / 16.4

MCH

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
uug	18.1	0.72	35	19.5 / 16.6	20.2 / 15.9	16.5 / 19.7

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

MCHC

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	34.9	1.35	35	37.6 / 32.2	38.9 / 30.9	32.6 / 37.2

MCV

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
fL	51.9	2.40	35	56.7 / 47.0	59.1 / 44.6	47.9 / 56.9

MONOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	9	4.6	35	18 / 0.0	23 / 0.0	0 / 19

MONOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1.1	0.62	35	2.4 / 0.0	3.0 / 0.0	0.0 / 2.3

NEUTROPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	16	7.1	35	30 / 1	37 / 0.0	7 / 48

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

NEUTROPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	2.0	1.02	35	4.0 / 0.0	5.1 / 0.0	1.0 / 6.9

PLATELET

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1247	301.1	35	1849 / 645	2150 / 344	810 / 2116

PROTIME

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	14.9	2.24	35	19.4 / 10.4	21.6 / 8.2	12.9 / 20.8

RED CELLS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mil/uL	8.57	0.437	35	9.44 / 7.69	9.88 / 7.26	7.72 / 9.58

RETICULOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1.5	0.70	5	2.9 / 0.1	3.6 / 0.0	0.5 / 2.3

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

WHITE CELL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	12.9	2.98	35	18.8 / 6.9	21.8 / 3.9	7.7 / 19.3

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Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

APTT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	18.8	5.49	34	29.8 / 7.8	35.3 / 2.4	11.2 / 31.5

BASOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	0	0.0	34	0 / 0	0 / 0	0 / 0

BASOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.0	0.00	34	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0

EOSINOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	2	1.2	34	4 / 0.0	6 / 0.0	0 / 5

EOSINOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.2	0.13	34	0.4 / 0.0	0.6 / 0.0	0.0 / 0.6

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

HEMATOCRIT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	42.4	2.79	34	48.0 / 36.8	50.8 / 34.1	35.8 / 47.8

HEMOGLOBIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	14.9	0.71	34	16.3 / 13.5	17.0 / 12.8	13.1 / 16.4

LYMPHOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	74	8.9	34	92 / 56	101 / 47	49 / 84

LYMPHOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	6.7	2.07	34	10.9 / 2.6	12.9 / 0.5	3.3 / 11.1

MCH

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
uug	18.9	0.64	34	20.1 / 17.6	20.8 / 17.0	17.5 / 19.8

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

MCHC

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	35.2	1.19	34	37.5 / 32.8	38.7 / 31.6	33.8 / 37.8

MCV

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
fL	53.7	2.09	34	57.9 / 49.5	60.0 / 47.4	49.5 / 58.0

MONOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	8	4.9	34	18 / 0.0	23 / 0.0	0 / 19

MONOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.7	0.44	34	1.6 / 0.0	2.0 / 0.0	0.0 / 1.8

NEUTROPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	16	7.3	34	31 / 2	38 / 0.0	5 / 38

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

NEUTROPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1.4	0.59	34	2.6 / 0.2	3.2 / 0.0	0.4 / 3.0

PLATELET

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1201	282.0	34	1765 / 637	2047 / 355	793 / 1874

PROTIME

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	13.7	1.70	34	17.1 / 10.3	18.8 / 8.6	11.8 / 20.0

RED CELLS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mil/uL	7.90	0.483	34	8.87 / 6.94	9.35 / 6.45	6.61 / 8.71

RETICULOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1.9	0.76	5	3.4 / 0.4	4.2 / 0.0	0.7 / 2.6

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

WHITE CELL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	9.0	2.33	34	13.7 / 4.3	16.0 / 2.0	5.5 / 15.2

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Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

APTT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	18.8	5.49	34	29.8 / 7.8	35.3 / 2.4	11.2 / 31.5

EOSINOPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	2	1.2	34	4 / 0.0	6 / 0.0	0 / 5

EOSINOPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.2	0.13	34	0.4 / 0.0	0.6 / 0.0	0.0 / 0.6

HEMATOCRIT

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	42.4	2.79	34	48.0 / 36.8	50.8 / 34.1	35.8 / 47.8

HEMOGLOBIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	14.9	0.71	34	16.3 / 13.5	17.0 / 12.8	13.1 / 16.4

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

LYMPHOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	74	8.9	34	92 / 56	101 / 47	49 / 84

LYMPHOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	6.7	2.07	34	10.9 / 2.6	12.9 / 0.5	3.3 / 11.1

MCH

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
uug	18.9	0.64	34	20.1 / 17.6	20.8 / 17.0	17.5 / 19.8

MCHC

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	35.2	1.19	34	37.5 / 32.8	38.7 / 31.6	33.8 / 37.8

MCV

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
fL	53.7	2.09	34	57.9 / 49.5	60.0 / 47.4	49.5 / 58.0

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

MONOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	8	4.9	34	18 / 0.0	23 / 0.0	0 / 19

MONOCYTE - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	0.7	0.44	34	1.6 / 0.0	2.0 / 0.0	0.0 / 1.8

NEUTROPHIL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	16	7.3	34	31 / 2	38 / 0.0	5 / 38

NEUTROPHIL - ABS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1.4	0.59	34	2.6 / 0.2	3.2 / 0.0	0.4 / 3.0

PLATELET

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	1201	282.0	34	1765 / 637	2047 / 355	793 / 1874

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

PROTIME

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
seconds	13.7	1.70	34	17.1 / 10.3	18.8 / 8.6	11.8 / 20.0

RED CELLS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mil/uL	7.90	0.483	34	8.87 / 6.94	9.35 / 6.45	6.61 / 8.71

RETICULOCYTE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
%	1.9	0.76	5	3.4 / 0.4	4.2 / 0.0	0.7 / 2.6

WHITE CELL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
thous/uL	9.0	2.33	34	13.7 / 4.3	16.0 / 2.0	5.5 / 15.2

WIL Research Laboratories, Inc.
Historical Control Data
Crl:CD®(SD)IGS rats from 13-week studies

SERUM CHEMISTRY DATA
SCHEDULED NECROPSY

Abbreviation Key:

Abs = Absolute

g/dL = grams/deciliter

mg/dL = milligrams/deciliter

mEq/L = milliEquivalents/Liter

U/L = international unit/liter

In the Report Header, **Report Type** is designated by **ALL DATA** or **Excluding +/- 5 S.D.** depending upon the data set.

In the **ALL DATA** serum chemistry report, the parameter Gamma Glutamyltransferase (labeled as **Glutamyl Transfer)** was observed with all values equal to zero. As a result, in the **Excluding +/- 5 S.D.** serum chemistry report where values equal to +/- 5 S.D. were excluded, this parameter was excluded due to the values being equal to zero.

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17- 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97- 10/01
Report Type: **ALL DATA**

A/G RATIO

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
NA	1.66	0.280	210	2.22 / 1.10	2.50 / 0.82	0.86 / 2.39

ALANINE TRANSFER

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	37	9.1	210	56 / 19	65 / 10	21 / 79

ALBUMIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	4.3	0.32	210	4.9 / 3.6	5.2 / 3.3	3.0 / 5.1

ALKALINE PHOS'TS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	99	28.7	210	156 / 41	185 / 13	50 / 210

ASPARTAT TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	86	18.1	210	122 / 49	140 / 31	53 / 155

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17- 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97- 10/01
Report Type: **ALL DATA**

CALCIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	10.3	0.81	210	11.9 / 8.7	12.7 / 7.9	7.4 / 12.9

CHLORIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	100	4.7	210	109 / 91	114 / 86	67 / 107

CHOLESTEROL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	62	16.2	210	95 / 30	111 / 14	31 / 126

CREATINE KINASE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	243	127.2	15	497 / 0.0	624 / 0.0	103 / 506

CREATININE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.3	0.07	210	0.4 / 0.1	0.5 / 0.0	0.1 / 0.4

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17- 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97- 10/01
Report Type: **ALL DATA**

GLOBULIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	2.6	0.35	210	3.3 / 1.9	3.7 / 1.6	1.8 / 3.8

GLUCOSE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	151	46.8	210	245 / 57	291 / 11	73 / 339

GLUTAMYL TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	0.2	0.91	198	2.0 / 0.0	2.9 / 0.0	0.0 / 12.0

PHOSPHORUS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	7.4	1.40	210	10.2 / 4.6	11.6 / 3.2	4.5 / 11.4

POTASSIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	5.60	1.128	210	7.86 / 3.35	8.99 / 2.22	3.10 / 10.50

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17- 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97- 10/01
Report Type: **ALL DATA**

SODIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	144	6.3	210	156 / 131	163 / 125	96 / 153

TOTAL BILI

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.2	0.06	210	0.3 / 0.1	0.3 / 0.0	0.1 / 0.4

TOTAL PROTEIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	6.9	0.39	210	7.7 / 6.1	8.1 / 5.7	5.8 / 8.3

TRIGLYCERIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	72	25.5	112	123 / 21	148 / 0.0	19 / 136

UREA NITROGEN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	14.2	3.07	210	20.3 / 8.1	23.4 / 5.0	6.8 / 33.9

Sex: M	Study Type: SUBCHRONIC	Number of Studies/Control Groups: 15 / 16
Species: RAT	Age: 17- 21 Weeks	Range of Study Dates: 12/97- 10/01
Strain: IGS		Report Type: **ALL DATA**

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Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

A/G RATIO

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
NA	1.66	0.280	210	2.22 / 1.10	2.50 / 0.82	0.86 / 2.39

ALANINE TRANSFER

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	37	9.1	210	56 / 19	65 / 10	21 / 79

ALBUMIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	4.3	0.32	210	4.9 / 3.6	5.2 / 3.3	3.0 / 5.1

ALKALINE PHOS'TS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	99	28.7	210	156 / 41	185 / 13	50 / 210

ASPARTAT TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	86	18.1	210	122 / 49	140 / 31	53 / 155

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

CALCIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	10.3	0.81	210	11.9 / 8.7	12.7 / 7.9	7.4 / 12.9

CHLORIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	100	3.5	208	107 / 93	111 / 90	81 / 107

CHOLESTEROL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	62	16.2	210	95 / 30	111 / 14	31 / 126

CREATINE KINASE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	243	127.2	15	497 / 0.0	624 / 0.0	103 / 506

CREATININE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.3	0.07	210	0.4 / 0.1	0.5 / 0.0	0.1 / 0.4

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

GLOBULIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	2.6	0.35	210	3.3 / 1.9	3.7 / 1.6	1.8 / 3.8

GLUCOSE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	151	46.8	210	245 / 57	291 / 11	73 / 339

GLUTAMYL TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	0.1	0.34	197	0.8 / 0.0	1.1 / 0.0	0.0 / 2.0

PHOSPHORUS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	7.4	1.40	210	10.2 / 4.6	11.6 / 3.2	4.5 / 11.4

POTASSIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	5.60	1.128	210	7.86 / 3.35	8.99 / 2.22	3.10 / 10.50

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

SODIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	144	4.3	208	153 / 136	157 / 131	117 / 153

TOTAL BILI

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.2	0.06	210	0.3 / 0.1	0.3 / 0.0	0.1 / 0.4

TOTAL PROTEIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	6.9	0.39	210	7.7 / 6.1	8.1 / 5.7	5.8 / 8.3

TRIGLYCERIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	72	25.5	112	123 / 21	148 / 0.0	19 / 136

UREA NITROGEN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	14.1	2.75	209	19.6 / 8.6	22.4 / 5.8	6.8 / 22.3

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

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Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

A/G RATIO

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
NA	2.12	0.502	211	3.12 / 1.11	3.62 / 0.61	0.86 / 3.93

ALANINE TRANSFER

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	40	30.3	211	100 / 0.0	131 / 0.0	18 / 299

ALBUMIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	4.9	0.55	211	6.0 / 3.8	6.5 / 3.2	3.1 / 6.8

ALKALINE PHOS'TS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	52	19.7	211	92 / 13	112 / 0.0	16 / 142

ASPARTAT TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	107	142.3	211	392 / 0.0	534 / 0.0	48 / 2010

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

CALCIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	10.4	0.84	211	12.1 / 8.7	12.9 / 7.9	7.7 / 13.3

CHLORIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	101	4.5	211	110 / 92	114 / 87	70 / 109

CHOLESTEROL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	75	19.9	211	114 / 35	134 / 15	33 / 149

CREATINE KINASE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	273	170.8	15	615 / 0.0	785 / 0.0	92 / 624

CREATININE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.3	0.09	209	0.5 / 0.1	0.6 / 0.0	0.1 / 0.8

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

GLOBULIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	2.4	0.39	211	3.2 / 1.6	3.6 / 1.2	1.5 / 3.6

GLUCOSE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	137	31.3	211	200 / 74	231 / 43	83 / 260

GLUTAMYL TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	0.2	0.50	200	1.3 / 0.0	1.8 / 0.0	0.0 / 2.0

PHOSPHORUS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	6.6	1.66	211	10.0 / 3.3	11.6 / 1.7	3.2 / 12.4

POTASSIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	5.60	1.441	211	8.48 / 2.72	9.92 / 1.28	2.90 / 11.80

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

SODIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	143	5.9	211	155 / 131	161 / 125	98 / 151

TOTAL BILI

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.2	0.13	211	0.5 / 0.0	0.6 / 0.0	0.1 / 1.5

TOTAL PROTEIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	7.2	0.52	211	8.3 / 6.2	8.8 / 5.7	6.0 / 8.8

TRIGLYCERIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	52	21.9	112	95 / 8	117 / 0.0	21 / 157

UREA NITROGEN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	15.7	3.32	210	22.3 / 9.0	25.6 / 5.7	8.3 / 32.1

Sex: F	Study Type: SUBCHRONIC	Number of Studies/Control Groups: 15 / 16
Species: RAT	Age: 17 - 21 Weeks	Range of Study Dates: 12/97 - 10/01
Strain: IGS		Report Type: **ALL DATA**

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Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

A/G RATIO

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
NA	2.12	0.502	211	3.12 / 1.11	3.62 / 0.61	0.86 / 3.93

ALANINE TRANSFER

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	38	21.4	209	80 / 0.0	102 / 0.0	18 / 173

ALBUMIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	4.9	0.55	211	6.0 / 3.8	6.5 / 3.2	3.1 / 6.8

ALKALINE PHOS'TS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	52	19.7	211	92 / 13	112 / 0.0	16 / 142

ASPARTAT TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	98	54.2	210	206 / 0.0	261 / 0.0	48 / 531

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

CALCIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	10.4	0.84	211	12.1 / 8.7	12.9 / 7.9	7.7 / 13.3

CHLORIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	101	3.5	209	108 / 94	111 / 90	78 / 109

CHOLESTEROL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	75	19.9	211	114 / 35	134 / 15	33 / 149

CREATINE KINASE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	273	170.8	15	615 / 0.0	785 / 0.0	92 / 624

CREATININE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.3	0.08	208	0.5 / 0.1	0.5 / 0.1	0.1 / 0.6

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

GLOBULIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	2.4	0.39	211	3.2 / 1.6	3.6 / 1.2	1.5 / 3.6

GLUCOSE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	137	31.3	211	200 / 74	231 / 43	83 / 260

GLUTAMYL TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	0.2	0.50	200	1.3 / 0.0	1.8 / 0.0	0.0 / 2.0

PHOSPHORUS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	6.6	1.66	211	10.0 / 3.3	11.6 / 1.7	3.2 / 12.4

POTASSIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	5.60	1.441	211	8.48 / 2.72	9.92 / 1.28	2.90 / 11.80

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 17 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

SODIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	143	3.3	208	150 / 137	153 / 133	119 / 151

TOTAL BILI

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.2	0.08	209	0.4 / 0.1	0.4 / 0.0	0.1 / 0.8

TOTAL PROTEIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	7.2	0.52	211	8.3 / 6.2	8.8 / 5.7	6.0 / 8.8

TRIGLYCERIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	52	21.9	112	95 / 8	117 / 0.0	21 / 157

UREA NITROGEN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	15.7	3.32	210	22.3 / 9.0	25.6 / 5.7	8.3 / 32.1

Sex: F	Study Type: SUBCHRONIC	Number of Studies/Control Groups: 15 / 16
Species: RAT	Age: 17 - 21 Weeks	Range of Study Dates: 12/97 - 10/01
Strain: IGS		Report Type: **Excluding +/- 5 S.D.**

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WIL Research Laboratories, Inc.
Historical Control Data
Crl:CD®(SD)IGS rats from 13-week studies

SERUM CHEMISTRY DATA
RECOVERY NECROPSY

Abbreviation Key:

Abs = Absolute

g/dL = grams/deciliter

mg/dL = milligrams/deciliter

mEq/L = milliEquivalents/Liter

U/L = international unit/liter

In the Report Header, **Report Type** is designated by **ALL DATA** or **Excluding +/- 5 S.D.** depending upon the data set.

In the **ALL DATA** serum chemistry report, the parameter Gamma Glutamyltransferase (labeled as **Glutamyl Transfer)** was observed with all values equal to zero. As a result, in the **Excluding +/- 5 S.D.** serum chemistry report where values equal to +/- 5 S.D. were excluded, this parameter was excluded due to the values being equal to zero.

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

A/G RATIO

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
NA	1.63	0.206	35	2.05 / 1.22	2.25 / 1.02	1.27 / 2.05

ALANINE TRANSFER

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	42	11.3	35	65 / 20	76 / 8	25 / 66

ALBUMIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	4.3	0.16	35	4.7 / 4.0	4.8 / 3.9	4.0 / 4.8

ALKALINE PHOS'TS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	90	29.9	35	150 / 31	180 / 1	47 / 174

ASPARTAT TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	90	19.5	35	129 / 51	149 / 31	57 / 132

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

CALCIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	10.6	0.79	35	12.1 / 9.0	12.9 / 8.2	9.6 / 12.3

CHLORIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	101	2.1	35	105 / 96	107 / 94	96 / 105

CHOLESTEROL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	75	19.1	35	113 / 37	132 / 18	41 / 108

CREATINE KINASE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	251	126.1	10	503 / 0.0	629 / 0.0	122 / 527

CREATININE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.3	0.09	35	0.5 / 0.1	0.6 / 0.0	0.2 / 0.6

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

GLOBULIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	2.7	0.30	35	3.3 / 2.1	3.6 / 1.8	2.1 / 3.4

GLUCOSE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	169	57.5	35	284 / 54	342 / 0.0	104 / 294

GLUTAMYL TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	0.0	0.00	35	0.0 / 0.0	0.0 / 0.0	0.0 / 0.0

PHOSPHORUS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	7.0	1.70	35	10.5 / 3.6	12.2 / 1.9	1.8 / 11.0

POTASSIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	6.03	1.130	35	8.29 / 3.77	9.42 / 2.64	4.72 / 9.52

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

SODIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	144	3.0	35	151 / 138	154 / 135	139 / 150

TOTAL BILI

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.2	0.05	35	0.3 / 0.1	0.3 / 0.1	0.1 / 0.3

TOTAL PROTEIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	7.0	0.32	35	7.7 / 6.4	8.0 / 6.1	6.4 / 7.9

TRIGLYCERIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	101	33.7	15	169 / 34	202 / 0	48 / 179

UREA NITROGEN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	16.1	3.21	35	22.5 / 9.7	25.7 / 6.4	11.5 / 29.0

Sex: M	Study Type: SUBCHRONIC	Number of Studies/Control Groups: 5 / 5
Species: RAT	Age: 22 - 25 Weeks	Range of Study Dates: 04/98 - 01/01
Strain: IGS		Report Type: **ALL DATA**

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Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

A/G RATIO

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
NA	1.63	0.206	35	2.05 / 1.22	2.25 / 1.02	1.27 / 2.05

ALANINE TRANSFER

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	42	11.3	35	65 / 20	76 / 8	25 / 66

ALBUMIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	4.3	0.16	35	4.7 / 4.0	4.8 / 3.9	4.0 / 4.8

ALKALINE PHOS'TS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	90	29.9	35	150 / 31	180 / 1	47 / 174

ASPARTAT TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	90	19.5	35	129 / 51	149 / 31	57 / 132

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

CALCIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	10.6	0.79	35	12.1 / 9.0	12.9 / 8.2	9.6 / 12.3

CHLORIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	101	2.1	35	105 / 96	107 / 94	96 / 105

CHOLESTEROL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	75	19.1	35	113 / 37	132 / 18	41 / 108

CREATINE KINASE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	251	126.1	10	503 / 0.0	629 / 0.0	122 / 527

CREATININE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.3	0.09	35	0.5 / 0.1	0.6 / 0.0	0.2 / 0.6

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

GLOBULIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	2.7	0.30	35	3.3 / 2.1	3.6 / 1.8	2.1 / 3.4

GLUCOSE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	169	57.5	35	284 / 54	342 / 0.0	104 / 294

PHOSPHORUS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	7.0	1.70	35	10.5 / 3.6	12.2 / 1.9	1.8 / 11.0

POTASSIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	6.03	1.130	35	8.29 / 3.77	9.42 / 2.64	4.72 / 9.52

SODIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	144	3.0	35	151 / 138	154 / 135	139 / 150

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

TOTAL BILI

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.2	0.05	35	0.3 / 0.1	0.3 / 0.1	0.1 / 0.3

TOTAL PROTEIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	7.0	0.32	35	7.7 / 6.4	8.0 / 6.1	6.4 / 7.9

TRIGLYCERIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	101	33.7	15	169 / 34	202 / 0	48 / 179

UREA NITROGEN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	16.1	3.21	35	22.5 / 9.7	25.7 / 6.4	11.5 / 29.0

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

A/G RATIO

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
NA	2.28	0.520	34	3.32 / 1.24	3.85 / 0.72	1.33 / 3.28

ALANINE TRANSFER

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	81	105.3	34	291 / 0.0	397 / 0.0	19 / 503

ALBUMIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	5.3	0.58	34	6.4 / 4.1	7.0 / 3.5	4.0 / 6.5

ALKALINE PHOS'TS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	49	23.3	34	96 / 3	119 / 0.0	23 / 114

ASPARTAT TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	164	204.0	34	572 / 0.0	776 / 0.0	60 / 913

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

CALCIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	10.9	1.18	34	13.3 / 8.5	14.4 / 7.3	9.6 / 13.9

CHLORIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	101	2.0	34	105 / 97	107 / 95	97 / 106

CHOLESTEROL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	87	31.8	34	150 / 23	182 / 0.0	45 / 166

CREATINE KINASE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	324	169.1	10	663 / 0.0	832 / 0.0	90 / 701

CREATININE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.3	0.07	34	0.5 / 0.2	0.5 / 0.1	0.2 / 0.5

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

GLOBULIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	2.4	0.37	34	3.1 / 1.6	3.5 / 1.3	1.7 / 3.0

GLUCOSE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	147	46.8	34	241 / 53	287 / 7	102 / 325

GLUTAMYL TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	0.3	1.09	34	2.5 / 0.0	3.6 / 0.0	0.0 / 6.0

PHOSPHORUS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	6.2	2.25	34	10.7 / 1.7	12.9 / 0.0	3.7 / 11.9

POTASSIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	6.12	2.168	34	10.46 / 1.78	12.63 / 0.0	4.62 / 14.80

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

SODIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	143	2.7	34	149 / 138	151 / 135	140 / 149

TOTAL BILI

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.2	0.08	34	0.4 / 0.1	0.5 / 0.0	0.1 / 0.4

TOTAL PROTEIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	7.6	0.53	34	8.7 / 6.6	9.2 / 6.1	6.8 / 8.8

TRIGLYCERIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	69	27.2	14	124 / 15	151 / 0.0	38 / 121

UREA NITROGEN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	17.1	2.65	34	22.4 / 11.8	25.1 / 9.2	9.9 / 22.1

Sex: F	Study Type: SUBCHRONIC	Number of Studies/Control Groups: 5 / 5
Species: RAT	Age: 22 - 25 Weeks	Range of Study Dates: 04/98 - 01/01
Strain: IGS		Report Type: **ALL DATA**

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Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

A/G RATIO

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
NA	2.28	0.520	34	3.32 / 1.24	3.85 / 0.72	1.33 / 3.28

ALANINE TRANSFER

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	81	105.3	34	291 / 0.0	397 / 0.0	19 / 503

ALBUMIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	5.3	0.58	34	6.4 / 4.1	7.0 / 3.5	4.0 / 6.5

ALKALINE PHOS'TS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	49	23.3	34	96 / 3	119 / 0.0	23 / 114

ASPARTAT TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	164	204.0	34	572 / 0.0	776 / 0.0	60 / 913

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

CALCIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	10.9	1.18	34	13.3 / 8.5	14.4 / 7.3	9.6 / 13.9

CHLORIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	101	2.0	34	105 / 97	107 / 95	97 / 106

CHOLESTEROL

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	87	31.8	34	150 / 23	182 / 0.0	45 / 166

CREATINE KINASE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	324	169.1	10	663 / 0.0	832 / 0.0	90 / 701

CREATININE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.3	0.07	34	0.5 / 0.2	0.5 / 0.1	0.2 / 0.5

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

GLOBULIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	2.4	0.37	34	3.1 / 1.6	3.5 / 1.3	1.7 / 3.0

GLUCOSE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	147	46.8	34	241 / 53	287 / 7	102 / 325

GLUTAMYL TRANSFE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
U/L	0.2	0.44	33	1.0 / 0.0	1.5 / 0.0	0.0 / 2.0

PHOSPHORUS

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	6.2	2.25	34	10.7 / 1.7	12.9 / 0.0	3.7 / 11.9

POTASSIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	6.12	2.168	34	10.46 / 1.78	12.63 / 0.0	4.62 / 14.80

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

SODIUM

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mEq/L	143	2.7	34	149 / 138	151 / 135	140 / 149

TOTAL BILI

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	0.2	0.08	34	0.4 / 0.1	0.5 / 0.0	0.1 / 0.4

TOTAL PROTEIN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
g/dL	7.6	0.53	34	8.7 / 6.6	9.2 / 6.1	6.8 / 8.8

TRIGLYCERIDE

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	69	27.2	14	124 / 15	151 / 0.0	38 / 121

UREA NITROGEN

Unit	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
mg/dL	17.1	2.65	34	22.4 / 11.8	25.1 / 9.2	9.9 / 22.1

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 22 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

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25-Apr-02

WIL Research Laboratories, Inc.
Historical Control Data
Crl:CD®(SD)IGS rats from 13-week studies

ORGAN WEIGHT DATA
SCHEDULED NECROPSY

Note:

Organ weights are presented in grams.
Organ weights relative to final body weights are presented in grams/100 grams of body weight.
Organ weights relative to brain weights are presented in grams/100 grams of brain weight.

In the Report Header, **Report Type** is designated by **ALL DATA** or
Excluding +/- 5 S.D. depending upon the data set.

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

ADRENAL GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0633	0.00973	205	0.0827 / 0.0438	0.0924 / 0.0341	0.0395 / 0.0886
OW relative to FBW:	0.012	0.0022	205	0.017 / 0.008	0.019 / 0.006	0.007 / 0.019
OW relative to brain:	3.045	0.4673	205	3.980 / 2.111	4.447 / 1.643	1.927 / 4.227

BRAIN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	2.08	0.091	205	2.26 / 1.90	2.35 / 1.81	1.84 / 2.38
OW relative to FBW:	0.408	0.0392	205	0.486 / 0.330	0.525 / 0.290	0.313 / 0.516
OW relative to brain:	NA					

EPIDIDYMIDES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.42	0.149	136	1.72 / 1.12	1.86 / 0.97	0.62 / 1.75
OW relative to FBW:	0.282	0.0358	136	0.354 / 0.210	0.389 / 0.174	0.121 / 0.367
OW relative to brain:	68.645	7.3009	136	83.247 / 54.043	90.548 / 46.742	31.156 / 85.000

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

FINAL BODY WEIGHT

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	514	51.0	205	616 / 412	667 / 361	398 / 653
OW relative to FBW:	NA					
OW relative to brain:	NA					

HEART

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.63	0.182	171	2.00 / 1.27	2.18 / 1.09	1.28 / 2.29
OW relative to FBW:	0.320	0.0349	171	0.390 / 0.250	0.425 / 0.215	0.249 / 0.432
OW relative to brain:	78.587	8.7749	171	96.137 / 61.038	104.912 / 52.263	59.722 / 115.075

KIDNEYS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	3.52	0.454	205	4.43 / 2.61	4.88 / 2.16	2.56 / 5.02
OW relative to FBW:	0.687	0.0847	205	0.857 / 0.518	0.942 / 0.433	0.513 / 1.126
OW relative to brain:	169.242	20.4362	205	210.114 / 128.370	230.550 / 107.933	121.905 / 240.704

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

LEFT CAUDA EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3087	0.03830	29	0.3853 / 0.2321	0.4236 / 0.1938	0.2133 / 0.3759
OW relative to FBW:	0.057	0.0081	29	0.073 / 0.041	0.082 / 0.033	0.042 / 0.071
OW relative to brain:	14.635	1.7768	29	18.189 / 11.082	19.965 / 9.305	9.784 / 17.565

LEFT EPIDIDYMIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.69	0.070	14	0.83 / 0.55	0.90 / 0.48	0.56 / 0.79
OW relative to FBW:	0.132	0.0179	14	0.168 / 0.096	0.185 / 0.078	0.110 / 0.167
OW relative to brain:	33.244	3.3864	14	40.017 / 26.471	43.403 / 23.085	25.688 / 38.916

LEFT TESTIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.72	0.152	29	2.02 / 1.41	2.17 / 1.26	1.34 / 2.04
OW relative to FBW:	0.319	0.0426	29	0.404 / 0.233	0.446 / 0.191	0.240 / 0.407
OW relative to brain:	81.407	7.6692	29	96.745 / 66.068	104.414 / 58.399	61.468 / 94.009

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

LIVER

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	14.1	2.13	205	18.3 / 9.8	20.4 / 7.7	10.3 / 20.5
OW relative to FBW:	2.728	0.2604	205	3.249 / 2.208	3.510 / 1.947	2.193 / 3.604
OW relative to brain:	675.823	97.5356	205	870.894 / 480.752	968.430 / 383.216	479.167 / 1028.643

LUNGS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.97	0.302	64	2.57 / 1.36	2.87 / 1.06	1.58 / 3.72
OW relative to FBW:	0.379	0.0667	64	0.512 / 0.246	0.579 / 0.179	0.307 / 0.714
OW relative to brain:	94.569	13.1441	64	120.857 / 68.281	134.001 / 55.137	77.143 / 166.071

PITUITARY

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0148	0.00264	69	0.0201 / 0.0096	0.0227 / 0.0069	0.0090 / 0.0203
OW relative to FBW:	0.003	0.0006	69	0.004 / 0.002	0.005 / 0.001	0.001 / 0.004
OW relative to brain:	0.716	0.1274	69	0.971 / 0.461	1.098 / 0.334	0.417 / 1.016

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

PROSTATE

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.03	0.287	165	1.60 / 0.45	1.89 / 0.16	0.34 / 1.97
OW relative to FBW:	0.201	0.0570	165	0.315 / 0.087	0.372 / 0.030	0.066 / 0.356
OW relative to brain:	49.423	13.7334	165	76.890 / 21.956	90.624 / 8.223	17.085 / 95.631

RIGHT CAUDA EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3166	0.03469	29	0.3860 / 0.2472	0.4206 / 0.2125	0.2573 / 0.4176
OW relative to FBW:	0.059	0.0072	29	0.073 / 0.044	0.080 / 0.037	0.044 / 0.077
OW relative to brain:	15.009	1.6254	29	18.260 / 11.758	19.885 / 10.133	12.551 / 19.514

RIGHT EPIDIDYMIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.71	0.056	29	0.82 / 0.60	0.88 / 0.54	0.62 / 0.84
OW relative to FBW:	0.132	0.0157	29	0.163 / 0.101	0.179 / 0.085	0.106 / 0.172
OW relative to brain:	33.719	2.9224	29	39.564 / 27.874	42.486 / 24.951	27.826 / 39.623

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

RIGHT TESTIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.72	0.136	29	1.99 / 1.45	2.13 / 1.31	1.39 / 1.97
OW relative to FBW:	0.319	0.0378	29	0.395 / 0.244	0.432 / 0.206	0.255 / 0.399
OW relative to brain:	81.546	6.7089	29	94.964 / 68.128	101.673 / 61.420	63.761 / 93.689

SALIVARY GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.8600	0.08176	20	1.0235 / 0.6965	1.1053 / 0.6147	0.7100 / 1.0600
OW relative to FBW:	0.170	0.0200	20	0.210 / 0.130	0.230 / 0.110	0.135 / 0.211
OW relative to brain:	41.941	3.9579	20	49.857 / 34.026	53.815 / 30.068	34.742 / 52.736

SEM VES/COAG GL.

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.6914	0.34771	14	2.3869 / 0.9960	2.7346 / 0.6483	1.1900 / 2.4200
OW relative to FBW:	0.327	0.0896	14	0.506 / 0.148	0.596 / 0.058	0.201 / 0.526
OW relative to brain:	81.466	16.5359	14	114.538 / 48.394	131.074 / 31.858	58.621 / 116.908

Sex: M | Study Type: SUBCHRONIC | Number of Studies/Control Groups: 15 / 16
Species: RAT | Age: 19 - 21 Weeks | Range of Study Dates: 12/97 - 10/01
Strain: IGS | Report Type: **ALL DATA**

SPLEEN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.84	0.137	191	1.11 / 0.56	1.25 / 0.42	0.53 / 1.30
OW relative to FBW:	0.163	0.0246	191	0.213 / 0.114	0.237 / 0.090	0.111 / 0.280
OW relative to brain:	40.196	6.3202	191	52.836 / 27.555	59.156 / 21.235	24.091 / 61.033

TESTES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	3.51	0.413	146	4.34 / 2.69	4.75 / 2.27	0.95 / 4.48
OW relative to FBW:	0.697	0.0928	146	0.883 / 0.512	0.976 / 0.419	0.186 / 0.934
OW relative to brain:	169.687	19.3654	146	208.418 / 130.956	227.783 / 111.591	47.739 / 224.000

TESTES/EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	4.92	0.730	30	6.38 / 3.46	7.11 / 2.73	1.52 / 5.77
OW relative to FBW:	0.950	0.1611	30	1.273 / 0.628	1.434 / 0.467	0.279 / 1.254
OW relative to brain:	235.248	35.9394	30	307.126 / 163.369	343.066 / 127.429	74.146 / 280.097

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

THYMUS GLAND

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3144	0.08100	191	0.4764 / 0.1524	0.5574 / 0.0714	0.1424 / 0.6067
OW relative to FBW:	0.062	0.0163	191	0.094 / 0.029	0.110 / 0.013	0.029 / 0.118
OW relative to brain:	15.149	3.9807	191	23.110 / 7.187	27.091 / 3.207	6.473 / 30.487

THYROID GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0268	0.00595	205	0.0388 / 0.0149	0.0447 / 0.0090	0.0091 / 0.0475
OW relative to FBW:	0.005	0.0012	205	0.008 / 0.003	0.009 / 0.002	0.002 / 0.008
OW relative to brain:	1.293	0.2900	205	1.873 / 0.713	2.163 / 0.423	0.420 / 2.189

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

ADRENAL GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0633	0.00973	205	0.0827 / 0.0438	0.0924 / 0.0341	0.0395 / 0.0886
OW relative to FBW:	0.012	0.0022	205	0.017 / 0.008	0.019 / 0.006	0.007 / 0.019
OW relative to brain:	3.045	0.4673	205	3.980 / 2.111	4.447 / 1.643	1.927 / 4.227

BRAIN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	2.08	0.091	205	2.26 / 1.90	2.35 / 1.81	1.84 / 2.38
OW relative to FBW:	0.408	0.0392	205	0.486 / 0.330	0.525 / 0.290	0.313 / 0.516
OW relative to brain:	NA					

EPIDIDYMIDES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.42	0.149	136	1.72 / 1.12	1.86 / 0.97	0.62 / 1.75
OW relative to FBW:	0.282	0.0358	136	0.354 / 0.210	0.389 / 0.174	0.121 / 0.367
OW relative to brain:	68.645	7.3009	136	83.247 / 54.043	90.548 / 46.742	31.156 / 85.000

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

FINAL BODY WEIGHT

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	514	51.0	205	616 / 412	667 / 361	398 / 653
OW relative to FBW:	NA					
OW relative to brain:	NA					

HEART

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.63	0.182	171	2.00 / 1.27	2.18 / 1.09	1.28 / 2.29
OW relative to FBW:	0.320	0.0349	171	0.390 / 0.250	0.425 / 0.215	0.249 / 0.432
OW relative to brain:	78.587	8.7749	171	96.137 / 61.038	104.912 / 52.263	59.722 / 115.075

KIDNEYS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	3.52	0.454	205	4.43 / 2.61	4.88 / 2.16	2.56 / 5.02
OW relative to FBW:	0.687	0.0847	205	0.857 / 0.518	0.942 / 0.433	0.513 / 1.126
OW relative to brain:	169.242	20.4362	205	210.114 / 128.370	230.550 / 107.933	121.905 / 240.704

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

LEFT CAUDA EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3087	0.03830	29	0.3853 / 0.2321	0.4236 / 0.1938	0.2133 / 0.3759
OW relative to FBW:	0.057	0.0081	29	0.073 / 0.041	0.082 / 0.033	0.042 / 0.071
OW relative to brain:	14.635	1.7768	29	18.189 / 11.082	19.965 / 9.305	9.784 / 17.565

LEFT EPIDIDYMIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.69	0.069	28	0.83 / 0.55	0.90 / 0.48	0.56 / 0.79
OW relative to FBW:	0.132	0.0176	28	0.167 / 0.097	0.184 / 0.079	0.110 / 0.167
OW relative to brain:	33.244	3.3231	28	39.890 / 26.598	43.213 / 23.275	25.688 / 38.916

LEFT TESTIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.72	0.152	29	2.02 / 1.41	2.17 / 1.26	1.34 / 2.04
OW relative to FBW:	0.319	0.0426	29	0.404 / 0.233	0.446 / 0.191	0.240 / 0.407
OW relative to brain:	81.407	7.6692	29	96.745 / 66.068	104.414 / 58.399	61.468 / 94.009

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

LIVER

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	14.1	2.13	205	18.3 / 9.8	20.4 / 7.7	10.3 / 20.5
OW relative to FBW:	2.728	0.2604	205	3.249 / 2.208	3.510 / 1.947	2.193 / 3.604
OW relative to brain:	675.823	97.5356	205	870.894 / 480.752	968.430 / 383.216	479.167 / 1028.643

LUNGS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.94	0.206	63	2.35 / 1.53	2.56 / 1.32	1.58 / 2.68
OW relative to FBW:	0.374	0.0518	63	0.477 / 0.270	0.529 / 0.218	0.307 / 0.597
OW relative to brain:	93.434	9.5804	63	112.595 / 74.274	122.176 / 64.693	77.143 / 125.234

PITUITARY

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0148	0.00264	69	0.0201 / 0.0096	0.0227 / 0.0069	0.0090 / 0.0203
OW relative to FBW:	0.003	0.0006	69	0.004 / 0.002	0.005 / 0.001	0.001 / 0.004
OW relative to brain:	0.716	0.1274	69	0.971 / 0.461	1.098 / 0.334	0.417 / 1.016

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

PROSTATE

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.03	0.287	165	1.60 / 0.45	1.89 / 0.16	0.34 / 1.97
OW relative to FBW:	0.201	0.0570	165	0.315 / 0.087	0.372 / 0.030	0.066 / 0.356
OW relative to brain:	49.423	13.7334	165	76.890 / 21.956	90.624 / 8.223	17.085 / 95.631

RIGHT CAUDA EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3166	0.03469	29	0.3860 / 0.2472	0.4206 / 0.2125	0.2573 / 0.4176
OW relative to FBW:	0.059	0.0072	29	0.073 / 0.044	0.080 / 0.037	0.044 / 0.077
OW relative to brain:	15.009	1.6254	29	18.260 / 11.758	19.885 / 10.133	12.551 / 19.514

RIGHT EPIDIDYMIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.71	0.056	29	0.82 / 0.60	0.88 / 0.54	0.62 / 0.84
OW relative to FBW:	0.132	0.0157	29	0.163 / 0.101	0.179 / 0.085	0.106 / 0.172
OW relative to brain:	33.719	2.9224	29	39.564 / 27.874	42.486 / 24.951	27.826 / 39.623

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

RIGHT TESTIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.72	0.136	29	1.99 / 1.45	2.13 / 1.31	1.39 / 1.97
OW relative to FBW:	0.319	0.0378	29	0.395 / 0.244	0.432 / 0.206	0.255 / 0.399
OW relative to brain:	81.546	6.7089	29	94.964 / 68.128	101.673 / 61.420	63.761 / 93.689

SALIVARY GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.8600	0.08176	20	1.0235 / 0.6965	1.1053 / 0.6147	0.7100 / 1.0600
OW relative to FBW:	0.170	0.0200	20	0.210 / 0.130	0.230 / 0.110	0.135 / 0.211
OW relative to brain:	41.941	3.9579	20	49.857 / 34.026	53.815 / 30.068	34.742 / 52.736

SEM VES/COAG GL.

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.6914	0.34771	14	2.3869 / 0.9960	2.7346 / 0.6483	1.1900 / 2.4200
OW relative to FBW:	0.327	0.0896	14	0.506 / 0.148	0.596 / 0.058	0.201 / 0.526
OW relative to brain:	81.466	16.5359	14	114.538 / 48.394	131.074 / 31.858	58.621 / 116.908

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

SPLEEN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.84	0.137	191	1.11 / 0.56	1.25 / 0.42	0.53 / 1.30
OW relative to FBW:	0.163	0.0246	191	0.213 / 0.114	0.237 / 0.090	0.111 / 0.280
OW relative to brain:	40.196	6.3202	191	52.836 / 27.555	59.156 / 21.235	24.091 / 61.033

TESTES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	3.53	0.355	145	4.24 / 2.82	4.60 / 2.46	1.61 / 4.48
OW relative to FBW:	0.701	0.0828	145	0.867 / 0.535	0.949 / 0.453	0.304 / 0.934
OW relative to brain:	170.528	16.5420	145	203.612 / 137.444	220.154 / 120.902	77.404 / 224.000

TESTES/EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	4.92	0.730	30	6.38 / 3.46	7.11 / 2.73	1.52 / 5.77
OW relative to FBW:	0.950	0.1611	30	1.273 / 0.628	1.434 / 0.467	0.279 / 1.254
OW relative to brain:	235.248	35.9394	30	307.126 / 163.369	343.066 / 127.429	74.146 / 280.097

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

THYMUS GLAND

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3144	0.08100	191	0.4764 / 0.1524	0.5574 / 0.0714	0.1424 / 0.6067
OW relative to FBW:	0.062	0.0163	191	0.094 / 0.029	0.110 / 0.013	0.029 / 0.118
OW relative to brain:	15.149	3.9807	191	23.110 / 7.187	27.091 / 3.207	6.473 / 30.487

THYROID GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0268	0.00595	205	0.0388 / 0.0149	0.0447 / 0.0090	0.0091 / 0.0475
OW relative to FBW:	0.005	0.0012	205	0.008 / 0.003	0.009 / 0.002	0.002 / 0.008
OW relative to brain:	1.293	0.2900	205	1.873 / 0.713	2.163 / 0.423	0.420 / 2.189

Version 1.0
17-May-02

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

ADRENAL GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0717	0.01100	206	0.0937 / 0.0497	0.1047 / 0.0387	0.0285 / 0.1187
OW relative to FBW:	0.026	0.0046	206	0.035 / 0.017	0.040 / 0.012	0.009 / 0.040
OW relative to brain:	3.775	0.5804	206	4.936 / 2.614	5.516 / 2.034	1.500 / 6.056

BRAIN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.90	0.092	206	2.09 / 1.72	2.18 / 1.63	1.64 / 2.16
OW relative to FBW:	0.683	0.0682	206	0.819 / 0.546	0.887 / 0.478	0.494 / 0.861
OW relative to brain:	NA					

FINAL BODY WEIGHT

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	281	28.1	206	337 / 225	366 / 197	218 / 409
OW relative to FBW:	NA					
OW relative to brain:	NA					

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

HEART

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.03	0.103	171	1.24 / 0.83	1.34 / 0.73	0.79 / 1.34
OW relative to FBW:	0.369	0.0364	171	0.442 / 0.296	0.478 / 0.260	0.287 / 0.490
OW relative to brain:	54.371	5.5763	171	65.523 / 43.218	71.100 / 37.642	41.237 / 70.157

KIDNEYS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	2.03	0.234	206	2.50 / 1.56	2.73 / 1.33	1.44 / 3.13
OW relative to FBW:	0.725	0.0883	206	0.902 / 0.549	0.990 / 0.461	0.515 / 1.218
OW relative to brain:	106.668	11.9567	206	130.581 / 82.755	142.538 / 70.798	77.295 / 165.608

LIVER

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	8.0	0.97	206	9.9 / 6.0	10.9 / 5.1	5.6 / 12.1
OW relative to FBW:	2.842	0.2896	206	3.422 / 2.263	3.711 / 1.974	2.250 / 4.085
OW relative to brain:	419.276	49.8134	206	518.903 / 319.650	568.717 / 269.836	309.392 / 614.796

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

LUNGS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.46	0.172	64	1.81 / 1.12	1.98 / 0.95	1.09 / 2.01
OW relative to FBW:	0.521	0.0637	64	0.649 / 0.394	0.712 / 0.330	0.409 / 0.664
OW relative to brain:	76.646	7.7179	64	92.081 / 61.210	99.799 / 53.492	60.914 / 101.026

OVARIES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.1069	0.02583	80	0.1586 / 0.0553	0.1844 / 0.0294	0.0553 / 0.1824
OW relative to FBW:	0.040	0.0095	80	0.059 / 0.021	0.068 / 0.011	0.023 / 0.062
OW relative to brain:	5.648	1.4376	80	8.523 / 2.773	9.961 / 1.335	2.926 / 10.077

OVARIES/OVIDUCTS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.1286	0.02459	126	0.1778 / 0.0794	0.2024 / 0.0548	0.0146 / 0.1889
OW relative to FBW:	0.045	0.0091	126	0.063 / 0.027	0.072 / 0.018	0.005 / 0.066
OW relative to brain:	6.759	1.2778	126	9.315 / 4.203	10.592 / 2.926	0.772 / 9.590

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

PITUITARY

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0185	0.00409	69	0.0267 / 0.0103	0.0307 / 0.0062	0.0096 / 0.0327
OW relative to FBW:	0.007	0.0014	69	0.009 / 0.004	0.011 / 0.002	0.004 / 0.012
OW relative to brain:	0.971	0.2042	69	1.379 / 0.562	1.583 / 0.358	0.500 / 1.668

SALIVARY GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.5195	0.07251	20	0.6645 / 0.3745	0.7370 / 0.3020	0.3800 / 0.6500
OW relative to FBW:	0.197	0.0254	20	0.248 / 0.146	0.273 / 0.121	0.167 / 0.253
OW relative to brain:	27.513	3.3698	20	34.253 / 20.774	37.623 / 17.404	20.994 / 33.871

SPLEEN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.55	0.088	191	0.72 / 0.37	0.81 / 0.28	0.36 / 0.88
OW relative to FBW:	0.197	0.0308	191	0.258 / 0.135	0.289 / 0.104	0.129 / 0.342
OW relative to brain:	28.873	4.5817	191	38.037 / 19.710	42.619 / 15.128	20.000 / 46.561

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

THYMUS GLAND

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.2808	0.06602	191	0.4128 / 0.1488	0.4789 / 0.0827	0.0818 / 0.4533
OW relative to FBW:	0.101	0.0240	191	0.149 / 0.053	0.173 / 0.029	0.026 / 0.163
OW relative to brain:	14.763	3.4088	191	21.581 / 7.945	24.990 / 4.537	4.305 / 24.266

THYROID GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0217	0.00586	206	0.0334 / 0.0099	0.0392 / 0.0041	0.0100 / 0.0562
OW relative to FBW:	0.008	0.0021	206	0.012 / 0.004	0.014 / 0.002	0.004 / 0.018
OW relative to brain:	1.138	0.3040	206	1.746 / 0.530	2.050 / 0.226	0.543 / 2.810

UTERUS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.72	0.305	127	1.33 / 0.11	1.63 / 0.0	0.36 / 2.36
OW relative to FBW:	0.255	0.1114	127	0.478 / 0.032	0.589 / 0.0	0.120 / 0.797
OW relative to brain:	37.743	16.3161	127	70.375 / 5.110	86.691 / 0.0	19.780 / 126.882

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **ALL DATA**

UTERUS/CERVIX

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.69	0.255	35	1.20 / 0.18	1.45 / 0.0	0.35 / 1.49
OW relative to FBW:	0.253	0.0952	35	0.443 / 0.063	0.539 / 0.0	0.123 / 0.540
OW relative to brain:	36.094	13.1796	35	62.453 / 9.735	75.633 / 0.0	17.500 / 72.283

UTERUS/VAGINA

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.89	0.258	9	1.41 / 0.37	1.66 / 0.12	0.63 / 1.54
OW relative to FBW:	0.315	0.0852	9	0.486 / 0.145	0.571 / 0.060	0.222 / 0.524
OW relative to brain:	45.103	12.5064	9	70.116 / 20.090	82.622 / 7.584	33.511 / 76.238

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

ADRENAL GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0717	0.01100	206	0.0937 / 0.0497	0.1047 / 0.0387	0.0285 / 0.1187
OW relative to FBW:	0.026	0.0046	206	0.035 / 0.017	0.040 / 0.012	0.009 / 0.040
OW relative to brain:	3.775	0.5804	206	4.936 / 2.614	5.516 / 2.034	1.500 / 6.056

BRAIN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.90	0.092	206	2.09 / 1.72	2.18 / 1.63	1.64 / 2.16
OW relative to FBW:	0.683	0.0682	206	0.819 / 0.546	0.887 / 0.478	0.494 / 0.861
OW relative to brain:	NA					

FINAL BODY WEIGHT

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	281	28.1	206	337 / 225	366 / 197	218 / 409
OW relative to FBW:	NA					
OW relative to brain:	NA					

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

HEART

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.03	0.103	171	1.24 / 0.83	1.34 / 0.73	0.79 / 1.34
OW relative to FBW:	0.369	0.0364	171	0.442 / 0.296	0.478 / 0.260	0.287 / 0.490
OW relative to brain:	54.371	5.5763	171	65.523 / 43.218	71.100 / 37.642	41.237 / 70.157

KIDNEYS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	2.03	0.234	206	2.50 / 1.56	2.73 / 1.33	1.44 / 3.13
OW relative to FBW:	0.725	0.0883	206	0.902 / 0.549	0.990 / 0.461	0.515 / 1.218
OW relative to brain:	106.668	11.9567	206	130.581 / 82.755	142.538 / 70.798	77.295 / 165.608

LIVER

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	8.0	0.97	206	9.9 / 6.0	10.9 / 5.1	5.6 / 12.1
OW relative to FBW:	2.842	0.2896	206	3.422 / 2.263	3.711 / 1.974	2.250 / 4.085
OW relative to brain:	419.276	49.8134	206	518.903 / 319.650	568.717 / 269.836	309.392 / 614.796

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

LUNGS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.46	0.172	64	1.81 / 1.12	1.98 / 0.95	1.09 / 2.01
OW relative to FBW:	0.521	0.0637	64	0.649 / 0.394	0.712 / 0.330	0.409 / 0.664
OW relative to brain:	76.646	7.7179	64	92.081 / 61.210	99.799 / 53.492	60.914 / 101.026

OVARIES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.1069	0.02583	80	0.1586 / 0.0553	0.1844 / 0.0294	0.0553 / 0.1824
OW relative to FBW:	0.040	0.0095	80	0.059 / 0.021	0.068 / 0.011	0.023 / 0.062
OW relative to brain:	5.648	1.4376	80	8.523 / 2.773	9.961 / 1.335	2.926 / 10.077

OVARIES/OVIDUCTS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.1286	0.02459	126	0.1778 / 0.0794	0.2024 / 0.0548	0.0146 / 0.1889
OW relative to FBW:	0.045	0.0091	126	0.063 / 0.027	0.072 / 0.018	0.005 / 0.066
OW relative to brain:	6.759	1.2778	126	9.315 / 4.203	10.592 / 2.926	0.772 / 9.590

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

PITUITARY

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0185	0.00409	69	0.0267 / 0.0103	0.0307 / 0.0062	0.0096 / 0.0327
OW relative to FBW:	0.007	0.0014	69	0.009 / 0.004	0.011 / 0.002	0.004 / 0.012
OW relative to brain:	0.971	0.2042	69	1.379 / 0.562	1.583 / 0.358	0.500 / 1.668

SALIVARY GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.5195	0.07251	20	0.6645 / 0.3745	0.7370 / 0.3020	0.3800 / 0.6500
OW relative to FBW:	0.197	0.0254	20	0.248 / 0.146	0.273 / 0.121	0.167 / 0.253
OW relative to brain:	27.513	3.3698	20	34.253 / 20.774	37.623 / 17.404	20.994 / 33.871

SPLEEN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.55	0.088	191	0.72 / 0.37	0.81 / 0.28	0.36 / 0.88
OW relative to FBW:	0.197	0.0308	191	0.258 / 0.135	0.289 / 0.104	0.129 / 0.342
OW relative to brain:	28.873	4.5817	191	38.037 / 19.710	42.619 / 15.128	20.000 / 46.561

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

THYMUS GLAND

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.2808	0.06602	191	0.4128 / 0.1488	0.4789 / 0.0827	0.0818 / 0.4533
OW relative to FBW:	0.101	0.0240	191	0.149 / 0.053	0.173 / 0.029	0.026 / 0.163
OW relative to brain:	14.763	3.4088	191	21.581 / 7.945	24.990 / 4.537	4.305 / 24.266

THYROID GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0217	0.00586	206	0.0334 / 0.0099	0.0392 / 0.0041	0.0100 / 0.0562
OW relative to FBW:	0.008	0.0021	206	0.012 / 0.004	0.014 / 0.002	0.004 / 0.018
OW relative to brain:	1.138	0.3040	206	1.746 / 0.530	2.050 / 0.226	0.543 / 2.810

UTERUS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.72	0.305	127	1.33 / 0.11	1.63 / 0.0	0.36 / 2.36
OW relative to FBW:	0.255	0.1114	127	0.478 / 0.032	0.589 / 0.0	0.120 / 0.797
OW relative to brain:	37.743	16.3161	127	70.375 / 5.110	86.691 / 0.0	19.780 / 126.882

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 19 - 21 Weeks

Number of Studies/Control Groups: 15 / 16
Range of Study Dates: 12/97 - 10/01
Report Type: **Excluding +/- 5 S.D.**

UTERUS/CERVIX

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.69	0.255	35	1.20 / 0.18	1.45 / 0.0	0.35 / 1.49
OW relative to FBW:	0.253	0.0952	35	0.443 / 0.063	0.539 / 0.0	0.123 / 0.540
OW relative to brain:	36.094	13.1796	35	62.453 / 9.735	75.633 / 0.0	17.500 / 72.283

UTERUS/VAGINA

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.89	0.258	9	1.41 / 0.37	1.66 / 0.12	0.63 / 1.54
OW relative to FBW:	0.315	0.0852	9	0.486 / 0.145	0.571 / 0.060	0.222 / 0.524
OW relative to brain:	45.103	12.5064	9	70.116 / 20.090	82.622 / 7.584	33.511 / 76.238

WIL Research Laboratories, Inc.
Historical Control Data
Crl:CD®(SD)IGS rats from 13-week studies

ORGAN WEIGHT DATA
RECOVERY NECROPSY

Note:

Organ weights are presented in grams.
Organ weights relative to final body weights are presented in grams/100 grams of body weight.
Organ weights relative to brain weights are presented in grams/100 grams of brain weight.

In the Report Header, **Report Type** is designated by **ALL DATA** or
Excluding +/- 5 S.D. depending upon the data set.

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

ADRENAL GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0590	0.01040	35	0.0798 / 0.0382	0.0902 / 0.0278	0.0375 / 0.0815
OW relative to FBW:	0.010	0.0017	35	0.014 / 0.007	0.015 / 0.005	0.006 / 0.015
OW relative to brain:	2.777	0.4866	35	3.750 / 1.803	4.236 / 1.317	1.842 / 3.603

BRAIN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	2.13	0.126	35	2.38 / 1.88	2.51 / 1.75	1.79 / 2.41
OW relative to FBW:	0.377	0.0385	35	0.454 / 0.300	0.493 / 0.262	0.304 / 0.447
OW relative to brain:	NA					

EPIDIDYMIDES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.50	0.090	15	1.68 / 1.32	1.77 / 1.23	1.37 / 1.66
OW relative to FBW:	0.270	0.0301	15	0.330 / 0.210	0.360 / 0.180	0.222 / 0.331
OW relative to brain:	72.986	6.6985	15	86.383 / 59.589	93.082 / 52.891	64.545 / 85.475

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

FINAL BODY WEIGHT

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	569	59.0	35	687 / 451	746 / 392	470 / 718
OW relative to FBW:	NA					
OW relative to brain:	NA					

HEART

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.67	0.193	35	2.05 / 1.28	2.25 / 1.09	1.29 / 2.09
OW relative to FBW:	0.294	0.0284	35	0.351 / 0.237	0.379 / 0.209	0.241 / 0.358
OW relative to brain:	78.451	8.9785	35	96.408 / 60.494	105.387 / 51.515	62.319 / 97.573

KIDNEYS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	3.68	0.460	35	4.60 / 2.76	5.06 / 2.30	2.80 / 5.02
OW relative to FBW:	0.650	0.0803	35	0.810 / 0.489	0.891 / 0.409	0.550 / 0.951
OW relative to brain:	173.056	19.4450	35	211.946 / 134.166	231.391 / 114.721	137.441 / 216.908

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

LEFT CAUDA EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3213	0.08000	10	0.4813 / 0.1613	0.5613 / 0.0812	0.1230 / 0.3950
OW relative to FBW:	0.055	0.0150	10	0.085 / 0.025	0.100 / 0.010	0.024 / 0.072
OW relative to brain:	14.658	3.6129	10	21.884 / 7.432	25.497 / 3.820	5.748 / 19.082

LEFT EPIDIDYMIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.6950	0.15544	10	1.0059 / 0.3841	1.1613 / 0.2287	0.2800 / 0.8400
OW relative to FBW:	0.119	0.0286	10	0.176 / 0.061	0.205 / 0.033	0.054 / 0.159
OW relative to brain:	31.671	6.6972	10	45.066 / 18.277	51.763 / 11.580	13.084 / 35.897

LEFT TESTIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.68	0.487	10	2.66 / 0.71	3.14 / 0.22	0.35 / 2.10
OW relative to FBW:	0.286	0.0873	10	0.461 / 0.112	0.548 / 0.025	0.067 / 0.398
OW relative to brain:	76.790	22.3619	10	121.514 / 32.066	143.876 / 9.704	16.355 / 96.135

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

LIVER

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	15.2	2.15	35	19.5 / 10.9	21.6 / 8.8	11.1 / 20.7
OW relative to FBW:	2.664	0.2026	35	3.069 / 2.258	3.271 / 2.056	2.194 / 2.980
OW relative to brain:	714.336	97.4425	35	909.221 / 519.451	1006.663 / 422.008	534.783 / 907.456

LUNGS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.98	0.223	15	2.43 / 1.54	2.65 / 1.31	1.71 / 2.55
OW relative to FBW:	0.360	0.0488	15	0.458 / 0.263	0.507 / 0.214	0.284 / 0.472
OW relative to brain:	92.986	10.1364	15	113.259 / 72.713	123.396 / 62.577	80.734 / 120.853

PITUITARY

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0151	0.00157	15	0.0182 / 0.0119	0.0198 / 0.0104	0.0118 / 0.0178
OW relative to FBW:	0.003	0.0004	15	0.004 / 0.002	0.004 / 0.002	0.002 / 0.003
OW relative to brain:	0.709	0.0836	15	0.876 / 0.542	0.960 / 0.458	0.527 / 0.844

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

PROSTATE

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.91	0.321	35	1.55 / 0.26	1.87 / 0.0	0.36 / 1.72
OW relative to FBW:	0.160	0.0566	35	0.273 / 0.046	0.330 / 0.0	0.076 / 0.300
OW relative to brain:	42.614	14.9907	35	72.596 / 12.633	87.586 / 0.0	17.094 / 79.263

RIGHT CAUDA EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3111	0.08592	10	0.4829 / 0.1393	0.5688 / 0.0533	0.1078 / 0.3937
OW relative to FBW:	0.053	0.0153	10	0.084 / 0.023	0.099 / 0.007	0.021 / 0.073
OW relative to brain:	14.238	4.0480	10	22.334 / 6.142	26.382 / 2.094	5.037 / 17.986

RIGHT EPIDIDYMIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.68	0.178	10	1.03 / 0.32	1.21 / 0.15	0.23 / 0.85
OW relative to FBW:	0.116	0.0308	10	0.177 / 0.054	0.208 / 0.023	0.044 / 0.146
OW relative to brain:	31.071	8.4075	10	47.886 / 14.256	56.294 / 5.849	10.748 / 41.063

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

RIGHT TESTIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.57	0.489	10	2.55 / 0.59	3.04 / 0.10	0.37 / 1.87
OW relative to FBW:	0.265	0.0810	10	0.428 / 0.103	0.509 / 0.022	0.071 / 0.350
OW relative to brain:	71.933	23.3604	10	118.654 / 25.212	142.014 / 1.852	17.290 / 90.338

SALIVARY GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.8100	0.04690	5	0.9038 / 0.7162	0.9507 / 0.6693	0.7700 / 0.8700
OW relative to FBW:	0.152	0.0077	5	0.168 / 0.137	0.175 / 0.129	0.146 / 0.164
OW relative to brain:	39.097	2.5937	5	44.284 / 33.909	46.878 / 31.316	36.493 / 42.647

SPLEEN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.85	0.139	35	1.12 / 0.57	1.26 / 0.43	0.48 / 1.14
OW relative to FBW:	0.149	0.0219	35	0.193 / 0.105	0.215 / 0.083	0.097 / 0.191
OW relative to brain:	39.924	7.3837	35	54.691 / 25.156	62.075 / 17.773	23.188 / 60.894

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

TESTES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	3.53	0.305	25	4.14 / 2.92	4.45 / 2.61	3.08 / 4.21
OW relative to FBW:	0.634	0.0798	25	0.793 / 0.474	0.873 / 0.394	0.480 / 0.854
OW relative to brain:	168.291	17.1428	25	202.577 / 134.006	219.720 / 116.863	143.925 / 200.498

THYMUS GLAND

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.2689	0.06564	35	0.4002 / 0.1376	0.4658 / 0.0720	0.1109 / 0.3891
OW relative to FBW:	0.047	0.0102	35	0.068 / 0.027	0.078 / 0.016	0.023 / 0.067
OW relative to brain:	12.626	2.9721	35	18.571 / 6.682	21.543 / 3.710	5.041 / 18.268

THYROID GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0285	0.00753	35	0.0436 / 0.0135	0.0511 / 0.0060	0.0134 / 0.0440
OW relative to FBW:	0.005	0.0012	35	0.007 / 0.003	0.009 / 0.001	0.003 / 0.008
OW relative to brain:	1.338	0.3343	35	2.007 / 0.670	2.341 / 0.335	0.713 / 2.085

Sex: M	Study Type: SUBCHRONIC	Number of Studies/Control Groups: 5 / 5
Species: RAT	Age: 23 - 25 Weeks	Range of Study Dates: 04/98 - 01/01
Strain: IGS		Report Type: **ALL DATA**

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17-May-02

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

ADRENAL GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0590	0.01040	35	0.0798 / 0.0382	0.0902 / 0.0278	0.0375 / 0.0815
OW relative to FBW:	0.010	0.0017	35	0.014 / 0.007	0.015 / 0.005	0.006 / 0.015
OW relative to brain:	2.777	0.4866	35	3.750 / 1.803	4.236 / 1.317	1.842 / 3.603

BRAIN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	2.13	0.126	35	2.38 / 1.88	2.51 / 1.75	1.79 / 2.41
OW relative to FBW:	0.377	0.0385	35	0.454 / 0.300	0.493 / 0.262	0.304 / 0.447
OW relative to brain:	NA					

EPIDIDYMIDES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.50	0.090	15	1.68 / 1.32	1.77 / 1.23	1.37 / 1.66
OW relative to FBW:	0.270	0.0301	15	0.330 / 0.210	0.360 / 0.180	0.222 / 0.331
OW relative to brain:	72.986	6.6985	15	86.383 / 59.589	93.082 / 52.891	64.545 / 85.475

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

FINAL BODY WEIGHT

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	569	59.0	35	687 / 451	746 / 392	470 / 718
OW relative to FBW:	NA					
OW relative to brain:	NA					

HEART

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.67	0.193	35	2.05 / 1.28	2.25 / 1.09	1.29 / 2.09
OW relative to FBW:	0.294	0.0284	35	0.351 / 0.237	0.379 / 0.209	0.241 / 0.358
OW relative to brain:	78.451	8.9785	35	96.408 / 60.494	105.387 / 51.515	62.319 / 97.573

KIDNEYS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	3.68	0.460	35	4.60 / 2.76	5.06 / 2.30	2.80 / 5.02
OW relative to FBW:	0.650	0.0803	35	0.810 / 0.489	0.891 / 0.409	0.550 / 0.951
OW relative to brain:	173.056	19.4450	35	211.946 / 134.166	231.391 / 114.721	137.441 / 216.908

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

LEFT CAUDA EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3213	0.08000	10	0.4813 / 0.1613	0.5613 / 0.0812	0.1230 / 0.3950
OW relative to FBW:	0.055	0.0150	10	0.085 / 0.025	0.100 / 0.010	0.024 / 0.072
OW relative to brain:	14.658	3.6129	10	21.884 / 7.432	25.497 / 3.820	5.748 / 19.082

LEFT EPIDIDYMIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.6950	0.15544	10	1.0059 / 0.3841	1.1613 / 0.2287	0.2800 / 0.8400
OW relative to FBW:	0.119	0.0286	10	0.176 / 0.061	0.205 / 0.033	0.054 / 0.159
OW relative to brain:	31.671	6.6972	10	45.066 / 18.277	51.763 / 11.580	13.084 / 35.897

LEFT TESTIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.68	0.487	10	2.66 / 0.71	3.14 / 0.22	0.35 / 2.10
OW relative to FBW:	0.286	0.0873	10	0.461 / 0.112	0.548 / 0.025	0.067 / 0.398
OW relative to brain:	76.790	22.3619	10	121.514 / 32.066	143.876 / 9.704	16.355 / 96.135

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

LIVER

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	15.2	2.15	35	19.5 / 10.9	21.6 / 8.8	11.1 / 20.7
OW relative to FBW:	2.664	0.2026	35	3.069 / 2.258	3.271 / 2.056	2.194 / 2.980
OW relative to brain:	714.336	97.4425	35	909.221 / 519.451	1006.663 / 422.008	534.783 / 907.456

LUNGS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.98	0.223	15	2.43 / 1.54	2.65 / 1.31	1.71 / 2.55
OW relative to FBW:	0.360	0.0488	15	0.458 / 0.263	0.507 / 0.214	0.284 / 0.472
OW relative to brain:	92.986	10.1364	15	113.259 / 72.713	123.396 / 62.577	80.734 / 120.853

PITUITARY

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0151	0.00157	15	0.0182 / 0.0119	0.0198 / 0.0104	0.0118 / 0.0178
OW relative to FBW:	0.003	0.0004	15	0.004 / 0.002	0.004 / 0.002	0.002 / 0.003
OW relative to brain:	0.709	0.0836	15	0.876 / 0.542	0.960 / 0.458	0.527 / 0.844

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

PROSTATE

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.91	0.321	35	1.55 / 0.26	1.87 / 0.0	0.36 / 1.72
OW relative to FBW:	0.160	0.0566	35	0.273 / 0.046	0.330 / 0.0	0.076 / 0.300
OW relative to brain:	42.614	14.9907	35	72.596 / 12.633	87.586 / 0.0	17.094 / 79.263

RIGHT CAUDA EPID

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.3111	0.08592	10	0.4829 / 0.1393	0.5688 / 0.0533	0.1078 / 0.3937
OW relative to FBW:	0.053	0.0153	10	0.084 / 0.023	0.099 / 0.007	0.021 / 0.073
OW relative to brain:	14.238	4.0480	10	22.334 / 6.142	26.382 / 2.094	5.037 / 17.986

RIGHT EPIDIDYMIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.68	0.178	10	1.03 / 0.32	1.21 / 0.15	0.23 / 0.85
OW relative to FBW:	0.116	0.0308	10	0.177 / 0.054	0.208 / 0.023	0.044 / 0.146
OW relative to brain:	31.071	8.4075	10	47.886 / 14.256	56.294 / 5.849	10.748 / 41.063

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

RIGHT TESTIS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.57	0.489	10	2.55 / 0.59	3.04 / 0.10	0.37 / 1.87
OW relative to FBW:	0.265	0.0810	10	0.428 / 0.103	0.509 / 0.022	0.071 / 0.350
OW relative to brain:	71.933	23.3604	10	118.654 / 25.212	142.014 / 1.852	17.290 / 90.338

SALIVARY GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.8100	0.04690	5	0.9038 / 0.7162	0.9507 / 0.6693	0.7700 / 0.8700
OW relative to FBW:	0.152	0.0077	5	0.168 / 0.137	0.175 / 0.129	0.146 / 0.164
OW relative to brain:	39.097	2.5937	5	44.284 / 33.909	46.878 / 31.316	36.493 / 42.647

SPLEEN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.85	0.139	35	1.12 / 0.57	1.26 / 0.43	0.48 / 1.14
OW relative to FBW:	0.149	0.0219	35	0.193 / 0.105	0.215 / 0.083	0.097 / 0.191
OW relative to brain:	39.924	7.3837	35	54.691 / 25.156	62.075 / 17.773	23.188 / 60.894

Sex: M
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

TESTES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	3.53	0.305	25	4.14 / 2.92	4.45 / 2.61	3.08 / 4.21
OW relative to FBW:	0.634	0.0798	25	0.793 / 0.474	0.873 / 0.394	0.480 / 0.854
OW relative to brain:	168.291	17.1428	25	202.577 / 134.006	219.720 / 116.863	143.925 / 200.498

THYMUS GLAND

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.2689	0.06564	35	0.4002 / 0.1376	0.4658 / 0.0720	0.1109 / 0.3891
OW relative to FBW:	0.047	0.0102	35	0.068 / 0.027	0.078 / 0.016	0.023 / 0.067
OW relative to brain:	12.626	2.9721	35	18.571 / 6.682	21.543 / 3.710	5.041 / 18.268

THYROID GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0285	0.00753	35	0.0436 / 0.0135	0.0511 / 0.0060	0.0134 / 0.0440
OW relative to FBW:	0.005	0.0012	35	0.007 / 0.003	0.009 / 0.001	0.003 / 0.008
OW relative to brain:	1.338	0.3343	35	2.007 / 0.670	2.341 / 0.335	0.713 / 2.085

Sex: M	Study Type: SUBCHRONIC	Number of Studies/Control Groups: 5 / 5
Species: RAT	Age: 23 - 25 Weeks	Range of Study Dates: 04/98 - 01/01
Strain: IGS		Report Type: **Excluding +/- 5 S.D.**

Version 1.0
17-May-02

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

ADRENAL GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0651	0.00806	34	0.0812 / 0.0489	0.0893 / 0.0409	0.0495 / 0.0847
OW relative to FBW:	0.023	0.0036	34	0.030 / 0.016	0.034 / 0.012	0.016 / 0.033
OW relative to brain:	3.384	0.4488	34	4.281 / 2.486	4.730 / 2.037	2.619 / 4.425

BRAIN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.93	0.139	34	2.21 / 1.65	2.35 / 1.51	1.33 / 2.10
OW relative to FBW:	0.678	0.0755	34	0.829 / 0.527	0.905 / 0.452	0.473 / 0.849
OW relative to brain:	NA					

FINAL BODY WEIGHT

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	287	30.3	34	348 / 226	378 / 196	232 / 405
OW relative to FBW:	NA					
OW relative to brain:	NA					

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

HEART

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.01	0.096	34	1.20 / 0.81	1.29 / 0.72	0.85 / 1.33
OW relative to FBW:	0.352	0.0277	34	0.407 / 0.296	0.435 / 0.269	0.296 / 0.401
OW relative to brain:	52.373	6.1290	34	64.631 / 40.115	70.760 / 33.986	43.147 / 70.677

KIDNEYS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	2.00	0.229	34	2.45 / 1.54	2.68 / 1.31	1.58 / 2.65
OW relative to FBW:	0.697	0.0686	34	0.835 / 0.560	0.903 / 0.492	0.591 / 0.915
OW relative to brain:	103.666	12.1994	34	128.065 / 79.267	140.264 / 67.068	86.473 / 137.594

LIVER

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	8.2	1.29	34	10.8 / 5.6	12.1 / 4.3	5.9 / 13.2
OW relative to FBW:	2.859	0.2818	34	3.422 / 2.295	3.704 / 2.013	2.379 / 3.384
OW relative to brain:	427.651	73.8827	34	575.416 / 279.886	649.299 / 206.003	299.492 / 670.558

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

LUNGS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.42	0.145	13	1.71 / 1.13	1.86 / 0.98	1.21 / 1.67
OW relative to FBW:	0.511	0.0460	13	0.603 / 0.419	0.649 / 0.373	0.424 / 0.591
OW relative to brain:	72.548	6.2517	13	85.051 / 60.045	91.303 / 53.793	61.421 / 84.343

OVARIES

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.1089	0.02004	10	0.1490 / 0.0689	0.1691 / 0.0488	0.0822 / 0.1369
OW relative to FBW:	0.039	0.0067	10	0.053 / 0.026	0.059 / 0.019	0.030 / 0.049
OW relative to brain:	5.762	1.0953	10	7.953 / 3.572	9.048 / 2.477	3.971 / 7.243

OVARIES/OVIDUCTS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.1144	0.01926	24	0.1529 / 0.0758	0.1721 / 0.0566	0.0862 / 0.1517
OW relative to FBW:	0.040	0.0078	24	0.055 / 0.024	0.063 / 0.016	0.022 / 0.052
OW relative to brain:	5.916	1.0787	24	8.073 / 3.759	9.152 / 2.680	4.124 / 7.647

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

PITUITARY

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0176	0.00372	14	0.0251 / 0.0102	0.0288 / 0.0065	0.0123 / 0.0253
OW relative to FBW:	0.006	0.0015	14	0.009 / 0.003	0.011 / 0.002	0.004 / 0.009
OW relative to brain:	0.903	0.1825	14	1.268 / 0.539	1.451 / 0.356	0.606 / 1.228

SALIVARY GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.5060	0.03578	5	0.5776 / 0.4344	0.6133 / 0.3987	0.4700 / 0.5600
OW relative to FBW:	0.188	0.0374	5	0.263 / 0.114	0.301 / 0.076	0.143 / 0.241
OW relative to brain:	26.852	1.5675	5	29.987 / 23.717	31.554 / 22.149	25.263 / 28.571

SPLEEN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.53	0.072	34	0.68 / 0.39	0.75 / 0.32	0.36 / 0.73
OW relative to FBW:	0.187	0.0279	34	0.243 / 0.131	0.271 / 0.104	0.139 / 0.267
OW relative to brain:	27.756	3.9102	34	35.576 / 19.935	39.486 / 16.025	19.780 / 38.421

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

THYMUS GLAND

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.2177	0.06054	34	0.3388 / 0.0967	0.3993 / 0.0361	0.0876 / 0.3657
OW relative to FBW:	0.076	0.0203	34	0.116 / 0.035	0.137 / 0.015	0.029 / 0.122
OW relative to brain:	11.364	3.3963	34	18.156 / 4.571	21.553 / 1.175	4.635 / 19.248

THYROID GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0220	0.00629	34	0.0345 / 0.0094	0.0408 / 0.0031	0.0120 / 0.0400
OW relative to FBW:	0.008	0.0021	34	0.012 / 0.003	0.014 / 0.001	0.004 / 0.014
OW relative to brain:	1.143	0.3372	34	1.818 / 0.469	2.155 / 0.132	0.635 / 2.032

UTERUS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.73	0.166	19	1.07 / 0.40	1.23 / 0.24	0.51 / 1.03
OW relative to FBW:	0.255	0.0498	19	0.354 / 0.155	0.404 / 0.105	0.171 / 0.352
OW relative to brain:	37.807	8.7846	19	55.376 / 20.238	64.161 / 11.453	26.984 / 53.368

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **ALL DATA**

UTERUS/CERVIX

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.74	0.200	15	1.14 / 0.34	1.34 / 0.14	0.52 / 1.17
OW relative to FBW:	0.263	0.0816	15	0.426 / 0.100	0.507 / 0.018	0.184 / 0.453
OW relative to brain:	38.921	10.2797	15	59.481 / 18.362	69.760 / 8.082	26.341 / 58.794

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

ADRENAL GLANDS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	0.0651	0.00806	34	0.0812 / 0.0489	0.0893 / 0.0409	0.0495 / 0.0847
OW relative to FBW:	0.023	0.0036	34	0.030 / 0.016	0.034 / 0.012	0.016 / 0.033
OW relative to brain:	3.384	0.4488	34	4.281 / 2.486	4.730 / 2.037	2.619 / 4.425

BRAIN

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.93	0.139	34	2.21 / 1.65	2.35 / 1.51	1.33 / 2.10
OW relative to FBW:	0.678	0.0755	34	0.829 / 0.527	0.905 / 0.452	0.473 / 0.849
OW relative to brain:	NA					

FINAL BODY WEIGHT

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	287	30.3	34	348 / 226	378 / 196	232 / 405
OW relative to FBW:	NA					
OW relative to brain:	NA					

Sex: F
Species: RAT
Strain: IGS

Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

HEART

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	1.01	0.096	34	1.20 / 0.81	1.29 / 0.72	0.85 / 1.33
OW relative to FBW:	0.352	0.0277	34	0.407 / 0.296	0.435 / 0.269	0.296 / 0.401
OW relative to brain:	52.373	6.1290	34	64.631 / 40.115	70.760 / 33.986	43.147 / 70.677

KIDNEYS

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	2.00	0.229	34	2.45 / 1.54	2.68 / 1.31	1.58 / 2.65
OW relative to FBW:	0.697	0.0686	34	0.835 / 0.560	0.903 / 0.492	0.591 / 0.915
OW relative to brain:	103.666	12.1994	34	128.065 / 79.267	140.264 / 67.068	86.473 / 137.594

LIVER

	Mean	S.D.	N	Mean +/- 2 S.D.	Mean +/- 3 S.D.	Observed Low/High Value
Absolute OW:	8.2	1.29	34	10.8 / 5.6	12.1 / 4.3	5.9 / 13.2
OW relative to FBW:	2.859	0.2818	34	3.422 / 2.295	3.704 / 2.013	2.379 / 3.384
OW relative to brain:	427.651	73.8827	34	575.416 / 279.886	649.299 / 206.003	299.492 / 670.558

Sex: F
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Study Type: SUBCHRONIC
Age: 23 - 25 Weeks

Number of Studies/Control Groups: 5 / 5
Range of Study Dates: 04/98 - 01/01
Report Type: **Excluding +/- 5 S.D.**

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UTERUS

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OW relative to brain:	37.807	8.7846	19	55.376 / 20.238	64.161 / 11.453	26.984 / 53.368

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Study Type: SUBCHRONIC
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UTERUS/CERVIX

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OW relative to FBW:	0.263	0.0816	15	0.426 / 0.100	0.507 / 0.018	0.184 / 0.453
OW relative to brain:	38.921	10.2797	15	59.481 / 18.362	69.760 / 8.082	26.341 / 58.794

Version 1.0
17-May-02

A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

ATTACHMENT B

Serum Analysis (Wildlife International, Ltd.)

THE ANALYSIS OF HEXABROMOCYCLODODECANE (HBCD-AS SEPARATE ALPHA, BETA, AND GAMMA DIASTEREOMERS) CONCENTRATIONS IN RODENT BLOOD SERUM FROM A 90-DAY ORAL (GAVAGE) TOXICITY STUDY IN RATS

IN SUPPORT OF

WIL RESEARCH LABORATORIES, INC. STUDY NO.: WIL-186012

WILDLIFE INTERNATIONAL, LTD. PROJECT NO.: 439C-135

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

SPONSOR: Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel

TITLE: A 90-Day Oral (Gavage) Toxicity Study of HBCD in Rats

WIL RESEARCH LABORATORIES, INC. STUDY NO.: WIL-186012

WILDLIFE INTERNATIONAL, LTD. PROJECT NO.: 439C-135

ANALYTICAL STUDY COMPLETION: June 7, 2002

The portion of this study performed by Wildlife International, Ltd. was conducted in compliance with Good Laboratory Practice Standards as published by the U.S. Environmental Protection Agency in 40 CFR Part 792, 17 August 1989, and OECD Principles of Good Laboratory Practice [C(97)186/Final] with the following exception:

Characterization of the reference substances and stability under storage conditions at the testing facility were not determined in accordance with Good Laboratory Practice Standards.

PRINCIPAL INVESTIGATOR:

Jon A. MacGregor
Scientist
Wildlife International, Ltd.

6-7-02
DATE

QUALITY ASSURANCE STATEMENT

The portion of this study performed by Wildlife International, Ltd. was examined for compliance with Good Laboratory Practice Standards as published by the U.S. Environmental Protection Agency in 40 CFR Part 792, 17 August 1989, and OECD Principles of Good Laboratory Practice, [C(97)186/Final]. The dates of all inspections and audits and the dates that any findings were reported to the Study Director and Laboratory Management were as follows:

		DATE REPORTED TO:	
ACTIVITY:	DATE CONDUCTED:	STUDY DIRECTOR:	MANAGEMENT:
Matrix Fortification	May 10, 2002	May 22, 2002	May 22, 2002
Raw Data, Draft Report	June 5 to 7, 2002	June 7, 2002	June 7, 2002
Final Report	June 7, 2002	June 7, 2002	June 7, 2002

James H. Coleman
James H. Coleman
Quality Assurance Representative

6-7-02
DATE

REPORT APPROVAL

SPONSOR: Chemical Manufacturers Association's Brominated Flame Retardant Industry Panel

TITLE: A 90-Day Oral (Gavage) Toxicity Study of HBCD in Rats

WIL RESEARCH LABORATORIES, INC. STUDY NO.: WIL-186012

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PRINCIPAL INVESTIGATOR:

Jon A. MacGregor, B.S.
Wildlife International, Ltd.
Scientist

6/7/02
DATE

MANAGEMENT:

Willard B. Nixon, Ph.D.
Wildlife International, Ltd.
Director, Chemistry

6/7/02
DATE

PERSONNEL INVOLVED IN THE STUDY

The following key Wildlife International. Ltd. personnel were involved in the conduct or management of this study:

1. Willard B. Nixon, Ph.D., Director, Chemistry
2. Timothy Z. Kendall, Supervisor
3. Jon A. MacGregor, Scientist
4. Kenneth Chafey, Senior Chemist

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Introduction

Rodent blood serum samples were collected by WIL Research Laboratories, Inc. from the control Group 5 and test Group 6, 90-day oral (gavage) toxicity study to determine concentration of the test article hexabromocyclododecane (HBCD) as individual alpha, beta and gamma diastereomers. The animals from the control Group 5 and test Group 6 were those selected for the fat collection/analysis of HBCD (as the individual diastereomers). Following collection, the serum samples were maintained at approximately-20 °C until shipment for analysis. The blood serum samples collected on Study Days 2, 55, and 89 were shipped by overnight delivery to the Wildlife International, Ltd analytical chemistry facility in Easton, Maryland for analysis using high performance liquid chromatography with mass spectrometry (HPLC/MS). Upon receipt at the analytical facility the samples were logged in and stored in a freezer at approximately –24 °C until analyzed. The study was identified at the analytical facility as Wildlife International, Ltd. Project Number 439C-135. Rodent blood serum samples were received frozen on May 8, 2002 and analyzed between May 10 and May 21, 2002.

Analytical Standards

Separate analytical standards of the alpha, beta and gamma diastereomers of HBCD were received from Albemarle Chemical Corporation on October 30, 2000 and assigned the Wildlife International, Ltd identification numbers of 5417, 5418, and 5419, respectively, upon receipt. The standards were described as white powders and were identified, as: HBCD, Alpha; HBCD, Beta; HBCD, Gamma; CAS number 3194-55-6. The standards had reported purities of 99.4%, 100% and 98.7%, respectively, and were stored under ambient conditions. These analytical standards were used to prepare combined calibration standards and concurrent matrix fortification samples for this study.

Analytical Method

The analytical methodology for the analysis of HBCD in rodent blood serum samples was developed by Wildlife International, Ltd. The method employed an initial volumetric dilution of the blood serum samples with a tetrahydrofuran (THF) : NANOpure® water solution (55:45, v/v). The dilutions were mixed well and an aliquot of each was filtered through a 0.2 µm Acrodisk filter. The filtered solutions were then volumetrically diluted further, if necessary with THF: NANOpure® water (50:50, v/v) . The final diluted solutions were transferred to autosampler vials and submitted for

analysis by LC/MS. A method flow chart for the analysis of HBCD (as alpha, beta and gamma diastereomers) in rodent blood serum is presented in Figure 1.

Concentrations of HBCD (as separate alpha, beta and gamma diastereomers) were determined by high performance liquid chromatography using a Hewlett-Packard Model 1100 High Performance Liquid Chromatograph (HPLC) equipped with a Perkin-Elmer API 100LC Mass Spectrometer and Perkin-Elmer APCI Heated Nebulizer ion source. Chromatographic separations were achieved using a Javelin C-18 guard column (20 mm x 2 mm) attached to a YMC AM C-18 analytical column (150 mm × 4.6 mm, 3-µm particle size). Note: chromatographic difficulties were encountered throughout the analyses as a result of suspected precipitation of the aqueous soluble protein constituents of the serum in the high organic solvent HPLC mobile phase. This precipitate clogged the analytical column end frits and irreversibly bound to the C-18 packing material, resulting in increasingly higher back pressure with each injection and loss of chromatographic resolution and peak shape. Guard columns and in-line filters were used to minimize the effects on the analytical columns. However, several columns were still compromised during the course of these analyses. The typical instrument parameters are summarized in Table 1.

Fortification/Calibration Stocks and Standards

Combined primary stocks of alpha, beta, and gamma HBCD diastereomers were prepared for use in the study by accurately weighing 0.0500 g (corrected for active ingredient) of each of the individual analytical standards and volumetrically dissolving them in tetrahydrofuran (THF) solvent. The primary stock solutions contained 1000 µg a.i. (alpha, beta, or gamma HBCD)/mL. Combined standard working solutions were prepared from the primary stock solution by dilution as appropriate with THF, yielding standard solutions that ranged from 1.00 to 100 µg a.i. (alpha, beta and gamma HBCD)/mL. The combined standards were used to prepare both the concurrent matrix fortification samples and calibration standards using the following dilution schemes:

Combined Standard Working Solutions:

Stock Concentration (µg a.i./mL)	Stock Aliquot (mL)	Final Diluted Volume (mL)	Combined Standard Concentration (µg a.i./mL)	Dilution Solvent
1000	5.00	50.0	100	THF
100	5.00	50.0	10.0	THF
10.0	5.00	50.0	1.00	THF

Combined Calibration Standards:

Combined Stock Concentration (mg a.i./mL)	Stock Aliquot (mL)	Final Diluted Volume (mL)	Combined Standard Concentration (mg a.i./L)	Dilution Solvent
0.0100	0.0500	100	0.00500	50% THF: 50% NANOpure® water
0.0100	0.100	100	0.0100	50% THF: 50% NANOpure® water
0.0100	0.200	100	0.0200	50% THF: 50% NANOpure® water
0.0100	0.300	100	0.0300	50% THF: 50% NANOpure® water
0.0100	0.500	100	0.0500	50% THF: 50% NANOpure® water
0.00500(mg a.i./L)	0.500	5.00	0.000500	50% THF: 50% NANOpure® water (for extended LOQ only)

All stocks and standards were prepared using a combination of Class A volumetric flasks, volumetric pipets, and/or gas tight syringes. Each stock solution was assigned a unique identification code, which was recorded on a stock preparation log sheet.

Calibration Curve and Limits of Quantitation

Combined calibration standards ranging from 0.00500 to 0.0500 mg a.i./ L of alpha, beta, and gamma HBCD diastereomers were prepared for the analysis of the study samples. For each analysis set, a set of calibration standards was injected at the beginning and end of the analytical run. In addition, a minimum of one standard was injected following every five test samples. Sample results not bracketed by the upper limit of the calibration range in each analysis set were diluted and re-analyzed in a separate analytical set or added to the end of each set, concurrently. A calibration curve for each diastereomer was derived from a weighted (1/x) regression analysis using the instrumental responses of each individual component of the combined calibration standards. Separate regression equations for the potential quantitation of each diastereomer were generated using the peak area responses of each individual component versus their respective concentrations in the combined standards. Typical calibration curves for the alpha, beta, and gamma HBCD diastereomers are presented in Figures 2-4, respectively. The concentration of HBCD in the rodent blood serum samples was determined by substituting the peak area responses of each HBCD component into the appropriate weighted (1/x) regression equation as follows:

HBCD in sample (µg a.i./g) = [(peak area – y-intercept)/slope] x (Final volume/Initial mass) x dilution factor

$$\% \text{ Recovery (QCs only)} = \frac{\text{Measured HBCD concentration (µg a.i./g)}}{\text{Nominal HBCD concentration (µg a.i./g)}} \times 100$$

Representative ion chromatograms of low and high combined calibration standards are presented in Figures 5 and 6, respectively.

The method limit of quantitation (LOQ) for the analysis of rodent blood serum samples was originally set at 0.0500 µg a.i./g (same as rodent fat tissue analyses), calculated as the product of the lowest calibration standard (0.00500 mg a.i./L) and the dilution factor of the matrix blank samples (10) analyzed concurrently with each set of test samples. This LOQ was used for the Group 6 (treatment) analyses. However, at the request of the sponsor, the LOQ for the Group 5 (control) samples was extended to 0.00500 µg a.i./g by preparing, analyzing, and adding a 0.000500 mg a.i./L (approximate instrument limit of detection) into the original calibration curve data. The standard was linear in relation to the original calibration curve, thus validating its use to lower the LOQ of the selected Group 5 (control) samples in this data set. By comparing the chromatogram of the extended standard against the control sample chromatograms from the original analysis set data (modified to the same scaling), it is evident that no traces of HBCD diastereomers were present, even at the lower extended LOQ.

Control Matrix and Sample Handling

Rodent blood serum from stock animals (I.D. WIL-186012) received from WIL Research Laboratories, Inc. was used for the preparation of concurrently analyzed quality control samples. The material was received frozen on April 23, 2002, was logged in and stored in a freezer at approximately -80 °C at the analytical testing facility. At the time of each analysis set, the control matrix (alternating male and female) was removed from freezer storage and allowed to thaw to ambient temperature. The matrix was mixed well and an appropriate number of control blood serum aliquots (0.500 g each) were then weighed and fortified as necessary to serve as concurrent matrix fortifications for each analytical sample set. The control matrix was then returned to freezer storage until needed for next analytical sample set.

Definitive rodent blood serum study samples from days 2, 55 and 89 of exposure were received frozen from WIL Research Laboratories, Inc. on May 8, 2002. The samples were logged in and stored in a freezer at approximately –24 °C. The Group 5 (control) samples from days 2, 55, and 89 were analyzed first, followed by the Group 6 (treatment) samples in chronological order. At the time of each analysis set, the study samples for each particular set was logged out of freezer storage, and

allowed to thaw to ambient temperature. The samples were then mixed well to insure homogeneity. Subsequently, approximately 0.500 gram aliquots (nominal) of each study sample were weighed into labeled 5-mL class A volumetric flasks for processing and analysis. Duplicate sample aliquots were weighed for analysis when sample size permitted.

Rodent Blood Serum Matrix Blank and Fortification Samples

Along with the actual rodent blood serum sample analyses, four rodent blood serum matrix blank quality control samples were analyzed to determine possible interferences. No interferences were observed at or above the LOQ during the study (Table 2). A representative ion chromatogram of a rodent blood serum matrix blank sample is presented in Figure 7.

For the preparation of matrix fortification (QC) samples, control rodent blood serum matrix was fortified with alpha, beta, and gamma HBCD using a combined standard solution of HBCD prepared in THF. Quality control samples were prepared and analyzed concurrently with each sample set to determine the analytical method procedural recovery. For all analytical sets, QC samples were prepared at 0.100, 1.00 and 10.0 µg a.i./g of rodent blood serum. The use of male and female control matrix was alternated with each sample set. The procedural recoveries of alpha, beta and gamma HBCD from the male serum matrix ranged from 75.5 to 107% of nominal concentrations (Table 2). The procedural recoveries of alpha, beta and gamma HBCD from the female serum matrix ranged from 80.4 to 105% of nominal concentrations. The overall mean procedural recoveries for alpha, beta, and gamma for the study were 89.3 ± 7.6%, 95.3 ± 9.0%, and 90.3 ± 8.8%, respectively. A representative ion chromatogram of a rodent blood serum matrix fortification is presented in Figure 8.

Example Calculations

The analytical result and percent recovery (as alpha diastereomer) for rodent blood serum quality control sample 439C-135-MMAS-1 (0.100 µg a.i./g nominal concentration), from the Group 5 (control) analytical sample set, were calculated using the following equations:

$$\text{HBCD –alpha in sample (µg a.i./g)} = \frac{(\text{peak area} - \text{y-intercept})}{\text{slope}} \times \text{overall dilution factor}$$

Peak area =3440
Y-intercept = 177.5910

Slope =399738.1875
(Note: Regression = 1/x weighted)
Initial Mass (M_i) = 0.500 g
Primary final volume (V_f) = 5.00 mL
Primary dilution factor (V_f/M_i) = 10.0

$$\text{HBCD –alpha diastereomer in sample (µg a.i./g)} = \frac{(3440 - 177.5910)}{399738.1875} \times 10.0$$

$$\text{HBCD – alpha diastereomer in sample (µg a.i./g)} = 0.0816$$

$$\text{\% Recovery} = \frac{\text{measured HBCD concentration (µg a.i./g)}}{\text{nominal HBCD concentration (µg a.i./g)}} \times 100$$

$$\text{\% Recovery} = \frac{0.0816 \text{ µg a.i./g}}{0.100 \text{ µg a.i./g}} \times 100$$

$$\text{\% Recovery} = 81.6\ \%$$

The above equations and calculations were applied to the analytical data for separate quantitation of the beta and gamma diastereomers of HBCD also.

RESULTS

Rodent Blood Serum Sample Analysis

Rodent blood serum samples (male and female) were collected from Group 5 (control) and Group 6 (1000 mg/kg/day-treatment) on Days 2, 55, and 89 of the study and analyzed for HBCD concentrations (measured as separate alpha, beta, and gamma diastereomers).

Measured concentrations of HBCD (as alpha, beta, and gamma diastereomers) in the Group 5 (control) samples (male and female) collected on the Days 2, 55, and 89 were all less than the extended LOQ of 0.005 µg a.i./g (Table 3). A representative ion chromatogram of a Group 5 (control) rodent blood serum sample on Day 2 at the original and extended LOQ are presented in Figures 9 and 10, respectively. The extended low-level calibration standard at 0.000500 mg a.i./L for direct comparison is presented in Figure 11.

Measured concentrations of HBCD (as alpha, beta and gamma diastereomers) in the Group 6 (1000 mg/kg/day) male rodent blood serum samples collected on Days 2, 55, and 89 ranged from 0.371 to 0.912 µg a.i./g, 0.0228 to 0.109 µg a.i./g, and 0.102 to 0.395 µg a.i./g, respectively (Table 4).

Measured concentrations of HBCD (as alpha, beta and gamma diastereomers) in the Group 6 (1000 mg/kg/day) female rodent blood serum samples collected on Days 2, 55 and 89 ranged from 0.822 to 1.91 µg a.i./g; 0.0548 to 0.123 µg a.i./g; and 0.110 to 0.311 µg a.i./g, respectively (Table 5). Representative ion chromatograms of Group 6 (1000 mg/kg/day) rodent blood serum samples on Day 2 and Day 89 are presented in Figures 12 and 13, respectively. Plots of the days of exposure versus the mean measured HBCD diastereomer concentrations for the male and female rodents are presented in Figure 14 and 15, respectively.

Table 1

Typical HPLC/MS Operational Parameters

INSTRUMENT:	Hewlett-Packard Model 1100 High Performance Liquid Chromatograph with a Perkin-Elmer API 100LC Mass Spectrometer
ION SOURCE:	Perkin-Elmer APCI Heated Nebulizer Operated in Selective Ion Monitoring (SIM) Mode
ANALYTICAL COLUMN:	YMC AM C-18 Column (150 mm × 4.6 mm, 3-µm particle size)
GUARD COLUMN:	Javelin C-18 Guard Column (20 x 2mm) in series with a 0.2 µm fritted in-line pre-filter assembly
OVEN TEMPERATURE:	40 °C
STOP TIME:	12.00 min
FLOW RATE:	0.750 mL/min
MOBILE PHASE:	85% Acetonitrile :15% NANOpure Water® with 0.1% Formic Acid:
INJECTION VOLUME:	100 µL
POST-COLUMN SWITCHING PROGRAM:	Time: 0.00 — Column 1(to waste) Time: 3.00 — Column 2 (to Detector)
HBCD DIASTEREOMER PEAK RETENTION TIMES:	Alpha- ~ 5.9 to ~ 7.0 minutes Beta- ~ 6.4 to ~ 7.6 minutes Gamma- ~ 7.9 to 9.9 minutes
HBCD MONITORED MASS:	640.7 amu

Table 2

Matrix Blanks and Fortifications Analyzed Concurrently During Rodent Blood Serum Sample Analyses

Sample Number (439C-135-)[1]	Concentration of HBCD (µg a.i./g of blood serum)				Percent Recovery[3]		
	Fortified	Measured (alpha[2])	Measured (beta)	Measured (gamma)	alpha	beta	gamma
MMAB-1	0.00	<0.0500	<0.0500	<0.0500	--	--	--
MMAS-1	0.100	0.0816	0.0827	0.0755	81.6	82.7	75.5
MMAS-2	1.00	0.901	0.982	0.930	90.1	98.2	93.0
MMAS-3	10.0	9.63	9.87	8.14	96.3	98.7	81.4
FMAB-2	0.00	<0.0500	<0.0500	<0.0500	--	--	--
FMAS-4	0.100	0.0851	0.0824	0.0822	85.1	82.4	82.2
FMAS-5	1.00	0.804	0.870	0.872	80.4	87.0	87.2
FMAS-6	10.0	6.85[4]	3.58[4]	2.29[4]	68.5[4]	35.8[4]	22.9[4]
MMAB-3	0.00	<0.0500	<0.0500	<0.0500	--	--	--
MMAS-7	0.100	0.0868	0.0860	0.0879	86.8	86.0	87.9
MMAS-8	1.00	0.942	0.984	0.978	94.2	98.4	97.8
MMAS-9	10.0	10.7	10.5	10.6	107	106	106
FMAB-4	0.00	<0.0500	<0.0500	<0.0500	--	--	--
FMAS-10	0.100	0.0882	0.105	0.0893	88.2	105	89.3
FMAS-11	1.00	0.879	1.02	0.991	87.9	102	99.1
FMAS-12	10.0	8.46	10.2	9.34	84.6	102	93.4
				Mean =	89.3%	95.3%	90.3%
				Std. Dev. =	7.6%	9.0%	8.8%
				N =	11	11	11

[1]Prefix M denotes male rodent serum matrix; Prefix F denotes female rodent serum matrix.

[2]The limits of quantitation (LOQ) were calculated as the product of the lowest combined calibration standard concentration and the dilution factor of the matrix blank sample analyzed in each analysis set.

[3]Results were generated using MacQuan, version 1.6 software. Manual calculations may differ slightly.

[4]Outlier, due to unstable fortification stock solution. Measured value not used in statistical calculations. Verification of fortification stock solution used in preparation of QC sample gave results of 64.8, 36.8, and 18.9 percent of nominal for the alpha, beta, and gamma diastereomers of HBCD. Fresh stock solutions prepared for subsequent analyses.

Table 3

Measured Concentrations of Hexabromocyclododecane (HBCD) in Group 5 (Control) Rodent Blood Serum Samples from a 90 Day Oral (Gavage) Test

Nominal Test Concentration (mg/kg/day)	Sample Number (WIL-186012-)	Sampling Time (Day)	Measured Concentration of HBCD[1] (µg a.i./g of blood serum)			Mean/Standard Deviation (µg a.i./g of blood serum)		
			alpha	beta	gamma	alpha	beta	gamma
0.00 (Group 5)	43301-A[2]	2	<0.00500	<0.00500	<0.00500	<0.00500	<0.00500	<0.00500
	43317-A	2	<0.00500	<0.00500	<0.00500	--	--	--
	43408-A	2	<0.00500	<0.00500	<0.00500			
	43415-A	2	<0.00500	<0.00500	<0.00500			
	43337-A	55	<0.00500	<0.00500	<0.00500	<0.00500	<0.00500	<0.00500
	43370-A	55	<0.00500	<0.00500	<0.00500	--	--	--
	43469-A	55	<0.00500	<0.00500	<0.00500			
	43470-A	55	<0.00500	<0.00500	<0.00500			
	43375-A	89	<0.00500	<0.00500	<0.00500	<0.00500	<0.00500	<0.00500
	43387-A	89	<0.00500	<0.00500	<0.00500	--	--	--
	43472-A	89	<0.00500	<0.00500	<0.00500			
	43473-A	89	<0.00500	<0.00500	<0.00500			

[1] The limit of quantitation (LOQ) for the control analyses was calculated as the product of the extended low-level calibration standard (0.000500 mg a.i./L) and the dilution factor of the matrix blank samples (10).
[2] Suffixes of A and B denote duplicate aliquots of same sample, if sample size permitted.

Table 4

Measured Concentrations of Hexabromocyclododecane (HBCD) in Group 6 (1000 mg/kg/day)- Male Rodent Blood Serum Samples from a 90 Day Oral (Gavage) Test

Nominal Test Concentration (mg/kg/day)	Sample Number (WIL-186012-)	Sampling Time (Day)	Measured Concentration of HBCD[1] (µg a.i./g of blood serum)			Mean/Standard Deviation (µg a.i./g of blood serum)		
			alpha	beta	gamma	alpha	beta	gamma
1000 (Group 6)	43286-A	2	0.371	0.0254[3]	0.120	0.427 ±0.0407	0.0370 ±0.0149	0.251 ±0.161
	43286-B	2	0.434	0.0228[3]	0.102			
	43287-A	2	0.432	0.0505	0.395			
	43287-B	2	0.469	0.0492[3]	0.385			
	43352-A	55	0.651	0.0775	0.107	0.563 ±0.187	0.0790 ±0.0200	0.178 ±0.0490
	43352-B	55	0.781	0.106[3]	0.193			
	43343-A	55	0.375	0.0579	0.194			
	43343-B	55	0.444	0.0745[3]	0.219			
	43353-A	89	0.912	0.106	0.305	0.762 ±0.257	0.0929 ±0.0253	0.282 ±0.0552
	43353-B	89	0.909	0.109[3]	0.322			
	43356-A	89	0.465	0.0637	0.219			

[1] The limit of quantitation (LOQ) was calculated as the product of the lowest calibration standard and the dilution factor of the matrix blank samples analyzed with each analysis set.
[2] Suffixes of A and B denote duplicate aliquots of same sample, if sample size permitted.
[3] Reported values extrapolated from calibration curve.

Table 5

Measured Concentrations of Hexabromocyclododecane (HBCD) in Group 6 (1000 mg/kg/day) Female Rodent Blood Serum Samples from a 90 Day Oral (Gavage) Test

Nominal Test Concentration (mg/kg/day)	Sample Number (WIL-186012-)	Sampling Time (Day)	Measured Concentration of HBCD[1] (µg a.i./g of blood serum)			Mean/Standard Deviation (µg a.i./g of blood serum)		
			alpha	beta	gamma	alpha	beta	gamma
1000 (Group 6)	43404-A	2	0.879	0.0548	0.119	0.883 ±0.0547	0.0668 ±0.0124	0.159 ±0.0491
	43404-B	2	0.822	0.0667	0.119			
	43406-A	2	0.876	0.0616	0.180			
	43406-B	2	0.955	0.0839	0.219			
	43482-A	55	1.44	0.119	0.170	1.33 ±0.159	0.118 ±0.00611	0.137 ±0.0304
	43488-A	55	1.15	0.111	0.132			
	43488-B	55	1.41	0.123[3]	0.110[3]			
	43493-A	89	1.78	0.0896	0.226	1.73 ±0.148	0.0932 ±0.00262	0.265 ±0.0431
	43493-B	89	1.91	0.0947	0.230			
	43494-A	89	1.60	0.0955	0.311			
	43494-B	89	1.61	0.0930	0.291			

[1] The limits of quantitation (LOQ) were calculated as the product of the lowest calibration standard and the dilution factor of the matrix blank samples analyzed with each analysis set.

[2] Suffixes of A and B denote duplicate aliquots of same sample, if sample size permitted.

[3] Reported values extrapolated from calibration curve.

Prepare all glassware by successively rinsing with a 5% solution of KOH in methanol(Base), followed by tap water, followed by 10% HCL (Acid), followed by tap water, followed by acetone, followed by THF. Allow glassware to set or remove solvent residues using nitrogen.

Prepare combined HBCD (alpha, beta, gamma diastereomers) calibration standards (0.00500 to 0.0500 mg a.i./L) in THF: NANOpure® water (50:50, v/v) solution using gas tight syringes and class A volumetric flasks.

Remove rodent blood serum control matrix and/or definitive study samples from freezer storage and allow to thaw to room temperature. Mix well to ensure homogeneity.

Weigh 0.500 g. (nominal) of rat blood serum sample and/or control matrix for QCs directly into a tared 5-mL class A volumetric flask. Fortify concurrent matrix fortification samples using appropriate volumes of HBCD stock solutions prepared in tetrahydrofuran (THF) solvent. Swirl to mix. Prepare matrix blank sample the same way, with the exception of the addition of HBCD test substance.

Adjust each sample to 5.0 mL final volume using a solution of THF: NANOpure® water (55:45, v/v) solution. Mix well. Filter sample through a 0.2 µm PTFE Acrodisk into a culture tube. Volumetrically dilute QCs further with THF:NANOpure® water (50:50,v/v) into the range of calibration standards.

Transfer an aliquot of each final filtered sample to an autosampler vial and submit for LC/MS analysis.

OPTIONAL: Following initial screening analysis, volumetrically dilute an aliquot of each initial diluted sample from autosampler vial into the calibration standard range, if necessary, using THF: NANOpure® water (50:50, v/v). Transfer an aliquot of each final re-diluted sample to an autosampler vial and submit for further LC/MS analysis.

Figure 1. Analytical method flow chart for the analysis of hexabromocyclododecane (HBCD) in rodent blood serum.

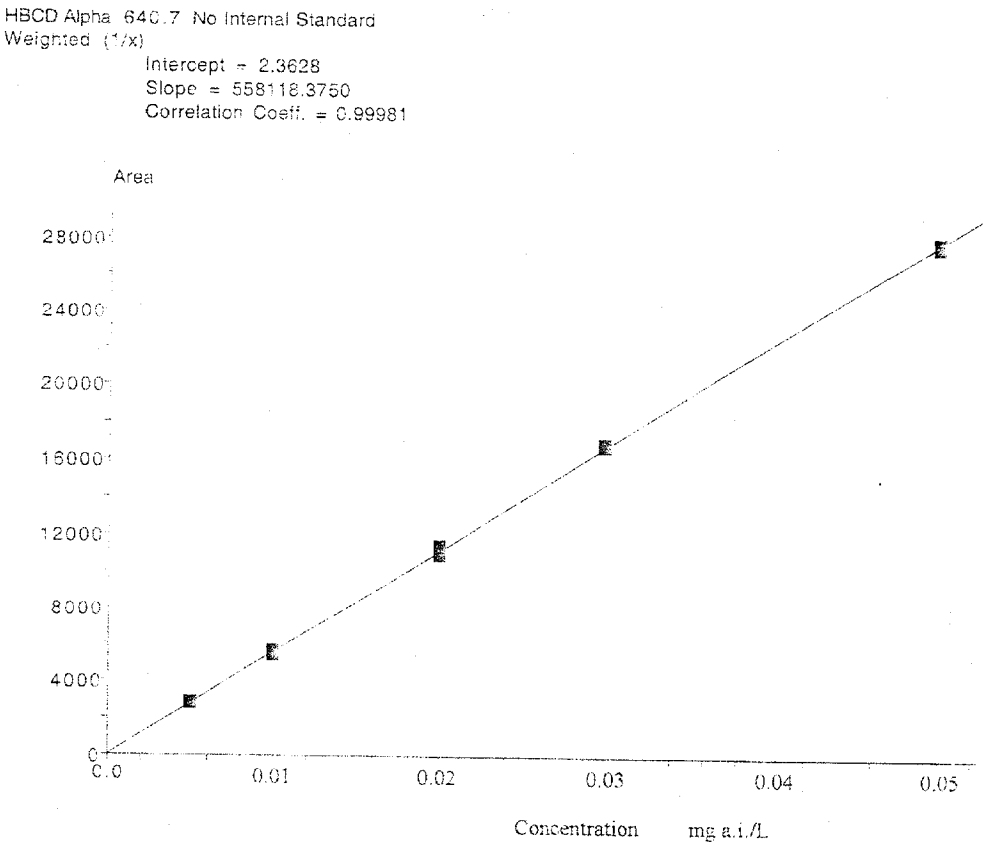


Figure 2. A typical calibration curve for alpha diastereomer of hexabromocyclododecane (HBCD).

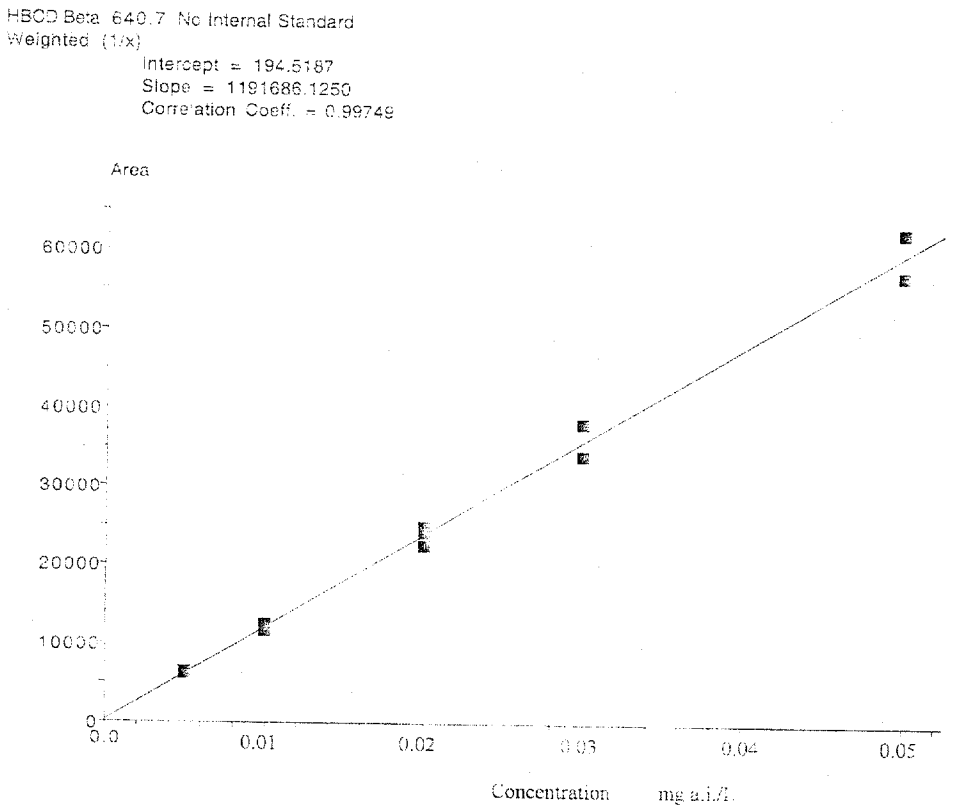


Figure 3. A typical calibration curve for beta diastereomer of hexabromocyclododecane (HBCD).

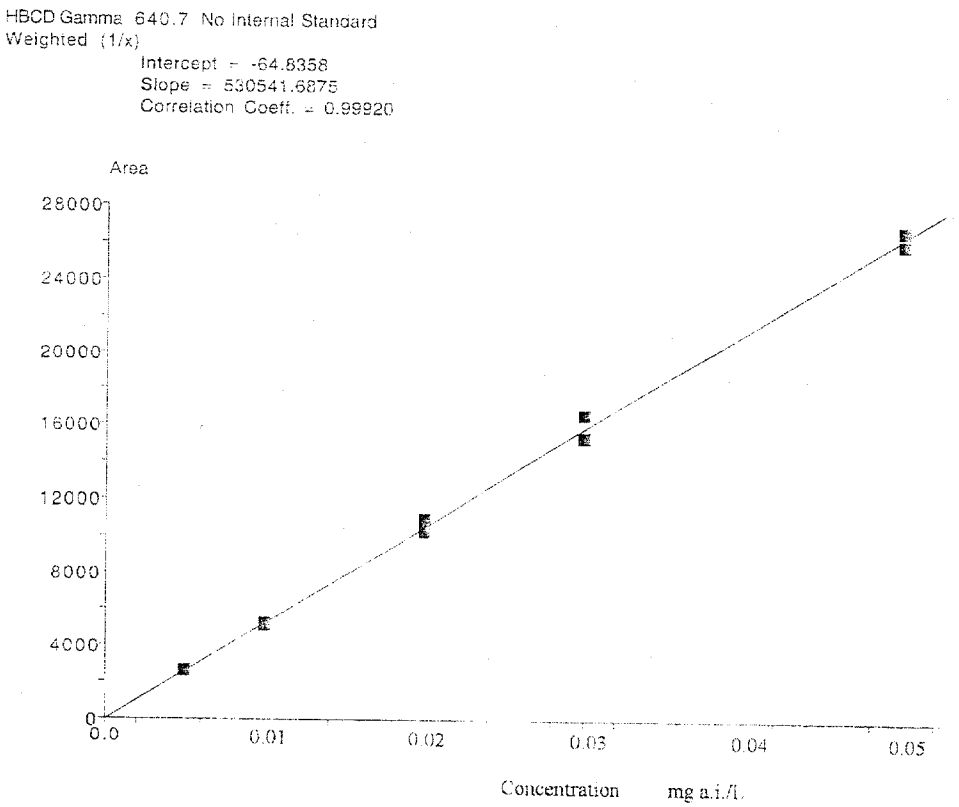


Figure 4. A typical calibration curve for gamma diastereomer of hexabromocyclododecane (HBCD).

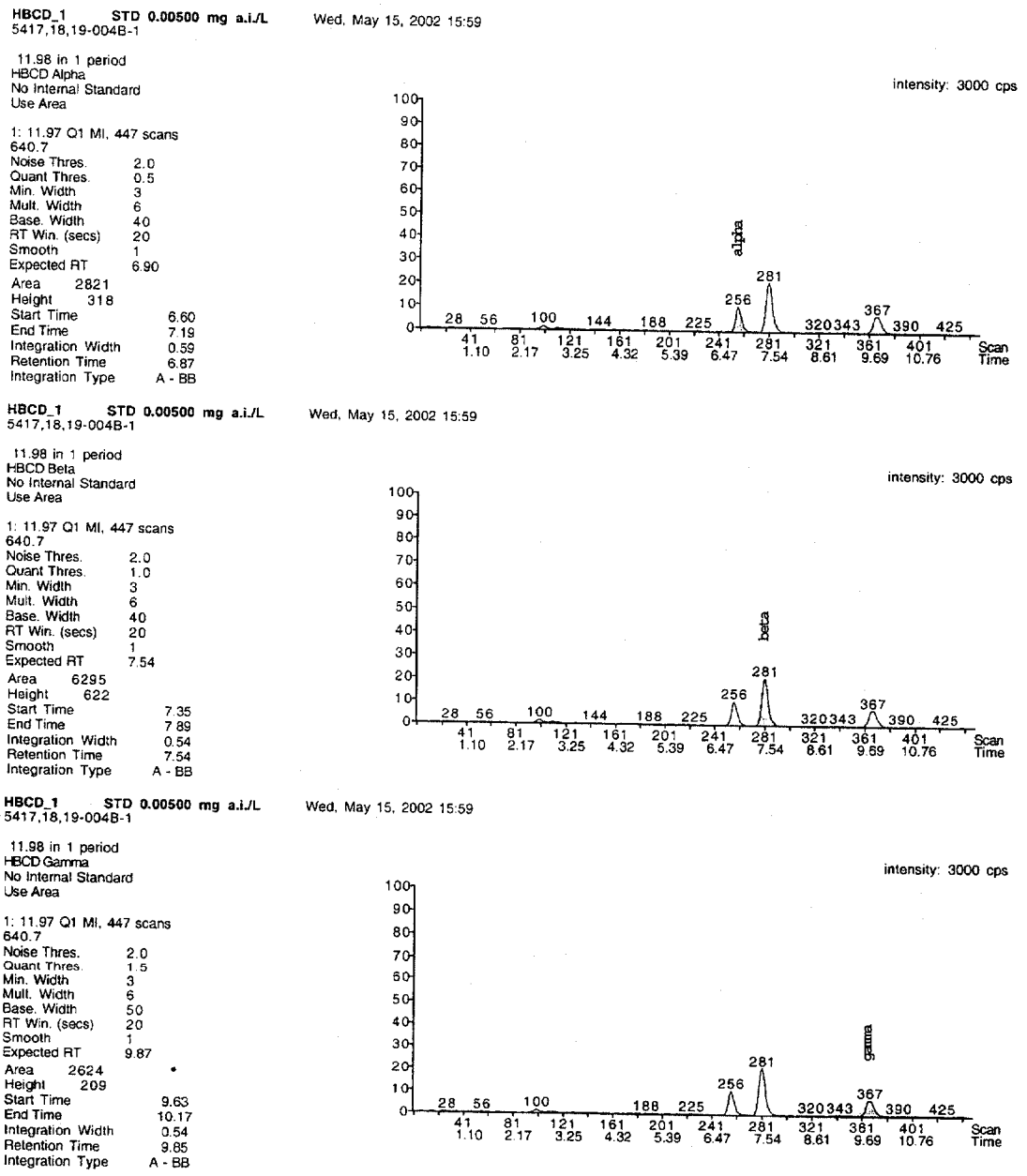


Figure 5. A representative ion chromatogram of a low-level combined alpha, beta, gamma HBCD diastereomer standard (0.00500 mg a.i./L)

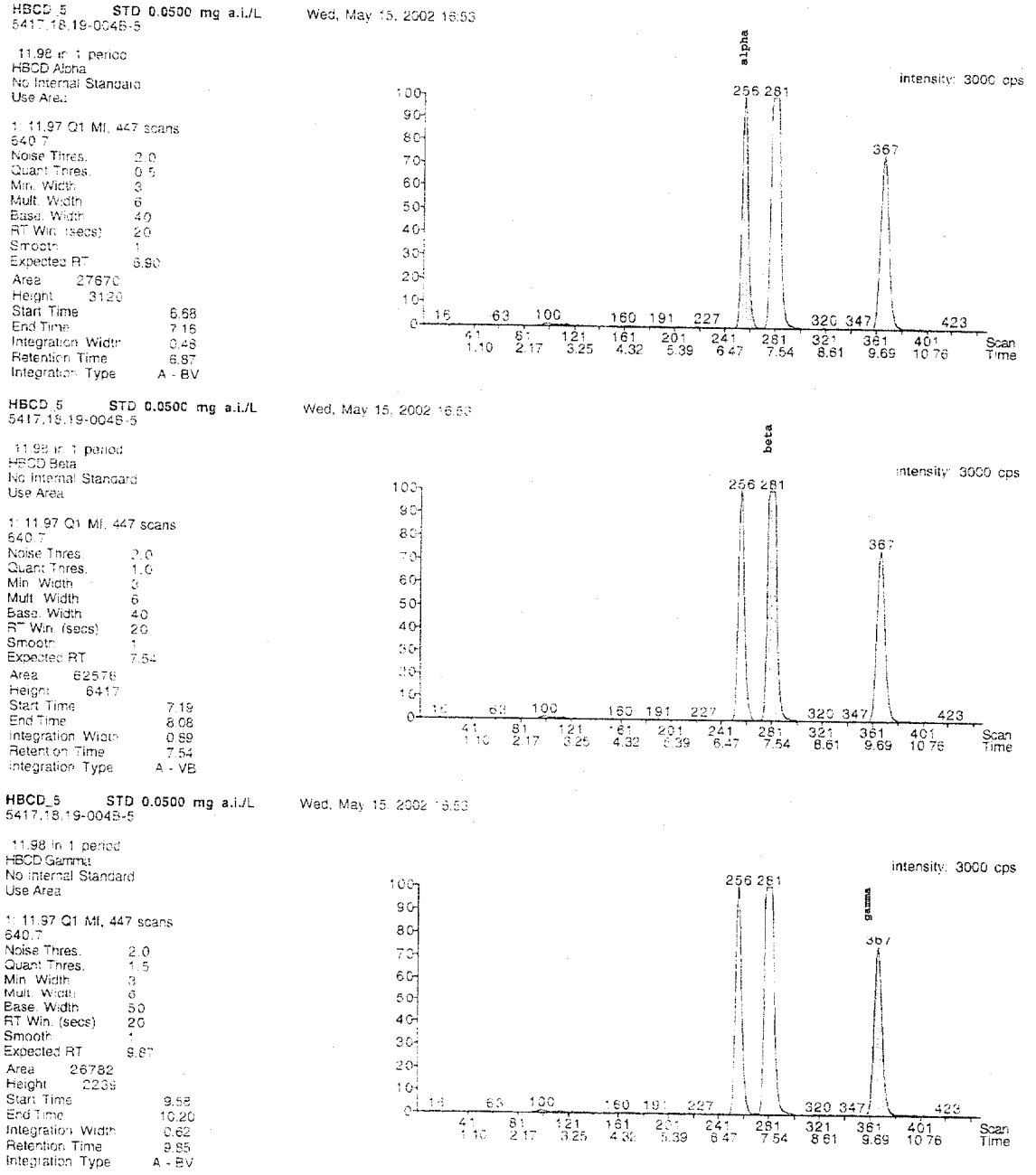


Figure 6. A representative ion chromatogram of a high-level combined alpha, beta, gamma HBCD diastereomer standard (0.0500 mg a.i./L)

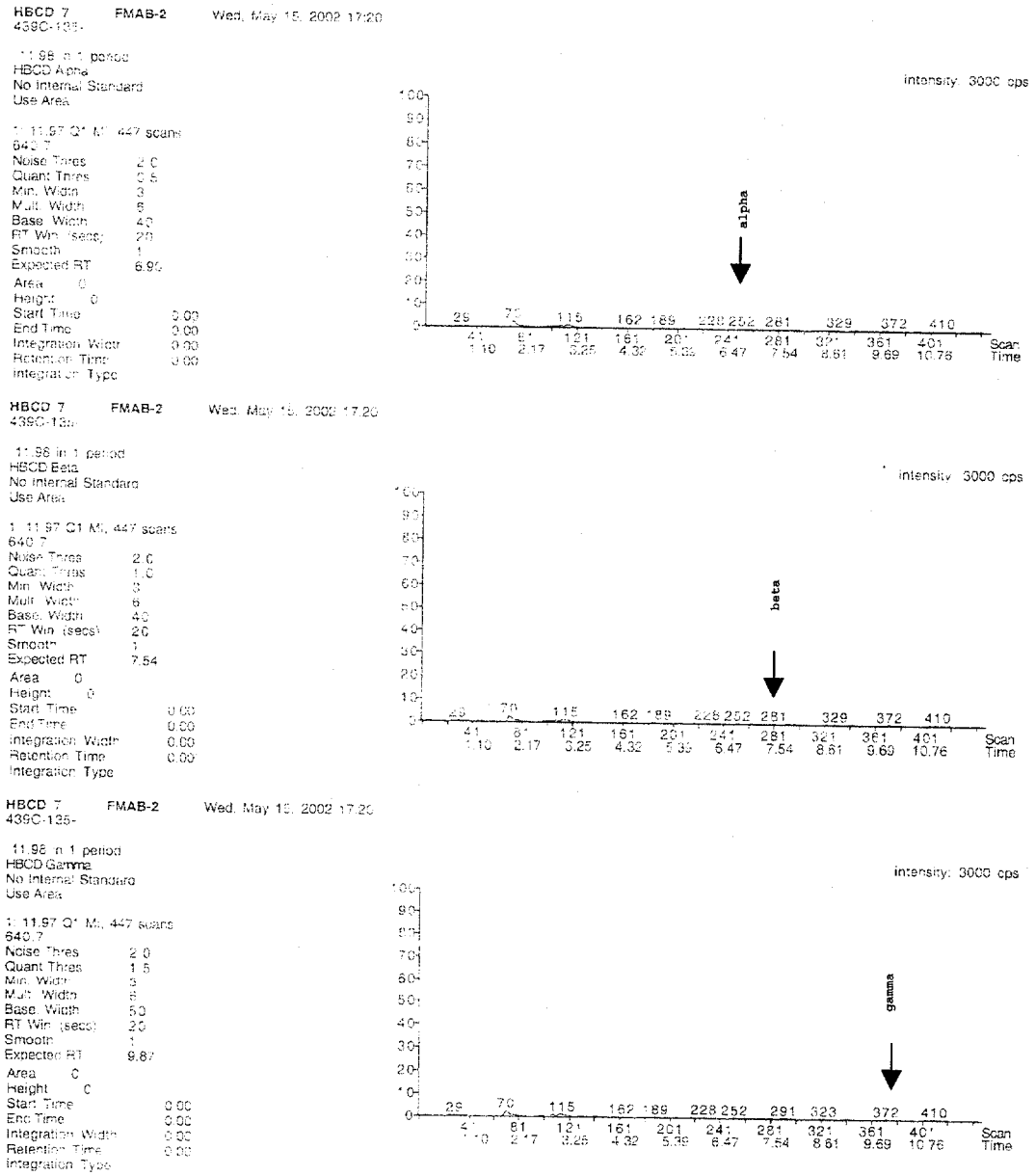


Figure 7. A representative ion chromatogram of a rodent blood serum matrix blank sample (439C-135-FMAB-2). Arrows indicate approximate retention time of alpha, beta, gamma diastereomers of HBCD.

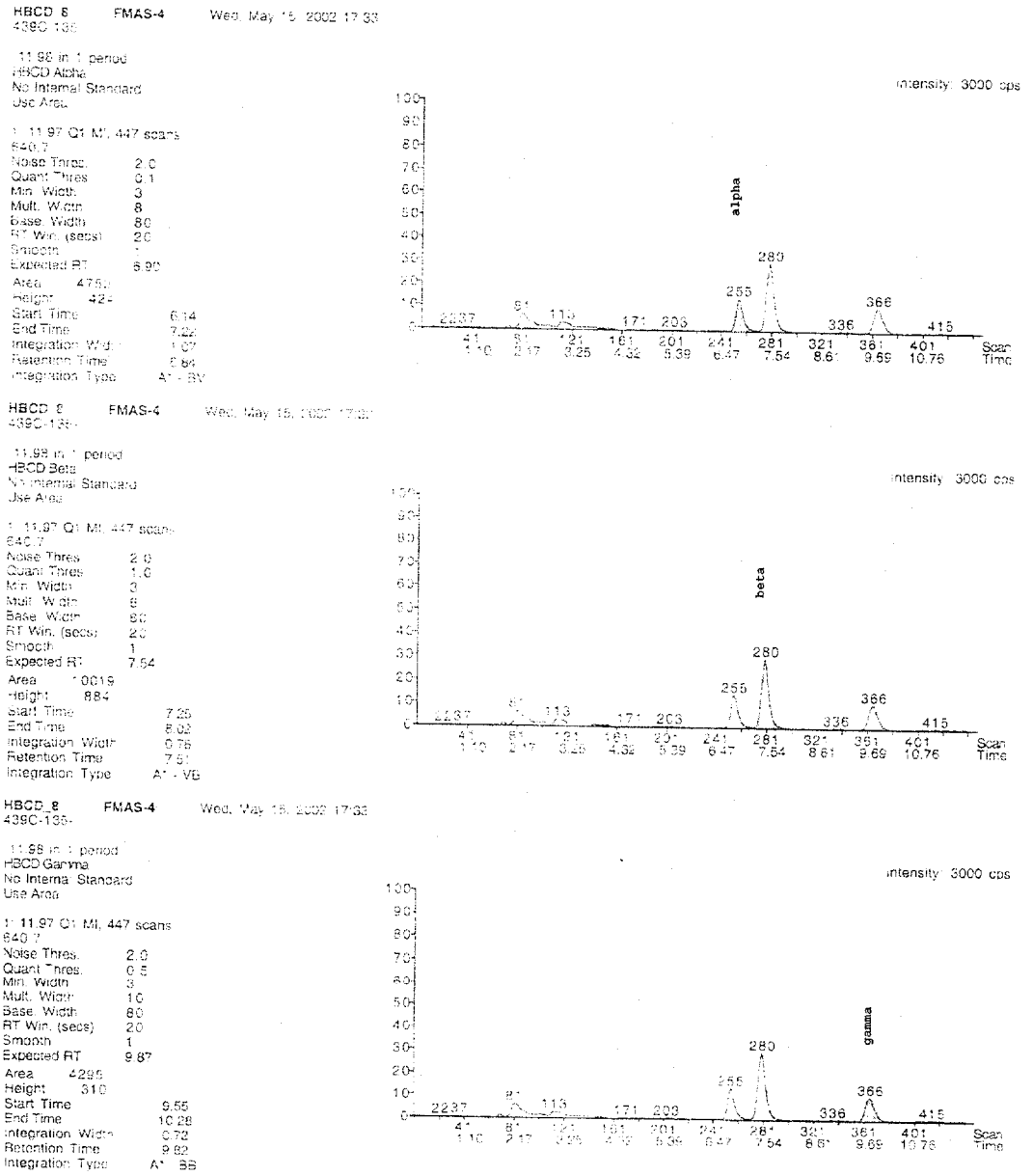


Figure 8. A representative ion chromatogram of a rodent blood serum matrix fortification sample (439C-135-FMAS-4), 0.100 µg alpha, beta, gamma HBCD diastereomer/g nominal concentration

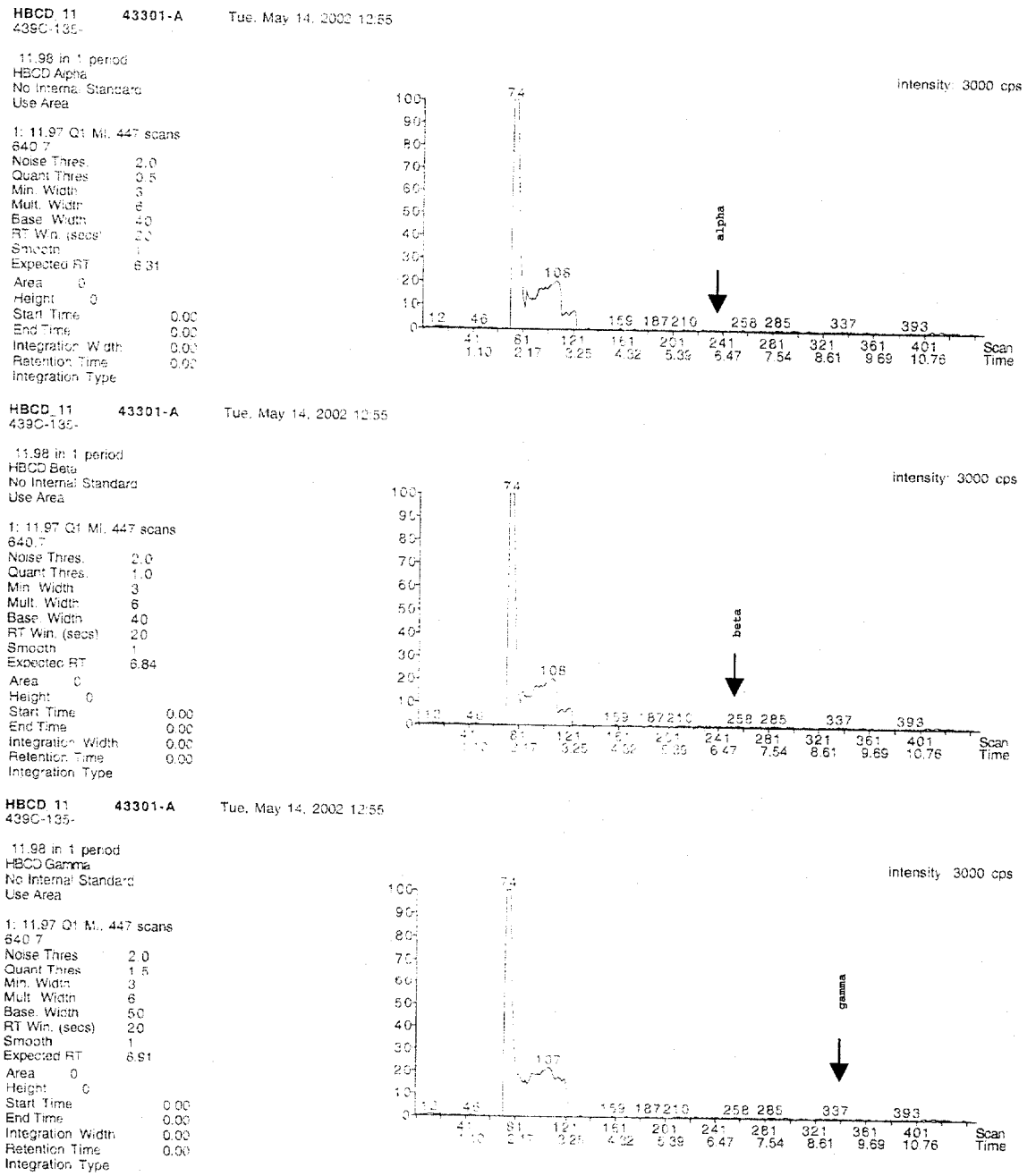


Figure 9. A representative ion chromatogram of a control group rodent blood serum study sample at Day 2 (439C-135-43301-A), 0.00 mg HBCD test substance/kg/day treatment level) displayed at scaling of original LOQ of 0.0500 µg a.i./g. Arrows indicate approximate retention time of alpha, beta, gamma diastereomers of HBCD.

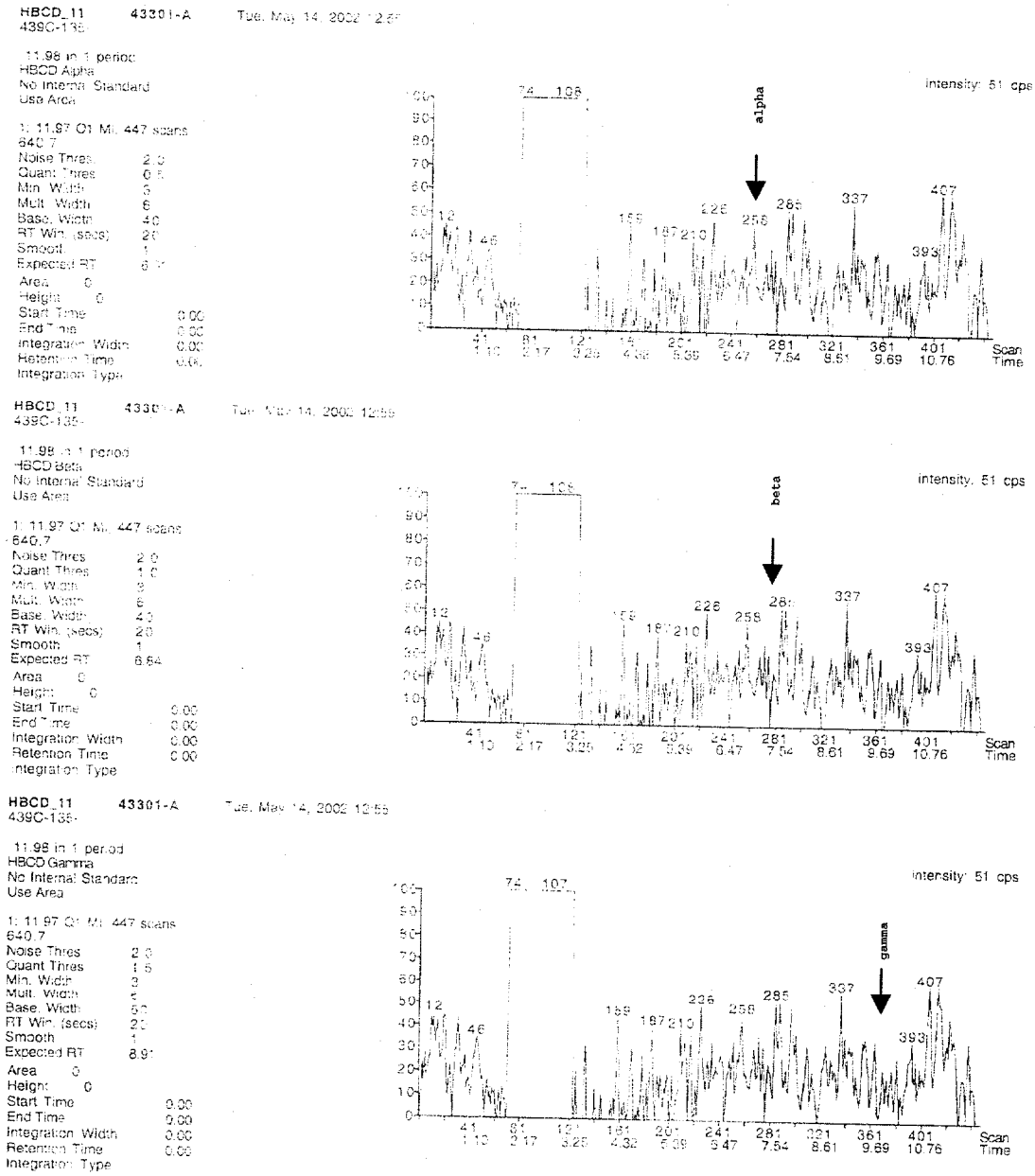


Figure 10. A representative ion chromatogram of a control group rodent blood serum study sample at Day 2 (439C-135-43301-A), 0.00 mg HBCD test substance/kg/day treatment level) displayed at scaling of extended LOQ of 0.00500 µg a.i./g. Arrows indicate approximate retention time of alpha, beta, gamma diastereomers of HBCD.

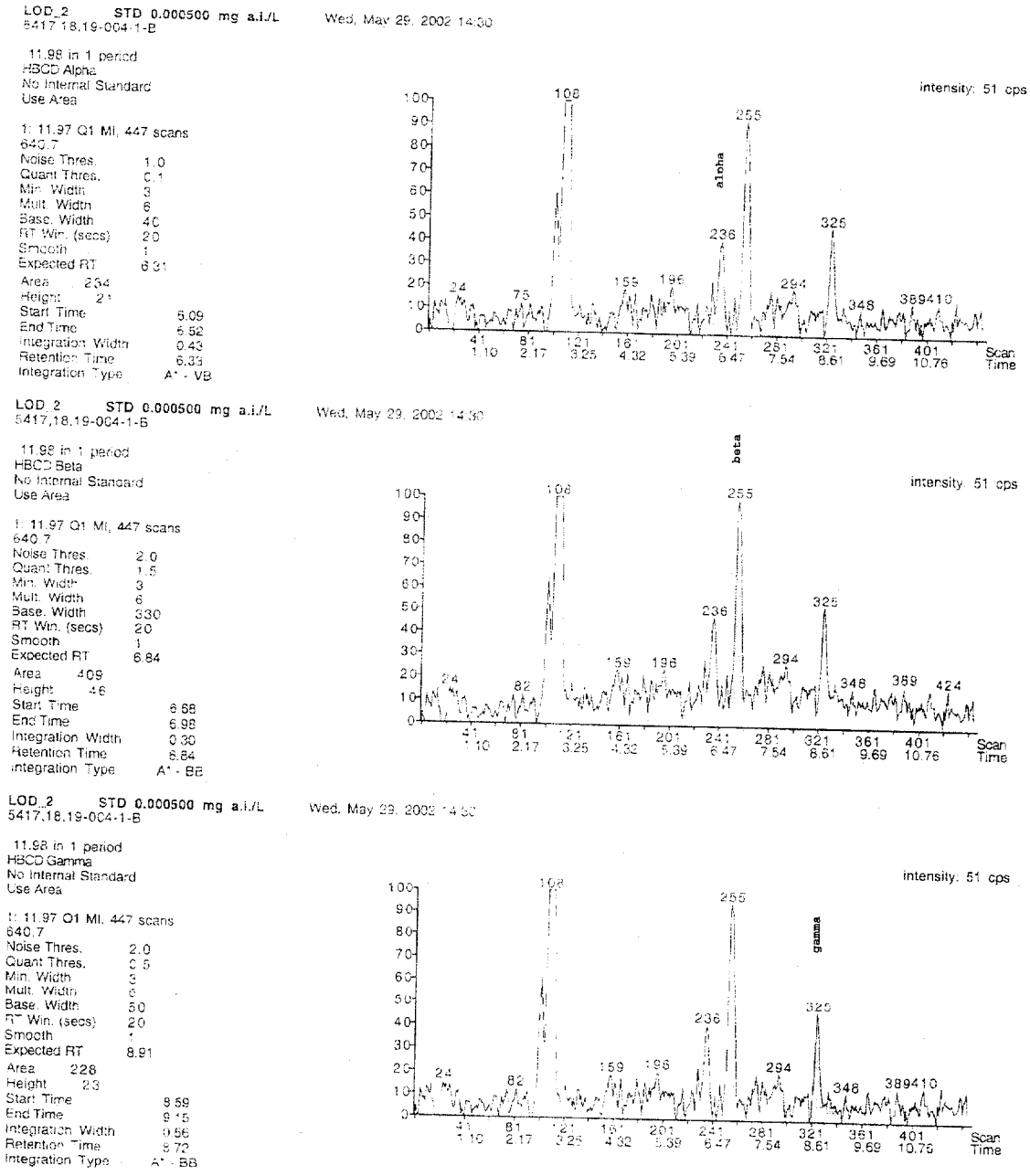


Figure 11. A representative ion chromatogram of a low-level combined alpha, beta, gamma HBCD diastereomer standard (0.000500 mg a.i./L) for the extended LOQ.

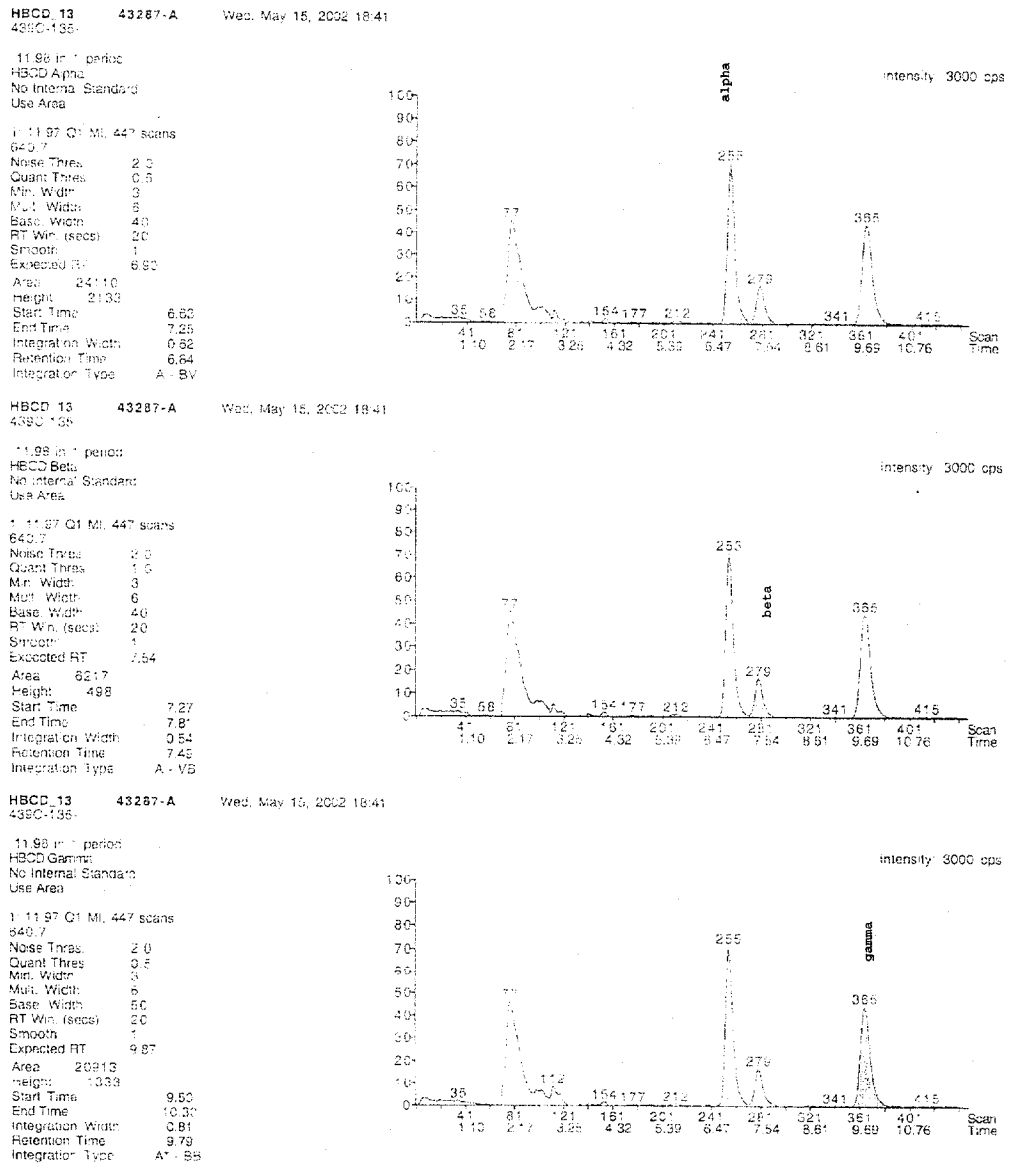


Figure 12. A representative ion chromatogram of a treatment group rodent blood serum study sample at Day 2 (439C-135-43287-A; 1000 mg HBCD test substance/kg/day treatment level).

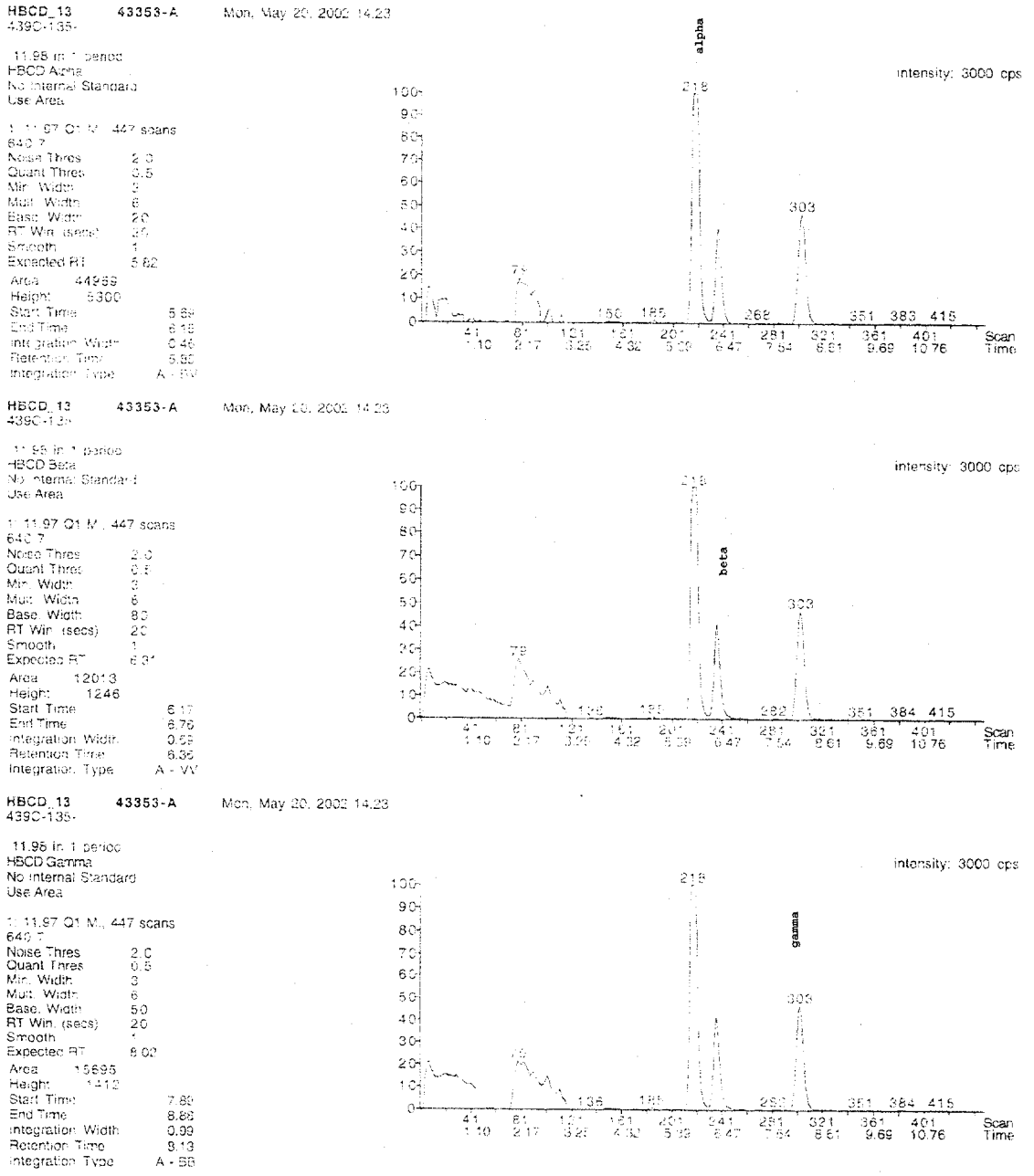


Figure 13. A representative ion chromatogram of a treatment group rodent blood serum study sample at Day 89 (439C-135-43353-A; 1000 mg HBCD test substance/kg/day treatment level)

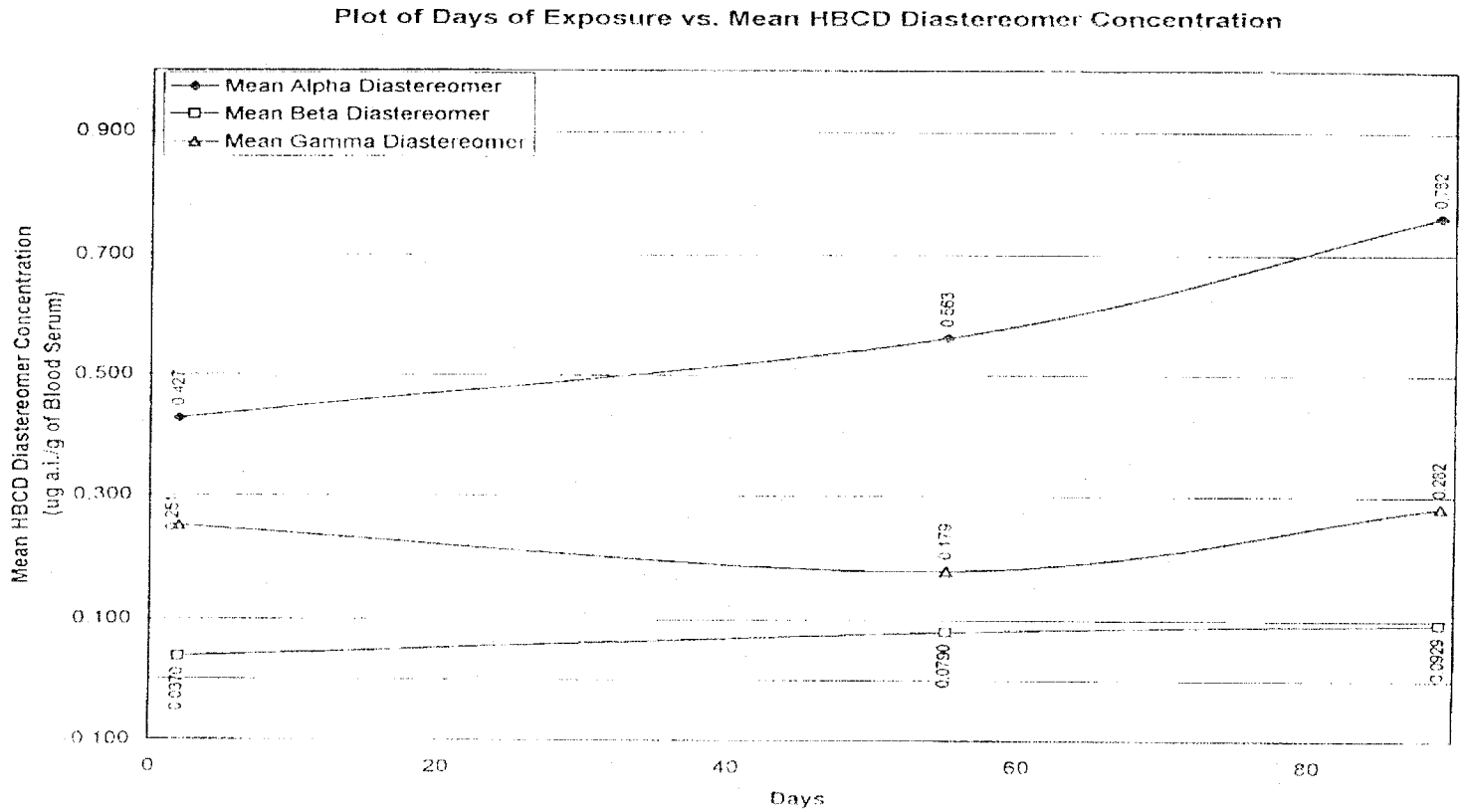


Figure 14. Plot of Days of Exposure vs. Mean Diastereomer Concentration – Male Rodents

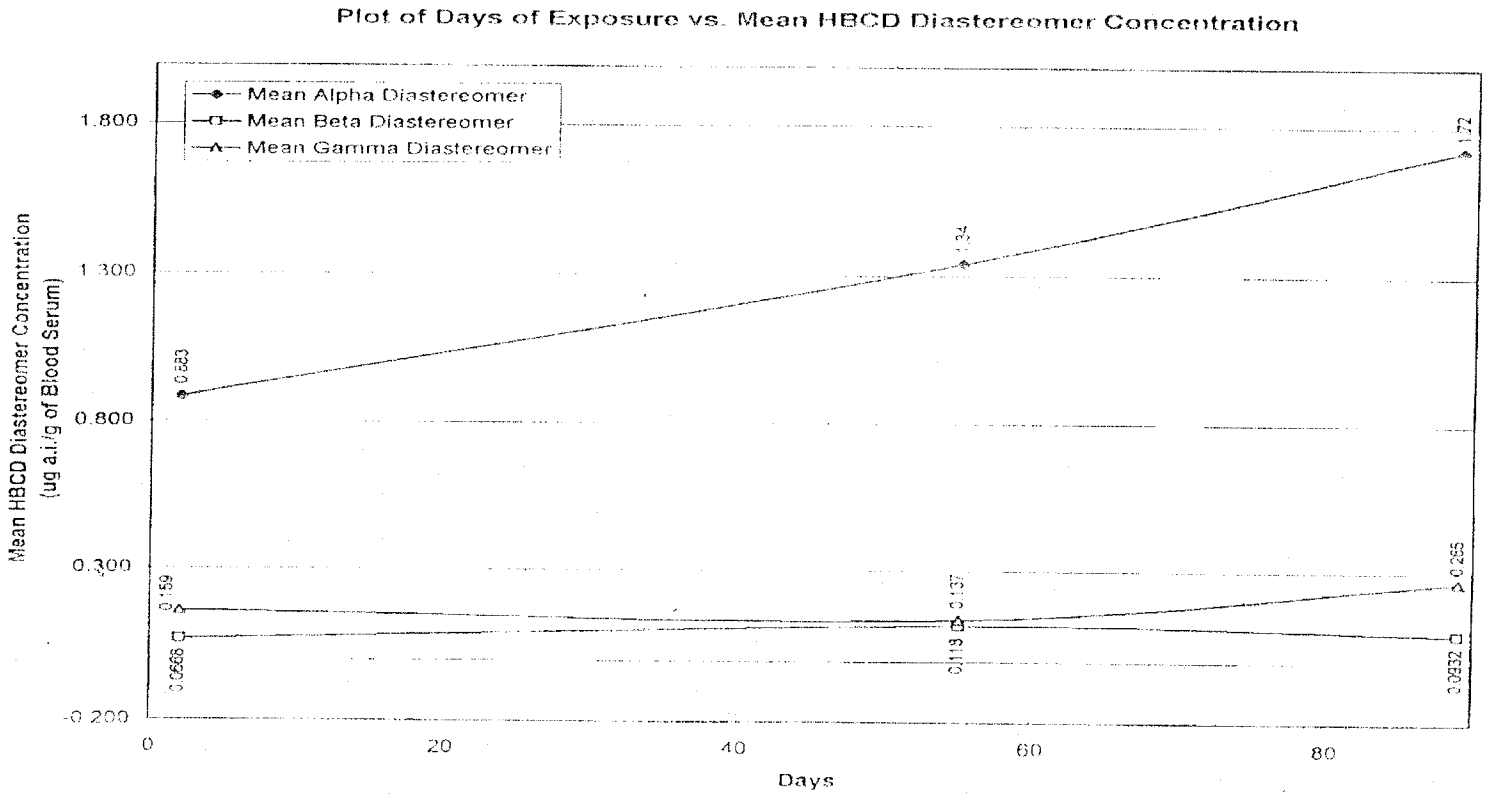


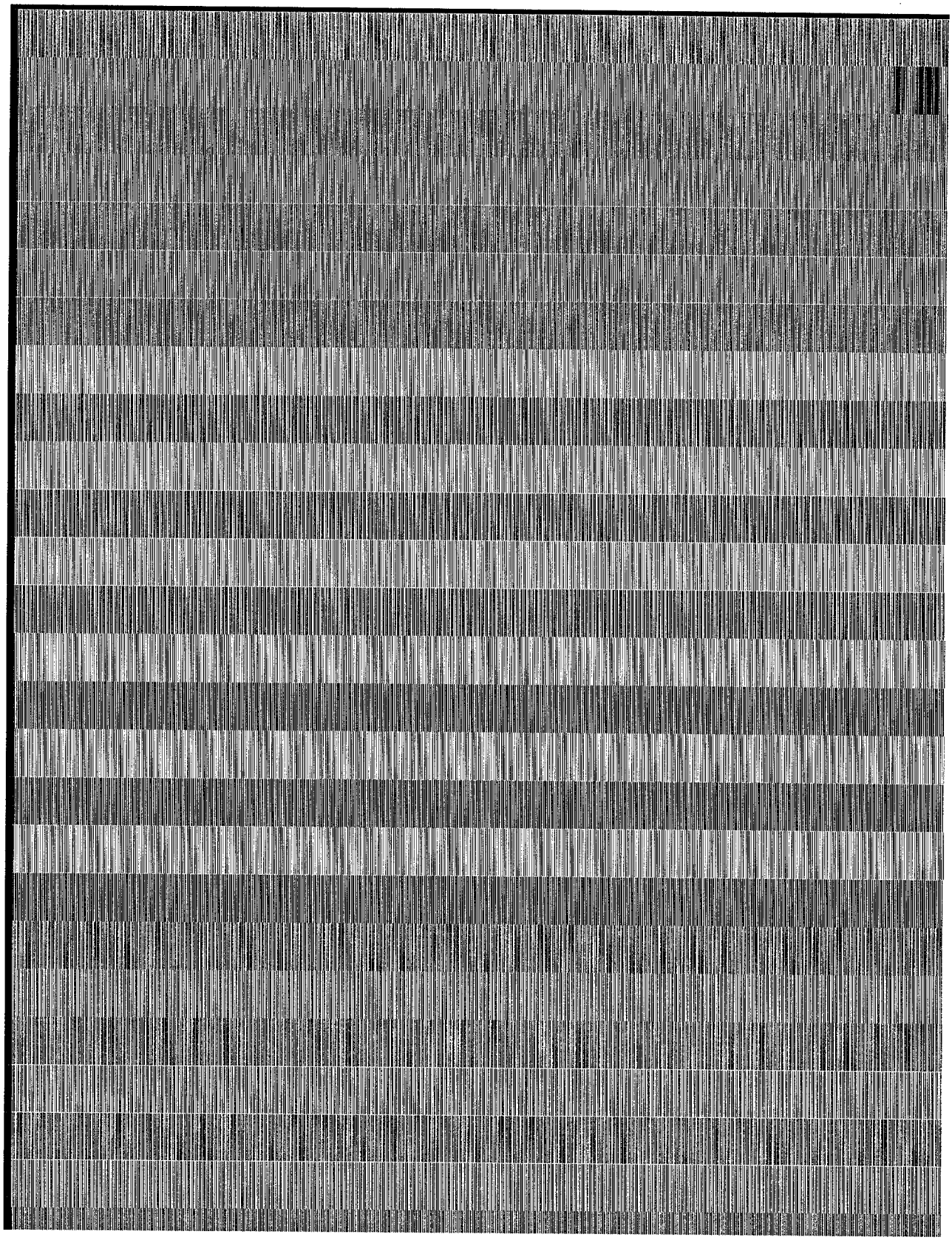
Figure 15. Plot of Days of Exposure vs. Mean Diastereomer Concentration – Female Rodents

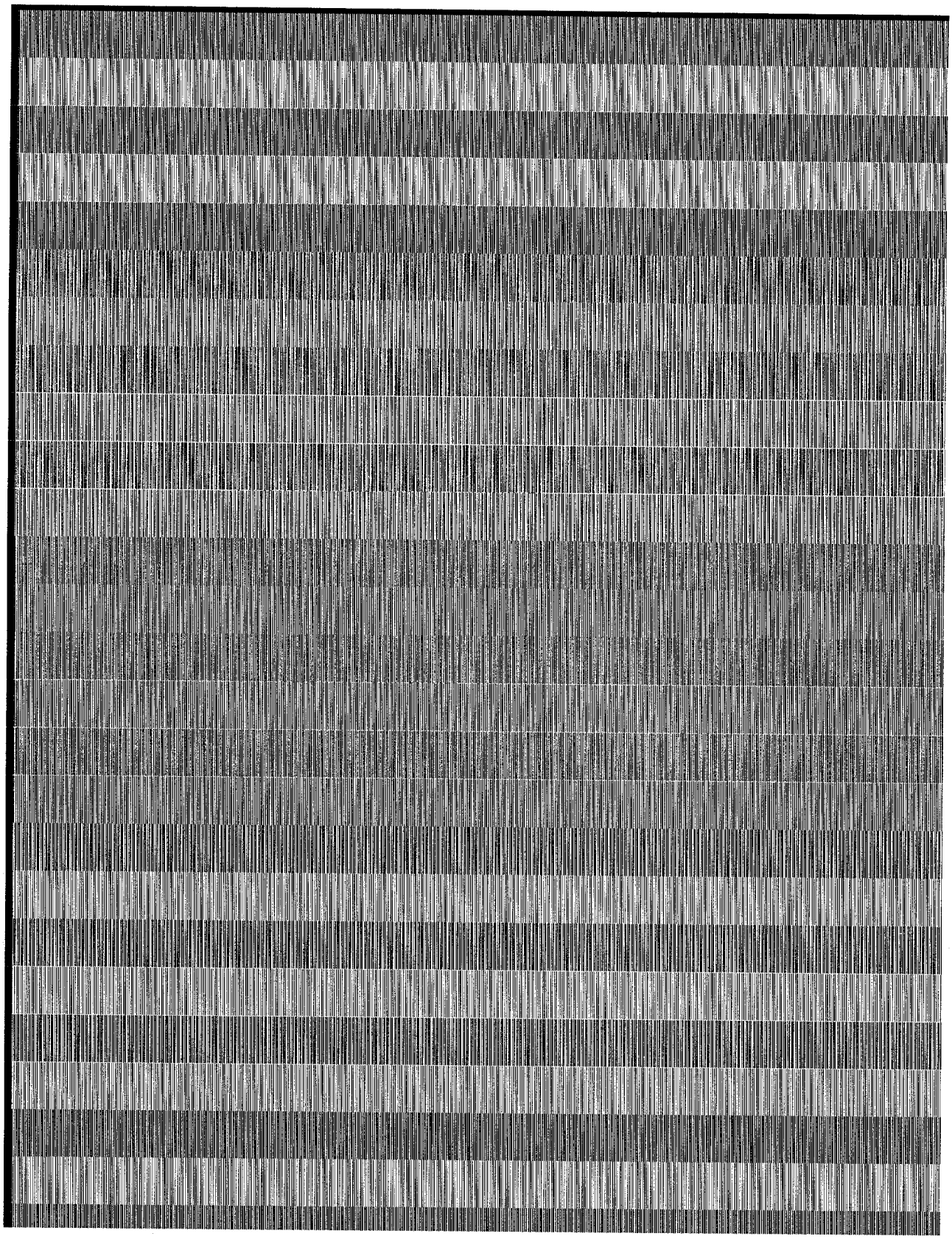
WIL-186012
CMA-BFRIP

A 90-Day Oral (Gavage) Toxicity
Study of HBCD in Rats

ATTACHMENT C

Protocol Amendments V and VI





Study Number: WIL-186012

PROTOCOL AMENDMENT VI

Sponsor: Brominated Flame Retardant Industry Panel
Chemical Manufacturer's Association

A. Title of Study:

A 90-Day Oral (Gavage) Toxicity Study of HBCD in Rats

B. Protocol Modifications:

1) **IX. Statistical Methods:**

For hormonal data (TSH, T4, T3) additional statistical analyses will be conducted. For the purposes of statistical analysis, individual animal data reported as "UR" (under range) in the individual animal data tables will be replaced arbitrarily by "0." This will result in different means and standard deviations than originally reported. These new means can only be considered estimates of the actual means. It was deemed to be more appropriate to analyze these means statistically non-parametrically. These newly configured hormonal data will be analyzed first by the Kruskal-Wallis Test (a non-parametric ANOVA)(2). If the Kruskal-Wallis Test(2) is positive, the treatment groups will be compared to the control group (Group 1) by the Mann-Whitney U-Test(2).

2) **XIII. Reports:**

The revised individual animal and summary hormone data tables, with the new statistical analysis, will be included in a report addendum.

C. Reasons for Protocol Modifications:

1) The amendment provided for a more thorough evaluation of the thyroidal hormone data.

2) This change provides the vehicle for reporting.

Approved By:

Brominated Flame Retardant Industry Panel
Chemical Manufacturer's Association:

Wendy K. Sherman — July 1, 2002
Wendy Sherman — Date
Sponsor Representative

Prepared By:

WIL Research Laboratories, Inc.

Christopher P. Chengelis, Ph.D., D.A.B.T. — 20 June 02
Study Director — Date

TETRABROMOBISPHENOL-A: AN ACTIVATED SLUDGE, RESPIRATION INHIBITION TEST

WILDLIFE INTERNATIONAL, LTD. PROJECT NUMBER: 439E-107A

Organisation for Economic Cooperation and Development
OECD Guideline 209

and

Council of European Communities Directive 67/548/EEC
Annex V, Guideline C.11

AUTHORS:
Edward C. Schaefer
Abul I. Siddiqui

STUDY INITIATION DATE: November 21, 2001

STUDY COMPLETION DATE: March 27, 2002

SUBMITTED TO:

American Chemistry Council's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209

Wildlife International, Ltd.

8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

SPONSOR: American Chemistry Council's Brominated Flame Retardant Industry Panel

TITLE: Tetrabromobisphenol-A: An Activated Sludge, Respiration Inhibition Test

WILDLIFE INTERNATIONAL, LTD. PROJECT NUMBER: 439E-107A

STUDY COMPLETION: March 27, 2002

This study was conducted in compliance with Good Laboratory Practice Standards as published by the U.S. Environmental Protection Agency in EPA 40 CFR Part 160, 17 August 1989; OECD Principles of Good Laboratory Practices (ENV/MC/CHEM (98) 17), and Japan MAFF 59 NohSan, Notification No. 3850, Agricultural Production Bureau, with the following exceptions:

The reference substance, obtained from Aldrich Chemical Company (Milwaukee, WI), was not characterized in compliance with Good Laboratory Practice Standards.

The stability of the reference substance under conditions of storage at the test site was not determined in accordance with Good Laboratory Practice Standards.

The homogeneity and stability of the reference material in the carrier was not determined in accordance with Good Laboratory Practice Standards.

STUDY DIRECTOR:

Edward C. Schaefer
Manager, Biodegradation

27 MARCH 2002
DATE

SPONSOR REPRESENTATIVE:

Ms. Wendy Sherman
American Chemistry Council's
Brominated Flame Retardant Industry Panel

March 25, 2002
DATE

QUALITY ASSURANCE STATEMENT

This study was examined for compliance with Good Laboratory Practice as published by the U.S. Environmental Protection Agency in EPA 40 CFR Part 160, 17 August 1989; OECD Principles of Good Laboratory Practices (ENV/MC/CHEM (98) 17); and Japan MAFF 59 NohSan, Notification No, 3850, Agricultural Production Bureau; Wildlife International, Ltd. Standard Operating Procedures and the study protocol. The dates of all inspections and audits and the dates that any findings were reported to the Study Director and Laboratory Management were as follows:

ACTIVITY:	DATE CONDUCTED:	DATE REPORTED TO: STUDY DIRECTOR:	MANAGEMENT
Initial Trial: 439E-107			
Test Substance Preparation And Test Initiation	December 12, 2001	December 12, 2001	March 22, 2002
D. O. Measurements	December 12, 2001	December 12, 2001	December 14, 2001
Definitive Trial: 439E-107A			
Test Substance Preparation	December 19, 2001	December 19, 2001	March 26, 2002
Data & Draft Report	January 14 &18, 2002	January 18, 2002	January 22, 2002
Final Report	March 26, 2002	March 26, 2002	March 27, 2002

Robert N. McGee, B.S.
Quality Assurance Representative

March 27, 2002
DATE

REPORT APPROVAL

SPONSOR: American Chemistry Council's Brominated Flame Retardant Industry Panel

TITLE: Tetrabromobisphenol-A: An Activated Sludge, Respiration Inhibition Test

WILDLIFE INTERNATIONAL, LTD. PROJECT NUMBER: 439E-107A

STUDY DIRECTOR:

Edward C. Schaefer
Manager, Biodegradation

27 MARCH 2002
DATE

MANAGEMENT:

Henry O. Krueger, Ph.D.
Director, Aquatic Toxicology and Non-Target Plants

27 Mar 02
DATE

STUDY INFORMATION

Study Initiation Date:	November 21, 2001
Experimental Start Date:	December 11, 2001
Experimental Termination Date:	December 19, 2001
Study Completion Date:	March 27, 2002

Study Director:	Edward C. Schaefer
Sponsor:	American Chemistry Council's Brominated Flame Retardant Industry Panel 1300 Wilson Boulevard Arlington, Virginia 22209
Sponsor's Representative:	Ms. Wendy Sherman
Study Personnel:	Edward C. Schaefer, B.S., Manager, Biodegradation Henry O. Krueger, Ph.D., Director, Aquatic Toxicology and Non-Target Plants Abul Siddiqui, B.A., Scientist, Biodegradation

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ABSTRACT

The effect of the test substance on activated sludge microorganisms was assessed by the Activated Sludge Respiration Inhibition Test Method (OECD Guideline 209). The test contained control, reference and treatment groups. The control group was used to determine the background respiration rate of the sludge and was not dosed with the test or reference substance. The reference group was dosed with 3,5-dichlorophenol, a known inhibitor of respiration, at nominal concentrations of 3, 15 and 50 mg/L. The test substance was dosed at a limit concentration of 15 mg/L. After an exposure period of approximately three hours, the respiration rates of the test solutions were measured using a dissolved oxygen meter. The individual respiration rates of the two controls were 15.3 and 17.1 mg O_2/L/hr. The difference between the two control respiration rates was 10.5% and was within the 15% difference limit established for the test. The validity of the test was further supported by the results from the 3,5-dichlorophenol reference group, which resulted in an EC50 of 9.6 mg/L. The EC50 was within the 5 to 30 mg/L range considered acceptable for the test. An average of approximately 1.9 percent inhibition was observed in the treatment group. Following is a summary of the results:

Treatment/Nominal Concentration	Respiration Rate mg O_2/L/hour	Percent Inhibition
Control 1	15.3	NA
Control 2	17.1	NA
3,5-dichlorophenol 3 mg/L	15.3	5.9
3,5-dichlorophenol 15 mg/L	4.9	69.9
3,5-dichlorophenol 50 mg/L	2.4	85.2
Tetrabromobisphenol-A 15 mg/L	15.9	1.9
Tetrabromobisphenol-A 15 mg/L	15.9	1.9
Tetrabromobisphenol-A 15 mg/L	15.9	1.9

NA – Not applicable

INTRODUCTION

The purpose of this test is to provide a screening method to identify substances that may adversely affect aerobic microbial treatment plants and to indicate suitable non-inhibitory test substance concentrations for use in biodegradability tests.

This study was conducted by Wildlife International, Ltd. for the American Chemistry Council's Brominated Flame Retardant Industry Panel at the Wildlife International, Ltd. biodegradation facility in Easton, Maryland. Original raw data generated by Wildlife International, Ltd. and the original final report are filed under Project Number 439E-107A in the archives located on the Wildlife International, Ltd. site.

OBJECTIVE

The objective of this study was to assess the effects of tetrabromobisphenol-A oxide on activated sludge microorganisms by measuring the respiration rate.

EXPERIMENTAL DESIGN

The test contained control, reference, and treatment groups. The control group was used to determine the background respiration rate of the sludge and was not exposed to the test or reference substances. The reference group was dosed with 3,5-dichlorophenol, a known inhibitor of respiration, at nominal concentrations of 3, 15 and 50 mg/L. The test substance was tested at a limit concentration of 15 mg/L, in triplicate.

MATERIALS AND METHODS

This study was conducted according to the procedures outlined in the protocol, "Tetrabromobisphenol A: An Activated Sludge, Respiration Inhibition Test," (Appendix II). The protocol was based on the procedures specified in the OECD Guideline for Testing of Chemicals, Method 209 (1) and Council of the European Communities, Guideline C.11, Activated Sludge, Respiration Inhibition Test (2).

Test Substance

The test substance used in this study was a composite of the following three samples:

Manufacturer:	Bromide Compounds Ltd
Sample ID:	Tetrabromobisphenol-A
Description	Powder
Purity	>99% Tetrabromobisphenol-A
Lot No.:	000135
CAS No:	Not given
Expiration Date:	Not given
Date Received:	August 17, 2000
Wildlife International, Ltd. ID:	5354

Manufacturer:	Great Lakes Chemical Corporation
Sample ID:	Tetrabromobisphenol A
Description	White powder
Purity	Not given
Batch No.:	008JG21C
CAS No:	00079-94-7
Expiration Date:	Not given
Date Received:	July 25, 2000
Wildlife International, Ltd. ID:	5315

Manufacturer:	Albemarle Corporation
Sample ID:	Tetrabromobisphenol-A (TBBPA)
Description	White powder
Purity	Not given
Lot No.:	25938C-1
CAS No:	79-94-7
Expiration Date:	Not given
Date Received:	July 27, 2000
Wildlife International, Ltd. ID:	5318

The composite tetrabromobisphenol-A sample was prepared on September 19, 2000 and was assigned Wildlife International Ltd. identification number 5381. The composite sample was prepared by combining equal parts of the three manufacturers' products and mixing for approximately ten minutes.

The test substance was administered to the treatment group by direct weight addition.

Reference Substance

A stock solution of the reference substance, 3,5-dichlorophenol was prepared by dissolving 500 mg in 10 mL of 1N NaOH and then diluting to 30 mL with NANOpure® water. While stirring, enough 1N H_2SO_4 was added to reach the point of incipient precipitation. The solution of 3,5-dichlorophenol then was diluted to 1 L with NANOpure® water. The reference substance was administered by volumetric addition. Following is a description of the reference substance used in this study.

Name:	3,5-dichlorophenol
Manufacturer:	Aldrich Chemical Co., Milwaukee, WI
Lot Number:	02611ES
Physical Description:	White solid
Handling Precautions:	Standard laboratory precautions
Date Received:	January 24, 2000
Expiration Date:	January 24, 2005
Purity:	99.1%
Storage Conditions:	Ambient
CAS Number:	591-35-5
Wildlife International, Ltd. ID:	5179

Test Conditions and Apparatus

Control, reference, and treatment test mixtures were incubated at 20 ± 2°C and aerated for three hours at a rate sufficient to provide aerobic conditions and maintain solids in suspension. The mixtures were prepared and aerated in 500 mL plastic Erlenmeyer flasks and then transferred into 300 mL biochemical oxygen demand (BOD) bottles to conduct the dissolved oxygen (DO) measurements.

Test Inoculum

Activated sludge was collected from the Denton Wastewater Treatment Plant, Denton, Maryland on December 18, 2001. The Denton facility receives wastes from predominately domestic sources. The sludge was sieved using a 2 mm screen and allowed to settle for approximately 30 minutes. After the settling period, the supernatant was removed and the total suspended solids (TSS) concentration of the settled sludge was determined.

The sludge was maintained in the laboratory for 1 day prior to use. Approximately 50 mL of synthetic sewage (Protocol, Appendix II) was added to each liter of activated sludge and the sludge was continuously aerated. Before use, the pH and total suspended solids concentration of the activated sludge were determined.

Procedure

Test mixtures were prepared at 15 minute intervals starting with the first control. The control contained 9.6 mL of synthetic sewage, 120 mL of inoculum, and enough municipal water to bring the total volume up to 300 mL. The mixture was promptly aerated at a rate sufficient to provide aerobic conditions and keep the solids in suspension. Subsequent mixtures contained 9.6 mL of synthetic sewage, 120 mL of inoculum, the appropriate amount of test substance or reference substance stock solution, and enough municipal water to bring the total volume up to 300 mL. Finally, a second control was prepared. All mixtures were aerated for three hours.

Sample Analysis

After three hours of aeration, the contents of the first vessel were transferred to a BOD bottle and the respiration rate was measured over a period of up to 10 minutes. Dissolved oxygen readings were recorded every 10 seconds for 10 minutes or until the DO dropped below 1.0 mg/L, whichever came first using a YSI Model 50B Dissolved Oxygen Meter. The respiration rate in subsequent vessels was determined in an identical manner at 15 minute intervals so that the contact time of the test substance with the activated sludge was three hours.

Calculations

A respiration rate was calculated for each test mixture and expressed in mg O_2/L/hour. The rate was calculated using DO values between approximately 6.5 mg O_2/L and 2.5 mg O_2/L, or over a 10 minute period if the DO did not reach approximately 2.5 mg O_2/L. The respiration rate was calculated using the following equation:

$$\textit{Respiration Rate} = \textit{(initial DO – final DO)/(final time – initial time)}$$

Percent inhibition was calculated using the following equation:

$$\textit{Percent Inhibition} = 1 - \frac{2R_s}{RC_1 + RC_2} \; X\,100$$

where:

R_s = oxygen consumption rate at a given concentration of the test substance
RC_1 = oxygen consumption rate, Control 1
RC_2 = oxygen consumption rate, Control 2

Statistical Analyses

When the dose response pattern allows for the calculation of an EC50 value, the data are analyzed using the computer program of C.E. Stephan (3). The program was designed to calculate the EC50 value and the 95% confidence interval by probit analysis, the moving average, or binomial probability with nonlinear interpolation (4, 5, 6). The EC50 value for the reference group was calculated using nonlinear interpolation.

RESULTS AND DISCUSSION

The temperature range during the maintenance of the sludge and during the test was 20-22° C. The measured total suspended solids (TSS) concentration and pH of the sludge on the day of testing was 3640 mg/L and 7.8, respectively.

Respiration rates and percent inhibitions are presented in Table 1. The respiration rates in the two controls were 15.3 and 17.1 mg O_2/L/hr. The difference between the two control respiration rates was 10.5% and was within the 15% difference limit established for the test. The validity of the test was

further supported by the results from the 3,5-dichlorophenol reference group, which resulted in an EC50 of 9.6 mg/L. The EC50 was within the 5 to 30 mg/L range considered acceptable for the test.

Minimal inhibitory effects upon respiration were observed at a tetrabromobisphenol-A concentration of 15 mg/L. The average respiration rate for the treatment group was 15.9 ± 0.0 O_2/L/hr and was slightly lower than the average respiration rate of the control (16.2 ± 1.3 mg O_2/L/hr). The average percent inhibition observed was approximately 1.9%.

CONCLUSION

Minimal inhibitory effects upon respiration were observed at a tetrabromobisphenol-A concentration of 15 mg/L. The average percent inhibition observed was approximately 1.9%.

REFERENCES

1. **Organisation for Economic Cooperation and Development.** 1989. *Activated Sludge Respiration Inhibition Test.* OECD Guideline 209.

2. **Council of the European Communities.** Directive 67/548/EEC. Annex V. Guideline C.11, *Activated Sludge Respiration Inhibition Test.*

3. **Stephan, C.E.** 1977. "Methods for Calculating an LC50," *Aquatic Toxicology and Hazard Evaluations.* American Society for Testing and Materials. Publication Number STP 634, pp 65-84.

4. **Finney, D.J.** 1971. *Statistical Methods in Biological Assay,* second edition. Griffin Press, London.

5. **Thompson, W.R.** 1947. *Bacteriological Reviews,* Vol. II, No. 2: 115-145.

6. **Stephan, C.E.** 1977. "Methods for Calculating an LC50," *Aquatic Toxicology and Hazard Evaluations.* American Society for Testing and Materials. Publication Number STP 634, pp 65-84.

Table 1

Respiration Rates and Percent Inhibitions

Treatment/Nominal Concentration	Respiration Rate mg O_2/L/hour	Percent Inhibition
Control 1	15.3	NA
Control 2	17.1	NA
3,5-dichlorophenol 3 mg/L	15.3	5.9
3,5-dichlorophenol 15 mg/L	4.9	69.9
3,5-dichlorophenol 50 mg/L	2.4	85.2
Tetrabromobisphenol-A 15 mg/L	15.9	1.9
Tetrabromobisphenol-A 15 mg/L	15.9	1.9
Tetrabromobisphenol-A 15 mg/L	15.9	1.9

NA – Not applicable.

APPENDIX I

Measured Dissolved Oxygen (DO) Concentrations (mg O_2/L)

Time (min./sec.)	Control 1	Reference			Treatment			Control 2
		3 mg/L	15 mg/L	50 mg/L	Rep A 15 mg/L	Rep B 15 mg/L	Rep C 15 mg/L	
00:10	**8.4**	**8.4**	**8.5**	**9.0**	**8.0**	**8.2**	**8.1**	**8.1**
00:20	8.4	8.4	8.7	9.1	8.0	8.2	8.1	8.1
00:30	8.3	8.3	8.7	9.2	8.0	8.2	8.1	8.0
00:40	8.3	8.3	8.6	9.2	7.9	8.1	8.0	8.0
00:50	8.3	8.2	8.6	9.2	7.9	8.1	8.0	7.9
00:60	8.2	8.2	8.6	9.2	7.9	8.0	7.9	7.9
00:70	8.2	8.2	8.6	9.2	7.8	8.0	7.9	7.9
00.80	8.2	8.1	8.6	9.2	7.8	7.9	7.8	7.8
00.90	8.1	8.1	8.6	9.2	7.7	7.9	7.8	7.8
01.00	8.1	8.1	8.6	9.2	7.7	7.8	7.8	7.7
01:10	8.0	8.0	8.6	9.1	7.6	7.8	7.7	7.7
01:20	8.0	8.0	8.6	9.1	7.6	7.8	7.7	7.6
01:30	8.0	7.9	8.5	9.1	7.6	7.7	7.6	7.6
01:40	7.9	7.9	8.5	9.1	7.5	7.7	7.6	7.5
01:50	7.9	7.9	8.5	9.1	7.5	7.6	7.6	7.5
01:60	7.8	7.8	8.5	9.1	7.4	7.6	7.5	7.4
01:70	7.8	7.8	8.5	9.0	7.4	7.5	7.5	7.4
01:80	7.7	7.7	8.5	9.0	7.3	7.5	7.4	7.4
01:90	7.7	7.7	8.5	9.0	7.3	7.4	7.4	7.3
02:00	7.7	7.6	8.4	9.0	7.2	7.4	7.3	7.3
02:10	7.6	7.6	8.4	9.0	7.2	7.4	7.3	7.2
02:20	7.6	7.6	8.4	9.0	7.2	7.3	7.2	7.2
02:30	7.5	7.5	8.4	9.0	7.1	7.3	7.2	7.1
02:40	7.5	7.5	8.4	9.0	7.1	7.2	7.1	7.1
02:50	7.4	7.4	8.3	9.0	7.0	7.2	7.1	7.0
02:60	7.4	7.4	8.3	9.0	7.0	7.1	7.0	7.0
02:70	7.4	7.4	8.3	9.0	6.9	7.1	7.0	6.9
02:80	7.3	7.3	8.3	9.0	6.9	7.0	7.0	6.9
02:90	7.3	7.3	8.3	9.0	6.8	7.0	6.9	6.8
03:00	7.2	7.2	8.2	8.9	6.8	7.0	6.9	6.8
03:10	7.2	7.2	8.2	8.9	6.8	6.9	6.8	6.7
03:20	7.1	7.2	8.2	8.9	6.7	6.9	6.8	6.7
03:30	7.1	7.1	8.2	8.9	6.7	6.8	6.7	6.6
03:40	7.0	7.1	8.2	8.9	6.6	6.8	6.7	6.6
03:50	7.0	7.0	8.2	8.9	6.6	6.7	6.6	6.5
03:60	6.9	7.0	8.1	8.9	6.6	6.7	6.6	6.5
03:70	6.9	6.9	8.1	8.9	6.5	6.6	6.6	6.4
03:80	6.9	6.9	8.1	8.9	6.5	6.6	6.5	6.4
03:90	6.8	6.8	8.1	8.8	6.4	6.6	6.5	6.3
04:00	6.8	6.8	8.0	8.8	6.4	6.5	6.4	6.3
04:10	6.7	6.8	8.0	8.8	6.3	6.5	6.4	6.2
04:20	6.7	6.7	8.0	8.8	6.3	6.4	6.3	6.2
04.30	6.6	6.7	8.0	8.8	6.2	6.4	6.3	6.1
04.40	6.6	6.6	7.9	8.8	6.2	6.3	6.2	6.1
04:50	6.6	6.6	7.9	8.8	6.1	6.3	6.2	6.1
04:60	6.5	6.5	7.9	8.8	6.1	6.2	6.1	6.0
04:70	6.5	6.5	7.9	8.8	6.1	6.2	6.1	6.0
04:80	6.4	6.4	7.9	8.8	6.0	6.1	6.1	5.9
04:90	6.4	6.4	7.9	8.7	6.0	6.1	6.0	5.9
05:00	6.4	6.4	7.9	8.7	5.9	6.1	6.0	5.8
05:10	6.3	6.3	7.8	8.7	5.9	6.0	5.9	5.8
05:20	6.3	6.3	7.8	8.7	5.8	6.0	5.9	5.7
05:30	6.3	6.2	7.8	8.7	5.8	5.9	5.8	5.7
05:40	6.2	6.2	7.8	8.7	5.7	5.9	5.8	5.6
05:50	6.2	6.1	7.8	8.7	5.7	5.8	5.7	5.6
05:60	6.1	6.1	7.8	8.7	5.6	5.8	5.7	5.5
05:70	6.1	6.1	7.8	8.6	5.6	5.7	5.6	5.5
05:80	6.0	6.0	7.7	8.6	5.5	5.7	5.6	5.4
05:90	6.0	6.0	7.7	8.6	5.5	5.6	5.6	5.4
06:00	**5.9**	**5.9**	**7.7**	**8.6**	**5.4**	**5.6**	**5.5**	**5.3**

Bold numbers indicate dissolved oxygen concentrations used to calculate respiration rates.

APPENDIX II

Protocol

PROTOCOL

TETRABROMOBISPHENOL A: AN ACTIVATED SLUDGE, RESPIRATION INHIBITION TEST

Organization for Economic Cooperation and Development
OECD Guideline 209

and

Council of European Communities Directive 67/548/EEC
Annex V, Guideline C.11

Submitted to

American Chemistry Council's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209

Wildlife International, Ltd.

8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600

November 7, 2001

Wildlife International, Ltd.

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TETRABROMOBISPHENOL A: AN ACTIVATED SLUDGE,
RESPIRATION INHIBITION TEST

SPONSOR:	American Chemistry Council's Brominated Flame Retardant Industry Panel 1300 Wilson Boulevard Arlington, Virginia 22209
SPONSOR'S REPRESENTATIVE:	Ms. Wendy Sherman
TESTING FACILITY:	Wildlife International, Ltd. 8598 Commerce Drive Easton, Maryland 21601
STUDY DIRECTOR:	Edward C. Schaefer
LABORATORY MANAGEMENT:	Henry O. Krueger, Ph.D. Manager of Aquatic Toxicology & Non-Target Plants

FOR LABORATORY USE ONLY

Proposed Dates:

Experimental Start Date: 12/04/01 Experimental Termination Date: 12/10/01

Project No.: 439E-107

Test Concentrations: 15 mg/L

Test Substance No.: 5381 Reference Substance No. (if applicable): 5179

PROTOCOL APPROVAL

STUDY DIRECTOR	DATE 11/21/01
LABORATORY MANAGEMENT	DATE 11/21/01
SPONSOR'S REPRESENTATIVE	DATE 11/16/01

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INTRODUCTION

The purpose of this test is to provide a screening method to identify substances that may adversely affect aerobic microbial treatment plants and to indicate suitable non-inhibitory test substance concentrations for use in biodegradability tests.

OBJECTIVE

The objective of the study will be to assess the effects of the test substance on activated sludge microorganisms by measuring the respiration rate. An EC50 will be calculated, if possible.

EXPERIMENTAL DESIGN

The test will contain control, reference, and treatment groups. The control group is used to determine the background respiration rate of the sludge and will not be exposed to the test substance. The reference group will be dosed with 3,5-dichlorophenol, a known inhibitor of respiration, at concentrations of 3, 15, and 50 mg/l. The test substance will be tested at a limit concentration of 15 mg/l, in triplicate.

MATERIALS AND METHODS

Test methods are based on the procedures specified in the OECD Guideline for Testing of Chemicals, Method 209 (1) and Council of the European Communities, Guideline C.11, Activated Sludge, Respiration Inhibition Test (2).

Test Substance

The test substance consisted of a composite of TBBPA samples received from three manufacturers. The material's identity and date received from each of the manufacturers is given below:

Manufacturer	Lot/Batch	Date Received	Wildlife International Ltd. Identification Number
Great Lakes Chemical Corporation	008JG21C	July 25, 2000	5315
Albemarle Corporation	25938C-1	July 27, 2000	5318
Bromine Compounds, Ltd.	000135	August 17, 2000	5354

The composite test substance was assigned Wildlife International Ltd. identification number 5381 and is being stored under ambient conditions.

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The Sponsor is responsible for all information related to the test substance and agrees to accept any unused test substance and/or test substance containers remaining at the end of the study.

The test substance will be administered by direct weight addition. Direct weight addition is the most appropriate route of administration of insoluble materials.

Stock Solution Preparation

A stock solution of 3,5-dichlorophenol will be prepared by dissolving 500 mg in 10 mL of 1N NaOH and then diluting to 30 mL with NANO™pure water. While stirring, enough 1N H_2SO_4 (approximately 8 mL) will be added to reach the point of incipient precipitation. The solution of 3,5-dichlorophenol then will be diluted to 1 L with NANO™pure water. The reference substance will be administered by volumetric addition.

Test System

The biological test system is a consortium of microorganisms common to the activated sludge treatment process. The organisms responsible for the decomposition of organic materials are principally aerobic, and facultative bacteria. The test system was chosen because it is representative of a treatment process that may receive the test substance.

Test Conditions and Apparatus

Control, reference, and treatment test mixtures will be incubated at 20 ± 2°C and aerated for 3 hours at a rate sufficient to maintain solids in suspension. The mixtures will be prepared and aerated in 500 mL plastic Erlenmeyer flasks and then transferred into a 300 mL Biochemical Oxygen Demand (BOD) bottle to conduct dissolved oxygen (DO) measurements. Test mixtures will be identified by project number, test substance identification and test concentration.

Test Inoculum

Activated sludge from the Denton Wastewater Treatment Plant, Denton, Maryland will be used as the inoculum for the test. The sludge will be sieved using a 2 mm screen and then allowed to settle for approximately 30 minutes. The supernatant above the settled solids will be drained and the total

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suspended solids (TSS) concentration of the settled sludge will be determined. Based on the result, the concentration of the sludge will be adjusted to 4000 mg/L (± 10%) by diluting with Nanopure® water.

If the sludge cannot be used on the day of collection or if the same batch is required to be used on subsequent days (maximum four days), 50 mL of synthetic sewage (Appendix II) will be added to each liter of activated sludge at the end of each working day. The sludge will be aerated overnight at 20 ± 2°C. Before use, the pH and total suspended solids concentration of the activated sludge will be determined and, if necessary, adjusted to pH 6.0 - 8.0 and a solids concentration of 4000 mg/L (± 10%).

Procedure

Test mixtures will be prepared at 15 minute intervals starting with the first control. The control will contain 9.6 mL of synthetic sewage, 120 mL of inoculum and enough municipal water to bring the total volume up to 300 mL. The mixture will be promptly aerated at a rate sufficient to keep the solids in suspension. Subsequent mixtures will contain 9.6 mL of synthetic sewage, 120 mL of inoculum, the appropriate amount of test or reference substance, and enough municipal water to bring the total volume up to 300 mL. Finally, a second control will be prepared. All mixtures will be aerated for three hours.

Sample Analysis

After three hours of aeration, the contents of the first vessel will be transferred to a BOD bottle and the respiration rate will be measured over a period of up to 10 minutes. Dissolved oxygen readings will be recorded every 10 seconds for 10 minutes or until the DO drops below 1.0 mg/L, which ever occurs first, The respiration rate in subsequent vessels will be determined in an identical manner at 15 minute intervals so that the contact time of the test substance with the activated sludge is three hours.

Calculations

A respiration rate will be calculated for each test mixture and expressed in mg O_2/L/hour. The rate will be calculated using DO values between approximately 6.5 mg O_2/L and 2.5 mg O_2/L, or over a 10 minute period if the DO does not reach approximately 2.5 mg O_2/L. The respiration rate will be calculated as follows:

$$\textit{Respiration Rate} = \textit{(initial DO} - \textit{final DO)/(final time} - \textit{initial time)}$$

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The percent inhibition for each test substance concentration will be calculated using the following equation and plotted against concentration on log paper:

$$Percent\ Inhibition = 1 - \frac{2R_s}{RC_1 + RC_2} \ X\ 100$$

where

R_s = oxygen consumption rate at a given concentration of the test substance

RC_1 = oxygen consumption rate, Control 1

RC_2 = oxygen consumption rate, Control 2

An EC50 value will be derived, if possible, based on the percent inhibition versus test substance concentration. Confidence limits (95%) for the EC50 will be determined using standard statistical procedures (3).

Quality Control

The test is considered valid only if the following criteria are met:

- the two control respiration rates are within 15% of each other;
- the EC50 (3 hours) of 3,5-dichlorophenol is in the accepted range of 5 to 30 mg/L.

RECORDS TO BE MAINTAINED

Records to be maintained will include, but not limited to, the following:

1. A copy of the signed protocol.
2. Identification and characterization of the test substance as provided by Sponsor.
3. Test initiation and termination dates.
4. Experimental initiation and termination dates.
5. Stock solution concentration calculations and solution preparation.
6. Activated sludge source and pretreatment details.
7. Test temperature and duration.
8. Reference substance results.

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9. All dissolved oxygen measurements.
10. Temperature range recorded during test period.
11. Inhibition curve and method for calculation of EC50.
12. If calculated, EC50 and 95% confidence limits.
13. A copy of the final report.

FINAL REPORT

A final report of the results of the study will be prepared by Wildlife International, Ltd. The report is to include, but is not limited to, the following when applicable:

1. Name and address of facility performing the study.
2. Dates on which the study was initiated and completed.
3. A statement of compliance signed by the Study Director addressing any exceptions to Good Laboratory Practice Standards.
4. Objectives and procedures stated in the approved protocol, including any changes in the original protocol.
5. Identification and characterization of the test substance as provided by Sponsor including name, CAS number, percent active, and other characteristics, if provided by the Sponsor.
6. A description of the transformations and calculations performed on the data.
7. A description of the methods used and reference to any standard method employed.
8. A description of the test system.
9. A description of the preparation of the test solutions, the testing concentration(s), the route of administration, and the duration of the test.
10. A description of all circumstances that may of affected the quality or integrity of the data.
11. The name of the study director, the names of other scientists or professionals, and the names of all supervisory personnel, involved in the study.
12. The signed and dated reports of each of the individual scientists or other professionals involved in the study, if applicable.
13. The location where the raw data and final report are to be stored.
14. A statement prepared by the Quality Assurance Unit listing the dates that the study inspections and audits were made and the dates of any findings were reported to the Study Director and Management.

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15. If it is necessary to make corrections or additions to a final report after it has been accepted, such changes will be made in the form of an amendment issued by the Study Director. The amendment will clearly identify the part of the final report that is being amended and the reasons for the amendment, and will be signed by the Study Director.
16. A copy of the signed protocol and amendments.

CHANGING OF PROTOCOL

Planned changes to the protocol will be in the form of written amendments signed by the Study Director and the Sponsor's Representative. Amendments will be considered as part of the protocol and will be attached to the final protocol. Any other changes will be in the form of written deviations signed by the Study Director and filed with the raw data. All changes to the protocol will be indicated in the final report.

GOOD LABORATORY PRACTICES

This study will be conducted in accordance with Good Laboratory Practice Standards for EPA (40 CFR Part 160); OECD Principles of Good Laboratory Practices (ENV/MC/CHEM (98) 17); and Japan MAFF (59 NohSan, Notification No. 3850, Agricultural Production Bureau). Each study conducted by Wildlife International, Ltd. is routinely examined by the Wildlife International, Ltd. Quality Assurance Unit for compliance with Good Laboratory Practices, Standard Operating Procedures and the specified protocol. A statement of compliance with Good Laboratory Practices will be prepared for all portions of the study conducted by Wildlife International, Ltd. Raw data for all work performed at Wildlife International, Ltd. and a copy of the final report will be filed by project number in archives located on the Wildlife International, Ltd. site, or at an alternative location to be specified in the final report.

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REFERENCES

1 **Organisation for Economic Cooperation and Development.** 1989. *Activated Sludge Respiration Inhibition Test.* OECD Guideline 209.

2 **Council of the European Communities.** Directive 67/548/EEC. Annex V. Guideline C.11, *Activated Sludge Respiration Inhibition Test.*

3 **Stephan, C.E.** 1977. "Methods for Calculating an LC50," *Aquatic Toxicology and Hazard Evaluations.* American Society for Testing and Materials. Publication Number STP 634, pp 65-84.

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APPENDIX I

IDENTIFICATION OF TEST SUBSTANCE BY SPONSOR

To be Completed by Sponsor

I. Test Substance Identity (name to be used in the report): Tetrabromobisphenol-A

Reference Standard (if applicable): N/A

Test Substance Sample Code or Batch Number: Wildlife International, Ltd. No. 5381

Test Substance Purity (% Active Ingredient): 98.91% Expiration Date: August 1, 2002

II. Test Substance Characterization

Have the identity, strength, purity and composition or other characteristics which appropriately define the test substance and reference standard been determined prior to its use in this study in accordance with GLP Standards? X Yes ___ No

III. Test Substance Storage Conditions

Please indicate the recommended storage conditions at Wildlife International, Ltd..

Ambient temperature; protect from light and moisture

Has the stability of the test substance under these storage conditions been determined in accordance with GLP Standards? X Yes ___ No

Other pertinent stability information:

N/A

IV. Toxicity Information:

Mammalian: Rat LD50 > 5 g/kg Mouse LD50: > 10 g/kg

Aquatic:	Invertebrate Toxicity (EC/LC50)	Fish Toxicity (LC50)
	N/A	N/A

Other Toxicity Information (including findings of chronic and subchronic tests):

V. Classification of the Compound:

_____Insecticide _____Herbicide _____Fungicide

_____Microbial Agent _____Economic Poison

Other: Halogenated flame retardant

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APPENDIX II. SYNTHETIC SEWAGE

The synthetic sewage provides the necessary nutrients required for bacterial metabolism. It is prepared by dissolving the following amounts of substances in 1 liter of municipal water:

16.0 g peptone
11.0 g meat extract
3.0 g urea
0.7 g NaCl
0.4 g $CaCl_2$ $2H_2O$
0.2 g $MgSO_4$ $7H_2O$
2.8 g K_2HPO_4

Reagent grade chemicals or better will be used when available. The constituents of the synthetic sewage are not known to contain any contaminants that are reasonable expected to be present and are known to be capable of interfering with the study.

TETRABROMOBISPHENOL A: A TOXICITY TEST TO DETERMINE THE EFFECTS OF THE TEST SUBSTANCE ON SEEDLING EMERGENCE OF SIX SPECIES OF PLANTS

FINAL REPORT

WILDLIFE INTERNATIONAL, LTD. PROJECT NUMBER: 439-102

OECD Guideline for Testing of Chemicals
Proposal for Revision of Guideline 208: Terrestrial Non-Target Plant Tests

and

U.S. Environmental Protection Agency
Series 850 - Ecological Effects Test Guidelines
OPPTS Number 850.4100 and 850.4225

AUTHORS:

John R. Porch
Timothy Z. Kendall
Henry O. Krueger, Ph.D.

STUDY INITIATION DATE: November 7, 2001

STUDY COMPLETION DATE: March 5, 2002

Submitted to

American Chemistry Council's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209

Wildlife International, Ltd.
8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

SPONSOR: American Chemistry Council's Brominated Flame Retardant Industry Panel

TITLE: Tetrabromobisphenol A: A Toxicity Test to Determine the Effects of the Test Substance on Seedling Emergence of Six Species of Plants

WILDLIFE INTERNATIONAL, LTD. PROJECT NO.: 439-102

STUDY COMPLETION: March 5, 2002

This study was conducted in compliance with Good Laboratory Practice Standards as published by the U.S. Environmental Protection Agency in 40 CFR Parts 160 and 792, 17 August 1989; OECD Principles of Good Laboratory Practice (ENV/MC/CHEM(98)17); and Japan MAFF, 11 NohSan, Notification No. 6283, Agricultural Production Bureau, 1 October 1999.

STUDY DIRECTOR:

John R. Porch — 5 March 02

John R. Porch — Date

QUALITY ASSURANCE STATEMENT

This study was examined for compliance with Good Laboratory Practice Standards as published by the U.S. Environmental Protection Agency in 40 CFR Parts 160 and 792, 17 August 1989; OECD Principles of Good Laboratory Practice (ENV/MC/CHEM(98)17); and Japan MAFF, 11 NohSan, Notification No. 6283, Agricultural Production Bureau, 1 October 1999. The dates of all audits and inspections and the dates that any findings were reported to the Study Director and Laboratory Management were as follows:

		DATE REPORTED TO:	
ACTIVITY	DATE CONDUCTED	STUDY DIRECTOR	MANAGEMENT
Test Substance Preparation	November 14, 2001	November 14, 2001	November 14, 2001
Initiation	November 14, 2001	November 14, 2001	November 15, 2001
Matrix Fortifications	November 15, 2001	November 15, 2001	November 15, 2001
Observations and Height Measurements	December 5, 2001	December 5, 2001	December 5, 2001
Analytical Data and Draft Report	January 8, 2002	January 8, 2002	January 8, 2002
Biological Data and Draft Report	January 7-10, 2002	January 10, 2002	March 5, 2002
Final Report	March 4, 2002	March 4, 2002	March 5, 2002

Kimberly A. Hoxter
Kimberly A. Hoxter
Quality Assurance Representative

3-5-02
Date

REPORT APPROVAL

SPONSOR: American Chemistry Council's Brominated Flame Retardant Industry Panel

TITLE: Tetrabromobisphenol A: A Toxicity Test to Determine the Effects of the Test Substance on Seedling Emergence of Six Species of Plants

WILDLIFE INTERNATIONAL, LTD. PROJECT NO.: 439-102

STUDY DIRECTOR:

John R. Porch — 5 March 02
John R. Porch
Supervisor, Non-Target Plants and Insects
Date

CHEMISTRY PRINCIPAL INVESTIGATOR:

Timothy Z. Kendall — 3/5/02
Timothy Z. Kendall
Supervisor
Date

WILDLIFE INTERNATIONAL, LTD. MANAGEMENT:

Henry O. Krueger — 5 Mar 02
Henry O. Krueger, Ph.D.
Director, Aquatic Toxicology and Non-Target Plants
Date

Willard B. Nixon — 3/5/02
Willard B. Nixon, Ph.D.
Director, Analytical Chemistry
Date

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SUMMARY

WILDLIFE INTERNATIONAL, LTD. PROJECT NO: 439-102

TEST SUBSTANCE: Tetrabromobisphenol A

STUDY TITLE: Tetrabromobisphenol A: A Toxicity Test to Determine the Effects of the Test Substance on Seedling Emergence of Six Species of Plants

GUIDELINES: OECD Guideline for Testing of Chemicals, Proposal for Revision of Guideline 208: Terrestrial Non-Target Plant Tests
OPPTS 850.4100 (Public Draft)
OPPTS 850.4225 (Public Draft)

NOMINAL TEST LEVELS: 0 (Control), 20, 78, 313, 1250, 5000 mg/kg dry soil

TEST DATES:

STUDY INITIATION:	November 7, 2001
Experimental Start (OECD):	November 14, 2001
Experimental Start (EPA):	November 14, 2001
Experimental Termination:	December 7, 2001
STUDY COMPLETION:	March 5, 2002

LENGTH OF TEST: 21 days

TEST SPECIES: Corn (*Zea mays*), Cucumber (*Cucumis sativa*), Onion (*Allium cepa*), Ryegrass (*Lolium perenne*), Soybean (*Glycine max*), Tomato (*Lycopersicon esulentum*)

RESULTS: The NOEC, LOEC, and lowest Effect Concentration (EC_x) for each of the six test species is listed below. This summary is based on the most sensitive endpoints only, complete results are presented in the text and tables.

RESULTS[1]:	Corn	Cucumber	Onion	Ryegrass	Soybean	Tomato
Most sensitive endpoint(s)	Dry Weight	Dry Weight, Height	Dry Weight, Height	Dry Weight, Height	-[2]	Dry Weight, Height
NOEC	313	20	313	78	5000	313
LOEC	1250	78	1250	313	>5000	1250
EC_{25}	>5000	73	460	49	>5000	422
EC_{50}	>5000	1672	4264	459	>5000	>5000
LC_{50}	>5000	>5000	>5000	>5000	>5000	>5000

[1] Results are presented as mg Tetrabromobisphenol A/kg soil dry weight.
[2] " –" indicates that endpoint or concentration could not be obtained because there were no effects observed

INTRODUCTION

This seedling emergence study was conducted for American Chemistry Council's Brominated Flame Retardant Industry Panel at the Wildlife International, Ltd. greenhouse facility in Easton, Maryland. The in-life portion of the test was conducted from November 14, 2001 to December 5, 2001. Raw data generated at Wildlife International, Ltd., the study protocol, and a copy of the final report were filed in the archives located on the Wildlife International, Ltd. site. Key personnel involved in the study are listed in Appendix 1.

PURPOSE

The purpose of the study was to determine the effects of Tetrabromobisphenol A (TBBPA) on the seedling emergence and growth of six species of non-target plants.

EXPERIMENTAL DESIGN

The experimental design for this study consisted of a negative control and five treatment groups. Each group had four replicate pots with ten seeds planted in each pot. Test concentrations of TBBPA were made by soil incorporation to each treatment group prior to the planting of seeds. The nominal test substance concentrations were 20, 78, 313, 1250, and 5000 mg of TBBPA per kilogram of dry soil (mg/kg). A control group, which received no test substance incorporation, was maintained concurrently.

Seeds were impartially assigned to prelabelled growth pots on the day of test initiation. The replicate pots were placed in a randomized block design on a greenhouse table after planting. Observations of emergence were made on Days 7, 14, and 21. A general assessment of seedling condition was made on Day 7, while observations of height, shoot dry weight, and assignment of plant condition scores were made only on Day 21.

MATERIALS AND METHODS

The study was conducted according to the procedures outlined in the protocol, "Tetrabromobisphenol A: A Toxicity Test to Determine the Effects of the Test Substance on Seedling Emergence of Six Species of Plants" (Appendix 2). The methods used in conducting this study were based upon procedures specified in the OECD Proposal for Revision of Guideline 208: Terrestrial Non-Target Plant Tests (1) and the U.S. Environmental Protection Agency Series 850 - Ecological Effects Test Guidelines OPPTS Numbers 850.4100 (2) and 850.4225 (3).

Test Substance

The test substance consisted of a composite of Tetrabromobisphenol A samples received from three manufacturers. The material's identity and date received from each of the manufacturers is given below:

Manufacturer	Lot/Batch	Date Received	Wildlife International, Ltd. Identification Number
Great Lakes Chemical Corporation	1008JE04B	August 16, 2001	5722
Albemarle Corporation	25115T-1	August 16, 2001	5721
Bromine Compounds, Ltd.	010040	August 31, 2001	5733

The composite test substance was assigned Wildlife International, Ltd. identification number 5754 and was stored under ambient conditions. The composite test substance was shipped to Albemarle Corporation for characterization and purity analyses (Appendix 3). The results of the analyses indicated the composite test substance was homogeneous. The conclusion of the characterization was that the test article had a purity of 99.17%.

Preparation and Soil Incorporation of Test Substance

The test soil was prepared by mixing TBBPA into bulk test soil with a measured soil moisture of 15%. Test substance for treatment groups 20, 78, 313, 1250, and 5000 mg/kg was prepared by weighing five known weights (1.0, 4.0, 16.0, 63.8, and 255.0 g) of TBBPA. Approximately 60 kg of bulk soil was measured into a soil mixer, and weighed test substance was added for each test concentration. The test substance and bulk soil were then mixed for ten minutes in order to prepare the test soil for each treatment group. Soils were mixed from lowest to highest concentration to avoid cross-contamination. The negative control soil was prepared in the same manner as the other test groups, but no test substance was added. At the completion of mixing, the test soils were sampled to provide material for analytical confirmation of the test concentrations. Analytical samples were stored at ambient room conditions after their collection until they were analyzed.

Test Species

The common and scientific names for the six species tested, the seed source, and their approximate planting depths are listed below:

Test Species / Variety:	Seed Source:	Planting Depth
Corn (*Zea mays*) / Mandan Bride	Johnny's Selected Seeds, Albion, ME, USA	20 mm
Onion (*Allium cepa*) / Texas Grano	Territorial Seed Co., Cottage Grove, OR, USA	6 mm
Ryegrass (*Lolium perenne*) / Manhattan 3	Meyer Seed Co., Baltimore, MD, USA	6 mm
Cucumber (*Cucumis sativa*) / Straight Eight	Meyer Seed Co., Baltimore, MD, USA	20 mm
Soybean (*Glycine max*) / Green Envy	Johnny's Selected Seeds, Albion, ME, USA	20 mm
Tomato (*Lycopersicon esculentum*) /Rutgers	Meyer Seed Co., Baltimore, MD, USA	6 mm

These species were chosen because they represent ecologically important families, and are readily cultivated test organisms that are widely used in research. Seeds were selected from a single size class within each species in order to reduce the potential for bias from differing seed sizes. Seeds used in this study were not treated with fungicides, insecticides or repellents prior to test initiation.

Test Soil

The soil used for the test represented a loam soil, and was composed of kaolinite clay, industrial quartz sand, and peat mixed in a 2:25:1 ratio (w:w:w). Crushed limestone was added to buffer the pH of the soil, and a slow-release fertilizer was added to provide nutrients essential for plant growth. A sample of soil representative of that used in this study was sent to Agvise Laboratories, Inc., in Northwood, North Dakota, for analysis of the particle size distribution and organic matter content of the soil. The soil was determined to consist of 49% sand, 30% silt, and 21% clay, with an organic matter content of 2.1%. The soil pH was measured by Wildlife International Ltd. to be 7.79. A copy of the complete report from Agvise Laboratories, Inc. was filed in the archives at Wildlife International, Ltd. along with the raw data for this study.

Planting of Seeds

Seeds were planted in plastic pots (approximately 16 cm in diameter and 12 cm deep) on the day of test substance application. A template was used to gently compact the soil and leave ten uniform holes for planting. One indiscriminately selected seed was then planted in each hole, for a total of ten seeds in each pot. Holes were then closed by slightly depressing the soil surface.

Watering of Seedlings

Water lost through transpiration and evaporation was replaced by subirrigation with well water from the greenhouse facility. Seedlings were subirrigated to minimize the potential for the leaching of the test substance through the soil. Subirrigation trays were filled to a predetermined

depth to help standardize the amount of water delivered to each tray. The days on which watering occurred are listed in Appendix 5.

Environmental Conditions

The environmental conditions (temperature and relative humidity) of the test are summarized in Appendix 5. The temperature within the greenhouse was controlled with a Wadsworth MicroStep S/A Environmental Control System. Artificial lighting (high pressure sodium) was used to supplement natural sunlight in order to provide a uniform 14-hour photoperiod. The temperature and relative humidity within the greenhouse were continuously monitored during the test with the Wadsworth control system.

Pesticide and Metal Screening of Well Water and Soil

The well water and soil used for plant studies are analyzed periodically for pesticide and metals. No analytes were measured at levels that were expected to have an impact on the study. Reports for the latest analyses are stored in the archives at the Wildlife International, Ltd. site in Easton, Maryland.

Observations and Measurements

Observations on Days 7 and 14 were made primarily to document seedling emergence, although the general condition of test seedlings was assessed on Day 7. Observations on Day 21 were made to document seedling emergence and growth, and to determine the condition of individual seedlings following the application of the test substance. Observations consisted of noting whether emergence had or had not occurred, and assessing the condition of each seedling. Emergence was defined as the presence of visible plant tissue at the surface of the soil. Seedling condition was described by noting the presence or absence of possible signs of phytotoxicity such as necrosis, leaf wrinkle, chlorosis, plant lodging or plant stunting. Each emerged seedling was then assigned a numerical score (see Table 1) that described the plant condition (4). Condition score is a subjective or qualitative assessment that determines whether damage is slight, moderate, or severe. A score of 10 does not mean that 10% of the plant is showing the effect (e.g. chlorosis), merely that the severity of the effect (e.g. chlorosis) is very slight.

The growth of emerged seedlings was evaluated by assessing the height and dry weight of living seedlings at test termination. Seedling height was measured to the nearest whole centimeter from the surface of the soil to the tip of the tallest leaf (corn, onion, and ryegrass) or to

the apical meristem (cucumber, soybean, and tomato). Seedlings were then clipped at soil level; the shoots of all living seedlings within a replicate were placed in a labeled bag, and dried. The total dry weight of the replicate was determined, and the mean dry weight per shoot was calculated by dividing the total weight by the number of seedlings weighed.

Analytical Sampling

On the day of test soil preparation (November 14, 2001), three soil samples were collected from the 20, 78, 313, 1250, and 5000 mg/kg treatment groups to verify the test concentrations and determine the homogeneity of the test substance in the carrier (soil). One sample was collected from the control group. Samples were stored at ambient room conditions until analysis was begun on November 15, 2001. Chemical analysis of the soil used in this study was performed by Wildlife International, Ltd. (Appendix 4). The test substance was used to prepare calibration standards.

Data Analyses

Statistical analyses were used to aid in the evaluation of effects of test substance application on seedling emergence, survival, mean shoot weight, and seedling height. These variables were defined for statistical analysis as follows:

Seedling Emergence:

The number of emerged seedlings per ten planted seeds in each pot.

Survival:

The number of emerged seedlings in each pot that were living at test termination per ten planted seeds.

Mean Shoot Weight:

The average dry shoot weight of living emerged seedlings in each pot.

Height:

The average height of living emerged seedlings in each pot.

Test data were evaluated to determine the no-observed-effect-concentration (NOEC) and lowest-observable-effect-concentration (LOEC) for condition and growth. The NOEC is defined as the maximum test substance concentration that shows no adverse phytotoxic effects and below which no phytotoxic effects are manifested. The LOEC is defined as the lowest test substance concentration used in the study that shows an adverse effect on a variable of interest. Mean seedling emergence, survival, weight, and height of the control and treatment groups were compared with Dunnett's t-test, using the DUNNETT option of the GLM (general linear model)

procedure of SAS version 8 (5). Significance was determined at the level of 0.05 ($p<0.05$). Dunnett's test was used to aid in establishing the NOEC by determining which treatment groups differed significantly from the control group.

Statistical analyses for species also included the determination of effect rates (EC estimates) and their confidence limits using the non-linear regression analysis of Bruce and Versteeg (6) when reductions in test endpoints among one or more treatment groups were 25% or more relative to control means. Analyses were conducted using the NLIN procedure of SAS version 8 (5). EC_x values (i.e. EC_{25} and EC_{50}) were defined as the test substance application rates that caused an x% change in the treatment group mean emergence, dry weight, or height relative to the control group. EC_x estimates were calculated using nominal test concentrations and treatment group mean values with the following equation:

$$R = \begin{cases} R_0 \cdot \Phi[(\log(EC_x)-\log(C))/\sigma+Z_x] & C>0 \\ R_0 & C=0 \end{cases}$$

where

R	= the predicted biotic response at concentration C
R_0	= the predicted biotic response for controls
$\Phi[\ ]$	= the cumulative area under the standard, normal distribution
$\log(EC_x)$	= the logarithm of the predicted ER giving an x percentage of decrease in the biological parameter vs. the control
Z_x	= the normal deviate above which x percentage of the area of the standard normal distribution lies.
σ	= the standard deviation of the normal distribution

Effects on survival were designated as LC_x values, and were calculated using the method described above.

RESULTS AND DISCUSSION

Analytical Chemistry

The results of analyses to measure concentrations of TBBPA in the soil samples collected during the test are presented in Appendix 4.

Biological Results

The results of the test are summarized for each species in Tables 2 through 7. Complete results are presented by species in Appendices 6 through 11.

Corn

There were no apparent adverse treatment-related effects on emergence, height or condition of corn seedlings. Mean emergence at test termination in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 9.25, 10.00, 9.25, 9.50, 9.25, and 9.75 seedlings per 10 planted seeds, respectively (Table 2). Mean height of seedlings at test termination in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 39.7, 44.1, 41.5, 39.2, 35.9, and 35.8 cm, respectively. None of the treatment group mean heights was significantly different ($p>0.05$) from the control means. The emerged seedlings generally appeared normal at test termination, excluding incidental mortality. The LC_{50} for corn seedlings, and the EC_{25} and the EC_{50} with respect to height was determined to be >5000 mg/kg soil dry weight.

There were apparent adverse treatment-related effects observed on dry weight of corn seedlings. The mean dry weight of seedlings in the control and the 20, 78, 313, 1250, 5000 mg/kg treatment groups was 0.45, 0.48, 0.45, 0.41, 0.36, and 0.36 g, respectively. The mean weights for the 1250 and 5000 mg/kg groups were significantly different ($p<0.05$) from the control mean. Therefore, the LOEC and NOEC for corn with respect to weight were 1250 mg/kg and 313 mg/kg, respectively. Since none of the treatment group weights was 25% less than the control mean, the EC_{25} and EC_{50} for corn weight were determined to be >5000 mg/kg.

Cucumber

There were no apparent adverse treatment-related effects on the emergence and condition of cucumber seedlings. Mean emergence at test termination in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 8.50, 9.50, 8.75, 8.75, 9.25, and 7.50 seedlings per 10 planted seeds, respectively (Table 3). The emerged seedlings generally appeared normal at test termination. There were isolated individuals with signs of leaf curl, necrosis, and mortality; however, none of these conditions appeared dose-responsive, and none were attributed to treatment. The LC_{50} for cucumber seedlings was determined to be >5000 mg/kg.

There were apparent adverse treatment-related effects on height and dry weight of cucumber seedlings. The mean height of seedlings at test termination in the control and the 20, 78, 313, 1250 and 5000 mg/kg treatment groups was 9.7, 9.4, 7.5, 6.5, 5.3, and 4.7 cm, respectively. Mean height of the 78, 313, 1250, 5000 mg/kg groups was significantly different ($p<0.05$) from the control mean. The LOEC and NOEC for cucumber seedlings with respect to height were 78 and 20 mg/kg, respectively. The EC_{25} for cucumber height was determined to be 131 mg/kg, and

the EC_{50} was determined to be 2603 mg/kg. The mean dry weight of seedlings in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 0.35, 0.32, 0.28, 0.20, 0.17, and 0.16 g, respectively. Mean weight of the 78, 313, 1250, and 5000 mg/kg groups was significantly different ($p<0.05$) from control means. The LOEC and NOEC for cucumber seedlings with respect to weight was 78 and 20 mg/kg, respectively. The EC_{25} for cucumber weight was determined to be 73 mg/kg, and the EC_{50} was determined to be 1672 mg/kg.

Onion

There were no apparent adverse treatment-related effects on seedling emergence, and condition of onion seedlings. The mean emergence of seedlings at test termination in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 9.00, 9.00, 9.50, 9.75, 9.25, and 9.00 seedlings per 10 planted seeds, respectively (Table 4). The emerged seedlings generally appeared normal at test termination, excluding incidental mortality. The LC_{50} was determined to be >5000 mg/kg.

There were apparent adverse treatment-related effects on the height and dry weight of onion seedlings. The mean height of seedlings at test termination for the control, and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 7.4, 7.9, 7.6, 7.2, 5.9, and 4.9 cm, respectively. Mean heights of the 1250 and 5000 mg/kg groups were significantly different ($p<0.05$) from the control means. The LOEC and the NOEC for onion seedlings with respect to height were 1250 and 313 mg/kg, respectively. The EC_{25} for onion height was determined to be 1948 mg/kg. Since none of the treatment group height were reduced by 50%, the EC_{50} was determined to be >5000 mg/kg. The mean weight of seedlings at test termination for the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 13, 13, 11, 10, 9, and 6 mg, respectively. Mean weights of the 1250 and 5000 mg/kg groups were significantly different ($p<0.05$) different from the control means. The LOEC and the NOEC for onion seedlings with respect to weight was 1250 and 313 mg/kg, respectively. The EC_{25} for onion weight was determined to be 460 mg/kg, the EC_{50} for onion weight was determined to be 4264 mg/kg.

Ryegrass

There were no apparent treatment-related effects on seedling emergence, and condition of ryegrass seedlings. The mean emergence of seedlings at test termination for the control, and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 9.25, 9.50, 9.25, 9.00, 8.75, and 8.25

seedlings per 10 planted seeds, respectively (Table 5). The emerged seedlings generally appeared normal, showing no signs of toxicity. The LC_{50} was determined to be >5000 mg/kg.

There were apparent adverse treatment-related effects on height and dry weight of ryegrass seedlings. Mean height at test termination for the control, and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 15.4, 15.7, 13.0, 9.6, 7.2, and 7.5 cm, respectively. Mean heights of the 313, 1250, and 5000 mg/kg groups were significantly different ($p<0.05$) from the control means. The LOEC and the NOEC for ryegrass seedlings with respect to height were 313 and 78 mg/kg, respectively. The EC_{25} for ryegrass dry weight was determined to be 114 mg/kg, the EC_{50} for ryegrass weight was determined to be 1801 mg/kg. Mean weights at test termination for the control, and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups were 21, 23, 17, 9, 7, and 7 mg, respectively. Mean weights of the 313, 1250, and 5000 mg/kg groups were significantly different ($p<0.05$) from the control means. The LOEC and NOEC for ryegrass seedlings with respect to weight were 313 and 78 mg/kg, respectively. The EC_{25} for ryegrass dry weight was determined to be 49 mg/kg, and the EC_{50} for ryegrass dry weight was determined to be 459 mg/kg.

Soybean

There were no apparent treatment-related effects on seedling emergence, height, dry weight, and condition of soybeans. Mean emergence at test termination in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 10.00, 9.50, 10.00, 10.00, 9.75, and 9.50 seedlings per 10 planted seeds, respectively (Table 6). Mean height at test termination in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 22.1, 22.7, 22.3, 22.4, 22.8, and 21.0 cm, respectively. None of the treatment group mean heights was significantly different ($p>0.05$) from the control means. The mean dry weight of seedlings in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 0.46, 0.48, 0.51, 0.47, 0.48, and 0.49 g, respectively. None of the treatment group mean weights was significantly different ($p>0.05$) from the control means. Since group mean weights and heights were not reduced by 25% (relative to the control mean), the EC_{25} and EC_{50} for weights and heights were determined to be >5000 mg/kg. The emerged seedlings generally appeared normal at test termination. There were a few individual plants that exhibited conditional ratings for leaf curl and stem curl; however, these cases were isolated and not considered treatment-related. The LC_{50} for soybean seedlings was therefore determined to be >5000 mg/kg.

Tomato

There were no apparent treatment-related effects on the emergence, and condition of tomato seedlings. The mean emergence at test termination in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 9.50, 8.75, 9.00, 9.25, 9.25, and 9.00 seedlings per 10 planted seeds, respectively (Table 7). Emerged seedlings generally appeared normal at test termination, excluding incidental mortality. The LC_{50} for tomato seedlings was determined to be >5000 mg/kg.

There were apparent treatment-related effects on height and dry weight of tomato seedlings. The mean height of seedlings at test termination for the control, and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 5.6, 5.0, 5.0, 4.8, 4.4, and 4.6 cm, respectively. Mean heights of the 1250 and 5000 mg/kg treatment groups were significantly different ($p<0.05$) from the control means. The LOEC and the NOEC for tomato seedlings with respect to height were 1250 and 313 mg/kg, respectively. The mean weight of seedlings at test termination in the control and the 20, 78, 313, 1250, and 5000 mg/kg treatment groups was 0.044, 0.039, 0.040, 0.033, 0.029, and 0.022 g, respectively. Mean weights of the 1250 and 5000 mg/kg treatment groups were significantly different ($p<0.05$) from the control means. The LOEC and the NOEC for tomato with respect to dry weight were 1250 and 313 mg/kg, respectively. The EC_{25} for tomato dry weight was determined to be 422 mg/kg, and the EC_{50} for tomato dry weight was determined to be >5000 mg/kg.

CONCLUSIONS

There were no adverse treatment-related effects on soybean seedling growth resulting from soil incorporated TBBPA. Therefore, the NOEC for soybean was the highest concentration tested, 5000 mg/kg, and the LOEC was not determined. Treatment-related effects on seedling growth were observed in corn, cucumber, onion, ryegrass, and tomato. The most sensitive endpoint for corn was seedling dry weight, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. EC_{25} and EC_{50} for corn was determined to be >5000 mg/kg. The NOEC and LOEC for both seedling dry weight and height of cucumber – the most sensitive endpoints – were 20 and 78 mg/kg, respectively. The EC_{25} and EC_{50} values for dry weight of cucumber were determined to be 73 and 1672 mg/kg, respectively. The most sensitive endpoints for onion were seedling dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The EC_{25} and EC_{50} values for onion dry weight were determined to be 460 and 4264 mg/kg, respectively. The most sensitive endpoints for ryegrass were observed in dry weight and

height, which resulted in a NOEC of 78 mg/kg, and a LOEC of 313 mg/kg. The EC_{25} and EC_{50} values for dry weight were 49 mg/kg and 459 mg/kg, respectively. The most sensitive endpoints for tomato were observed in dry weight and height, which resulted in a NOEC of 313 mg/kg, and a LOEC of 1250 mg/kg. The value for the EC_{25} for tomato was determined to be 422 mg/kg; the EC_{50} was determined to be >5000 mg/kg.

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Table 1

Seedling Condition Rating System

The rating system below was used to help evaluate the health of seedlings on Day 21. Assigned scores by treatment group are reported on the following pages.

Rating	Category	Description
0	No Effect	No noticeable effect
10		Effect barely noticeable
20	Slight Effect	Some effect, not apparently detrimental
30		Effect more pronounced, not obviously detrimental
40		Effect moderate, plants appear able to recover
50	Moderate Effect	More lasting effect, recovery somewhat doubtful
60		Lasting effect, recovery doubtful
70		Heavy injury, loss of individual leaves
80	Severe Effect	Plant nearly destroyed, a few surviving leaves
90		Occasional surviving leaves
100	Complete Effect	Death of entire plant

Rating scale adapted from:

Frans, Robert E. and Ronald E. Talbert. 1977. Design of Field Experiments and the Measurement and Analysis of Plant Responses. Pages 15-23 in B. Truelove, ed. Research Methods in Weed Science. Southern Weed Science Society, Auburn University, Alabama.

Table 2

Effects of Tetrabromobisphenol A on Seedling Emergence, Survival, Shoot Dry Weight, and Height in a 21-Day Seedling Emergence Test with CORN

Test Concentration (mg/kg)	Number of Emerged Seedlings (% Reduction) Day 7	Day 14	Day 21	Seedling Survival (% Reduction)	Dry Weight (g) (% Reduction)	Seedling Height (cm) (% Reduction)
Control	9.00 ± 1.15	9.25 ± 0.96	9.25 ± 0.96	9.00 ± 1.15	0.45 ± 0.071	39.7 ± 4.57
20	10.00 ± 0.00 (-11%)	10.00 ± 0.00 (-8%)	10.00 ± 0.00 (-8%)	10.00 ± 0.00 (-11%)	0.48 ± 0.008 (-8%)	44.1 ± 1.04 (-11%)
78	9.00 ± 0.82 (0%)	9.25 ± 0.96 (0%)	9.25 ± 0.96 (0%)	9.00 ± 0.82 (0%)	0.45 ± 0.063 (-1%)	41.5 ± 3.38 (-5%)
313	9.00 ± 1.41 (0%)	9.50 ± 0.58 (-3%)	9.50 ± 0.58 (-3%)	9.25 ± 0.96 (-3%)	0.41 ± 0.036 (8%)	39.2 ± 2.60 (1%)
1250	9.00 ± 0.82 (0%)	9.25 ± 0.50 (3%)	9.25 ± 0.50 (0%)	9.25 ± 0.50 (-3%)	0.36 ± 0.038* (19%)	35.9 ± 1.86 (10%)
5000	9.75 ± 0.50 (-8%)	9.75 ± 0.50 (-5%)	9.75 ± 0.50 (-5%)	9.75 ± 0.50 (-8%)	0.36 ± 0.046* (20%)	35.8 ± 1.73 (10%)

* Treatment group mean is significantly different from the control mean (Dunnett's test, $p<0.05$).

Table 3

Effects of Tetrabromobisphenol A on Seedling Emergence, Survival, Shoot Dry Weight, and Height in a 21-Day Seedling Emergence Test with CUCUMBER

Test Concentration (mg/kg)	Number of Emerged Seedlings (% Reduction) Day 7	Day 14	Day 21	Seedling Survival (% Reduction)	Dry Weight (g) (% Reduction)	Seedling Height (cm) (% Reduction)
Control	8.50 ± 1.29	8.50 ± 1.29	8.50 ± 1.29	8.50 ± 1.29	0.35 ± 0.037	9.7 ± 1.11
20	8.25 ± 1.50 (3%)	9.50 ± 1.00 (-12%)	9.50 ± 1.00 (-12%)	8.75 ± 1.50 (-3%)	0.32 ± 0.014 (9%)	9.4 ± 0.53 (3%)
78	8.00 ± 1.15 (6%)	8.50 ± 1.29 (0%)	8.75 ± 1.26 (-3%)	8.25 ± 1.71 (3%)	0.28 ± 0.056* (20%)	7.5 ± 1.72* (22%)
313	8.25 ± 1.71 (3%)	8.75 ± 1.26 (-3%)	8.75 ± 1.26 (-3%)	8.50 ± 1.29 (0%)	0.20 ± 0.035* (42%)	6.5 ± 1.21* (33%)
1250	9.00 ± 1.41 (-6%)	9.00 ± 1.41 (-6%)	9.25 ± 1.50 (-9%)	9.25 ± 1.50 (-9%)	0.17 ± 0.011* (50%)	5.3 ± 0.46* (45%)
5000	6.75 ± 2.06 (21%)	7.50 ± 2.38 (12%)	7.50 ± 2.38 (12%)	7.50 ± 2.38 (12%)	0.16 ± 0.020* (54%)	4.7 ± 0.53* (52%)

* Treatment group mean is significantly different from the control mean (Dunnett's test, $p<0.05$).

Table 4

Effects of Tetrabromobisphenol A on Seedling Emergence, Survival, Shoot Dry Weight, and Height in a 21-Day Seedling Emergence Test with ONION

Test Concentration (mg/kg)	Number of Emerged Seedlings (% Reduction) Day 7	Day 14	Day 21	Seedling Survival (% Reduction)	Dry Weight (mg) (% Reduction)	Seedling Height (cm) (% Reduction)
Control	8.50 ± 1.29	9.00 ± 1.41	9.00 ± 1.41	9.00 ± 1.41	0.013 ± 0.0021	7.4 ± 0.78
20	9.00 ± 1.15 (-6%)	9.00 ± 1.55 (0%)	9.00 ± 1.55 (0%)	8.25 ± 1.71 (8%)	0.013 ± 0.0034 (1%)	7.9 ± 0.85 (-7%)
78	9.25 ± 0.50 (-9%)	9.50 ± 0.58 (-6%)	9.50 ± 0.58 (-6%)	9.50 ± 0.58 (-6%)	0.011 ± 0.0020 (15%)	7.6 ± 0.46 (-3%)
313	9.50 ± 0.58 (-12%)	9.75 ± 0.50 (-8%)	9.75 ± 0.50 (-8%)	9.75 ± 0.50 (-8%)	0.010 ± 0.0027 (21%)	7.2 ± 0.62 (2%)
1250	9.00 ± 0.82 (-6%)	9.25 ± 0.50 (-3%)	9.25 ± 0.50 (-3%)	9.00 ± 0.00 (0%)	0.009 ± 0.0019* (33%)	5.9 ± 0.31* (21%)
5000	8.25 ± 0.96 (3%)	9.00 ± 0.00 (0%)	9.00 ± 0.00 (0%)	8.50 ± 0.58 (6%)	0.006 ± 0.0012* (52%)	4.9 ± 0.28* (33%)

* Treatment group mean is significantly different from the control mean (Dunnett's test, $p<0.05$).

Table 5

Effects of Tetrabromobisphenol A on Seedling Emergence, Survival, Shoot Dry Weight, and Height in a 21-Day Seedling Emergence Test with RYEGRASS

Test Concentration (mg/kg)	Number of Emerged Seedlings (% Reduction) Day 7	Day 14	Day 21	Seedling Survival (% Reduction)	Dry Weight (mg) (% Reduction)	Seedling Height (cm) (% Reduction)
Control	9.00 ± 0.82	9.25 ± 0.96	9.25 ± 0.96	9.25 ± 0.96	0.021 ± 0.0012	15.4 ± 1.29
20	8.75 ± 1.26 (3%)	9.50 ± 0.58 (-3%)	9.50 ± 0.58 (-3%)	9.50 ± 0.58 (-3%)	0.023 ± 0.0056 (-8%)	15.7 ± 1.85 (-2%)
78	9.25 ± 0.96 (-3%)	9.00 ± 0.82 (3%)	9.25 ± 0.50 (0%)	9.25 ± 0.50 (0%)	0.017 ± 0.0066 (21%)	13.0 ± 1.56 (16%)
313	8.75 ± 0.96 (3%)	9.00 ± 0.82 (3%)	9.00 ± 0.82 (3%)	9.00 ± 0.82 (3%)	0.009 ± 0.0039* (55%)	9.6 ± 1.75* (37%)
1250	8.00 ± 1.63 (11%)	8.50 ± 1.73 (8%)	8.75 ± 1.89 (5%)	8.75 ± 1.89 (5%)	0.007 ± 0.0030* (65%)	7.2 ± 1.15* (53%)
5000	7.75 ± 2.06 (14%)	8.25 ± 1.26 (11%)	8.25 ± 1.26 (11%)	8.25 ± 1.26 (11%)	0.007 ± 0.0032* (67%)	7.5 ± 0.93* (51%)

* Treatment group mean is significantly different from the control mean (Dunnett's test, $p<0.05$).

Table 6

Effects of Tetrabromobisphenol A on Seedling Emergence, Survival, Shoot Dry Weight, and Height in a 21-Day Seedling Emergence Test with SOYBEAN

Test Concentration (mg/kg)	Number of Emerged Seedlings (% Reduction) Day 7	Day 14	Day 21	Seedling Survival (% Reduction)	Dry Weight (g) (% Reduction)	Seedling Height (cm) (% Reduction)
Control	9.50 ± 0.58	10.00 ± 0.00	10.00 ± 0.00	10.00 ± 0.00	0.46 ± 0.014	22.1 ± 2.03
20	9.00 ± 0.82 (5%)	9.50 ± 0.58 (5%)	9.50 ± 0.58 (5%)	9.50 ± 0.58 (5%)	0.48 ± 0.041 (-3%)	22.7 ± 1.60 (-3%)
78	9.25 ± 0.50 (3%)	10.00 ± 0.00 (0%)	10.00 ± 0.00 (0%)	10.00 ± 0.00 (0%)	0.51 ± 0.028 (-10%)	22.3 ± 2.09 (-1%)
313	9.50 ± 0.58 (0%)	10.00 ± 0.00 (0%)	10.00 ± 0.00 (0%)	10.00 ± 0.00 (0%)	0.47 ± 0.051 (-1%)	22.4 ± 2.81 (-1%)
1250	9.50 ± 0.58 (0%)	9.75 ± 0.50 (3%)	9.75 ± 0.50 (3%)	9.75 ± 0.50 (3%)	0.48 ± 0.054 (-3%)	22.8 ± 2.11 (-3%)
5000	9.00 ± 0.00 (5%)	9.25 ± 0.50* (8%)	9.50 ± 0.58 (5%)	9.50 ± 0.58 (5%)	0.49 ± 0.049 (-7%)	21.0 ± 1.86 (5%)

* Treatment group mean was significantly different from the control mean (Dunnett's test, $p<0.05$)

Table 7

Effects of Tetrabromobisphenol A on Seedling Emergence, Survival, Shoot Dry Weight, and Height in a 21-Day Seedling Emergence Test with TOMATO

Test Concentration (mg/kg)	Number of Emerged Seedlings (% Reduction) Day 7	Day 14	Day 21	Seedling Survival (% Reduction)	Dry Weight (g) (% Reduction)	Seedling Height (cm) (% Reduction)
Control	5.00 ± 2.31	9.50 ± 0.58	9.50 ± 0.58	9.25 ± 0.50	0.044 ± 0.0088	5.6 ± 0.38
20	7.75 ± 2.06 (-55%)	8.75 ± 0.96 (8%)	8.75 ± 0.96 (8%)	8.75 ± 0.96 (5%)	0.039 ± 0.0115 (12%)	5.0 ± 0.84 (11%)
78	4.75 ± 1.26 (5%)	9.00 ± 0.82 (5%)	9.00 ± 0.82 (5%)	9.00 ± 0.82 (3%)	0.040 ± 0.0087 (9%)	5.0 ± 0.74 (11%)
313	7.50 ± 1.73 (-50%)	9.00 ± 0.00 (5%)	9.25 ± 0.50 (3%)	9.00 ± 0.82 (3%)	0.033 ± 0.0065 (26%)	4.8 ± 0.20 (13%)
1250	4.75 ± 2.87 (5%)	9.25 ± 1.50 (3%)	9.25 ± 1.50 (3%)	9.25 ± 1.50 (0%)	0.029 ± 0.0055* (34%)	4.4 ± 0.56* (21%)
5000	6.25 ± 1.71 (-25%)	9.00 ± 0.82 (5%)	9.00 ± 0.82 (5%)	9.00 ± 0.82 (3%)	0.022 ± 0.0031* (50%)	4.6 ± 0.21* (18%)

* Treatment group mean is significantly different from the control mean (Dunnett's test, $p<0.05$).

Table 8

Observed NOEC and Calculated ECx Estimates for
Tetrabromobisphenol A on Seedling Emergence, Survival, Height, and Dry Weight
in a 21-Day Seedling Emergence Test

Species	Endpoint (NOEC) (mg/kg)		Estimate	Lower 95% CL (mg/kg)	Upper 95% CL
Corn	Emergence (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Survival (5000)	LC_{25}	>5000	-	-
		LC_{50}	>5000	-	-
	Height (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Dry Weight (313)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
Cucumber	Emergence (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Survival (5000)	LC_{25}	>5000	-	-
		LC_{50}	>5000	-	-
	Height (20)	EC_{25}	131	8.03	2150
		EC_{50}	2600	506	13400
	Dry Weight (20)	EC_{25}	72.6	1.74	3040
		EC_{50}	1670	194	14400
Onion	Emergence (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Survival (5000)	LC_{25}	>5000	-	-
		LC_{50}	>5000	-	-
	Height (313)	EC_{25}	1950	668	5680
		EC_{50}	>5000	-	-
	Dry Weight (313)	EC_{25}	460	150	1410
		EC_{50}	4260	2240	8140
Ryegrass	Emergence (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Survival (5000)	LC_{25}	>5000	-	-
		LC_{50}	>5000	-	-
	Height (78)	EC_{25}	114	0.871	14900
		EC_{50}	1800	111	29300
	Dry Weight (78)	EC_{25}	48.5	0.202	11700
		EC_{50}	459	16.3	12900
Soybean	Emergence (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Survival (5000)	LC_{25}	>5000	-	-
		LC_{50}	>5000	-	-
	Height (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Dry Weight (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
Tomato	Emergence (5000)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Survival (5000)	LC_{25}	>5000	-	-
		LC_{50}	>5000	-	-
	Height (313)	EC_{25}	>5000	-	-
		EC_{50}	>5000	-	-
	Dry Weight (313)	EC_{25}	422	81.2	2200
		EC_{50}	5460	1960	15200

Appendix 1

Personnel Involved In the Study

The following key personnel were involved in the conduct or management of this study:

(1) Henry O. Krueger, Ph.D., Director, Aquatic Toxicology and Non-Target Plants
(2) John R. Porch, Supervisor, Non-Target Plants and Insects
(3) Andrew J. Brignole, Biologist
(4) Timothy Z. Kendall, Supervisor
(5) Willard B. Nixon, Director, Analytical Chemistry

Appendix 2

Study Protocol and Deviations

PROTOCOL

TETRABROMOBISPHENOL A: A TOXICITY TEST TO DETERMINE THE EFFECTS OF THE TEST SUBSTANCE ON SEEDLING EMERGENCE OF SIX SPECIES OF PLANTS

U.S. Environmental Protection Agency
Series 850 - Ecological Effects Test Guidelines
OPPTS Number 850.4100 and 850.4225

and

OECD Guideline for Testing of Chemicals
Proposal for Revision of Guideline 208: Terrestrial Non-Target Plant Tests

Submitted to

American Chemistry Council's
Brominated Flame Retardant Industry Panel
1300 Wilson Boulevard
Arlington, Virginia 22209

Wildlife International, Ltd.

8598 Commerce Drive
Easton, Maryland 21601
(410) 822-8600

September 5, 2001

Wildlife International, Ltd.

TETRABROMOBISPHENOL A: A TOXICITY TEST TO DETERMINE THE EFFECTS OF THE TEST SUBSTANCE ON SEEDLING EMERGENCE OF SIX SPECIES OF PLANTS

SPONSOR:	American Chemistry Council's Brominated Flame Retardant Industry Panel 1300 Wilson Boulevard Arlington, Virginia 22209
SPONSOR'S REPRESENTATIVE:	Ms. Wendy Sherman
TESTING FACILITY:	Wildlife International, Ltd. 8598 Commerce Drive Easton, Maryland 21601
STUDY DIRECTOR:	John R. Porch Senior Biologist
LABORATORY MANAGEMENT:	Henry O. Krueger, Ph.D. Director of Aquatic Toxicology & Non-Target Plants

FOR LABORATORY USE ONLY

Proposed Dates:

Experimental Start Date: November 27, 2001 Experimental Termination Date: December 18, 2001

Project No.: 439-102

Test Concentrations: 0 (control), 20, 78, 313, 1250, 5000 mg/kg

Test Substance No.: 5754 Reference Substance No. (if applicable): N/A

PROTOCOL APPROVAL

STUDY DIRECTOR	DATE: 7 Nov 2001
LABORATORY MANAGEMENT	DATE: 11/6/01
SPONSOR'S REPRESENTATIVE	DATE: September 10, 2001

PROTOCOL NO. 439/090401/SEEDEM-10/SU439

Wildlife International, Ltd.

INTRODUCTION

Wildlife International, Ltd. will conduct a toxicity test with six species of plants to determine the effects of a test substance on seedling emergence and early growth. The test will be conducted at the Wildlife International, Ltd. plant testing facility near Easton, Maryland. The six species to be tested include rye grass, onion, corn, soybean, cucumber, and tomato. The study will be performed based on procedures in the U.S. Environmental Protection Agency Series 850 - Ecological Effects Test Guidelines OPPTS Number 850.4100 (1) and 850.4225 (2) and in the OECD Guideline for Testing of Chemicals: Proposal for Revision of Guideline 208: "Terrestrial Non-target Plant Tests" (3). Raw data for all work performed at Wildlife International, Ltd. and a copy of the final report will be filed by project number in archives located on the Wildlife International, Ltd. site, or at an alternative location to be specified in the final report.

OBJECTIVE

The objective of this study is to determine the effect of Tetrabromobisphenol A (TBBPA) on the seedling emergence and growth of six species of plants.

EXPERIMENTAL DESIGN

The target test concentration(s) will be selected by the Sponsor in consultation with Wildlife International, Ltd., and will be based upon information such as the results of exploratory range-finding toxicity data, known toxicity data, physical/chemical properties of the test substance or other relevant information. If necessary, the test concentrations to be used for each species will be added to the protocol by amendment.

For each plant species tested, seeds will be planted and exposed to a series of five concentrations of the test substance. A negative control and, if appropriate, a solvent control group will be maintained concurrently. There will be four replicates for each treatment and control group. Each replicate will consist of a growth pot containing ten seeds. The replicates will be placed on a benchtop in a greenhouse according to a randomized design. Data collected from all replicates within a treatment group will be combined for calculating EC25 and EC50 values, as well as the no-observed-effect concentration (NOEC) and lowest-observed-effect concentration (LOEC).

Wildlife International, Ltd.

One application of each of the various treatments will be made by soil incorporation of the test substance prior to planting seeds. The duration of the in-life portion of the test will be 21 days following planting, during which time possible phytotoxic effects of the test substance on seedling emergence and growth of emerged seedlings will be evaluated.

MATERIALS AND METHODS

Test Substance

The test substance consisted of a composite of TBBPA samples received from three manufacturers. The material's identity and date received from each of the manufacturers is given below:

Manufacturer	Lot/Batch	Date Received	Wildlife International Ltd. Identification Number
Great Lakes Chemical Corporation	1008JE04B	August 16, 2001	5722
Albemarle Corporation	25115T-1	August 16, 2001	5721
Bromine Compounds, Ltd.	010040	August 31, 2001	5733

The composite test substance was assigned Wildlife International Ltd. identification number 5754 and was stored under ambient conditions.

The Sponsor is responsible for all information related to the test substance and agrees to accept any unused test substance and/or test substance containers remaining at the end of the study.

Test Soil Preparation

Concentrations of the test substance in the soil will be prepared on a dry weight basis (e.g., mg test chemical/kg dry soil). The test substance will be incorporated into the soil for each treatment level prior to planting.

Species to be Tested

The six species of plants used in this study were chosen because they are economically important, and are readily cultivated test organisms that are widely used in research. The common and scientific names for the species and their approximate planting depths are listed below:

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Monocots:		Planting Depth
Rye Grass	*Lolium perenne*	6 mm
Onion	*Allium cepa*	6 mm
Corn	*Zea mays*	2.0 - 2.5 cm
Dicots:		
Soybean	*Glycine max*	2.0 - 2.5 cm
Cucumber	*Cucumis sativa*	2.0 - 2.5 cm
Tomato	*Lycopersicon esculentum.*	6 mm

Seeds will be selected from a single size class within each species. The seeds of most plant species are sorted according to size by the supplier prior to being obtained by Wildlife International, Ltd. However, in some cases it may be necessary to further sort seeds to form a more uniform size class that reduces the potential for bias from differing seed sizes.

Seeds used in this study will not have been treated with fungicides, insecticides or repellents prior to test initiation. Seeds will be obtained from a producer or supplier such as Meyer Seed Company, Baltimore, Maryland. Any documentation provided from the supplier concerning the identification and history of the seeds used will be included in the study data.

Test Soil

Test plants will be grown in pots with a sandy-loam soil substrate. Analyses will be performed at least once annually to characterize the soil. A sample of soil representative of that used in this study will be sent to Agvise Laboratories, Inc., in Northwood, North Dakota, for analysis of the particle size distribution and organic matter content of the soil. Soil characterization will include, but may not be limited to, the determination of particle size distribution, organic matter content, and pH. Those items relevant to the conduct of the study will be discussed in the final report. The complete report from Agvise Laboratories, Inc. will be filed in the archives located at Wildlife International, Ltd. The results of the characterization will be stored in the archives located at the Wildlife International, Ltd. site, and those items relevant to the conduct of the study will be discussed in the final report.

PROTOCOL NO. 439/090401/SEEDEM-10/SU439

Wildlife International, Ltd.

Pesticide and Metal Screening

Neither the well water nor the artificial soil are expected to have contaminants present in quantities known to be capable of interfering with the study. Analyses will be performed at least once annually to determine the concentrations of selected organic and inorganic constituents of water and soil used in this study. Results of the analyses will be stored in the archives located on the Wildlife International Ltd. site.

Environmental Conditions

The test will be conducted within a greenhouse. Environmental conditions, including temperature and light intensity, will be controlled using a Wadsworth MicroStep/SA environmental control system. Temperature and relative humidity in the study room will be continuously monitored with a Campbell Scientific data logger, and daily conditions throughout the test will be reported. A photoperiod of at least 14 hours light will be maintained during the test. Artificial lighting may be used to lengthen short-day photoperiods or to supplement natural sunlight on overcast days.

Test Procedure

Growth pots will be filled with test or control soil, and ten seeds of one species will be planted per replicate. The seeds will be planted at the appropriate depth and will be approximately equally spaced. Seeds will be assigned to test and control groups and planted in growth pots uniquely identified with a minimum of the species name, project number, treatment group designation, and replicate. This method of application was chosen because contaminated soil is the most likely route of exposure to plants. After planting, the growth pots will be placed on benches in the greenhouse in a randomized configuration to minimize bias from microclimates which may exist within the greenhouse. Initial watering will be done to the soil surface after planting. Thereafter, water will be supplied to the growth pots by sub-irrigation to help ensure that sufficient water is available for seedling growth. Records of the days that watering occurs and source of water used will be kept in the study data.

The growth pots will be observed weekly after test initiation in order to determine the number of emerged seedlings. The in-life portion of the test will terminate twenty-one days after initiation, however, the test may be extended at the discretion of the study director for one or more species. If any portion of the test is extended, the duration of and the reason for the extension will be documented in the data and discussed in the final report. At the termination of the in-life portion of

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the test, height measurements and the condition of the emerged seedlings will be recorded. The height of each living seedling within a replicate will be determined in order to calculate the mean seedling height per replicate. The exact method used to measure height may vary with species, and will be described in the raw data and included in the final report.

At the in-life phase termination, the condition of seedlings will be assessed utilizing a rating system based upon Frans and Talbert (4). A numerical rating will be assigned to help characterize changes in the seedlings' morphology including necrosis, chlorosis, general development, or any other characteristic that may be deemed a response of the seedling to the treatment. Ratings may range from 0 to 100, 0 indicating normal seedling appearance, 100 indicating emerged seedlings that have died prior to test termination. Intermediate scores reflect the severity of changes in plant condition. After final observations are completed, plants will be clipped at soil level and the above-ground portion (shoots) of all living plants within each replicate will be dried to a constant weight. The mean shoot dry weight of each replicate will be calculated.

Sampling for Analytical Measurements

On each day of test substance application, samples of the test soils will be collected for the analysis of the test substance. Samples will be placed in an appropriate storage container (e.g., glass or polypropylene bottles) and stored under conditions designated by the Sponsor until analyzed. Triplicate samples will be collected from the soil of each test concentration to verify concentrations and demonstrate homogeneity in the soil.

Experimental Group	Day 0
Control	1
Solvent Control (if needed)	1
Level 1-Low Concentration	3
Level 2	3
Level 3	3
Level 4	3
Level 5-High Concentration	3
Total Number of Samples = 17	

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The above numbers of samples represent those collected from the test and do not include quality control (QC) samples such as matrix blanks and fortifications prepared and analyzed during the analytical validation phase of the study.

Analytical Method Development and Verification

Wildlife International, Ltd. will develop appropriate analytical methods and validate them for Sponsor approval prior to their use in support of this study. If the Sponsor provides an analytical method, Wildlife International, Ltd. will demonstrate its validity to the Sponsor before being used in support of this study. All analytical methods accepted for use in this study will be added by protocol amendment and described in detail as an Appendix to the final report."

Analytical Chemistry

Chemical analysis of the samples will be performed by Wildlife International, Ltd. using High Performance Liquid Chromatography (HPLC). The methodology used to analyze the test samples will be documented in the raw data and summarized in the final report. Maximum sample holding times, prior to analysis, will not exceed one week from the date of the collection of samples.

Data Analyses

This section includes proposed statistical analyses. Additional tests or analyses may be performed when warranted at the discretion of the Study Director or by Sponsor request.

An evaluation of potential effects of the test substance on seedling emergence, the growth of emerged seedlings, as characterized by shoot weight and height, and seedling condition will be made. Statistical analyses will include the determination of effect concentrations (EC estimates), and the determination of which treatment groups differ significantly from the control group(s).

The 25 and 50% effect concentrations and their 95% confidence intervals will be determined when warranted using an appropriate technique, such as Probit analysis or linear interpolation. When possible, EC estimates will be made for mean seedling emergence, mean shoot weight and height of seedlings at test termination.

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The data will be evaluated to determine the lowest-observed-effect concentration (LOEC), defined as the lowest concentration of test substance used in the study that shows an adverse effect on a variable of interest. The no-observed-effect-concentration (NOEC) will be defined as the maximum concentration which shows no adverse phytotoxic effects and below which no phytotoxic effects are manifested. Dunnett's two-tailed test will be used to determine significant differences from the control(s) at the 0.05 level of significance. Significant differences from the control, or their absence, may help establish the LOEC and NOEC.

All statistical analyses will be performed on a personal computer using commercially available statistical software programs (5, 6). The specific statistical tests and the programs used to perform the tests will be described in the final report of the study.

RECORDS TO BE MAINTAINED

Records to be maintained for data generated by Wildlife International, Ltd. will include but not be limited to:

1. Copy of signed protocol.
2. Identification and characterization of the test substance, if provided by the Sponsor.
3. Dates of initiation and termination of the test.
4. Test soil calculation and preparation.
5. Observations.
6. The methods used to analyze test substance concentrations and the results of analytical measurements.
7. Statistical calculations, if applicable.
8. Test conditions (temperature, humidity, etc.).
9. Calibration records for application equipment.
10. Copy of final report.

FINAL REPORT

A final report of the results of the study will be prepared by Wildlife International, Ltd. The report will include, but not be limited to, the following, when applicable.

1. Name and address of the facility performing the study.

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2. Dates upon which the study was initiated and completed, and the definitive experimental start and termination dates.
3. A statement of compliance signed by the Study Director addressing any exceptions to Good Laboratory Practice Standards.
4. The test substance identification including name, chemical abstract number or code number, strength, purity, composition, and other information provided by the Sponsor.
5. A copy of the protocol and protocol amendments.
6. Stability and solubility of the test substance under the conditions of administration, if provided by the Sponsor.
7. A description of the methods used to conduct the test.
8. A description of the test species, including the source and scientific name.
9. A description of the preparation of the test solutions.
10. The methods used to allocate seeds to test substrates and begin the test, the number of seeds and replicates per treatment, and the duration of the test.
11. A description of circumstances that may have affected the quality or integrity of the data.
12. The name of the Study Director and the names of other scientists, professionals, and supervisory personnel involved in the study.
13. A description of the transformations, calculations, and operations performed on the data, a summary and analysis of the biological data and analytical chemistry data, and a statement of the conclusions drawn from the analyses.
14. Statistical methods used to evaluate the data.
15. The signed and dated reports of each of the individual scientists or other professionals involved in the study, if applicable.
16. The location where raw data and final report are to be stored.
17. A statement prepared by the Quality Assurance Unit listing the dates that study inspections and audits were made and the dates of any findings reported to the Study Director and Management.
18. If it is necessary to make corrections or additions to a final report after it has been accepted, such changes will be made in the form of an amendment issued by the Study Director. The amendment will clearly identify the part of the final report that is being amended and the reasons for the amendment, and will be signed by the Study Director.

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CHANGING OF PROTOCOL

Planned changes to the protocol will be in the form of written amendments signed by the Study Director and the Sponsor's Representative. Amendments will be considered as part of the protocol and will be attached to the final protocol. Any other changes will be in the form of written deviations signed by the Study Director and filed with the raw data. All changes to the protocol will be indicated in the final report.

GOOD LABORATORY PRACTICES

This study will be conducted in accordance with Good Laboratory Practice Standards for EPA (40 CFR Part 160 and/or Part 792); OECD Principles of Good Laboratory Practice (ENV/MC/CHEM (98) 17); and Japan MAFF (11 NohSan, Notification No. 6283, Agricultural Production Bureau, 1 October 1999). Each study conducted by Wildlife International, Ltd. is routinely examined by the Wildlife International, Ltd. Quality Assurance Unit for compliance with Good Laboratory Practices, Standard Operating Procedures and the specified protocol. A statement of compliance with Good Laboratory Practices will be prepared for all portions of the study conducted by Wildlife International, Ltd. The Sponsor will be responsible for compliance with Good Laboratory Practices for procedures performed by other laboratories (e.g., residue analyses or pathology). Raw data for all work performed at Wildlife International, Ltd. and a copy of the final report will be filed by project number in archives located on the Wildlife International, Ltd. site or at an alternative location to be specified in the final report.

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REFERENCES

1 **U.S. Environmental Protection Agency.** 1996. Series 850- Ecological Effects Test Guidelines (*draft*), OPPTS Number 850.4100: Terrestrial Plant Toxicity, Tier I (Seedling Emergence).

2 **U.S. Environmental Protection Agency.** 1996. Series 850- Ecological Effects Test Guidelines (*draft*), OPPTS Number 850.4225: Terrestrial Plant Toxicity, Tier II (Seedling Emergence).

3 **OECD.** 1998. *Guideline for Testing of Chemicals, Proposal for Revision of Guideline 208: Terrestrial Non-target Plant Tests.* Organization for Economic Cooperation Development.

3 **Fraas, Robert E. and Ronald E. Talbert.** 1977. Design of Field Experiments and the Measurement and Analysis of Plant Responses. Pages 15-23 *in* B. Truelove, ed. Research Methods in Weed Science. Southern Weed Science Society, Auburn University, Alabama.

4 **SAS Institute, Inc.** 1989. SAS/STAT User's Guide , Version 6, Fourth Edition, Volume 1, Cary, NC, SAS Institute, Inc., 943 pp.

5 **Norberg-King, T.J.** 1993. *A Linear Interpolation Method for Sublethal Toxicity: The Inhibition Concentration (ICp) Approach (Version 2.0).* U.S. Environmental Protection Agency, Environmental Research Laboratory, Duluth, Minnesota.

Wildlife International, Ltd.

APPENDIX I

IDENTIFICATION OF TEST SUBSTANCE BY SPONSOR

To be Completed by Sponsor

I. Test Substance Identity (name to be used in the report): Tetrabromobisphenol-A

Reference Standard (if applicable): N/A

Test Substance Sample Code or Batch Number: Wildlife International, Ltd. No.5381

Test Substance Purity (% Active Ingredient): 98.91% Expiration Date: August 1, 2002

II. Test Substance Characterization

Have the identity, strength, purity and composition or other characteristics which appropriately define the test substance and reference standard been determined prior to its use in this study in accordance with GLP Standards? X Yes ___ No

III. Test Substance Storage Conditions

Please indicate the recommended storage conditions at Wildlife International, Ltd..

Ambient temperature; protect from light and moisture

Has the stability of the test substance under these storage conditions been determined in accordance with GLP Standards? X Yes ___ No

Other pertinent stability information:

N/A

IV. Toxicity Information:

Mammalian: Rat LD50 > 5 g/kg Mouse LD50: > 10 g/kg

Aquatic:	Invertebrate Toxicity (EC/LC50)	Fish Toxicity (LC50)
	N/A	N/A

Other Toxicity Information (including findings of chronic and subchronic tests):

V. Classification of the Compound:

_____Insecticide _____Herbicide _____Fungicide

_____Microbial Agent _____Economic Poison

Other: Halogenated flame retardant

DEVIATION FROM STUDY PROTOCOL

STUDY TITLE: Tetrabromobisphenol A: A Toxicity Test to Determine the Effects of the Test Substance on Seedling Emergence of Six Species of Plants

PROTOCOL NO.: 439/090401/SEEDEM-10/SU439 **DEVIATION NO.:** 1

SPONSOR: American Chemistry Council's Brominated Flame Retardant Industry Panel **PROJECT NO.:** 439-102

DATE(S) OF DEVIATION: As noted below

DEVIATION: November 14, 2001
Eleven seeds were planted in one replicate (Tomato 1250 mg/kg, C).

REASON:
Oversight. The replicate means were appropriately adjusted for the presence of the eleventh seedling. There will be no adverse impact on the study as a result of this deviation.

DEVIATION: November 14, 2001
The artificial soil used for the test was classified as a loam rather than a sandy-loam.

REASON:
Results of the soil characterization indicated that the sand content was slightly less than anticipated. There will be no adverse impact on the study as a result of this deviation.

DEVIATION: November 14, 2001
The initial watering for the test was not made on the soil surface.

REASON:
Surface watering is used to help surface-applied test substances move into the soil column. The procedure is not necessary for soil-incorporated applications. There will be no adverse impact on the study as a result of this deviation.

DEVIATION: November 21, 2001
Observations made on Day 7 included a general assessment of seedling condition.

REASON:
Oversight. Seedling conditions are routinely observed to monitor the progress of the test. There will be no adverse impact on the study as a result of this deviation.

DEVIATION: November 14, 2001

The analytical method was not amended to the protocol.

REASON:

The protocol states in the "Analytical Method Development and Verification" section that the analytical methods used would be amended to the protocol. However, the next section, "Analytical Methods," clearly identifies the method as HPLC. The first reference should have been removed from the protocol upon the inclusion of the "Analytical Methods" section. There will be no adverse impact on the study as a result of this deviation.

STUDY DIRECTOR — DATE 5 March 02

LABORATORY MANAGEMENT — DATE 5 March 02

Appendix 3
Certificate of Analysis

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PFR 11/02/01

ALBEMARLE CORPORATION
RESEARCH AND DEVELOPMENT DEPARTMENT

FINAL REPORT ON THE CHEMICAL CHARACTERIZATION (IDENTITY, PURITY AND HOMOGENEITY) OF TETRABROMOBISPHENOL-A (TBBPA), WIL TEST SUBSTANCE 5754, COMPOSITED FROM WIL 5733, 5721 AND 5722

I.	Reference Protocol Number:	TBBPA-10-01-2001
II.	Sponsor:	American Chemistry Council Brominated Flame Retardant Industry Panel 1300 Wilson Boulevard Arlington, Virginia 22209 Study Monitor: Wendy K. Sherman
III.	Analytical Testing Facilities:	Albemarle Corporation Albemarle Technical Center 8000 GSRI Avenue Baton Rouge, LA 70820 Study Chemist: Paul F. Ranken, Ph. D.
IV.	Dates of Performance:	Study Initiation Date: September 28, 2001 Study Completion Date: November 2, 2001
V.	Test Article:	Tetrabromobisphenol-A (WIL Test Substance 5754). The test article is a composite of WIL #5733, 5721, and 5722 which are samples of commercial products from Albemarle Corporation, Great Lakes Chemical Corporation and the Dead Sea Bromine Group. The composite was prepared by Wildlife International Ltd., Easton, MD 21601.
VI.	Objective/Methodology:	This study was initiated to confirm the identity of the test article, to demonstrate the homogeneity of the test article and to demonstrate the purity of the test article. The identity of one sample of the test article, designated Characterization Sample, was confirmed by Fourier Transform Infrared Spectroscopy using SOP No. ARS-284-R4. In this procedure, the sample infrared spectrum was compared to a standard reference spectrum

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of TBBPA. The homogeneity of the test article was demonstrated by determining the purity of six separate test article samples which were taken from the top, middle and bottom of the right side of the bulk container and from the top, middle and bottom of the left side of the bulk container. The purity (area % TBBPA) of the six samples was determined by High Performance Liquid Chromatography (HPLC) using SOP No. ARS-443-R1. The homogeneity of the test article was established by demonstrating that all six samples had the same purity (< 5% difference of the TBBPA area % for each sample compared to the average TBBPA area % of the six samples). The six test article samples were further characterized by measuring the concentration (area%) of three potential impurities: tribromophenol, tribromobisphenol-A and o,p'-tetrabromobisphenol-A. Chain of Custody and sample handling were conducted according to established standard operating procedures.

VII. Results:

Table 1 and table 2 contain the test article analytical data from the study. The identity of the test article was confirmed by Fourier Transform Infrared Spectroscopy. The homogeneity of the test article was confirmed by HPLC analysis; all six test article samples had the same purity (<5% difference of the TBBPA area% for each sample compared to the average TBBPA area% of the six samples). Further characterization of the six test article samples was accomplished by measuring the concentration of three expected impurities. There were no circumstances that may have affected the quality or integrity of the data.

VIII. Regulatory Requirements:

The study conformed to the requirements of EPA TSCA (40 CFR Part 792) Good Laboratory Practice Regulations and the

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OECD [C(97)186/Final] Good Laboratory Practice Regulations.

IX. Data/Record Retention:

All original log books, spectra and reports will be forwarded to the Quality Assurance Unit (QAU) for a final review prior to filing in the designated Health and Environment archives at Albemarle Corporation, Health and Environment Department, 451 Florida Street, Baton Rouge, LA 70801.

Paul F. Ranken November 2, 2001

Paul F. Ranken, Ph. D. DATE
STUDY CHEMIST

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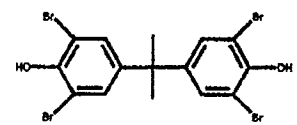
4

CONCLUSIONS AND TEST ARTICLE ANALYTICAL DATA. 1.

CHEMICAL NAME: Tetrabromobisphenol-A
C.A.S. No.: 79-94-7
MOLECULAR FORMULA: $C_{15}H_{12}Br_4O_2$
PHYSICAL FORM: White Powder
CHEMICAL STRUCTURE:



ANALYSIS	RESULTS			ANALYSIS DATES	ANALYST
FT-IR	The sample FT-IR spectrum matched that of the reference spectrum. All spectra are on file with the original data.			10/12/01	W. T. Cobb
HPLC					
Sample	Purity (area% TBBPA)	Average	Difference (%) from average		
middle right	99.14	99.17	<5%	10/25/01	J. S. Arroyave
middle left	99.18	99.17	<5%	10/25/01	J. S. Arroyave
bottom right	99.09	99.17	<5%	10/25/01	J. S. Arroyave
top right	99.19	99.17	<5%	10/25/01	J. S. Arroyave
top left	99.16	99.17	<5%	10/25/01	J. S. Arroyave
bottom left	99.23	99.17	< 5%	10/25/01	J. S. Arroyave

CONCLUSION: Based on these analytical data, the test article identity was confirmed as tetrabromobisphenol-A. The composite sample was shown to be homogeneous with a purity of 99.17%.

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Conclusions and Test Article Data. 2.

Characterization of Test Article by HPLC (Area%)

	TBBPA	Tribromophenol	TriBPA	o,p'-TBBPA
Middle Right	99.14	Not detected	0.82	0.04
Middle Left	99.18	Not detected	0.76	0.06
Bottom Right	99.09	Not detected	0.84	0.06
Top Right	99.19	Not detected	0.78	0.04
Top Left	99.16	Not detected	0.8	0.04
Bottom Left	99.23	Not detected	0.72	0.04

Appendix 4

Analysis of Tetrabromobisphenol A (TBBPA) in Soil Samples From a Seedling Emergence Test

Analytical Method

The method used for the analysis of Tetrabromobisphenol A (TBBPA) in soil samples was developed by Wildlife International, Ltd. Samples were processed as follows:

Soil samples (10.0 g) were weighed into French square bottles. To each sample, 100 mL of methanol acidified with phosphoric acid was added and samples were sonically disrupted for approximately 10 minutes at a setting of approximately 60. Following disruption the samples were allowed to cool undisturbed for approximately 5 minutes. An aliquot of each sample was transferred into a microcentrifuge tube and centrifuged for approximately 5 minutes. The methanolic extract was volumetrically diluted using 50% methanol : 50% NANOpure® water. An aliquot of each diluted extract was transferred to an autosampler vial for immediate HPLC analysis. A method flowchart for the analysis of sediment samples is provided in Figure 1

Concentrations of TBBPA were determined by high performance liquid chromatography using a Hewlett-Packard Model 1100 High Performance Liquid Chromatograph (HPLC) equipped with an Agilent Series 1100 Variable Wavelength Detector. Chromatographic separations were achieved using a YMC Pack ODS AM analytical column (150 x 4.6 mm, 3 µm particle size). The instrument parameters are summarized in Table 1 and a method flow chart is provided in Figure 1.

Calibration Curve

Calibration standards containing TBBPA ranging from 0.100 to 1.00 mg/L were prepared in 50% methanol : 50% NANOpure® water and analyzed with the sample set. A linear regression analysis was generated using the peak area responses versus the respective concentrations of the calibration standards. A representative calibration curve for TBBPA is presented in Figure 2. The concentration of TBBPA in the samples was determined by substituting the peak area responses into the linear regression equation. Representative chromatograms of low and high calibration standards for TBBPA are presented in Figures 3 and 4, respectively.

Example Calculations

A sample calculation of sample number 439-102-16 having a nominal concentration of 5000 mg/Kg TBBPA in the soil follows:

Initial mass (M_1) : 10.0 grams
Initial final volume (V_1): 100 mL
Secondary dilution (V_2): 0.150 → 100 mL
Dilution Factor (V_1/M_1) x (V_2) = 6667
Peak Area: 43.89433
Linear regression equation:
Slope: 60.9319
$Y_{Intercept}$: -0.2275

$$\text{Concentration TBBPA (mg/Kg)} = \frac{(\text{Peak area} - Y_{intercept}) \times \text{Dilution factor}}{\text{Slope}}$$

$$\text{Concentration TBBPA (mg/Kg)} = \frac{(43.89433 + 0.2275) \times 6667}{60.9319}$$

$$\text{Concentration TBBPA (mg/Kg)} = 4828 \text{ mg/Kg}^*$$

$$\text{Percent of Nominal Conc.} = \frac{4828 \text{ mg/Kg}}{5000 \text{ mg/Kg}} \times 100$$

$$\text{Percent of Nominal Conc.} = 96.6\%^*$$

* Results were generated using Excel 2000 in the full precision mode. Manual calculations may differ slightly.

RESULTS

Sample Analysis

Soil samples were collected from a study designed to determine the effects of Tetrabromobisphenol A (TBBPA) on the seedling emergence of non-target plants. Samples were processed on November 15, 2001 and analyzed on November 15 and 16, 2001. Concentrations of TBBPA in soil in the range of 20 to 5000 mg/Kg yielded percent recoveries from 67.3 to 96.6%. The mean percent recoveries of triplicate samples at 20, 78, 313, 1250 and 5000 mg/Kg were 80.0, 82.1, 80.8, 84.7 and 91.9%, respectively. Quality control samples fortified at 15.0, 100 and 5000 mg/Kg yielded percent recoveries of 97.9, 94.9 and 99.4%, respectively. The control sample was devoid of TBBPA. Analytical results for all exposure and quality control samples are presented in Table 2. A chromatogram of a control sample (439-102-1) is presented in Figure 5. A representative chromatogram of a soil extract (439-102-16) is presented in Figure 6.

Table 1

HPLC Operational Parameters

INSTRUMENT:	Hewlett-Packard Model 1100 High Performance Liquid Chromatograph with an Agilent Series 1100 Variable Wavelength Detector			
ANALYTICAL COLUMN:	YMC Pack ODS AM (150 mm x 4.6 mm, 3 µm particle size)			
FLOW RATE:	1.000 mL/min			
OVEN TEMPERATURE:	40°C			
MOBILE PHASE:	Solvent A: 0.1% H_3PO_4 Solvent B: CH_3CN			
GRADIENT:	Time (min.)	% A	%B	Flow (mL/min)
	0.01	90.0	10.0	1.000
	1.00	90.0	10.0	1.000
	8.00	5.00	95.0	1.000
	10.00	5.00	95.0	1.000
	10.10	90.0	10.0	1.000
	15.00	90.0	10.0	1.000
INJECTION VOLUME:	100.0 µL			
TBBPA RETENTION TIME:	Approximately 10.9 minutes			
PRIMARY ANALYTICAL WAVELENGTH:	286 nm			

Table 2

Measured Concentration of Tetrabromobisphenol A in Samples from a Seedling Emergence Study

Nominal Test Concentration (mg/Kg)	Sample Number (439-102)[1]	Measured Concentration (mg/Kg)[2,3]	Percent of Nominal[3] (%)	Mean Concentration (mg/Kg)	Mean Percent of Nominal (%)
0.0	MAB-1	< LOQ	--	--	--
15.0	MAS-1	14.7	97.9	--	--
100	MAS-2	94.9	94.9	--	--
5000	MAS-3	4970	99.4	--	--
Negative Control	1	< LOQ	--	--	--
20	2	15.1	75.7	16	80.0
	3	15.9	79.7		
	4	16.7	83.5		
78	5	61.5	78.8	64	82.1
	6	71.0	91.0		
	7	60.1	77.1		
313	8	211	67.3	253	80.8
	9	287	91.5		
	10	261	83.3		
1250	11	970	77.6	1059	84.7
	12	1047	83.8		
	13	1161	92.9		
5000	14	4289	85.8	4595	91.9
	15	4669	93.4		
	16	4828	96.6		

[1] MAB refers to an unfortified matrix blank. MAS refers to a fortified quality control sample.

[2] The limit of quantitation (LOQ) was defined as 10.0 mg/Kg, calculated as the product of the lowest calibration standard concentration (0.100 mg/L) and the dilution factor of the matrix blank sample (100).

[3] Results were generated using Excel 2000 in the full precision mode. Manual calculations may differ slightly.

METHOD OUTLINE FOR THE PROCESSING OF
TETRABROMOBISPHENOL A IN SOIL

Rinse 8 oz. French square bottles with methanol

↓

Transfer the requisite volume of sediment to the French square bottles. Fortify samples with the appropriate Tetrabromobisphenol A stock solution or the test substance. Unfortified sediment will serve as the matrix blank samples.

↓

Using a class A volumetric pipette, add 100 mL of acidified methanol to each sample.

↓

Sonic disrupt the samples for approximately 10 minutes at a setting of approximately 60.

↓

Allow the samples to settle and cool for approximately five minutes.

↓

Transfer an aliquot of each sample into microcentrifuge tubes and centrifuge for approximately five minutes.

↓

Volumetrically dilute the centrifuged methanol extract using the requisite volume of 50% methanol : 50% water.

↓

Transfer an aliquot of each diluted extract to an autosampler vial. Submit samples for HPLC/UV analysis.

Figure 1. A method flowchart for the analysis of TBBPA in soil samples.

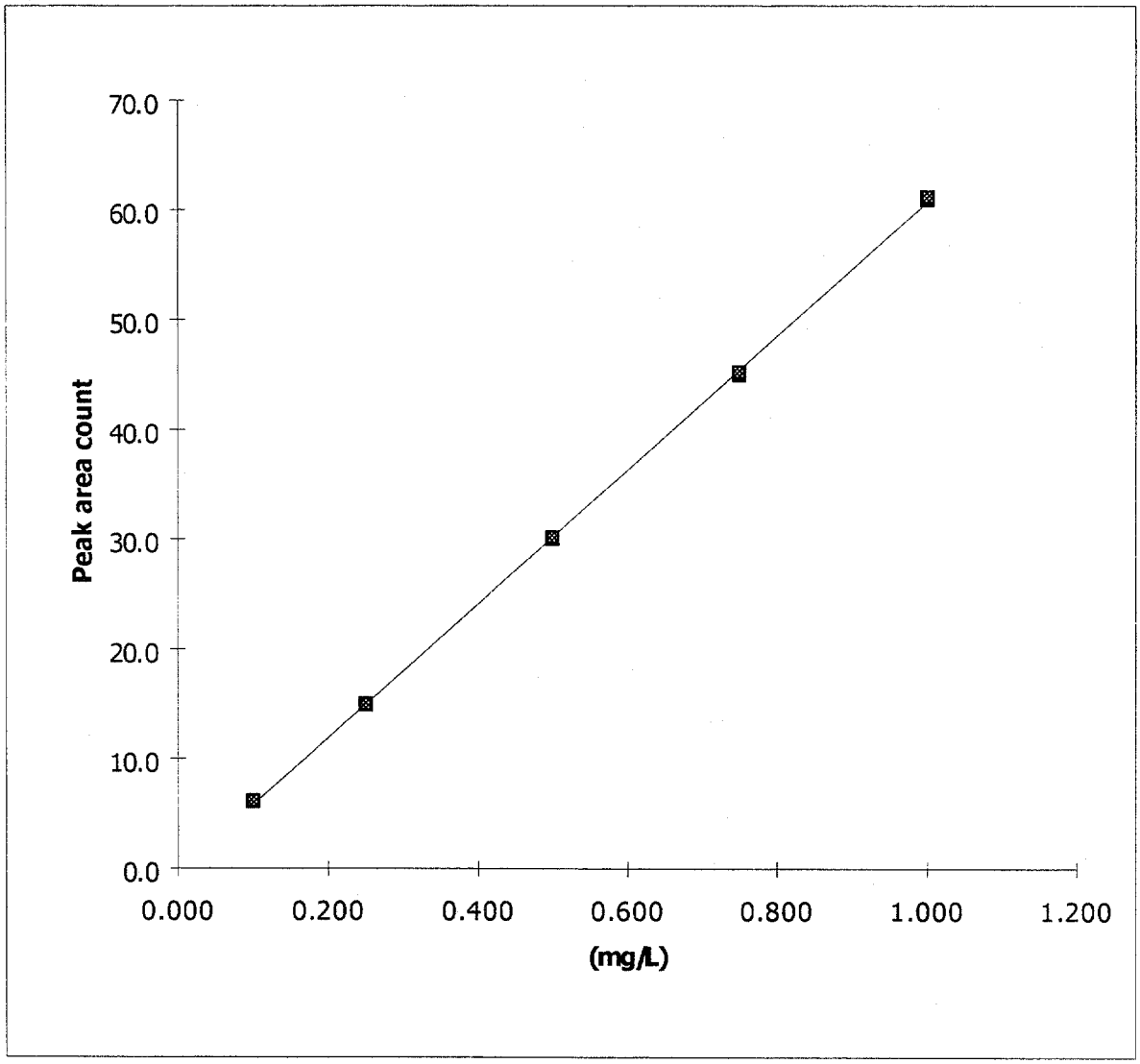


Figure 2. A representative calibration curve for TBBPA. Slope = 60.9319; Y-Intercept = -0.2275; $r^2 = 0.9998$.

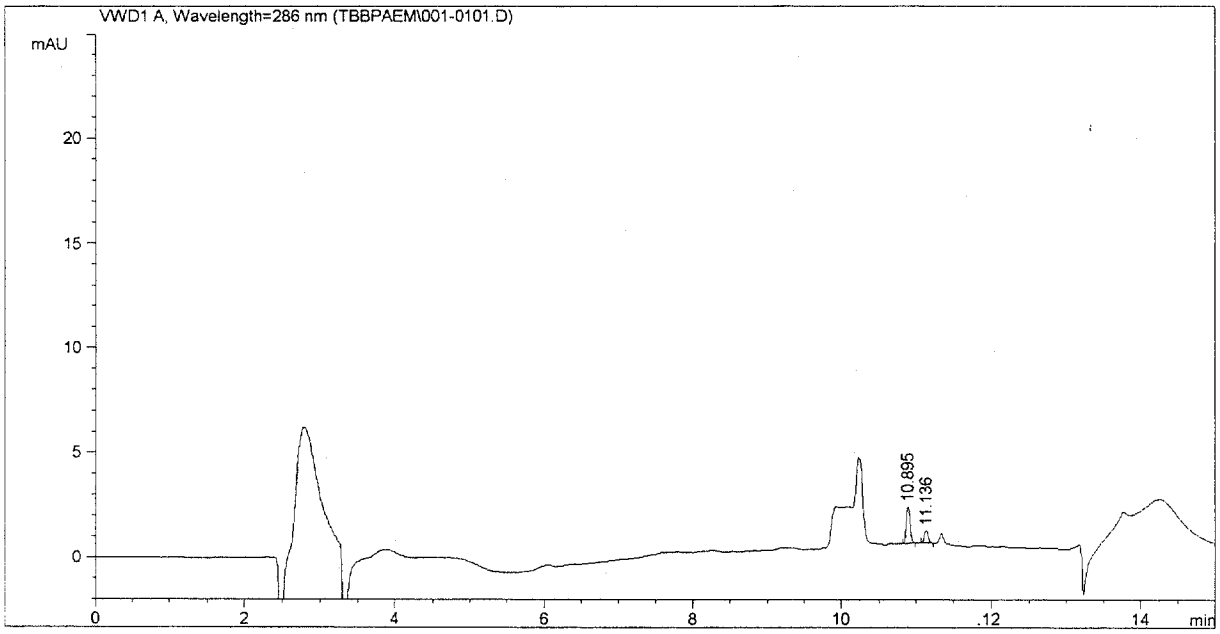


Figure 3. A representative chromatogram of a 0.100 mg/L calibration standard.

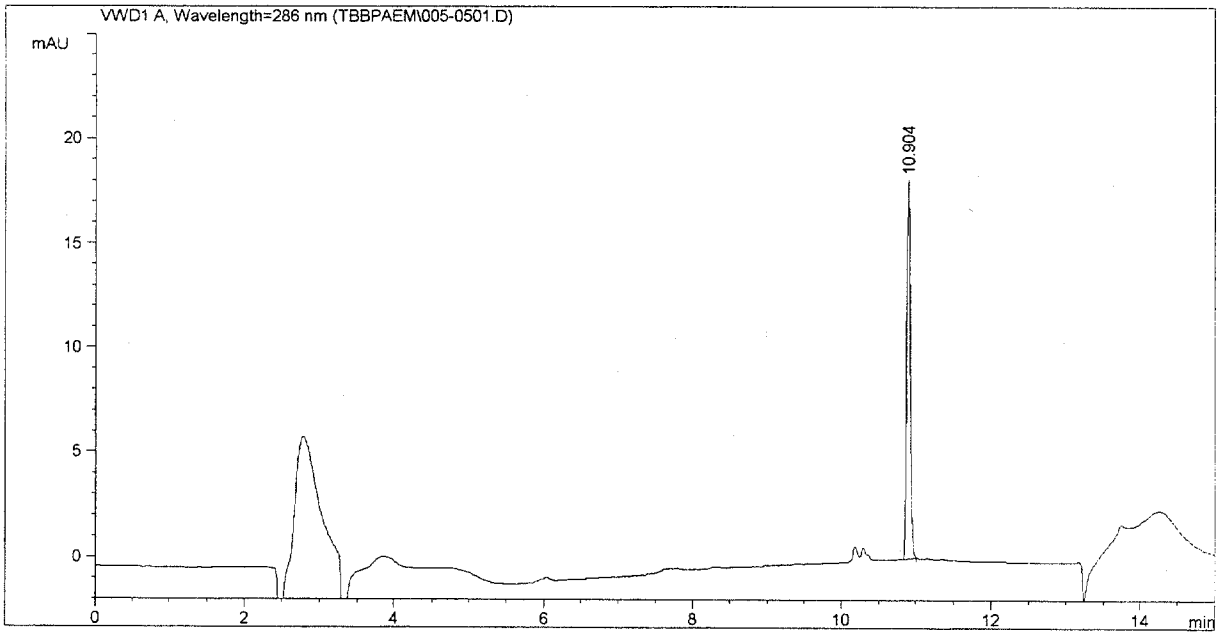


Figure 4. A representative chromatogram of a 1.00 mg/L calibration standard.

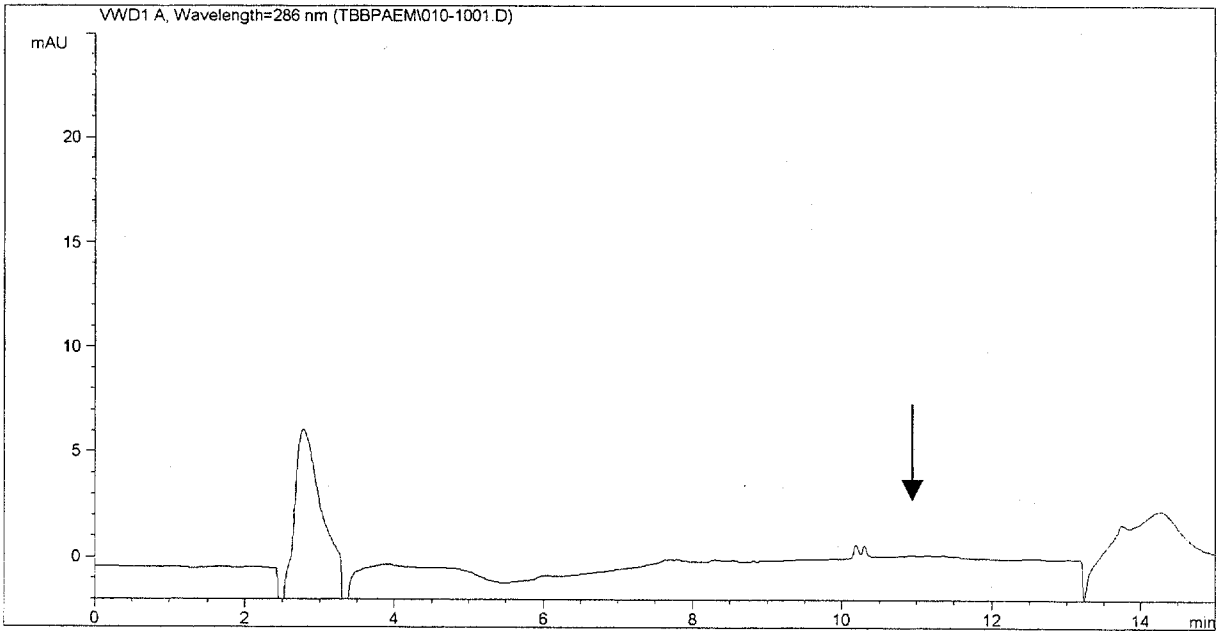


Figure 5. A representative chromatogram of a control sample (439-102-1). The arrow indicates the retention time of TBBPA.

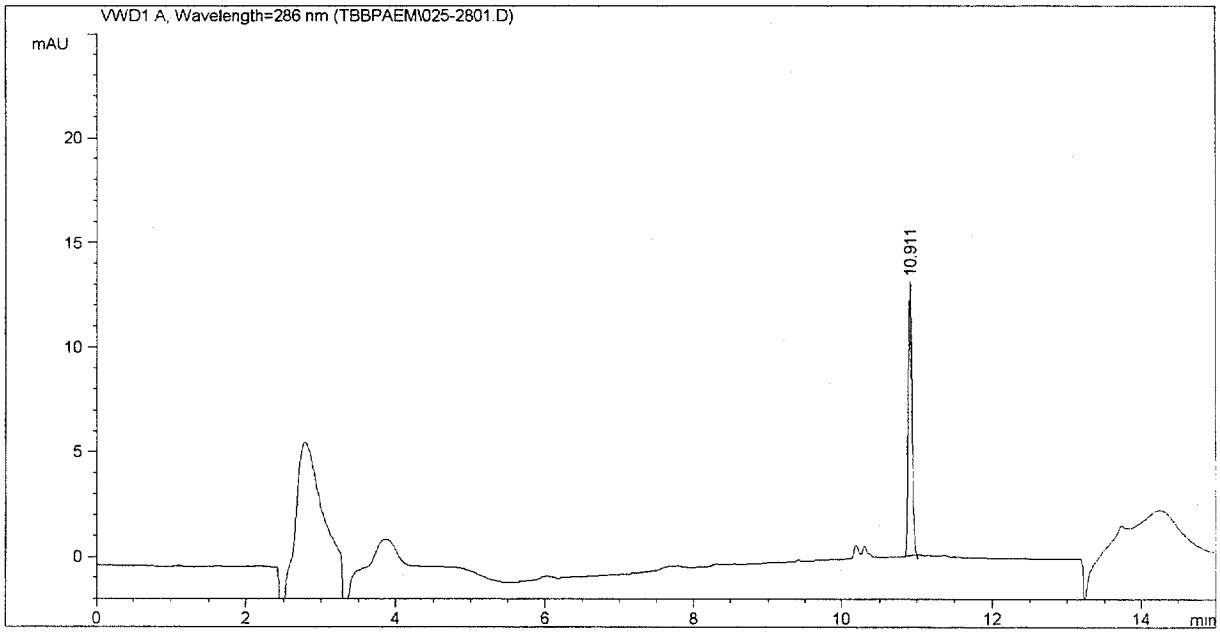


Figure 6. A representative chromatogram of a soil extract (439-102-16, 5000 mg/Kg nominal concentration).

Appendix 5

Environmental Conditions

Date	Temperature (°C)			Relative Humidity (%)		
	Minimum	Maximum	Mean	Minimum	Maximum	Mean
11/14/01[1]	16	26	20	17	72	39
11/15/01	16	27	21	20	63	39
11/16/01	17	29	21	21	63	42
11/17/01[1]	16	26	20	27	63	44
11/18/01[1]	16	27	20	21	54	38
11/19/01	16	27	21	30	81	50
11/20/01	16	27	20	13	81	40
11/21/01[1]	16	27	20	12	51	33
11/22/01	16	28	20	14	47	32
11/23/01[1]	16	27	20	16	57	34
11/24/01	17	25	21	46	75	60
11/25/01	18	26	21	42	83	64
11/26/01[1]	17	27	21	31	85	59
11/27/01	17	25	20	35	75	53
11/28/01	18	26	21	47	80	66
11/29/01	18	26	21	49	81	68
11/30/01	18	26	22	54	85	70
12/01/01	17	28	21	36	83	61
12/02/01[2]	16	27	20	22	55	39
12/03/01[1]	16	32	21	19	55	37
12/04/01	16	27	21	20	57	40
12/05/01	17	29	21	17	59	40

[1] Indicates days on which all species were watered.
[2] Indicates days on which only cucumber, soybean and ryegrass were watered.

Appendix 6.1

Corn Emergence

Day 7

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	8	8	10	*4*	9.00	1.15
20 mg/kg	10	10	10	10	*4*	10.00	0.00
78 mg/kg	10	8	9	9	*4*	9.00	0.82
313 mg/kg	10	9	10	7	*4*	9.00	1.41
1250 mg/kg	9	10	8	9	*4*	9.00	0.82
5000 mg/kg	10	10	9	10	*4*	9.75	0.50

Day 14

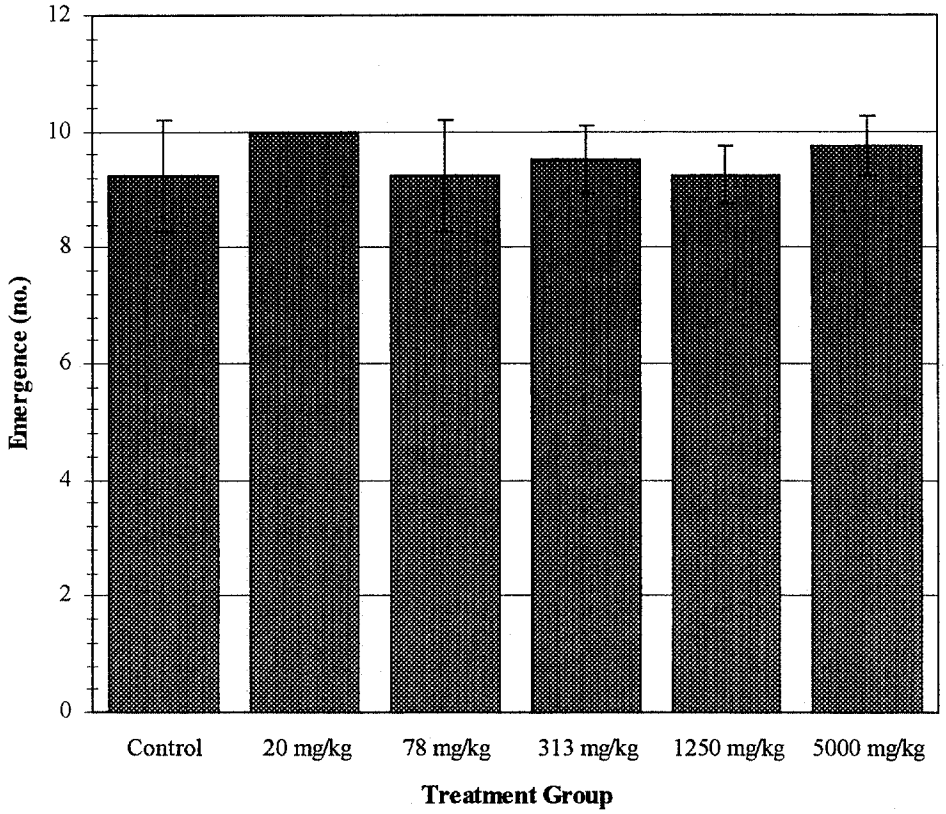
Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	8	9	10	*4*	9.25	0.96
20 mg/kg	10	10	10	10	*4*	10.00	0.00
78 mg/kg	10	8	10	9	*4*	9.25	0.96
313 mg/kg	10	9	10	9	*4*	9.50	0.58
1250 mg/kg	9	10	9	9	*4*	9.25	0.50
5000 mg/kg	10	10	9	10	*4*	9.75	0.50

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	8	9	10	*4*	9.25	0.96
20 mg/kg	10	10	10	10	*4*	10.00	0.00
78 mg/kg	10	8	10	9	*4*	9.25	0.96
313 mg/kg	10	9	10	9	*4*	9.50	0.58
1250 mg/kg	9	10	9	9	*4*	9.25	0.50
5000 mg/kg	10	10	9	10	*4*	9.75	0.50

Appendix 6.2

Mean Corn Emergence on Day 21



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

Appendix 6.3

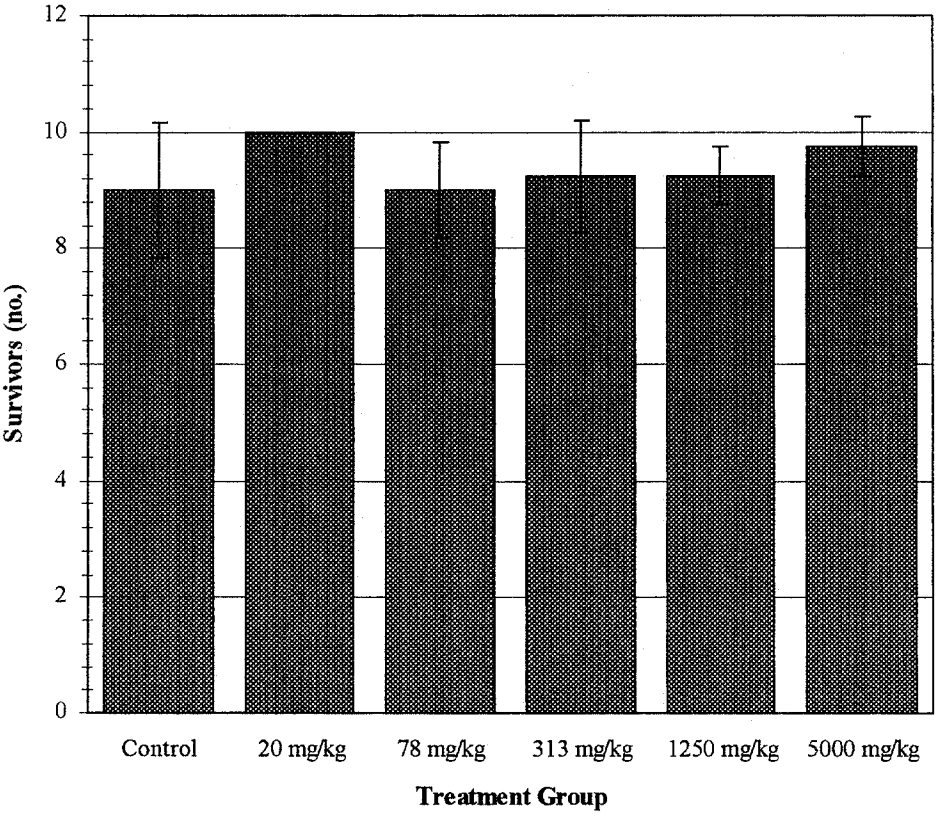
Corn 21-Day Survival

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	8	8	10	*4*	9.00	1.15
20 mg/kg	10	10	10	10	*4*	10.00	0.00
78 mg/kg	10	8	9	9	*4*	9.00	0.82
313 mg/kg	10	9	10	8	*4*	9.25	0.96
1250 mg/kg	9	10	9	9	*4*	9.25	0.50
5000 mg/kg	10	10	9	10	*4*	9.75	0.50

Appendix 6.4

Mean Corn 21-Day Survival



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

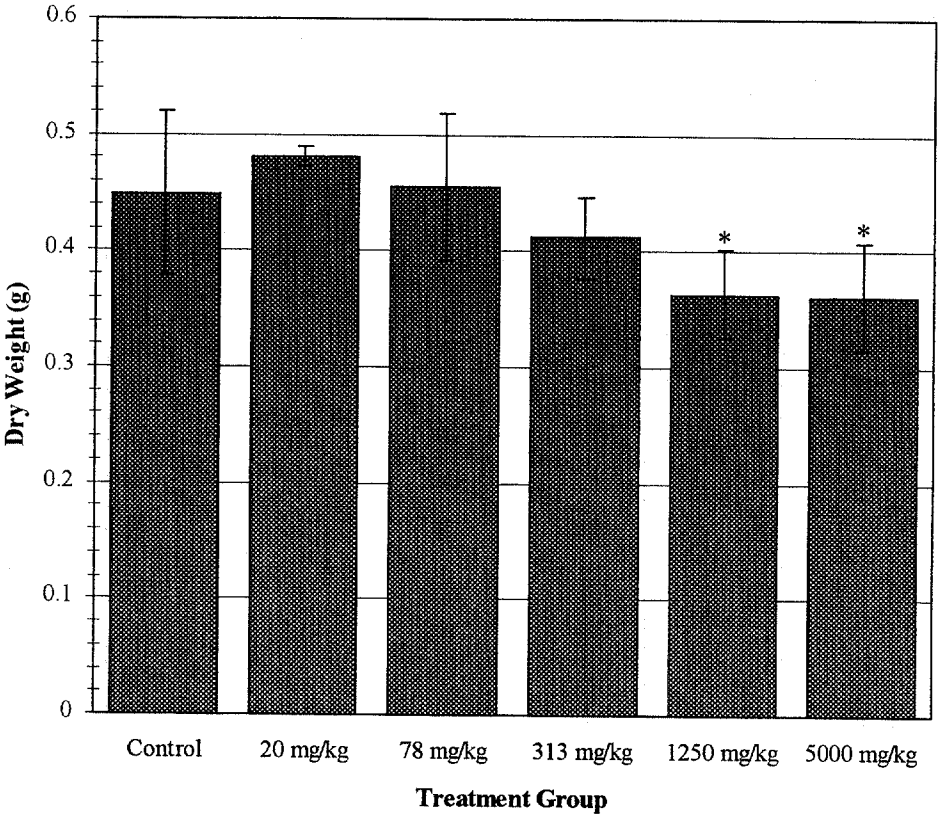
Appendix 6.5

Corn Mean Seedling Dry Weight, Day 21

Treatment Group	Mean Weight (g) per Plant of Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	0.49	0.49	0.47	0.34	*4*	0.45	0.071
20 mg/kg	0.48	0.49	0.48	0.47	*4*	0.48	0.008
78 mg/kg	0.42	0.55	0.43	0.41	*4*	0.45	0.063
313 mg/kg	0.43	0.42	0.43	0.36	*4*	0.41	0.036
1250 mg/kg	0.32	0.36	0.37	0.41	*4*	0.36	0.038
5000 mg/kg	0.35	0.42	0.31	0.36	*4*	0.36	0.046

Appendix 6.6

Mean Corn Dry Weight



* Treatment group mean is significantly different from the control mean (Dunnett's test, $p<0.05$).

Appendix 6.7

Corn Seedling Height on Day 21

Treatment Group	Replicate	Height (cm) for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	42	41	33	48	42	38	37	45	36	48	*10*	41.0	5.06
	B	.	.	46	52	40	43	26	32	51	45	*8*	41.9	9.00
	C	.	.	42	40	44	46	37	46	40	48	*8*	42.9	3.76
	D	35	39	40	18	33	34	31	32	35	32	*10*	32.9	6.01
20 mg/kg	A	39	50	44	49	44	43	38	42	49	32	*10*	43.0	5.64
	B	48	42	42	37	48	44	45	39	52	41	*10*	43.8	4.57
	C	46	42	38	44	50	34	45	51	50	42	*10*	44.2	5.47
	D	42	44	43	47	45	41	48	50	44	51	*10*	45.5	3.37
78 mg/kg	A	37	39	35	32	45	38	38	41	40	41	*10*	38.6	3.57
	B	40	40	50	52	54	61	29	44	.	.	*8*	46.3	10.04
	C	43	46	44	47	44	39	35	37	38	.	*9*	41.4	4.28
	D	.	42	33	42	41	43	42	43	41	30	*9*	39.7	4.74
313 mg/kg	A	44	29	42	38	42	46	42	34	38	47	*10*	40.2	5.55
	B	.	34	49	41	42	35	40	33	45	31	*9*	38.9	6.03
	C	49	51	46	44	37	42	40	39	30	41	*10*	41.9	6.08
	D	.	.	41	37	42	39	34	23	27	43	*8*	35.8	7.30
1250 mg/kg	A	.	39	39	33	35	29	26	30	35	34	*9*	33.3	4.39
	B	33	38	46	38	39	43	34	35	35	33	*10*	37.4	4.35
	C	.	36	37	38	36	29	36	33	47	28	*9*	35.6	5.55
	D	.	33	37	42	44	28	38	33	38	41	*9*	37.1	5.06
5000 mg/kg	A	18	35	43	36	40	47	39	42	30	26	*10*	35.6	8.76
	B	39	41	35	43	52	41	37	41	35	19	*10*	38.3	8.35
	C	.	33	35	31	31	32	38	36	35	42	*9*	34.8	3.60
	D	38	32	16	45	42	27	37	37	39	32	*10*	34.5	8.32

The "." symbol indicates that the seedling either did not emerge or died prior to measurement.

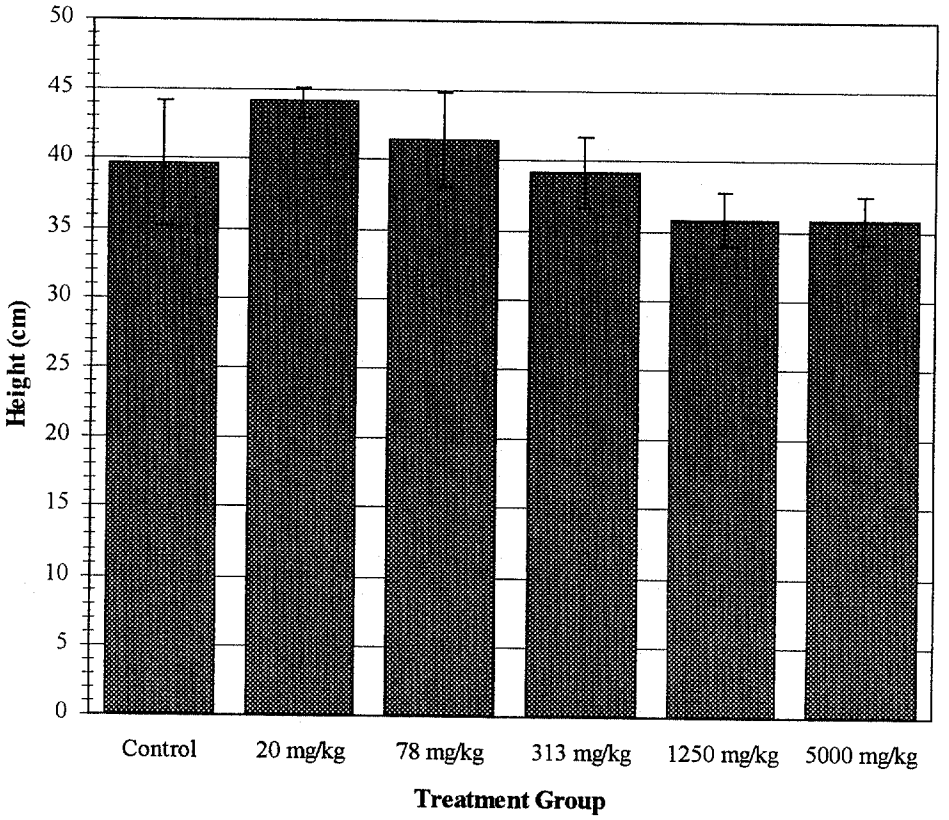
Appendix 6.8

Corn Mean Seedling Height on Day 21

Treatment Group	Mean Height (cm) for Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	41.0	41.9	42.9	32.9	*4*	39.7	4.57
20 mg/kg	43.0	43.8	44.2	45.5	*4*	44.1	1.04
78 mg/kg	38.6	46.3	41.4	39.7	*4*	41.5	3.38
313 mg/kg	40.2	38.9	41.9	35.8	*4*	39.2	2.60
1250 mg/kg	33.3	37.4	35.6	37.1	*4*	35.9	1.86
5000 mg/kg	35.6	38.3	34.8	34.5	*4*	35.8	1.73

Appendix 6.9

Mean Corn Height on Day 21



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$)

Appendix 6.10

Corn Seedling Condition, Day 21

Treatment Group T	Replicate	Condition (score.sign)[1] for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	C	.	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	11	33.3
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
20 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
78 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	.	.	*8*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	100.-	*10*	10	31.6
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
313 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	.	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	11	33.3
1250 mg/kg	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
5000 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0

[1]The "." symbol indicates that the seedling did not emerge. A score of 0 indicates a normal seedling, while a score of 100 indicates a dead seedling. Intermediate scores are assigned to indicate the relative severity of observed signs of toxicity.

Appendix 7.1

Cucumber Emergence

Day 7

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	8	7	10	9	*4*	8.50	1.29
20 mg/kg	7	9	7	10	*4*	8.25	1.50
78 mg/kg	7	9	9	7	*4*	8.00	1.15
313 mg/kg	9	8	10	6	*4*	8.25	1.71
1250 mg/kg	9	10	7	10	*4*	9.00	1.41
5000 mg/kg	7	9	7	4	*4*	6.75	2.06

Day 14

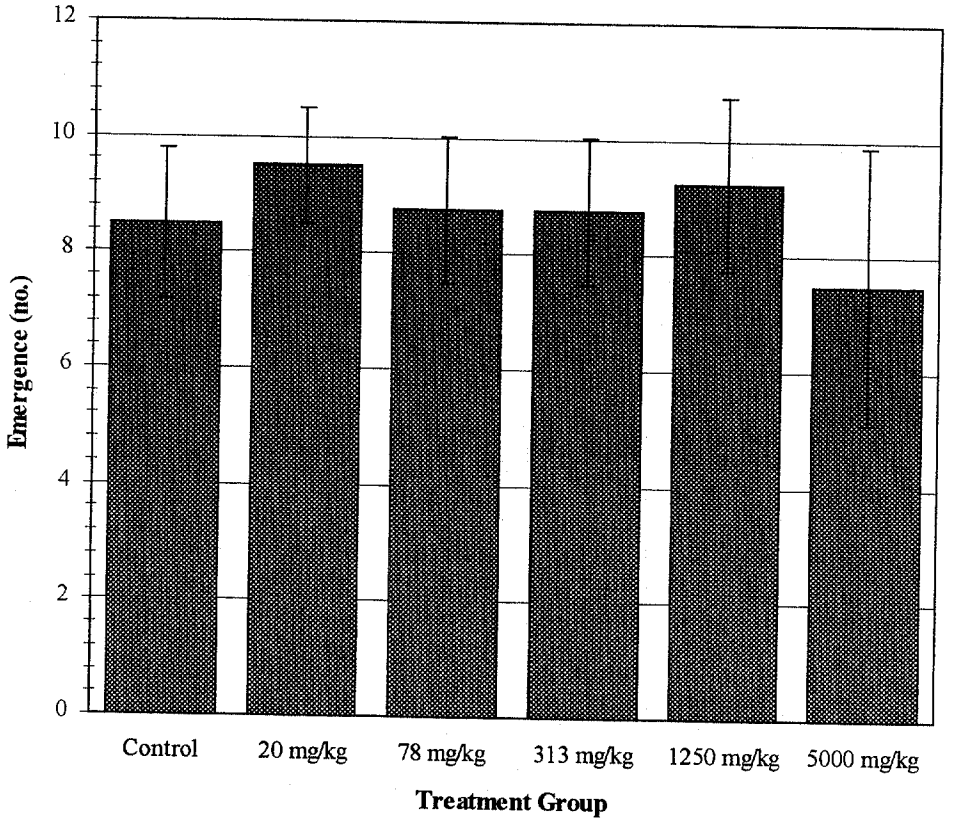
Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	8	7	10	9	*4*	8.50	1.29
20 mg/kg	8	10	10	10	*4*	9.50	1.00
78 mg/kg	7	9	10	8	*4*	8.50	1.29
313 mg/kg	9	9	10	7	*4*	8.75	1.26
1250 mg/kg	9	10	7	10	*4*	9.00	1.41
5000 mg/kg	9	9	8	4	*4*	7.50	2.38

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	8	7	10	9	*4*	8.50	1.29
20 mg/kg	8	10	10	10	*4*	9.50	1.00
78 mg/kg	7	9	10	9	*4*	8.75	1.26
313 mg/kg	9	9	10	7	*4*	8.75	1.26
1250 mg/kg	10	10	7	10	*4*	9.25	1.50
5000 mg/kg	9	9	8	4	*4*	7.50	2.38

Appendix 7.2

Mean Cucumber Emergence on Day 21



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$)

Appendix 7.3

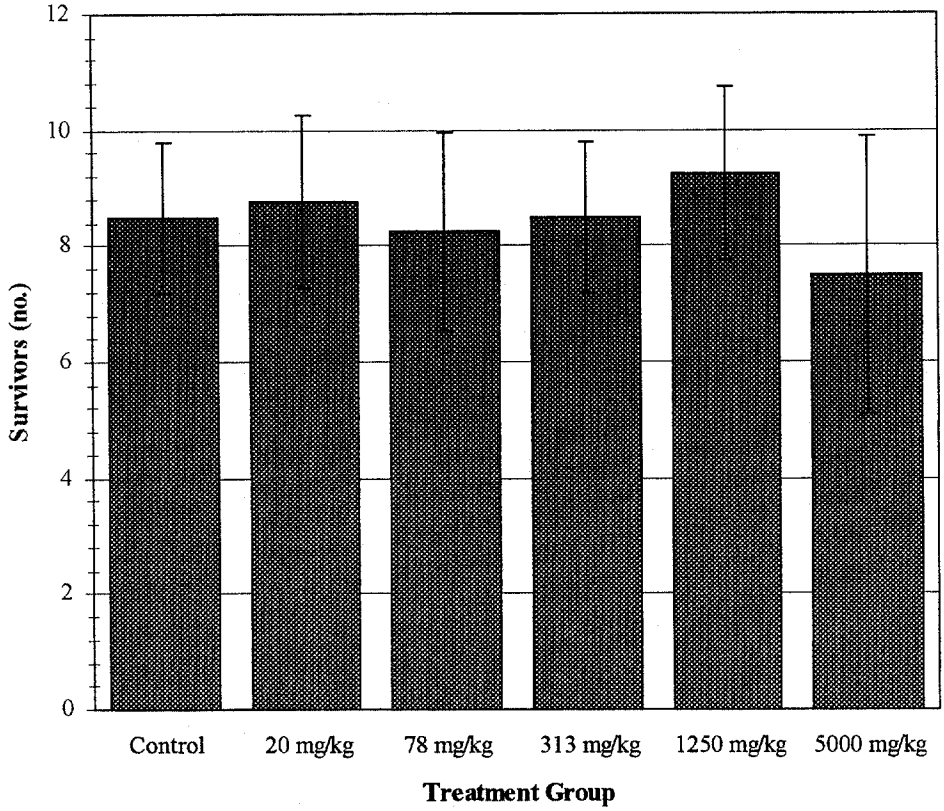
Cucumber 21-Day Survival

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	8	7	10	9	*4*	8.50	1.29
20 mg/kg	8	10	7	10	*4*	8.75	1.50
78 mg/kg	6	9	10	8	*4*	8.25	1.71
313 mg/kg	8	9	10	7	*4*	8.50	1.29
1250 mg/kg	10	10	7	10	*4*	9.25	1.50
5000 mg/kg	9	9	8	4	*4*	7.50	2.38

Appendix 7.4

Mean Cucumber 21-Day Survival



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

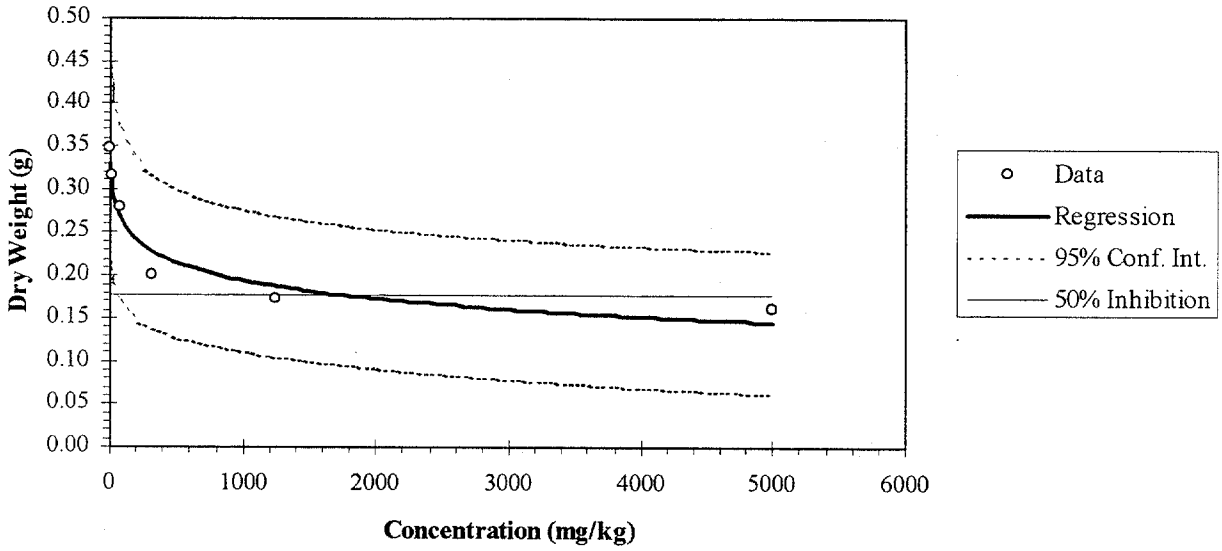
Appendix 7.5

Cucumber Mean Seedling Dry Weight, Day 21

Treatment Group	Mean Weight (g) per Plant of Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	0.38	0.38	0.32	0.31	*4*	0.35	0.037
20 mg/kg	0.33	0.30	0.31	0.32	*4*	0.32	0.014
78 mg/kg	0.32	0.34	0.25	0.22	*4*	0.28	0.056
313 mg/kg	0.25	0.19	0.21	0.16	*4*	0.20	0.035
1250 mg/kg	0.16	0.18	0.18	0.17	*4*	0.17	0.011
5000 mg/kg	0.13	0.18	0.16	0.17	*4*	0.16	0.020

Appendix 7.6

Mean Cucumber Dry Weight



Curve Parameters

EC_{25}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
72.6440	1.73700	3038.79	0.3567	2.0193	0.92881

EC_{50}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
1672.25	194.223	14394.61	0.3567	2.0193	0.92881

Appendix 7.7

Cucumber Seedling Height on Day 21

Treatment Group	Replicate	Height (cm) for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	.	.	9	9	10	9	13	10	16	10	*8*	10.8	2.49
	B	.	.	.	9	11	9	12	13	9	9	*7*	10.3	1.70
	C	10	12	13	10	3	6	13	8	10	10	*10*	9.5	3.14
	D	.	10	10	8	8	10	8	5	8	7	*9*	8.2	1.64
20 mg/kg	A	.	.	8	11	7	10	8	7	9	9	*8*	8.6	1.41
	B	2	8	8	9	8	10	13	12	13	11	*10*	9.4	3.27
	C	.	.	.	10	12	8	11	9	10	8	*7*	9.7	1.50
	D	8	10	9	11	10	9	11	9	11	10	*10*	9.8	1.03
78 mg/kg	A	.	.	.	.	7	5	7	7	8	4	*6*	6.3	1.51
	B	.	8	12	5	10	14	9	11	8	9	*9*	9.6	2.60
	C	9	8	3	10	8	8	12	8	8	9	*10*	8.3	2.26
	D	.	.	3	5	6	7	6	7	6	7	*8*	5.9	1.36
313 mg/kg	A	.	.	5	7	5	10	6	7	9	5	*8*	6.8	1.91
	B	.	7	7	9	7	7	5	7	8	8	*9*	7.2	1.09
	C	5	8	9	7	5	10	7	7	8	7	*10*	7.3	1.57
	D	.	.	.	3	7	3	5	4	5	6	*7*	4.7	1.50
1250 mg/kg	A	4	8	7	5	4	6	5	4	7	1	*10*	5.1	2.02
	B	6	7	8	6	8	5	5	7	5	3	*10*	6.0	1.56
	C	.	.	.	6	5	6	4	2	5	7	*7*	5.0	1.63
	D	7	5	5	6	5	6	5	4	4	5	*10*	5.2	0.92
5000 mg/kg	A	.	5	5	6	5	7	2	1	6	3	*9*	4.4	2.01
	B	.	4	6	6	6	4	5	7	5	6	*9*	5.4	1.01
	C	.	4	4	5	7	4	4	4	4	.	*8*	4.5	1.07
	D	.	.	.	.	.	.	4	4	4	5	*4*	4.3	0.50

The "." symbol indicates that the seedling either did not emerge or died prior to measurement.

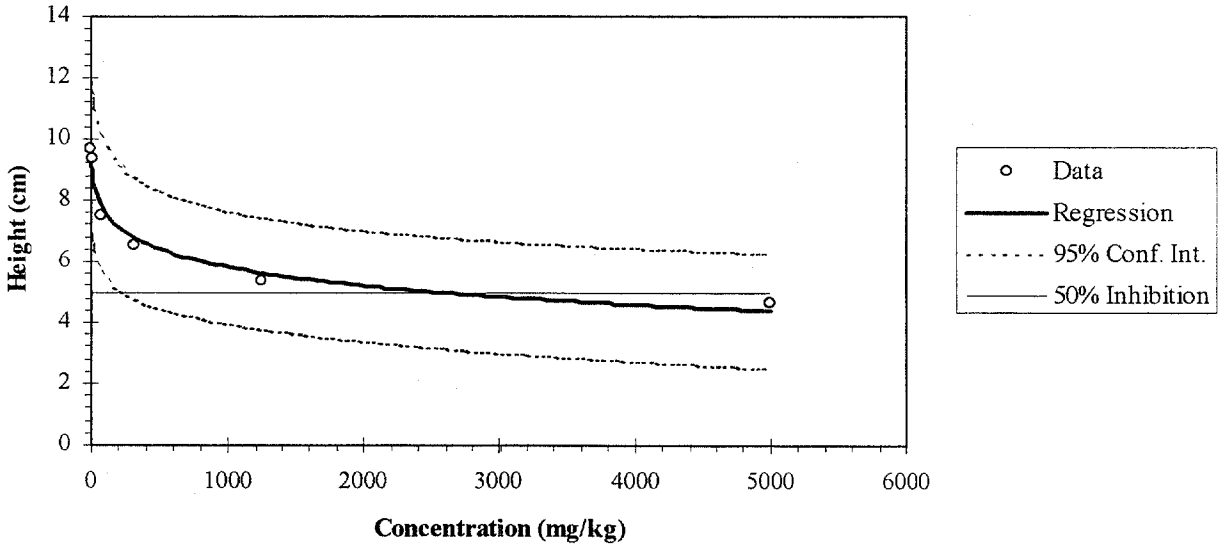
Appendix 7.8

Cucumber Mean Seedling Height on Day 21

Treatment Group	Mean Height (cm) for Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10.8	10.3	9.5	8.2	*4*	9.7	1.11
20 mg/kg	8.6	9.4	9.7	9.8	*4*	9.4	0.53
78 mg/kg	6.3	9.6	8.3	5.9	*4*	7.5	1.72
313 mg/kg	6.8	7.2	7.3	4.7	*4*	6.5	1.21
1250 mg/kg	5.1	6.0	5.0	5.2	*4*	5.3	0.46
5000 mg/kg	4.4	5.4	4.5	4.3	*4*	4.7	0.53

Appendix 7.9

Mean Cucumber Height on Day 21



Curve Parameters

EC_{25}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
131.341	8.02971	2148.33	9.9218	1.9229	0.94272

EC_{50}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
2602.56	506.407	13375.19	9.9218	1.9229	0.94272

Appendix 7.10

Cucumber Seedling Condition, Day 21

Treatment Group	Replicate	Condition (score.sign)[1] for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	B	.	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*7*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
20 mg/kg	A	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	B	30.LC	0.-	30.LC	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	6	12.6
	C	100.-	100.-	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	30	48.3
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
78 mg/kg	A	.	.	.	100.-	0.-	0.-	0.-	0.-	0.-	50.LC	*7*	21	39.3
	B	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	.	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	11	33.3
313 mg/kg	A	.	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	11	33.3
	B	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	.	.	.	0.-	0.-	30.LC	0.-	0.-	0.-	0.-	*7*	4	11.3
1250 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	80.N	*10*	8	25.3
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*7*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
5000 mg/kg	A	.	0.-	0.-	0.-	0.-	0.-	50.LC	80.N	0.-	0.-	*9*	14	29.6
	B	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	.	*8*	0	0.0
	D	.	.	.	.	.	.	0.-	0.-	0.-	0.-	*4*	0	0.0

[1]The "." symbol indicates that the seedling did not emerge. A score of 0 indicates a normal seedling, while a score of 100 indicates a dead seedling. Intermediate scores are assigned to indicate the relative severity of observed signs of toxicity. LC – Leaf Curl, N - Necrosis

Appendix 8.1

Onion Emergence

Day 7

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	8	10	7	9	*4*	8.50	1.29
20 mg/kg	10	8	8	10	*4*	9.00	1.15
78 mg/kg	9	10	9	9	*4*	9.25	0.50
313 mg/kg	10	10	9	9	*4*	9.50	0.58
1250 mg/kg	8	10	9	9	*4*	9.00	0.82
5000 mg/kg	9	8	7	9	*4*	8.25	0.96

Day 14

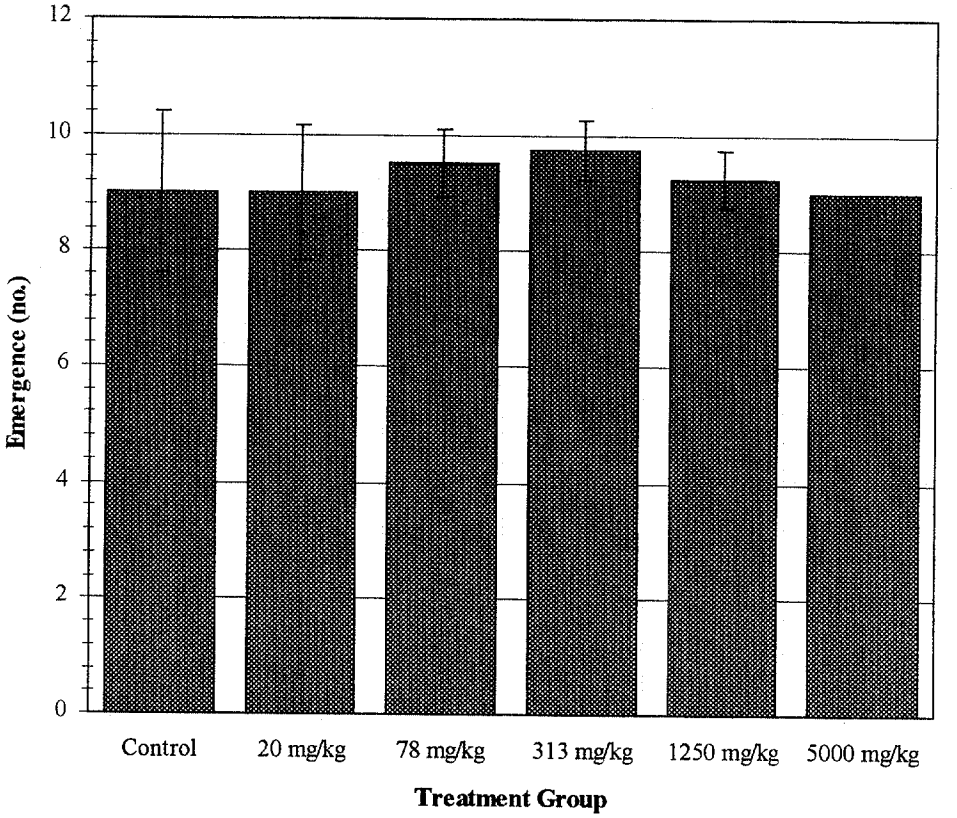
Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	9	10	7	10	*4*	9.00	1.41
20 mg/kg	10	8	8	10	*4*	9.00	1.55
78 mg/kg	10	10	9	9	*4*	9.50	0.58
313 mg/kg	10	10	10	9	*4*	9.75	0.50
1250 mg/kg	9	10	9	9	*4*	9.25	0.50
5000 mg/kg	9	9	9	9	*4*	9.00	0.00

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	9	10	7	10	*4*	9.00	1.41
20 mg/kg	10	8	8	10	*4*	9.00	1.55
78 mg/kg	10	10	9	9	*4*	9.50	0.58
313 mg/kg	10	10	10	9	*4*	9.75	0.50
1250 mg/kg	9	10	9	9	*4*	9.25	0.50
5000 mg/kg	9	9	9	9	*4*	9.00	0.00

Appendix 8.2

Mean Onion Emergence on Day 21



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

Appendix 8.3

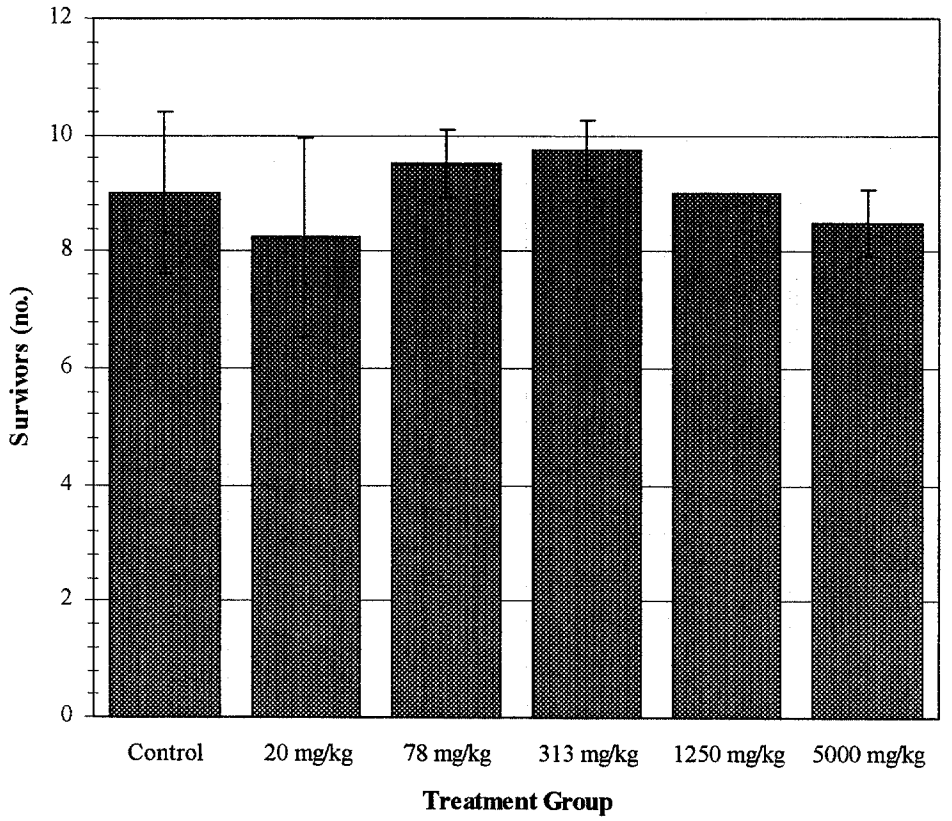
Onion 21-Day Survival

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	9	10	7	10	*4*	9.00	1.41
20 mg/kg	9	8	6	10	*4*	8.25	1.71
78 mg/kg	10	10	9	9	*4*	9.50	0.58
313 mg/kg	10	10	10	9	*4*	9.75	0.50
1250 mg/kg	9	9	9	9	*4*	9.00	0.00
5000 mg/kg	9	9	8	8	*4*	8.50	0.58

Appendix 8.4

Mean Onion 21-Day Survival



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

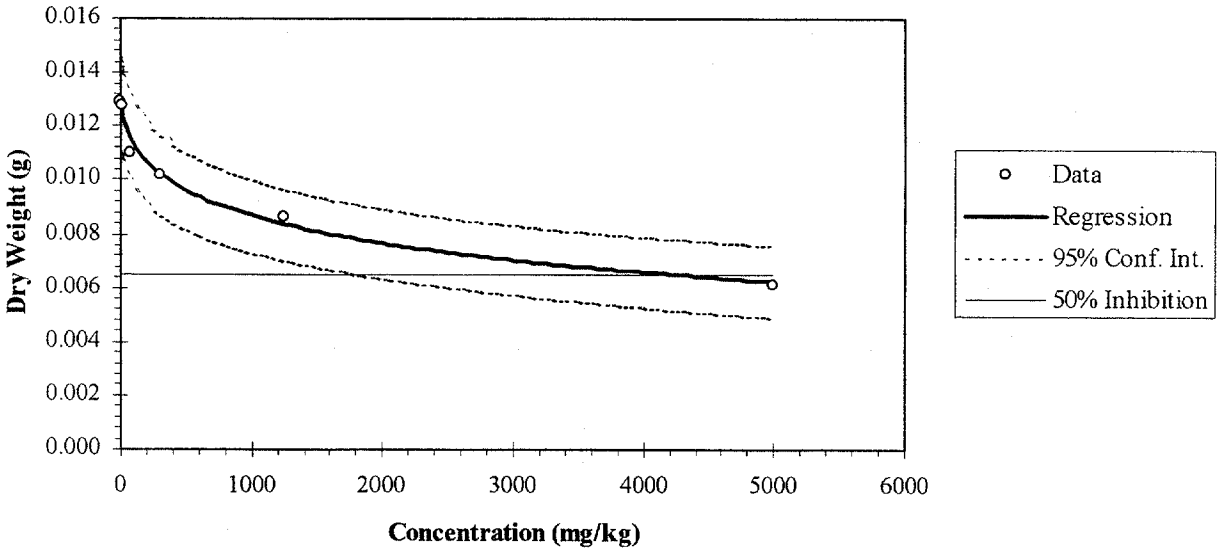
Appendix 8.5

Onion Mean Seedling Dry Weight, Day 21

Treatment Group	Mean Weight (g) per Plant of Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	0.012	0.016	0.011	0.012	*4*	0.013	0.0021
20 mg/kg	0.013	0.016	0.013	0.008	*4*	0.013	0.0034
78 mg/kg	0.014	0.010	0.010	0.010	*4*	0.011	0.0020
313 mg/kg	0.014	0.010	0.009	0.008	*4*	0.010	0.0027
1250 mg/kg	0.011	0.007	0.009	0.008	*4*	0.009	0.0019
5000 mg/kg	0.008	0.006	0.006	0.005	*4*	0.006	0.0012

Appendix 8.6

Mean Onion Dry Weight



Curve Parameters

EC_{25}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
459.727	150.349	1405.72	0.0130	1.4341	0.98599

EC_{50}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
4263.83	2235.12	8135.80	0.0130	1.4341	0.98599

Appendix 8.7

Onion Seedling Height on Day 21

Treatment Group	Replicate	Height (cm) for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	.	2	7	8	7	13	4	5	11	8	*9*	7.2	3.38
	B	9	9	9	7	8	6	7	14	8	7	*10*	8.4	2.22
	C	.	.	.	7	8	8	6	6	4	13	*7*	7.4	2.82
	D	9	6	8	6	9	7	6	5	6	3	*10*	6.5	1.84
20 mg/kg	A	.	9	9	8	7	10	8	7	12	11	*9*	9.0	1.73
	B	.	.	5	10	10	6	7	7	8	7	*8*	7.5	1.77
	C	.	.	.	.	7	7	6	7	7	8	*6*	7.0	0.63
	D	6	8	6	8	7	8	9	13	8	7	*10*	8.0	2.00
78 mg/kg	A	9	9	9	9	8	9	8	10	9	1	*10*	8.1	2.56
	B	8	9	7	7	8	7	7	9	9	8	*10*	7.9	0.88
	C	.	7	8	4	7	8	7	7	8	9	*9*	7.2	1.39
	D	.	7	7	8	9	6	7	3	11	7	*9*	7.2	2.17
313 mg/kg	A	7	6	7	6	3	7	6	7	7	8	*10*	6.4	1.35
	B	8	9	8	8	7	6	13	8	6	6	*10*	7.9	2.08
	C	7	4	7	8	7	8	9	8	7	8	*10*	7.3	1.34
	D	.	8	6	8	3	7	7	13	6	7	*9*	7.2	2.64
1250 mg/kg	A	.	9	4	6	8	5	7	7	6	2	*9*	6.0	2.12
	B	.	2	8	3	6	6	2	7	10	7	*9*	5.7	2.78
	C	.	6	7	6	4	3	6	5	6	7	*9*	5.6	1.33
	D	.	8	2	10	6	6	6	4	11	3	*9*	6.2	3.03
5000 mg/kg	A	.	6	5	10	4	6	3	4	5	5	*9*	5.3	2.00
	B	.	4	5	5	4	4	4	5	6	5	*9*	4.7	0.71
	C	.	.	4	5	5	5	5	6	3	6	*8*	4.9	0.99
	D	.	.	2	3	4	9	4	7	6	4	*8*	4.9	2.30

The "." symbol indicates that the seedling either did not emerge or died prior to measurement.

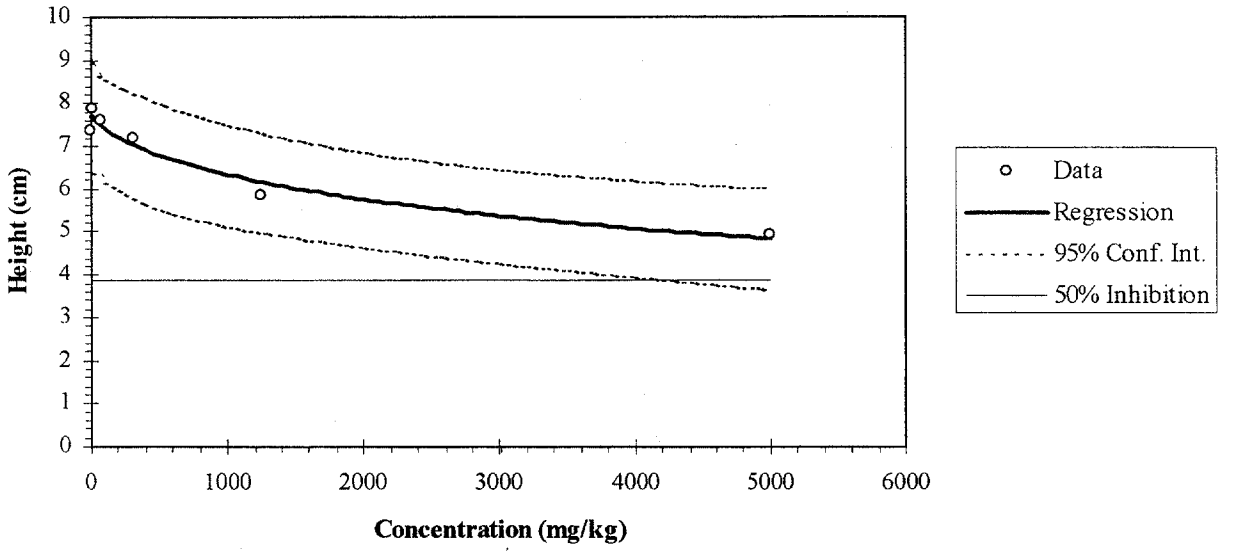
Appendix 8.8

Onion Mean Seedling Height on Day 21

Treatment Group	Mean Height (cm) for Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	7.2	8.4	7.4	6.5	*4*	7.4	0.78
20 mg/kg	9.0	7.5	7.0	8.0	*4*	7.9	0.85
78 mg/kg	8.1	7.9	7.2	7.2	*4*	7.6	0.46
313 mg/kg	6.4	7.9	7.3	7.2	*4*	7.2	0.62
1250 mg/kg	6.0	5.7	5.6	6.2	*4*	5.9	0.31
5000 mg/kg	5.3	4.7	4.9	4.9	*4*	4.9	0.28

Appendix 8.9

Mean Onion Height on Day 21



Curve Parameters

EC_{25}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
1947.60	668.344	5675.45	7.7132	1.1634	0.95034

Appendix 8.10

Onion Seedling Condition, Day 21

Treatment Group	Replicate	Condition (score.sign)[1] for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*7*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
20 mg/kg	A	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	10	31.6
	B	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	C	.	.	100.-	100.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	25	46.3
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
78 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
313 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
1250 mg/kg	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	10	31.6
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
5000 mg/kg	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	C	.	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	11	33.3
	D	.	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	11	33.3

[1]The "." symbol indicates that the seedling did not emerge. A score of 0 indicates a normal seedling, while a score of 100 indicates a dead seedling. Intermediate scores are assigned to indicate the relative severity of observed signs of toxicity.

Appendix 9.1

Ryegrass Emergence

Day 7

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	8	9	9	*4*	9.00	0.82
20 mg/kg	7	10	9	9	*4*	8.75	1.26
78 mg/kg	10	9	10	8	*4*	9.25	0.96
313 mg/kg	8	8	10	9	*4*	8.75	0.96
1250 mg/kg	8	6	8	10	*4*	8.00	1.63
5000 mg/kg	10	8	8	5	*4*	7.75	2.06

Day 14

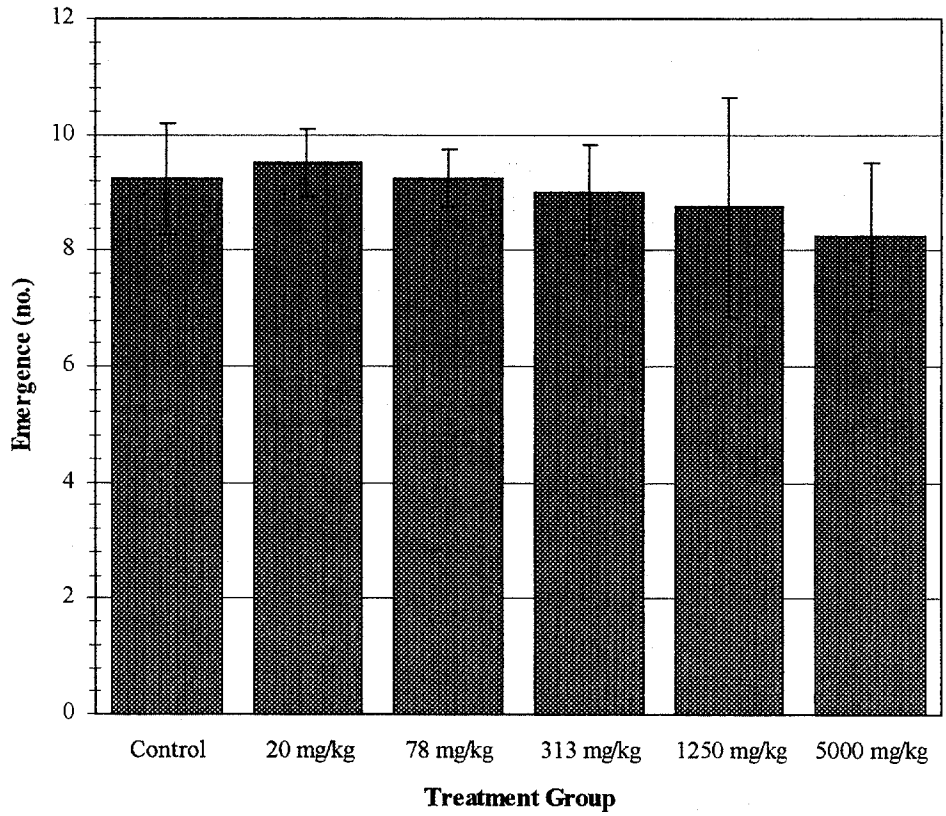
Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	8	9	10	*4*	9.25	0.96
20 mg/kg	9	10	9	10	*4*	9.50	0.58
78 mg/kg	8	9	10	9	*4*	9.00	0.82
313 mg/kg	8	9	10	9	*4*	9.00	0.82
1250 mg/kg	9	6	9	10	*4*	8.50	1.73
5000 mg/kg	10	8	8	7	*4*	8.25	1.26

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	8	9	10	*4*	9.25	0.96
20 mg/kg	9	10	9	10	*4*	9.50	0.58
78 mg/kg	9	9	10	9	*4*	9.25	0.50
313 mg/kg	9	8	10	9	*4*	9.00	0.82
1250 mg/kg	9	6	10	10	*4*	8.75	1.89
5000 mg/kg	10	8	8	7	*4*	8.25	1.26

Appendix 9.2

Mean Ryegrass Emergence on Day 21



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

Appendix 9.3

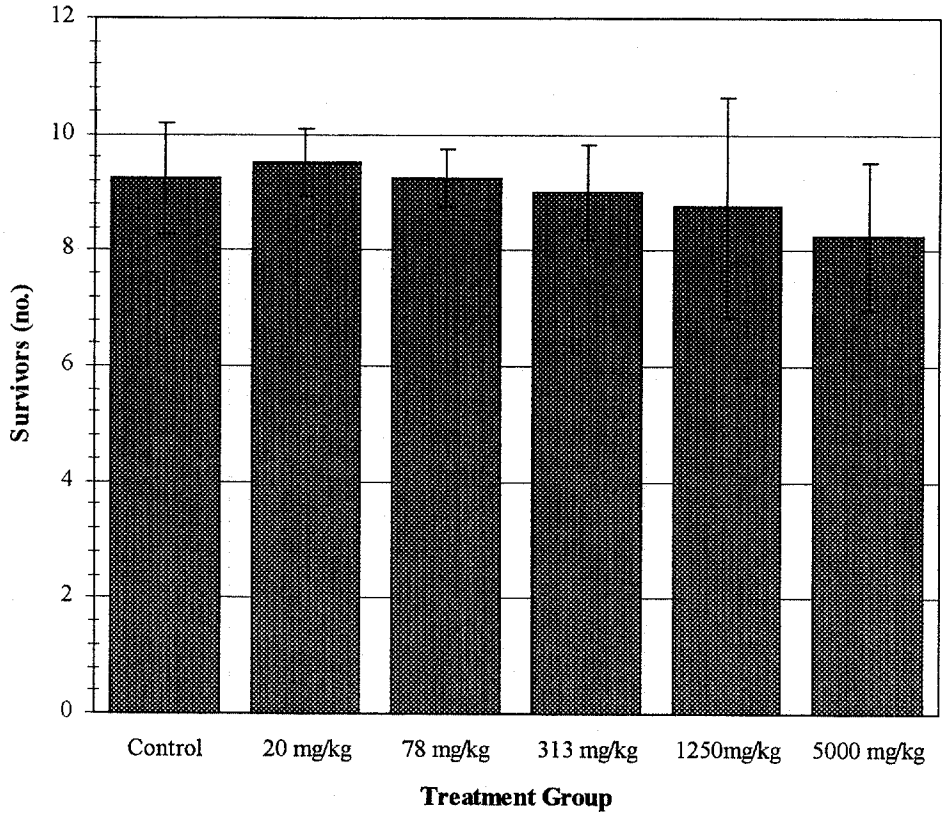
Ryegrass 21-Day Survival

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	8	9	10	*4*	9.25	0.96
20 mg/kg	9	10	9	10	*4*	9.50	0.58
78 mg/kg	9	9	10	9	*4*	9.25	0.50
313 mg/kg	9	8	10	9	*4*	9.00	0.82
1250 mg/kg	9	6	10	10	*4*	8.75	1.89
5000 mg/kg	10	8	8	7	*4*	8.25	1.26

Appendix 9.4

Mean Ryegrass 21-Day Survival



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$)

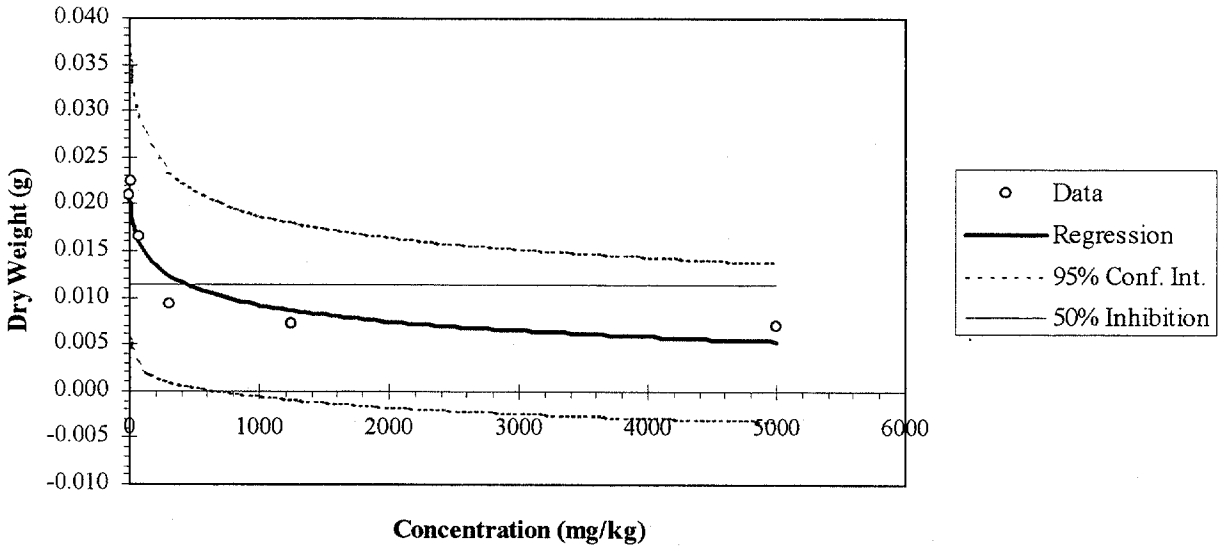
Appendix 9.5

Ryegrass Mean Seedling Dry Weight, Day 21

Treatment Group	Mean Weight (g) per Plant of Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	0.020	0.023	0.020	0.021	*4*	0.021	0.0012
20 mg/kg	0.030	0.023	0.020	0.017	*4*	0.023	0.0056
78 mg/kg	0.016	0.017	0.025	0.009	*4*	0.017	0.0066
313 mg/kg	0.004	0.009	0.014	0.010	*4*	0.009	0.0039
1250 mg/kg	0.007	0.003	0.010	0.009	*4*	0.007	0.0030
5000 mg/kg	0.006	0.009	0.010	0.003	*4*	0.007	0.0032

Appendix 9.6

Mean Ryegrass Dry Weight



Curve Parameters

EC_{25}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
48.5177	0.20188	11660.04	0.0226	1.4469	0.84141

EC_{50}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
458.987	16.2892	12930.04	0.0226	1.4469	0.84141

Appendix 9.7

Ryegrass Seedling Height on Day 21

Treatment Group	Replicate	Height (cm) for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	15	16	14	14	17	17	15	17	15	2	*10*	14.2	4.44
	B	.	.	16	7	16	16	22	16	16	15	*8*	15.5	4.07
	C	.	21	22	15	13	17	16	18	15	17	*9*	17.1	2.89
	D	18	18	12	9	12	19	12	16	14	16	*10*	14.6	3.31
20 mg/kg	A	.	15	24	8	17	19	14	18	23	18	*9*	17.3	4.80
	B	19	20	19	16	12	20	16	19	17	13	*10*	17.1	2.85
	C	.	15	7	14	13	17	17	14	16	20	*9*	14.8	3.60
	D	13	15	18	14	8	6	17	13	18	13	*10*	13.5	3.98
78 mg/kg	A	.	8	12	10	8	15	17	13	18	11	*9*	12.4	3.64
	B	.	10	14	17	15	19	14	15	10	7	*9*	13.4	3.78
	C	17	12	21	19	12	15	10	9	15	18	*10*	14.8	3.99
	D	.	9	13	12	10	10	5	18	11	12	*9*	11.1	3.48
313 mg/kg	A	.	6	9	4	4	8	8	12	10	9	*9*	7.8	2.68
	B	.	.	13	14	10	10	7	7	8	6	*8*	9.4	2.92
	C	11	18	14	8	12	9	21	9	8	10	*10*	12.0	4.42
	D	.	8	15	7	16	7	10	7	8	6	*9*	9.3	3.67
1250 mg/kg	A	.	6	6	11	7	7	7	9	6	10	*9*	7.7	1.87
	B	.	.	.	.	7	5	6	6	4	5	*6*	5.5	1.05
	C	6	4	8	12	8	8	4	8	11	11	*10*	8.0	2.79
	D	8	8	7	9	9	8	5	6	11	6	*10*	7.7	1.77
5000 mg/kg	A	9	6	8	7	9	7	8	9	6	11	*10*	8.0	1.56
	B	.	.	10	8	6	5	15	12	7	6	*8*	8.6	3.46
	C	.	.	9	5	5	9	6	7	8	7	*8*	7.0	1.60
	D	5	6	6	7	7	7	8	.	.	.	*7*	6.6	0.98

The "." symbol indicates that the seedling either did not emerge or died prior to measurement.

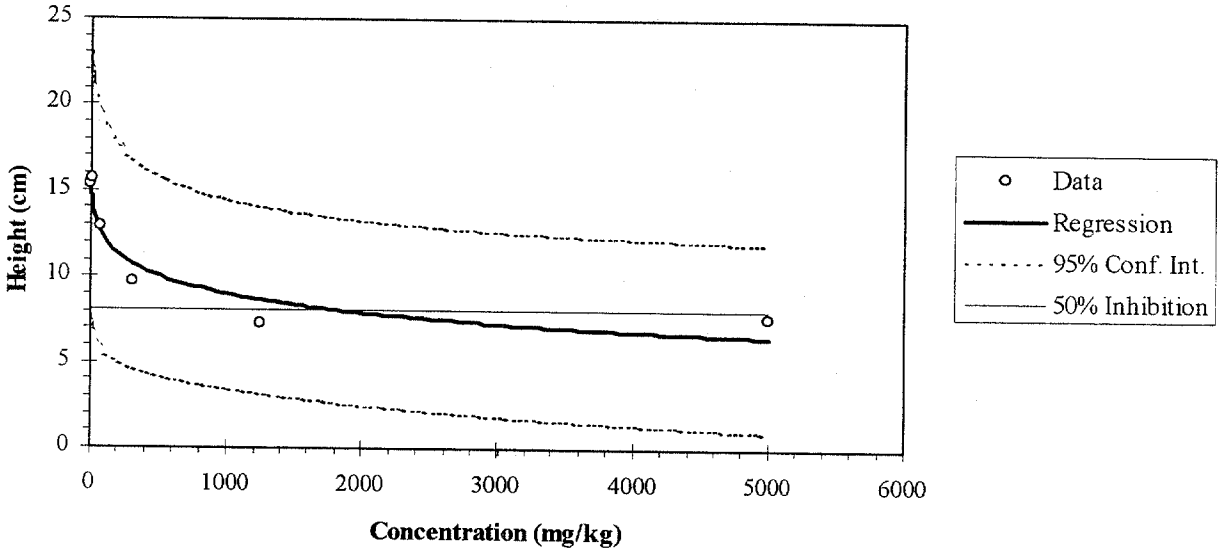
Appendix 9.8

Ryegrass Mean Seedling Height on Day 21

Treatment Group	Mean Height (cm) for Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	14.2	15.5	17.1	14.6	*4*	15.4	1.29
20 mg/kg	17.3	17.1	14.8	13.5	*4*	15.7	1.85
78 mg/kg	12.4	13.4	14.8	11.1	*4*	13.0	1.56
313 mg/kg	7.8	9.4	12.0	9.3	*4*	9.6	1.75
1250 mg/kg	7.7	5.5	8.0	7.7	*4*	7.2	1.15
5000 mg/kg	8.0	8.6	7.0	6.6	*4*	7.5	0.93

Appendix 9.9

Mean Ryegrass Height on Day 21



Curve Parameters

EC_{25}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
113.815	0.87116	14869.62	16.1050	1.7781	0.86700

EC_{50}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
1801.36	110.688	29315.68	16.1050	1.7781	0.86700

Appendix 9.10

Ryegrass Seedling Condition, Day 21

Treatment Group	Replicate	Condition (score.sign)[1] for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
20 mg/kg	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
78 mg/kg	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
313 mg/kg	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
1250 mg/kg	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	.	.	.	.	0.-	0.-	0.-	0.-	0.-	0.-	*6*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
5000 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	C	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	.	.	.	*7*	0	0.0

[1]The "." symbol indicates that the seedling did not emerge. A score of 0 indicates a normal seedling, while a score of 100 indicates a dead seedling. Intermediate scores are assigned to indicate the relative severity of observed signs of toxicity.

Appendix 10.1

Soybean Emergence

Day 7

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	9	10	9	*4*	9.50	0.58
20 mg/kg	10	8	9	9	*4*	9.00	0.82
78 mg/kg	9	9	10	9	*4*	9.25	0.50
313 mg/kg	10	9	9	10	*4*	9.50	0.58
1250 mg/kg	10	10	9	9	*4*	9.50	0.58
5000 mg/kg	9	9	9	9	*4*	9.00	0.00

Day 14

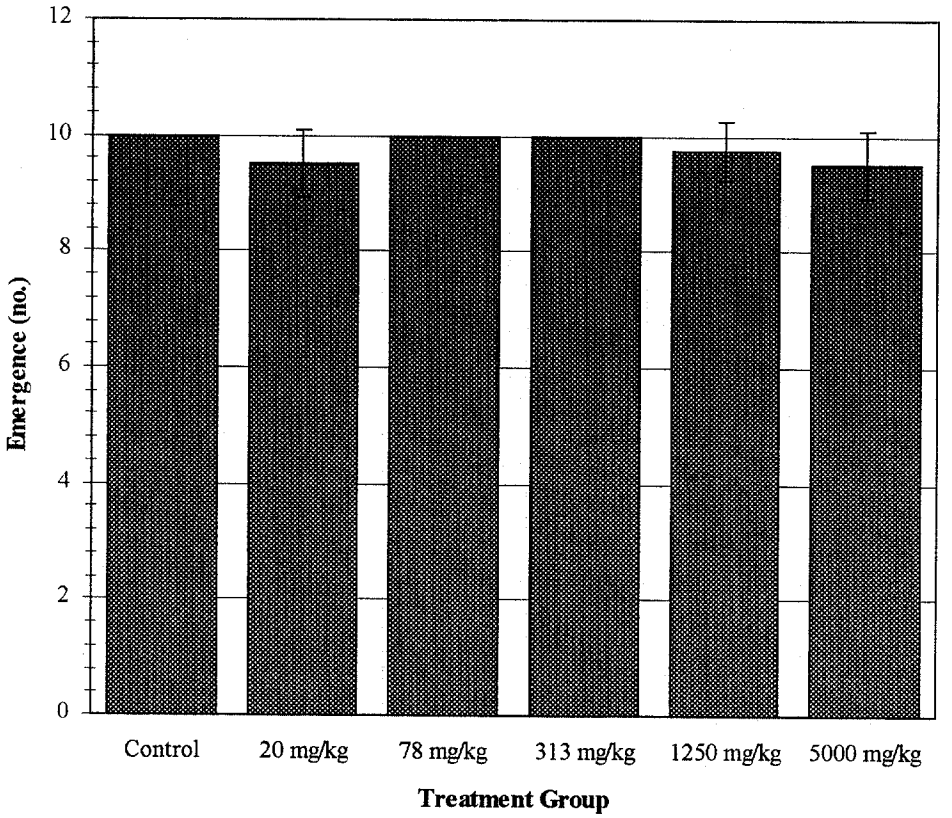
Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	10	10	10	*4*	10.00	0.00
20 mg/kg	10	9	9	10	*4*	9.50	0.58
78 mg/kg	10	10	10	10	*4*	10.00	0.00
313 mg/kg	10	10	10	10	*4*	10.00	0.00
1250 mg/kg	10	10	9	10	*4*	9.75	0.50
5000 mg/kg	9	9	10	9	*4*	9.25	0.50

Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	10	10	10	*4*	10.00	0.00
20 mg/kg	10	9	9	10	*4*	9.50	0.58
78 mg/kg	10	10	10	10	*4*	10.00	0.00
313 mg/kg	10	10	10	10	*4*	10.00	0.00
1250 mg/kg	10	10	9	10	*4*	9.75	0.50
5000 mg/kg	10	9	10	9	*4*	9.50	0.58

Appendix 10.2

Mean Soybean Emergence on Day 21



No treatment group mean is significantly different from the control mean (Dunnett's test, $p > 0.05$).

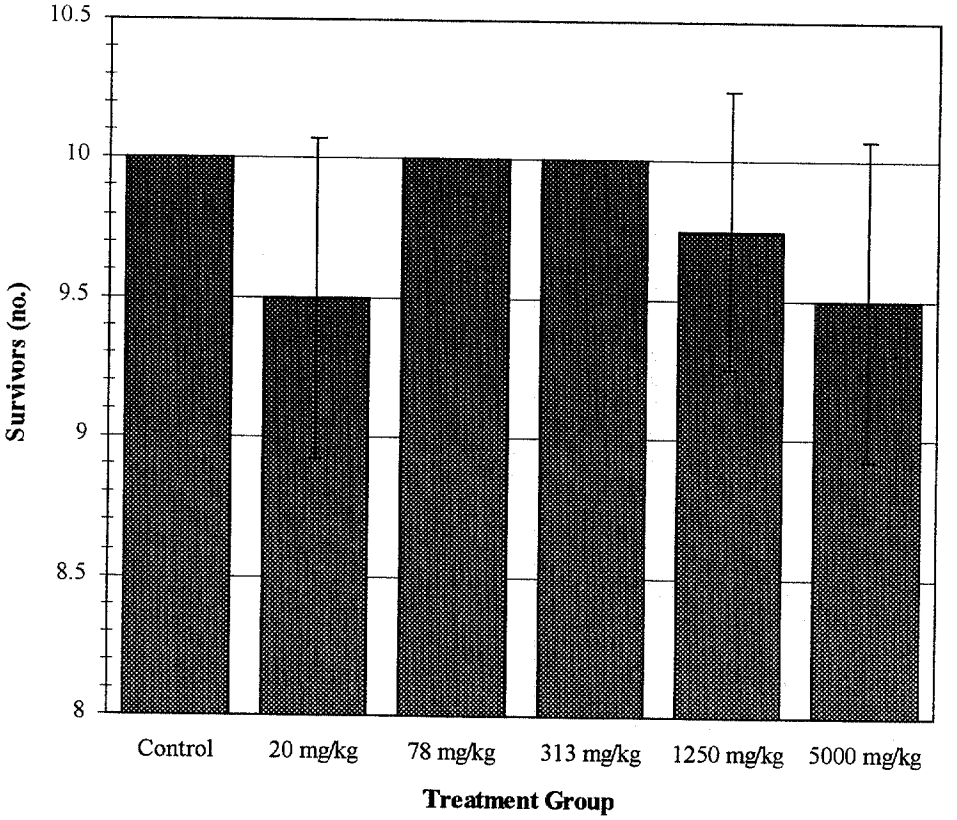
Appendix 10.3

Soybean 21-Day Survival

Treatment Group	Day 21 Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	10	10	10	10	*4*	10.00	0.00
20 mg/kg	10	9	9	10	*4*	9.50	0.58
78 mg/kg	10	10	10	10	*4*	10.00	0.00
313 mg/kg	10	10	10	10	*4*	10.00	0.00
1250 mg/kg	10	10	9	10	*4*	9.75	0.50
5000 mg/kg	10	9	10	9	*4*	9.50	0.58

Appendix 10.4

Mean Soybean 21-Day Survival



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

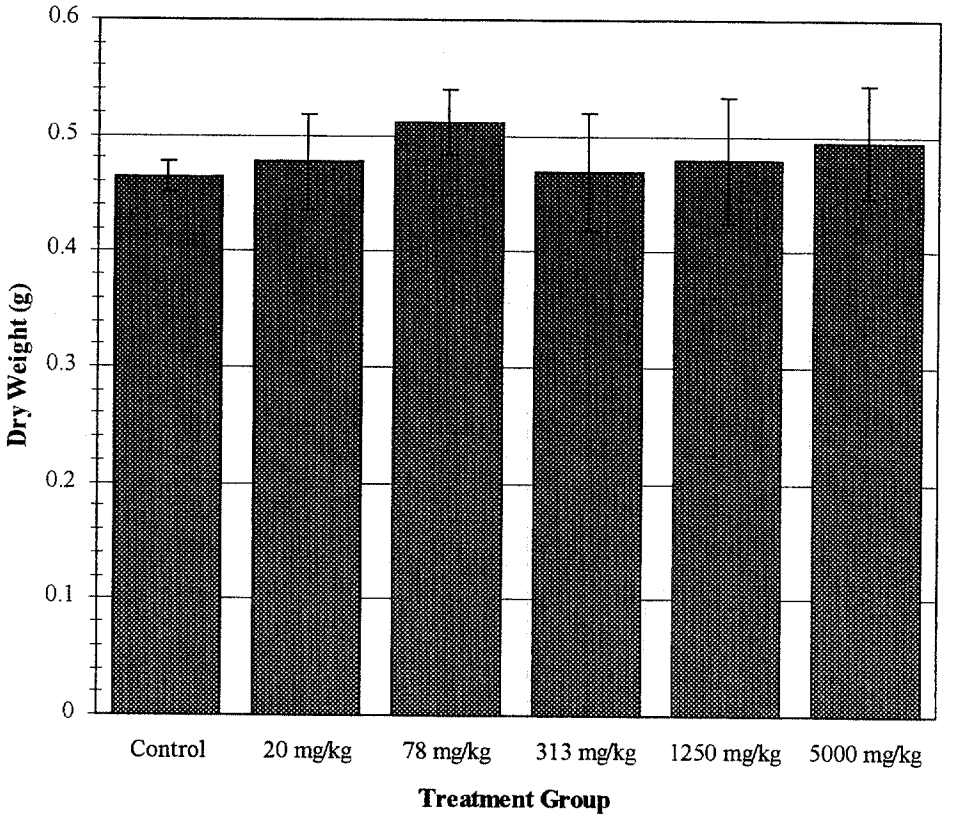
Appendix 10.5

Soybean Mean Seedling Dry Weight, Day 21

Treatment Group	Mean Weight (g) per Plant of Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	0.48	0.47	0.46	0.45	*4*	0.46	0.014
20 mg/kg	0.47	0.54	0.44	0.46	*4*	0.48	0.041
78 mg/kg	0.55	0.49	0.51	0.49	*4*	0.51	0.028
313 mg/kg	0.51	0.50	0.40	0.47	*4*	0.47	0.051
1250 mg/kg	0.52	0.43	0.53	0.43	*4*	0.48	0.054
5000 mg/kg	0.45	0.50	0.47	0.56	*4*	0.49	0.049

Appendix 10.6

Mean Soybean Dry Weight



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

Appendix 10.7

Soybean Seedling Height on Day 21

Treatment Group	Replicate	Height (cm) for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	27	19	24	20	23	26	19	27	20	25	*10*	23.0	3.27
	B	30	20	26	25	21	24	27	26	23	21	*10*	24.3	3.13
	C	21	22	21	20	21	19	21	25	23	21	*10*	21.4	1.65
	D	20	23	22	22	24	18	19	20	10	18	*10*	19.6	3.95
20 mg/kg	A	23	26	29	29	15	24	24	24	27	25	*10*	24.6	3.98
	B	.	20	21	28	21	24	25	23	25	23	*9*	23.3	2.50
	C	.	22	25	25	26	24	17	23	17	16	*9*	21.7	3.94
	D	19	19	22	24	20	21	22	19	25	20	*10*	21.1	2.13
78 mg/kg	A	18	25	32	28	21	22	25	27	24	21	*10*	24.3	4.06
	B	21	24	23	20	20	24	25	24	23	16	*10*	22.0	2.75
	C	26	26	22	28	24	18	25	17	27	21	*10*	23.4	3.78
	D	11	22	21	25	23	20	18	17	24	14	*10*	19.5	4.50
313 mg/kg	A	5	19	26	26	27	24	21	19	27	17	*10*	21.1	6.76
	B	13	20	32	29	29	12	29	30	25	24	*10*	24.3	7.12
	C	10	21	23	18	17	11	16	28	24	22	*10*	19.0	5.72
	D	26	25	21	27	22	26	25	26	27	25	*10*	25.0	2.00
1250 mg/kg	A	22	26	27	26	18	25	11	28	24	23	*10*	23.0	5.10
	B	21	21	23	23	24	28	21	23	24	17	*10*	22.5	2.84
	C	.	27	23	27	29	23	28	27	19	26	*9*	25.4	3.17
	D	15	24	23	21	19	23	18	24	16	20	*10*	20.3	3.27
5000 mg/kg	A	19	21	22	31	5	27	30	25	28	3	*10*	21.1	9.81
	B	.	20	19	14	23	24	3	18	23	24	*9*	18.7	6.75
	C	20	24	21	25	25	17	19	21	15	25	*10*	21.2	3.55
	D	.	21	21	24	20	27	19	27	24	26	*9*	23.2	3.07

The "." symbol indicates that the seedling either did not emerge or died prior to measurement.

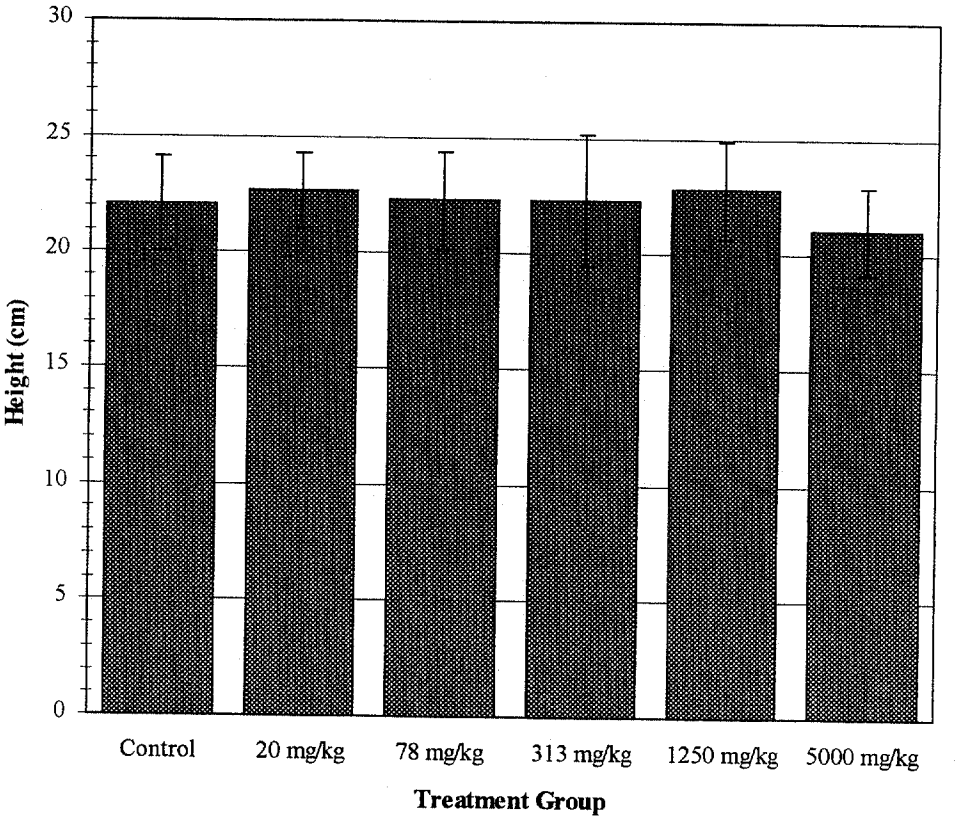
Appendix 10.8

Soybean Mean Seedling Height on Day 21

Treatment Group	Mean Height (cm) for Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	23.0	24.3	21.4	19.6	*4*	22.1	2.03
20 mg/kg	24.6	23.3	21.7	21.1	*4*	22.7	1.60
78 mg/kg	24.3	22.0	23.4	19.5	*4*	22.3	2.09
313 mg/kg	21.1	24.3	19.0	25.0	*4*	22.4	2.81
1250 mg/kg	23.0	22.5	25.4	20.3	*4*	22.8	2.11
5000 mg/kg	21.1	18.7	21.2	23.2	*4*	21.0	1.86

Appendix 10.9

Mean Soybean Height on Day 21



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

Appendix 10.10

Soybean Seedling Condition, Day 21

Treatment Group	Replicate	Condition (score.sign)[1] for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
20 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
78 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	20.LC	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	30.LC	*10*	5	10.8
313 mg/kg	A	60.LC	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	6	19.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
1250 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
5000 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	.	0.-	0.-	0.-	0.-	0.-	70.LC	0.-	10.SC	0.-	*9*	9	23.2
	C	0.-	0.-	0.-	0.-	0.-	30.LC	0.-	0.-	0.-	0.-	*10*	3	9.5
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0

[1]The "." symbol indicates that the seedling did not emerge. A score of 0 indicates a normal seedling, while a score of 100 indicates a dead seedling. Intermediate scores are assigned to indicate the relative severity of observed signs of toxicity. LC – Leaf Curl, SC – Stem Curl

Appendix 11.1

Tomato Emergence

Day 7

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	7	3	7	3	*4*	5.00	2.31
20 mg/kg	8	10	8	5	*4*	7.75	2.06
78 mg/kg	5	6	5	3	*4*	4.75	1.26
313 mg/kg	8	8	9	5	*4*	7.50	1.73
1250 mg/kg	1	8	5	5	*4*	4.75	2.87
5000 mg/kg	7	8	6	4	*4*	6.25	1.71

Day 14

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	9	10	10	9	*4*	9.50	0.58
20 mg/kg	8	10	8	9	*4*	8.75	0.96
78 mg/kg	10	9	8	9	*4*	9.00	0.82
313 mg/kg	9	9	9	9	*4*	9.00	0.00
1250 mg/kg	7	10	10	10	*4*	9.25	1.50
5000 mg/kg	9	10	8	9	*4*	9.00	0.82

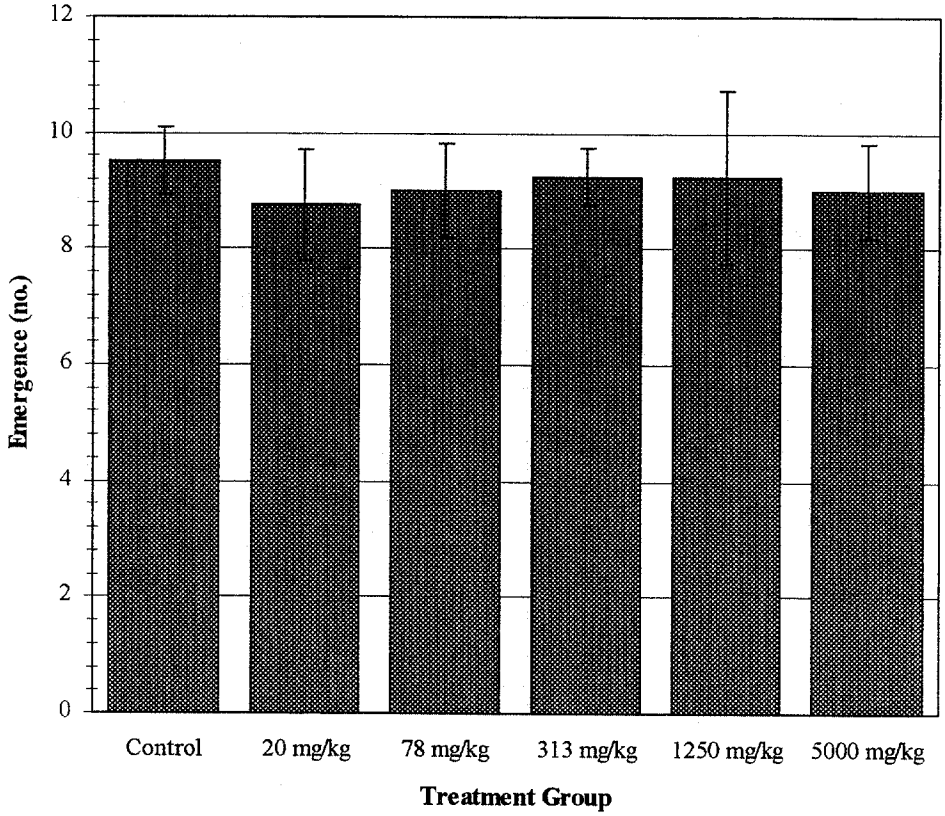
Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	9	10	10	9	*4*	9.50	0.58
20 mg/kg	8	10	8	9	*4*	8.75	0.96
78 mg/kg	10	9	8	9	*4*	9.00	0.82
313 mg/kg	10	9	9	9	*4*	9.25	0.50
1250 mg/kg	7	10	10[1]	10	*4*	9.25	1.50
5000 mg/kg	9	10	8	9	*4*	9.00	0.82

[1] An eleventh seedling was observed in this replicate on Day 21. Mean emergence was based on 10 emerged seedlings per 10 planted seeds.

Appendix 11.2

Mean Tomato Emergence on Day 21



No treatment group mean is significantly different from the control mean (Dunnettt's test, $p>0.05$).

Appendix 11.3

Tomato 21-Day Survival

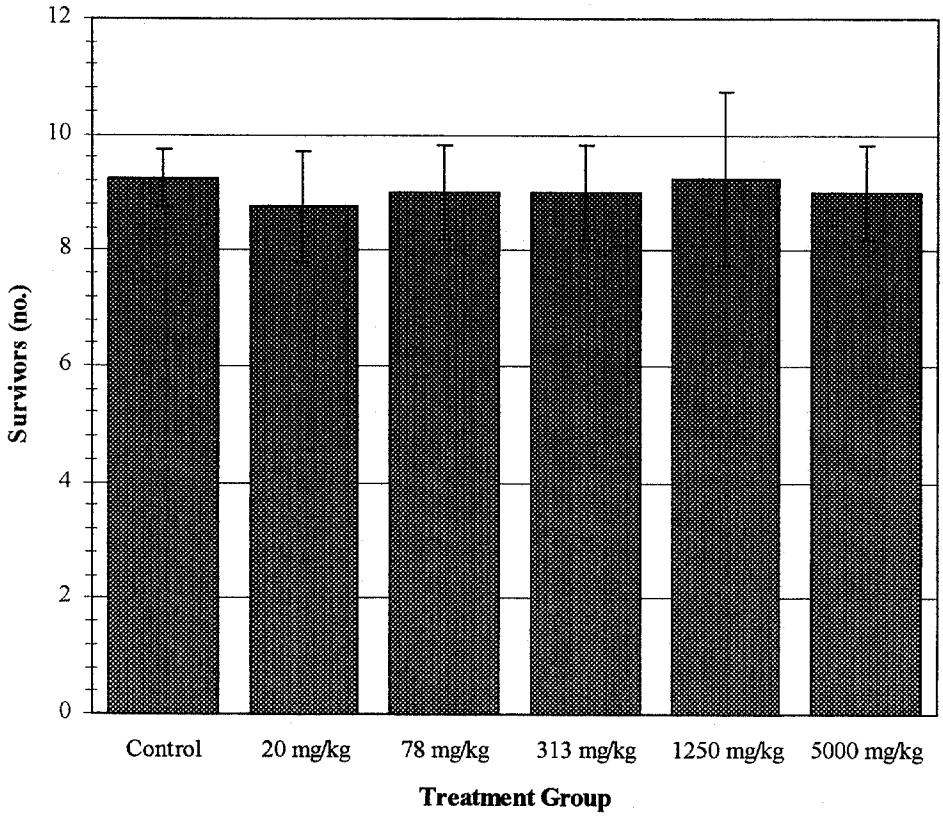
Day 21

Treatment Group	Number of Emerged Seedlings in Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	9	10	9	9	*4*	9.25	0.50
20 mg/kg	8	10	8	9	*4*	8.75	0.96
78 mg/kg	10	9	8	9	*4*	9.00	0.82
313 mg/kg	10	8	9	9	*4*	9.00	0.82
1250 mg/kg	7	10	10[1]	10	*4*	9.25	1.50
5000 mg/kg	9	10	8	9	*4*	9.00	0.82

[1] An eleventh seedling was observed in this replicate on Day 21. Mean survival was based on 10 surviving seedlings per 10 planted seeds.

Appendix 11.4

Mean Tomato 21-Day Survival



No treatment group mean is significantly different from the control mean (Dunnett's test, $p>0.05$).

Appendix 11.5

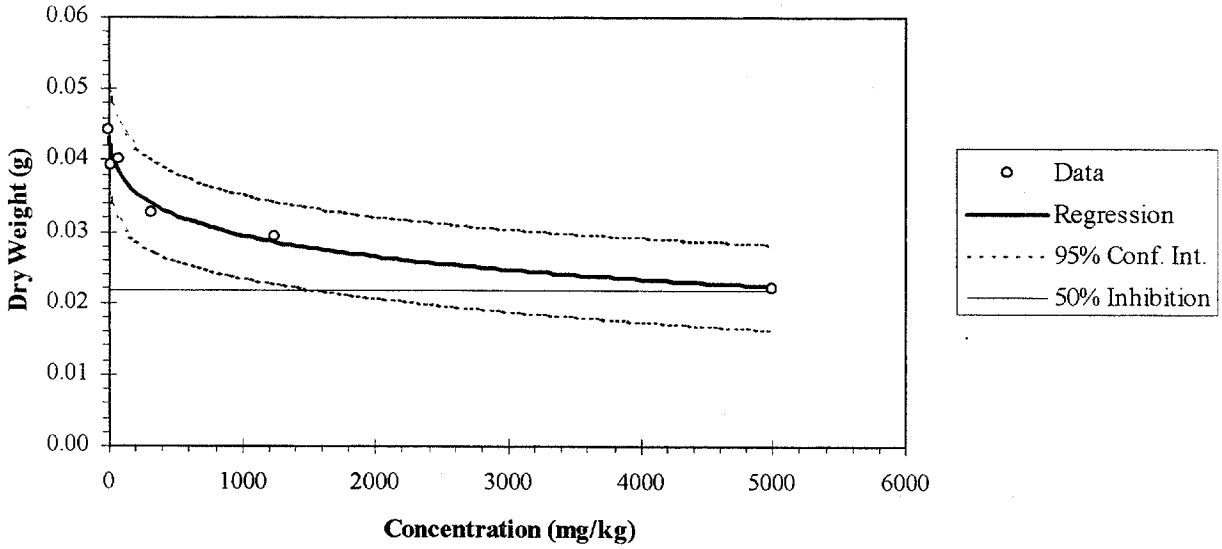
Tomato Mean Seedling Dry Weight, Day 21

Treatment Group	Mean Weight (g) per Plant of Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	0.034	0.048	0.040	0.054	*4*	0.044	0.0088
20 mg/kg	0.039	0.035	0.055	0.028	*4*	0.039	0.0115
78 mg/kg	0.049	0.046	0.036	0.030	*4*	0.040	0.0087
313 mg/kg	0.041	0.025	0.032	0.032	*4*	0.033	0.0065
1250 mg/kg	0.024	0.037	0.027[1]	0.029	*4*	0.029	0.0055
5000 mg/kg	0.020	0.019	0.024	0.026	*4*	0.022	0.0031

[1] Eleven plants were observed in replicate. Weight was not adjusted for consideration of eleventh plant weighed.

Appendix 11.6

Mean Tomato Dry Weight



Curve Parameters

EC_{25}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
422.182	81.1895	2195.84	0.0438	1.6476	0.97168

EC_{50}	Lower 95% Confidence Limit	Upper 95% Confidence Limit	R_0	σ	r^2
5455.07	1962.00	15167.01	0.0438	1.6476	0.97168

Appendix 11.7

Tomato Seedling Height on Day 21

Treatment Group	Replicate	Height (cm) for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	.	4	7	3	5	5	5	6	7	4	*9*	5.1	1.36
	B	4	6	3	5	5	11	7	5	6	7	*10*	5.9	2.18
	C	.	5	6	5	5	5	6	6	5	6	*9*	5.4	0.53
	D	.	6	7	7	7	6	3	7	4	6	*9*	5.9	1.45
20 mg/kg	A	.	.	7	7	5	7	5	6	4	5	*8*	5.8	1.16
	B	3	4	4	4	5	6	6	5	5	4	*10*	4.6	0.97
	C	.	.	4	7	3	7	8	6	4	6	*8*	5.6	1.77
	D	.	4	3	3	5	5	5	4	4	3	*9*	4.0	0.87
78 mg/kg	A	4	5	5	6	5	6	6	8	6	4	*10*	5.5	1.18
	B	.	4	5	4	5	7	7	7	5	7	*9*	5.7	1.32
	C	4	3	4	6	5	4	5	6	.	.	*8*	4.6	1.06
	D	.	3	4	4	2	5	4	4	5	6	*9*	4.1	1.17
313 mg/kg	A	4	6	6	6	6	5	4	5	3	6	*10*	5.1	1.10
	B	.	.	4	5	5	4	4	3	5	7	*8*	4.6	1.19
	C	.	4	2	5	4	4	5	5	6	8	*9*	4.8	1.64
	D	.	6	7	4	3	4	4	4	4	8	*9*	4.9	1.69
1250 mg/kg	A	.	.	.	3	4	3	3	3	5	4	*7*	3.6	0.79
	B	4	6	4	3	3	5	6	6	7	4	*10*	4.8	1.40
	C[1]	5	5	5	4	6	4	4	4	5	4	*10*	4.6	0.70
	D	3	5	6	5	5	5	5	6	2	4	*10*	4.6	1.26
5000 mg/kg	A	3	4	7	5	4	4	5	5	5	.	*9*	4.7	1.12
	B	4	3	4	3	4	5	3	4	6	7	*10*	4.3	1.34
	C	.	.	4	4	5	5	4	3	4	8	*8*	4.6	1.51
	D	.	4	5	5	5	7	5	4	4	4	*9*	4.8	0.97

The "." symbol indicates that the seedling either did not emerge or died prior to measurement.

[1] An eleventh seedling 3 cm tall was observed in this replicate, but was dropped from calculation of the replicate mean.

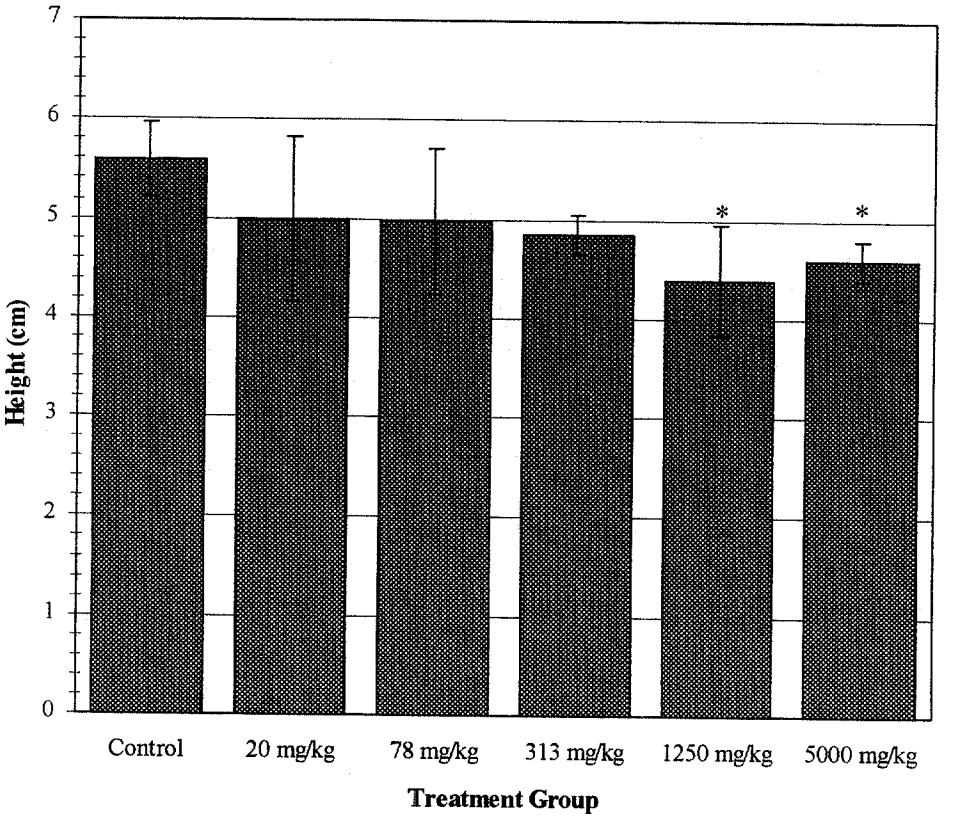
Appendix 11.8

Tomato Mean Seedling Height on Day 21

Treatment Group	Mean Height (cm) for Replicate: A	B	C	D	*n*	Mean	Std. Dev.
Control	5.1	5.9	5.4	5.9	*4*	5.6	0.38
20 mg/kg	5.8	4.6	5.6	4.0	*4*	5.0	0.84
78 mg/kg	5.5	5.7	4.6	4.1	*4*	5.0	0.74
313 mg/kg	5.1	4.6	4.8	4.9	*4*	4.8	0.20
1250 mg/kg	3.6	4.8	4.6	4.6	*4*	4.4	0.56
5000 mg/kg	4.7	4.3	4.6	4.8	*4*	4.6	0.21

Appendix 11.9

Mean Tomato Height on Day 21



* Treatment group mean is significantly different from the control mean (Dunnett's test, $p<0.05$).

Appendix 11.10

Tomato Seedling Condition, Day 21

Treatment Group	Replicate	Condition (score.sign)[1] for Plant Number:										*n*	Mean	Std. Dev.
		1	2	3	4	5	6	7	8	9	10			
Control	A	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	10	31.6
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
20 mg/kg	A	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
78 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	C	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	.	.	*8*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
313 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	B	.	100.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	11	33.3
	C	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0
1250 mg/kg	A	.	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*7*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C[2]	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	D	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
5000 mg/kg	A	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	.	*9*	0	0.0
	B	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*10*	0	0.0
	C	.	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*8*	0	0.0
	D	.	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	0.-	*9*	0	0.0

[1] The "." symbol indicates that the seedling did not emerge. A score of 0 indicates a normal seedling, while a score of 100 indicates a dead seedling. Intermediate scores are assigned to indicate the relative severity of observed signs of toxicity.

[2] An eleventh apparently normal seedling was observed in this replicate.