CALVERT
LABORATORIES, INC.

Final Report

TITLE: A 7-Day Oral Toxicokinetic Study with GB67B in Rats

Calvert Study No.: 0440RE27.002

Sponsor Study No.: TL-GB67B-RTK-09-1

Testing Facility:
Calvert Laboratories, Inc.
Scott Technology Park
130 Discovery Drive
Scott Township, PA 18447

Study Sponsor:
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
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Date: 1 June 2009

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I. Table of Contents

Appendix IV – Protocol, Amendments and Deviations

II. List of Abbreviations

CFR	Code of Federal Regulations
DABT	Diplomate of the American Board of Toxicology
DACLAM	Diplomate of the American College of Laboratory Animal Medicine
EDTA	Ethylenediamine tetraacetic acid
FDA	Food and Drug Administration
GLP	Good Laboratory Practice
IACUC	Institutional Animal Care and Use Committee
ILAR	Institute for Laboratory Animal Resources
MSDS	Material Safety Data Sheet
QAU	Quality Assurance Unit
SOP	Standard Operating Procedure
USDA	United States Department of Agriculture
M01/F01	Group 1 Male/Group 2 Female
M02/F02	Group 2 Male/Group 2 Female
M03/F03	Group 3 Male/Group 3 Female
M04/F04	Group 4 Male/Group 4 Female

III. Regulatory Compliance and Signatures

Calvert Study No.: 0440RE27.002

Title: A 7-Day Oral Toxicokinetic Study with GB67B in Rats

A. Regulatory Compliance

1. Calvert Laboratories-Conducted Study Elements

This was a non-regulated study. All parts of this study conducted by Calvert Laboratories, Inc. were performed according to SOPs and the protocol. There was no formal involvement of the Quality Assurance Unit.

2. Sponsor-Conducted Study Elements

The following portion of the study was conducted by the Sponsor or a Sponsor-enlisted subcontractor

- Dosing formulation, bioanalytical and toxicokinetic analyses

3. Guidelines for Study Design

The design and scope of this study were based on consideration of the study objective in relation to the overall product development strategy.

B. Study Director Signature

I, the undersigned, hereby declare that this report is a true and accurate record of the results obtained. No circumstances occurred during the study that were considered to have significantly affected the overall quality or integrity of the data obtained.

Cesar V. Mujer, Ph.D. — 1 June 2009

Cesar V. Mujer, Ph.D.
Study Director
Calvert Laboratories, Inc.

Date

C. Signatures of Other Responsible Personnel

Scientific Oversight and Report Review

1 Jun 2009

Scientific Management
Calvert Laboratories, Inc.

Date

IV. Summary

A. Title

A 7-Day Oral Toxicokinetic Study with GB67B in Rats

B. Objective

The purpose of this study was to evaluate the toxicity and toxicokinetics of GB67B when administered once daily, via oral gavage, for seven consecutive days to Sprague Dawley rats.

C. Methods

The test article, GB67B, was supplied by the Sponsor as a white powder. The test article was then prepared into dosing solutions for oral administration via gavage. Forty experimentally naïve Sprague Dawley rats (20 males and 20 females), approximately 7 weeks old and weighing 177-262 grams for males and females at the outset of the study were assigned to treatment groups as shown in the tables below.

Toxicology Groups

Group	Daily Dose Level (mg/kg/day)	Concentration (mg/ml)	Dose Volume* (ml/kg)	Number of Animals**	
				Male	Female
1. Control (Vehicle)	0	0	5	2	2
2. Low-Dose	30	6	5	2	2
3. Mid-Dose	90	18	5	2	2
4. High-Dose	180	36	5	2	2

*The test article was administered once daily for 7 consecutive days by oral gavage.
**On Day 8, all surviving animals were euthanized by CO_2 asphyxiation and necropsied.

Toxicokinetic Groups

Group	Daily Dose Level (mg/kg/day)	Concentration (mg/ml)	Dose Volume* (ml/kg)	Number of Animals**	
				Male	Female
5. Low dose	30	6	5	4	4
6. Mid dose	90	18	5	4	4
7. High Dose	180	36	5	4	4

*The test article was administered once daily for 7 consecutive days by oral gavage.
**On Day 1 and Day 7, whole blood samples (~0.3 mL/sample) were collected from 2 animals/sex/group in Groups 5-7 via retroorbital puncture at the specified timepoints after a single dose. Immediately following their final blood collection on Day 7, all animals were euthanized by CO_2 asphyxiation and carcasses were appropriately discarded with no necropsy.

Animals were dosed once daily for 7 consecutive days. Mortality and clinical observations were evaluated daily. Body weights were recorded prior to dose administration on Days 1, 4 and 7. Food consumption was recorded on Day 1 and Day 7. Blood for evaluation of hematology, coagulation and clinical chemistry parameters was collected on Day 8. Blood for toxicokinetic evaluation was collected from animals in the toxicokinetic groups at selected timepoints on Day 1 and Day 7. All surviving animals in the toxicology groups were sacrificed on Day 8. Selected tissues were harvested at necropsy and selected organs weighed. At the completion of necropsy, tissues were not retained and carcasses were appropriately discarded.

D. Results and Conclusions

There was no test article-related mortality observed in the study. All animals survived until their scheduled sacrifice on Day 8.

There were clinical signs of test article-related effects in one of the High dose group M04 (180 mg/kg/day) animals. Clinical signs included soft feces and ruffled fur coat.

There were test article-related effects on body weights and body weight gains. At the completion of the study, the mean body weight of M04 animals was lower when compared to Groups M01, M02 and M03 animals. In terms of mean body weight gains, M04 animals lost body weights on Days 1-4 and Days 4-7 when compared to body weight gains of animals in Groups M01, M02 and M03.

There were test article-related effects on food consumption. Lower group mean food consumption was noted in Group 4 animals on Days 1-7 when compared to the respective food consumption of animals in Groups 1, 2 and 3.

There were test article-related effects on red blood cell parameters. Group mean levels of White Blood Cells (WBC), Platelets (PLT), Absolute Neutrophils (# NEUT), and Absolute Monocytes (# MONO) were higher in M04/F04 animals when compared to Group 1 controls. Likewise, the level of PLT was also higher in Group 3 animals when compared to Group 1. In addition, F04 animals had higher mean levels of Monocytes (% MONO), Lymphocytes (# LYMPH) and Absolute Large Unstained Cells (# LUC). F03 animals had higher mean levels of # NEUT when compared to F01. The values for the above hematology parameters were outside the historical database limits for this stock of rats in this laboratory.

There were no test article-related effects on erythrocyte morphology. RBC morphology was normocytic and normochromic. There were no test article-related effects in group mean coagulation parameters.

There were test article-related effects in group mean clinical chemistry parameters in groups M03 and M04. Group mean Glucose (GLU) level was higher in M03 when compared to M01. Group mean Blood Urea Nitrogen (BUN), Alanine Aminotransferase (ALT) and Potassium (K) levels were higher in M04 when compared to M01. These levels were outside the historical database limits for this stock of rats.

There were no test article-related gross necropsy findings. However, lower absolute spleen weights, spleen-to-body weight ratios, and spleen-to-brain weight ratios were observed in M04 animals when compared to M01 control.

In conclusion, the test article GB67B caused toxicological and biological effects when administered daily to Sprague Dawley rats via oral gavage. Daily doses of 180 mg/kg/day GB67B (High-dose) administered over a 7-day period caused clinical signs of intolerance including soft feces, ruffled fur coat, reduced body weight and body weight gains in M04 rats. The test article also lowered food consumption and increased the levels of some hematology parameters in Groups 3 and 4 rats, elevated the levels of a few clinical chemistry parameters in M03 and M04 rats, and reduced the spleen weights in M04 rats.

V. General Information

A. Key Study Dates

Study Initiation Date:	26 Jan 2009
Animal Receipt Date:	28 Jan 2009
Experimental Start Date:	28 Jan 2009
First Day of Dosing:	5 Feb 2009
Necropsy:	12 Feb 2009
Experimental Completion Date:	12 Feb 2009

B. Responsible Personnel

Study Director:	Cesar V. Mujer, Ph.D.
Study Coordinator:	Renee Tanner, B.S., ALAT
Project Leader:	Jennifer Jenson, B.S.
Primary Technician:	Melissa Cicchella, B.S.
Pharmacy Technicians:	Nicholas Acri, B.S. and Christina Jackson, B.S.
Staff Veterinarian:	Laurie Serfilippi, V.M.D., DACLAM
Medical Technologist:	Beth Williams, M.S., M.T. (ASCP)
Sponsor Representative:	Randy Howard, Ph.D.
Principal Investigator - Toxicokinetics and Dose Formulation Analysis:	Rick Arrendale, Ph.D.

C. Objective

The purpose of this study was to evaluate the toxicity and toxicokinetics of GB67B when administered once daily, via oral gavage, for seven consecutive days to Sprague Dawley rats.

D. Rationale for the Study

Studies in laboratory animals provide the best means of assessing the safety and tolerability of prospective pharmaceuticals intended for human use. According to the Sponsor, this study was necessitated by the absence of appropriate non-animal alternatives and was required by a regulatory agency. The information obtained from this study does not unnecessarily duplicate the results of previous studies and could not be obtained by other means.

VI. Materials and Methods

A. Test Article

1. Test Article

Identification: GB67B

Lot/Batch No. : Not Available

Expiration Date: Not Available

Physical Description: White powder

Storage Conditions: Refrigerated (2-8 °C) and protected from light

Stability: Stability was determined by the Sponsor. Stability data was not provided by the Sponsor.

2. Vehicle

Identification: DMSO/45% Beta-cyclodextrin (20/80)

Vehicle Components

Component	Supplier	Lot or Batch #	Expiration Date	Description	Storage
β-cyclodextrin	Sigma	05002E	28 Jan 2012	White powder	Room temperature
Sterile Water for Injection, USP	Baxter	C745059	Jul 2009	Clear colorless liquid	Room temperature
DMSO	Sigma	00296JJ	05 Dec 2011	Clear colorless liquid	Room temperature

Lot/Batch No. : 04 Feb 2009

Expiration Date: 11 Feb 2009

Physical Description: Clear colorless slightly viscous liquid

Storage Conditions: Room temperature

3. *Dose Preparation*

The test article was prepared according to Calvert SOPs on test article formulation. Dosing preparations were stored at room temperature following preparation and utilized within 4 hours of completion of preparation. Each day prior to dosing, a 5X stock solution of test article in DMSO was made, and then the stock was diluted with 4 parts of 45% Beta-cyclodextrin by vortexing at room temperature.

4. *Formulated Test Article Analysis*

On Day 1 and Day 7, 1-ml samples of each dosing solution including the control article, were obtained from top, middle and bottom to determine the concentration, homogeneity, and/or stability of the test article in vehicle. These samples were stored at approximately -70° C or lower. These samples were returned to, and analytical evaluation was done under the direction of:

Rick Arrendale, Ph.D.
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322
Phone: (770) 337-6472
Fax: (404) 727-3677
Email: rarrend@emory.edu

The client had analyzed the High-dose dosing solution used in the study by HPLC and determined that high levels of the drug were present. However, the Dosing Formulation Report was not available for inclusion in this final report.

5. *Reserve Archive Samples*

A retention sample of the test article was not maintained at Calvert.

6. *Accountability and Disposition*

Test material accountability was maintained according to Calvert SOPs. After the end of the study, unused material was returned to:

Randy Howard, Ph.D.
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322
Cell: (319) 541-7809
Email: rbhowar@emory.edu

B. Test System (Animals and Animal Care)

1. Description

Species:	Rat
Stock:	Sprague-Dawley (Hsd: SD)
Total Number:	40 (20 males and 20 females)
Gender:	Male and female
Age Range:	Approximately 7 weeks at start of dosing; records of dates of birth for animals used in this study are retained in the Calvert archives.
Body Weight Range:	177-262 grams for males and females at the outset (Day 1) of the study.
Animal Source:	Harlan
Experimental History:	Purpose-bred and experimentally naïve at the outset of the study.
Identification:	Eartag and cage card.

2. Rationale for Choice of Species and Number of Animals

The rat is a standard rodent species used in toxicology studies based upon the substantial amounts of published historical data (1). The rat is a species of choice because there are previous pharmacology studies showing activity of the test article that have been conducted in the rats. Use of the rat will allow calculation of therapeutic index, using the previous rat efficacy results.

The total number of animals used in this study is considered to be the minimum number necessary to provide a preliminary assessment of the tolerability in rodents (2).

3. Husbandry

Housing:	Animals were group-housed by sex upon receipt and individually housed upon assignment to study in compliance with National Research Council "Guide for the Care and Use of Laboratory Animals". The room in which the animals were kept is documented in the study records. No other species were kept in the same room.
Lighting:	12 hours light/12 hours dark
Room Temperature:	19.8 to 20.3°C
Relative Humidity:	44-56.7%
Food:	All animals had access to Harlan Teklad Rodent Diet (certified) or equivalent *ad libitum*, unless otherwise specified. The lot number(s) and specifications of each lot used are archived at Calvert. No contaminants were known to be present in the certified diet at levels that would be expected to interfere with the results of this study. Analysis of the diet was limited to that performed by the manufacturer, records of which are maintained in the Calvert archives.
Water:	Water was available *ad libitum,* to each animal via an automatic watering device. The water is routinely analyzed for contaminants as per Calvert SOP's. No contaminants were known to be present in the water at levels that would be expected to interfere with the results of this study. Results of the water analysis are maintained in the Calvert archives.

Acclimation: Study animals were acclimated to their housing for a minimum of five days prior to their first day of dosing.

4. *Prestudy Health Screen and Selection Criteria*

All animals received for this study were assessed as to their general health by a member of the veterinary staff or other authorized personnel. During the acclimation period, each rat was observed at least once daily for any abnormalities or for the development of infectious disease. Only animals that were suitable for use were assigned to this study.

5. *Assignment to Study Groups*

Animals were assigned to study groups by a computerized randomization program (LABCAT In Life module version 8.0), developed by Innovative Program Associates, Inc. 303 Wall Street, Princeton, NJ 08540-1515) designed to achieve similar group mean body weights.

Rats were given the following identification numbers and identified by ear tag:

Toxicology Groups

Group Number	Males	Females
1	5001-5002	5003-5004
2	5005-5006	5007-5008
3	5009-5010	5011-5012
4	5013-5014	5015-5016

Toxicokinetic Groups

Group Number	Males	Females
5	5017-5020	5021-5024
6	5025-5028	5029-5032
7	5033-5036	5037-5040

6. *Humane Care of Animals*

Treatment of animals was in accordance with the study protocol and also in accordance with Calvert SOP's which adhere to the regulations outlined in the USDA Animal Welfare Act (9 CFR Parts 1, 2 and 3) and the conditions specified in the Guide for the Care and Use of Laboratory Animals (ILAR

publication, 1996, National Academy Press). The Calvert IACUC approved the study protocol prior to finalization.

C. Test Article Administration

1. Group Assignments and Dose Levels

Toxicology Groups

Group	Daily Dose Level (mg/kg/day)	Concentration (mg/ml)	Dose Volume* (ml/kg)	Number of Animals**	
				Male	Female
1. Control (Vehicle)	0	0	5	2	2
2. Low-Dose	30	6	5	2	2
3. Mid-Dose	90	18	5	2	2
4. High-Dose	180	36	5	2	2

*The test article was administered once daily for 7 consecutive days by oral gavage.
**On Day 8, all surviving animals were euthanized by CO_2 asphyxiation and necropsied.

Toxicokinetic Groups

Group	Daily Dose Level (mg/kg/day)	Concentration (mg/ml)	Dose Volume* (ml/kg)	Number of Animals**	
				Male	Female
5. Low-dose	30	6	5	4	4
6. Mid-dose	90	18	5	4	4
7. High-Dose	180	36	5	4	4

*The test article was administered once daily for 7 consecutive days by oral gavage.
**On Day 1 and Day 7, whole blood samples (~0.3 mL/sample) were collected from 2 animals/sex/group in Groups 5-7 by retroorbital puncture at the specified timepoints after a single dose. Immediately following their final blood collection on Day 7, all animals were euthanized by CO_2 asphyxiation and carcasses were appropriately discarded with no necropsy.

2. Dosing

Route: Oral via gavage

Frequency: Once daily for a minimum of 7 consecutive days at the maximum dose volume of 5 ml/kg.

Procedure: Doses were administered once daily. Each animal received a mg/kg dose based upon its most recent body weight.

Groups 1-4 animals were euthanized by CO_2 asphyxiation and necropsied on Day 8.

3. *Justification for Route, Dose Levels and Dosing Schedule*

The oral route was chosen as it is the intended route of administration in humans.

Dose levels were selected by the Sponsor. The data from this study will be utilized to establish toxicity of the test article as an oral formulation.

D. In-Life Observations and Measurements (Groups 1-4)

1. *Mortality/Morbidity*

Frequency: Twice daily (a.m. and p.m.) on Days 1-7 and once prior to sacrifice on Day 8.

Each animal observed for evidence of death or impending death (as per Calvert SOP VET-14).

2. *Clinical Observations*

Frequency: Prior to dose administration on Day 1, one hour post-dose, and as necessary. Once prior to scheduled sacrifice on Day 8.

3. *Body Weight*

Frequency: At the time of randomization/selection and prior to dose administration on Days 1, 4 and 7.

A fasted body weight was recorded prior to scheduled sacrifice on Day 8.

4. Food Consumption

Frequency — Full feeder weights and/or feeder weigh backs were recorded on Day 1 and Day 7.

E. Clinical Pathology Evaluation (Groups 1-4)

1. Sample Collection

Blood samples for evaluation of hematology, coagulation and serum chemistry parameters were collected from all surviving animals prior to terminal sacrifice on Day 8. Animals were anesthetized by CO_2 inhalation prior to blood collection. Immediately following exsanguination by cardiocentesis for terminal blood collection, rats were returned to the CO_2 chamber to ensure euthanasia. Animals were fasted overnight (approximately 12-24 hours) prior to blood collection for clinical chemistry evaluation.

2. Collection Procedures, Processing and Analysis

a) Hematology

Method of Collection: Cardiocentesis

Anticoagulant: EDTA

Parameters Analyzed:

Hematology Parameters	
Red Blood Cell Count (RBC) and Morphology	Platelet count (PLT)
White Blood Cell Count (WBC)*	Hematocrit (HCT)
Mean Corpuscular Hemoglobin (MCH)	Hemoglobin (HGB)
Mean Corpuscular Hemoglobin Concentration (MCHC)	Reticulocyte Count (Retic)
Mean Corpuscular Volume (MCV)	

*Total and differential white blood cell counts, including neutrophils, monocytes, basophils, eosinophils, lymphocytes and large unstained cells

b) Coagulation

Method of Collection: Cardiocentesis

Anticoagulant: Sodium Citrate

Parameters Analyzed:

Coagulation Parameters	
Activated Partial Thromboplastin Time (APTT)	Prothrombin Time (PT)

c) Serum Clinical Chemistry

Method of Collection: Cardiocentesis

Anticoagulant: None

Parameters Analyzed:

Clinical Chemistry Parameters	
Alanine Aminotransferase (ALT)	Globulin (calculated)(GLOB)
Albumin (ALB)	Glucose (GLU)
Albumin/Globulin ratio (calculated)(A/G)	Phosphorus (PHOS)
Alkaline Phosphatase (ALP)	Potassium (K)
Aspartate Aminotransferase (AST)	Sodium (NA)
Calcium (CA)	Total Bilirubin (T-BIL)
Chloride (CL)	Total Protein (TP)
Cholesterol (CHOL)	Triglycerides (TRIG)
Creatinine (CREAT)	Urea Nitrogen (BUN)

F. Terminal Procedures and Anatomic Pathology (Groups 1-4)

1. Termination

a) Scheduled Sacrifice

All surviving animals were euthanized by CO_2 asphyxiation on Day 8 and necropsied.

b) Final Body Weight

A fasted terminal body weight was recorded prior to sacrifice on Day 8. This body weight was used to calculate organ-to-body weight ratios.

2. Necropsy

A gross necropsy was performed by Calvert personnel on all animals that were sacrificed or found dead during the study. The necropsy included examination of:

- the external body surface
- all orifices
- the cranial, thoracic and abdominal cavities and their contents.

All abnormalities were described completely and recorded. No tissues were collected and carcasses were appropriately discarded.

3. *Organ Weights*

At scheduled sacrifice on Day 8, the following organs were weighed before fixation, after dissection of excess fat and other excess tissues. Paired organs were weighed together.

Organs Weighed		
Adrenals	Brain	Heart
Kidneys	Liver	Lungs
Ovaries	Pituitary	Spleen
Testes	Thyroids/parathyroids	

Organ-to-body weight and organ-to-brain weight ratios were calculated using the final body weight obtained prior to necropsy.

G. Toxicokinetic In-Life Observations and Measurements (Groups 5-7)

1. *Mortality*

Frequency: Twice daily for 7 consecutive days (a.m. and p.m.)

Each animal observed for evidence of death or impending death (as per Calvert SOP VET-14).

2. *Clinical Observations*

Frequency: Observations were recorded as needed, but not reported.

3. *Body Weight*

Frequency: At the time of randomization/selection and prior to dose administration on Days 1, 4 and 7.

4. Toxicokinetics

a) Blood Sampling

On Day 1 and Day 7, whole blood samples (~0.3 mL/sample) were collected from 2 animals/sex/group in Groups 5-7 by retroorbital puncture at the following timepoints after a single dose:

0 hour (predose)	2 hours post-dose
30 minutes post-dose	4 hours post-dose
1 hour post-dose	8 hours post-dose

Each animal was bled no more than three times on each TK day. Animals were not fasted prior to collection. Animals were anesthetized by CO_2 inhalation and blood samples were collected into blood collection tubes containing potassium EDTA. Blood samples were centrifuged at approximately 3000 rpm for approximately 10 minutes to separate the plasma. The resultant plasma was dispensed into appropriately labeled tubes and stored frozen at approximately -70°C.

Samples were shipped on dry ice with prior notification to the Sponsor at the following address:

Randy Howard, Ph.D.
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322
Cell: (319) 541-7809
Email: rbhowar@emory.edu

Results of the Bioanalytical Evaluation Report are presented in Appendix III. Using a PE Sciex API 4000 LC-MS/MS system, the practical detection limits in the rat plasma were all below quantitation limits for GB67B (see pp. 8-13 of Appendix III). Although HPLC analysis indicated the presence of the drug in the dosing solution (High-dose), it appears that the drug was rapidly broken down or metabolized during absorption.

5. Euthanasia

Each animal in Groups 5-7 was euthanized by CO_2 asphyxiation following their final blood collection. Necropsy was not performed and the carcasses were appropriately discarded.

VII. Records and Reports

A. Data Collection and Analysis

In-Life data (clinical observations, body weights, feeder weights, dose administration) were collected using LABCAT In-Life module version 8.0 or on paper when necessary. Necropsy data was collected on paper. Any other data not collected on-line was manually tabulated for inclusion in the report.

In-Life data was tabulated and/or statistically evaluated using the LABCAT In-Life module version 8.0. Necropsy data was hand-tabulated or tabulated and/or statistically evaluated using the LABCAT Organ Weights/Necropsy module version 3.28. All LABCAT modules were developed by Innovative Program Associates, Inc. (303 Wall Street, Princeton, NJ 08540-1515).

Statistical analysis was not be performed since N<3 animals per group.

B. Storage of Records

Test article preparation (or test article information), test article tracking, in-life data, necropsy data, protocol, protocol amendments (if applicable), draft report(s) that have been submitted to a regulatory agency, and the original final report generated as a result of this study will be archived at Calvert, 105 Edella Road, Suite 100, Clarks Summit, PA 18411. After 2 years, the Sponsor will be contacted to determine final disposition of all study materials.

All analytical and bioanalytical data will be archived in the Emory Institute for Drug Discovery, Emory University, 1515 Dickey Drive, Atlanta, GA 30322.

VIII. Results and Discussion

A. In-Life Observations

1. Mortality/Morbidity

There were no early deaths during the study. All animals survived until their scheduled sacrifice on Day 8.

2. *Clinical Observations*

There were clinical signs of test article-related effects in one of the high dose group M04 (180 mg/kg/day) animals. Clinical signs included soft feces and ruffled fur coat. Soft feces were noted pre-dose in animal # 5014 on Days 3, 4 and 5, and post-dose on Days 4 and 8. Ruffled fur coat was noted in this animal (#5014) pre-dose on Day 5 and post-dose on Days 4, 5 and 8. Additionally, soft feces were noted post-dose in low dose group M02 (30 mg/kg/day) animal #s 5005 and 5006 on Day 2.

3. *Body Weight*

There were test article-related effects on body weights and body weight gains. At the completion of the study, the mean body weight of Group M04 animals was 24.3% lower when compared to M01 animals.

In terms of mean body weight gains, Group M04 animals lost body weights on Days 1-4 and Days 4-7 when compared to body weight gains of animals in Groups M01, M02 and M03.

4. *Food Consumption*

There were test article-related effects on food consumption during the study. Lower group mean food consumption was noted in Group 4 animals on Days 1-7 when compared to the respective food consumption of animals in Groups 1, 2 and 3.

B. Clinical Pathology

1. *Hematology*

There were test article-related effects on red blood cell parameters. Group mean levels of White Blood Cells (WBC), Platelets (PLT), Absolute Neutrophils (# NEUT), and Absolute Monocytes (# MONO) were higher in Group 4 animals when compared to Group 1 controls. Likewise, the level of PLT was also higher in Group 3 animals when compared to Group 1. In addition, F04 animals had higher mean levels of Monocytes (% MONO), Lymphocytes (# LYMPH) and Absolute Large Unstained Cells (# LUC) and F03 animals had higher mean levels of # NEUT when compared to F01.

The values for the above hematology parameters were outside the historical database limits for this stock of rats in this laboratory. The normal historical limits are: Males: WBC=4.05-15.51, PLT=631-1455, # NEUT=0.0-3.3, # MONO=0.02-0.8; Females: WBC=2.16-12.50, PLT=657-1421, # NEUT=0.0-1.92, # MONO=0.00-0.60, %MONO=1.3-6.5, # LYMPH=1.64-10.12 and # LUC=0.00-0.18.

2. Erythrocyte Morphology

There were no test article-related effects on erythrocyte morphology. RBC morphology was normocytic and normochromic.

3. Coagulation

There were no test article-related effects in group mean coagulation parameters. Except for a slight increase in group mean Prothrombin Time (PT) in group M04 of 19.65 seconds, the coagulation parameters were normal in all dose groups. The normal historical limits for PT were from 16.4-19.4 seconds among male rats.

4. Clinical Chemistry

There were test article-related effects in group mean clinical chemistry parameters in groups M03 and M04. Group mean level of Glucose (GLU) was higher in group M03 animals when compared to M01. Group mean levels of Blood Urea Nitrogen (BUN), Alanine Aminotransferase (ALT) and Potassium (K) were higher in group M04 animals when compared to M01.

The historical limits for the above parameters are: GLU=73-169, BUN=10-26, ALT=22-62 and K=5.1-7.5.

C. Postmortem Observations

1. Gross Necropsy Findings

There were no findings noted at necropsy that were test article-related. One male (# 5009, M03) was observed to have the right testis (0.30 g) smaller than the left (1.15 g). All other animals had no visible macroscopic abnormalities.

2. *Organ Weights*

Test article-related findings in absolute spleen weights were noted at necropsy. Lower absolute spleen weights, spleen-to-body weight ratios, and spleen-to-brain weight ratios were observed in M04 animals when compared to M01 control.

IX. Conclusion

The test article GB67B caused toxicological and biological effects when administered daily to Sprague Dawley rats via oral gavage. Daily doses of 180 mg/kg/day GB67B (High-dose) administered over a 7-day period caused clinical signs of intolerance including soft feces, ruffled fur coat, reduced body weight and body weight gains in M04 rats. The test article also lowered food consumption and increased the levels of some hematology parameters in Group 4 rats, elevated the levels of a few clinical chemistry parameters in M03 and M04 rats, and reduced the spleen weights in M04 rats.

X. References

1. Speid, L.H., Lumley, C. E., and Walker, S. R. (1990). Harmonization of Guidelines for Toxicity Testing of Pharmaceuticals by 1992. *Regulatory Toxicology and Pharmacology*. 12: 179-211.

2. Gad, Shayne C. (2002) *Drug Safety Evaluation*. John Wiley and Sons, Inc., New York, pp. 130-175.

XI. Tables

TABLE 1 – Summary of Observations by Period

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

Data collected by Labcat v8.0; Report generated by v8.0

TABLE 1 - Summary of Observations by Period

Study Id:	0440RE27.002
Study Name:	0440RE27.002

Group Gender :	Male	**Study Phase :**	In-Life
Subject Gender :	Male	**Scheduled AND UnScheduled**	

Day 1

Group ID / N	M01 2	M02 2	M03 2	M04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 2

Group ID / N	M01 2	M02 2	M03 2	M04 2
1 Hour Post-dose Normal	2 100.00 %	-	2 100.00 %	2 100.00 %
1 Hour Post-dose Soft Feces	-	2 100.00 %	-	-
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 3

Group ID / N	M01 2	M02 2	M03 2	M04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	1 50.00 %
Predose Soft Feces	-	-	-	1 50.00 %

Day 4

Group ID / N	M01 2	M02 2	M03 2	M04 2
1 Hour Post-dose Loose Feces	-	-	-	1 50.00 %
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	1 50.00 %

TABLE 1 - Summary of Observations by Period

Study Id:	0440RE27.002
Study Name:	0440RE27.002

Group Gender :	Male	**Study Phase :**	In-Life
Subject Gender :	Male	**Scheduled AND UnScheduled**	

Day 4

	M01 2	M02 2	M03 2	M04 2
1 Hour Post-dose Ruffled Fur Coat	-	-	-	1 50.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	1 50.00 %
Predose Soft Feces	-	-	-	1 50.00 %

Day 5

Group ID N	M01 2	M02 2	M03 2	M04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	1 50.00 %
1 Hour Post-dose Ruffled Fur Coat	-	-	-	1 50.00 %
1 Hour Post-dose Soft Feces	-	-	-	1 50.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	1 50.00 %
Predose Ruffled Fur Coat	-	-	-	1 50.00 %
Predose Soft Feces	-	-	-	1 50.00 %

Day 6

Group ID N	M01 2	M02 2	M03 2	M04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	1 50.00 %
1 Hour Post-dose Soft Feces	-	-	-	1 50.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 7

TABLE 1 - Summary of Observations by Period

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group Gender : Male
Subject Gender : Male
Study Phase : In-Life
Scheduled AND UnScheduled

Day 7

Group ID N	M01 2	M02 2	M03 2	M04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	1 50.00 %
1 Hour Post-dose Soft Feces	-	-	-	1 50.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 8

Group ID N	M01 2	M02 2	M03 2	M04 2
Appears Normal	2 100.00 %	2 100.00 %	2 100.00 %	1 50.00 %
Ruffled Fur Coat	-	-	-	1 50.00 %
Soft Feces	-	-	-	1 50.00 %

Group Gender : Female
Subject Gender : Female
Study Phase : In-Life
Scheduled AND UnScheduled

Day 1

Group ID N	F01 2	F02 2	F03 2	F04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 2

Group ID N	F01 2	F02 2	F03 2	F04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

TABLE 1 - Summary of Observations by Period

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group Gender : Female
Subject Gender : Female
Study Phase : In-Life
Scheduled AND UnScheduled

Day 3

Group ID / N	F01 2	F02 2	F03 2	F04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 4

Group ID / N	F01 2	F02 2	F03 2	F04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 5

Group ID / N	F01 2	F02 2	F03 2	F04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 6

Group ID / N	F01 2	F02 2	F03 2	F04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

Day 7

Group ID / N	F01 2	F02 2	F03 2	F04 2
1 Hour Post-dose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %
Predose Normal	2 100.00 %	2 100.00 %	2 100.00 %	2 100.00 %

TABLE 1 - Summary of Observations by Period

Study Id:	0440RE27.002
Study Name:	0440RE27.002

Group Gender :	Female	**Study Phase :**	In-Life
Subject Gender :	Female	**Scheduled AND UnScheduled**	

Day 8

	Group ID	**F01**	**F02**	**F03**	**F04**
	N	**2**	**2**	**2**	**2**
Appears Normal		2	2	2	2
		100.00 %	100.00 %	100.00 %	100.00 %

-- No Data available

TABLE 2 – Summary of Body Weight by Group

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

Data collected by Labcat v8.0; Report generated by v8.0

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002

TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

TABLE 2 - Summary of Body Weight by Group (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group Gender : Male **Subject Gender :** Male
Study Phase : In-Life

Period:	Group ID:	M01	M02	M03	M04
Day 1	N	2	2	2	2
	Mean	246.5	243.0	244.5	238.0
	SD	9.19	11.31	10.61	1.41
Day 4	N	2	2	2	2
	Mean	265.5	259.5	259.0	221.5
	SD	10.61	9.19	15.56	19.09
Day 7	N	2	2	2	2
	Mean	279.5	271.0	275.5	211.5
	SD	10.61	5.66	14.85	27.58

Group Gender : Female **Subject Gender :** Female
Study Phase : In-Life

Period:	Group ID:	F01	F02	F03	F04
Day 1	N	2	2	2	2
	Mean	184.5	189.0	193.0	192.5
	SD	4.95	15.56	5.66	3.54
Day 4	N	2	2	2	2
	Mean	198.0	193.0	197.0	189.5
	SD	7.07	4.24	1.41	0.71
Day 7	N	2	2	2	2
	Mean	194.5	201.5	204.5	188.5
	SD	9.19	6.36	9.19	4.95

TABLE 3 – Summary of Body Weight Changes

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

Data collected by Labcat v8.0; Report generated by v8.0

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS STUDY NUMBER: 0440RE27.002

TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

TABLE 3 - Summary of Body Weight Changes (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group Gender : Male **Study Phase :** In-Life
Subject Gender : Male

Period	Group ID:	M01	M02	M03	M04
Day 1 - 4	N	2	2	2	2
	Mean	19.0	16.5	14.5	-16.5
	SD	1.41	2.12	4.95	20.51
Day 4 - 7	N	2	2	2	2
	Mean	14.0	11.5	16.5	-10.0
	SD	0.00	3.54	0.71	8.49

Group Gender : Female **Study Phase :** In-Life
Subject Gender : Female

Period	Group ID:	F01	F02	F03	F04
Day 1 - 4	N	2	2	2	2
	Mean	13.5	4.0	4.0	-3.0
	SD	2.12	11.31	4.24	2.83
Day 4 - 7	N	2	2	2	2
	Mean	-3.5	8.5	7.5	-1.0
	SD	2.12	2.12	10.61	5.66

TABLE 4 – Summary of Feed Consumption By Group

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

Data collected by Labcat v8.0; Report generated by v8.0

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002

TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

TABLE 4 - Summary of Feed Consumption By Group (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group Gender : Male **Study Phase :** In-Life
Subject Gender : Male

Period	Group Id:	M01	M02	M03	M04
Day 1 - 7	N	2	2	2	2
	Mean	175.0	152.0	162.5	73.5
	SD	2.83	0.00	3.54	40.31

Group Gender : Female **Study Phase :** In-Life
Subject Gender : Female

Period	Group Id:	F01	F02	F03	F04
Day 1 - 7	N	2	2	2	2
	Mean	116.0	122.5	120.5	89.0
	SD	1.41	0.71	9.19	7.07

TABLE 5 – Hematology Group Summary

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

Data collected by Labcat v8.0; Report generated by v8.0

TABLE 5 – Hematology Group Summary

Abbr	Description	Units
WBC	White Blood Cells	x10e3/µL
RBC	Red Blood Cells	x10e6/µL
HGB	Hemoglobin	g/dL
HCT	Hematocrit	%
#LYMPH	Lymphocytes	x10e3/µL
%LYMPH	Lymphocytes - %	%
MCV	Mean Corpuscular Volume	fL
MCHC	Mean Corpuscular Hemoglobin Concentration	g/dL
MCH	Mean Corpuscular Hemoglobin	pg
#MONO	Absolute Monocytes	x10e3/µL
%MONO	Monocytes - %	%
#NEUT	Absolute Neutrophil	x10e3/µL
%NEUT	Neutrophil - %	%
PLT	Platelets	x10e3/µL
#BASO	Absolute Basophil	x10e3/µL
%BASO	Basophil - %	%
#EOS	Absolute Eosinophil	x10e3/µL
%EOS	Eosinophil - %	%
%LUC	Large Unstained Cells - %	%
#LUC	Absolute Large Unstained Cells	x10e3/µL
%RETIC	Reticuloyctes - %	%
#RETIC	Absolute Reticulocyte	x10e9/L

TABLE 5 - Hematology Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002
Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M01 (0 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	13.865	7.680	14.80	46.25	60.25	19.30	32.00	1,184.0	13.60	81.45	3.15	0.75	0.60	0.45
SD	1.6617	0.0141	0.283	0.778	0.919	0.424	1.131	56.57	6.364	8.415	1.344	0.636	0.141	0.071

Group ID: M02 (30 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	10.050	8.125	15.25	48.15	59.30	18.75	31.60	1,292.5	13.45	80.20	3.90	0.80	0.65	1.00
SD	5.1619	0.3323	0.778	2.616	0.849	0.212	0.141	174.66	3.748	1.131	3.253	0.424	0.071	0.283

Group ID: M03 (90 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	15.215	7.995	14.95	47.95	60.00	18.70	31.20	1,762.0	12.95	80.95	4.00	0.65	0.90	0.55
SD	1.0677	0.1485	0.071	0.071	0.990	0.283	0.000	292.74	0.071	0.778	0.990	0.212	0.000	0.071

Group ID: M04 (180 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	17.395	8.350	15.65	48.75	58.35	18.75	32.15	1,944.5	25.85	67.70	5.45	0.15	0.50	0.30
SD	4.8861	0.0849	0.495	1.909	2.899	0.636	0.354	474.47	5.869	2.404	2.051	0.212	0.707	0.424

Group ID: M01 (0 mg/kg/day)

	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2	2	2
Mean	1.835	11.365	0.425	0.095	0.080	0.070	4.355	334.40
SD	0.6576	2.5244	0.1344	0.0778	0.0141	0.0141	0.3323	26.022

Group ID: M02 (30 mg/kg/day)

	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2	2	2
Mean	1.250	8.090	0.475	0.070	0.070	0.095	4.155	337.35
SD	0.3111	4.2568	0.5303	0.0000	0.0424	0.0212	0.3748	16.758

Group ID: M03 (90 mg/kg/day)

TABLE 5 - Hematology Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Day on Test 8 **Observation Date** 02/12/2009

	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2	2	2
Mean	1.970	12.315	0.605	0.100	0.130	0.090	4.160	331.75
SD	0.1556	0.9829	0.1202	0.0424	0.0141	0.0000	0.6223	43.770

Group ID: M04 (180 mg/kg/day)

	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2	2	2
Mean	4.355	11.840	0.995	0.035	0.105	0.070	2.535	211.50
SD	0.2475	3.7335	0.6152	0.0495	0.1485	0.0990	0.1768	13.011

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F01 (0 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	9.835	7.860	15.00	45.30	57.65	19.05	33.10	1,328.0	12.25	80.60	3.95	1.05	1.00	1.15
SD	0.7142	0.3253	0.424	1.273	0.778	0.212	0.000	217.79	3.323	0.000	2.192	0.071	0.424	0.778

Group ID: F02 (30 mg/kd/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	10.145	7.990	15.05	46.05	57.60	18.85	32.75	1,318.0	12.10	81.95	2.90	1.10	0.80	1.10
SD	0.7000	0.0000	0.071	0.212	0.283	0.071	0.354	195.16	1.556	0.495	0.566	0.849	0.283	0.566

Group ID: F03 (90 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	14.545	7.925	14.65	45.25	57.10	18.50	32.40	1,826.0	27.30	65.90	4.00	0.95	0.95	0.95
SD	0.5728	0.2899	0.636	2.051	0.566	0.141	0.141	41.01	14.991	15.132	0.566	0.212	0.212	0.071

Group ID: F04 (180 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	17.640	7.160	13.50	41.70	58.20	18.90	32.45	2,179.5	15.25	72.65	8.65	0.90	0.85	1.75
SD	1.1738	0.0990	0.424	1.273	0.990	0.283	0.071	521.14	11.243	17.607	3.889	0.566	0.071	1.768

Group ID: F01 (0 mg/kg/day)

	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2	2	2
Mean	1.220	7.935	0.380	0.100	0.095	0.110	2.670	210.20
SD	0.4101	0.5728	0.1838	0.0141	0.0354	0.0707	0.2970	31.820

Group ID: F02 (30 mg/kd/day)

TABLE 5 - Hematology Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Day on Test 8 **Observation Date** 02/12/2009

	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2	2	2
Mean	1.230	8.310	0.295	0.110	0.085	0.105	2.595	207.25
SD	0.2404	0.5233	0.0778	0.0707	0.0212	0.0495	1.0394	83.368

Group ID: F03 (90 mg/kg/day)

	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2	2	2
Mean	4.015	9.545	0.585	0.140	0.140	0.135	3.545	282.75
SD	2.3405	1.8314	0.1061	0.0283	0.0283	0.0212	1.2374	108.399

Group ID: F04 (180 mg/kg/day)

	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2	2	2
Mean	2.760	12.710	1.550	0.160	0.145	0.315	3.360	240.70
SD	2.1637	2.2627	0.7920	0.1131	0.0212	0.3323	0.3536	28.850

' ' No data collected

TABLE 6 – Morphology Observations

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

Data collected by Labcat v8.0; Report generated by v8.0

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002

TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

TABLE 6 - Morphology Observations

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Study Phase: In-Life | **Group Id:** M01 (0 mg/kg/day)
GroupGender: Male | **Subject Id:** 5001

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** M01 (0 mg/kg/day)
GroupGender: Male | **Subject Id:** 5002

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** M02 (30 mg/kg/day)
GroupGender: Male | **Subject Id:** 5005

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** M02 (30 mg/kg/day)
GroupGender: Male | **Subject Id:** 5006

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** M03 (90 mg/kg/day)
GroupGender: Male | **Subject Id:** 5009

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** M03 (90 mg/kg/day)
GroupGender: Male | **Subject Id:** 5010

TABLE 6 - Morphology Observations

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Study Phase: In-Life | **Group Id:** M03 (90 mg/kg/day)
GroupGender: Male | **Subject Id:** 5010

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** M04 (180 mg/kg/day)
GroupGender: Male | **Subject Id:** 5013

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** M04 (180 mg/kg/day)
GroupGender: Male | **Subject Id:** 5014

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** F01 (0 mg/kg/day)
GroupGender: Female | **Subject Id:** 5003

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** F01 (0 mg/kg/day)
GroupGender: Female | **Subject Id:** 5004

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** F02 (30 mg/kd/day)
GroupGender: Female | **Subject Id:** 5007

TABLE 6 - Morphology Observations

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Study Phase: In-Life | **Group Id:** F02 (30 mg/kd/day)
GroupGender: Female | **Subject Id:** 5007

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** F02 (30 mg/kd/day)
GroupGender: Female | **Subject Id:** 5008

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** F03 (90 mg/kg/day)
GroupGender: Female | **Subject Id:** 5011

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** F03 (90 mg/kg/day)
GroupGender: Female | **Subject Id:** 5012

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** F04 (180 mg/kg/day)
GroupGender: Female | **Subject Id:** 5015

Accession Number

Schedule DOT = 8 | **Day on Test** 8 | **Observation Date** 02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

Study Phase: In-Life | **Group Id:** F04 (180 mg/kg/day)
GroupGender: Female | **Subject Id:** 5016

Accession Number

TABLE 6 - Morphology Observations

Study ID:	0440RE27.002
Study Name:	0440RE27.002

Study Phase:	In-Life	**Group Id:**	F04 (180 mg/kg/day)
GroupGender:	Female	**Subject Id:**	5016

Accession Number

Schedule	DOT = 8	**Day on Test**	8	**Observation Date**	02/12/2009

Observation		Details
NN	Normocytic & Normochromic	

TABLE 7 – Coagulation Group Summary

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

Data collected by Labcat v8.0; Report generated by v8.0

Abbr	Description	Units
PT	Prothrombin Time	sec
APTT	Activated Partial Thromboplastin Time	sec

TABLE 7 - Coagulation Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M01 (0 mg/kg/day)

	PT	APTT
N	2	2
Mean	18.35	10.55
SD	0.212	0.071

Group ID: M02 (30 mg/kg/day)

	PT	APTT
N	2	2
Mean	18.40	9.30
SD	0.707	3.394

Group ID: M03 (90 mg/kg/day)

	PT	APTT
N	2	2
Mean	17.80	9.35
SD	0.000	0.071

Group ID: M04 (180 mg/kg/day)

	PT	APTT
N	2	2
Mean	19.65	11.30
SD	3.323	1.556

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F01 (0 mg/kg/day)

	PT	APTT
N	2	2
Mean	18.70	9.10
SD	0.283	2.404

Group ID: F02 (30 mg/kd/day)

	PT	APTT
N	2	2
Mean	19.15	8.90
SD	1.202	0.141

TABLE 7 - Coagulation Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F03 (90 mg/kg/day)

	PT	APTT
N	2	2
Mean	17.90	8.35
SD	0.141	0.212

Group ID: F04 (180 mg/kg/day)

	PT	APTT
N	2	2
Mean	19.15	10.15
SD	0.636	1.202

'' No data collected

TABLE 8 – Clinical Chemistry Group Summary

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

Data collected by Labcat v8.0; Report generated by v8.0

TABLE 8 – Clinical Chemistry Group Summary

Abbr	Description	Units
AST	Aspartate Aminotransferase	U/L
ALT	Alanine Aminotransferase	U/L
GLU	Glucose	mg/dL
BUN	Blood Urea Nitrogen	mg/dL
CREAT	Creatinine	mg/dL
PHOS	Inorganic Phosphorous	mg/dL
TRIG	Triglycerides	mg/dL
CHOL	Cholesterol	mg/dL
TP	Total Protein	g/dL
NA	Sodium	mEq/L
K	Potassium	mEq/L
CL	Chloride	mEq/L
TBILI	Total Bilirubin	mg/dL
ALP	Alkaline Phosphatase	U/L
CA	Calcium	mg/dL
GLOB	Globulin	g/dL
ALB	Albumin	g/dL
A/G	Albumin Globulin Ratio	g/dL

TABLE 8 - Clinical Chemistry Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M01 (0 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP	AST	ALT	CHOL	CA	NA	K
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	128.0	22.5	0.330	11.15	6.00	3.25	0.120	162.5	97.5	59.0	90.5	11.375	146.5	7.20
SD	5.66	0.71	0.0000	0.636	0.000	0.071	0.0283	14.85	33.23	15.56	3.54	0.2758	0.71	0.424

Group ID: M02 (30 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP	AST	ALT	CHOL	CA	NA	K
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	125.5	20.0	0.330	11.40	6.35	3.45	0.130	168.5	103.5	48.5	74.5	11.545	148.5	6.80
SD	20.51	0.00	0.0000	0.141	0.071	0.071	0.0141	34.65	36.06	2.12	16.26	0.1909	0.71	0.424

Group ID: M03 (90 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP	AST	ALT	CHOL	CA	NA	K
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	174.0	20.0	0.330	12.30	6.15	3.35	0.110	149.5	85.0	59.5	95.5	11.925	146.0	7.50
SD	25.46	0.00	0.0000	1.273	0.071	0.071	0.0141	9.19	16.97	19.09	6.36	0.2192	1.41	0.849

Group ID: M04 (180 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP	AST	ALT	CHOL	CA	NA	K
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	116.0	40.5	0.275	12.55	4.80	2.55	0.125	122.0	123.5	77.0	98.5	10.865	148.5	8.25
SD	5.66	28.99	0.0495	1.768	0.424	0.354	0.0071	42.43	71.42	41.01	31.82	0.8415	0.71	1.485

Group ID: M01 (0 mg/kg/day)

	CL	TRIG	GLOB	A/G
N	2	2	2	2
Mean	100.5	35.0	2.75	1.15
SD	0.71	9.90	0.071	0.071

Group ID: M02 (30 mg/kg/day)

	CL	TRIG	GLOB	A/G
N	2	2	2	2
Mean	99.5	28.5	2.90	1.20
SD	0.71	2.12	0.141	0.141

Group ID: M03 (90 mg/kg/day)

TABLE 8 - Clinical Chemistry Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Day on Test 8 **Observation Date** 02/12/2009

	CL	TRIG	GLOB	A/G
N	2	2	2	2
Mean	102.0	43.5	2.80	1.20
SD	0.00	13.44	0.000	0.000

Group ID: M04 (180 mg/kg/day)

	CL	TRIG	GLOB	A/G
N	2	2	2	2
Mean	105.0	46.5	2.25	1.10
SD	0.00	33.23	0.071	0.141

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F01 (0 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP	AST	ALT	CHOL	CA	NA	K
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	120.5	19.5	0.360	10.50	6.30	3.60	0.115	116.0	90.0	44.5	69.0	11.630	145.0	6.90
SD	10.61	0.71	0.0424	0.141	0.000	0.000	0.0071	33.94	4.24	4.95	16.97	0.1273	0.00	0.141

Group ID: F02 (30 mg/kd/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP	AST	ALT	CHOL	CA	NA	K
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	103.5	17.5	0.315	11.10	6.30	3.45	0.135	97.0	80.5	40.5	77.0	11.805	146.0	7.40
SD	3.54	0.71	0.0212	0.707	0.000	0.071	0.0212	4.24	0.71	4.95	4.24	0.0919	0.00	0.566

Group ID: F03 (90 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP	AST	ALT	CHOL	CA	NA	K
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	121.0	17.0	0.305	10.85	5.55	3.15	0.115	94.0	68.5	33.0	65.0	11.300	145.0	7.55
SD	24.04	1.41	0.0071	0.354	0.778	0.354	0.0071	11.31	7.78	2.83	1.41	0.4667	0.00	0.212

Group ID: F04 (180 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP	AST	ALT	CHOL	CA	NA	K
N	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Mean	141.0	17.5	0.270	11.55	5.30	2.75	0.115	113.5	57.0	34.0	71.5	11.540	146.5	7.30
SD	19.80	3.54	0.0141	0.778	0.566	0.071	0.0071	48.79	4.24	2.83	3.54	0.2121	3.54	0.849

Group ID: F01 (0 mg/kg/day)

	CL	TRIG	GLOB	A/G
N	2	2	2	2
Mean	99.5	41.0	2.70	1.30
SD	2.12	4.24	0.000	0.000

Group ID: F02 (30 mg/kd/day)

TABLE 8 - Clinical Chemistry Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Day on Test 8 **Observation Date** 02/12/2009

	CL	TRIG	GLOB	A/G
N	2	2	2	2
Mean	101.5	37.5	2.85	1.25
SD	0.71	9.19	0.071	0.071

Group ID: F03 (90 mg/kg/day)

	CL	TRIG	GLOB	A/G
N	2	2	2	2
Mean	100.5	52.5	2.40	1.35
SD	2.12	21.92	0.424	0.071

Group ID: F04 (180 mg/kg/day)

	CL	TRIG	GLOB	A/G
N	2	2	2	2
Mean	103.5	48.5	2.55	1.10
SD	2.12	6.36	0.495	0.141

'' No data collected

TABLE 9 – Incidence of Gross Findings

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

-- = No Data available

Data hand recorded; Report generated in LABCAT Necropsy v.3.28

TABLE 9
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INCIDENCE OF GROSS FINDINGS

SEX: MALE

FATES: Day 8 Sacrifice

GROUP:	1-M	2-M	3-M	4-M
ADRENALS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
BRAIN				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
HEART				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
KIDNEYS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
LIVER				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
LUNGS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
PITUITARY				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
SPLEEN				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
TESTES				
No. of Observations	2	2	2	2
Right small				
(Right 0.304g, Left 1.1537g)	0	0	1 50%	0
NO GROSS FINDINGS	2 100%	2 100%	1 50%	2 100%

TABLE 9
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INCIDENCE OF GROSS FINDINGS

SEX: MALE

FATES: Day 8 Sacrifice

GROUP:	1-M	2-M	3-M	4-M
THYROIDS/PARATHYROIDS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
GROSS FINDINGS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%

TABLE 9
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INCIDENCE OF GROSS FINDINGS

SEX: FEMALE

FATES: Day 8 Sacrifice

GROUP:	1-F	2-F	3-F	4-F
ADRENALS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
BRAIN				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
HEART				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
KIDNEYS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
LIVER				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
LUNGS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
PITUITARY				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
SPLEEN				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
OVARIES				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%

TABLE 9
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INCIDENCE OF GROSS FINDINGS

SEX: FEMALE

FATES: Day 8 Sacrifice

GROUP:	1-F	2-F	3-F	4-F
THYROIDS/PARATHYROIDS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%
GROSS FINDINGS				
No. of Observations	2	2	2	2
NO GROSS FINDINGS	2 100%	2 100%	2 100%	2 100%

TABLE 10 – Absolute Organ Weights

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

-- = No Data available

Data hand recorded; Report generated in LABCAT Necropsy v.3.28

TABLE 10
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

ABSOLUTE ORGAN WEIGHTS

SEX: MALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-M	2-M	3-M	4-M
BODY WEIGHT (G)(ABSOLUTE)				
MEAN	250	240	246	189
SD	5.7	5.7	11.3	26.9
N	2	2	2	2
ADRENALS (G)(ABSOLUTE)				
MEAN	0.050	0.045	0.060	0.059
SD	0.0092	0.0113	0.0035	0.0099
N	2	2	2	2
BRAIN (G)(ABSOLUTE)				
MEAN	1.66	1.75	1.67	1.58
SD	0.191	0.035	0.304	0.007
N	2	2	2	2
HEART (G)(ABSOLUTE)				
MEAN	1.01	0.92	0.98	0.77
SD	0.021	0.035	0.064	0.099
N	2	2	2	2
KIDNEYS (G)(ABSOLUTE)				
MEAN	2.05	1.96	2.12	1.57
SD	0.014	0.042	0.269	0.255
N	2	2	2	2
LIVER (G)(ABSOLUTE)				
MEAN	8.03	8.13	8.82	7.63
SD	0.502	0.460	0.658	1.534
N	2	2	2	2
LUNGS (G)(ABSOLUTE)				
MEAN	1.30	1.17	1.70	1.09
SD	0.035	0.007	0.495	0.049
N	2	2	2	2

TABLE 10
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

ABSOLUTE ORGAN WEIGHTS

SEX: MALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-M	2-M	3-M	4-M
PITUITARY (G)(ABSOLUTE)				
MEAN	0.002	0.006	0.004	0.006
SD	0.0000	0.0014	0.0000	0.0035
N	2	2	2	2
SPLEEN (G)(ABSOLUTE)				
MEAN	0.59	0.54	0.65	0.31
SD	0.021	0.028	0.021	0.078
N	2	2	2	2
TESTES (G)(ABSOLUTE)				
MEAN	3.299	3.091	2.725	3.115
SD	0.2008	0.2645	1.2509	0.1902
N	2	2	2	2
THYROIDS/PARATHYROIDS (G)(ABSOLUTE)				
MEAN	0.014	0.015	0.012	0.010
SD	0.0099	0.0035	0.0064	0.0057
N	2	2	2	2

TABLE 10
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

ABSOLUTE ORGAN WEIGHTS

SEX: FEMALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-F	2-F	3-F	4-F
BODY WEIGHT (G)(ABSOLUTE)				
MEAN	177	178	188	171
SD	7.8	2.8	5.7	5.7
N	2	2	2	2
ADRENALS (G)(ABSOLUTE)				
MEAN	0.066	0.059	0.064	0.075
SD	0.0042	0.0007	0.0099	0.0049
N	2	2	2	2
BRAIN (G)(ABSOLUTE)				
MEAN	1.62	1.61	1.53	1.71
SD	0.085	0.049	0.240	0.099
N	2	2	2	2
HEART (G)(ABSOLUTE)				
MEAN	0.77	0.78	0.81	0.75
SD	0.042	0.057	0.042	0.064
N	2	2	2	2
KIDNEYS (G)(ABSOLUTE)				
MEAN	1.47	1.53	1.61	1.53
SD	0.021	0.127	0.028	0.141
N	2	2	2	2
LIVER (G)(ABSOLUTE)				
MEAN	5.84	5.82	6.96	6.98
SD	0.156	0.205	0.629	NA
N	2	2	2	1
LUNGS (G)(ABSOLUTE)				
MEAN	1.15	1.12	1.22	1.15
SD	0.057	0.042	0.170	0.106
N	2	2	2	2

NA-Not Applicable

TABLE 10
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

ABSOLUTE ORGAN WEIGHTS

SEX: FEMALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-F	2-F	3-F	4-F
PITUITARY (G)(ABSOLUTE)				
MEAN	0.006	0.006	0.003	0.005
SD	0.0014	0.0014	0.0000	0.0049
N	2	2	2	2
SPLEEN (G)(ABSOLUTE)				
MEAN	0.55	0.45	0.54	0.51
SD	0.000	0.014	0.042	0.071
N	2	2	2	2
OVARIES (G)(ABSOLUTE)				
MEAN	0.113	0.114	0.097	0.137
SD	0.0000	0.0311	0.0453	0.0007
N	2	2	2	2
THYROIDS/PARATHYROIDS (G)(ABSOLUTE)				
MEAN	0.015	0.013	0.014	0.010
SD	0.0042	0.0007	0.0042	0.0007
N	2	2	2	2

TABLE 11 – Relative Organ-to-Body Weight Ratios

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

-- = No Data available

Data hand recorded; Report generated in LABCAT Necropsy v.3.28

TABLE 11
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

RELATIVE ORGAN-TO-BODY WEIGHT RATIOS

SEX: MALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-M	2-M	3-M	4-M
ADRENALS (% BODY WEIGHT)				
MEAN	0.020	0.019	0.025	0.032
SD	0.0042	0.0042	0.0021	0.0099
N	2	2	2	2
BRAIN (% BODY WEIGHT)				
MEAN	0.666	0.732	0.675	0.842
SD	0.0615	0.0318	0.0926	0.1160
N	2	2	2	2
HEART (% BODY WEIGHT)				
MEAN	0.407	0.386	0.401	0.408
SD	0.0007	0.0240	0.0078	0.0057
N	2	2	2	2
KIDNEYS (% BODY WEIGHT)				
MEAN	0.820	0.817	0.860	0.830
SD	0.0240	0.0368	0.0693	0.0163
N	2	2	2	2
LIVER (% BODY WEIGHT)				
MEAN	3.209	3.389	3.585	4.018
SD	0.1280	0.2715	0.1018	0.2411
N	2	2	2	2
LUNGS (% BODY WEIGHT)				
MEAN	0.519	0.490	0.687	0.584
SD	0.0262	0.0141	0.1697	0.0573
N	2	2	2	2
PITUITARY (% BODY WEIGHT)				
MEAN	0.001	0.003	0.002	0.003
SD	0.0000	0.0007	0.0000	0.0014
N	2	2	2	2

TABLE 11
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

RELATIVE ORGAN-TO-BODY WEIGHT RATIOS

SEX: MALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-M	2-M	3-M	4-M
SPLEEN (% BODY WEIGHT)				
MEAN	0.234	0.225	0.263	0.160
SD	0.0028	0.0071	0.0205	0.0184
N	2	2	2	2
TESTES (% BODY WEIGHT)				
MEAN	1.319	1.287	1.098	1.659
SD	0.0509	0.0792	0.4575	0.1351
N	2	2	2	2
THYROIDS/PARATHYROIDS (% BODY WEIGHT)				
MEAN	0.006	0.007	0.005	0.006
SD	0.0042	0.0021	0.0028	0.0035
N	2	2	2	2

TABLE 11
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

RELATIVE ORGAN-TO-BODY WEIGHT RATIOS

SEX: FEMALE — FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-F	2-F	3-F	4-F
ADRENALS (% BODY WEIGHT)				
MEAN	0.038	0.034	0.034	0.044
SD	0.0035	0.0007	0.0042	0.0014
N	2	2	2	2
BRAIN (% BODY WEIGHT)				
MEAN	0.918	0.902	0.816	1.000
SD	0.0078	0.0424	0.1527	0.0247
N	2	2	2	2
HEART (% BODY WEIGHT)				
MEAN	0.437	0.438	0.431	0.441
SD	0.0049	0.0255	0.0092	0.0226
N	2	2	2	2
KIDNEYS (% BODY WEIGHT)				
MEAN	0.831	0.859	0.857	0.894
SD	0.0481	0.0580	0.0106	0.0530
N	2	2	2	2
LIVER (% BODY WEIGHT)				
MEAN	3.310	3.267	3.696	4.180
SD	0.0580	0.0629	0.2234	NA
N	2	2	2	1
LUNGS (% BODY WEIGHT)				
MEAN	0.653	0.629	0.651	0.669
SD	0.0608	0.0141	0.1096	0.0396
N	2	2	2	2
PITUITARY (% BODY WEIGHT)				
MEAN	0.004	0.004	0.002	0.003
SD	0.0007	0.0007	0.0000	0.0028
N	2	2	2	2

NA-Not Applicable

TABLE 11
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

RELATIVE ORGAN-TO-BODY WEIGHT RATIOS

SEX: FEMALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-F	2-F	3-F	4-F
SPLEEN (% BODY WEIGHT)				
MEAN	0.312	0.253	0.288	0.298
SD	0.0141	0.0042	0.0311	0.0318
N	2	2	2	2
OVARIES (% BODY WEIGHT)				
MEAN	0.064	0.064	0.052	0.081
SD	0.0028	0.0170	0.0255	0.0035
N	2	2	2	2
THYROIDS/PARATHYROIDS (% BODY WEIGHT)				
MEAN	0.009	0.007	0.008	0.007
SD	0.0028	0.0000	0.0021	0.0007
N	2	2	2	2

TABLE 12 – Relative Organ-to-Brain Weight Ratios

Group	Sex	Dose Level
M01	Male	0 mg/kg/day
M02	Male	30 mg/kg/day
M03	Male	90 mg/kg/day
M04	Male	180 mg/kg/day
F01	Female	0 mg/kg/day
F02	Female	30 mg/kg/day
F03	Female	90 mg/kg/day
F04	Female	180 mg/kg/day

-- = No Data available

Data hand recorded; Report generated in LABCAT Necropsy v.3.28

TABLE 12
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

RELATIVE ORGAN-TO-BRAIN WEIGHT RATIOS

SEX: MALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-M	2-M	3-M	4-M
ADRENALS (% BRAIN WEIGHT)				
MEAN	3.025	2.570	3.715	3.745
SD	0.8980	0.6930	0.8839	0.6435
N	2	2	2	2
HEART (% BRAIN WEIGHT)				
MEAN	61.29	52.70	59.81	48.88
SD	5.756	0.955	7.099	6.060
N	2	2	2	2
KIDNEYS (% BRAIN WEIGHT)				
MEAN	123.99	111.68	127.99	99.65
SD	15.068	0.170	7.234	15.712
N	2	2	2	2
LIVER (% BRAIN WEIGHT)				
MEAN	483.44	462.80	535.35	483.92
SD	25.279	16.864	58.266	95.254
N	2	2	2	2
LUNGS (% BRAIN WEIGHT)				
MEAN	78.42	66.96	101.07	69.52
SD	11.109	0.948	11.271	2.828
N	2	2	2	2
PITUITARY (% BRAIN WEIGHT)				
MEAN	0.120	0.340	0.245	0.350
SD	0.0141	0.0707	0.0495	0.2263
N	2	2	2	2
SPLEEN (% BRAIN WEIGHT)				
MEAN	35.29	30.79	39.52	19.35
SD	2.772	2.234	8.492	4.851
N	2	2	2	2

TABLE 12
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

RELATIVE ORGAN-TO-BRAIN WEIGHT RATIOS

SEX: MALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-M	2-M	3-M	4-M
TESTES (% BRAIN WEIGHT)				
MEAN	198.755	176.315	159.495	197.785
SD	10.7268	18.6181	45.9973	11.1935
N	2	2	2	2
THYROIDS/PARATHYROIDS (% BRAIN WEIGHT)				
MEAN	0.880	0.880	0.735	0.635
SD	0.6930	0.1838	0.5162	0.3606
N	2	2	2	2

TABLE 12
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

RELATIVE ORGAN-TO-BRAIN WEIGHT RATIOS

SEX: FEMALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-F	2-F	3-F	4-F
ADRENALS (% BRAIN WEIGHT)				
MEAN	4.085	3.710	4.285	4.355
SD	0.4738	0.1556	1.3223	0.0354
N	2	2	2	2
HEART (% BRAIN WEIGHT)				
MEAN	47.53	48.68	53.82	44.12
SD	0.127	5.028	11.229	1.167
N	2	2	2	2
KIDNEYS (% BRAIN WEIGHT)				
MEAN	90.59	95.49	106.69	89.39
SD	6.053	10.875	18.611	3.090
N	2	2	2	2
LIVER (% BRAIN WEIGHT)				
MEAN	360.74	362.68	463.53	425.61
SD	9.291	23.964	113.971	NA
N	2	2	2	1
LUNGS (% BRAIN WEIGHT)				
MEAN	71.18	69.86	79.85	66.89
SD	7.220	4.801	1.457	2.333
N	2	2	2	2
PITUITARY (% BRAIN WEIGHT)				
MEAN	0.370	0.375	0.200	0.315
SD	0.0707	0.1061	0.0283	0.2758
N	2	2	2	2
SPLEEN (% BRAIN WEIGHT)				
MEAN	34.00	28.07	35.52	29.76
SD	1.782	1.747	2.807	2.411
N	2	2	2	2

NA-Not Applicable

TABLE 12
CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

RELATIVE ORGAN-TO-BRAIN WEIGHT RATIOS

SEX: FEMALE FATES: Day 8 Sacrifice

DOSE:(mg/kg/day)	0	30	90	180
GROUP:	1-F	2-F	3-F	4-F
OVARIES (% BRAIN WEIGHT)				
MEAN	6.985	7.135	6.185	8.055
SD	0.3606	2.1567	1.9870	0.5020
N	2	2	2	2
THYROIDS/PARATHYROIDS (% BRAIN WEIGHT)				
MEAN	0.930	0.775	0.950	0.615
SD	0.3111	0.0212	0.4243	0.0778
N	2	2	2	2

XIII. Appendices

Appendix I—Individual Animal Data

Observation Frequency by Subject

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M01 (0 mg/kg/day)
Group Gender : Male

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5001	Male	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal
5002	Male	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal

Group ID : M02 (30 mg/kg/day)
Group Gender : Male

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5005	Male	In-Life	S	1	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	2	1 Hour Post-dose Soft Feces
		In-Life	S	3-7	1 Hour Post-dose Normal
		In-Life	S	8	Appears Normal
5006	Male	In-Life	S	1	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	2	1 Hour Post-dose Soft Feces
		In-Life	S	3-7	1 Hour Post-dose Normal
		In-Life	S	8	Appears Normal

Group ID : M03 (90 mg/kg/day)
Group Gender : Male

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5009	Male	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal
5010	Male	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal

Group ID : M04 (180 mg/kg/day)
Group Gender : Male

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5013	Male	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal
5014	Male	In-Life	S	1-3	1 Hour Post-dose Normal
		In-Life	S	1-2	Predose Normal

Observation Frequency by Subject

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M04 (180 mg/kg/day)
Group Gender : Male

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5014	Male	In-Life	S	3-5	Predose Soft Feces
		In-Life	S	4	1 Hour Post-dose Loose Feces
		In-Life	S	4-5	1 Hour Post-dose Ruffled Fur Coat
		In-Life	S	5-7	1 Hour Post-dose Soft Feces
		In-Life	S	5	Predose Ruffled Fur Coat
		In-Life	S	6-7	Predose Normal
		In-Life	S	8	Ruffled Fur Coat
		In-Life	S	8	Soft Feces

Group ID : F01 (0 mg/kg/day)
Group Gender : Female

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5003	Female	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal
5004	Female	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal

Group ID : F02 (30 mg/kd/day)
Group Gender : Female

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5007	Female	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal
5008	Female	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal

Group ID : F03 (90 mg/kg/day)
Group Gender : Female

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5011	Female	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal
5012	Female	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal

Group ID : F04 (180 mg/kg/day)
Group Gender : Female

Observation Frequency by Subject

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : F04 (180 mg/kg/day)
Group Gender : Female

Subject ID	Subject Gender	Study Phase	S/U	Interval	Observations & Details
5015	Female	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal
5016	Female	In-Life	S	1-7	1 Hour Post-dose Normal
		In-Life	S	1-7	Predose Normal
		In-Life	S	8	Appears Normal

S - Scheduled, U - Unscheduled

Individual Mortality Report

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M01 (0 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life

Subject ID	Subject Gender	Fate	DOT	Fate Date	Fate Comments	User Name
5001	Male	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella
5002	Male	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella

Group ID : M02 (30 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life

Subject ID	Subject Gender	Fate	DOT	Fate Date	Fate Comments	User Name
5005	Male	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella
5006	Male	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella

Group ID : M03 (90 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life

Subject ID	Subject Gender	Fate	DOT	Fate Date	Fate Comments	User Name
5009	Male	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella
5010	Male	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella

Group ID : M04 (180 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life

Subject ID	Subject Gender	Fate	DOT	Fate Date	Fate Comments	User Name
5013	Male	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella
5014	Male	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella

Group ID : F01 (0 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life

Subject ID	Subject Gender	Fate	DOT	Fate Date	Fate Comments	User Name
5003	Female	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella
5004	Female	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella

Group ID : F02 (30 mg/kd/day) **Group Gender :** Female

Individual Mortality Report

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : F02 (30 mg/kd/day) **Group Gender :** Female
Study Phase : In-Life

Subject ID	Subject Gender	Fate	DOT	Fate Date	Fate Comments	User Name
5007	Female	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella
5008	Female	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella

Group ID : F03 (90 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life

Subject ID	Subject Gender	Fate	DOT	Fate Date	Fate Comments	User Name
5011	Female	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella
5012	Female	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella

Group ID : F04 (180 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life

Subject ID	Subject Gender	Fate	DOT	Fate Date	Fate Comments	User Name
5015	Female	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella
5016	Female	Terminal sacrifice	8	02/12/2009 9:44:52AM		mcicchella

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002

TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

Individual Body Weight (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M01 (0 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male
Scheduled and UnScheduled

Subject ID / Days	1	4	7
5001	253	273	287
5002	240	258	272
N	2	2	2
Mean	246.5	265.5	279.5
Median	247	266	280
SD	9.19	10.61	10.61
StdErr	6.50	7.50	7.50

Group ID : M02 (30 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male
Scheduled and UnScheduled

Subject ID / Days	1	4	7
5005	235	253	267
5006	251	266	275
N	2	2	2
Mean	243.0	259.5	271.0
Median	243	260	271
SD	11.31	9.19	5.66
StdErr	8.00	6.50	4.00

Group ID : M03 (90 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male
Scheduled and UnScheduled

Subject ID / Days	1	4	7
5009	237	248	265
5010	252	270	286
N	2	2	2
Mean	244.5	259.0	275.5
Median	245	259	276
SD	10.61	15.56	14.85
StdErr	7.50	11.00	10.50

Group ID : M04 (180 mg/kg/day) **Group Gender :** Male

Individual Body Weight (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M04 (180 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male
Scheduled and UnScheduled

Subject ID / Days	1	4	7
5013	237	235	231
5014	239	208	192
N	2	2	2
Mean	238.0	221.5	211.5
Median	238	222	212
SD	1.41	19.09	27.58
StdErr	1.00	13.50	19.50

Group ID : F01 (0 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female
Scheduled and UnScheduled

Subject ID / Days	1	4	7
5003	188	203	201
5004	181	193	188
N	2	2	2
Mean	184.5	198.0	194.5
Median	185	198	195
SD	4.95	7.07	9.19
StdErr	3.50	5.00	6.50

Group ID : F02 (30 mg/kd/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female
Scheduled and UnScheduled

Subject ID / Days	1	4	7
5007	200	196	206
5008	178	190	197
N	2	2	2
Mean	189.0	193.0	201.5
Median	189	193	202
SD	15.56	4.24	6.36
StdErr	11.00	3.00	4.50

Group ID : F03 (90 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female
Scheduled and UnScheduled

Individual Body Weight (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : F03 (90 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female
Scheduled and UnScheduled

Subject ID / Days	1	4	7
5011	189	196	211
5012	197	198	198
N	2	2	2
Mean	193.0	197.0	204.5
Median	193	197	205
SD	5.66	1.41	9.19
StdErr	4.00	1.00	6.50

Group ID : F04 (180 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female
Scheduled and UnScheduled

Subject ID / Days	1	4	7
5015	190	189	192
5016	195	190	185
N	2	2	2
Mean	192.5	189.5	188.5
Median	193	190	189
SD	3.54	0.71	4.95
StdErr	2.50	0.50	3.50

- No data available (f) - Subject previously fated * -Terminal Body Weight x -Excluded Data SD -Standard Deviation

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002

TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

Individual Body Weight Changes (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M01 (0 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male

Subject ID / Days	1 - 4	4 - 7	Net Change
5001	20	14	34
5002	18	14	32
N	2	2	2
Mean	19.0	14.0	33.0
SD	1.41	0.00	1.41

Group ID : M02 (30 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male

Subject ID / Days	1 - 4	4 - 7	Net Change
5005	18	14	32
5006	15	9	24
N	2	2	2
Mean	16.5	11.5	28.0
SD	2.12	3.54	5.66

Group ID : M03 (90 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male

Subject ID / Days	1 - 4	4 - 7	Net Change
5009	11	17	28
5010	18	16	34
N	2	2	2
Mean	14.5	16.5	31.0
SD	4.95	0.71	4.24

Group ID : M04 (180 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male

Subject ID / Days	1 - 4	4 - 7	Net Change
5013	-2	-4	-6
5014	-31	-16	-47

Individual Body Weight Changes (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M04 (180 mg/kg/day) **Group Gender :** Male
Study Phase : In-Life **Subject Gender :** Male

N	2	2	2
Mean	-16.5	-10.0	-26.5
SD	20.51	8.49	28.99

Group ID : F01 (0 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female

Days / Subject ID	1 - 4	4 - 7	Net Change
5003	15	-2	13
5004	12	-5	7

N	2	2	2
Mean	13.5	-3.5	10.0
SD	2.12	2.12	4.24

Group ID : F02 (30 mg/kd/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female

Days / Subject ID	1 - 4	4 - 7	Net Change
5007	-4	10	6
5008	12	7	19

N	2	2	2
Mean	4.0	8.5	12.5
SD	11.31	2.12	9.19

Group ID : F03 (90 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female

Days / Subject ID	1 - 4	4 - 7	Net Change
5011	7	15	22
5012	1	0	1

N	2	2	2
Mean	4.0	7.5	11.5
SD	4.24	10.61	14.85

Group ID : F04 (180 mg/kg/day) **Group Gender :** Female
Study Phase : In-Life **Subject Gender :** Female

Individual Body Weight Changes (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : F04 (180 mg/kg/day)
Study Phase : In-Life
Group Gender : Female
Subject Gender : Female

Days / Subject ID	1 - 4	4 - 7	Net Change
5015	-1	3	2
5016	-5	-5	-10
N	2	2	2
Mean	-3.0	-1.0	-4.0
SD	2.83	5.66	8.49

(f) - Subject previously fated

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002

TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

Individual Feed Consumption (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M01 (0 mg/kg/day) **Study Phase :** In-Life
Group Gender : Male **Subject Gender :** Male

Subject Id	Days: 1 - 7
5001	177
5002	173
N	2
Mean	175.0
SD	2.83

Group ID : M02 (30 mg/kg/day) **Study Phase :** In-Life
Group Gender : Male **Subject Gender :** Male

Subject Id	Days: 1 - 7
5005	152
5006	152
N	2
Mean	152.0
SD	0.00

Group ID : M03 (90 mg/kg/day) **Study Phase :** In-Life
Group Gender : Male **Subject Gender :** Male

Subject Id	Days: 1 - 7
5009	160
5010	165
N	2
Mean	162.5
SD	3.54

Group ID : M04 (180 mg/kg/day) **Study Phase :** In-Life
Group Gender : Male **Subject Gender :** Male

Subject Id	Days: 1 - 7
5013	102
5014	45

Individual Feed Consumption (g)

Study Id: 0440RE27.002
Study Name: 0440RE27.002

Group ID : M04 (180 mg/kg/day) **Study Phase :** In-Life
Group Gender : Male **Subject Gender :** Male

N	2
Mean	73.5
SD	40.31

Group ID : F01 (0 mg/kg/day) **Study Phase :** In-Life
Group Gender : Female **Subject Gender :** Female

Days: / Subject Id	1 - 7
5003	117
5004	115

N	2
Mean	116.0
SD	1.41

Group ID : F02 (30 mg/kd/day) **Study Phase :** In-Life
Group Gender : Female **Subject Gender :** Female

Days: / Subject Id	1 - 7
5007	122
5008	123

N	2
Mean	122.5
SD	0.71

Group ID : F03 (90 mg/kg/day) **Study Phase :** In-Life
Group Gender : Female **Subject Gender :** Female

Days: / Subject Id	1 - 7
5011	127
5012	114

N	2
Mean	120.5
SD	9.19

Group ID : F04 (180 mg/kg/day) **Study Phase :** In-Life
Group Gender : Female **Subject Gender :** Female

Individual Feed Consumption (g)

Study Id:	0440RE27.002
Study Name:	0440RE27.002

Group ID :	F04 (180 mg/kg/day)	**Study Phase :**	In-Life
Group Gender :	Female	**Subject Gender :**	Female

Days: / Subject Id	1 - 7
5015	94
5016	84
N	2
Mean	89.0
SD	7.07

- No data available * -Subject fated this period x -Excluded Data SD -Standard Deviation

Individual Hematology By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M01 (0 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
5001	12.69	7.69	14.6	46.8	60.9	19.0	31.2	1,144
5002	15.04	7.67	15.0	45.7	59.6	19.6	32.8	1,224 P
N	2	2	2	2	2	2	2	2
Mean	13.865	7.680	14.80	46.25	60.25	19.30	32.00	1,184.0
SD	1.6617	0.0141	0.283	0.778	0.919	0.424	1.131	56.57

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
5001	18.1	75.5	4.1	1.2	0.7	0.4	2.30	9.58
5002	9.1	87.4	2.2	0.3	0.5	0.5	1.37	13.15
N	2	2	2	2	2	2	2	2
Mean	13.60	81.45	3.15	0.75	0.60	0.45	1.835	11.365
SD	6.364	8.415	1.344	0.636	0.141	0.071	0.6576	2.5244

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
5001	0.52	0.15	0.09	0.06	4.59	352.8
5002	0.33	0.04	0.07	0.08	4.12	316.0
N	2	2	2	2	2	2
Mean	0.425	0.095	0.080	0.070	4.355	334.40
SD	0.1344	0.0778	0.0141	0.0141	0.3323	26.022

Group ID: M02 (30 mg/kg/day)

Individual Hematology By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M02 (30 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
5005	6.40	7.89	14.7	46.3	58.7	18.6	31.7	1,169
5006	13.70	8.36	15.8	50.0	59.9	18.9	31.5	1,416 P
N	2	2	2	2	2	2	2	2
Mean	10.050	8.125	15.25	48.15	59.30	18.75	31.60	1,292.5
SD	5.1619	0.3323	0.778	2.616	0.849	0.212	0.141	174.66

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
5005	16.1	79.4	1.6	1.1	0.6	1.2	1.03	5.08
5006	10.8	81.0	6.2	0.5	0.7	0.8	1.47	11.10
N	2	2	2	2	2	2	2	2
Mean	13.45	80.20	3.90	0.80	0.65	1.00	1.250	8.090
SD	3.748	1.131	3.253	0.424	0.071	0.283	0.3111	4.2568

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
5005	0.10	0.07	0.04	0.08	4.42	349.2
5006	0.85	0.07	0.10	0.11	3.89	325.5
N	2	2	2	2	2	2
Mean	0.475	0.070	0.070	0.095	4.155	337.35
SD	0.5303	0.0000	0.0424	0.0212	0.3748	16.758

Group ID: M03 (90 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
5009	15.97	8.10	15.0	48.0	59.3	18.5	31.2	1,555 P
5010	14.46	7.89	14.9	47.9	60.7	18.9	31.2	1,969 P

Individual Hematology By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M03 (90 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
N	2	2	2	2	2	2	2	2
Mean	15.215	7.995	14.95	47.95	60.00	18.70	31.20	1,762.0
SD	1.0677	0.1485	0.071	0.071	0.990	0.283	0.000	292.74

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
5009	13.0	81.5	3.3	0.8	0.9	0.5	2.08	13.01
5010	12.9	80.4	4.7	0.5	0.9	0.6	1.86	11.62
N	2	2	2	2	2	2	2	2
Mean	12.95	80.95	4.00	0.65	0.90	0.55	1.970	12.315
SD	0.071	0.778	0.990	0.212	0.000	0.071	0.1556	0.9829

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
5009	0.52	0.13	0.14	0.09	3.72	300.8
5010	0.69	0.07	0.12	0.09	4.60	362.7
N	2	2	2	2	2	2
Mean	0.605	0.100	0.130	0.090	4.160	331.75
SD	0.1202	0.0424	0.0141	0.0000	0.6223	43.770

Group ID: M04 (180 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
5013	20.85	8.29	16.0	50.1	60.4	19.2	31.9	1,609 P
5014	13.94	8.41	15.3	47.4	56.3	18.3	32.4	2,280
N	2	2	2	2	2	2	2	2
Mean	17.395	8.350	15.65	48.75	58.35	18.75	32.15	1,944.5
SD	4.8861	0.0849	0.495	1.909	2.899	0.636	0.354	474.47

Individual Hematology By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M04 (180 mg/kg/day)

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
5013	21.7	69.4	6.9	0.3	1.0	0.6	4.53	14.48
5014	30.0	66.0	4.0	0.0	0.0	0.0	4.18	9.20
N	2	2	2	2	2	2	2	2
Mean	25.85	67.70	5.45	0.15	0.50	0.30	4.355	11.840
SD	5.869	2.404	2.051	0.212	0.707	0.424	0.2475	3.7335

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
5013	1.43	0.07	0.21	0.14	2.66	220.7
5014	0.56	0.00	0.00	0.00	2.41	202.3
N	2	2	2	2	2	2
Mean	0.995	0.035	0.105	0.070	2.535	211.50
SD	0.6152	0.0495	0.1485	0.0990	0.1768	13.011

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F01 (0 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
5003	9.33	8.09	15.3	46.2	57.1	18.9	33.1	1,174 P
5004	10.34	7.63	14.7	44.4	58.2	19.2	33.1	1,482 P
N	2	2	2	2	2	2	2	2
Mean	9.835	7.860	15.00	45.30	57.65	19.05	33.10	1,328.0
SD	0.7142	0.3253	0.424	1.273	0.778	0.212	0.000	217.79

Individual Hematology By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F01 (0 mg/kg/day)

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
5003	9.9	80.6	5.5	1.0	1.3	1.7	0.93	7.53
5004	14.6	80.6	2.4	1.1	0.7	0.6	1.51	8.34
N	2	2	2	2	2	2	2	2
Mean	12.25	80.60	3.95	1.05	1.00	1.15	1.220	7.935
SD	3.323	0.000	2.192	0.071	0.424	0.778	0.4101	0.5728

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
5003	0.51	0.09	0.12	0.16	2.88	232.7
5004	0.25	0.11	0.07	0.06	2.46	187.7
N	2	2	2	2	2	2
Mean	0.380	0.100	0.095	0.110	2.670	210.20
SD	0.1838	0.0141	0.0354	0.0707	0.2970	31.820

Group ID: F02 (30 mg/kd/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
5007	9.65	7.99	15.1	45.9	57.4	18.9	33.0	1,180 P
5008	10.64	7.99	15.0	46.2	57.8	18.8	32.5	1,456 P
N	2	2	2	2	2	2	2	2
Mean	10.145	7.990	15.05	46.05	57.60	18.85	32.75	1,318.0
SD	0.7000	0.0000	0.071	0.212	0.283	0.071	0.354	195.16

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
5007	11.0	82.3	2.5	1.7	1.0	1.5	1.06	7.94
5008	13.2	81.6	3.3	0.5	0.6	0.7	1.40	8.68

Individual Hematology By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F02 (30 mg/kd/day)

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
N	2	2	2	2	2	2	2	2
Mean	12.10	81.95	2.90	1.10	0.80	1.10	1.230	8.310
SD	1.556	0.495	0.566	0.849	0.283	0.566	0.2404	0.5233

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
5007	0.24	0.16	0.10	0.14	1.86	148.3
5008	0.35	0.06	0.07	0.07	3.33	266.2
N	2	2	2	2	2	2
Mean	0.295	0.110	0.085	0.105	2.595	207.25
SD	0.0778	0.0707	0.0212	0.0495	1.0394	83.368

Group ID: F03 (90 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
5011	14.95	8.13	15.1	46.7	57.5	18.6	32.3	1,855
5012	14.14	7.72	14.2	43.8	56.7	18.4	32.5	1,797
N	2	2	2	2	2	2	2	2
Mean	14.545	7.925	14.65	45.25	57.10	18.50	32.40	1,826.0
SD	0.5728	0.2899	0.636	2.051	0.566	0.141	0.141	41.01

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
5011	37.9	55.2	4.4	0.8	0.8	1.0	5.67	8.25
5012	16.7	76.6	3.6	1.1	1.1	0.9	2.36	10.84
N	2	2	2	2	2	2	2	2
Mean	27.30	65.90	4.00	0.95	0.95	0.95	4.015	9.545
SD	14.991	15.132	0.566	0.212	0.212	0.071	2.3405	1.8314

Individual Hematology By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8

Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F03 (90 mg/kg/day)

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
5011	0.66	0.12	0.12	0.15	4.42	359.4
5012	0.51	0.16	0.16	0.12	2.67	206.1
N	2	2	2	2	2	2
Mean	0.585	0.140	0.140	0.135	3.545	282.75
SD	0.1061	0.0283	0.0283	0.0212	1.2374	108.399

Group ID: F04 (180 mg/kg/day)

	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
5015	18.47	7.09	13.2	40.8	57.5	18.7	32.5	2,548
5016	16.81	7.23	13.8	42.6	58.9	19.1	32.4	1,811
N	2	2	2	2	2	2	2	2
Mean	17.640	7.160	13.50	41.70	58.20	18.90	32.45	2,179.5
SD	1.1738	0.0990	0.424	1.273	0.990	0.283	0.071	521.14

	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC	#NEUT	#LYMPH
5015	23.2	60.2	11.4	1.3	0.9	3.0	4.29	11.11
5016	7.3	85.1	5.9	0.5	0.8	0.5	1.23	14.31
N	2	2	2	2	2	2	2	2
Mean	15.25	72.65	8.65	0.90	0.85	1.75	2.760	12.710
SD	11.243	17.607	3.889	0.566	0.071	1.768	2.1637	2.2627

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
5015	2.11	0.24	0.16	0.55	3.11	220.3
5016	0.99	0.08	0.13	0.08	3.61	261.1

Individual Hematology By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F04 (180 mg/kg/day)

	#MONO	#EOS	#BASO	#LUC	%RETIC	#RETIC
N	2	2	2	2	2	2
Mean	1.550	0.160	0.145	0.315	3.360	240.70
SD	0.7920	0.1131	0.0212	0.3323	0.3536	28.850

'' No data collected x-Excluded data P – Platelets clumped

Individual Coagulation By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8

Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M01 (0 mg/kg/day)

	PT	APTT
5001	18.2	10.5
5002	18.5	10.6
N	2	2
Mean	18.35	10.55
SD	0.212	0.071

Group ID: M02 (30 mg/kg/day)

	PT	APTT
5005	17.9	6.9
5006	18.9	11.7
N	2	2
Mean	18.40	9.30
SD	0.707	3.394

Group ID: M03 (90 mg/kg/day)

	PT	APTT
5009	17.8	9.3
5010	17.8	9.4
N	2	2
Mean	17.80	9.35
SD	0.000	0.071

Group ID: M04 (180 mg/kg/day)

Individual Coagulation By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M04 (180 mg/kg/day)

	PT	APTT
5013	17.3	10.2
5014	22.0	12.4
N	2	2
Mean	19.65	11.30
SD	3.323	1.556

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F01 (0 mg/kg/day)

	PT	APTT
5003	18.5	7.4
5004	18.9	10.8
N	2	2
Mean	18.70	9.10
SD	0.283	2.404

Group ID: F02 (30 mg/kd/day)

	PT	APTT
5007	20.0	9.0
5008	18.3	8.8
N	2	2
Mean	19.15	8.90
SD	1.202	0.141

Group ID: F03 (90 mg/kg/day)

Individual Coagulation By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F03 (90 mg/kg/day)

	PT	APTT
5011	17.8	8.2
5012	18.0	8.5
N	2	2
Mean	17.90	8.35
SD	0.141	0.212

Group ID: F04 (180 mg/kg/day)

	PT	APTT
5015	19.6	11.0
5016	18.7	9.3
N	2	2
Mean	19.15	10.15
SD	0.636	1.202

'' No data collected x-Excluded data

Individual Clinical Chemistry By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8

Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M01 (0 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
5001	132	22	0.33	10.7	6.0	3.2	0.10	152
5002	124	23	0.33	11.6	6.0	3.3	0.14	173
N	2	2	2	2	2	2	2	2
Mean	128.0	22.5	0.330	11.15	6.00	3.25	0.120	162.5
SD	5.66	0.71	0.0000	0.636	0.000	0.071	0.0283	14.85

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
5001	121	70	93	11.18	147	6.9	101	28
5002	74	48	88	11.57	146	7.5	100	42
N	2	2	2	2	2	2	2	2
Mean	97.5	59.0	90.5	11.375	146.5	7.20	100.5	35.0
SD	33.23	15.56	3.54	0.2758	0.71	0.424	0.71	9.90

	GLOB	A/G
5001	2.8	1.1
5002	2.7	1.2
N	2	2
Mean	2.75	1.15
SD	0.071	0.071

Group ID: M02 (30 mg/kg/day)

Individual Clinical Chemistry By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M02 (30 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
5005	111	20	0.33	11.3	6.4	3.4	0.14	193
5006	140	20	0.33	11.5	6.3	3.5	0.12	144
N	2	2	2	2	2	2	2	2
Mean	125.5	20.0	0.330	11.40	6.35	3.45	0.130	168.5
SD	20.51	0.00	0.0000	0.141	0.071	0.071	0.0141	34.65

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
5005	129	47	86	11.41	149	6.5	99	30
5006	78	50	63	11.68	148	7.1	100	27
N	2	2	2	2	2	2	2	2
Mean	103.5	48.5	74.5	11.545	148.5	6.80	99.5	28.5
SD	36.06	2.12	16.26	0.1909	0.71	0.424	0.71	2.12

	GLOB	A/G
5005	3.0	1.1
5006	2.8	1.3
N	2	2
Mean	2.90	1.20
SD	0.141	0.141

Group ID: M03 (90 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
5009	192	20	0.33	11.4	6.1	3.3	0.12	143
5010	156	20	0.33	13.2	6.2	3.4	0.10	156

Individual Clinical Chemistry By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8

Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M03 (90 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
N	2	2	2	2	2	2	2	2
Mean	174.0	20.0	0.330	12.30	6.15	3.35	0.110	149.5
SD	25.46	0.00	0.0000	1.273	0.071	0.071	0.0141	9.19

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
5009	73	46	100	11.77	147	6.9	102	34
5010	97	73	91	12.08	145	8.1	102	53
N	2	2	2	2	2	2	2	2
Mean	85.0	59.5	95.5	11.925	146.0	7.50	102.0	43.5
SD	16.97	19.09	6.36	0.2192	1.41	0.849	0.00	13.44

	GLOB	A/G
5009	2.8	1.2
5010	2.8	1.2
N	2	2
Mean	2.80	1.20
SD	0.000	0.000

Group ID: M04 (180 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
5013	112	20	0.31	11.3	5.1	2.8	0.13	92
5014	120	61	0.24	13.8	4.5	2.3	0.12	152
N	2	2	2	2	2	2	2	2
Mean	116.0	40.5	0.275	12.55	4.80	2.55	0.125	122.0
SD	5.66	28.99	0.0495	1.768	0.424	0.354	0.0071	42.43

Individual Clinical Chemistry By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Male **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Male

Day on Test 8 **Observation Date** 02/12/2009

Group ID: M04 (180 mg/kg/day)

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
5013	73	48	121	11.46	149	7.2	105	70
5014	174	106	76	10.27	148	9.3	105	23
N	2	2	2	2	2	2	2	2
Mean	123.5	77.0	98.5	10.865	148.5	8.25	105.0	46.5
SD	71.42	41.01	31.82	0.8415	0.71	1.485	0.00	33.23

	GLOB	A/G
5013	2.3	1.2
5014	2.2	1.0
N	2	2
Mean	2.25	1.10
SD	0.071	0.141

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F01 (0 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
5003	113	19	0.39	10.6	6.3	3.6	0.11	92
5004	128	20	0.33	10.4	6.3	3.6	0.12	140
N	2	2	2	2	2	2	2	2
Mean	120.5	19.5	0.360	10.50	6.30	3.60	0.115	116.0
SD	10.61	0.71	0.0424	0.141	0.000	0.000	0.0071	33.94

Individual Clinical Chemistry By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F01 (0 mg/kg/day)

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
5003	87	41	57	11.72	145	6.8	98	38
5004	93	48	81	11.54	145	7.0	101	44
N	2	2	2	2	2	2	2	2
Mean	90.0	44.5	69.0	11.630	145.0	6.90	99.5	41.0
SD	4.24	4.95	16.97	0.1273	0.00	0.141	2.12	4.24

	GLOB	A/G
5003	2.7	1.3
5004	2.7	1.3
N	2	2
Mean	2.70	1.30
SD	0.000	0.000

Group ID: F02 (30 mg/kd/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
5007	106	18	0.30	10.6	6.3	3.4	0.12	94
5008	101	17	0.33	11.6	6.3	3.5	0.15	100
N	2	2	2	2	2	2	2	2
Mean	103.5	17.5	0.315	11.10	6.30	3.45	0.135	97.0
SD	3.54	0.71	0.0212	0.707	0.000	0.071	0.0212	4.24

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
5007	80	44	80	11.74	146	7.0	102	31
5008	81	37	74	11.87	146	7.8	101	44

Individual Clinical Chemistry By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F02 (30 mg/kd/day)

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
N	2	2	2	2	2	2	2	2
Mean	80.5	40.5	77.0	11.805	146.0	7.40	101.5	37.5
SD	0.71	4.95	4.24	0.0919	0.00	0.566	0.71	9.19

	GLOB	A/G
5007	2.9	1.2
5008	2.8	1.3
N	2	2
Mean	2.85	1.25
SD	0.071	0.071

Group ID: F03 (90 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
5011	138	16	0.31	10.6	5.0	2.9	0.12	86
5012	104	18	0.30	11.1	6.1	3.4	0.11	102
N	2	2	2	2	2	2	2	2
Mean	121.0	17.0	0.305	10.85	5.55	3.15	0.115	94.0
SD	24.04	1.41	0.0071	0.354	0.778	0.354	0.0071	11.31

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
5011	63	35	64	10.97	145	7.4	99	68
5012	74	31	66	11.63	145	7.7	102	37
N	2	2	2	2	2	2	2	2
Mean	68.5	33.0	65.0	11.300	145.0	7.55	100.5	52.5
SD	7.78	2.83	1.41	0.4667	0.00	0.212	2.12	21.92

Individual Clinical Chemistry By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F03 (90 mg/kg/day)

	GLOB	A/G
5011	2.1	1.4
5012	2.7	1.3
N	2	2
Mean	2.40	1.35
SD	0.424	0.071

Group ID: F04 (180 mg/kg/day)

	GLU	BUN	CREAT	PHOS	TP	ALB	TBILI	ALP
5015	155	15	0.28	12.1	5.7	2.8	0.12	148
5016	127	20	0.26	11.0	4.9	2.7	0.11	79
N	2	2	2	2	2	2	2	2
Mean	141.0	17.5	0.270	11.55	5.30	2.75	0.115	113.5
SD	19.80	3.54	0.0141	0.778	0.566	0.071	0.0071	48.79

	AST	ALT	CHOL	CA	NA	K	CL	TRIG
5015	60	36	74	11.69	144	7.9	102	44
5016	54	32	69	11.39	149	6.7	105	53
N	2	2	2	2	2	2	2	2
Mean	57.0	34.0	71.5	11.540	146.5	7.30	103.5	48.5
SD	4.24	2.83	3.54	0.2121	3.54	0.849	2.12	6.36

	GLOB	A/G
5015	2.9	1.0
5016	2.2	1.2

Individual Clinical Chemistry By Group Summary

Study ID: 0440RE27.002
Study Name: 0440RE27.002

Group Gender: Female **Study Phase:** In-Life **Schedule:** DOT = 8
Subject Gender: Female

Day on Test 8 **Observation Date** 02/12/2009

Group ID: F04 (180 mg/kg/day)

	GLOB	A/G
N	2	2
Mean	2.55	1.10
SD	0.495	0.141

' ' No data collected x-Excluded data

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL NECROPSY OBSERVATIONS

SEX: MALE GROUP: 1-M
DOSE: 0(mg/kg/day)

ANIMAL ID	FATE	DAY	LOCATION	OBSERVATION
5001	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>
5002	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>

DAY-Days on Test

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL NECROPSY OBSERVATIONS

SEX: MALE GROUP: 2-M
DOSE: 30(mg/kg/day)

ANIMAL ID	FATE	DAY	LOCATION	OBSERVATION
5005	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>
5006	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>

DAY-Days on Test

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL NECROPSY OBSERVATIONS

SEX: MALE GROUP: 3-M
DOSE: 90(mg/kg/day)

ANIMAL ID	FATE	DAY	LOCATION	OBSERVATION
5009	Day 8 Sacrifice	8	TESTES	Right small;Right 0.304, Left 1.1537
5010	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>

DAY-Days on Test

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL NECROPSY OBSERVATIONS

SEX: MALE GROUP: 4-M
DOSE: 180(mg/kg/day)

ANIMAL ID	FATE	DAY	LOCATION	OBSERVATION
5013	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>
5014	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>

DAY-Days on Test

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL NECROPSY OBSERVATIONS

SEX: FEMALE GROUP: 1-F
DOSE: 0(mg/kg/day)

ANIMAL ID	FATE	DAY	LOCATION	OBSERVATION
5003	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>
5004	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>

DAY-Days on Test

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL NECROPSY OBSERVATIONS

SEX: FEMALE GROUP: 2-F
DOSE: 30(mg/kg/day)

ANIMAL ID	FATE	DAY	LOCATION	OBSERVATION
5007	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>
5008	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>

DAY-Days on Test

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL NECROPSY OBSERVATIONS

SEX: FEMALE GROUP: 3-F
DOSE: 90(mg/kg/day)

ANIMAL ID	FATE	DAY	LOCATION	OBSERVATION
5011	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>
5012	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>

DAY-Days on Test

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL NECROPSY OBSERVATIONS

SEX: FEMALE GROUP: 4-F
DOSE: 180(mg/kg/day)

ANIMAL ID	FATE	DAY	LOCATION	OBSERVATION
5015	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>
5016	Day 8 Sacrifice	8		<NO ORGANS WITH GROSS FINDINGS>

DAY-Days on Test

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: MALE

GROUP: 1-M
DOSE: 0(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5001	5002
BODY WEIGHT (G)	254	246
ADRENALS (G)	0.043	0.056
% BODY WEIGHT	0.017	0.023
% BRAIN WEIGHT	2.389	3.660
BRAIN (G)	1.80	1.53
% BODY WEIGHT	0.71	0.62
HEART (G)	1.03	1.00
% BODY WEIGHT	0.41	0.41
% BRAIN WEIGHT	57.22	65.36
KIDNEYS (G)	2.04	2.06
% BODY WEIGHT	0.80	0.84
% BRAIN WEIGHT	113.33	134.64
LIVER (G)	8.38	7.67
% BODY WEIGHT	3.30	3.12
% BRAIN WEIGHT	465.56	501.31
LUNGS (G)	1.27	1.32
% BODY WEIGHT	0.50	0.54
% BRAIN WEIGHT	70.56	86.27
PITUITARY (G)	0.002	0.002
% BODY WEIGHT	0.001	0.001
% BRAIN WEIGHT	0.111	0.131
SPLEEN (G)	0.60	0.57
% BODY WEIGHT	0.24	0.23
% BRAIN WEIGHT	33.33	37.25
TESTES (G)	3.441	3.157
% BODY WEIGHT	1.355	1.283
% BRAIN WEIGHT	191.167	206.340

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: MALE

GROUP: 1-M
DOSE: 0(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5001	5002
THYROIDS/PARATHYROIDS (G)	0.007	0.021
% BODY WEIGHT	0.003	0.009
% BRAIN WEIGHT	0.389	1.373

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: MALE

GROUP: 2-M
DOSE: 30(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5005	5006
BODY WEIGHT (G)	236	244
ADRENALS (G)	0.037	0.053
% BODY WEIGHT	0.016	0.022
% BRAIN WEIGHT	2.079	3.064
BRAIN (G)	1.78	1.73
% BODY WEIGHT	0.75	0.71
HEART (G)	0.95	0.90
% BODY WEIGHT	0.40	0.37
% BRAIN WEIGHT	53.37	52.02
KIDNEYS (G)	1.99	1.93
% BODY WEIGHT	0.84	0.79
% BRAIN WEIGHT	111.80	111.56
LIVER (G)	8.45	7.80
% BODY WEIGHT	3.58	3.20
% BRAIN WEIGHT	474.72	450.87
LUNGS (G)	1.18	1.17
% BODY WEIGHT	0.50	0.48
% BRAIN WEIGHT	66.29	67.63
PITUITARY (G)	0.007	0.005
% BODY WEIGHT	0.003	0.002
% BRAIN WEIGHT	0.393	0.289
SPLEEN (G)	0.52	0.56
% BODY WEIGHT	0.22	0.23
% BRAIN WEIGHT	29.21	32.37
TESTES (G)	2.904	3.278
% BODY WEIGHT	1.231	1.343
% BRAIN WEIGHT	163.146	189.480

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: MALE

GROUP: 2-M
DOSE: 30(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5005	5006
THYROIDS/PARATHYROIDS (G)	0.018	0.013
% BODY WEIGHT	0.008	0.005
% BRAIN WEIGHT	1.011	0.751

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: MALE

GROUP: 3-M
DOSE: 90(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5009	5010
BODY WEIGHT (G)	238	254
ADRENALS (G)	0.063	0.058
% BODY WEIGHT	0.026	0.023
% BRAIN WEIGHT	4.345	3.085
BRAIN (G)	1.45	1.88
% BODY WEIGHT	0.61	0.74
HEART (G)	0.94	1.03
% BODY WEIGHT	0.39	0.41
% BRAIN WEIGHT	64.83	54.79
KIDNEYS (G)	1.93	2.31
% BODY WEIGHT	0.81	0.91
% BRAIN WEIGHT	133.10	122.87
LIVER (G)	8.36	9.29
% BODY WEIGHT	3.51	3.66
% BRAIN WEIGHT	576.55	494.15
LUNGS (G)	1.35	2.05
% BODY WEIGHT	0.57	0.81
% BRAIN WEIGHT	93.10	109.04
PITUITARY (G)	0.004	0.004
% BODY WEIGHT	0.002	0.002
% BRAIN WEIGHT	0.276	0.213
SPLEEN (G)	0.66	0.63
% BODY WEIGHT	0.28	0.25
% BRAIN WEIGHT	45.52	33.51
TESTES (G)	1.841	3.610
% BODY WEIGHT	0.774	1.421
% BRAIN WEIGHT	126.966	192.021

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: MALE

GROUP: 3-M
DOSE: 90(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5009	5010
THYROIDS/PARATHYROIDS (G)	0.016	0.007
% BODY WEIGHT	0.007	0.003
% BRAIN WEIGHT	1.103	0.372

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: MALE

GROUP: 4-M
DOSE: 180(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5013	5014
BODY WEIGHT (G)	208	170
ADRENALS (G)	0.052	0.066
% BODY WEIGHT	0.025	0.039
% BRAIN WEIGHT	3.291	4.204
BRAIN (G)	1.58	1.57
% BODY WEIGHT	0.76	0.92
HEART (G)	0.84	0.70
% BODY WEIGHT	0.40	0.41
% BRAIN WEIGHT	53.16	44.59
KIDNEYS (G)	1.75	1.39
% BODY WEIGHT	0.84	0.82
% BRAIN WEIGHT	110.76	88.54
LIVER (G)	8.71	6.54
% BODY WEIGHT	4.19	3.85
% BRAIN WEIGHT	551.27	416.56
LUNGS (G)	1.13	1.06
% BODY WEIGHT	0.54	0.62
% BRAIN WEIGHT	71.52	67.52
PITUITARY (G)	0.008	0.003
% BODY WEIGHT	0.004	0.002
% BRAIN WEIGHT	0.506	0.191
SPLEEN (G)	0.36	0.25
% BODY WEIGHT	0.17	0.15
% BRAIN WEIGHT	22.78	15.92
TESTES (G)	3.250	2.981
% BODY WEIGHT	1.563	1.754
% BRAIN WEIGHT	205.696	189.873

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: MALE

GROUP: 4-M
DOSE: 180(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5013	5014
THYROIDS/PARATHYROIDS (G)	0.006	0.014
% BODY WEIGHT	0.003	0.008
% BRAIN WEIGHT	0.380	0.892

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: FEMALE

GROUP: 1-F
DOSE: 0(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5003	5004
BODY WEIGHT (G)	182	171
ADRENALS (G)	0.063	0.069
% BODY WEIGHT	0.035	0.040
% BRAIN WEIGHT	3.750	4.423
BRAIN (G)	1.68	1.56
% BODY WEIGHT	0.92	0.91
HEART (G)	0.80	0.74
% BODY WEIGHT	0.44	0.43
% BRAIN WEIGHT	47.62	47.44
KIDNEYS (G)	1.45	1.48
% BODY WEIGHT	0.80	0.87
% BRAIN WEIGHT	86.31	94.87
LIVER (G)	5.95	5.73
% BODY WEIGHT	3.27	3.35
% BRAIN WEIGHT	354.17	367.31
LUNGS (G)	1.11	1.19
% BODY WEIGHT	0.61	0.70
% BRAIN WEIGHT	66.07	76.28
PITUITARY (G)	0.007	0.005
% BODY WEIGHT	0.004	0.003
% BRAIN WEIGHT	0.417	0.321
SPLEEN (G)	0.55	0.55
% BODY WEIGHT	0.30	0.32
% BRAIN WEIGHT	32.74	35.26
OVARIES (G)	0.113	0.113
% BODY WEIGHT	0.062	0.066
% BRAIN WEIGHT	6.726	7.244

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: FEMALE

GROUP: 1-F
DOSE: 0(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5003	5004
THYROIDS/PARATHYROIDS (G)	0.012	0.018
% BODY WEIGHT	0.007	0.011
% BRAIN WEIGHT	0.714	1.154

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: FEMALE

GROUP: 2-F
DOSE: 30(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5007	5008
BODY WEIGHT (G)	180	176
ADRENALS (G)	0.060	0.059
% BODY WEIGHT	0.033	0.034
% BRAIN WEIGHT	3.822	3.598
BRAIN (G)	1.57	1.64
% BODY WEIGHT	0.87	0.93
HEART (G)	0.82	0.74
% BODY WEIGHT	0.46	0.42
% BRAIN WEIGHT	52.23	45.12
KIDNEYS (G)	1.62	1.44
% BODY WEIGHT	0.90	0.82
% BRAIN WEIGHT	103.18	87.80
LIVER (G)	5.96	5.67
% BODY WEIGHT	3.31	3.22
% BRAIN WEIGHT	379.62	345.73
LUNGS (G)	1.15	1.09
% BODY WEIGHT	0.64	0.62
% BRAIN WEIGHT	73.25	66.46
PITUITARY (G)	0.007	0.005
% BODY WEIGHT	0.004	0.003
% BRAIN WEIGHT	0.446	0.305
SPLEEN (G)	0.46	0.44
% BODY WEIGHT	0.26	0.25
% BRAIN WEIGHT	29.30	26.83
OVARIES (G)	0.136	0.092
% BODY WEIGHT	0.076	0.052
% BRAIN WEIGHT	8.662	5.610

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: FEMALE

GROUP: 2-F
DOSE: 30(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5007	5008
THYROIDS/PARATHYROIDS (G)	0.012	0.013
% BODY WEIGHT	0.007	0.007
% BRAIN WEIGHT	0.764	0.793

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: FEMALE

GROUP: 3-F
DOSE: 90(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5011	5012
BODY WEIGHT (G)	192	184
ADRENALS (G)	0.071	0.057
% BODY WEIGHT	0.037	0.031
% BRAIN WEIGHT	5.221	3.353
BRAIN (G)	1.36	1.70
% BODY WEIGHT	0.71	0.92
HEART (G)	0.84	0.78
% BODY WEIGHT	0.44	0.42
% BRAIN WEIGHT	61.76	45.88
KIDNEYS (G)	1.63	1.59
% BODY WEIGHT	0.85	0.86
% BRAIN WEIGHT	119.85	93.53
LIVER (G)	7.40	6.51
% BODY WEIGHT	3.85	3.54
% BRAIN WEIGHT	544.12	382.94
LUNGS (G)	1.10	1.34
% BODY WEIGHT	0.57	0.73
% BRAIN WEIGHT	80.88	78.82
PITUITARY (G)	0.003	0.003
% BODY WEIGHT	0.002	0.002
% BRAIN WEIGHT	0.221	0.176
SPLEEN (G)	0.51	0.57
% BODY WEIGHT	0.27	0.31
% BRAIN WEIGHT	37.50	33.53
OVARIES (G)	0.065	0.129
% BODY WEIGHT	0.034	0.070
% BRAIN WEIGHT	4.779	7.588

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: FEMALE

GROUP: 3-F
DOSE: 90(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5011	5012
THYROIDS/PARATHYROIDS (G)	0.017	0.011
% BODY WEIGHT	0.009	0.006
% BRAIN WEIGHT	1.250	0.647

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: FEMALE

GROUP: 4-F
DOSE: 180(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5015	5016
BODY WEIGHT (G)	175	167
ADRENALS (G)	0.078	0.071
% BODY WEIGHT	0.045	0.043
% BRAIN WEIGHT	4.382	4.329
BRAIN (G)	1.78	1.64
% BODY WEIGHT	1.02	0.98
HEART (G)	0.80	0.71
% BODY WEIGHT	0.46	0.43
% BRAIN WEIGHT	44.94	43.29
KIDNEYS (G)	1.63	1.43
% BODY WEIGHT	0.93	0.86
% BRAIN WEIGHT	91.57	87.20
LIVER (G)	0.16@	6.98
% BODY WEIGHT	0.09	4.18
% BRAIN WEIGHT	8.99	425.61
LUNGS (G)	1.22	1.07
% BODY WEIGHT	0.70	0.64
% BRAIN WEIGHT	68.54	65.24
PITUITARY (G)	0.009	0.002
% BODY WEIGHT	0.005	0.001
% BRAIN WEIGHT	0.506	0.122
SPLEEN (G)	0.56	0.46
% BODY WEIGHT	0.32	0.28
% BRAIN WEIGHT	31.46	28.05
OVARIES (G)	0.137	0.138
% BODY WEIGHT	0.078	0.083
% BRAIN WEIGHT	7.697	8.415

@ Suspected recording error, removed from Organ Weight summary tables

CALVERT LABORATORIES, INC.
A 7-DAY ORAL TOXICOKINETIC STUDY WITH GB67B IN RATS
STUDY NUMBER: 0440RE27.002
TEST ARTICLE: GB67B
SPONSOR: EMORY INSTITUTE FOR DRUG DISCOVERY

INDIVIDUAL ORGAN WEIGHTS

SEX: FEMALE

GROUP: 4-F
DOSE: 180(mg/kg/day)
FATES: Day 8 Sacrifice

ANIMAL ID:	5015	5016
THYROIDS/PARATHYROIDS (G)	0.010	0.011
% BODY WEIGHT	0.006	0.007
% BRAIN WEIGHT	0.562	0.671

Appendix II—Test Article Information & Dosing Solution Analyses

Test article information (Certificate of Analysis) and Dosing Solution Analyses Report were not available for inclusion in this report.

Appendix III—Bioanalytical Report

Study Title:

Analysis of Rodent Plasma Samples for GB67B, GB97 and GB594

Ricerca Project Number: **024347**

Study Completed:

22-May-2009

Author:

Xiaohong Hou, M.D., Ph.D.

Testing Facility:
Ricerca Biosciences, LLC
Discovery Biology
7528 Auburn Road
Concord OH 44077

Study Sponsor:
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
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Approvals

Study Title: Analysis of Rodent Plasma Samples for GB67B, GB97 and GB594

Document Number: 024347-1

Testing Facility: Ricerca Biosciences, LLC
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Xiaohong Hou, M.D., Ph.D.
Discovery Biology
Ricerca Biosciences, LLC

Date: 5/22/09

Testing Facility Management

James R. Szabo, D.V.M., Ph.D., DACVP
Vice President, Biology Services
Ricerca Biosciences, LLC

Date: 22 May 2009

Introduction

Objectives

The objectives of this bioanalytical study were to analyze mouse plasma from mouse PK studies for three compounds (GB67B, GB97, and GB594) and to analyze rat plasma from a rat toxicology study for GB67B conducted outside Ricerca.

Methods

Extraction Method

GB67B

1. Prepare a 1 mg/ml of test article in MeOH.
2. Serial diluted test articles from 1 mg/mL in MeOH to obtain 1000, 800, 400, 100, 50, 10, 5 and 2.5, µg/mL stock.
3. Spiked 10 µL of the each stock in 490 µL of mouse or rat plasma to make standard mouse and rat plasma curves at 20000, 16000, 8000, 2000, 1000, 200, 100 and 50 ng/mL.
4. Prepare an internal standard (IS) (GB67B-d9) stock at 0.5 µg/mL in ACN.
5. Transfer 40 µL of the standards and samples to new tubes and quench by 250 µL of IS in ACN, vortex, and spin at 14000 rpm for 10 min at 5 °C.
6. The supernatant were transferred in low-volume plastic HPLC vials for LC/MS/MS.

GB97

1. Prepare a 271 µg/ml of test article in MeOH.
2. Spiked 271 µg/mL of the stock solution in mouse plasma and make a serial dilution from mouse plasma to obtain a standard mouse plasma curve at 20000, 16000, 8000, 4000, 2000, 800, 400 and 200 ng/mL.
3. Prepare an internal standard (IS) (GB97-d9) stock at 2.5 µg/mL in CAN.
4. Transfer 50 µL of the standards and samples to new tubes and quench by 250 µL of IS in ACN, vortex, and spin at 14000 rpm for 10 min at 5 °C.
5. The supernatant were transferred in low-volume plastic HPLC vials for LC/MS/MS.

GB594

1. Prepare a 400 µg/ml of test article in MeOH.
2. Spiked 400 µg/mL of the stock solution in mouse plasma and make a serial dilution from mouse plasma to obtain a standard mouse plasma curve at 20000, 16000, 8000, 2000, 1000, 200, 100 and 50 ng/mL
3. Prepare an internal standard (IS) (GB594-d9) stock at 2.5 µg/mL in ACN
4. Transfer 50 µL of the standards and samples to new tubes and quench by 250 µL of IS in ACN, vortex, and spin at 14000 rpm for 10 min at 5 °C
5. The supernatant were transferred in low-volume plastic HPLC vials for LC/MS/MS.

Bioanalytical Method

Test Article: GB67B

Mass spectrometer:	PE Sciex API 4000 LC-MS/MS System
HPLC Column:	Phenomenex Synergi MAX-RP 4µ 150 x 2.0 mm with Security Guard
Buffers:	A = 1% formic acid in 5 mM ammonium acetate B = 1% formic acid in methanol
Isocratic:	Time (min) %B 0 68 3.0 Stop Note: The column flow before 1.3 minutes was diverted to waste.
Flow Rate:	0.5 mL/min
Injection Volume:	4 µL
Ionization:	Positive
MRM:	209.1 → 181.2 (GB67B) 218.1 → 190.2 (GB67B-d9, IS)

Test Article:GB97

Mass spectrometer:	PE Sciex API 4000 LC-MS/MS System
HPLC Column:	Phenomenex Synergi MAX-RP 4µ 150 x 2.0 mm with Security Guard
Buffers:	A = 1% formic acid in 5 mM ammonium acetate B = 1% formic acid in methanol
Isocratic:	Time (min) %B 0 80 3.0 Stop Note: The column flow before 1.0 minute was diverted to waste.
Flow Rate:	0.5 mL/min
Injection Volume:	6 µL
Ionization:	Positive
MRM:	242.4 → 167.1 (GB97) 251.4 → 176.1 (GB97-d9, IS)

Test Article: GB594

Mass spectrometer:	PE Sciex API 4000 LC-MS/MS System
HPLC Column:	Phenomenex Synergi POLAR-RP 4µ 50 x 2.0 mm with Security Guard
Buffers:	A = 1% formic acid in 5 mM ammonium acetate B = 1% formic acid in methanol
Gradient:	Time (min) %B 0 10 0.2 10 2.0 95 2.8 95 2.9 10 5.6 Stop Note: The column flow before 1.5 minutes was diverted to waste.
Injection Volume:	5 µL
Ionization:	Positive
MRM:	260.1 → 57.1 (GB594) 269.1 → 66.1 (GB594-d9, IS)

Results

Analytical Results of Mouse Plasma

Analysis result for GB-67B

Std Curve weighted 1/x*x
Intercept = 0.018
Slope = 0.00161
Correlation Coeff = 0.9981

Group	Dose/Route	GB-67B/MPK-08-1	Mouse Number	Dosing Time	Schedule Sample Time	Concentration (ng/mL)
1 (8h)	30mg/kg i.p	1	1	800	1600	No Peak
		2	2	802	1602	No Peak
		3	3	804	1604	No Peak
		4	4	806	1606	No Peak
2 (6h)	30mg/kg i.p	5	1	810	1410	No Peak
		6	2	812	1412	No Peak
		7	3	814	1414	No Peak
		8	4	816	1416	No Peak
3 (4h)	30mg/kg	9	1	820	1220	No Peak
		10	2	822	1222	No Peak
		11	3	824	1224	No Peak
		12	4	826	1226	No Peak
4 (2h)	30mg/kg .i.p	13	1	830	1030	No Peak
		14	2	832	1032	No Peak
		15	3	834	1034	No Peak
		16	4	836	1036	No Peak
5 (1h)	30mg/kg	17	1	840	940	No Peak
		18	2	842	942	No Peak
		19	3	844	944	No Peak
		20	4	846	946	No Peak
6 (30m)	30mg/kg i.p	21	1	1020	1050	No Peak
		22	2	1022	1052	BLQ
		23	3	1024	1054	No Peak
		24	4	1026	1056	No Peak
7 (15m)	30mg/kg	25	1	1100	1115	No Peak
		26	2	1102	1117	No Peak
		27	3	1104	1119	No Peak
		28	4	1106	1121	No Peak
8 (5m)	30mg/kg i.p	29	1	1140	1145	No Peak
		30	2	1142	1147	No Peak
		31	3	1150	1155	No Peak
		32	4	1152	1157	No Peak
Vehicle Control	i.p	33	1	1200	1230	No Peak

BLQ: blow limit of quantitation

Analysis result for GB-97

Std Curve weighted 1/x*x
Intercept = -0.0177
Slope = 0.00104
Correlation Coeff = 0.9978

Group	Dose/Route	GB-97/-MPK-08-1	Animal	Collection Time (nominal)	Collection Time (actual)	Concentration (ng/mL)
G1	30mg/kg/i.p.	1	1	1600	NA	No Peak
		2	2	1602	NA	No Peak
		3	3	1604	NA	No Peak
		4	4	1606	NA	No Peak
G2	30mg/kg/i.p.	5	1	1410	NA	No Peak
		6	2	1412	NA	No Peak
		7	3	1414	NA	No Peak
		8	4	1416	NA	No Peak
G3	30mg/kg/i.p.	9	1	1220	NA	No Peak
		10	2	1222	NA	No Peak
		11	3	1224	NA	No Peak
		12	4	1226	NA	No Peak
G4	30mg/kg/i.p.	13	1	1030	NA	No Peak
		14	2	1032	NA	No Peak
		15	3	1034	NA	No Peak
		16	4	1036	NA	No Peak
G5	30mg/kg/i.p.	17	1	940	NA	No Peak
		18	2	942	NA	No Peak
		19	3	944	NA	No Peak
		20	4	946	NA	No Peak
G6	30mg/kg/i.p.	21	1	1050	NA	330
		22	2	1052	NA	214
		23	3	1054	NA	253
		24	4	1056	NA	182
G7	30mg/kg/i.p.	25	1	1115	NA	1559
		26	2	1117	NA	176
		27	3	1119	NA	802
		28	4	1121	NA	1448
G8	30mg/kg/i.p.	29	1	1145	NA	2813
		30	2	1147	NA	1373
		31	3	1155	NA	1742
		32	4	1157		305
Vehicle Control	i.p.	33	1	1230	NA	No Peak

Analysis result for GB594

Std Curve weighted 1/x*x
Intercept = -0.0223
Slope = 0.00186
Correlation Coeff = 0.9939

Group	Dose/Route	GB-594/MPK-08-1	Animal	Collection Time (nominal)	Concentration (ng/mL)
G1	30mg/kg/i.p.	1	1	1600	No Peak
		2	2	1602	No Peak
		3	3	1604	No Peak
		4	4	1606	No Peak
G2	30mg/kg/i.p.	5	3	1414	No Peak
		6	4	1416	No Peak
G3	30mg/kg/i.p.	7	1	1220	No Peak
		8	2	1222	No Peak
		9	3	1224	No Peak
		10	4	1226	No Peak
G4	30mg/kg/i.p.	11	1	1030	No Peak
		12	2	1032	No Peak
		13	3	1034	No Peak
		14	4	1036	No Peak
G5	30mg/kg/i.p.	15	1	940	110
		16	2	942	118
		17	3	944	72.9
		18	4	946	BLQ
G6	30mg/kg/i.p.	19	1	1050	463
		20	2	1052	326
		21	3	1054	619
		22	4	1056	251
G7	30mg/kg/i.p.	23	1	1115	2567
		24	2	1117	1555
		25	3	1119	2023
		26	4	1121	1080
G8	30mg/kg/i.p.	27	1	1145	1501
		28	2	1147	1003
		29	3	1155	1106
		30	4	1157	2189
Vehicle Control	i.p.	31	1	1230	No Peak

BLQ: blow limit of quantitation

Analytical Results of Rat Plasma

Std Curve weighted 1/x*x
Intercept = -0.00614
Slope = 0.00183
Correlation Coeff = 0.9992

DAY 1 (05-Feb-2009) RAT PLASMA SAMPLES (5017-5039)

GB-67B/ 044RE27.003	Animal	Sex	Group	Dose (mg/kg/day)	Predose Sample	Time of Dose	1 hour Postdose	Differ-ence	4 hours Postdose	Differ-ence	Conc. (ng/mL)
	5017	M	5	6							
0001					7:09	8:00					No Peak
0002							9:00	1:00			No Peak
0003									12:00	4:00	No Peak
	5019	M	5	6							
0004					7:11	8:03					No Peak
0005							9:03	1:00			No Peak
0006									12:03	4:00	No Peak
	5021	F	5	6							
0007					7:13	8:06					No Peak
0008							9:06	1:00			No Peak
0009									12:06	4:00	No Peak
	5023	F	5	6							
0010					7:15	8:09					No Peak
0011							9:09	1:00			No Peak
0012									12:09	4:00	No Peak
	5025	M	6	18							
0013					7:17	8:12					No Peak
0014							9:12	1:00			No Peak
0015									12:12	4:00	No Peak
	5027	M	6	18							
0016					7:19	8:15					No Peak
0017							9:15	1:00			No Peak
0018									12:15	4:00	No Peak
	5029	F	6	18							
0019					7:22	8:18					No Peak
0020							9:18	1:00			No Peak
0021									12:18	4:00	No Peak
	5031	F	6	18							
0022					7:24	8:21					No Peak
0023							9:21	1:00			No Peak
0024									12:21	4:00	No Peak
	5033	M	7	36							
0025					7:26	8:24					No Peak
0026							9:24	1:00			No Peak
0027									12:24	4:00	No Peak
	5035	M	7	36							
0028					7:28	8:27					No Peak
0029							9:27	1:00			No Peak
0030									12:27	4:00	No Peak
	5037	F	7	36							
0031					7:30	8:30					No Peak
0032							9:30	1:00			No Peak
0033									12:30	4:00	No Peak
	5039	F	7	36							
0034					7:32	8:33					No Peak
0035							9:33	1:00			No Peak
0036									12:33	4:00	No Peak

DAY 1 (05-Feb-2009) RAT PLASMA SAMPLES (2018-5040A)

GB-67B/ 044RE27.002	Animal	Sex	Group	Dose (mg/kg/day)	Time of Dose	30 min Posdose	Differ-ence	2 hours Postdose	Differ-ence	Conc. (ng/mL)
	5018	M	5	6						
0037					8:01	8:31	0:30			No Peak
0038								10:01	2:00	No Peak
	5020	M	5	6						
0039					8:04	8:34	0:30			No Peak
0040								10:04	2:00	No Peak
	5022	F	5	6						
0041					8:07	8:37	0:30			No Peak
0042								10:07	2:00	No Peak
	5024	F	5	6						
0043					8:10	8:40	0:30			No Peak
0044								10:10	2:00	No Peak
	5026	M	6	18						
0045					8:13	8:43	0:30			No Peak
0046								10:13	2:00	No Peak
	5028	M	6	18						
0047					8:16	8:46	0:30			No Peak
0048								10:16	2:00	No Peak
	5030	F	6	18						
0049					8:19	8:49	0:30			No Peak
0050								10:19	2:00	No Peak
	5032	F	6	18						
0051					8:22	8:52	0:30			No Peak
0052								10:22	2:00	No Peak
	5034	M	7	36						
0053					8:25	8:55	0:30			No Peak
0054								10:25	2:00	No Peak
	5036	M	7	36						
0055					8:28	8:58	0:30			No Peak
0056								10:28	2:00	No Peak
	5038	F	7	36						
0057					8:31	9:01	0:30			No Peak
0058								10:31	2:00	No Peak
	5040	F	7	36						
0059					8:34	9:04	0:30			No Peak
0060								10:34	2:00	No Peak

DAY 1 (5 Feb 2009) RAT PLASMA SAMPLES (5018-5040B)

GB-67B/044RE27.003	Animal	Sex	Group	Dose (mg/kgday)	Time of Dose	8 hours Postdose	Difference	Conc. (ng/mL)
0061	5018	M	5	6	8:01	16:01	8:00	No Peak
0062	5020	M	5	6	8:04	16:04	8:00	No Peak
0063	5022	F	5	6	8:07	16:07	8:00	No Peak
0064	5024	F	5	6	8:10	16:10	8:00	No Peak
0065	5026	M	6	18	8:13	16:13	8:00	No Peak
0066	5028	M	6	18	8:16	16:16	8:00	No Peak
0067	5030	F	6	18	8:19	16:19	8:00	No Peak
0068	5032	F	6	18	8:22	16:22	8:00	No Peak
0069	5034	M	7	36	8:25	16:25	8:00	No Peak
0070	5036	M	7	36	8:28	16:28	8:00	No Peak
0071	5038	F	7	36	8:31	16:31	8:00	No Peak
0072	5040	F	7	36	8:34	16:34	8:00	No Peak

DAY 7 (11 Feb 2009) RAT PLASMA SAMPLES (5017-5039)

Std Curve weighted 1/x*x
Intercept = 0.00133
Slope = 0.00155
Correlation Coeff = 0.9993

GB-67B/ 044RE27.002	Animal	Sex	Group	Dose (mg/kg/day)	Predose Sample	Time of Dose	1 hour Postdose	Differ-ence	4 hours Postdose	Differ-ence	Conc. (ng/mL)
	5017	M	5	6							
0073					7:15	8:00					No Peak
0074							9:00	1:00			No Peak
0075									12:00	4:00	No Peak
	5019	M	5	6							
0076					7:18	8:03					No Peak
0077							9:03	1:00			No Peak
0078									12:03	4:00	No Peak
	5021	F	5	6							
0079					7:19	8:06					No Peak
0080							9:06	1:00			No Peak
0081									12:06	4:00	No Peak
	5023	F	5	6							
0082					7:21	8:09					No Peak
0083							9:09	1:00			No Peak
0084									12:09	4:00	No Peak
	5025	M	6	18							
0085					7:24	8:12					No Peak
0086							9:12	1:00			No Peak
0087									12:12	4:00	No Peak
	5027	M	6	18							
0088					7:27	8:15					No Peak
0089							9:15	1:00			No Peak
0090									12:15	4:00	No Peak
	5029	F	6	18							
0091					7:29	8:18					No Peak
0092							9:18	1:00			No Peak
0093									12:18	4:00	No Peak
	5031	F	6	18							
0094					7:32	8:21					No Peak
0095							9:21	1:00			No Peak
0096									12:21	4:00	No Peak
	5033	M	7	36							
0097					7:34	8:24					No Peak
0098							9:24	1:00			No Peak
0099									12:24	4:00	No Peak
	5035	M	7	36							
0100					7:36	8:27					No Peak
0101							9:27	1:00			No Peak
0102									12:27	4:00	No Peak
	5037	F	7	36							
0103					7:38	8:30					No Peak
0104							9:30	1:00			No Peak
0105									12:30	4:00	No Peak
	5039	F	7	36							
0106					7:40	8:33					No Peak
0107							9:33	1:00			No Peak
0108									12:33	4:00	No Peak

DAY 7 (11 Feb 2009) RAT PLASMA SAMPLES (5018-5040A)

GB-67B/ 044RE27.003	Animal	Sex	Group	Dose (mg/kg/day)	Time of Dose	30 minutes Postdose	Differ-ence	2 hours Postose	Differ-ence	Conc. (ng/mL)
	5018	M	5	6						
0109					8:01	8:31	0:30			No Peak
0110								10:01	2:00	No Peak
	5020	M	5	6						
0111					8:04	8:34	0:30			No Peak
0112								10:04	2:00	No Peak
	5022	F	5	6						
0113					8:07	8:37	0:30			No Peak
0114								10:07	2:00	No Peak
	5024	F	5	6						
0115					8:10	8:40	0:30			No Peak
0116								10:10	2:00	No Peak
	5026	M	6	18						
0117					8:13	8:43	0:30			No Peak
0118								10:13	2:00	No Peak
	5028	M	6	18						
0119					8:16	8:46	0:30			No Peak
0120								10:16	2:00	No Peak
	5030	F	6	18						
0121					8:19	8:49	0:30			No Peak
0122								10:19	2:00	No Peak
	5032	F	6	18						
0123					8:22	8:52	0:30			No Peak
0124								10:22	2:00	No Peak
	5034	M	7	36						
0125					8:25	8:55	0:30			No Peak
0126								10:25	2:00	No Peak
	5036	M	7	36						
0127					8:28	8:58	0:30			No Peak
0128								10:28	2:00	No Peak
	5038	F	7	36						
0129					8:31	9:01	0:30			No Peak
0130								10:31	2:00	No Peak
	5040	F	7	36						
0131					8:34	9:04	0:30			No Peak
0132								10:34	2:00	No Peak

DAY 7 (11 Feb 2009) RAT PLASMA SAMPLES (5018-5040B)

GB-67B/ 044RE27.002	Animal	Sex	Group	Dose (mg/kg/day)	Time of dose	8 hours Postdose	Difference	Conc. (ng/mL)
0133	5018	M	5	6	8:01	16:01	8:00	No Peak
0134	5020	M	5	6	8:04	16:04	8:00	No Peak
0135	5022	F	5	6	8:07	16:07	8:00	No Peak
0136	5024	F	5	6	8:10	16:10	8:00	No Peak
0137	5026	M	6	18	8:13	16:13	8:00	No Peak
0138	5028	M	6	18	8:16	16:16	8:00	No Peak
0139	5030	F	6	18	8:19	16:19	8:00	No Peak
0140	5032	F	6	18	8:22	16:22	8:00	No Peak
0141	5034	M	7	36	8:25	16:25	8:00	No Peak
0142	5036	M	7	36	8:28	16:28	8:00	No Peak
0143	5038	F	7	36	8:31	16:31	8:00	No Peak
0144	5040	F	7	36	8:34	16:34	8:00	No Peak

Figure 1: GB67B-MPK-08-1-027 (upper) and GB67B_d_9 (internal standard, lower)

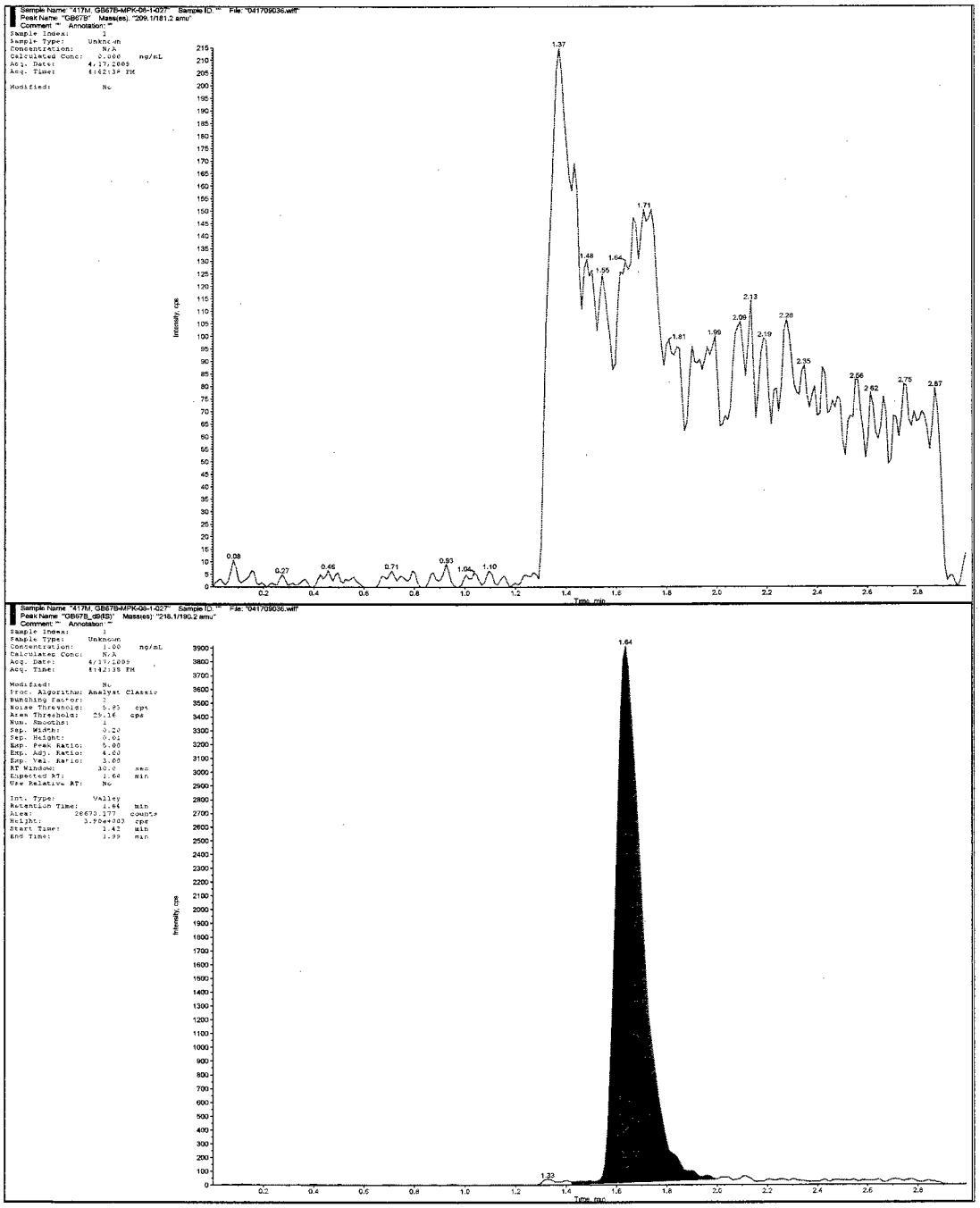


Figure 2: Typical Chromatograms of GB67B in a Mouse Plasma Standard Curve Sample (LLOQ 50 ng/mL) GB67B (upper) and GB67B_d_9 (internal standard, lower)

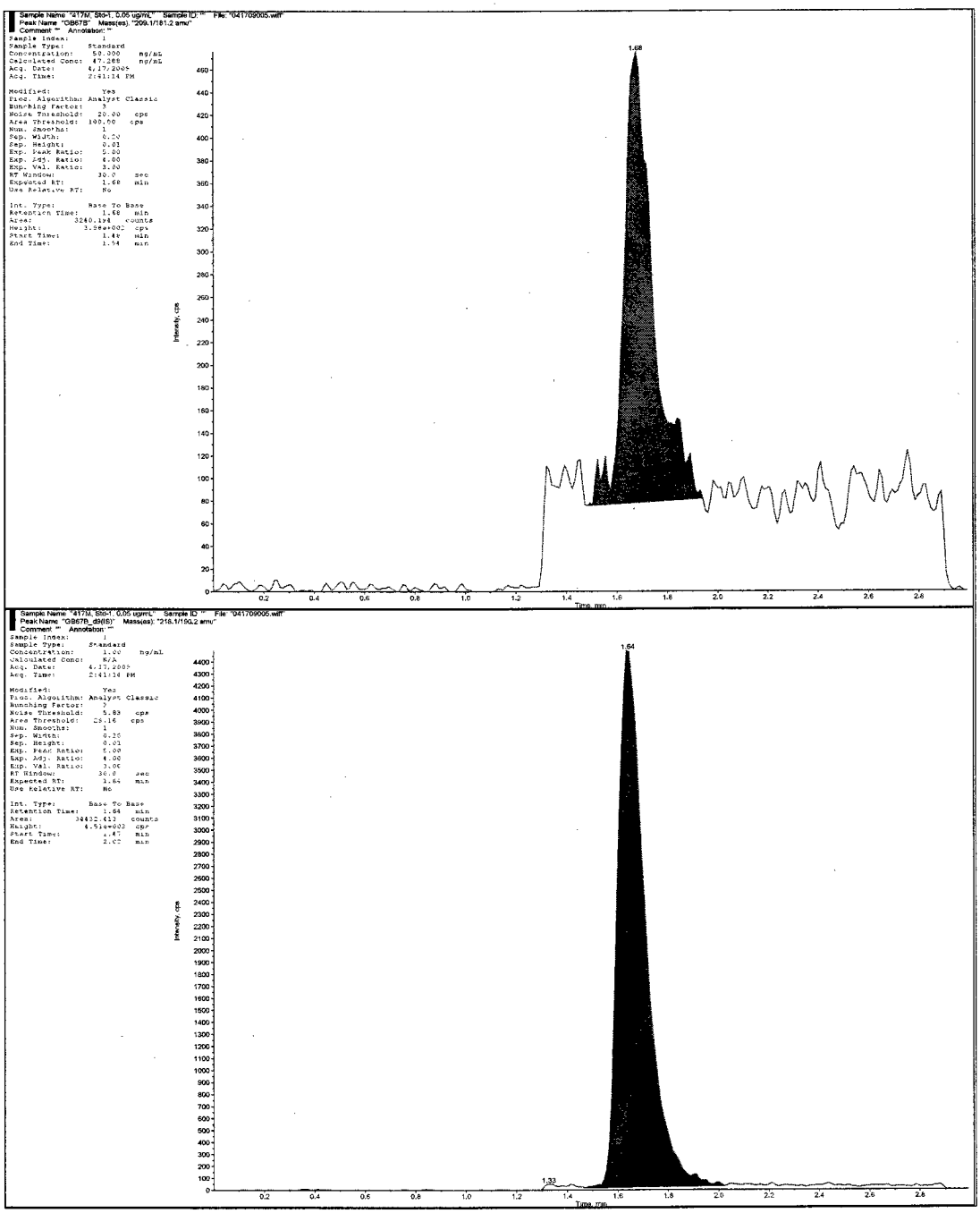


Figure 3: Typical Chromatograms of GB67B in a Mouse Plasma Standard Curve Sample (ULOQ 20 µg/mL) GB67B (upper) and GB67B_d_9 (internal standard, lower)

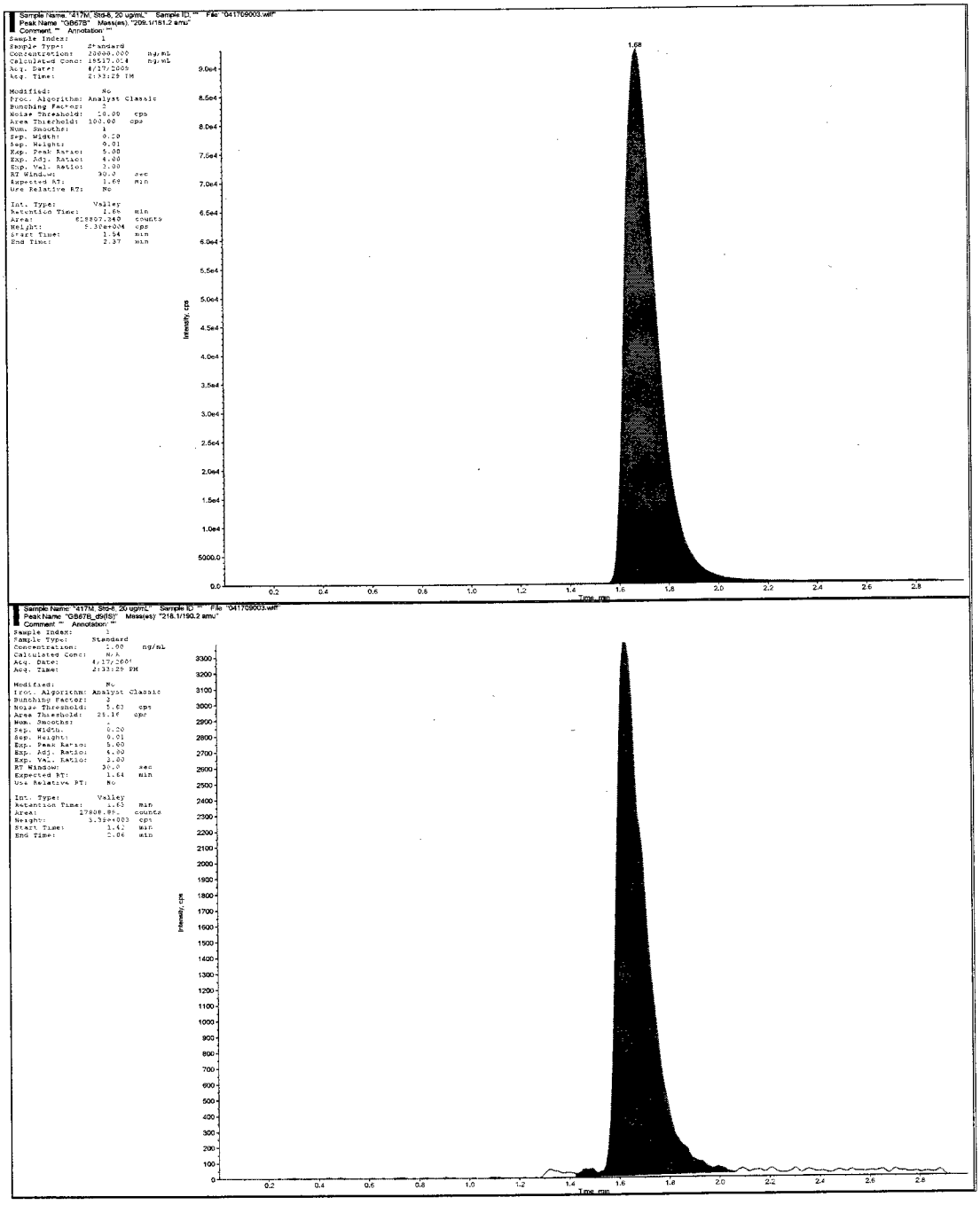


Figure 4: GB97-MPK-08-1-0029 (upper) and GB97_d_9 (internal standard, lower)

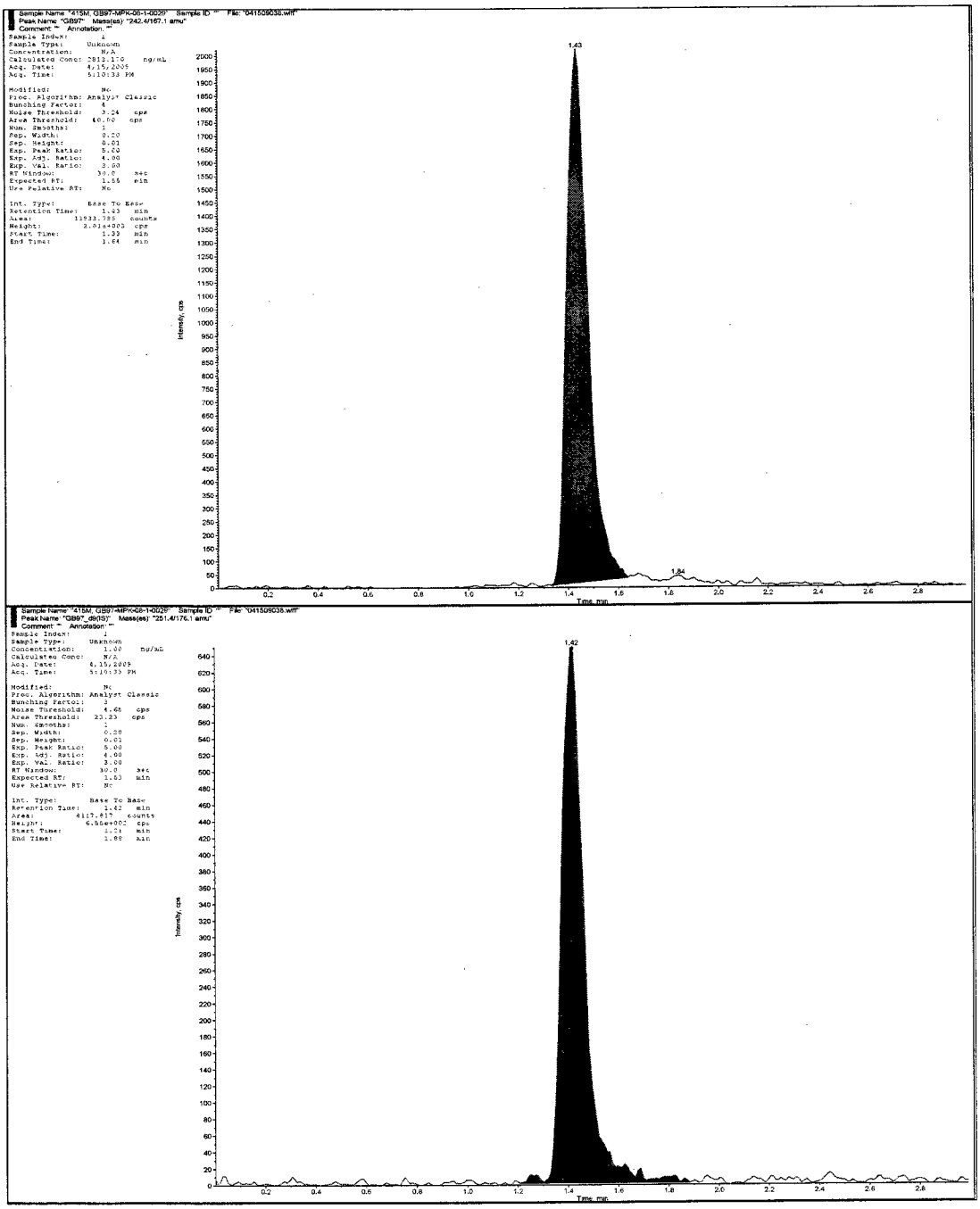


Figure 5: Typical Chromatograms of GB97 in a Mouse Plasma Standard Curve Sample (LLOQ 200 ng/mL) GB97 (upper) and GB97_d_9 (internal standard, lower)

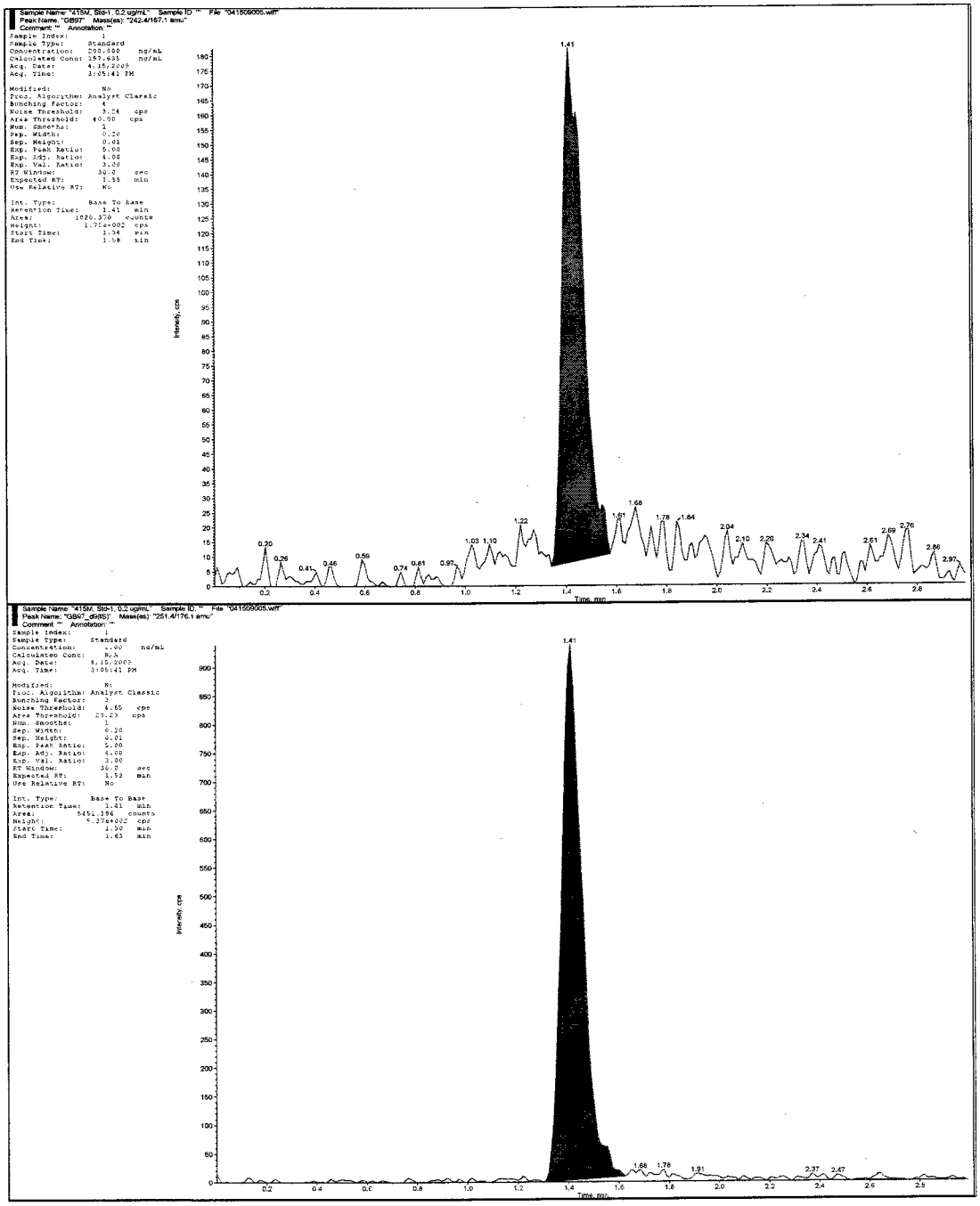


Figure 6: Typical Chromatograms of GB97 in a Mouse Plasma Standard Curve Sample (ULOQ 20 µg/mL) GB97 (upper) and GB97_d_9 (internal standard, lower)

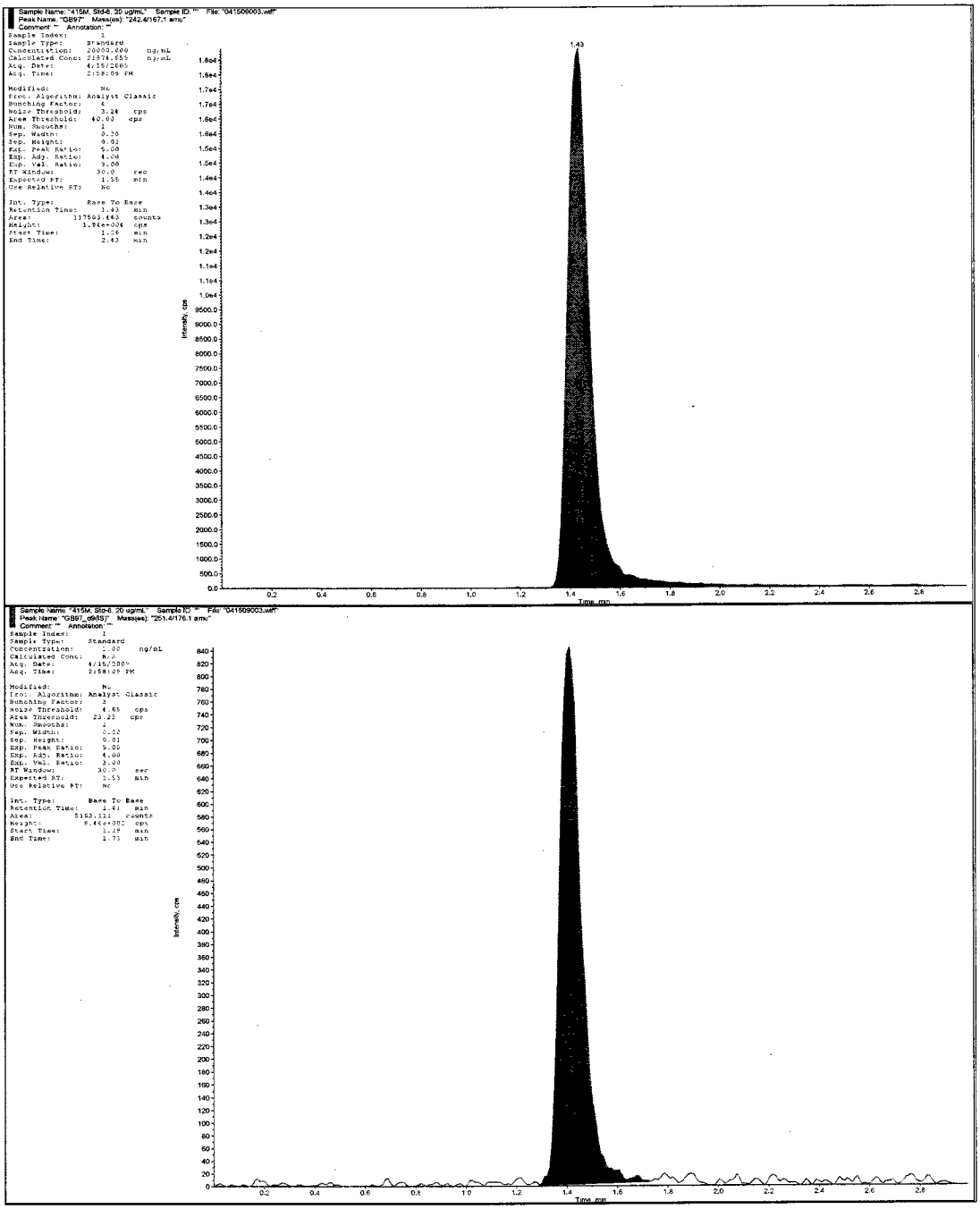


Figure 7: GB594-MPK-08-1-027 (upper) and GB594_d_9 (internal standard, lower)

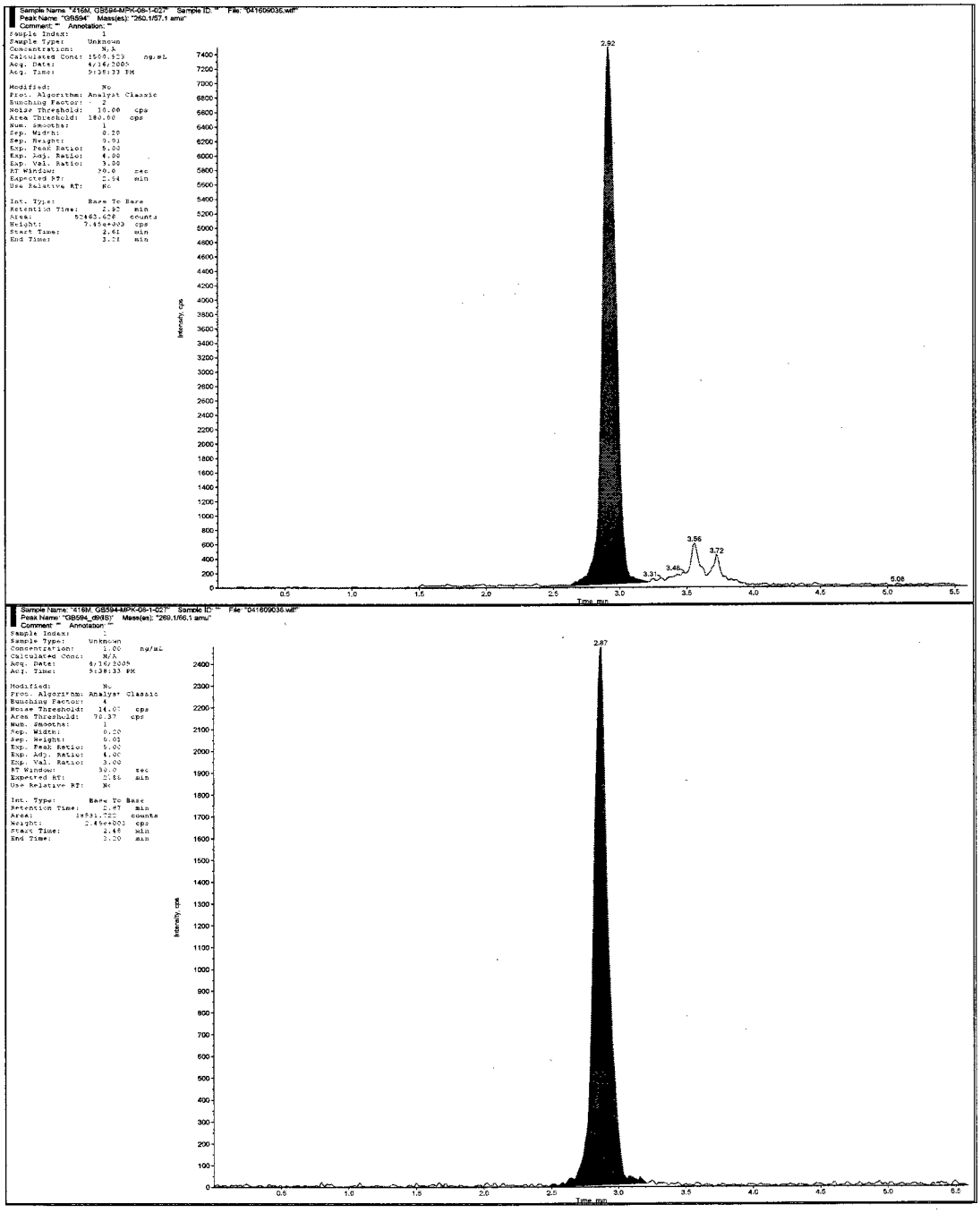


Figure 8: Typical Chromatograms of GB594 in a Mouse Plasma Standard Curve Sample (LLOQ 50 ng/mL) GB594 (upper) and GB594_d_9 (internal standard, lower)

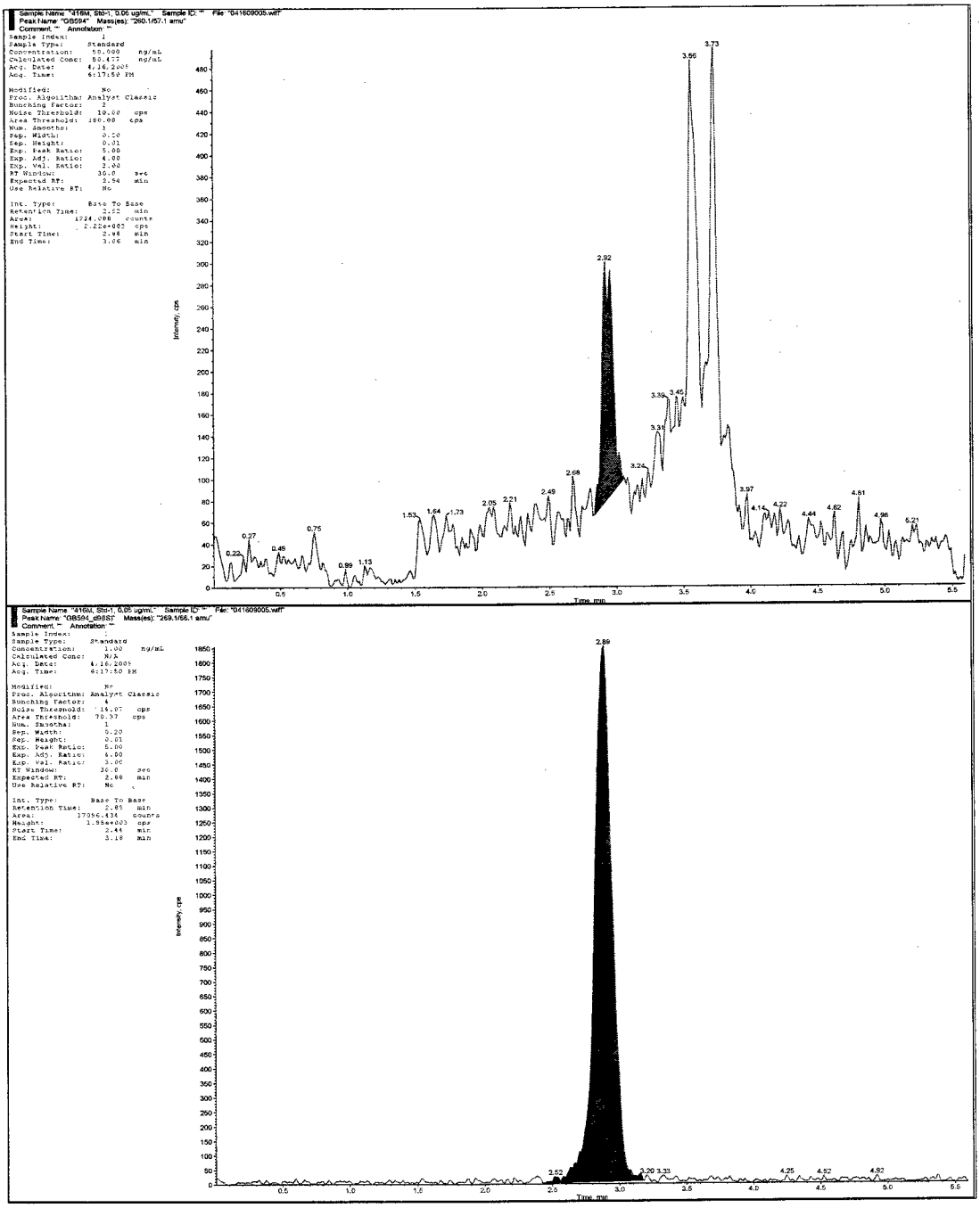


Figure 9: Typical Chromatograms of GB594 in a Mouse Plasma Standard Curve Sample (ULOQ 20 µg/mL) GB594 (upper) and GB594_d_9 (internal standard, lower)

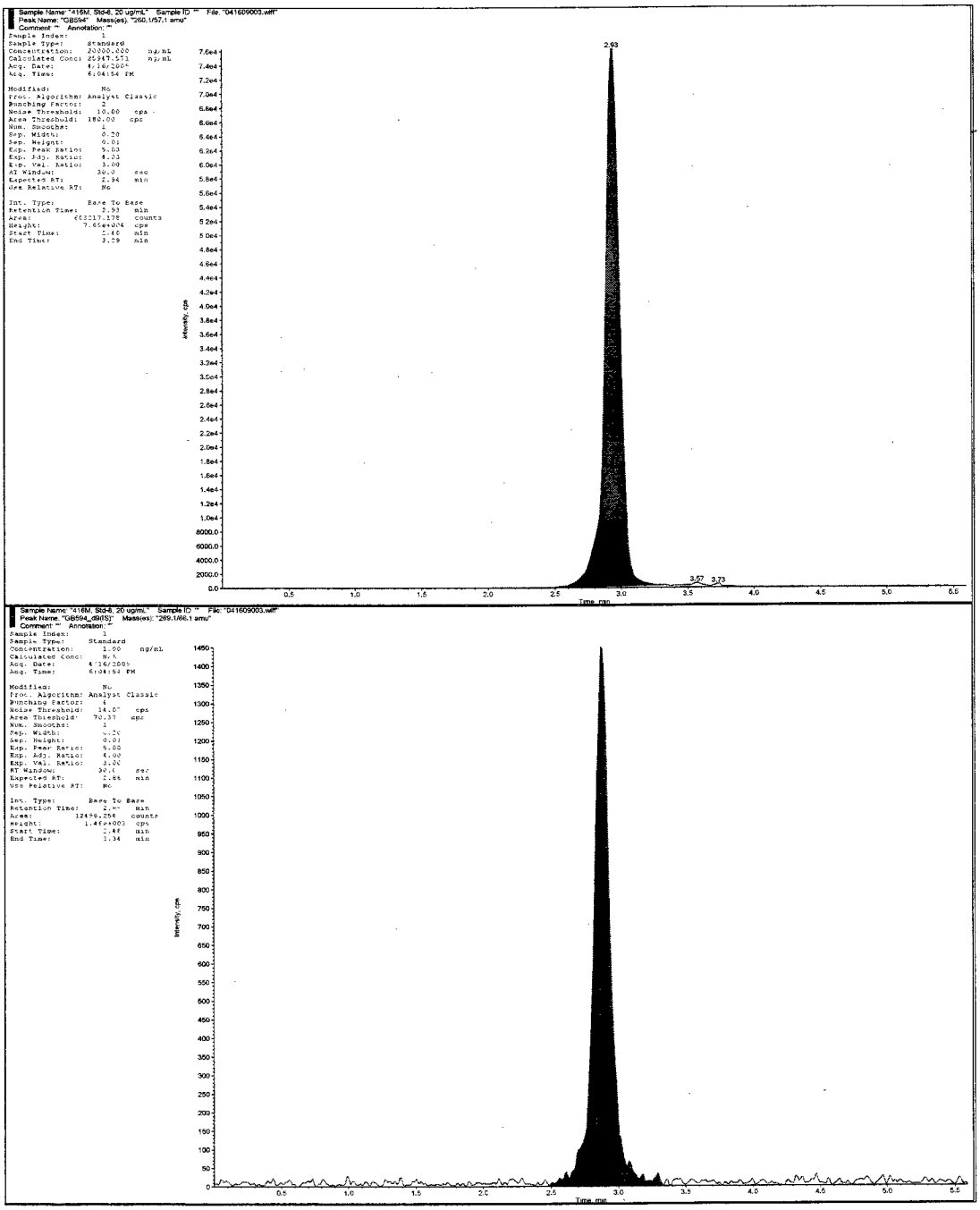


Figure 10: GB67B 5030, day1, 30 min (upper) and GB67B_d_9 (internal standard, lower)

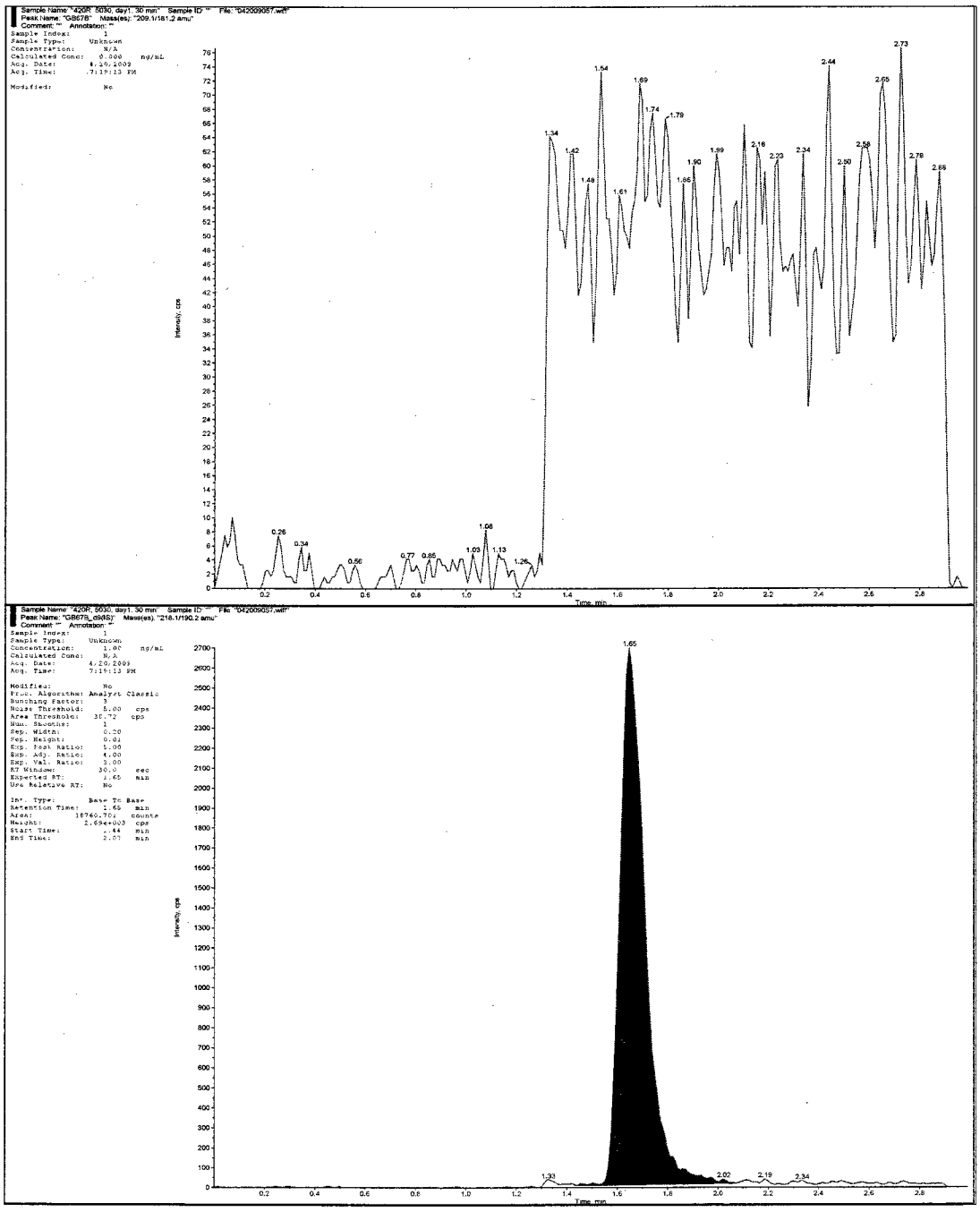


Figure 11: Typical Chromatograms of GB67B in a Rat Plasma Standard Curve Sample (LLOQ 50 ng/mL) GB67B (upper) and GB67B_d_9 (internal standard, lower)

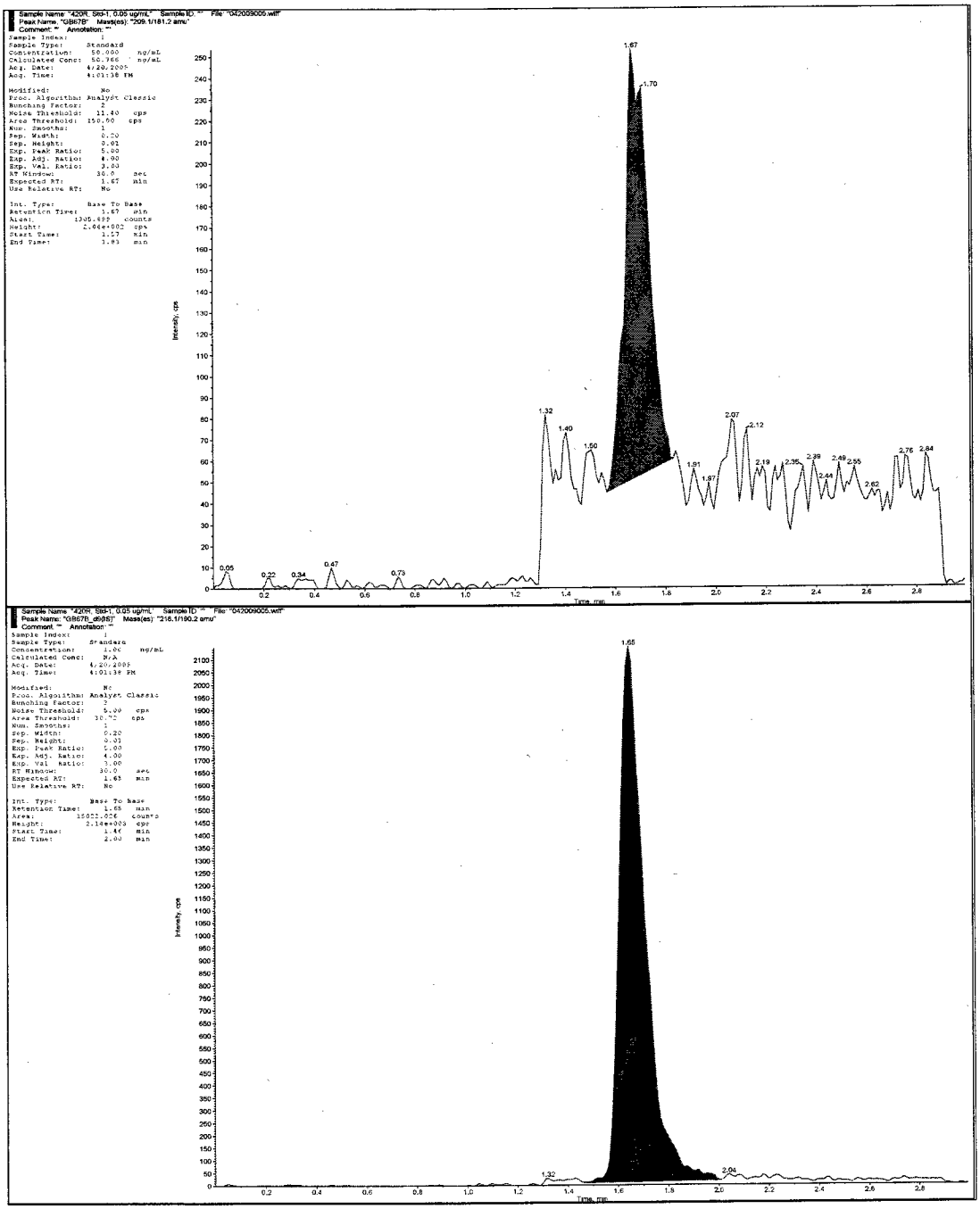
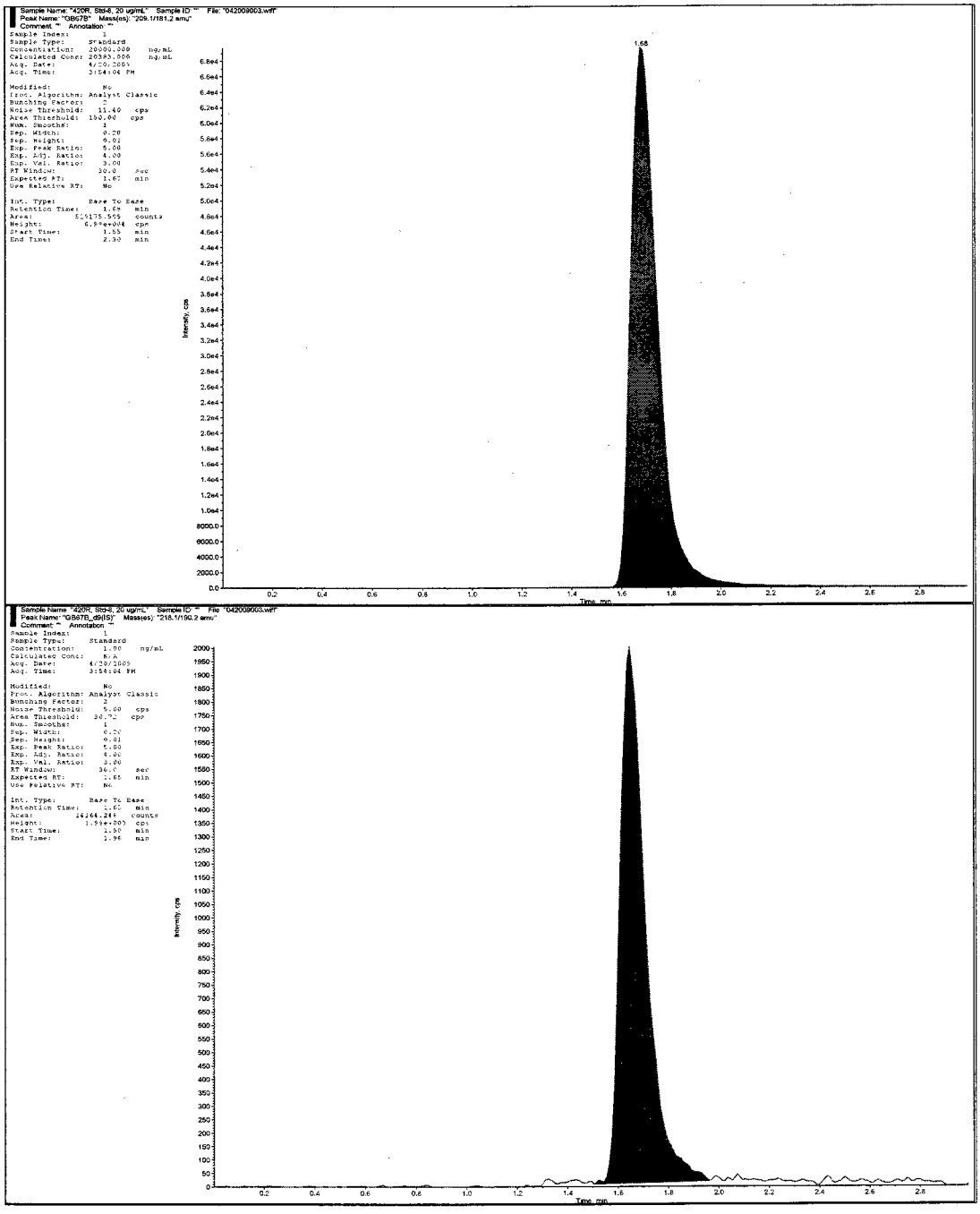


Figure 12: Typical Chromatograms of GB67B in a Rat Plasma Standard Curve Sample (ULOQ 20 µg/mL) GB67B (upper) and GB67B_d_9 (internal standard, lower)



Appendix IV—Protocol, Amendments and Deviations

CALVERT
LABORATORIES, INC.

Study Protocol

Title: A 7-Day Oral Toxicokinetic Study with GB67B in Rats

Calvert Study No.: 0440RE27.002

Sponsor Study No.: TL-GB67B-RTK-09-1

Testing Facility:
Calvert Laboratories, Inc.
Scott Technology Park
100 Discovery Drive
Olyphant, PA 18447

Study Sponsor:
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322

I. Table of Contents

II. Introduction

A. Title

A 7-Day Oral Toxicokinetic Study with GB67B in Rats

B. Objective

The purpose of this study is to evaluate the toxicity and toxicokinetics of GB67B when administered once daily, via oral gavage, for seven consecutive days to Sprague Dawley rats.

C. Regulatory Compliance

This is a non-regulated study. However, it will be run according to the Standard Operating Procedures (SOPs) of Calvert. There will be no formal involvement of the Quality Assurance Unit.

D. Calvert Study Number

0440RE27.002

E. Sponsor Study Number

TL-GB67B-RTK-09-1

F. Testing Facility

Calvert Laboratories, Inc. (Calvert)
Scott Technology Park
100 Discovery Drive
Olyphant, PA 18447

G. Sponsor

Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322

H. Study Director

Cesar V. Mujer, Ph.D.
Calvert Laboratories, Inc.
Scott Technology Park
100 Discovery Drive
Olyphant, PA 18447
Phone: (570) 585-2304
Fax: (570) 586-3450
E-mail: cesar.mujer@calvertlabs.com

I. Sponsor Representative

Randy Howard, Ph.D.
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322
Cell: (319) 541-7809
Email: rbhowar@emory.edu

J. Principal Investigator – Toxicokinetics and Dose Formulation Analysis

Rick Arrendale, Ph.D.
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322
Cell: (770) 337-6472
Email: rarrend@emory.edu

K. Key Study Dates

Proposed Experimental Start Date:	28 January 2009
Proposed First Day of Dosing:	5 February 2009
Proposed Necropsy:	12 February 2009
Proposed Experimental Completion Date:	12 February 2009

III. Materials and Methods

A. Test Article

1. Test Article

Identification:	GB67B
Lot/Batch No. :	To be documented in the study data.
Physical Description:	To be documented in the study data.
Storage Conditions:	Refrigerated (2-8°C) and protected from light

2. Vehicle

Identification	DMSO/45% Beta-cyclodextrin (20/80)
Lot/Batch No.:	To be documented in the study data.
Physical Description:	Semi-viscous solution
Storage Conditions:	Room temperature

3. Dose Preparation

The test article will be prepared according to Calvert SOPs on test article formulation. Dosing preparations will be stored at room temperature following preparation and utilized within 4 hours of completion of preparation. Each day prior to dosing, make a 5X stock solution in DMSO, then dilute stock with 4 parts room temperature 45% Beta-cyclodextrin while vortexing.

4. Formulated Test Article Analysis

On Day 1 and Day 7, 1-ml samples of each dosing solution including the control article, will be obtained from top, middle and bottom to determine the concentration, homogeneity, and/or stability of the test article in vehicle. These samples will be stored at approximately -70° C or lower. These samples will be returned to, and analytical evaluation will be done under the direction of:

Rick Arrendale, Ph.D.
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322
Phone: (770) 337-6472
Fax: (404) 727-3677
Email: rarrend@emory.edu

5. Reserve Archive Samples

A retention sample of the test article will not be maintained at Calvert.

6. Accountability and Disposition

Unused test article will be returned to the Sponsor or designee at the termination of this study or, if necessary, retained for use on related future studies. The Sponsor will be notified in advance of shipping and a transmittal letter will accompany the shipment. The material will be packed in a suitable container to maintain the conditions specified by the Sponsor during transit plus an adequate margin of safety to account for any possible transit delays. If returned to the Sponsor, unused material will be returned to:

Randy Howard, Ph.D.
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322
Cell: (319) 541-7809
Email: rbhowar@emory.edu

B. Test System (Animals and Animal Care)

1. Description

Species:	Rat
Stock:	Sprague-Dawley (Hsd: SD)
Total Number:	40 (20 males and 20 females)

Gender:	Male and female
Age Range:	7-8 weeks at start of dosing; records of dates of birth for animals used in this study will be retained in the Calvert archives.
Body Weight Range:	150-275 grams for the males and females at the outset (Day 1) of the study.
Animal Source:	Harlan
Experimental History:	Purpose-bred and experimentally naïve at the outset of the study.
Identification:	Ear tag and cage card.

2. *Rationale for Choice of Species and Number of Animals*

The rat is a standard rodent species used in toxicology studies based upon the substantial amounts of published historical data (1). The rat is a species of choice because there are previous pharmacology studies showing activity of the test article that have been conducted in the rats. Use of the rat will allow calculation of therapeutic index, using the previous rat efficacy results.

The total number of animals used in this study is considered to be the minimum number necessary to provide a preliminary assessment of the tolerability in rodents (2).

3. *Husbandry*

Housing:	Animals will be group-housed by sex upon receipt and individually housed upon assignment to study in compliance with National Research Council "Guide for the Care and Use of Laboratory Animals." The room in which the animals will be kept will be documented in the study records. No other species will be kept in the same room.

Lighting:	12 hours light/12 hours dark, except when room lights will be turned on/off during the light/dark cycle to accommodate study procedures.
Room Temperature:	18 to 26°C
Relative Humidity:	30-70%
Food:	All animals will have access to Harlan Teklad Rodent Diet (certified) or equivalent, *ad libitum*, unless otherwise specified. The lot number(s) and specifications of each lot used are archived at Calvert. No contaminants are known to be present in the certified diet at levels that would be expected to interfere with the results of this study. Analysis of the diet was limited to that performed by the manufacturer, records of which will be maintained in the Calvert archives.
Water:	Water will be available *ad libitum,* to each animal via an automatic watering device. The water is routinely analyzed for contaminants as per Calvert SOP's. No contaminants are known to be present in the water at levels that would be expected to interfere with the results of this study. Results of the water analysis will be maintained in the Calvert archives.
Acclimation:	Study animals will be acclimated to their housing for a minimum of five days prior to their first day of dosing.

4. Prestudy Health Screen and Selection Criteria

All animals received for this study will be assessed as to their general health by a member of the veterinary staff or other authorized personnel. During the acclimation period, each animal will be observed at least once daily for any abnormalities or for the development of infectious disease. Only animals that are determined to be suitable for use will be assigned to

this study. Any animals considered unacceptable for use in this study will be replaced with animals of similar age and weight from the same vendor.

5. Assignment to Study Groups

Animals will be assigned to study groups by a computerized randomization program (LABCAT In Life module version 8.0), developed by Innovative Program Associates, Inc. 303 Wall Street, Princeton, NJ 08540-1515) designed to achieve similar group mean body weights.

6. Humane Care of Animals

Treatment of animals will be in accordance with the study protocol and also in accordance with Calvert SOP's which adhere to the regulations outlined in the USDA Animal Welfare Act (9 CFR Parts 1, 2 and 3) and the conditions specified in the Guide for the Care and Use of Laboratory Animals (ILAR publication, 1996, National Academy Press). The Calvert Institutional Animal Care and Use Committee (IACUC) will approve the study protocol prior to finalization to insure compliance with acceptable standard animal welfare and humane care.

No alternative test systems exist which have been adequately validated to permit replacement of the use of live animals in this study. Every effort has been made to obtain the maximum amount of information while reducing to a minimum the number of animals required for this study. The assessment of pain and distress in study animals and the use or non-use of pain alleviating medications will be in accordance with Standard Operating Procedure VET-19, Criteria for Assessing Pain and Distress in Laboratory Animals. The study will be terminated in part or whole for humane reasons if unnecessary pain occurs. To the best of our knowledge, this study is not unnecessary or duplicative.

C. Test Article Administration

1. Group Assignments and Dose Levels

Group	Daily Dose Level (mg/kg/day)	Concentration (mg/ml)	Dose Volume* (ml/kg)	Number of Animals**	
				Male	Female
1. Control (Vehicle)	0	0	5	2	2
2. Low-Dose	30	6	5	2	2
3. Mid-Dose	90	18	5	2	2
4. High-Dose	180	36	5	2	2

*The test article will be administered once daily for 7 consecutive days by oral gavage.

**On Day 8, all surviving animals will be euthanized by CO_2 asphyxiation and necropsied.

Toxicokinetic Groups

Group	Daily Dose Level (mg/kg/day)	Concentration (mg/ml)	Dose Volume* (ml/kg)	Number of Animals**	
				Male	Female
5. Low dose	30	6	5	4	4
6. Mid dose	90	18	5	4	4
7. High Dose	180	36	5	4	4

*The test article will be administered once daily for 7 consecutive days by oral gavage.

**On Day 1 and Day 7, whole blood samples (~0.3 mL/sample) will be collected from 2 animals/sex/group in Groups 5-7 via retroorbital puncture at the specified timepoints after a single dose. Immediately following their final blood collection on Day 7, all animals will be euthanized by CO_2 asphyxiation and carcasses with be appropriately discarded with no necropsy.

2. Dosing

Route: Oral via gavage

Frequency: Once daily for a minimum of 7 consecutive days at the maximum dose volume of 5 ml/kg.

Procedure: Doses will be administered once daily. Each animal will receive a mg/kg dose based upon its most recent body weight.

All animals will be euthanized by CO_2 asphyxiation and necropsied on Day 8.

3. Justification for Route, Dose Levels and Dosing Schedule

The oral route was chosen as it is the intended route of administration in humans.

Dose levels were selected by the Sponsor. The data from this study will be utilized to establish toxicity of the test article as an oral formulation.

D. In-Life Observations and Measurements (Groups 1-4)

1. Mortality/Morbidity

Frequency:	Twice daily (a.m. and p.m.) on Days 1-7 and once prior to sacrifice on Day 8. Each animal observed for evidence of death or impending death (as per Calvert SOP VET-14).

2. Clinical Observations

Frequency:	Prior to dose administration on Day 1, one hour post-dose, and as necessary. Once prior to scheduled sacrifice on Day 8.

3. Body Weight

Frequency:	At the time of randomization/selection and prior to dose administration on Days 1, 4 and 7. A fasted body weight will be recorded prior to scheduled sacrifice on Day 8.

4. Food Consumption

Frequency	Full feeder weights and/or feeder weigh backs will be recorded on Day 1 and Day 7.

E. Clinical Pathology Evaluation (Groups 1-4)

1. Sample Collection

Blood samples for evaluation of hematology, coagulation and serum chemistry parameters will be collected from all surviving animals prior to terminal sacrifice on Day 8. Animals will be anesthetized by CO_2 inhalation

prior to blood collection. Immediately following exsanguination by cardiocentesis for terminal blood collection, rats will be returned to the CO_2 chamber to ensure euthanasia. Animals will be fasted overnight (approximately 12-24 hours) prior to blood collection for clinical chemistry evaluation.

2. *Collection Procedures, Processing and Analysis*

a) Hematology

Method of Collection: Cardiocentesis

Anticoagulant: EDTA

Parameters Analyzed:

Hematology Parameters	
Red Blood Cell Count (RBC) and Morphology	Platelet count (PLT)
White Blood Cell Count (WBC)*	Hematocrit (HCT)
Mean Corpuscular Hemoglobin (MCH)	Hemoglobin (HGB)
Mean Corpuscular Hemoglobin Concentration (MCHC)	Reticulocyte Count (Retic)
Mean Corpuscular Volume (MCV)	

*Total and differential white blood cell counts, including neutrophils, monocytes, basophils, eosinophils, lymphocytes and large unstained cells

b) Coagulation

Method of Collection: Cardiocentesis

Anticoagulant: Sodium Citrate

Parameters Analyzed:

Coagulation Parameters	
Activated Partial Thromboplastin Time (APTT)	Prothrombin Time (PT)

c) Serum Clinical Chemistry

Method of Collection: Cardiocentesis

Anticoagulant: None

Parameters Analyzed:

Clinical Chemistry Parameters	
Alanine Aminotransferase (ALT)	Globulin (calculated)(GLOB)
Albumin (ALB)	Glucose (GLU)
Albumin/Globulin ratio (calculated)(A/G)	Phosphorus (PHOS)
Alkaline Phosphatase (ALP)	Potassium (K)
Aspartate Aminotransferase (AST)	Sodium (NA)
Calcium (CA)	Total Bilirubin (T-BIL)
Chloride (CL)	Total Protein (TP)
Cholesterol (CHOL)	Triglycerides (TRIG)
Creatinine (CREAT)	Urea Nitrogen (BUN)

F. Terminal Procedures and Anatomic Pathology (Groups 1-4)

1. Termination

a) Scheduled Sacrifice

All surviving animals will be euthanized by CO_2 asphyxiation on Day 8 and necropsied.

b) Non-Scheduled Sacrifice

Any animal determined to be moribund during the study will be euthanized by CO_2 asphyxiation and necropsied. A final body weight (non-fasted) will be recorded for such animals.

c) Final Body Weight

A fasted terminal body weight will be recorded prior to sacrifice on Day 8. This body weight will be used to calculate organ-to-body weight ratios.

2. Necropsy

A gross necropsy will be performed by Calvert personnel on all animals that are sacrificed or found dead during the study. The necropsy will include examination of:

- the external body surface
- all orifices
- the cranial, thoracic and abdominal cavities and their contents.

All abnormalities will be described completely and recorded. If a necropsy cannot be performed immediately on any animal found dead, it will be refrigerated until necropsy can be performed. No tissues will be collected and carcasses will be appropriately discarded.

3. *Organ Weights*

At scheduled sacrifice on Day 8, the following organs (when present) will be weighed before fixation, after dissection of excess fat and other excess tissues. Organ weights will not be recorded for animals found dead or sacrificed moribund. Paired organs will be weighed together unless gross abnormalities are present, in which case they will be weighed separately.

Organs Weighed		
Adrenals	Brain	Heart
Kidneys	Liver	Lungs
Ovaries	Pituitary	Spleen
Testes	Thyroids/parathyroids	

Organ-to-body weight and organ-to-brain weight ratios will be calculated using the final body weight obtained prior to necropsy.

G. Toxicokinetic In-Life Observations and Measurements (Groups 5-7)

1. *Mortality*

Frequency: Twice daily for 7 consecutive days (a.m. and p.m.)

Each animal observed for evidence of death or impending death (as per Calvert SOP VET-14).

2. *Clinical Observations*

Frequency: Observations will be recorded as needed, but not reported.

3. *Body Weight*

Frequency: At the time of randomization/selection and prior to dose administration on Days 1, 4 and 7.

4. Toxicokinetics

a) Blood Sampling

On Day 1 and Day 7, whole blood samples (~0.3 mL/sample) will be collected from 2 animals/sex/group in Groups 5-7 via retroorbital puncture at the following timepoints after a single dose:

0 hour (predose)	2 hours post-dose
30 minutes post-dose	4 hours post-dose
1 hour post-dose	8 hours post-dose

Each animal will be bled no more than three times on each TK day. Animals will not be fasted prior to collection. Animals will be anesthetized by CO_2 inhalation and blood samples will be collected into blood collection tubes containing potassium EDTA. Blood samples will be centrifuged at approximately 3000 rpm for approximately 10 minutes to separate the plasma. The resultant plasma will be dispensed into appropriately labeled tubes and stored frozen at approximately -70°C.

Samples will be shipped on dry ice with prior notification to the Sponsor at the following address:

Randy Howard, Ph.D.
Emory Institute for Drug Discovery
Emory University
1515 Dickey Drive
Atlanta, GA 30322
Cell: (319) 541-7809
Email: rbhowar@emory.edu

The final bioanalytical report will be provided to the Study Director for inclusion in the final report.

5. Euthanasia

Each animal in Groups 5-7 will be euthanized by CO_2 asphyxiation following their final blood collection. Necropsy will not be performed and the carcasses will be appropriately discarded.

IV. Records and Reports

A. Data Collection and Analysis

In-Life data (clinical observations, body weights, feeder weights, dose administration) will be collected using LABCAT In-Life module version 8.0 or on paper when necessary. Necropsy data will be collected on paper. Any other data not collected on-line will be manually tabulated for inclusion in the report.

In-Life data will be tabulated and/or statistically evaluated using the LABCAT In-Life module version 8.0. Necropsy data will be hand-tabulated or tabulated and/or statistically evaluated using the LABCAT Organ Weights/Necropsy module version 3.28. All LABCAT modules were developed by Innovative Program Associates, Inc. (303 Wall Street, Princeton, NJ 08540-1515).

Statistical analysis will be performed on In-Life data when 3 or more animals are present in 2 or more dose groups. Statistical analysis will not be performed if N<3 animals per group. For In-Life parameters, the homogeneity of the data will be determined by Bartlett's Test. If the data is homogeneous, a one-way analysis of variance will be performed to assess statistical significance. If statistically significant differences between the means are found, Dunnett's test will be used to determine the degree of significance from the control means ($p < 0.05$ and $p< 0.01$). If the data is non-homogeneous, the Kruskal-Wallis non-parametric analysis will be performed to assess statistical significance. If statistically significant differences between the means are found ($p<0.05$, $p<0.01$), the Mann-Whitney U-Test will be used to determine the degree of significance from the control means ($p < 0.05$ and $p< 0.01$). If only 2 dose groups are present for evaluation, the Mann-Whitney U-test will be used to assess statistical significance between the 2 groups.

B. Storage of Records

Test article preparation (or test article information), test article tracking, in-life data, necropsy data, protocol, protocol amendments (if applicable), draft report(s) that have been submitted to a regulatory agency, and the original final report generated as a result of this study will be archived at Calvert, 105 Edella Road, Suite 100, Clarks Summit, PA 18411. After 2 years, the Sponsor will be contacted to determine final disposition of all study materials.

All analytical data will be archived in the Emory Institute for Drug Discovery, Emory University, 1515 Dickey Drive, Atlanta, GA 30322.

Six months following the submission of the audited draft report, if there are no client comments generated by the Sponsor and/or Study Monitor, the Sponsor/Study Monitor will be notified and the report will be finalized and archived according to the terms stated in the protocol.

V. Miscellaneous

A. Confidentiality Statement

The information contained herein is for the personal use of the intended recipient(s).

B. References

1. Speid, L.H., Lumley, C. E., and Walker, S. R. (1990). Harmonization of Guidelines for Toxicity Testing of Pharmaceuticals by 1992. *Regulatory Toxicology and Pharmacology*. 12: 179-211.

2. Gad, Shayne C. (2002) *Drug Safety Evaluation*. John Wiley and Sons, Inc., New York, pp. 130-175.

VI. Protocol Approval Signatures

Cesar V. Mujer, Ph.D.
Study Director
Calvert Laboratories, Inc.

26 Jan 2009
Date

Scientific Management
Calvert Laboratories, Inc.

26 Jan 2009
Date

IACUC
Calvert Laboratories, Inc.

26 JAN 2009
Date

Randy Howard, Ph.D.
Sponsor Representative
Emory University

1/22/09
Date

CALVERT
LABORATORIES, INC.

PROTOCOL AMENDMENTS

STUDY NUMBER: 0440RE27.002

STUDY TITLE: A 7-Day Oral Toxicokinetic Study with GB67B in Rats

AMENDMENT NUMBER: 1

EFFECTIVE DATE: 6 February 2009

ORIGINAL PROTOCOL STATEMENT:

III. Materials and Methods

D. In-Life Observations and Measurements (Groups 1-4)

2. Clinical Observations

Frequency: Prior to dose administration on Day 1, one hour post-dose, and as necessary. Once prior to scheduled sacrifice on Day 8.

AMENDED PROTOCOL STATEMENT:

III. Materials and Methods

D. In-Life Observations and Measurements (Groups 1-4)

2. Clinical Observations

Frequency: Prior to dose administration on Days 1-7, one hour post-dose, and as necessary. Once prior to scheduled sacrifice on Day 8.

REASON FOR CHANGE:

Clarification that clinical observations will be collected prior to dose administration on Days 1-7.

ORIGINAL PROTOCOL STATEMENT:

III. Materials and Methods

F. Terminal Procedures and Anatomic Pathology (Groups 1-4)

3. Organ Weights

At scheduled sacrifice on Day 8, the following organs (when present) will be weighed before fixation, after dissection of excess fat and other excess tissues.

AMENDED PROTOCOL STATEMENT:

III. Materials and Methods

F. Terminal Procedures and Anatomic Pathology (Groups 1-4)

3. Organ Weights

At scheduled sacrifice on Day 8, the following organs (when present) will be weighed after dissection of excess fat and other excess tissues.

REASON FOR CHANGE:

Clarification that organs will not be put in fixative after weighing.

SIGNATURES:

Cesar V. Mujer, Ph.D.
Study Director
Calvert Laboratories, Inc.

6 Feb 2009
Date

Scientific Management
Calvert Laboratories, Inc.

5 Feb 2009
Date

IACUC
Calvert Laboratories, Inc.

5 FEB. 2009
Date

Randy Howard, Ph.D.
Sponsor Representative
Emory University

2/4/09
Date

Protocol Deviations

There were no Protocol Deviations noted during the conduct of the study.