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FYI-07-01596

Re: For Your Information Submission:

The enclosed information is submitted on behalf of Dow Corning Corporation, Midland, Michigan, 48686-0994, on a For-Your-Information (FYI) basis as a follow-up to submissions made concerning decamethylcyclopentasiloxane (DMCPS), which chemical substance was the subject of a health and safety data rule issued under Section 8(d) of the Toxic Substances Control Act (TSCA) and with an effective date of June 14, 1993 (sunset date June 30, 1998), as codified at 40 CFR 716 (Health and Safety Data Reporting). The information presented in this submission was generated as part of our Siloxane Research Program. This program was the subject of a memorandum of understanding, dated April 9, 1996, between Dow Corning and EPA.

Listed Chemical Substance:

541-02-6 Decamethylcyclopentasiloxane (DMCPS, D_5)

Final Study Report:

Disposition of ^{14}C-Decamethylcyclopentasiloxane (D_5), in Fischer 344 Rats when Delivered in Various Carriers Following the Administration of a Single Oral Dose

Dow Corning Corporation
2003-I0000-52391
December 9, 2003

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Dow Corning Corporation
Midland, Michigan 48686-0994
Phone: (989) 496-4000
www.dowcorning.com

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES (HES)
TECHNICAL REPORT

Report No.:	2003-I0000-52391
Title:	Disposition of ^{14}C-Decamethylcyclopentasiloxane (D_5), in Fischer 344 Rats when Delivered in Various Carriers Following the Administration of a Single Oral Dose
Study No.:	9550
Test Article:	^{14}C-Decamethylcyclopentasiloxane (^{14}C- D_5)
Study Director:	Marina L. Jovanovic, M.S. Associate Toxicology Specialist
Sponsor:	Dow Corning Corporation
HES Management:	Steven D. Crofoot, M.S. Team Leader, Toxicology Health and Environmental Sciences
Testing Facility:	Dow Corning Corporation Health and Environmental Sciences 2200 W. Salzburg Road Midland, MI 48686-0994
Study Completion Date:	December 9, 2003
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ABSTRACT

The disposition of ^{14}C labeled decamethylcyclopentasiloxane (^{14}C-D_5) was evaluated in male and female Fischer 344 rats following a single, oral administration of 1000 mg of ^{14}C-D_5 in corn oil/kg of body weight. Additional female rats were dosed with neat ^{14}C-D_5 and ^{14}C-D_5 in simethicone fluid to evaluate any effect that the carrier may have on the absorption and disposition of D_5 following oral administration. Animals (N=4/sex and N=4 females/carrier) were housed in glass metabolism cages for collection of urine, feces and expired volatiles. At 168 hr post-dose, animals were sacrificed and selected tissues and remaining carcasses were collected. All samples were analyzed for radioactivity content. In addition to radioactivity, feces and expired volatiles were analyzed for parent D_5 concentration. A separate group of jugular vein cannulated animals (N=6/sex and N=6 females/carrier) were used to determine radioactivity and parent D_5 concentration in blood at 15 min, 1, 6, 12, 24, 48, 72, 96, 120, 144 and 168 hr post dosing. Whole-body autoradiography (WBA) was used for qualitative *in vivo* assessment of tissue distribution of radioactivity in male and female rats following a single oral administration of ^{14}C-D_5 in corn oil. Rats in the WBA groups were sacrificed at 3, 12, 24, 48, 96 and 168 hr post-dose.

The majority of administered dose, regardless of sex or carrier, was excreted in feces. The absorption of D_5 based on radioactivity recovered in urine, expired volatiles, expired CO_2, tissues and carcass in males and females dosed with ^{14}C-D_5 in corn oil was 21.82 and 19.62% of administered dose, respectively. Both sexes showed similar patterns of disposition (Urine: 4.70 and 4.37%; Expired volatiles: 13.36 and 10.37%; Expired CO_2: 0.92 and 0.97%; Tissues: 0.38 and 0.49%; Carcass: 2.46 and 3.43% for males and females, respectively). Qualitative assessment of tissue distribution (WBA) showed that the radioactivity was systemically available and distributed to major organs such as bone marrow, liver, kidney and fat. Statistical analysis of blood curves showed significant difference between radioactivity and parent area under the curves (AUC) for both males and females when ^{14}C-D_5 was administered in corn oil indicating presence of metabolites in the blood ($AUC_{metabolites} = AUC_{radioactivity} - AUC_{parent}$).

Absorption of D_5 was also compared between various carriers. Data obtained from the blood curve analysis showed that the test article was most readily absorbed when delivered in corn oil and least available for absorption when carried in the simethicone fluid. Both radioactivity and parent blood AUCs were significantly different among the three carriers with the largest AUC obtained with ^{14}C-D_5 in corn oil ($AUC_{radioactivity}$ =1035.47 µg equivalent D_5*hr/g and AUC_{parent} = 879.50 µg D_5*hr/g) when compared with neat ^{14}C-D_5 ($AUC_{radioactivity}$ = 270.46 µg equivalent D_5*hr/g, AUC_{parent} = 188.00

μg D_5*hr/g) and ^{14}C-D_5 in simethicone fluid ($AUC_{radioactivity}$ = 85.76 μg equivalent D_5*hr/g, AUC_{parent} = 54.70 μg D_5*hr/g).

In contrast, the mass balance data showed that 19.62%, 25.81% and 9.94% of administered ^{14}C-D_5 was absorbed when delivered in corn oil, in simethicone fluid or as neat ^{14}C-D_5, respectively. The majority of the absorbed dose (radioactivity found in the expired volatiles, CO_2, urine, tissues and carcass) was found in expired volatile traps (charcoal tubes) particularly when the dose was delivered in simethicone fluid (e.g. ^{14}C-D_5 trapped in charcoal tubes accounted for 93.13% of the absorbed dose in simethicone dosed animals). In addition, the entire radioactivity in the expired volatiles was attributed to parent D_5. The discrepancy between absorption assessed by blood curve analysis and mass balance data analysis may be caused by evaporation of ^{14}C-D_5 from the excreted fecal matter that remained in the body of the cage. Animals dosed with corn oil and especially simethicone had a higher occurrence of loose fecal matter that adhered to the side of the cages. Results of a follow-up experiment (HES Study No. 9748) demonstrated that the evaporation of ^{14}C-D_5 from the fecal matter, that could not be removed from the body of the cage throughout the experiment, could significantly contribute to the radioactivity trapped in the charcoal tubes giving false high values for expired volatiles and absorption of D_5.

HPLC profile evaluation of urine and feces showed that entire radioactivity in the urine consisted of polar metabolites, whereas in the feces the majority was parent D_5 with a trace non-polar metabolite.

In summary, approximately 20% of ^{14}C-D_5 delivered in corn oil was absorbed after single oral administration in Fischer 344 rats based on radioactivity found in urine, expired volatiles, CO_2, carcass and tissues. In addition, this study indicated that the oral absorption of D_5 could be influenced by the carrier used to deliver ^{14}C-D_5.

GLP COMPLIANCE STATEMENT

The study was conducted in compliance with Environmental Protection Agency (EPA) Toxic Substances Control Act (TSCA) Good Laboratory Practice Standards 40 CFR part 792, with the exception of the use of software SAS®, v. 8.2 that was not validated to the GLP standards. Deviations to the Protocol are listed in the Experimental Design section of the main report and Appendix A. There were no circumstances that would negatively impact or bias the results of this study.

The Dow Corning Health and Environmental Sciences (HES) Quality Assurance Unit monitored the study in accordance with Dow Corning HES Standard Operating Procedures.

Marina Jovanovic 12/09/2003

Marina L. Jovanovic, M.S. Date
Associate Toxicology Specialist
Study Director

Steven D. Crofoot 12/4/2003

Steven D. Crofoot, M.S. Date
Team Leader, Toxicology
Health and Environmental Sciences

QUALITY ASSURANCE STATEMENT

Title: Disposition of ^{14}C-Decamethylcyclopentasiloxane (D_5), in Fischer 344 Rats when Delivered in Various Carriers Following the Administration of a Single, Oral Dose

Study Number: 9550

This study has been audited by the Dow Corning Corporation Health and Environmental Sciences Quality Assurance Unit according to approved Standard Operating Procedures to assure that the raw data are accurately reflected within this final report. The following are the inspection dates and the dates inspection findings were reported.

Dates of Inspection	Phase Inspected	Findings Reported to Study Director	Findings Reported to Management
06 Jan 01	Draft Protocol Review	18 Jan 01	19 Jan 01
01 Feb 01	Dosing	06 Feb 01	14 Feb 01
01 May 01	Whole Body Autoradiography (Sectioning)	15 May 01	22 May 01
30 May 01	Part 2 Stability and Homogeneity of ^{14}C-D_5 in Simethicone	30 May 01	02 Jun 01
30 Jan - 07, 12 Feb 03	Draft Final Report and Associated Raw Data (Binder 1)	12 Feb 03	03 Mar 03
06-07 Feb 03	Autoradiography portion of the Draft Final Report and Associated Raw Data	07 Feb 03	06 Mar 03
5-10, 19-20 Feb 03	Appendix B of the Draft Final Report with supporting Raw Data	20 Feb 03	03 Mar 03
24 Feb – 05 Mar 03	Individual Scientist Report and Associated Raw Data	10 Apr 03	29 Apr 03
18 Feb – 05 Mar 03	Draft Final Report and Associated Raw Data (Volume 2, Part 2 and Statistical Analyses)	05 Mar 03	08 Apr 03
29 Oct 03	Wet Specimen Verification	29 Oct 03	31 Oct 03

Joyce L. Henry
Manager, Quality Assurance
Dow Corning Corporation
Health & Environmental Sciences

01 Dec 03
Date

APPROVAL SIGNATURES

This report consists of pages 1 through 267 including Tables 1 through 17, Figures 1 through 18 and Appendices A through D.

Marina Jovanovic 12/09/2003

Marina L. Jovanovic, M.S. Date
Associate Toxicology Specialist
Study Director

Steven D. Crofoot 12/4/2003

Steven D. Crofoot, M.S. Date
Team Leader, Toxicology
Health and Environmental Sciences

STUDY INFORMATION

Study Initiation Date:	01/22/2001
Experimental Start Date:	02/01/2001
Experimental Termination Date:	05/16/2002
Study Completion Date:	12/09/2003
Study Director:	Marina L. Jovanovic, M.S. Associate Toxicology Specialist
Sponsor:	Dow Corning Corporation 2200 W. Salzburg Rd. Midland, MI 48686-0994
Management:	Steven D. Crofoot Team Leader, Toxicology Health and Environmental Sciences Roy A. Campbell Team Leader, Analytical Chemistry Health and Environmental Sciences
Key Study Personnel:	James W. Crissman, D.V.M., Ph.D.,D.A.C.V.P. Brian Marinik, Study coordinator Debra A. McNett, Bioanalytical support Jane M. Regan, H.T./M.L.T. (A.S.C.P.) Trevor Newhook, Biostatistician Joseph M. Tobin, Supervisor

OBJECTIVE

This study had two objectives: 1) to determine the absorption and excretory pathways of the test article, ^{14}C-decamethylcyclopentasiloxane (^{14}C-D_5) following oral administration in corn oil, and 2) to evaluate any effect that the carrier may have on the absorption and disposition of D_5 following oral administration.

INTRODUCTION

Oral ingestion in humans may be a route of exposure to decamethylcyclopentasiloxane (D_5). Oral ingestion may also represent a potential route of exposure in the animal inhalation studies. It is possible that rats, when grooming themselves, may intake some of the material that was deposited on the pelt during the inhalation exposure. This study was conducted to provide absorption, distribution, metabolism and elimination (ADME) data that would be useful in understanding this route of exposure. Oral gavage is a common and an accepted method of administration of test chemicals in pharmacokinetic and metabolism studies.

The experimental design of this study followed test guidelines and Tier 1 data requirements for the health effects testing of pesticides and toxic substances issued in August 1998 by the United States EPA. In the first part, animals were dosed with ^{14}C-D_5 suspended in corn oil (CO). In the second part of this study ^{14}C-D_5 was orally administered as neat material, and also delivered in the carrier known as "simethicone fluid" (SF). Corn oil is a commonly used carrier for hydrophobic materials that are administered by oral gavage. The second carrier selected for D_5 delivery is similar to the simethicone fluid that is currently used in commercially available antacid/antiflatulent products that may contain small amounts of D_5.

In essence, three experimental approaches were used to provide Absorption, Distribution, Metabolism and Elimination (ADME) data:
1) Rats were housed in glass metabolism cages for quantitative assessment of D_5 excretion and absorption after oral administration; 2) A group of jugular vein cannulated rats were used to obtain estimates of blood concentration and basic pharmacokinetic parameters (e.g. area under the curve, AUC and half-life) and 3) Whole-body autoradiography (WBA) was used for qualitative *in vivo* assessment of tissue distribution of radiolabeled D_5 and its potential metabolites, and for tracking the transient time of radioactivity through the gastrointestinal tract.

TEST SYSTEM

A. Species: *Rattus norvegicus*

B. Strain: CDF® (Fischer 344)/CrlBR

C. Source: The Charles River Breeding Laboratories, Inc.
(Supplier location is documented in the study records)

D. Number of groups: 18

E. Number of Animals:

Part 1 (D_5 in Corn Oil):

Mass balance (MB) groups:	Group 1 (CO controls):	2 females
	Group 2 (CO controls):	2 males
	Group 3 (CO):	4 females
	Group 4 (CO):	4 males
Whole body autoradiography (WBA):	Group 5 (CO):	6 females
	Group 6 (CO):	6 males
Blood kinetics (BK):	Group 7 (CO controls):	2 females (C)
	Group 8 (CO controls):	2 males (C)
	Group 9 (CO):	6 females (C)
	Group 10 (CO):	6 males (C)

Part 2 (D_5 neat and in simethicone fluid):

Mass balance (MB) groups:	Group 11 (Neat controls):	2 females
	Group 12 (SF controls):	2 females
	Group 13 (Neat):	4 females
	Group 14 (SF):	4 females
Blood kinetics (BK):	Group 15 (Neat controls):	2 females (C)
	Group 16 (SF controls):	2 females (C)

Group 17 (Neat): 6 females (C)
Group 18 (SF): 6 females (C)

C = jugular cannulated rats CO = Corn Oil SF = Simethicone Fluid

F. Total Number: Non-cannulated (NC): 36 (24 females and 12 males)
Cannulated (C): 32 (24 females and 8 males)

G. Special Consideration: In Part 1, rats were randomized and assigned to groups 1, 2, 3, 4, 5 and 6.
In Part 2 rats were randomized and assigned to groups 11, 12, 13 and 14.

In Parts 1 and 2, 32 animals were jugular vein cannulated by the supplier prior to arrival at the testing facility. Rats with patent cannulae were randomized and assigned to the groups 7, 8, 9, 10 in Part 1, and to groups 15, 16, 17 and 18 in Part 2.

H. Body Weight Range: Females: 133-156 g at start of in-life
Males: 179-226 g at start of in-life

I. Approximate Age: 9-10 weeks at start of in-life

J. Quarantine: 1 day for cannulated rats
7 days for non-cannulated rats

K. Identification Method:

Upon receipt in the Toxicology Department, each animal received a Q number. While in quarantine, the date received and release number for the shipment of animals was included on the cage tags. At the end of the quarantine period non-cannulated and cannulated rats were weighed, randomized and uniquely identified by a metal ear-tag displaying the animal number as documented in the study records. Cannulated rats were also checked for cannula patency after they were released from quarantine, and then randomly assigned to control and exposure groups. Individual cage tags (study number, animal number, group number, dose level, species/strain, sex, and study director) were placed on the outside of each cage. Cannulated

rats (Part 1: rats No. Q0041 and Q0037) and non-cannulated rat No.Q0004 in Part 2 were uniquely identified only by individual cage tags (see Deviations).

L. Method of Euthanasia:

1. **Scheduled animal termination**

   Immediately prior to euthanasia, animals in Mass Balance (MB) groups were placed in the pre-weighed anesthesia chambers primed with methoxyflurane and weighed. Inadvertently, the body weight of animal No. C9163 was not taken at the termination time point (see Deviations). All animals in the MB groups were euthanized by exsanguination *via* cardiac puncture under methoxyflurane anesthesia. Animals in the WBA groups (Part 1) were euthanized by CO_2 asphyxiation.

   Cannulated rats were euthanized by CO_2 asphyxiation after last blood collection. If the last blood collection *via* the jugular cannula was not successful, blood was collected by an open thoracic cardiac puncture under methoxyflurane anesthesia. All rats were weighed prior to euthanasia with the exception of rats in the control groups in Part 1 whose weights were taken after they have been euthanized.

2. **Unscheduled death and termination**

   Three female cannulated rats in the blood kinetics groups died during the conduct of the Part 1. Rat No. C9191 died during the blood collection. Rats No. C9186 and No. C9187 showed clinical signs that could be associated with the jugular cannula surgery and were found dead prior to a final blood collection (168hr). In Part 2, two female cannulated rats died: rat No. C9214 died in the process of obtaining blood, and rat No. C9213 died from unknown causes when it escaped from the cage. Appropriate records are maintained in the study files to allow tracking of the animal fate.

JUSTIFICATION FOR SELECTION OF THE TEST SYSTEM

This species and strain of animal is recognized as appropriate for toxicity studies. Fischer 344 female and male rats have previously been used in pharmacokinetic and metabolism studies of various silicone materials, and data obtained in this study can be used as historical data. The use of both sexes in the Part 1 enabled detection any potential gender-related differences in absorption of D_5 from GI tract. The number of animals used in the mass balance groups was selected to provide statistical power (N=4). Based on previous work with D_4 (HES Study No. 8546), the minimum number of time points were chosen for the WBA to allow visual assessment of the *in vivo*

distribution pattern of radioactivity, as well as to track the transient time of radioactivity in the gastrointestinal tract. Blood collection time points in the Blood Kinetics group were selected based on previous work (HES Study No. 8546). In Part 2, only female rats were used to evaluate the effect that a carrier may have on the absorption and disposition of D_5 following oral administration.

METHOD OF RANDOMIZATION

Upon release from quarantine, non-cannulated rats in both parts of the study were weighed, and then randomized by weight stratification into test groups using a table of random numbers generated by MicroSoft® Excel version 9.0 (Table 1). Cannulated rats were checked for cannula patency prior to the randomization. In Part 1, all the cannulae were patent, while in Part 2, three rats were excluded prior to the randomization process due to the cannula not being patent. Rats with patent cannulae that were excluded in a weight stratified randomization process (one female, No. Q0041 and two males, No. Q0033 and Q0037, in Part 1, and one female rat No. Q0034 in Part 2 were treated as extra rats for substitution. This was considered necessary due to difficulties known to occur when jugular vein cannulated rats are used. All animals were within ± 20 % of the mean body weight for the group to which they were assigned. Animals not used on the study were returned to the Animal Resources Group.

SPECIFIC HOUSING AND MAINTENANCE

A. Animal Receipt and Quarantine

All animals received from Charles River Laboratories were judged to be in good health and suitable as test animals. The attending veterinarian or his designee examined all animals before release from quarantine. However, rat No. C9183 was found in a poor health and it died one day prior to dosing. Rat No. Q0041 was randomly selected to replace rat No. C9183. Also, on the day of dosing rat No. C9197 in the blood kinetics group was judged by the attending veterinarian to be in poor health and was removed from the study. Rat No. Q0037 was randomly selected to replace rat No. C9197.

B. Animal housing

Animals were individually housed in suspended wire-mesh cages (7"x10"x7") during quarantine and upon release from quarantine. The cages were elevated above Bed-O'Cobs® bedding, and were subjected to routine cleaning. Animals that were used in the MB groups were transferred to individual Roth-style glass metabolism cages and allowed to acclimate overnight to this experimental environment prior to administration of test article. Animals that were used in BK

and WBA groups continued to be housed individually in suspended wire-mesh cages throughout the conduct of the study. Rats that were not used on the study were returned to the Animal Resources Group.

All animals were housed in an environmentally controlled animal room (12-hour fluorescent-light/dark cycle, 64-79°F, 30-70% humidity, 10-15 air changes per hour) through the in-life part of the study. Temperature and humidity were monitored twice a day on weekdays and once a day during the weekend. The light cycle was only interrupted periodically for sample collection. Such interruptions were necessary for the conduct of the study, and are not considered to have an impact on the study outcome. Air-flow and animal condition in the glass metabolism cages were monitored twice a day (am/pm) during the experiment. Air-flow in the metabolism cages was kept in the range of 500-600 ml/min. Cage temperature was checked at the time of sample collection and was kept in the range of 68-72°F.

A commercial diet of Purina® Certified Rodent Chow No. 5002 (Lot No. SEP 19 00, 1A and FEB 12 01 1B) and reverse osmosis water (Edstrom Industries, Inc. Waterford, WI) were available *ad libitum*. Periodic analysis of the certified feed for the presence of heavy metals and pesticides was performed and provided by the manufacturer to ensure that none were present in concentrations expected to affect the outcome of the study. Results of the most recent water analysis provided by an independent laboratory (Ann Arbor Technical Services, Ann Arbor, MI) and feed analysis were reviewed by the Study Director. Documentation of study director reviews was placed in the study records. There were no contaminants in the water or feed identified at levels that would interfere with the integrity of the study.

ANIMAL WELFARE ACT COMPLIANCE

This study complied with all applicable sections of the final rules of the Animal Welfare Act regulations (9 CFR, Part 1, 2 and 3) and was approved by the Laboratory Animal Care and Use Committee (LACUC) before animals were ordered.

TEST ARTICLE and CARRIER INFORMATION

Test article characterization was done in compliance with the EPA Toxic Substances Control Act (TSCA), and Good Laboratory Practice Regulations (40 CFR Part 792).

TEST ARTICLE I

The characterization of the unlabeled test article (D_5) identified below included a visual inspection, purity by gas chromatography (GC) with thermal conductivity detector (TCD) and GC with mass spectrometry (MS) to verify the identity of the major component as D_5 (HES Study No. 8824, HES report No. 1997-I0000-43682). Records of characterization are maintained in the HES Archive. Documentation of study director review is kept in the study files. Any remaining test article was disposed of by study personnel. This is documented in the study records.

- Identification: Decamethylcyclopentasiloxane (supplied as Dow Corning™ 1693 Fluid)
- Lot No.: LL014002
- CAS No.: 541-02-6
- Physical Description: colorless liquid
- Handling Precautions: Good ventilation recommended, wear impervious gloves, safety glasses with side shields or safety goggles
- Stability: Chemically stable
  (Refer to MSDS)
- Expiration Date: Extended to March 04, 2004
- Purity: 99.44 % by GC/TCD
- Solubility: Soluble in toluene, hexane, acetone, ethanol, tetrahydrofuran etc. (Angelotti , 1991; Varaprath *et al.*, 1998)
- Analytical Procedure to Verify Test Article: GC/MS

- Storage Conditions: Room temperature (refer to MDMS)
- Supplier: Dow Corning Corporation
  2200 W. Salzburg Road
  Midland, MI 48686-0994
- Reserve Sample: A sample is retained in the HES Test Article
  Archives, Dow Corning Corporation
  Midland, MI 48686-0994

TEST ARTICLE II

Chemical identity and radiochemical purity of the labeled test article (^{14}C-D_5) was determined using gas chromatography/mass spectrometry (GC/MS) and high performance liquid chromatography (HPLC) with a radioactivity flow-through detector (RAD), respectively (Study No. 9551). Records of the characterization are maintained in the HES Archive. Documentation of study director review was placed in the study records. Any remaining test article was disposed of by study personnel. This is documented in the study records.

- Identification: ^{14}C-Decamethylcyclopentasiloxane (^{14}C- D_5)
- Lot No.: 001227
- Specific Activity: 23.85 mCi/mmol (80.69 μCi/mg) as determined by Wizard Laboratories, Inc.
- Radiochemical Purity 99.37 % (HES Study No. 9551)
- Solubility: Soluble in hexane, heptane, toluene, tetrahydrofuran etc. (Angelotti , 1991; Varaprath *et al.*, 1998)
- Physical Description: Colorless, odorless liquid

- Handling Precautions: Good ventilation recommended, wear impervious gloves, safety glasses with side shields or safety goggles
- Stability: Chemically stable (refer to MSDS)
- Expiration Date: 12/17/2002
- Analytical Procedure to Verify Test Article: GC/MS and HPLC/ Radiometric Flow Detector
- Storage Conditions: -20°C Freezer
- Supplier: Wizard Laboratories, Inc.
  2785 B Del Monte Street
  West Sacramento, CA 95691
- Reserve Sample: A sample retained in the HES Test Article Archives, Dow Corning Corporation, Midland, MI 48686-0994.

Unlabeled D_5 (Lot No. LL014002) and ^{14}C labeled D_5 (Lot No. 001227) were combined and the HES test article control and characterization group assigned a new reference No. 001227D to a diluted ^{14}C-D_5 stock. Specific activity of ^{14}C-D_5 (Ref. No. 001227D) was determined to be 5.758 mCi/g by liquid scintillation analysis.

TEST ARTICLE CARRIERS

Corn Oil

- Identification: Corn oil
- Lot No.: 86H0059
- CAS No.: 8001-30-7

- Physical Description: Yellow, clear liquid
- Handling precautious: None
- Stability: Stable at room temperature
- Purity: 100% pure corn oil
- Expiration Date: 02/10/2003
- Solubility: N.A.
- Storage conditions: Room temperature
- Supplier: Sigma, St. Louis, MO

Simethicone Fluid

This carrier, identified as simethicone fluid (SF), was analyzed for D_5 and D_4 content by the HES Analytical Chemistry Group at Dow Corning Corporation (HES Study No. 9561). The observed concentrations of D_5 and D_4 in SF (material No. 01539213) were 5.5 ± 0.3 ppm (RSD = 4.6%) and 12.9 ± 1.8 ppm (RSD = 13.8%), respectively (n = 12). Records of characterization are maintained in the HES Archive. Documentation of study director review is kept in the study files.

- Identification: 01539213 (supplied as Dow Corning® Q7-2243 LVA, Simethicone USP; PDMS 700cSt.)
- Batch No.: 0000720506
- Physical Description: Translucent gray liquid (refer to MSDS)
- Stability: Chemically stable (refer to MSDS)
- Purity: The test article is representative of material No. 01539213
- Expiration Date: May 15, 2002
- Solubility: Soluble in toluene, hexane, chloroform, tetrahydrofuran etc. (Angelotti, 1991; Varaprath *et al.*,1998)

- Storage conditions: Room temperature (refer to MSDS)
- Supplier: Dow Corning Corporation
  2200 W. Salzburg Road
  Midland, MI 48686-0994

DOSING SOLUTIONS

In Part 1, a single oral dose of ^{14}C-D_5 was delivered in corn oil, and in Part 2 a single oral dose of ^{14}C-D_5 was delivered in simethicone fluid or as neat material. The volume of administered dosing solutions (D_5 in corn oil and simethicone fluid) was targeted at 10 ml/kg body weight to deliver a nominal dose of 1000 mg D_5/kg body weight. Rats in CO and SF control groups were dosed with appropriate carrier, while rats in neat control groups were not dosed (Table 1).

Neat Test Article

Appropriate volumes of labeled test article, ^{14}C-D_5, Ref. No.001227D, were added to unlabeled D_5, lot No. LL014002 and mixed well to achieve a specific activity of 0.30 µCi/mg of dosing solution. This radioactivity content was sufficient to provide a radioactivity of approximately 30 µCi /100 g of body weight (0.3 mCi/kg of body weight), at a targeted nominal dose of 1000 mg D_5/kg of body weight (Table 2 and 5). The dose of 1000 mg/kg of body weight was selected based on EPA recommendations for test substances of low toxicity. Dosing test article was stored in -20°C freezer following final dilution. Radiochemical purity of the dosing test article was verified within three days prior to dosing using HPLC with radiometric detection (see Deviations). Radioactivity concentration in the dosing test article (specific activity) was measured by liquid scintillation analysis on the day of dosing prior to initiation. Documentations of these analyses are maintained in the study records.

D_5 in Corn oil

Homogeneity and six-day stability of ^{14}C-D_5 in corn oil were evaluated by extracting/diluting in tetrahydrofuran (THF) and analyzing by HPLC/RAD, by liquid scintillation counting (LSC), and by GC/MS against THF solvent standards of D_5. These analyses were performed by the HES Analytical Chemistry Group at Dow Corning Corporation. Records of stability and homogeneity were reviewed by the study director.

Specific activity of corn oil dosing solution was determined to be 0.036 mCi/g on the days of dosing. D_5 concentration was determined to be 125.26 mg/g of dosing solution. This dosing solution delivered approximately 36 µCi radioactivity/100 g of body weight (0.36 mCi/kg of body weight), and

a nominal dose of 1000 mg D_5/ kg of body weight (Table 2, 3 and 4). The dosing solution was stored at refrigeration temperature (4 ± 4°C).

D_5 in Simethicone Fluid

Stability and homogeneity of ^{14}C-D_5 in simethicone fluid were evaluated by extracting/diluting in tetrahydrofuran (THF) and analyzing by HPLC/RAD, LSC, and GC-MS against THF solvent standards of D_5. These analyses were performed by the HES Analytical Chemistry Group at Dow Corning Corporation. Records of stability and homogeneity were reviewed by the study director.

Specific activity of this dosing solution was determined to be 0.029 mCi/g on the days of dosing. The concentration of D_5 was determined to be 97.47 mg/g of dosing solution. D_5 in the simethicone dosing solution delivered approximately 29 μCi radioactivity/100 g of body weight (0.29 mCi/kg of body weight, and a nominal dose of 1000 mg D_5/ kg of body weight (Table 2 and 5). The dosing solution was stored at refrigeration temperature.

EXPERIMENTAL DESIGN

ROUTE AND RATIONALE OF TEST MATERIAL ADMINISTRATION

Oral administration of the test article was selected as the exposure route since this represents a potential although minor route for human exposure and is an accepted method of administration of test chemicals in pharmacokinetic and metabolism studies when this is an expected route of human exposure.

ORGANIZATION OF TEST GROUPS

The study consisted of two parts defined by the carrier in dosing solution (Part 1: ^{14}C-D_5 in corn oil; Part 2: neat ^{14}C-D_5 or ^{14}C-D_5 in simethicone fluid). The first part consisted of MB, WBA, and BK groups, and the second part consisted of MB, and BK groups as outlined in Table 1. Each part was performed as a separate experiment. In the Part 1, rats in the MB and WBA exposure groups were dosed on the same day and rats in the BK exposure group were dosed on a separate day. In the Part 2, rats in MB and BK exposure groups were dosed on separate days.

TEST ARTICLE ADMINISTRATION

Rats in MB groups (groups 1-4, 11-14) were placed into the individual glass metabolism cages for overnight acclimation after their release from quarantine and prior to dosing. On the respective

days of dosing, all rats were weighed prior to dosing. Dose calculated on the body weight was delivered using a syringe equipped with curved stainless steel feeding needle. Immediately after dosing, animals in MB groups were returned to the glass metabolism cages while animals in WBA and BK groups were returned and housed in the suspended wire-mesh cages.

Part 1. Rats in all exposure groups (MB, WBA and BK) were dosed with ^{14}C-D_5 in corn oil by oral gavage. Administered dose was determined gravimetrically. An average dose of 1008 mg D_5/kg body weight was delivered in 8 g of dosing solution/kg body weight. Control animals in groups 1, 2 and 7, 8 were dosed with an average of 8 g corn oil/kg body weight. Animals in MB groups were returned to the individual glass metabolism for 168 hours. Animals in WBA and BK groups were returned to the suspended wire-mesh cages after dosing and housed for maximum 168 hours.

Part 2. Rats in the MB and BK exposure groups 13 and 17 were dosed with neat ^{14}C-D_5 at an average dose of 1004 mg D_5/kg body weight. Control animals in groups 11 and 15 were not dosed. Animals in the MB and BK exposure groups 14 and 18 were dosed with ^{14}C-D_5 in simethicone at an average dose of 985 mg D_5/kg body weight delivered in 10 g dosing solution/kg body weight. Administered doses were determined gravimetrically. Control animals in groups 12 and 16 were dosed with an average of 10 g simethicone fluid/kg body weight. Animals in MB groups were returned to the individual glass metabolism cages for 168 hours. Animals in BK groups were returned to the suspended wire-mesh cages after dosing and housed for a maximum 168 hours.

At the end of the exposure, rats were euthanized as described in the section Test System: L. Method of Euthanasia.

SAMPLE COLLECTION

Mortality/Morbidity/Daily Observations

All animals were observed in their cages for mortality, morbidity, and signs of distress daily by study personnel through the completion of the in-life phase of the study. Female rat No. C9202 in the MB group was removed from the study and replaced with rat No. Q0004 that was randomly selected. This was necessary due to injury that occurred in attempt during delivery of the dosing solution. Also, female rat No. C9183 and male rat No. C9197 in BK groups were in poor health prior to the experimental start and were replaced with rats No. Q0041 and No. Q0037, respectively. All the

female and some of male cannulated rats in Part 1 appeared to be in the poor health close to 168 hr- blood collection time point (e.g. corneal opacities, porphyrin staining, urine staining perineum). Female rat No. C9189 was in a near moribund condition and two female rats No. C9186 and No. C9187, died before the last blood collection from causes related to the jugular cannula surgery. Female rats No. C9191 (Part 1) and C9214 (Part 2) died in the process of obtaining blood. Female rat No. C9213 in the BK group escaped from the cage and was found dead by the study personnel. The study director was notified when animals were found dead.

Mass balance groups

Immediately following dose administration, animals in the MB groups were returned to individual glass metabolism cages for collection of urine, feces, expired CO_2 and expired volatiles at scheduled times (Table 6). At the same time, control animals in groups 1, 2, 11 and 12 were placed in glass metabolism cages for collection of the excreta on a daily basis beginning at 24 hr post-dose until 168 hours post-dose.

Glass Metabolism Cage Set-up and Operation:

Twelve Roth-style glass metabolism cages were set-up and used in each part of the study. Each cage was set up and operated at target conditions and flow rates of 0.5-1 Lit per min for a minimum of 24 hours prior to housing of animals. During this time, the system was evaluated for leaks by monitoring flow rates using flow meters and if necessary, appropriate actions were taken to assure the leaks were corrected and the system was sealed. In addition, evaluation of Roth-style metabolism cage system operation and integrity plus the trapping of volatile ^{14}C-D_5 from the metabolism cages onto charcoal tubes was assessed in a separate study prior to initiation of the exposure period (Study No. 9549).

Roth-style glass metabolism cages were set up and operated in a manner that allowed adequate and uninterrupted airflow. Connections between parts were made using Tygon® tubing. For connections leading from the exhaust side of the chamber, Teflon® tubing was used.

The room air was drawn through the cages using a vacuum pump. The airflow rate through each chamber was monitored using a calibrated flow meter and was maintained between 500-600 ml per minute. The room air entering the system was passed through a

series of Drierite® and Ascerite® canisters designed to remove H_2O and CO_2, respectively. Cage temperatures were recorded once in the A.M. and once in the P.M. every day during animal housing in the metabolism cages.

Glass tubes containing charcoal were used for trapping expired volatiles. Urine and feces were collected over dry ice and CO_2 was collected in 4N KOH traps (gas towers). Tissues and remaining carcasses were collected at the sacrifice time points.

Excreta Collection

Urine

The Roth-style glass metabolism cages that were used were modified to allow direct collection of urine into 4 oz. glass jars. Jars were pre-weighed and labeled with a minimum of study No., animal number, group number and collection interval. While collecting, each jar was maintained on dry ice. At the appropriate time point, the collection jars were removed from the cage, capped and placed in an -80 °C freezer for storage.

Feces

The Roth style glass metabolism cages being used were modified to allow direct collection of feces into 4 oz. glass jars. Jars were pre-weighed and labeled with a minimum of study number, animal number, group number and collection interval. While collecting, each jar was maintained on dry ice. At the appropriate time point, the jars were removed from the cage, capped and placed in a -80°C freezer for storage.

Expired Volatiles

Glass tubes containing charcoal were used for trapping expired volatiles. Glass tubes were supplied closed at each end and were opened by etching and breaking of each end. Each tube was then attached in-line on the exhaust side of the cage. One tube was used per cage, per collection interval. Each tube was labeled with a minimum of study number, animal number, group number and collection interval. At the appropriate time point, the charcoal tubes were removed, capped and placed in a -20 °C freezer for storage. Charcoal tubes were transferred to a cold room (4 ± 4°C) to be cracked and desorbed in toluene.

Carbon Dioxide (CO_2)

Cage exhaust air was passed through a glass gas trap filled with 128-209 g of 4N potassium hydroxide (KOH). Each gas trap was filled with fresh KOH prior to initiation of collections. At the appropriate collection interval, KOH was collected into pre-weighed 8 oz. glass jars labeled with a minimum of study No., animal No., group No. and collection interval. Jars with collected KOH were capped and kept at refrigeration temperature.

Metabolism Cage Rinse

Each glass metabolism cage was rinsed with THF following removal of the animal. The rinse was collected in a pre-weighed jar. The cage rinse was kept at 4 ± 4°C for storage.

Tissues and carcass

At the terminal sacrifice time point (168 hours post-dosing), MB animals were placed into individual chambers containing methoxyflurane vapor and anesthetized. Anesthetized rats were euthanized by exsanguination *via* cardiac puncture. The maximum volume of blood possible was collected into a heparinized Vacutainer® tube until the heart beat and blood flow appeared to stop. Blood collected by open thoracic cardiac puncture was added into a jar prepared for carcass collection. At this time, liver, lungs, perirenal fat, gastrointestinal (GI) tract, kidney, adrenals, spleen and reproductive organs (ovaries and testis) were collected. Upon removal, the GI tract was mechanically emptied of its contents by squeezing segments of GI tract with hemostats. GI contents were collected into the empty, pre-weighed glass jars. In addition, tools that are used to clean the GI tract were rinsed with up to 2 ml of reverse osmosis (RO) water into the jar containing GI contents as needed and documented in the study records. All tissues were excised, blotted of excess blood, and separately added to a predetermined amount of 35% tetraethylammonium hydroxide (TEAH) for solubilization at ambient temperature. Residual carcasses were placed into the pre-weighed jars that were pre-filled with 35% TEAH to be solubilized *in toto* at room temperature. Tissue weights were determined by subtracting tare weights of the jars containing TEAH from total weights after tissues had been added into TEAH.

Control Animals

Rats in control groups 1, 2, 11 and 12 were housed in glass metabolism cages under the same environmental conditions as animals in the exposure groups. Excreta collected at the 24 hr time point were used as a matrix background. At the terminal sacrifice time point (168 hours post-dose), rats in the control groups were euthanized by exsanguination *via* cardiac puncture under

methoxyflurane anesthesia and selected tissues and organs were collected as defined in Table 6. Each Roth-style glass metabolism cage was rinsed with THF following removal of the animal.

Whole Body Autoradiography

Immediately after dose administration, animals in the WBA Group were returned to wire-mesh cages for exposure durations of 3, 12, 24, 48, 96 and 168 hr (Tables 1 and 6). All animals were observed in their cages for mortality, morbidity, and signs of distress daily by study personnel through the completion of the in-life phase of the study.

At 3, 12, 24, 96 and 168 hr time points animals in WBA Groups 5 and 6 were weighed and sacrificed by CO_2 asphyxiation, and immediately frozen in a hexane/dry ice bath at approximately -75°C for approximately 20-40 minutes and stored at -80 ± 10°C. The frozen carcasses were positioned within a frame and embedded in a 4% aqueous solution of carboxymethylcellulose, which supported the carcass for sectioning. Blocks were stored at -80°C (± 10°C) until sectioned.

Blood Kinetics Groups

Immediately after dose administration, cannulated animals in BK groups were returned to wire-mesh cages for collection of blood samples *via* jugular cannula at scheduled time points (15 and 60 min, and 6, 12, 24, 48, 72, 96, 120, 144 and 168 hours post-dose). During blood collections from the jugular cannula, an aliquot of blood (approximately 300 µl) was collected, immediately transferred into a pre-weighed glass vial containing THF and glass beads, and processed for analysis of total radioactivity, unchanged D_5 concentrations and metabolite profile evaluation. Throughout the conduct of the study, a few animals developed non-patent cannulas at later time points or died due to complications associated with jugular cannula surgery. If no blood was obtained, the sample for that time point was considered lost.

Control Animals

Blood samples from the control animals were obtained only at the 24 hr time point (Table 1 and 6).

SAMPLE PROCESSING AND ANALYSIS

Mass Balance Groups

Radioactivity of all samples collected was quantified by liquid scintillation analysis. Each sample was counted for 10 minutes or a 2 sigma %value of two, whichever came first. All counts were converted to absolute radioactivity (disintegration per minute, dpm) by automatic quench correction.

Results were corrected for matrix background radioactivity that was determined by using samples in the control groups.

Urine, KOH, and cage washes were weighed following collection and directly analyzed for radioactivity by liquid scintillation counter (LSC). Urine samples from 12, 24, 48, 72 and 96 hr time points were selected based on the level of radioactivity (approximately >25,000 dpm/g urine) and directly analyzed by HPLC/RAD to determine metabolic profile. Although urine samples from Part 2 had lower levels of radioactivity, same time points were analyzed for the consistency of the data.

Charcoal tubes that were used to trap expired volatiles were desorbed with toluene (main and back-up portion combined). Two aliquots of the toluene were taken for total radioactivity analysis by LSC. In addition, separate aliquots of the charcoal tube extracts were taken for analysis by GC/MS for determination of parent D_5 concentrations according to the method "Procedure for Determination of D_5 in Expired Volatiles (Charcoal Tubes)" given in Appendix A, Attachment B. This method was validated prior to this study and results from this validation can be found in the DC report No. 2001-I0000-50469. Instrumentation and GC/MS methodology was documented and included in the study file.

Feces and contents of the GI tract were homogenized using a tissue homogenizer prior to solubilization or extraction. Aliquots of the fecal and GI contents homogenates were taken and solubilized in 35% TEAH, decolorized with hydrogen peroxide and neutralized with isopropanol. At that time, aliquots of the solubilized feces and GI contents were analyzed by LSC for radioactivity content. In addition, a spiking experiment was performed to determine if the processing efficiency of fecal material was less than 100% under conditions used to analyze fecal samples. Fecal processing efficiency was determined by comparing the amount of radioactivity used for spiking control fecal pellets to the amount of radioactivity recovered after fecal homogenization with water and solubilization in 35% TEAH (see Appendix A for experimental details). Fecal solubilization processing efficiency was determined for D_5 in each carrier (D_5 in corn oil, D_5 in simethicone fluid, neat D_5) and was used to correct the mass balance results.

Separate aliquots of the fecal homogenates were kept frozen at -80°C until extraction with THF. Extracts of fecal homogenates were analyzed by LSC for radioactivity content in the extracts, and by GC/MS to determine the levels of parent (unchanged) D_5 present in samples according to the method "Procedure for Determination of D_5 in Biological Matrices (Plasma, Blood, Liver, Lung,

Feces, and Fat)" given in Appendix A, Attachment A. This method was validated prior to this study and results from this validation can be found in the DC report No. 2000-I0000-49032 (HES Study No. 8762). Instrumentation and GC/MS methodology are documented and included in the study file. In addition to parent D_5 quantitation by GC-MS, extracts of fecal homogenates from 12, 24, 48 and 72 hour time points had sufficient radioactivity to be further analyzed by qualitative analysis by HPLC/ RAD in order to evaluate the metabolite profile of individual radioactive components present in feces. GI contents homogenates were not extracted nor further analyzed by GC/MS because of insufficient level of radioactivity ($\leq$ 1210 dpm/g homogenate).

The tissues and carcasses were solubilized using 35%TEAH and aliquots of the solubilized samples were taken and analyzed by LSC to determine radioactivity content.

Control Animals

Samples collected from the control animals were processed and analyzed the same as samples from the dosed animals in mass balance groups. Results obtained from control animals were used to determine background levels of radioactivity and any background parent D_5. Matrix background radioactivity was used to correct radioactivity results for the exposure groups.

Whole Body Autoradiography

Animals from Groups 5 and 6 were euthanized, frozen and sectioned by placing the frozen block on a stage of a Cryomacrocut® microtome (Leica, Deerfield, IL) with the temperature maintained at approximately -25°C ± 5°. Parasagittal sections of a thickness of approximately 40 µm were collected onto adhesive tape at various levels to include organs and tissues of interest (Appendix D). The non-dehydrated sections were then mounted on a cardboard support, covered with a layer of plastic wrap, and placed immediately onto a Kodak BioMax MR® radiographic film and exposed at -80°C for 1, 2 and 4 weeks. At the end of the exposure period, films were developed on an Cordell MXR-14 automatic film processor (Cordell, Peabody, MA). After the film had been developed, non-dehydrated sections were disposed of as radioactive waste. One representative section from each level was dehydrated within the cryochamber for 48 to 72 hours and retained as a reference for comparison with the film.

The films were evaluated for visual clarity and artifacts. These artifacts might occur during preparation, processing, or developing due to the physiochemical properties of the test article.

Films from each time point were evaluated visually and tissues/organs were ranked by intensity of radioactivity using a gradient scale of grayness as an approximate reference value.

Blood Kinetics

The blood samples were extracted in THF and an aliquot of the extract was analyzed for unchanged D_5 content by GC/MS according to the approved method given in Appendix A, Attachment A. This method was validated prior to this study and results from this validation can be found in the DC report No. 2000-I0000-49032. Separate aliquots of extracts were taken and added to appropriate LSC cocktail and analyzed by LSC for radioactivity content. In addition to parent D_5 quantitation by GC/MS, blood extracts found to contain sufficient radioactivity (6, 12 and 24 hour time points) were analyzed by HPLC/RAD (Appendix A).

Control animals

Blood collected from the control animals at the 24 hr time-point was processed and analyzed the same as samples from the dosed animals. Results obtained from animals in the control groups were used to determine background radioactivity and any parent D_5 background for each carrier. Blood radioactivity in the exposure groups was corrected for matrix background radioactivity. However, corn oil blood extracts were corrected for background values obtained from the neat (not dosed) control animal blood extracts (See Deviations).

Sample Identification and Storage

Samples collected were identified by study number, test system number, target time point, identity/name of sample, date of collection and storage conditions. Samples were stored under following conditions:

KOH	Refrigerated (4 ± 4°C)
Charcoal tubes	-20 °C freezer
Toluene extracts	Refrigerated (4 ± 4°C)
Urine, Feces	-80°C freezer
Feces and GI contents homogenates	-80°C freezer
Solubilized carcass and tissues	Room temperature
THF extracts (blood, feces, GI contents)	Refrigerated (4 ± 4°C)
Cage rinses (THF)	Refrigerated (4 ± 4°C)
Frozen carcasses (WBA)	-80°C freezer

DATA ANALYSIS

Parameters evaluated

Radioactivity in excreta and tissues from the MB group is expressed in terms of percent of total radioactivity recovered relative to the amount of administered radioactivity. Radioactivity content is expressed in terms of μg equivalents D_5/g of sample. Radioactivity recovered in charcoal tubes (expired volatiles) is reported in μg equivalents D_5/hr. The calculation of μg equivalents D_5 was based on upon the specific activity of the dosing solution. The concentration of parent D_5 (unchanged D_5) in blood and feces is reported in μg D_5/g of sample. The concentration of parent D_5 in charcoal tubes is reported in μg D_5/hr.

- Absorption: The radioactivity recovered in urine, expired volatiles, expired CO_2, tissues (liver, lungs, perirenal fat, GI tract, kidney, adrenals, spleen, ovaries and testis), residual organs and tissues that were left behind in the remaining carcasses of the animals in the MB groups was considered to represent the absorbed portion of administered dose.
  The radioactivity recovered in urine, expired volatiles and expired CO_2 over 168 hours represent the portion of absorbed dose that was excreted. Radioactivity recovered in urine and charcoal tubes was compared with content of parent D_5 to evaluate relative metabolism of D_5 excreted in urine or exhaled, respectively.
- Elimination through GI tract (Dose excreted in feces): The radioactivity recovered in feces, and in the contents of GI tract and cage rinses represented the portion of administered dose eliminated through GI tract. Feces radioactivity was compared with parent D_5 found in feces to evaluate relative metabolism/degradation of D_5 excreted in feces.
- Blood kinetics: The radioactivity concentrations in blood are reported as μg equivalents D_5/g of sample based upon the specific activity of the dosing solution and compared to parent D_5 concentrations in blood. Blood kinetics data are used to generate pharmacokinetic parameters such as blood radioactivity AUC, blood parent D_5 AUC, distribution and elimination half-lives ($T_{1/2}$ ' and $T_{1/2}$ '') for radioactivity and parent D_5, maximum blood concentration (C_{max}) and the time of the peak concentration (T_{max}). Blood radioactivity AUC (expressed as μg equivalents D_5 *hr/g) was compared with blood parent D_5 AUC (expressed as μg D_5*hr/g) to evaluate relative metabolism of D_5. Parent D_5 AUCs were also used to evaluate relative availability of D_5 when administered in different carriers (Rowland and Tozer, 1989).
- Limits of quantitation: Values that are below the limits of quantification (LOQ) were considered equivalent to zero. The LOQ for radioactivity analyses was defined by matrix background radioactivity that was determined by using excreta of control animals collected 24 hr post-

dosing, and tissues collected at the sacrifice time point. The LOQ for parent analyses was defined in the methods for each of the matrices.

Statistical analysis

Numerical data obtained during the conduct of the study were processed using Microsoft Excel™ version 9.0. and subjected to calculation of group mean values and standard error of the mean, where appropriate.

Statistical analysis of the data were carried out using Microsoft Excel™ version 9.0 and/or SAS®, v. 8.2.

Part 1. Endpoints for statistical analysis included the absorption, disposition and elimination of ^{14}C-D_5 when delivered in corn oil. Gender effects on the endpoints were determined using analysis of variance (9). If the analysis of variance was significant, no multiple comparison test was required since only two groups were being compared.

The AUC of the time course of radiolabeled and parent D_5 was determined for blood, feces and expired air. Blood radioactivity AUC was compared to parent D_5 AUC for each gender to evaluate relative metabolism of the absorbed D_5 (Appendix C). The amount of metabolites in blood was calculated by subtracting the AUC of the parent D_5 from the AUC of the total radioactivity. Distribution and elimination half lives ($T_{1/2}$' and $T_{1/2}$") of D_5 in blood were calculated as 0.693/K where K is the distribution or elimination rate constant.

In addition, radioactivity and parent AUCs for feces and expired air were compared for the presence of metabolites. Differences in the AUC between sexes were determined by constructing a 95% confidence interval for the difference (AUC_{male} - AUC_{female}) using the method of Nedelman and Jia (12). Confidence intervals for the AUCs were constructed using the method of Nedelman, Gibansky and Lau (13). If the confidence interval did not contain the value zero, then the mean AUCs were considered to be significantly different.

Part 2. Endpoints for statistical analysis included the absorption, disposition and elimination of ^{14}C-D_5 when delivered either in neat or in simethicone fluid. Carrier effects on the endpoints were determined by comparing the results using the two carriers, corn oil and simethicone, with data obtained with neat D_5 using a one-way analysis of variance (9) followed by Tukey's multiple

comparison technique (10) carried out on the combined data set which included all the animals from Part 2 and the female animals from Part 1 of this study.

The area under the curve of the time course of radiolabeled and parent D_5 was determined for blood, feces and expired air. Blood AUCs for radioactivity were compared with parent D_5 AUC for each carrier to evaluate relative metabolism of absorbed D_5 (Appendix C). The amount of metabolites in blood was calculated by subtracting the AUC of the parent D_5 from the AUC of the total radioactivity. Distribution and elimination half lives ($T_{1/2}$' and $T_{1/2}$") of D_5 in blood was calculated as 0.693/K where K is the distribution or elimination rate constant, respectively.

In addition, radioactivity and parent AUCs for feces and expired volatiles were compared for the presence of metabolites. Area under the curve for corn oil was compared to AUCs for simethicone fluid and neat D_5, and AUC for neat was compared to AUC for simethicone fluid. Differences in the blood, feces and expired air AUCs between carriers were determined by the methods mentioned above in Part 1 (12,13). In all cases, the Type I error was controlled at 5 % ($\alpha = 0.05$). Data were analyzed to determine if the assumption of homogeneity of variance has been met using Levene's test (9). If that assumption did not hold, a suitable transformation was determined using the Box-Cox power method (10). If a transformation that equalizes variance could not be found, treatment effects was evaluated using Welch's ANOVA (9).

DEVIATIONS

a. A deviation occurred in the protocol with regard to the section XI.D (Dosing Solutions). Neat test article was prepared two weeks before dosing (protocol states no earlier than three days prior to use). However, radiochemical purity of the dosing test article was determined within three days prior to dosing using HPLC with radiometric detection. Radioactivity concentration in the dosing test article (specific activity) was verified by liquid scintillation analysis on the day of preparation and on the day of dosing prior to initiation. This was considered to have no impact on the study outcome.

b. A deviation occurred in the protocol with regard to the section VI.I (Body Weight Range). Male rats in Part 1 exceeded body weight range that was specified in the Protocol. However, age of the test system was within the protocol age limits (8-11 weeks). This was considered to have no impact on the study outcome.

c. A deviation occurred in the protocol with regard to the section VI.L (Identification Method). Rats No. Q0004, Q0037 and Q0041 were randomly selected to replace rats No. C9202, C9197 and C9183, respectively that appeared to be sick. Due to time constraints, those rats were not eartaged and were identified only by cage tags. This was considered to have no impact on the study outcome.

d. A deviation occurred in the protocol with regard to the section IX.C. (Environmental Conditions). Temperature and humidity of the source air for metabolism cages was not monitored as specified in Protocol. However, temperature and humidity was monitored in the room where the rats were housed. This was considered to have no impact on the study outcome.

e. Standards, blood QC samples and blood samples were centrifuged at 3030 rpm instead of 2800 rpm as stated in the "Procedure for Determination of D5 in Biological Matrices (Plasma, Blood, Liver, Lung, Feces and Fat)". This was considered to have no impact on the study outcome.

f. A deviation occurred in the protocol with regard to the section VI. M (Scheduled animal termination). Cannulated rats in control groups 7 and 8 were not weighed prior to but after the euthanasia by CO_2 asphyxiation. Inadvertently, body weight of rat No. C9163 was not taken at the termination time point. This was considered to have no impact on the study outcome.

g. A deviation occurred in the protocol with regard to section XII.G (Sample Processing and Analysis). Corn oil blood extracts were corrected for background values obtained from the neat (not dosed) control animal blood extracts. This was considered to have no impact on the study outcome.

h. A deviation occurred in the protocol with regard to section XII.C (Exposure method). Administered dose for animal No. C9177 in WBA group was determined volumetrically instead of gravimetrically because post-dose syringe weight was not taken due to technical difficulties. The weight of the dose was estimated based on density of corn oil dosing solution. This was considered to have no impact on the study outcome.

i. A deviation occurred in the protocol with regard to section XII.F (Sample Collection). Tools that were used to clean GI tract in animals C9164, C9167, C9169 were not rinsed with water because they did not become dirty during this procedure. Also tools that were used to clean GI

tract in control animals (C9158, C9159, C9160 and C9161) were not rinsed because they were only used for matrix background. This was considered to have no impact on the study outcome.

RESULTS AND DISCUSSION

Organization of test groups is presented in Table 1.

D_5 IN CORN OIL

The disposition of ^{14}C-D_5 was evaluated in male and female Fischer 344 rats following a single oral dose of 1000 mg D_5 in corn oil/kg body weight. A group of jugular vein cannulated animals were used to obtain estimates of blood concentrations. A separate group of rats dosed with ^{14}C-D_5 in corn oil was placed in glass metabolism cages for quantitative assessment of ^{14}C-D_5 excretion and absorption. Finally, whole body autoradiography was used for qualitative *in vivo* assessment of tissue distribution of radioactivity.

BLOOD KINETICS

This portion of the study was designed to provide data on blood kinetics for male and female Fischer 344 rats dosed with D_5 in corn oil. Individual dosing data are presented in Tables 4 and 5. Radioactivity and parent D_5 concentrations are presented in Table 7 and in Figure 1. Individual animal values are presented in Appendix B.

Blood curves were used to determine basic pharmacokinetic parameters. The area under the curve analysis for total radioactivity and parent D_5 in blood as well as values for T_{max}, C_{max} and $T_{½}$ are presented in Table 8. Statistical analysis (Appendix C) showed statistically significant difference between radioactivity and parent AUCs for both males and females when D_5 was administered in corn oil indicating presence of metabolites in blood ($AUC_{metabolites} = AUC_{radioactivity} - AUC_{parent}$). The parent AUC was significantly larger for males (1014.50 µg D_5 X hr/g) compared to females (879.50 µg D_5 X hr/g) but there was no difference in the radioactivity AUC between males (1121.48 µg equivalent D_5 X hr/g) and female (1035.47 µg equivalent D_5 X hr/g), respectively (Figure 1). However, this observation is not considered to be biologically significant due to the influence of the early time points on the calculation of the blood AUCs.

The maximum concentration of D_5 in blood (C_{max}) was achieved 6 hr after dosing for both males and females (Table 8). The maximum concentration of D_5 in males was 51.15 µg equivalents D_5/g of blood and 46.94 µg equivalents D_5/g of blood in females based on total radioactivity, and 62.49 µg D_5/g in males and 52.12 µg D_5/g in females based on D_5 parent analysis. Radioactivity and parent D_5 distribution half-lives ($T_{1/2}$') were 9.88 hr and 6.78 hr for males, respectively and 12.05 hr and 8.15 hr for females, respectively. Radioactivity and parent D_5 elimination half lives ($T_{½}$") were 81.15 hr and 166.80 hr for males, respectively and 240.36 hr and 160.91 hr for females, respectively as shown Table 8.

The blood extracts from samples collected at 6, 12, and 24 hours following dosing were analyzed by HPLC/RAD in order to determine the radioactivity profile in the blood extracts. HPLC/RAD data showed only one peak corresponding to parent D_5 indicating the presence of only parent D_5 at 6, 12 and 24 hr. Example HPLC/RAD chromatograms of a blood extract for males and females at 12 hr post-dosing with corn oil are presented in Figure 11.

MASS BALANCE

Following a single, oral dose of ^{14}C-D_5 in corn oil, animals were placed in glass metabolism cages for collection of expired volatiles, expired CO_2, urine, and feces at predetermined time points (Table 6). Rats in the control group were dosed with pure corn oil. Individual dosing data are presented in Table 2. At the terminal sacrifice time point (168 hours post-dosing) liver, lungs, perirenal fat, GI tract, kidney, adrenals, spleen, emptied GI tract, contents of GI tract, reproductive organs (ovaries and testis) and remaining carcasses were collected.

The radioactivity content was measured in all samples, and D_5 concentrations (µg equivalents D_5 per gram or per hour) were calculated based upon specific activity of administered dosing solution. In addition, percent dose recoveries in feces were corrected for the sample-processing efficiencies associated with analysis of the fecal samples. Fecal processing efficiency was determined in a spiking experiment under conditions used to analyze fecal samples (Appendix A). The feces processing efficiency was determined to be 88% for D_5 in corn oil and was used to correct fecal radioactivity results. The discrepancy from 100% was possibly due to the process of taking aliquots from the aqueous fecal homogenate samples containing highly lipophilic D_5 that tends to migrate to the glass jar rather than stay in the aqueous sample.

Elimination through GI tract (Dose excreted in feces). The majority of the administered dose was excreted in feces regardless of sex (Table 9 and Figure 4). Total radioactivity found in feces, contents of the GI tract and cage rinses, was determined to be 81.43 ± 5.91% and 80.03 ± 6.18% of administered dose for male and female rats, respectively. Cumulative percent dose excreted in feces was not significantly different between sexes. The majority of administered dose was excreted in feces within 48 hours (Figure 10, Appendix B). In addition to radioactivity content, fecal samples were analyzed by GC/MS for the levels of parent D_5. Average LOQ was determined to be 0.36 μg D_5/ g of feces. Average radioactivity and parent D_5 concentrations in feces per time point are presented in Table 12. Statistical analysis showed that there was no significant difference between feces radioactivity AUC and feces parent AUC in males and females (Figure 6). The feces extracts from samples collected at 12, 24, 48, and 72 hours following dosing were analyzed by HPLC/RAD in order to determine the metabolite profile of the radioactivity present in the feces extracts (Appendix A). Figure 14 shows representative chromatograms of 24-hour fecal samples from male and female rats dosed with D_5 in corn oil. The majority of the radioactivity found in all of the feces extracts corresponded to parent D_5 based on retention time comparisons (retention time ~51 minutes). Some of the samples had a small metabolite peak (≤ 6% of the radioactivity in all cases, Table 15) present that is yet unidentified that eluted fairly close to parent D_5 indicating that it is relatively non-polar (retention time ~45 minutes). Samples of GI contents homogenates were not further analyzed by GC/MSD or by HPLC/RAD because of insufficient level of radioactivity in the homogenates.

Absorption. Absorption of radioactivity, expressed as percent of administered dose (± standard error of the mean) in urine, expired volatiles, expired CO_2, tissues and carcasses, was determined to be 21.82 ± 4.37% and 19.62 ± 4.20% for male and female rats dosed with D_5 in corn oil, respectively (Table 10). Comparison of endpoints in males *vs.* females showed only significantly higher level of radioactivity in perirenal fat of females (0.052%) as compared to the males (0.024%) as shown in Appendix C.

The majority of the absorbed dose was excreted in urine (4.70 ± 0.38% and 4.37 ± 1.07% of administered dose for male and female rats, respectively) and expired volatiles (13.36 ± 4.76% and 10.37 ± 2.91% of administered dose for male and female rats, respectively) as shown in Table 10. Radioactivity recovered in urine and expired volatiles represent 75% and 83% of the absorbed dose for females and males, respectively (Table 11). Less than 5% of administered dose was recovered in tissues and remaining carcass, and less than 1% of administered dose was found in CO_2.

In addition to the radioactivity content, charcoal extracts (expired volatiles) were analyzed by GC/MS for parent D_5 (Appendix A and B). The average LOQ was 0.03 µg D_5/hr. Comparison of radioactivity and parent AUCs for D_5 in corn oil showed that all of the radioactivity trapped in charcoal tubes (expired volatiles) could be attributed to the parent D_5 (Figure 8). Average total radioactivity (µg Equivalents D_5/hr) and parent D_5 concentrations (µg D_5/hr) in expired volatiles are presented in Table 13.

In addition to radioactivity content, urine samples collected at 12, 24, 48, 72 and 96 hr were directly analyzed by HPLC/RAD to determine radioactivity profile. The radioactivity eliminated in the urine consisted entirely of polar metabolites of D_5. No parent D_5 was found in any of the urine samples regardless of gender at any of the time points investigated. There were 2 major metabolites common to all of the rats regardless of gender at the time points of 12, 24, 48 and 72 hours. These metabolites have been identified as methylsilanetriol [$CH_3Si(OH)_3$] and dimethylsilanediol ([$(CH_3)_2Si(OH)_2$] based on retention time comparison to urinary metabolite profiles performed previously in a separate HES study No. 8784. No confirmation of identity was conducted within this study. The mean results from the qualitative urinary metabolite profiles can be found in Table 14. This table shows the mean percent of radioactivity that can be attributed to individual metabolites from urine at 12, 24, 48, 72 and 96 hours following exposure. Data showed that methylsilanetriol represented approximately 30-40% of urine metabolites up to 72 hr time point, while at 96 hr it was the only metabolite detected in urine (100%). Dimethylsilanediol represented approximately 45-60% of urine metabolites at 12, 24, 48 and 72 hr, but it was not detected in urine at 96 hr post dosing (0%). Figure 12 shows representative HPLC/RAD chromatograms of 24-hour urine samples from rats dosed with D_5 in corn oil. Individual animal results from the qualitative metabolite profile analysis can be found in Appendix A.

WHOLE BODY AUTORADIOGRAPHY

The whole-body autoradiography portion of this study was performed concurrently with the mass balance and blood kinetic analysis following single, oral dose of ^{14}C-D_5 in corn oil administered to male and female Fischer 344 rats. Individual dosing data are presented in Table 3. All original films were reviewed and evaluated visually for the intensity of radioactivity. Tissues and organs within each animal were rated from highest to lowest as compared to background (Appendix D). Figures in this report are scanned images of the original autoradiographs (Figures 15,16, 17 and 18, and Appendix D). It should be noted that at the earlier time points (3 through 24 hours) the high intensity of radioactivity in the gastrointestinal tract tended to obscure adjacent organs rendering difficulty in visualization. Qualitative assessment of tissue distribution by WBA showed that the

radioactivity was systemically available and distributed to major organs such as bone marrow, liver, and fat. Both sexes showed comparatively similar patterns of disposition at each time point with differences in intensities of some organs and in sex specific organs.

Three hours following dosing, radioactivity was distributed throughout the rats of both sexes. In the female rat the highest concentration of radioactivity was found in the contents of the stomach, cecum, and small intestines and the ethmoturbinates. In the male rat the highest concentrations were also found in the contents of the stomach, cecum, and small intestines, as well as the contents of the urinary bladder. At twelve hours, the female had highest amounts in the contents of the stomach, cecum and brown fat. The male rat also exhibited highest amounts in the contents of the stomach, cecum and small intestines. Twenty-four and forty-eight hours after dose the highest concentrations for both the female and male were seen in the contents of the cecum, and colon and in brown fat. At 96 and 168 hours, both female and male rats had highest levels found only in the brown fat. In addition to the contents of GI tract and brown fat, radioactivity was found at lower concentrations in liver, bone marrow, harderian glands, preputial gland, kidneys and other organs (Table 16 and 17). Whole body autoradiography data supported mass balance data showing that the majority of administered D_5 in corn oil stayed in the GI tract and the majority was excreted in feces over 96 hours, and that a small amount of D_5 was absorbed and distributed to major organs and tissues.

CARRIER EFFECT ON D_5 ORAL ABSORPTION

In addition to corn oil, separate groups of female rats were dosed with ^{14}C-D_5 in simethicone fluid and with neat ^{14}C-D_5 in order to explore possible effects of a carrier on pharmacokinetics of D_5. A group of jugular vein cannulated animals were used to obtain estimates of blood concentrations, and a separate group of rats dosed with ^{14}C-D_5 in corn oil was placed in glass metabolism cages for quantitative assessment of ^{14}C-D_5 excretion and absorption. Rats in the SF control group were dosed with simethicone fluid while rats in neat control group were not dosed.

BLOOD KINETICS

Individual dosing data for animals in blood kinetic groups are presented in Table 5. Radioactivity and parent D_5 concentrations are presented in Table 7 and in Figures 2 and 3. Individual animal values are presented in Appendix B.

The blood curves showed the same trend in distribution and elimination of D_5 when delivered in various carriers but different levels of absorption (Figure 3). Both radioactivity and parent blood

AUCs were significantly different among the three carriers with the largest AUC obtained with D_5 in corn oil ($AUC_{radioactivity}$ =1035.47 μg equivalent D_5 X hr/g and AUC_{parent}=879.50 μg D_5 X hr/g) when compared with neat D_5 ($AUC_{radioactivity}$= 270.46 μg equivalent D_5 X hr/g and AUC_{parent} = 188.00 μg D_5*hr/g) and D_5 in simethicone ($AUC_{radioactivity}$= 85.76 μg equivalent D_5 X hr/g and AUC_{parent} = 54.70 μg D_5 X hr/g). The area under the curve analysis indicated that the D_5 was most readily absorbed when delivered in corn oil and least available for absorption when carried in the simethicone (Figure 2). Also, relative availability data, based on administered dose and parent AUC (Rowland and Tozer, 1989), showed that D_5 delivered in corn oil was 4.8 and 16.2 times more available than when delivered as neat or in simethicone fluid, respectively (Table 8). Review of the simethicone data suggested that statistical difference between radioactivity and parent AUC for D_5 (85.76 *vs.* 54.70 μg D_5 X hr/g) was probably caused by very low levels of D_5, background noise and variability at later time points when D_5 was present at concentrations that were close to LOQ (Appendix B). Average LOQ was determined to be 0.045 μg D_5/g of blood. It is believed that difference between radioactivity and parent AUC does not have biological significance.

Maximum concentration (C_{max}) of total radioactivity and parent D_5 was achieved 6 hr after dosing for D_5 in corn oil and neat D_5, and 12 hr after dosing for D_5 in simethicone (Table 8). Maximum concentrations for both total radioactivity and parent D_5 were highest for corn oil, and lowest for D_5 in simethicone (Radioactivity C_{max}: 46.94, 9.33 and 3.10 μg equivalents D_5/g for D_5 in corn oil, neat D_5 and D_5 in simethicone, respectively; Parent C_{max}: 52.12, 7.94 and 2.13 μg D_5/g for D_5 in corn oil, neat D_5 and D_5 in simethicone, respectively). Distribution half-lives ($T_{1/2}$') for both radioactivity and parent D_5 were in the same range regardless carrier (12.05-16.54 hr for radioactivity, and 8.15-17.16 hr for parent D_5). Elimination half lives ($T_{½}$") ranged between 45.45 hr and 240.36 hr for radioactivity, and between 116.77 and 242.21 for parent D_5 (Table 8).

The blood extracts from samples collected at 6, 12, and 24 hours following dosing by all three carriers were analyzed by HPLC/RAD in order to determine the radioactivity profile. All of the blood extracts analyzed either had no detectable peaks due to the low amount of radioactivity present or they only had one peak, corresponding to parent D_5 based on retention time comparisons (Appendix A), indicating that at early time points parent D_5 is quite similar to total radioactivity.

MASS BALANCE

Following a single, oral dose of ^{14}C-D_5 in simethicone fluid and neat ^{14}C-D_5, animals were placed in glass metabolism cages for collection of expired volatiles, expired CO_2, urine, and feces at predetermined time points (Table 6). Individual dosing data are presented in Table 2. At the terminal sacrifice time point (168 hours post-dosing) liver, lungs, perirenal fat, GI tract, kidney, adrenals, spleen, emptied GI tract, contents of GI tract, reproductive organs (ovaries and testis) and remaining carcasses were collected.

The radioactivity content was measured in all samples, and D_5 concentrations (µg equivalents D_5 per gram or per hour) were calculated based upon specific activity of administered dosing solution. In addition, percent dose recoveries in feces were corrected for the sample-processing efficiencies associated with analysis of the fecal samples. The sample-processing efficiencies were determined for each carrier in a spiking experiment under conditions used to analyze fecal samples (88% for corn oil, 89% for D_5 in simethicone fluid and 94% for neat D_5) as shown in Appendix A. The discrepancy from 100% could be due to the actual efficiency of the solubilization of the fecal samples, but it is more likely due to the process of taking aliquots from the aqueous fecal homogenate samples containing highly lipophilic D_5.

Elimination through GI tract (Dose excreted in feces). The majority of administered dose was excreted in feces regardless of carrier (Table 9, Figure 5). Total radioactivity found in feces, contents of GI tract and cage rinses, was determined to be 80.03 ± 6.18% of administered dose for female rats dosed with D_5 in corn oil, 68.31 ± 4.66% of administered dose for females dosed with D_5 in simethicone, and 84.95 ± 1.28% of administered dose for neat D_5 (Table 9). Cumulative percent dose excreted in feces was not significantly different among the carriers. The majority of administered dose was excreted in feces within 48 hours regardless of carrier (Figure 10 and Appendix B). In addition to radioactivity content, fecal samples were analyzed by GC/MS for the levels of parent D_5. Average LOQ was determined to be 0.36 µg D_5/ g of feces. Average radioactivity and parent D_5 concentrations in feces per time point are presented in Table 12. Statistical analysis showed that there was no significant difference between radioactivity AUC and parent AUC in feces when D_5 was administered in corn oil, simethicone or neat D_5 (Figure 7, Appendix C). Radioactivity found in the contents of GI tract was significantly higher when rats were dosed with D_5 in corn oil in comparison with neat D_5 and D_5 in simethicone fluid. Also contents of GI tract had higher radioactivity content after dosing with neat D_5 in comparison with simethicone fluid.

The feces extracts from samples collected at 12, 24, 48, and 72 hours following dosing by all three carriers were analyzed by HPLC/RAD in order to determine the metabolite profile of the radioactivity present in the feces extracts (Table 15 and Appendix A). The majority of the radioactivity present in all of the feces extracts corresponded to parent D_5 based on retention time comparisons (retention time ~51 minutes). Some of the samples had a small metabolite peak ($\leq$ 6% of the radioactivity in all cases) present that is yet unidentified that eluted fairly close to parent D_5 indicating that it is relatively non-polar (retention time ~45 minutes). Samples of GI contents homogenates were not further analyzed by GC/MSD or by HPLC/RAD because of insufficient level of radioactivity in the homogenates.

Absorption. Absorption of radioactivity, expressed as percent of administered dose (± standard error of the mean) in urine, expired volatiles, expired CO_2, tissues and carcasses, was compared among various carriers. Following administration of D_5 in corn oil, simethicone fluid or neat, absorption was 19.62 ± 4.20%, 25.81 ± 2.26% and 9.94 ± 0.99%, respectively (Table 10, Figure 5). The majority of the absorbed dose was excreted in urine and expired volatiles regardless of carrier as shown in Table 11.

Statistical analysis showed that percent dose recovered in adrenals, lungs, ovaries, fat, spleen, kidneys, liver, and emptied GI tract was significantly higher when rats were dosed with D_5 in corn oil in comparison with D_5 in simethicone fluid but not different from rats dosed with neat D_5 (Appendices B and C). Percent dose recovered in residual carcasses was statistically higher in rats dosed with D_5 in corn oil in comparison with D_5 in simethicone and neat D_5. Overall, rats dosed with D_5 in corn oil had higher percent dose distributed to tissues and carcass (Table 10, Figure 5).

Statistical analysis showed that percent dose recovered in urine (4.37 ± 1.07% of administered dose) and expired CO_2 (0.97 ± 0.15% of administered dose) was significantly higher when rats were dosed with D_5 in corn oil in comparison with D_5 in simethicone fluid (1.04 ± 0.13% of administered dose recovered in urine and 0.23 ± 0.02% of administered dose recovered in CO_2 traps) but not different from rats dosed with neat D_5. The radioactivity eliminated in the urine consisted entirely of polar metabolites of D_5. No parent D_5 was found in any of the urine samples regardless of carrier at any of the time points investigated. The metabolic profiles of the urine collected from the animals dosed with three different dosing carriers did not differ qualitatively. There were 2 major metabolites common to all of the rats regardless of dosing carrier at the time points of 12, 24, 48 and 72 hours. These metabolites have been identified as methylsilanetriol [$CH_3Si(OH)_3$] and dimethylsilanediol ([$(CH_3)_2Si(OH)_2$] based on retention time comparison to urinary metabolite profiles performed previously in a separate HES study No. 8784. No confirmation of identity was

conducted within this study. The mean results from the qualitative urinary metabolite profiles can be found in Table 14. This table shows the mean percent of radioactivity that can be attributed to individual metabolites from urine at 12, 24, 48, 72 and 96 hours following exposure. Up to 72 hr post-dose, methylsilanetriol represented approximately 30-50% of urine metabolites, and dimethylsilanediol represented approximately 45-60% of urine metabolites regardless of carrier. At 96 hr the ratio of the major metabolites in urine was different depending on the carrier. Methylsilanetriol represented 100% of the urine metabolites in corn oil group, and only 16 and 21% in neat and simethicone group, respectively. Ninety-six hours after dosing, dimethylsilanediol was not found in urine of animals dosed with D_5 in corn oil, but it represented 84% and 79% of the urine metabolites in neat and simethicone group, respectively. Figure 13 shows representative HPLC/RAD chromatograms of 96-hour urine samples from rats dosed with neat ^{14}C-D_5, ^{14}C-D_5 in corn oil and simethicone fluid.

Expired volatiles trapped in charcoal tubes were significantly higher in females dosed with ^{14}C-D_5 in simethicone (24.04% of administered dose) in comparison with ^{14}C-D_5 in corn oil (10.37% of administered dose) or neat ^{14}C-D_5 (5.16% of administered dose), as shown in Table 10 and Figure 5. Radioactivity recovered in expired volatiles represents 93% and 52% of the absorbed dose for ^{14}C-D_5 in simethicone and neat ^{14}C-D_5, respectively (Table 11). Parent analysis of charcoal tubes (expired volatiles) by GC/MS showed that all of the radioactivity trapped in charcoal tubes (expired volatiles) regardless of carrier could be attributed to the parent D_5 (Figure 9, Table 12). The average LOQ was 0.03 μg D_5/hr. Less than 1% of administered dose was recovered in tissues and remaining carcass of animals dosed with ^{14}C-D_5 in simethicone fluid, and less than 2% when dosed with neat ^{14}C-D_5.

CONCLUDING DISCUSSION

Review of blood kinetic and mass balance data provided conflicting information on absorption of D_5. Blood AUCs, tissue and carcass levels, radioactivity elimination in urine and CO_2, all indicated highest absorption of D_5 when administered in corn oil and lowest when administered in simethicone fluid. In contrast, when evaluating expired volatiles and overall mass balance data, of which expired volatiles were the main contributor, data suggested increased absorption of D_5 when administered in simethicone fluid, corn oil and neat respectively. Expired volatiles represented approximately 50% of absorption in animals dosed with corn oil and neat D_5, and 93% of absorbed dose in simethicone group (Table 11). During the course of the study it was noticed that simethicone and corn oil at the dose level of approximately 10 ml/ kg of body weight affected

consistency of fecal material causing difficulties in it's collection and removal from the body of the cage. Particularly animals dosed with simethicone fluid had significantly higher occurrence of loose fecal matter at earlier time points that was adhering to the side of the cages. In the rats dosed with ^{14}C-D_5 in the carriers it was also noticed that high radioactivity concentrations in expired volatiles occurred concurrently with the highest concentrations in the excreted fecal material (Figure 10). These observations may indicate that evaporation from the fecal material that remained inside the cage contributed to the radioactivity trapped in the charcoal tubes. Loose consistency of fecal material and considerable amount of fecal material that remained inside the cage might explain high levels of volatiles trapped in charcoal tubes especially with simethicone dosed animals. Cumulative radioactivity in expired volatiles in simethicone dosed rats (24.04% of applied dose) was significantly higher than corn oil (10.37% of applied dose) or neat (5.16% of applied dose). Given that the majority of the orally administered dose was eliminated in feces (Table 9), and that any volatiles that might have escaped from fecal material, which was not frozen and captured as intended, would be trapped in the same charcoal tubes that were used to collect expired volatiles and could potentially give false high values for expired volatiles and consequently high absorption values due to partitioning from the fecal matter into the air. At the same time, the % dose excreted in the feces appeared to be lower for the simethicone dosed rats (68.31% dose) because it was lost from the fecal material that remained inside the body of the cage and ended up in the expired volatile traps. This did not happen to the same extent in other groups where fecal material made it to the collection jar (stored on dry ice) as it is suppose to and volatilization of D_5 was prevented.

Results of a follow-up experiment (HES Study No. 9748) demonstrated that evaporation of ^{14}C-D_5 from the fecal matter that was not frozen and captured in collection jars but remained inside the body of the cage throughout the experiment could significantly contribute to the radioactivity trapped in the charcoal tubes giving false high values for expired volatiles and absorption of D_5.

The data from this study will be evaluated in a physiologically based pharmacokinetic model developed to assess the overall behavior of D_5 in the rat and eventually in humans. Once the model is developed with a base set of data on D_5 from different routes of exposure, including the oral absorption from corn oil (which demonstrated consistency between males and females), the model can be used to assess the data set from the different carriers to provide clarification on the effect of different carriers on relative absorption of D_5.

SUMMARY OF RESULTS

The majority of administered dose, regardless of sex or carrier, was excreted in feces. Approximately 20% of ^{14}C-D_5 delivered in corn oil appeared to be absorbed after single oral administration in Fischer 344 rats. Both sexes showed similar patterns of disposition with the majority of absorbed dose excreted in expired volatiles and urine. Statistical analysis of the blood curves indicated presence of metabolites in the blood. Qualitative assessment of tissue distribution (WBA) showed that the radioactivity was systemically available and distributed to major organs such as bone marrow, liver, kidney and fat. The study indicated that oral absorption of D_5 could be significantly influenced by the carrier used to deliver D_5. Blood kinetics data indicated that D_5 was most readily absorbed when delivered in corn oil and least available for absorption when carried in simethicone fluid.

ARCHIVE

Study related records inclusive of, but not limited to, study authorization, study correspondence, study protocol (including amendments and deviations), signatures of the study personnel involved in the conduct of the study, test article documentation, test system records, equipment verification and condition records, dosing records, sample collection records, sample processing records, films and reference sections for WBA, analytical data, Excel worksheets, and the final report, will be maintained in the archives of Dow Corning Corporation, Health and Environmental Sciences, Midland, MI.

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Table 1. Organization of Test Groups

	Group	Group ID	Sex	Number of animals	Target dose (mg D_5 / kg BW)	Exposure duration/ Sacrifice time points
Part 1 (^{14}C-D_5 in Corn Oil)	1	MB Control (CO) [1]	F	2	N.A. [1]	168 hr
	2	MB Control (CO)[1]	M	2	N.A. [1]	168 hr
	3	MB (CO)	F	4	1000	168 hr
	4	MB (CO)	M	4	1000	168 hr
	5	WBA (CO)	F	6	1000	up to 168 hr[4]
	6	WBA (CO)	M	6	1000	up to 168 hr[4]
	7	BK Control (CO)[1]	F	2	N.A. [1]	24 hr
	8	BK Control (CO)[1]	M	2	N.A. [1]	24 hr
	9	BK (CO)	F	6	1000	168 hr
	10	BK (CO)	M	6	1000	168 hr
Part 2	11	MB control (Neat) [2]	F	2	N.A. [2]	168 hr
	12	MB control (SF) [3]	F	2	N.A. [3]	168 hr
	13	MB (Neat)	F	4	1000	168 hr
	14	MB (SF)	F	4	1000	168 hr
	15	BK Control (Neat) [2]	F	2	N.A. [2]	24 hr
	16	BK Control (SF) [3]	F	2	N.A. [3]	24 hr
	17	BK (Neat)	F	6	1000	168 hr
	18	BK (SF)	F	6	1000	168 hr

[1] Control animals in Part 1 were dosed with pure corn oil

[2] Control animals in Part 2 (neat controls) were not dosed.

[3] Control animals in Part 2 (SF controls) were dosed with simethicone fluid.

[4] Sacrifice time points for rats of each sex in WBA were 3, 12, 24, 48, 96 and 168 hr.

MB = Mass balance group WBA = Whole body autoradiography group

BK = Blood kinetics group BW = Body weight

CO= Corn Oil SF = Simethicone Fluid F=Female M=Male

Table 2. Individual Dosing Data: Part 1 and 2/ Mass Balance Groups

Rat ID	Group	Sex	Dosing Solution[4),5)]	Body weight (g)	Dosing solution (g) / rat	mg D_5 per kg of body weight
C9158	1 (Ctrl)	F	CO[1)]	144.0	1.0959[1)]	0
C9159	1 (Ctrl)	F	CO[1)]	143.8	1.1287[1)]	0
C9160	2 (Ctrl)	M	CO[1)]	224.8	1.8329[1)]	0
C9161	2 (Ctrl)	M	CO[1)]	217.8	1.7725[1)]	0
C9162	3	F	^{14}C-D_5 in CO	143.1	1.0727	938.97
C9163	3	F	^{14}C-D_5 in CO	146.5	1.1243	961.30
C9164	3	F	^{14}C-D_5 in CO	139.6	1.1091	995.17
C9165	3	F	^{14}C-D_5 in CO	143.4	1.1206	978.84
C9166	4	M	^{14}C-D_5 in CO	223.6	1.9041	1066.67
C9167	4	M	^{14}C-D_5 in CO	227.2	1.9168	1056.77
C9168	4	M	^{14}C-D_5 in CO	224.2	1.9273	1076.78
C9169	4	M	^{14}C-D_5 in CO	228.1	1.9383	1064.41
C9198	11 (Ctrl)	F	Not dosed [2)]	140.1	N.A.[2)]	0
C9199	11 (Ctrl)	F	Not dosed [2)]	144.8	N.A. [2)]	0
C9204	12 (Ctrl)	F	Simethicone [3)]	147.4	1.4702[3)]	0[6)]
C9205	12 (Ctrl)	F	Simethicone [3)]	145.7	1.4410[3)]	0[6)]
C9200	13	F	Neat ^{14}C-D_5	147.7	0.1110	751.52
C9201	13	F	Neat ^{14}C-D_5	144.8	0.1685	1163.67
Q0004	13	F	Neat ^{14}C-D_5	160.6	0.1512	941.47
C9203	13	F	Neat ^{14}C-D_5	153.5	0.1457	949.19
C9206	14	F	^{14}C-D_5 in SF	141.4	1.1899	820.22
C9207	14	F	^{14}C-D_5 in SF	146.2	1.5360	1024.04
C9208	14	F	^{14}C-D_5 in SF	151.0	1.4373	927.77
C9209	14	F	^{14}C-D_5 in SF	151.1	1.5147	977.09

[1)] Rats in control groups 1 and 2 were dosed with pure corn oil. [2)] Rats in control group 11 were not dosed. [3)] Rats in control group 12 were dosed with simethicone fluid. [4)] D_5 concentration in corn oil (CO) dosing solution: 125.26 mg/g of dosing solution. [5)] D_5 concentration in simethicone (SF) dosing solution: 97.47 mg/g of dosing solution. [6)] Observed concentration of D_5 in SF was 5.5 ppm (0.00055%).

Table 3. Individual Dosing Data: Part 1/ Whole Body Autoradiography

Rat ID	Group	Sex	Dosing Solution[1]	Body weight	Dosing solution (g) / rat	mg D_5 per kg of body weight
C9170	5	F	^{14}C-D_5 in CO	134.7	0.9694	901.46
C9171	5	F	^{14}C-D_5 in CO	139.2	1.0525	947.10
C9172	5	F	^{14}C-D_5 in CO	143.9	1.0810	940.97
C9173	5	F	^{14}C-D_5 in CO	143.4	1.0520	918.92
C9174	5	F	^{14}C-D_5 in CO	139.1	1.0372	934.00
C9175	5	F	^{14}C-D_5 in CO	149.7	1.1077	926.86
C9176	6	M	^{14}C-D_5 in CO	223.2	1.8890	1060.11
C9177	6	M	^{14}C-D_5 in CO	221.0	1.8800	1065.56
C9178	6	M	^{14}C-D_5 in CO	226.2	1.9620	1086.47
C9179	6	M	^{14}C-D_5 in CO	231.2	1.9946	1080.64
C9180	6	M	^{14}C-D_5 in CO	225.9	1.8940	1050.21
C9181	6	M	^{14}C-D_5 in CO	231.6	1.9397	1049.08

[1)] D_5 concentration in corn oil (CO) dosing solution: 125.26 mg/g of dosing solution

Table 4. Individual Dosing Data: Blood Kinetics/ D_5 in Corn Oil (Part 1)

Rat ID	Group	Sex	Dosing Solution[1)]	Body weight (g)	Dosing solution (g) / rat	mg D_5 per kg of body weight
C9182	7	F	CO	148.1	1.1623	0
Q0041	7	F	CO	160.4	1.2191	0
C9184	8	M	CO	210.9	1.5769	0
C9185	8	M	CO	200.7	1.4826	0
C9186	9	F	^{14}C-D_5 in CO	148.8	1.2834	1080.37
C9187	9	F	^{14}C-D_5 in CO	153.7	1.2170	991.81
C9188	9	F	^{14}C-D_5 in CO	155.3	1.2264	989.17
C9189	9	F	^{14}C-D_5 in CO	151.4	1.2120	1002.74
C9190	9	F	^{14}C-D_5 in CO	155.4	1.1838	954.20
C9191	9	F	^{14}C-D_5 in CO	154.7	1.2759	1033.09
C9192	10	M	^{14}C-D_5 in CO	214.4	1.7205	1005.18
C9193	10	M	^{14}C-D_5 in CO	208.4	1.6409	986.27
C9194	10	M	^{14}C-D_5 in CO	211.4	1.7280	1023.88
C9195	10	M	^{14}C-D_5 in CO	222.3	1.7669	995.60
C9196	10	M	^{14}C-D_5 in CO	212.9	1.7713	1042.15
Q0037	10	M	^{14}C-D_5 in CO	210.7	1.7803	1058.38

[1)] D_5 concentration in corn oil (CO) dosing solution: 125.26 mg/g of dosing solution

Part 1: Rats in MB, WBA and BK exposure groups dosed with ^{14}C-D_5 in corn oil received an average dose of 1008 mg D_5 per kg of body weight delivered in 8 g dosing solution per kg of body weight.

Table 5. Individual Dosing Data: Blood Kinetics/ D_5 Neat and D_5 in Simethicone Fluid (Part 2)

Rat ID	Group	Sex	Dosing Solution	Body weight	Dosing solution (g) / rat	mg D_5 per kg of body weight
C9210	15	F	N.A.	141.8	0	0
C9211	15	F	N.A.	134.6	0	0
C9218	16	F	Simethicone	136.2	1.2984	0
C9219	16	F	Simethicone	147.3	1.4624	0
C9212	17	F	Neat ^{14}C-D_5	123.4	0.0861	697.73
C9213	17	F	Neat ^{14}C-D_5	126.8	0.1492	1176.66
C9214	17	F	Neat ^{14}C-D_5	149.0	0.1461	980.54
C9215	17	F	Neat ^{14}C-D_5	138.4	0.1623	1172.69
C9216	17	F	Neat ^{14}C-D_5	135.9	0.1640	1206.77
C9217	17	F	Neat ^{14}C-D_5	142.5	0.1432	1004.91
C9220	18	F	^{14}C-D_5 in SF[1)]	139.1	1.4429	1011.07
C9221	18	F	^{14}C-D_5 in SF	129.5	1.4435	1086.47
C9222	18	F	^{14}C-D_5 in SF	142.2	1.4487	993.001
C9223	18	F	^{14}C-D_5 in SF	140.1	1.4653	1019.43
C9224	18	F	^{14}C-D_5 in SF	144.7	1.4790	996.26
C9225	18	F	^{14}C-D_5 in SF	143.2	1.4637	996.28

[1)] D_5 concentration in simethicone fluid (SF) dosing solution: 97.47 mg/g of dosing solution

Part 2: Rats in MB and BK exposure groups dosed with neat ^{14}C-D_5 received an average dose of 1004 mg D_5 per kg of body weight. Rats in MB and BK exposure groups dosed with ^{14}C-D_5 in simethicone fluid received an average dose of 985 mg D_5 per kg of body weight delivered in 10 g of dosing solution per kg of body weight.

Table 6. Sample Collection Time Points

Groups	Exposure duration (hr)	Expired air (hr)	Urine (hr)	Feces (hr)	CO_2 (hr)	Tissues/ Carcasses (hr)
MB: 1, 2, 11,12 (Control)	N.A.*	24, 48, 72, 96, 120, 144, 168	24, 48, 72, 96, 120, 144, 168	24, 48, 72, 96, 120, 144, 168	24, 48, 72, 96, 120, 144, 168	168[1)]
MB: 3,4,13, 14	168	1, 2, 4, 6, 12, 24, 48, 72, 96, 120, 144, 168	6,12,24,48, 72, 96, 120, 144, 168	6,12,24,48, 72, 96, 120, 144, 168	24, 48, 72, 96, 120, 144, 168	168[1)]
WBA: 5, 6	Up to 168	-	-	-	-	3, 12, 24, 48, 96, 168[2)]
BK: 7, 8, 15, 16 (Control)	N.A.*	-	-	-	-	24[3)]
BK: 9, 10, 17, 18	168	N.A.	N.A.	N.A.	N.A.	Up to 168[4)]

*N.A. (not applicable) = Control rats in groups 1,2, 7 and 8 were dosed with pure control oil, rats in group 11 and 15 were not dosed, and control rats in group 12 and 16 were dosed with simethicone fluid.

[1)] Tissues collected in MB groups at sacrifice time points: liver, lungs, perirenal fat, emptied GI tract, kidneys, spleen, and reproductive organs (ovaries and testis).

[2)] Carcasses collected at sacrifice time point, frozen, embedded in 4% carboxymethylcellulose, and blocks stored at - 80°C.

[3)] Blood collected at 24 hr time point.

[4)] Blood collected 15 min, 60 min, and 6, 12, 24, 48, 72, 96, 120, 144 and 168 hr post-dosing.

Table 7. Blood Radioactivity Concentration *vs.* Parent D_5 in Fischer Rats Following Single, Oral Administration of ^{14}C-D_5 in Various Carriers

	Females						Males	
	D_5 in CO[1)]		D_5 Neat [2)]		D_5 in SF [3)]		D_5 in CO (n=6)	
Time Point	Radioactivity (µg Eq. D_5/g±SEM)	Parent (µg D_5/g±SEM)	Radioactivity (µg Eq. D_5/g±SEM)	Parent (µg $D_5$5/g±SEM)	Radioactivity (µg Eq. D_5/g±SEM)	Parent (µg D_5/g±SEM)	Radioactivity (µg Eq. D_5/g±SEM)	Parent (µg D_5/g±SEM)
15 min	0.241±0.081	0.215±0.042	0.133±0.044	0.093±0.037	0.025±0.016	0.000±0.000	0.129±0.039	0.202±0.035
1 hr	4.784±0.478	5.310±0.407	2.185±0.475	1.928±0.470	0.434±0.098	0.395±0.065	5.222±0.577	6.226±0.754
6 hr	46.936±9.783	52.121±8.972	9.328±0.846	7.943±0.708	2.168±0.392	1.578±0.308	51.149±2.930	62.490±4.261
12 hr	30.809±4.039	34.753±6.148	5.585±1.224	4.080±1.149	3.097±0.479	2.134±0.385	40.176±2.315	44.975±4.032
24 hr	13.718±1.489	10.185±1.396	5.790±3.547	4.023±3.088	1.393±0.311	0.612±0.227	16.815±2.000	11.517±1.980
48 hr	4.114±0.690	1.541±0.303	1.292±0.611	0.487±0.180	0.348±0.070	0.165±0.024	2.867±0.335	0.952±0.140
72 hr	1.611±0.155	0.593±0.060	0.481±0.179	0.242±0.03	0.205±0.046	0.173±0.043	1.038±0.142	0.285±0.035
96 hr	1.485±0.304	0.479±0.063	0.409±0.103	0.206±0.042	0.108±0.018	0.094±0.007	1.918±1.121	0.227±0.034
120 hr	0.793±0.214	0.447±0.060	0.243±0.163	0.152±0.031	0.115±0.046	0.087±0.026	0.579±0.097	0.190±0.030
144 hr	2.561±1.333	0.549±0.115	0.252±0.100	0.209±0.011	0.112±0.012	0.082±0.011	0.709±0.130	0.186±0.041
168 hr	0.868±0.278	0.331±0.109	0.152±0.104	0.118±0.015	0.032±0.032	0.101±0.011	0.613±0.116	0.191±0.049

[1)] 15 min-96 hr : n=6; 120 hr: n=5; 144 hr: n=4; 168 hr: n=3
[2)] 15 min-1 hr: n=6; 6-96 hr: n=5; 120-168 hr: n=3
[3)] 15min-120 hr: n= 6; 144 hr: n=5; 168 hr: n=6

Table 8. Summary of Pharmacokinetic Parameters in Blood from Fischer 344 Rats Following Single, Oral Administration of ^{14}C-D_5 in various carriers

Pharmacokinetics Parameters	Females			Males
	D_5 in CO	D_5 Neat	D_5 in SF	D_5 in CO
Radioactivity AUC (µg Eq. D_5 X hr/g)	1035.47$^{+\dagger}$	270.46†	85.76$^{+\dagger}$	1121.48^{+}
C_{max} (µg Eq.D_5/g)	46.94	9.33	3.10	51.15
T_{max} (hr post-dosing)	6	6	12	6
$T_{½}$' (hr)	Distribution = 12.05	Distribution = 15.68	Distribution = 16.54	Distribution = 9.88
$T_{½}$" (hr)	Elimination = 240.36	Elimination = 59.62	Elimination = 45.45	Elimination = 81.15
Parent AUC (µg D5 X hr/g)	879.50$^{+*\dagger}$	188.00†	54.70$^{+\dagger}$	1014.50^{+*}
C_{max} (µg D5/g)	52.12	7.94	2.13	62.49
T_{max} (hr post-dosing)	6	6	12	6
$T_{½}$' (hr)	Distribution = 8.15	Distribution = 11.00	Distribution = 17.16	Distribution = 6.78
$T_{½}$" (hr)	Elimination = 160.91	Elimination = 116.77	Elimination = 242.21	Elimination = 166.80
Relative Availability [1] in females			**Relative Availability [1)]**	
CO *vs.* Neat	4.8		Males *vs.* Females (CO)	1.1
CO *vs.* Simethicone	16.2			
Neat *vs.* Simethicone	3.4			

$^{+}$ Statistically significant difference between parent and radioactivity at α=0.05

* Statistically significant difference between sexes at α=0.05

† Statistically significant difference between carriers at α=0.05

[1)] Relative availability = (Parent AUC_A/Parent AUC_B)*($Dose_B$/$Dose_A$)

Table 9. Disposition of Radioactivity in Fischer 344 Rats Following Oral Administration of ^{14}C-D_5 Neat and in Various Carriers

Percent of Administered Dose ± Standard Error of the Mean

N/sex	Dosing solution	Average Dose (mg D_5/kg BW)	Absorbed[1)] (% Dose)	Eliminated through GI tract [2),3)] (% Dose)	Total recovered (% Dose)
Group 3 3/F	^{14}C-D_5 in CO	968.57	19.62 ± 4.20	80.03 ± 6.18	99.65 ± 2.66
Group 4 4/M	^{14}C-D_5 in CO	1066.16	21.82 ± 4.37	81.43 ± 5.91	103.24 ± 2.02
Group 13 3/F	^{14}C-D_5 Neat	951.46	9.94† ± 0.99	84.95 ± 1.28	94.88 ± 2.07
Group 14 3/F	^{14}C-D_5 in SF	937.28	25.81† ± 2.26	68.31 ± 4.66	94.13 ± 2.72

[1)] **Absorbed radioactivity** = Percent of administered dose recovered in urine, expired volatiles (charcoal tubes), CO_2 (KOH traps), tissues and remaining carcass (as defined in Table 8)

[2)] **Radioactivity eliminated through GI tract = Radioactivity excreted in feces =** Percent of administered dose recovered in feces, contents of GI tract and cage rinse.

[3)] Percent dose recovered in feces was corrected for the fecal sample processing efficiency: 88% for D_5 in Corn oil, 94% for neat D_5, and 89% for D_5 in simethicone fluid.

† Statistically significant difference between D_5 in simethicone and neat D_5 at $\alpha = 0.05$

Table 10. Disposition of Absorbed Radioactivity in Fischer 344 Rats Following Oral Administration of ^{14}C-D_5 In Various Carriers

Percent of administered dose ± Standard error of the Mean

N/Sex	Dosing Solution	Urine	Expired Volatiles	CO_2 (KOH)	Tissues[1)]	Remaining Carcass	Total Absorbed[2)]
Group 3 3/F	D_5 in CO	4.37* ± 1.07	10.37* ± 2.91	0.97* ± 0.15	0.49* ± 0.13	3.43*+ ± 0.45	19.62 ± 4.20
Group 4 4/M	D_5 in CO	4.70 ± 0.38	13.36 ± 4.76	0.92 ± 0.12	0.38 ± 0.09	2.46 ± 0.18	21.82 ± 4.37
Group 13 3/F	D_5 Neat	2.39 ± 0.55	5.16† ± 1.20	0.56 ± 0.15	0.20 ± 0.05	1.64+ ± 0.43	9.94† ± 0.99
Group 14 3/F	D_5 in SF	1.04* ± 0.13	24.04*† ± 2.14	0.23* ± 0.02	0.06* ± 0.00	0.45* ± 0.04	25.81† ± 2.26

[1)] **Tissues** collected at the sacrifice time point (168 hr post dosing): blood, liver, lungs, sample of perirenal fat, GI tract emptied of it's contents, kidney, adrenals, spleen and reproductive organs (ovaries or testis)

[2)] **Absorbed radioactivity** = Percent of administered dose recovered in urine, expired volatiles (charcoal tubes), CO_2 (KOH traps), tissues and remaining carcass. In Groups 3 and 4, 75% and 83% of the absorbed dose was excreted in expired air and urine. In Groups 13 and 14, 76% and 97% of the absorbed dose was excreted in expired air and urine.

* Statistically significant difference between D_5 in corn oil and simethicone fluid at $\alpha = 0.05$

+ Statistically significant difference between D_5 in corn oil and neat D_5 at $\alpha = 0.05$

† Statistically significant difference between D_5 in simethicone fluid and neat D_5 at $\alpha = 0.05$

Table 11. Distribution of the Total Absorbed Dose Following Oral Administration of ^{14}C-D_5 in Various Carriers

Percent of the total absorbed dose

N/Sex	Dosing Solution	Urine (%)	Expired Volatiles (%)	CO_2 (KOH) (%)	Tissues (%)	Remaining Carcass (%)
Group 3 3/F	D_5 in CO	22.24	52.84	4.93	2.50	17.48
Group 4 4/M	D_5 in CO	21.53	61.23	4.22	1.75	11.27
Group 13 3/F	D_5 Neat	24.00	51.91	5.65	1.97	16.42
Group 14 3/F	D_5 in SF	4.02	93.13	0.90	0.21	1.73

CO = corn oil SF = simethicone fluid

Table 12. Radioactivity *vs.* Parent D_5 Concentration in Feces of Fischer Rats Following Single, Oral Administration of ^{14}C-D_5 in Various Carriers

	Females						Males	
	D_5 in CO (n=3)		D_5 Neat (n=3)		D_5 in SF (n=3)		D_5 in CO (n=4)	
Time Point	Radioactivity (µg Equiv.D_5/g ±SEM)	Parent (µg D_5/g±SEM)	Radioactivity (µg Equiv.D_5/g ±SEM)	Parent (µg D_5/g ±SEM)	Radioactivity (µg Equiv.D_5/g ±SEM)	Parent (µg D_5/g±SEM)	Radioactivity (µg Equiv.D_5/g ±SEM)	Parent (µg D_5/g ±SEM)
6 hr	0.89±0.63	0.49±0.49	8.82±3.50	8.37±3.72	4055.61±1509.54	4397.60±1627.61	1.48±0.82	1.48±1.10
12 hr	694.71±681.59	1165.20±1151.14	10016.69±6368.76	9665.22±5986.74	11123.74±2746.33	11067.66±1710.20	1814.42±1556.67	1911.41±1894.93
24 hr	19524.90±4918.76	19142.84±5307.91	28270.04±2553.70	23332.70±2147.07	12104.29±1705.60	11133.75±1560.52	19971.48±4179.88	21818.20±5517.62
48 hr	9510.47±3082.54	11857.22±4891.26	7906.15±2373.61	7780.50±2430.36	4283.03±1664.00	4283.65±1697.24	11282.64±1285.55	12075.78±1409.61
72 hr	802.38±216.54	1410.07±913.34	501.56±153.65	420.94±161.09	283.91±188.94	218.07±151.52	1368.98±343.22	1319.62±341.10
96 hr	54.43±16.11	17.55±5.05	253.49±217.78	213.24±204.01	76.03±55.02	57.19±47.11	126.13±50.99	63.04±30.88
120 hr	43.61±12.77	1.18±0.45	14.10±5.01	0.70±0.14	6.38±0.56	0.61±0.34	29.15±4.60	2.68±1.43
144 hr	21.96±2.70	0.76±0.32	7.07±0.73	0.00±0.00	2.83±0.07	0.15±0.15	19.01±2.58	2.78±2.26
168 hr	43.47±23.97	23.73±22.55	133.35±124.45	118.11±118.11	2.95±0.56	0.13±0.13	22.66±8.37	4.15±3.81

Table 13. Radioactivity *vs.* Parent D_5 Concentration in Charcoal Tubes (Expired Volatiles) of Fischer Rats Following Single, Oral Administration of ^{14}C-D_5 in Various Carriers

	Females						Males	
	D_5 in CO (n=3)		D_5 Neat (n=3)		D_5 in SF (n=3)		D_5 in CO (n=4)	
Time Point	Radioactivity (µg Eq.D_5/hr ±SEM)	Parent (µg D_5/hr ±SEM)	Radioactivity (µg Eq.D_5/hr ±SEM)	Parent (µg D_5/hr ±SEM)	Radioactivity (µg Eq.D_5/hr ±SEM)	Parent (µg D_5/hr ±SEM)	Radioactivity (µg Eq.D_5/hr ±SEM)	Parent (µg D_5/hr±SEM)
1 hr	45.30±39.67	47.13±40.12	298.47±287.56	279.75±271.26	3.47±3.35	2.27±2.27	98.67±53.82	98.59±57.16
2 hr	7.86±1.97	7.32±2.03	40.30±30.25	33.30±25.45	72.68±47.17	63.50±41.86	10.59±2.89	6.92±2.47
4 hr	25.01±2.47	21.68±2.71	330.65±295.49	286.43±257.22	2459.60±476.63	2102.70±385.99	25.75±1.34	21.44±1.20
6 hr	48.32±2.36	41.85±2.16	140.56±112.87	124.08±103.61	2152.35±430.34	1868.02±336.85	50.27±2.09	44.05±2.10
12 hr	264.34±204.36	246.28±190.29	49.74±20.51	64.59±40.49	2232.16±18.65	1957.67±142.03	213.38±151.89	199.08±136.98
24 hr	940.11±175.70	1063.34±303.80	121.78±66.97	112.17±61.21	606.55±203.21	560.69±185.98	1796.24±813.05	2679.43±1575.51
48 hr	50.24±30.81	49.40±28.58	80.47±41.90	76.07±40.48	58.81±36.05	54.43±34.04	327.67±155.48	392.53±197.69
72 hr	5.74±1.05	5.14±0.63	58.16±27.84	55.67±26.72	19.06±14.36	17.59±13.56	39.80±25.73	38.71±26.29
96 hr	2.38±0.35	2.21±0.33	25.37±13.41	23.27±12.29	10.76±8.42	9.78±7.80	3.01±0.43	2.48±0.18
120 hr	1.04±0.57	1.04±0.56	6.03±5.33	5.34±4.78	1.54±0.96	1.26±0.85	1.32±0.31	1.16±0.18
144 hr	0.88±0.15	0.81±0.14	1.90±1.54	1.67±1.41	0.88±0.729	0.70±0.66	0.91±0.27	0.73±0.17
168 hr	0.81±0.16	0.82±0.18	2.53±2.23	2.15±1.94	0.47±0.37	0.35±0.30	0.70±0.15	0.69±0.10

CO = corn oil SF = simethicone fluid

Table 14. Summary of Urinary Metabolites as Percentages of the Total Urinary Radioactivity Following Single, Oral Administration of ^{14}C-D_5

	De-Methylated % of Methylsilanetriol	De-Methylated % of Dimethyl-disiloxane-1,3,3,3-tetrol	De-Methylated % of Dimethyl-disiloxane-1,1,3,3-tetrol	% of Dimethyl-silanediol	De-Methylated % of 1,3,3-Trimethyl-disiloxane-1,1,3-triol	% of 1,1,3,3-Tetramethyl-disiloxane-1,3-diol	% of 1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Sum of De-methylated Peak Percentages
12 Hour Male CO	38% ± 5%	9% ± 1%	0% ± 0%	45% ± 4%	5% ± 3%	3% ± 3%	0% ± 0%	52% ± 5%
12 Hour Female CO	35% ± 3%	9% ± 8%	0% ± 0%	50% ± 11%	0% ± 0%	4% ± 7%	3% ± 5%	43% ± 6%
12 Hour Female Neat	39% ± 6%	0% ± 0%	0% ± 0%	57% ± 6%	0% ± 0%	4% ± 8%	0% ± 0%	39% ± 6%
12 Hour Female SF	43% ± 5%	0% ± 0%	0% ± 0%	57% ± 5%	0% ± 0%	0% ± 0%	0% ± 0%	43% ± 5%
24 Hour Male CO	32% ± 1%	9% ± 1%	2% ± 1%	48% ± 4%	5% ± 1%	3% ± 0%	0% ± 1%	48% ± 3%
24 Hour Female CO	31% ± 1%	10% ± 0%	0% ± 1%	46% ± 11%	6% ± 0%	5% ± 1%	0% ± 0%	48% ± 1%
24 Hour Female Neat	32% ± 2%	9% ± 2%	0% ± 0%	51% ± 6%	2% ± 3%	5% ± 1%	0% ± 0%	43% ± 4%
24 Hour Female SF	35% ± 4%	5% ± 6%	0% ± 0%	59% ± 5%	0% ± 0%	1% ± 3%	0% ± 0%	**39% ± 3% ***
48 Hour Male CO	29% ± 1%	11% ± 0%	2% ± 0%	53% ± 1%	3% ± 1%	2% ± 0%	0% ± 0%	45% ± 1%
48 Hour Female CO	29% ± 2%	11% ± 2%	2% ± 1%	52% ± 3%	3% ± 2%	3% ± 2%	0% ± 0%	45% ± 1%
48 Hour Female Neat	30% ± 3%	11% ± 1%	1% ± 1%	55% ± 5%	1% ± 1%	1% ± 2%	0% ± 0%	43% ± 4%
48 Hour Female SF	35% ± 3%	7% ± 8%	0% ± 0%	58% ± 6%	0% ± 0%	0% ± 0%	0% ± 0%	42% ± 6%
72 Hour Male CO	35% ± 1%	10% ± 2%	0% ± 0%	55% ± 3%	0% ± 0%	0% ± 0%	0% ± 0%	**45% ± 3% ***
72 Hour Female CO	29% ± 2%	9% ± 1%	0% ± 1%	58% ± 5%	1% ± 2%	2% ± 2%	0% ± 0%	39% ± 4%
72 Hour Female Neat	35% ± 4%	3% ± 6%	0% ± 0%	62% ± 3%	0% ± 0%	0% ± 0%	0% ± 0%	38% ± 3%
72 Hour Female SF	50% ± 34%	4% ± 7%	0% ± 0%	47% ± 31%	0% ± 0%	0% ± 0%	0% ± 0%	53% ± 31%
96 Hour Male CO	100% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	100% ± 0%
96 Hour Female CO	100% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	100% ± 0%
96 Hour Female Neat	16% ± 19%	0% ± 0%	0% ± 0%	84% ± 19%	0% ± 0%	0% ± 0%	0% ± 0%	**16% ± 19% ***
96 Hour Female SF	21% ± 29%	0% ± 0%	0% ± 0%	79% ± 29%	0% ± 0%	0% ± 0%	0% ± 0%	21% ± 29%

* indicates statistical difference when compared to female corn oil dosed animals ($p < 0.05$)

Table 15. Summary of Fecal Metabolites as Percentages of the Total Fecal Radioactivity

Timepoint/Sex/Carrier	% Unknown Metabolite	% of Decamethylcyclopentasiloxane (D_5 parent)
12 Hour /Male/CO	0% N.A.	100% N.A.
12 Hour /Female/CO	0% N.A.	100% N.A.
12 Hour /Female/Neat	0% ± 0%	100% ± 0%
12 Hour /Female/SF	0% ± 0%	100% ± 0%
24 Hour/Male/CO	3% ± 1%	97% ± 1%
24 Hour/Female/CO	1% ± 1%	99% ± 1%
24 Hour/Female/Neat	0% ± 0%	100% ± 0%
24 Hour/Female/SF	0% ± 0%	100% ± 0%
48 Hour/Male/CO	4% ± 1%	96% ± 1%
48 Hour/Female/CO	2% ± 2%	98% ± 2%
48 Hour/Female/Neat	1% ± 1%	99% ± 1%
48 Hour/Female/SF	0% ± 0%	100% ± 0%
72 Hour/Male/CO	0% ± 0%	100% ± 0%
72 Hour/Female/CO	0% ± 0%	100% ± 0%
72 Hour/Female/Neat	0% ± 0%	100% ± 0%
72 Hour/Female/SF	0% ± 0%	100% ± 0%

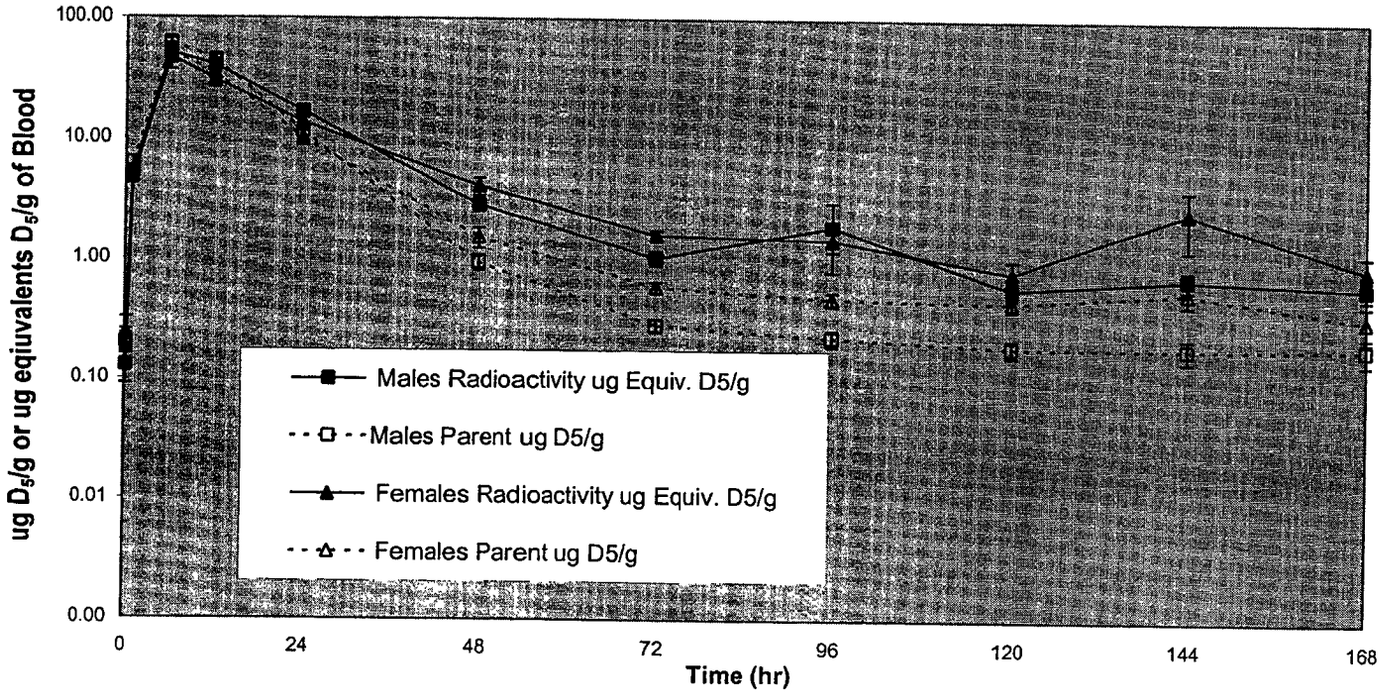
Table 16. Individual Qualitative Radioactive Concentrations in Male Fischer 344 Rats (WBA)

Animal	Time point	Highest Radioactive Conc.	Moderate Radioactive Conc.	Low Radioactivity Conc. (slightly above background)
C9176	3 hour	stomach/contents cecum/contents small intestine/contents bladder/contents	skin fat brown fat	liver seminal vesicle skeletal muscle bone marrow
C9177	12 hour	stomach/contents cecum/contents small intestine/contents	bladder/contents liver fat brown fat skin bone marrow harderian gland	eye (lens) seminal vesicle skeletal muscle epiglottis/soft palette
C9178	24 hour	cecum/contents colon/feces brown fat	liver fat skin bone marrow small intestine/contents	preputial gland Harderian gland spleen (red pulp) myocardium kidney (cortex) bladder/contents hard palette
C9179	48 hour	cecum/contents colon/feces brown fat	liver fat bone marrow	preputial gland skin Harderian gland spleen (red pulp) myocardium kidney (cortex) tongue lungs (speckled)
C9180	96 hour	brown fat	liver bone marrow skin fat	cecum/contents colon/feces preputial gland harderian gland spleen (red pulp) myocardium
C9181	168 hour	brown fat	liver bone marrow fat skin preputial gland	spleen (red pulp) myocardium

Table 17. Individual Qualitative Radioactive Concentrations in Female Fischer 344 Rats (WBA)

Animal	Time point	Highest Radioactivity Conc.	Moderate Radioactivity Conc.	Low Radioactivity Conc. (slightly above background)
C9170	3 hour	stomach/contents cecum/contents small intestine/contents ethmoturbinates	liver fat brown fat skin bone marrow	lung myocardium
C9171	12 hour	stomach/contents cecum/contents brown fat	liver fat skin bone marrow tongue esophagus ethmoturbinates	myocardium kidney (cortex) skeletal muscle eye (lens) Harderian gland
C9172	24 hour	cecum/contents colon/feces brown fat	liver fat skin bone marrow small intestine/contents	stomach/contents Harderian gland myocardium kidney (cortex) esophagus
C9173	48 hour	cecum/contents colon/feces brown fat	liver fat bone marrow	kidney (cortex) adrenal (cortex) Harderian gland skin tongue myocardium spleen (red pulp) ovarian structures(cyclical)
C9174	96 hour	brown fat	liver fat bone marrow colon/feces	cecum/contents skin myocardium spleen (red pulp) ovarian structures(cyclical) tongue
C9175	168 hour	brown fat	fat liver bone marrow	cecum/contents skin myocardium spleen (red pulp) ovarian structures(cyclical)

Figure 1. Blood Radioactivity Concentration and Blood Parent D_5 Concentration *vs.* Time in Male and Female Fischer Rats Following Single, Oral Administration of ^{14}C-D_5 in Corn Oil



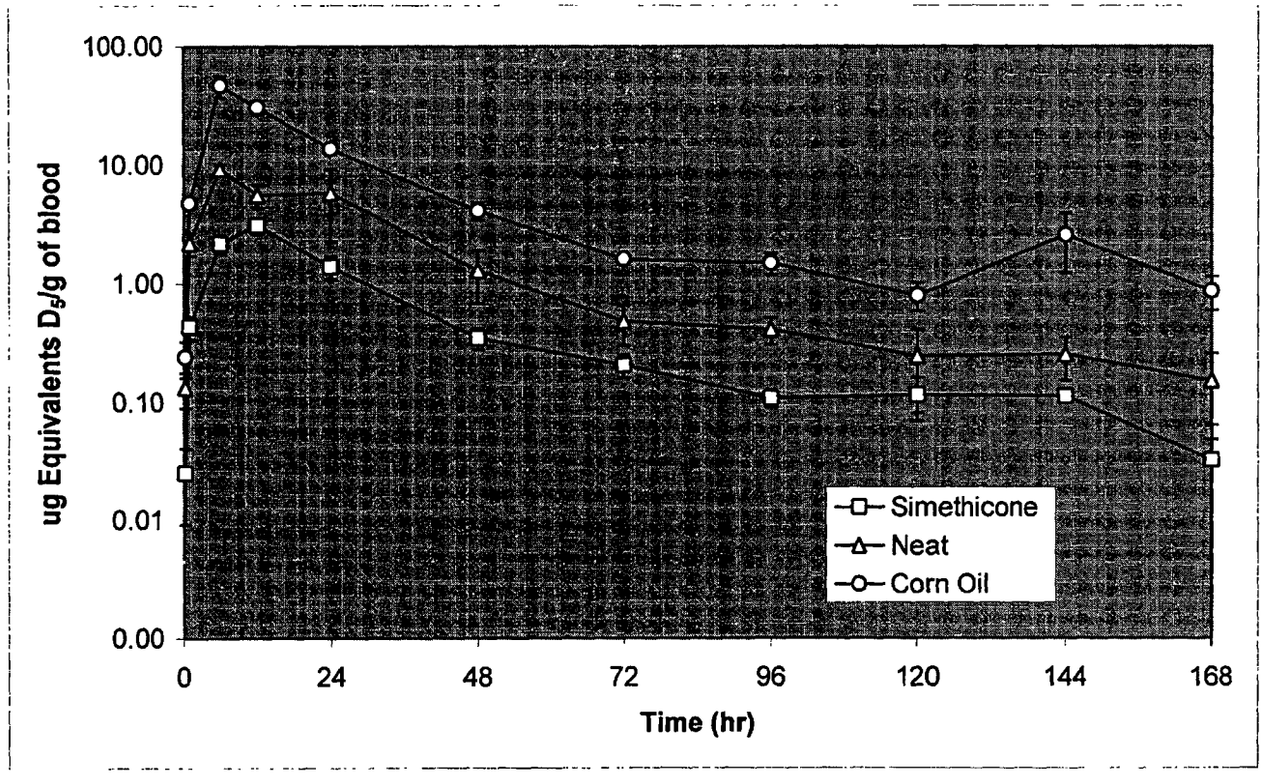
Areas Under The Blood Curves
(μg ^{14}C-Equivalents D_5 X hr/g or μg D_5 X hr/g)

Males
Radioactivity = 1121.48 ± 52.74
D_5 Parent = 1014.50 ± 56.13

Females
Radioactivity = 1035.47 ± 78.86
D_5 Parent = 879.50 ± 78.58

Data expressed as mean ± standard error of the mean

Figure 2. Blood Radioactivity Concentration *vs.* Time in Female Fischer Rats Following Single Oral Administration of ^{14}C-D_5 in Various Carriers



Areas Under The Blood Curves
(μg ^{14}C-Equivalents D_5 X hr/g)

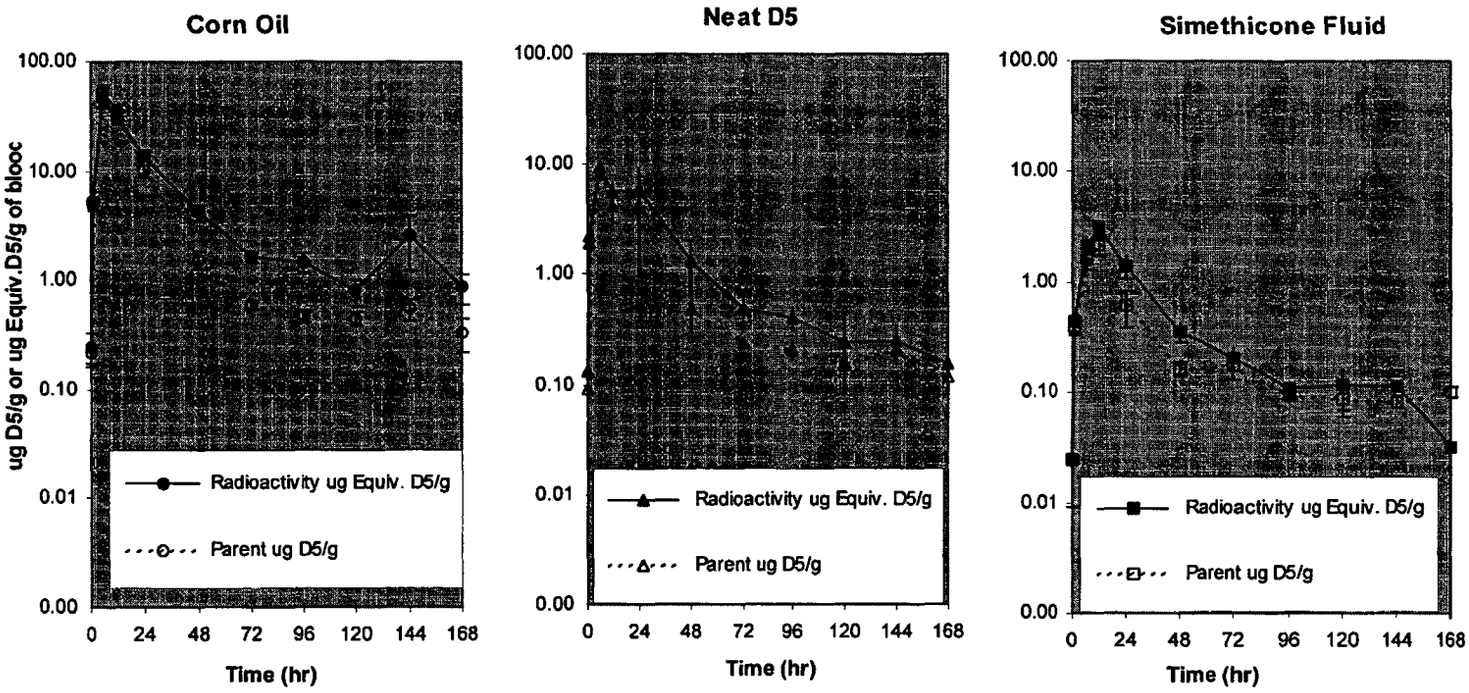
Corn Oil
Radioactivity = 1035.47 ± 78.86

Neat D_5
Radioactivity = 270.46 ± 66.25

Simethicone Fluid
Radioactivity = 85.76 ± 7.68

Data expressed as mean ± standard error of the mean

Figure 3. Comparison of Blood Radioactivity Concentration with Blood Parent D_5 Concentration *vs.* Time in Female Fischer Rats Following Single Oral Administration of ^{14}C-D_5 in Various Carriers



Areas Under The Blood Curves
(μg ^{14}C-Equivalents D_5 X hr/g or μg D_5 X hr/g)

Corn Oil
Radioactivity =1035.47 ± 78.86
Parent = 879.50 ± 78.58

Neat D_5
Radioactivity = 270.46 ± 66.25
Parent = 188.00 ± 56.79

Simethicone Fluid
Radioactivity = 85.76 ± 7.68
Parent = 54.70 ± 5.78

Data expressed as mean ± standard error of the mean

Figure 4. Disposition of Radioactivity in Female and Male Fischer 344 Rats Following Single Oral Dose of ^{14}C-D_5 in Corn Oil

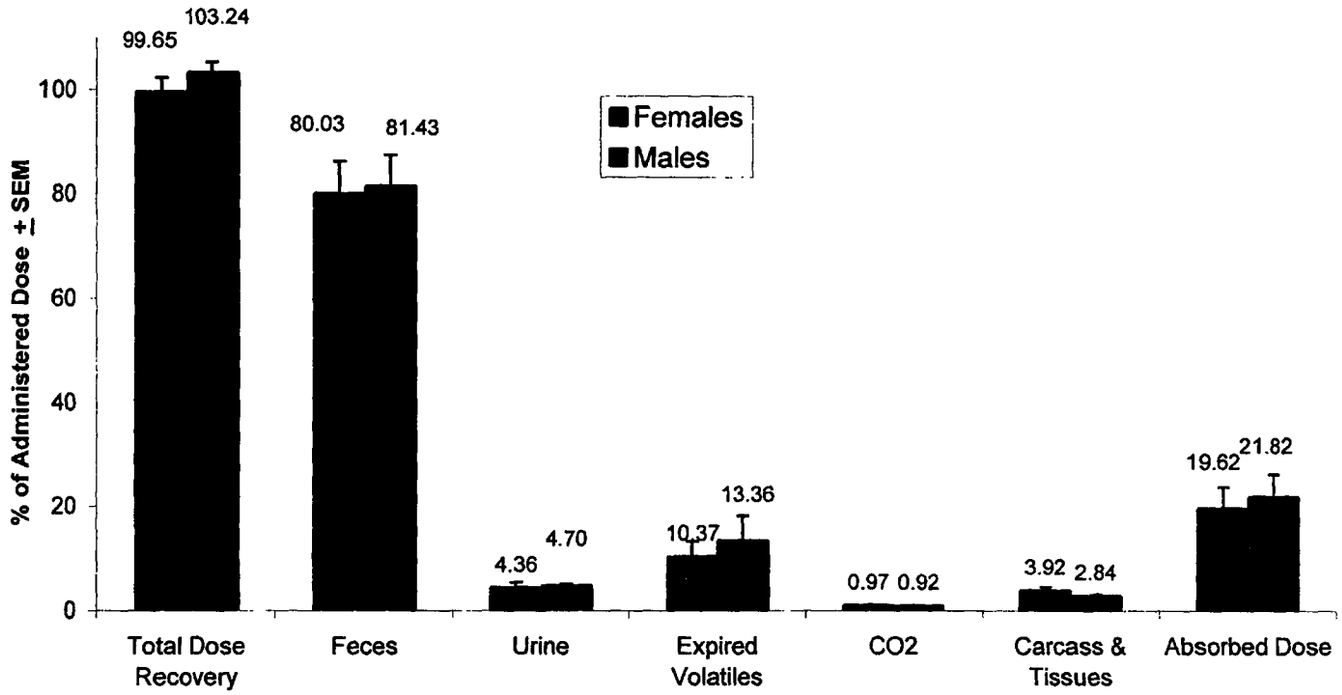
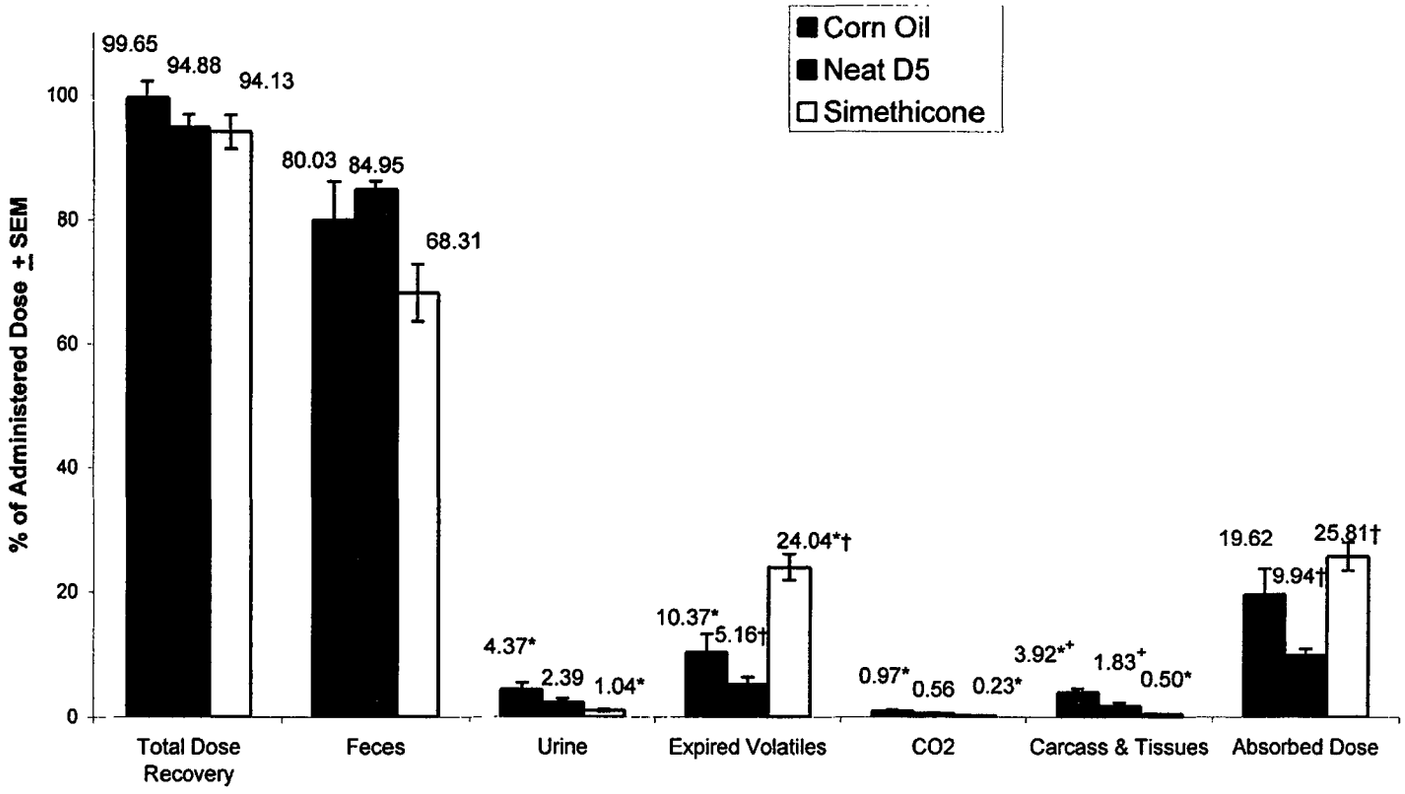


Figure 5. Disposition of Radioactivity in Female Fischer 344 Rats Following Single Oral Dose of ^{14}C-D_5 in Various Carriers

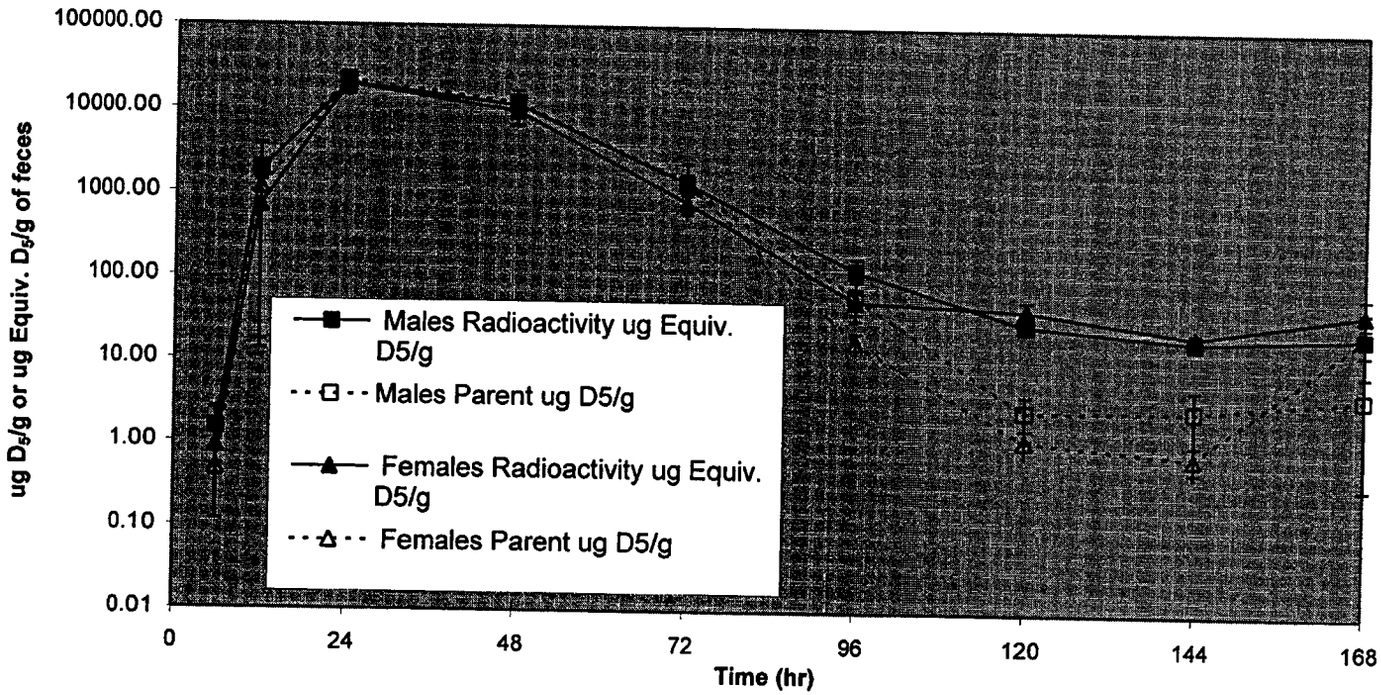


* Statistically significant difference between D_5 in corn oil and simethicone at $\alpha = 0.05$

\+ Statistically significant difference between D_5 in corn oil and neat D_5 at $\alpha = 0.05$

† Statistically significant difference between D_5 in simethicone oil and neat D_5 at $\alpha = 0.05$

Figure 6. Radioactivity *vs.* Parent D_5 Concentration in Feces of Male and Female Fischer Rats Following Single, Oral Administration of ^{14}C-D_5 in Corn Oil



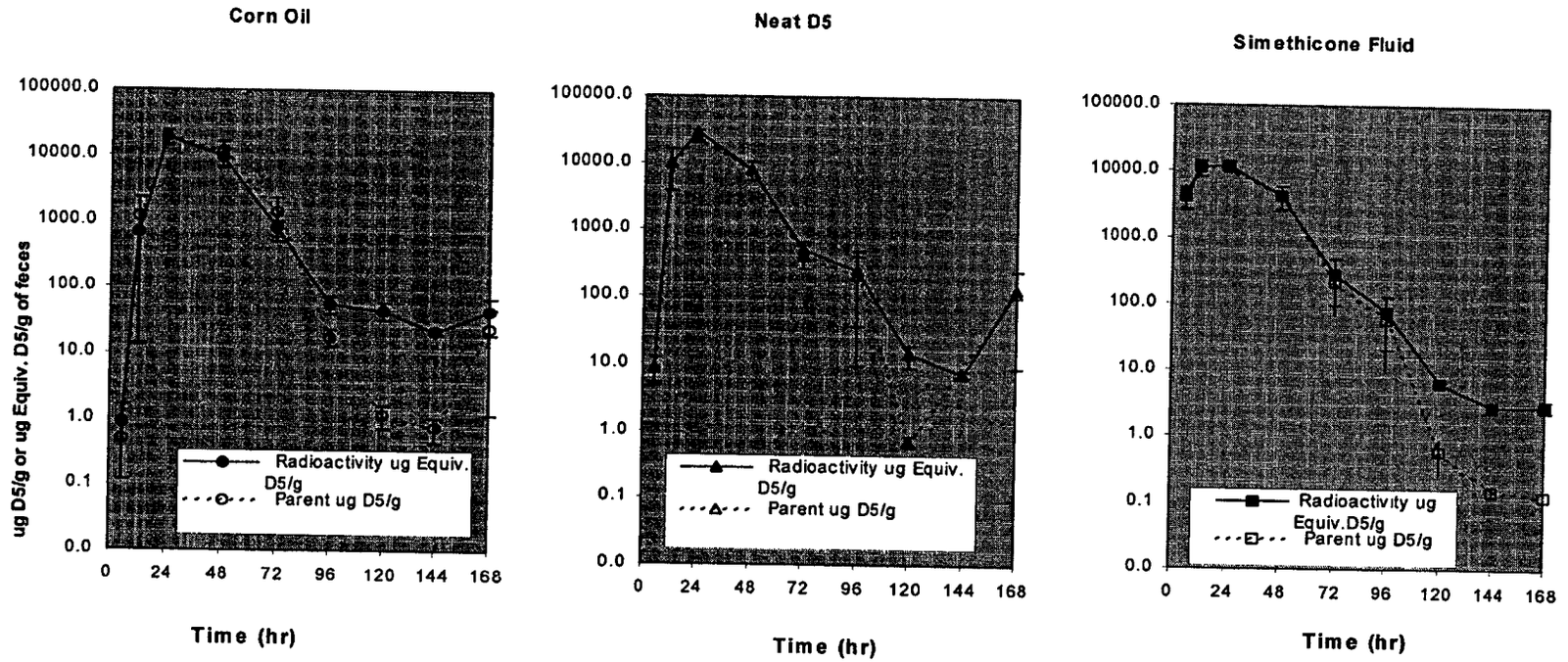
Areas Under The Fecal Curves

(μg ^{14}C-Equivalents D_5 X hr/g or μg D_5 X hr/g)

Males
Radioactivity = 616222.51 ± 80791.59
D_5 Parent = 660667.01 ± 104240.57
Data expressed as mean ± standard error of the mean

Females
Radioactivity = 551553.00 ± 104797.70
D_5 Parent = 603084.69 ± 132165.76

Figure 7. Radioactivity *vs.* Parent D_5 Concentration in Feces of Female Fischer Rats Following Single Oral Administration of ^{14}C-D_5 in Various Carriers



Areas Under The Fecal Curves
(µg ^{14}C-Equivalents D_5 X hr/g or µg D_5 X hr/g)

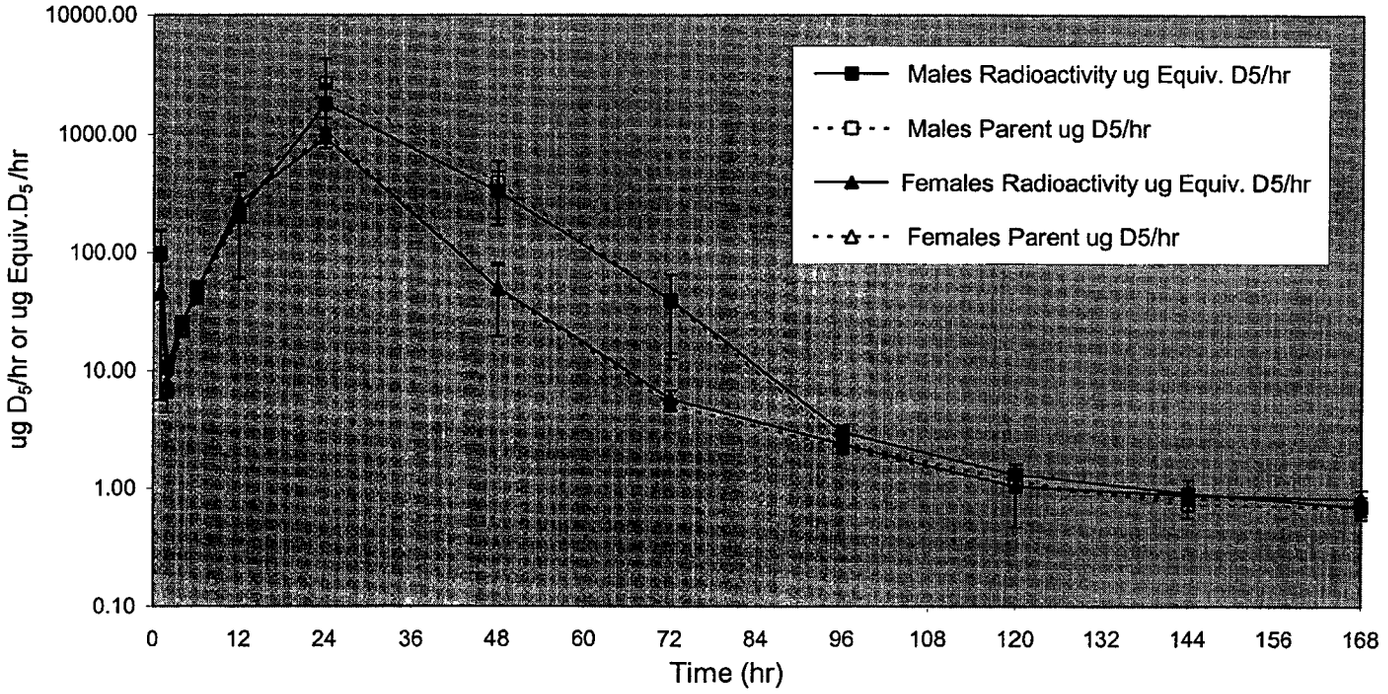
Corn Oil
Radioactivity = 551553.00 ± 104797.70
D_5 Parent = 603084.69 ± 132165.76

Neat D_5
Radioactivity = 761599.77 ± 85246.42
D_5 Parent = 663725.03 ± 79695.74

Simethicone Fluid
Radioactivity = 426286.15 ± 50416.29
D_5 Parent = 407934.79 ± 45319.79

Data expressed as mean ± standard error of the mean

Figure 8. Radioactivity *vs.* Parent D_5 Content in Charcoal Tubes Used to Trap Expired Volatiles in Male and Female Fischer Rats Following Single, Oral Administration of ^{14}C-D_5 in Corn Oil



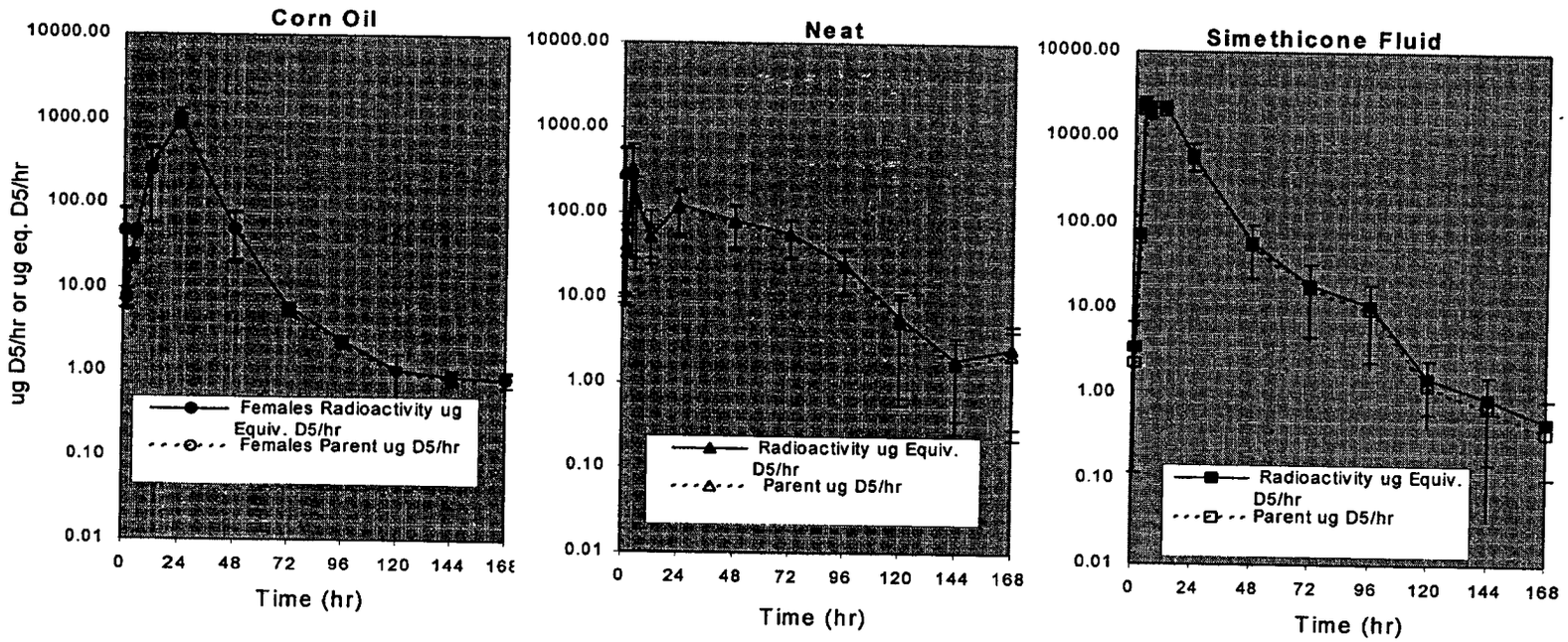
Areas Under The Expired Volatiles Curves

(μg ^{14}C-Equivalents D_5 X hr/g or μg D_5 X hr/g)

Males	**Females**
Radioactivity = 41800.33 ± 14976.19	Radioactivity = 20852.14 ± 3702.19
D_5 Parent = 58654.70 ± 28615.48	D_5 Parent = 22842.10 ± 5754.53

Data expressed as mean ± standard error of the mean

Figure 9. Radioactivity *vs.* Parent D_5 Content in Charcoal Tubes Used to Trap Expired Volatiles in Female Fischer Rats Following Single, Oral Administration of ^{14}C-D_5 in Various Carriers



Areas Under The Expired Volatiles Curves
(μg ^{14}C-Equivalents D_5 X hr/g or μg D_5 X hr/g)

Corn Oil
Radioactivity = 20852.14 ± 3702.19
D_5 Parent = 22842.10 ± 5754.53

Neat D_5
Radioactivity = 7944.34 ± 1921.83
D_5 Parent = 7544.77 ± 1823.12

Simethicone Fluid
Radioactivity = 44693.37 ± 4426.23
D_5 Parent = 39679.74 ± 4097.53

Data expressed as mean ± standard error of the mean

Figure 10. Radioactivity Content in Expired Volatiles and Fecal Material Over Time in Fischer Rats Following Single, Oral Administration of ^{14}C-D_5 in Various Carriers

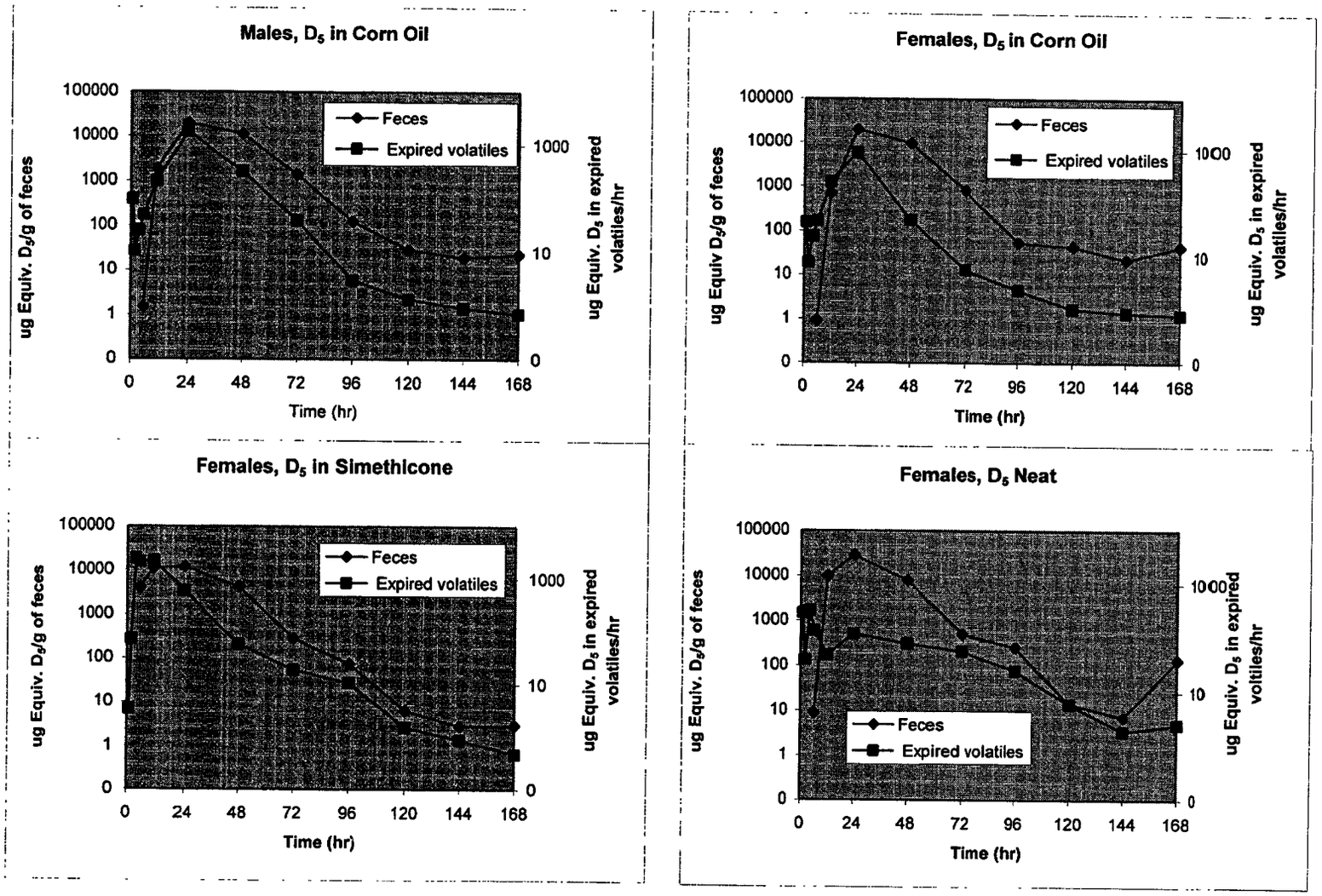


Figure 11. Example HPLC/RAD Chromatograms of a) ^{14}C-D_5 Standard, and Blood Obtained from b) Male and c) Female Rats at 12 Hours Following Corn Oil Dose

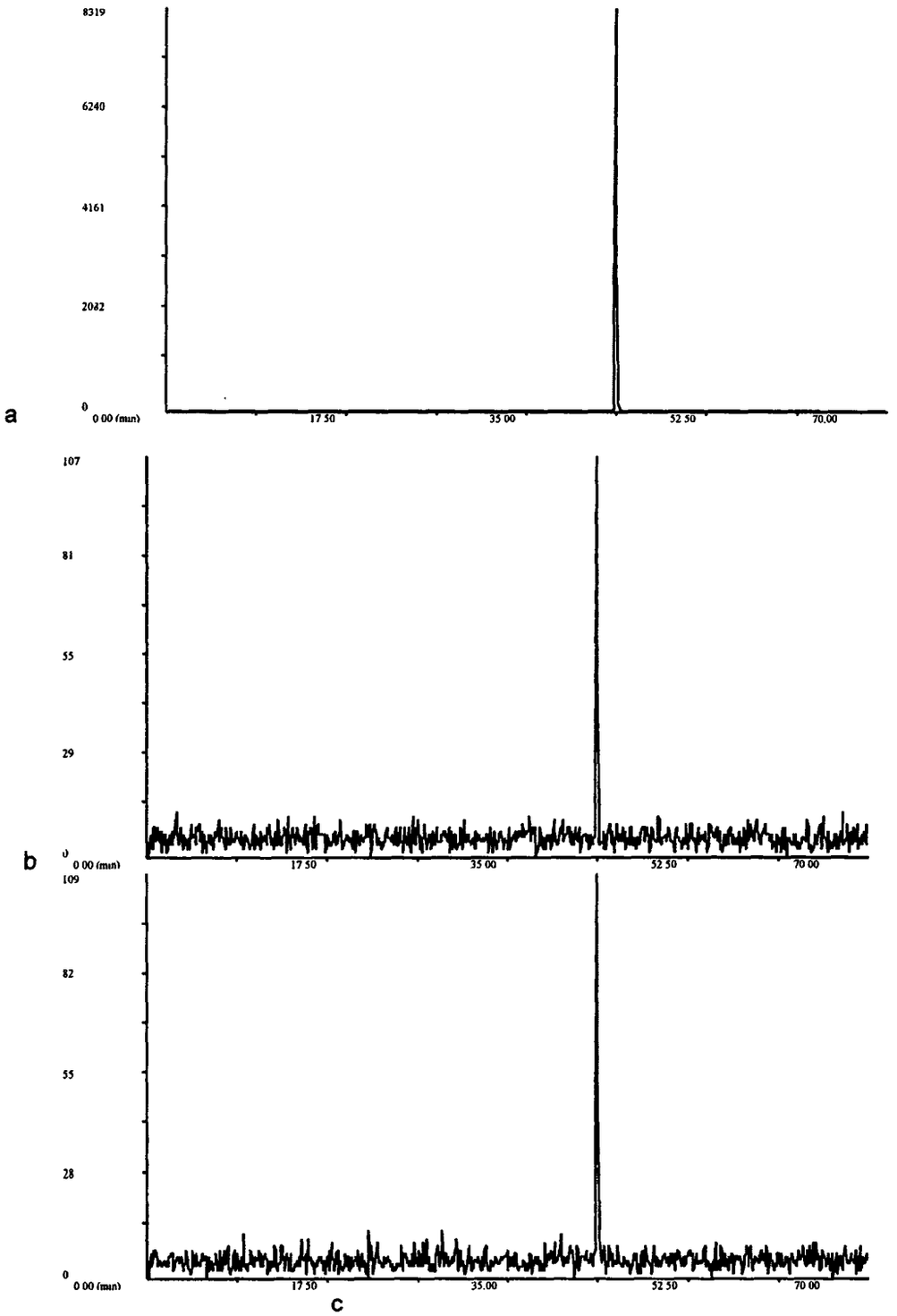


Figure 12. Example HPLC/RAD Chromatograms of a) ^{14}C-D_5 Standard, and Urine Samples Obtained from b) Male and c) Female Rats at 24 Hours Following Corn Oil Dose

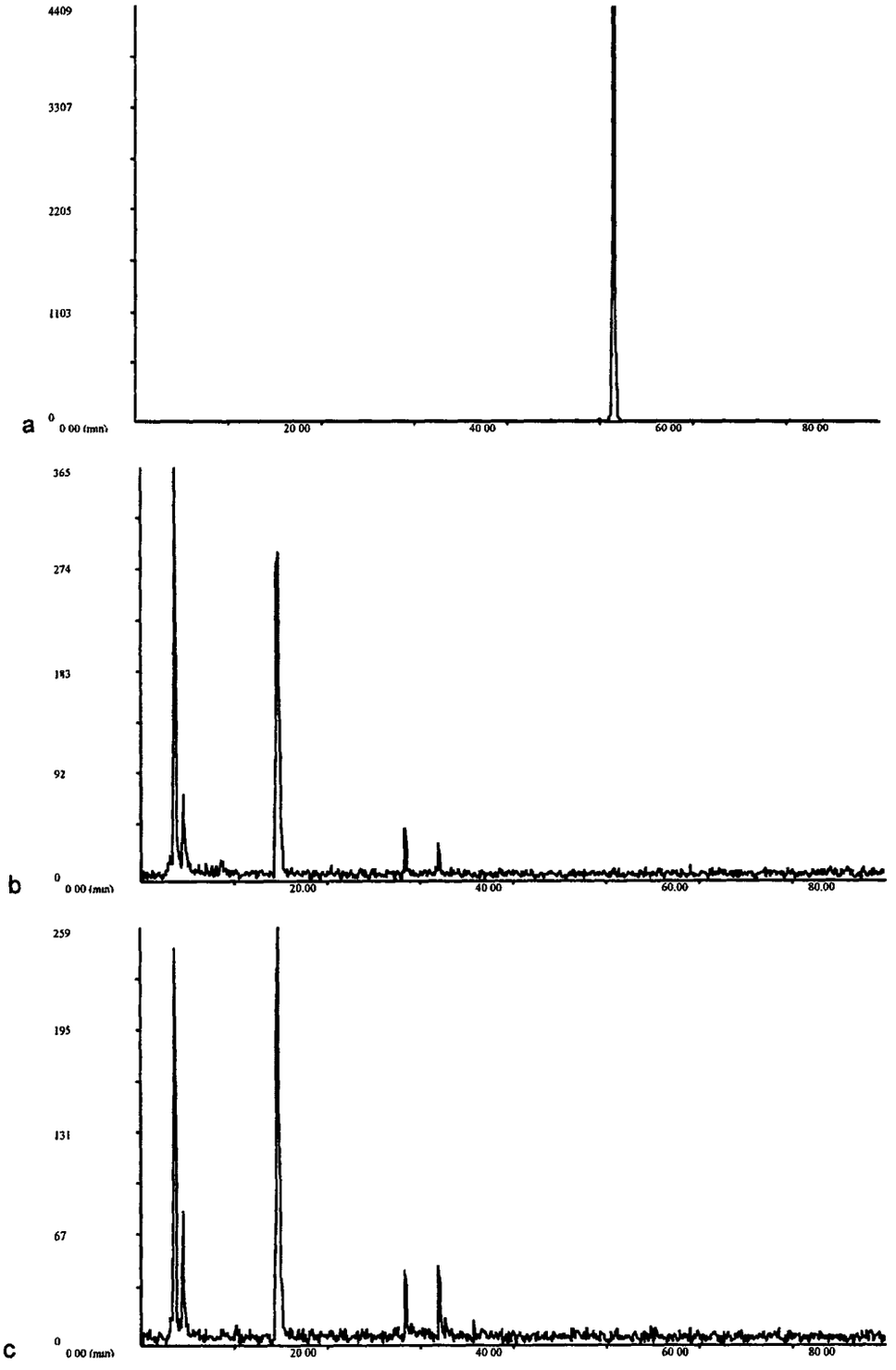


Figure 13. Example HPLC/RAD Chromatograms of Urine Samples from Female Rats at 96 Hours Following a) Corn Oil Dose, b) Neat ^{14}C-D_5 Dose, and c) Simethicone Dose

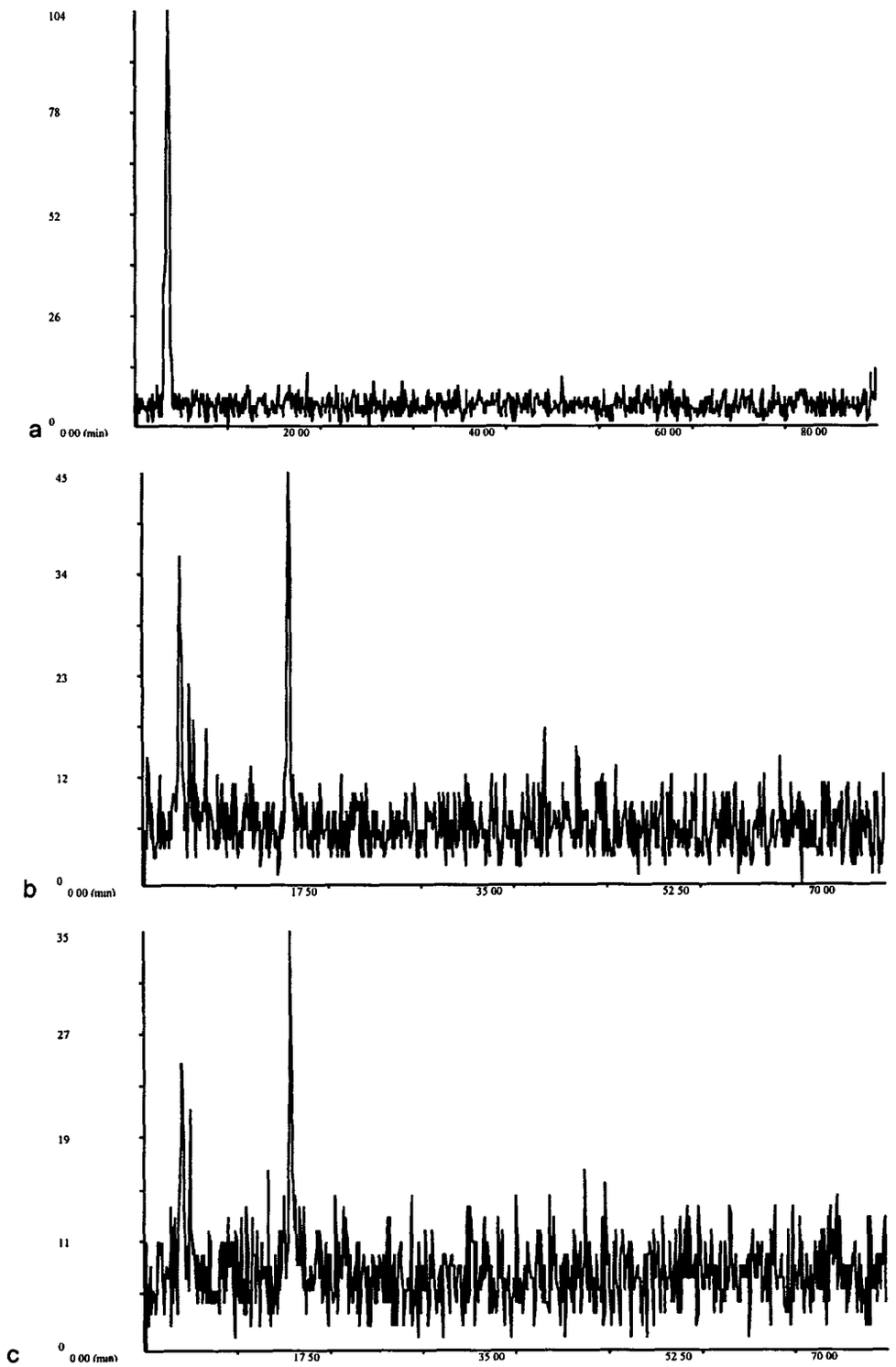


Figure 14. Example HPLC/RAD Chromatograms of a) ^{14}C-D_5 Standard, and Fecal Samples Obtained from b) Male and c) Female Rats at 24 Hours Following Corn Oil Dose

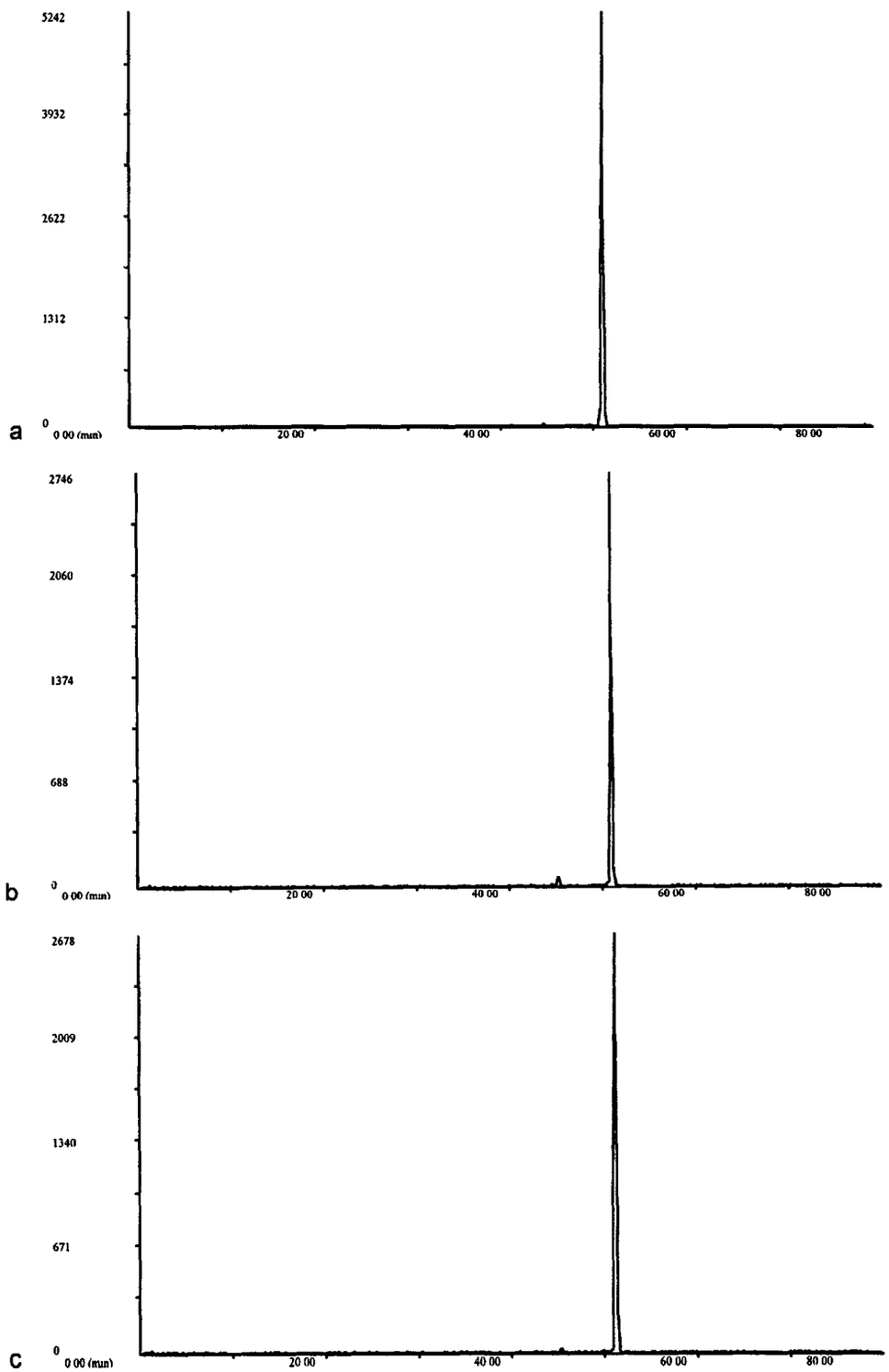


Figure 15. Whole Body Autoradiography of Female Fischer 344 Rats 3, 12, and 24 Hours Following Administration of a Single Oral Dose of ^{14}C-D_5 in Corn Oil

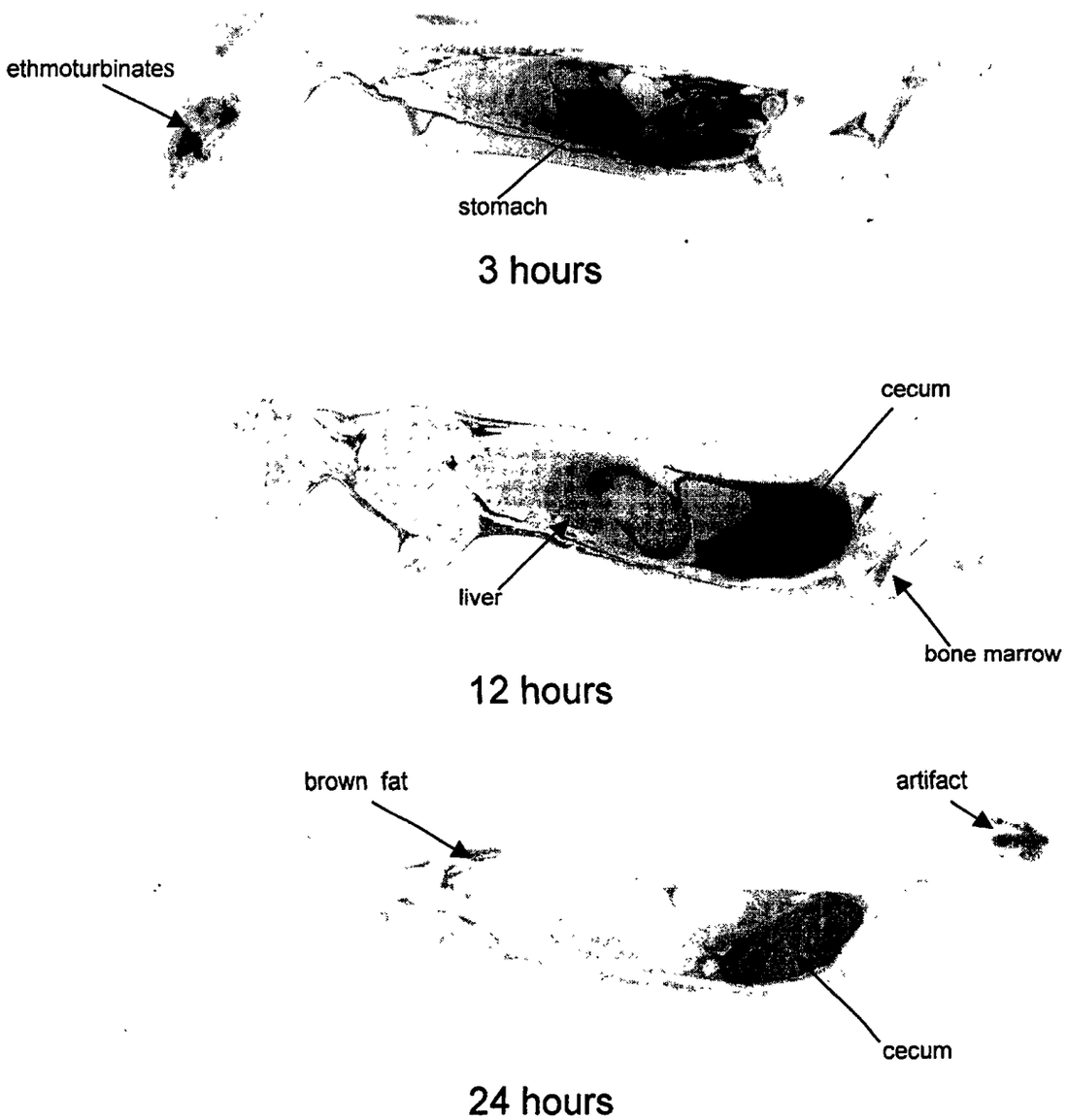
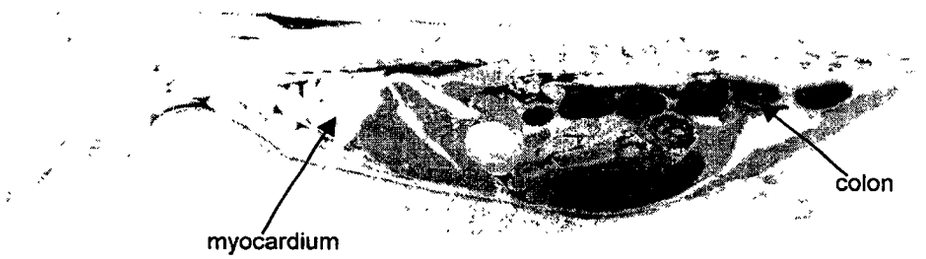
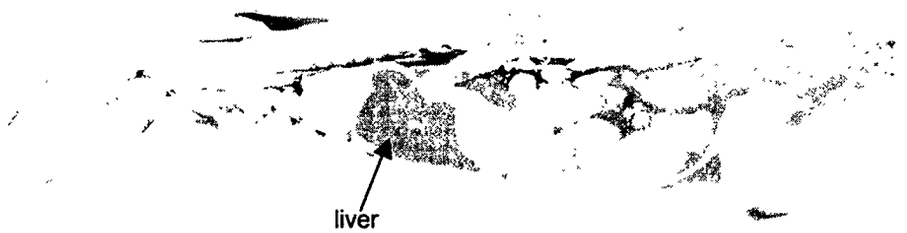


Figure 16. Whole Body Autoradiography of Female Fischer 344 Rats 48, 96 and 168 Hours Following Administration of a Single Oral Dose of ^{14}C-D_5 in Corn Oil



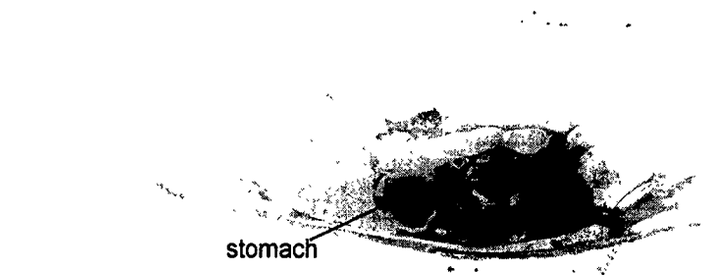
48 hours



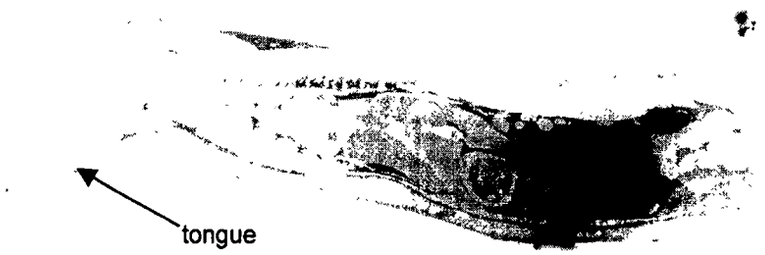
96 hours

168 hours

Figure 17. Whole Body Autoradiography of Male Fischer 344 Rats 3, 12, and 24 Hours Following Administration of a Single Oral Dose of ^{14}C-D_5 in Corn Oil



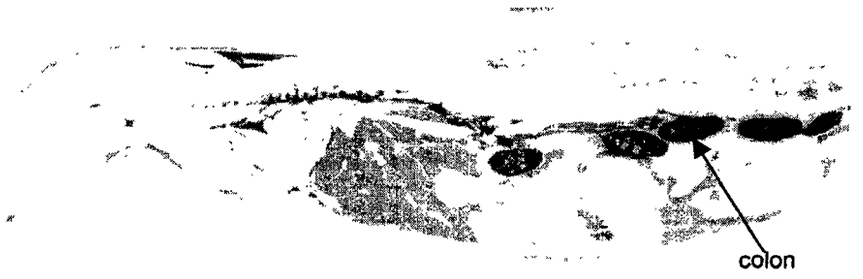
3 hours



12 hours

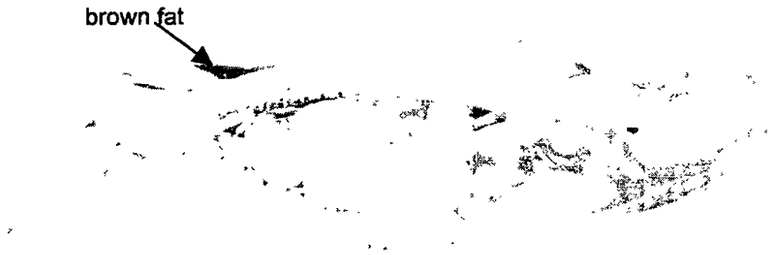
24 hours

Figure 18. Whole Body Autoradiography of Male Fischer 344 Rats 48, 96 and 168 Hours Following Administration of a Single Oral Dose of ^{14}C-D_5 in Corn Oil



48 hours

96 hours



168 hours

DOW CORNING CORPORATION
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CONTRIBUTING SCIENTIST REPORT

Title:	Parent Quantitation of D_5 in Feces, Expired Volatiles and Blood, and Qualitative Metabolite Profile Analysis in Urine, Feces and Blood
Study No.:	9550
Test Article:	^{14}C-Decamethylcyclopentasiloxane (^{14}C-D_5)
Study Director:	Marina L. Jovanovic, M.S. Associate Toxicology Specialist
Contributing Scientist:	Debra A. McNett, B.S. Analytical Specialist
Sponsor:	Dow Corning Corporation
HES Manager:	Roy A. Campbell, B.S. Manager, Analytical Chemistry
Testing Facility:	Dow Corning Corporation Health and Environmental Sciences Midland, MI 48686-0994
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ABSTRACT

The objective of the work reported in this contributing scientist report was to determine the concentration of parent D_5 in blood, feces and expired volatiles from male and female Fischer 344 rats following a single oral dose of ^{14}C-D_5 in corn oil as a carrier as well as in the same matrices from female Fischer 344 rats following single oral doses of ^{14}C-D_5 in simethicone and neat. In addition, the metabolic radioactive profile was determined in blood, urine and feces. The details of the study design for the complete study can be found in the main report. This contributing scientist report pertains to the parent D_5 analysis of samples from animals in the blood kinetics group and the mass balance group. At selected time points following exposure, blood samples were collected from animals in the blood kinetics groups and feces and expired volatile samples were collected from the mass balance groups from the two phases of this study. The first phase consisted of dosing male and female Fischer 344 rats with ^{14}C-D_5 in corn oil as the carrier. The second phase consisted of only female Fischer 344 rats and compared the dosing of ^{14}C-D_5 neat and in the carrier of simethicone to corn oil from the first phase.

Blood, feces and expired volatile samples (trapped on charcoal tube filters) were processed and analyzed for parent D_5 quantitation. Extraction of D_5 from the blood and feces matrices with tetrahydrofuran (THF) was performed according to a study specific procedure found in attachment A and the validated method from DCC study# 8762 [1]. The THF extracts were analyzed by gas chromatography with mass selective detection and the concentrations in the THF extracts were determined by comparison to standard curves of THF solvent standards. Charcoal tube samples were similarly processed and analyzed except with toluene as an extraction solvent. These extractions were performed according to a study specific procedure in attachment B and the validated method from DCC study #9105 [2]. In addition, the metabolic profile of blood, feces and urine was analyzed from each of the phases of this study. For blood and feces, the THF extracts at selected time points obtained from the processing for parent D_5 analysis were also used for the analysis of the metabolic profiles. Urine collected from the animals was analyzed directly by high performance liquid chromatography for the analysis of the metabolic profiles at various time points.

Analysis of blood, feces, and charcoal tubes collected from the rats orally dosed with D_5 in corn oil, simethicone, or neat revealed that parent D_5 concentrations were much higher in feces as compared to blood and charcoal tubes, and lowest in the blood. When comparing the area under the curves (AUC) from males and females dosed with D_5 in corn oil, the males had a statistically significant greater amount of parent D_5 than the females in the blood ($p=0.04$), but the same amount as the females in expired volatiles and feces (see SAS output). When the same comparison was made with the total radioactivity AUCs, which is parent plus any metabolites (see main report), there was not a difference between males and females in blood concentrations or feces and expired volatile concentrations. The amount of metabolites in the blood was statistically different from zero in both the males and the females dosed with D_5 in corn oil. Comparisons were also made then between the female rats that were dosed D_5 in corn oil, simethicone, or neat. When the AUCs resulting from the parent blood concentrations were compared, it

was found that the rats dosed with corn oil had significantly higher concentrations than with either simethicone or neat. The blood concentrations from the female rats dosed with D_5 neat were the next highest and they were statistically significant greater than the blood concentrations from the simethicone dosed animals, which had the lowest. The amount of metabolites in blood were statistically different from zero for females dosed both with D_5 in corn oil and in simethicone but not when dosed neat. Analysis of the expired volatiles also revealed significant differences between females dosed with corn oil, simethicone or neat. Each type of dose was different from the rest, however, in expired volatiles the highest amount of parent D_5 was found in simethicone dosed females, and followed by corn oil dosed and then neat dosed. The same trend was observed with radioactivity from expired volatiles (see main report), in fact the parent D_5 and radioactivity in the expired volatiles were not different within the same type of dose indicating that all of the expired volatiles was unchanged D_5. Comparisons were also made for feces from females dosed with D_5 in the different carriers and the only statistically different amounts of parent D_5 occurred between the females dosed neat and dosed in simethicone, with neat having a higher amount of parent D_5.

Analysis of blood, feces and urine for the metabolic profiles was performed. All of the selected blood extracts analyzed either had no detectable peaks due to the low amount of radioactivity present or they only had one peak, corresponding to parent D_5 based on retention time comparisons. The majority of the radioactivity present in all of the feces extracts corresponded to parent D_5 based on retention time comparisons with a minor amount ($\leq$ 6%) corresponding to a relatively non-polar metabolite that is yet unidentified. Unlike the blood and feces, the radioactivity eliminated in the urine consisted entirely of polar metabolites of D_5. No parent D_5 was found in any of the urine samples from any of the animals regardless of dosing carrier, gender or time point collected. There were 2 major metabolites common to all of the rats regardless of gender or dosing carrier at the time points of 12, 24, 48 and 72 hours. These metabolites have been identified as methylsilanetriol [$CH_3Si(OH)_3$] and dimethylsilanediol ([$(CH_3)_2Si(OH)_2$], monomerdiol) based on retention time comparison to urinary metabolite profiles performed previously in a separate study by Varaprath *et.al.*[3].

APPROVAL SIGNATURES

This report consists of pages 1 through 101 including Tables 1-10, Figures 1-10 and Attachments A through C.

Debra A. McNett Nov. 20, 2003

Debra A. McNett., B.S. Date
Analytical Specialist
Contributing Scientist
Bioanalytical Support

Roy A Campbell 20-Nov-2003

Roy A. Campbell, B.S. Date
Manager, Analytical Chemistry

OBJECTIVE

The objective of the work reported in this contributing scientist report was to determine the concentration of parent D_5 in blood, feces, and expired volatiles from male (corn oil carrier only) and female Fischer 344 rats following a single oral dose of D_5 in corn oil or simethicone dosing carriers or neat. An additional objective was to determine the metabolic radioactivity profile in the blood, feces and urine.

TEST, CONTROL, REFERENCE ARTICLE INFORMATION

This information is provided in the body of the main report.

ROUTE OF EXPOSURE

This information is provided in the body of the main report.

TEST SYSTEM

Species: *Rattus norvegicus*

Strains: Fischer 344 CDF

Sex and Number Used: Part 1 Corn Oil Dose:

- Mass Balance Groups (MB)
  - Group 1: 2 females controls
  - Group 3: 4 females test article dosed
  - Group 2: 2 males controls
  - Group 4: 4 males test article dosed
- Blood Kinetics Group (BK)
  - Group 7: 2 females controls
  - Group 9: 6 females test article dosed
  - Group 8: 2 males controls
  - Group 10: 6 males test article dosed

Part 2 D_5 Neat and Simethicone (SF) Dose:

- Mass Balance Group (MB)
  - Group 11: 2 females Neat controls
  - Group 13: 4 females Neat test article dosed
  - Group 12: 2 females SF controls
  - Group 14: 4 females SF test article dosed
- Blood Kinetics Group (BK)
  - Group 15: 2 females Neat controls
  - Group 17: 6 females Neat test article dosed
  - Group 16: 2 females SF controls
  - Group 18: 6 females SF test article dosed

The animals in all of the Blood Kinetics Groups (BK) for both part 1 and 2 were jugular vein cannulated by the supplier prior to arrival at the testing facility in order for blood to be drawn from these animals at various time points following dosing.

All other test system information can be found in the body of the main report.

EXPERIMENTAL DESIGN

1. Randomization

This information is provided in the body of the main report.

2. Dose Groups

The samples that were analyzed as part of this contributing scientist report were blood from the Blood Kinetics Groups and feces, expired volatiles (charcoal tubes), and urine from the Mass Balance Groups.

3. Test Article Preparation and Analysis

This information is provided in the body of the main report.

4. Test Article Administration

This information is provided in the body of the main report.

5. Sample Processing and Analysis

Blood Kinetics Groups

Blood

Blood was collected via the jugular cannula at scheduled time points of 15 and 60 min, and 6, 12, 24, 48, 72, 96, 120, 144 and 168 hours post-dose. During blood collections from the jugular cannula, an aliquot of blood (approximately 300 µL) was collected and immediately transferred into a pre-weighed glass vial containing tetrahydrofuran (THF), glass beads and the internal standard tetrakis(trimethylsiloxy)silane (M_4Q). The samples were then directly processed by extraction twice with THF according to the approved method given in attachment A of this contributing scientist report. This method was validated prior to this study and results from this validation are found in the DCC report no. 2000-I0000-49032 [1]. Quality control (QC) samples were prepared every day at the same time as the samples were processed as a check of the extraction and analysis

and were prepared by spiking varying amounts of D_5 into control blood and processed and analyzed in the same manner as study samples which were processed for analysis immediately following collection.

Parent D_5 was quantified in the blood samples and QC samples by comparing the extracts of these samples to calibration curves generated from THF solvent standards containing M_4Q and varying amounts of D_5. The various amounts of D_5 in the solvent standards were sufficient to cover the range of concentrations found in the study samples. The standards and samples were analyzed by gas chromatography with mass selective detection (GC-MS). The mass spectrometer was operated in the electron ionization (EI) and selected ion monitoring (SIM) modes. The fragment ions of m/z 355 and m/z 281 were monitored for D_5 and M_4Q quantitation, respectively. Remaining details pertaining to the preparation and analysis of the blood samples can be found in the procedure in attachment A.

In addition to parent D_5 quantitation by GC-MS, the metabolite profile of the blood extracts found to contain sufficient radioactivity (time points 6, 12, and 24 hours (see deviation)) was also determined by qualitative analysis by high performance liquid chromatography (HPLC) with radiometric detection (RAD). The conditions for the HPLC/RAD analysis can be found in Table 1.

Mass Balance Groups

Feces

The collected feces samples were removed from –80°C frozen storage and allowed to thaw on ice. They were then homogenized with 3:1 (v:w) cold Milli-Q water. On the same day that the feces samples were homogenized, aliquots of the homogenates were removed and placed in pre-weighed glass vials and weighed to obtain the homogenate aliquot weight. The homogenate aliquots were then placed back in –80°C frozen storage until the time of sample processing for parent analysis.

The fecal homogenate aliquots were extracted and analyzed according to the approved method given in attachment A of this contributing scientist report. This method was validated prior to this study and results from this validation are found

in the DCC report no. 2000-I0000-49032 [1]. The fecal homogenate aliquots were extracted three times with tetrahydrofuran (THF). The method employed the use of an internal standard, namely tetrakis(trimethylsiloxy)silane (M_4Q). This internal standard was added with the THF as part of the first extraction. Just as with the blood samples, quality control (QC) samples were prepared at the same time as the feces samples were processed as a check of the extraction and analysis and were prepared by spiking varying amounts of D_5 into control fecal homogenate and processed and analyzed in the same manner as the study samples. The only difference is that the fecal homogenate samples were processed all together and only one set of QC samples was prepared.

Parent D_5 was quantified in the fecal samples and QC samples by comparing the extracts of these samples to calibration curves generated from THF solvent standards containing M_4Q and varying amounts of D_5. The various amounts of D_5 in the solvent standards were sufficient to cover the range of concentrations found in the study samples. The standards and samples were analyzed by gas chromatography with mass selective detection (GC-MS). The mass spectrometer was operated in the electron ionization (EI) and selected ion monitoring (SIM) modes. The fragment ions of m/z 355 and m/z 281 were monitored for D_5 and M_4Q quantitation, respectively. Remaining details pertaining to the preparation and analysis of the feces samples can be found in the procedure in attachment A.

In addition to parent D_5 quantitation by GC-MS, the metabolite profile of the fecal extracts found to contain sufficient radioactivity (time points 12, 24, 48 and 72 hours) was also determined by qualitative analysis by high performance liquid chromatography (HPLC) with radiometric detection (RAD). The conditions for the HPLC/RAD analysis can be found in Table 1.

Urine

Urine samples collected from the mass balance groups found to contain sufficient radioactivity (time points 12, 24, 48, 72, and 96 hours) were removed from frozen storage, thawed on ice, and approximately 1 mL aliquots were removed to new vials. The urine aliquots were centrifuged at approximately (1790 – 2270) x g in order to remove the insoluble particulates from the urine. Aliquots of the clear urine supernatant

were then transferred to autosampler vials for direct qualitative analysis by high performance liquid chromatography (HPLC) with radiometric detection (RAD). The conditions for HPLC/RAD analysis can be found in Table 1.

Charcoal Tubes (Expired Volatiles)

The charcoal tubes containing the expired volatiles collected at the time points of 1, 2, 4, 6, 12, 24, 48, 72, 96, 120, 144 and 168 hours were processed and analyzed according to the method provided in Attachment B. This method was also validated prior to this study and the results can be found in DCC report no. 2001-I0000-50469 [2]. The charcoal tubes were removed from frozen storage and allowed to cool to approximately 4°C. The tubes were broken and the contents were placed in pre-weighed glass vials containing approximately 15 mL of a solution of toluene and M_4Q (toluene/ISTD). The charcoal samples were allowed to desorb in the toluene for at least 24 hours prior to drying aliquots with magnesium sulfate and subsequent GC-MS analysis. Like the feces, these samples were processed for analysis all together and one set of QC samples were prepared and processed in the same manner and at the same time as the charcoal tube samples. Remaining details pertaining to the preparation and analysis of the charcoal tube samples can be found in the procedure in Attachment B.

Fecal Spiking Experiment

A spiking experiment was performed with feces pellets after obtaining preliminary mass balance results from the radioactivity measurements for the study. This was done to determine if the processing efficiency of solubilizing feces was less than 100% and to be able to correct the mass balance results for this determined efficiency. Control feces pellets were placed into the same kind of jars as used for collections, spiked with 4.5 – 6.7 µCi D_5/g feces with the three different dosing solutions used for this study in triplicate (3 fecal samples for each dosing solution). The spike concentration was targeted to compare with the maximum found in feces collected from the animals in this study. After spiking, the samples were placed in the freezer for four days. After the fourth day, the samples were removed and diluted with Milli-Q water and homogenized in the same manner as study samples. Aliquots were removed from the homogenized samples the same day and solubilized with TEAH and processed for radioactivity measurements. The measured radioactivity was compared to the amount spiked in order to determine a processing efficiency.

6. Parameters Measured

Parent D_5 concentrations were measured in the blood from the blood kinetics groups and feces and expired volatiles (charcoal tubes) from the mass balance groups. The concentration of parent D_5 in blood and feces was reported as µg/gram sample and in the charcoal tubes as µg/hour. The calculations used to convert from peak areas generated from the GC-MS to µg/gram sample or µg/hour can be found in the procedures in attachment A or B, respectively. In addition, the qualitative metabolite profile was analyzed in selected blood and feces extracts and urine samples. The metabolites are reported as a percentage of the total radioactivity analyzed.

7. Statistical Methods

A description of the statistical methods used can be found in the main report.

8. Deviations

1. A deviation was reported in the protocol, section G. Sample Processing and Analysis, Blood Kinetics. The protocol stated that if sufficient radioactivity was present in the THF extracts (>25,000 dpm/g), then a qualitative assessment of the THF extracts would be done using HPLC with radiochemical detection. Only one blood sample (C9186 Female 6hr) analyzed by this method had radioactivity levels greater than 25,000 dpm/g of THF extract, however all of the 6, 12, and 24 hour samples collected following all three dose types were analyzed in this manner for comparison purposes. This deviation does not affect the outcome of the study.

2. A deviation was reported in the protocol, section H. Sample Identification and Storage. The protocol stated that THF extracts from blood would be stored at 4 ± 4°C, however from 6-11-01 to 6-12-01 blood extracts from the 72 hour time point were left in a refrigerator that was found to be not working properly. Stability tests were initiated proving stability of blood extracts for 24 hours at ambient temperature. The details pertaining to these stability results can be found in the study file. As a result of the stability analyses, this deviation does not affect the outcome of the study.

RESULTS AND DISCUSSION

Fecal Spiking Experiment

The processing efficiencies for fecal radioactivity analysis for each of the dosing solutions results are presented in Table 2. The processing efficiencies for corn oil, simethicone, and neat averaged 88%, 89%, and 94%, respectively. The discrepancy from 100% could be due to the actual efficiency of the solubilization of the fecal samples, but is more likely due to the process of taking aliquots from the aqueous homogenate sample. With D_5 being highly lipophilic, it tends to migrate to the glass jar rather than stay in the aqueous sample.

D_5 Parent Quantitation

Blood Kinetics D_5 Quantitation

The limit of quantitation for each analysis was determined to be the value of the lowest prepared solvent standard to meet acceptable accuracy (% relative error from prepared concentration) within ± 15%. The LOQ was approximately 18 ng D_5 present in the blood extract. The actual µg/gram LOQ depended on the actual sample size of blood obtained and averaged 0.045 µg D_5/g blood. The individual results from the analysis of the blood quality control samples (QC spikes) analyzed daily with the daily collection of blood samples are presented in Table 3. The majority of the blood QC spikes had accuracies within 15 % of the prepared concentration. Only two QC samples that were detectable had accuracies outside of 15% of the prepared concentrations at 15.4% and 17.5%. These samples were also at the lowest QC concentration spiked at approximately 23 ng.

The parent D_5 concentrations (µg/g) in blood from male and female rats dosed with D_5 in corn oil along with the female rats dosed with D_5 neat and in simethicone are presented as group means with standard errors of the means in Table 6. Graphical representations of these concentrations as functions of post exposure time are presented in Figures 1 and 2. The corresponding individual animal values for these parameters are presented in Attachment C.

Feces D_5 Quantitation

The limit of quantitation for each analysis of feces samples was determined to be the value of the lowest prepared solvent standard to meet acceptable accuracy (% relative error from prepared concentration) within ± 15%. The LOQ was approximately 21 ng D_5 present in the

fecal extract. The actual μg/g LOQ depended on the actual amount of feces obtained and averaged 0.36 μg D_5/g feces. The individual results from the analysis of the feces quality control samples (QC spikes) analyzed alongside the feces samples are presented in Table 4. All of the feces QC spikes had accuracies within 15 % of the prepared concentrations.

The parent D_5 concentrations (μg/g) in feces from male and female rats dosed with D_5 in corn oil along with the female rats dosed with D_5 neat and in simethicone are presented as group means with standard errors of the means in Table 7. Graphical representations of these concentrations as functions of post exposure time are presented in Figures 3 and 4. The corresponding individual animal values for these parameters are presented in Attachment C.

Expired Volatiles D_5 Quantitation

The limit of quantitation for each analysis of charcoal tube samples was determined to be the value of the lowest prepared solvent standard to meet acceptable accuracy (% relative error from prepared concentration) within ± 15%. The LOQ averaged 57 ng D_5/g of toluene extract for the two parts of this study. The actual μg/hr LOQ depended on the amount of toluene used to extract the charcoal tube and the number of hours that the sample was collected and averaged 0.03 μg D_5/hr using a sample collection time of 24 hours. The individual results from the analysis of the charcoal tube quality control samples (QC spikes) analyzed alongside the samples are presented in Table 5. All of the charcoal tube QC spikes that were detectable had accuracies within 15 % of the prepared concentrations.

The parent D_5 concentrations (μg/hr) in the charcoal tube samples collected from male and female rats dosed with D_5 in corn oil along with the female rats dosed with D_5 neat and in simethicone are presented as group means with standard errors of the means in Table 8. Graphical representations of these concentrations as functions of post exposure time are presented in Figures 5 and 6. The corresponding individual animal values for these parameters are presented in Attachment C.

Summary of Parent D_5 Quantitation

Analysis of blood, feces, and charcoal tubes collected from the rats orally dosed with D_5 in corn oil, simethicone, or neat revealed that parent D_5 concentrations were much higher in feces as compared to blood and charcoal tubes, and lowest in the blood. This is consistent with dosing

a highly lipophilic material such as D_5 where the majority of the dose was excreted in the feces unchanged.

When comparing the area under the curves (AUC) from males and females dosed with D_5 in corn oil, the males had a statistically significant greater amount of parent D_5 than the females in the blood ($p=0.04$) (see Figure 1), but the same amount as the females in expired volatiles (Figure 5) and feces (Figure 3). The second phase of this study included dosing D_5 to female rates in a different vehicle, simethicone fluid, as well as dosing without a vehicle (neat). Comparisons were also made then between the female rats that were dosed D_5 in corn oil, simethicone, or neat. When the AUCs resulting from the parent blood concentrations were compared, it was found that the rats dosed with corn oil had significantly higher concentrations than with either simethicone or neat (see Figure 2). The blood concentrations from the female rats dosed with D_5 neat were the next highest and they were statistically and significantly greater than the blood concentrations from the simethicone dosed animals, which had the lowest. This indicates that the D_5 dose was most readily absorbed when dosed in the corn oil vehicle, followed by neat and then simethicone.

Analysis of the expired volatiles also revealed significant differences between females dosed with corn oil, simethicone or neat. Each type of dose was different from the rest, however, in expired volatiles the highest amount of D_5 was found in simethicone dosed females, followed by corn oil dosed and then neat dosed (see Figure 6). The parent D_5 and radioactivity (see main report) in the expired volatiles were not different within the same type of dose indicating that all of the expired volatiles was unchanged D_5. Comparisons were also made for feces from females dosed with the different carriers and the only statistically different amounts of parent D_5 occurred between the females dosed neat and dosed in simethicone, with neat having a higher amount of parent D_5 (see Figure 4).

Qualitative Metabolite Profile Analysis

Blood

The blood extracts from samples collected at 6, 12, and 24 hours following dosing by all three carriers were analyzed by HPLC with radiometric detection in order to determine the metabolite profile of the radioactivity present in the blood extracts. Example HPLC chromatograms of 12 hour blood extracts from male and female rats dosed with D_5 in corn oil as well as a standard of ^{14}C-D_5 are presented in Figure 7. All of the blood extracts analyzed either had no detectable

peaks due to the low amount of radioactivity present or they only had one peak, corresponding to parent D_5 based on retention time comparisons. This is consistent with the parent quantitation and radioactivity quantitation (main report) results, indicating that at these early time points, parent D_5 is quite similar to the total radioactivity.

Feces

The feces extracts from samples collected at 12, 24, 48, and 72 hours following dosing by all three carriers were analyzed by HPLC with radiometric detection in order to determine the metabolite profile of the radioactivity present in the feces extracts. The mean results from the qualitative fecal metabolite profile can be found in Table 9. Example chromatograms of 24 hour feces extracts from male and female rats dosed with D_5 in corn oil as well as a standard of ^{14}C-D_5 are presented in Figure 8. The majority of the radioactivity present in all of the feces extracts corresponded to parent D_5 based on retention time comparisons (retention time ~51 minutes). Some of the samples at 24 and 48 hours following dosing did have a small metabolite peak that was present in one animal as high as 6% (See individual animal data in Attachment C). This metabolite is yet unidentified, but it eluted fairly close to parent D_5, indicating that it is relatively non-polar (retention time ~45 minutes).

Urine

The mean results from the qualitative urinary metabolite profile analysis can be found in Table 10. This table shows the mean percent of radioactivity that can be attributed to individual metabolites from urine at 12, 24, 48, 72, and 96 hours following exposure. Figure 9 shows representative chromatograms of urine samples at 24 hours from male and female rats dosed with D_5 in corn oil and Figure 10 shows representative chromatograms of urine samples at 96 hours from female rats dosed with corn oil, neat or with simethicone. Unlike the blood and feces, the radioactivity eliminated in the urine consisted entirely of polar metabolites of D_5. No parent D_5 was found in any of the urine samples from any of the animals regardless of dosing carrier, gender or time point collected. There were 2 major metabolites common to all of the rats regardless of gender or dosing carrier at the time points of 12, 24, 48 and 72 hours. These metabolites have been identified as methylsilanetriol [$CH_3Si(OH)_3$] and dimethylsilanediol [$(CH_3)_2Si(OH)_2$] based on retention time comparison to urinary metabolite profiles performed previously in a separate study by Varaprath et.al.[3] No confirmation of identity was conducted within this study. Interestingly at 96 hours, the corn oil dosed animals (both males and females)

displayed only the methylsilanetriol metabolite while the simethicone and neat dosed animals contained mostly the dimethylsilanediol metabolite.

Individual animal results from the qualitative metabolite profile analyses of blood, feces and urine can be found in Attachment C.

ARCHIVE

Study related records, inclusive of, but not limited to sample preparation records, Excel worksheets, and the final report, will be maintained in the archives of Dow Corning Corporation, Midland, MI.

REFERENCES

1. HES Study No. 8762. Plotzke, K.P., McNett, D.A., Charbonneau, C., Tobin, J.M., and Nader, P., "Validation of Analytical Chemistry Methods for the Determination of Decamethylcyclopentasiloxane (D_5) in Dose Solution, Inhalation Chamber Atmosphere, Various Biological Matrices, Including its Metabolite Profile, as well as the Purity of the Test Article". Dow Corning Report #2000-I0000-49032.
2. HES Study No. 9105. McNett, D.A., Tobin, J.M., and Mast, T.J., "Absorption, Distribution, Metabolism, and Excretion (ADME) Study of 14C-Decamethylcyclopentasiloxane (D5) in the Rat Following a Single Nose-only Vapor Inhalation Exposure to 14C-D5 at Two Dose Levels". Dow Corning Report #2001-I0000-50469.
3. HES Study No. 8784. Varaprath, S., McMahon, J., Plotzke, K.P., "Non-Regulated Study: Metabolites of Decamehtylcycopentasiloxane (D_5) in Rat Urine". Dow Corning Report #1999-I0000-47584.

Table 1. HPLC/RAD Analysis Conditions for Qualitative Metabolite Profiling of Blood, Feces and Urine

Instrument:	Hewlett Packard 1050 High Performance Liquid Chromatograph/Packard Radiomatic FLO-ONE Detector
Column:	Alltima C-18, 5 um, 250 x 4.6 mm
Mobile Phase for Blood:	A: Water B: 50:50 Acetonitrile:Tetrahydrofuran
Mobile Phase for Feces & Urine:	A: Water B: Acetonitrile
Gradient:	Time (min) %A %B 0 100 0 20 100 0 40 0 100 60 0 100 65 100 0 80 100 0
Injection:	100µL injection, except 1 sample C9191 blood 6hr at 60µL
Flow Rate:	HPLC at 1.0mL/min Radiomatic at 3.0mL/min
Liquid Scintillation Cocktail:	Ultima Flo M

Table 2. Results from the Fecal Processing Efficiency Experiment

	µCi/g feces	µCi/g feces spiked	% Processing Efficiency	Average % Processing Efficiency
Corn Oil 1	4.71	5.29	89%	88%
Corn Oil 2	5.50	6.29	88%	
Corn Oil 3	4.00	4.54	88%	
Simethicone 1	6.50	6.43	101%	89%
Simethicone 2	4.23	5.18	82%	
Simethicone 3	3.87	4.52	86%	
Neat 1	6.50	6.65	98%	94%
Neat 2	5.48	6.44	85%	
Neat 3	4.51	4.55	99%	

Table 3. Accuracy Results from the Blood Quality Control (QC) Samples

QC Samples from Part 1

Preparation Date	2/5/2001			2/6/2001			2/7/2001			2/8/2001		
Blood QC Name	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference
QC-low -1-A	25.40	27.70	9.07%	27.35	28.27	3.37%	28.00	25.41	-9.28%	26.05	25.85	-0.78%
QC-low-1-B	22.14	26.02	17.52%	28.00	27.28	-2.58%	26.70	26.30	-1.51%	24.75	25.45	2.82%
QC-low-2-A	65.78	69.43	5.55%	65.78	70.17	6.67%	66.43	67.63	1.80%	63.82	64.40	0.90%
QC-low-2-B	63.82	68.92	7.98%	60.57	62.46	3.12%	65.78	66.13	0.54%	64.48	63.92	-0.86%
QC-high-1-A	477.39	519.91	8.91%	477.39	523.36	9.63%	488.94	527.67	7.92%	477.39	524.40	9.85%
QC-high-1-B	485.09	534.70	10.23%	488.94	524.40	7.25%	488.94	530.69	8.54%	473.54	525.88	11.05%
QC-high-2-A	6512.48	6794.66	4.33%	7150.96	7417.32	3.72%	7150.96	7502.56	4.92%	7023.26	7407.43	5.47%
QC-high-2-B	6640.17	6861.67	3.34%	7278.65	7624.32	4.75%	7278.65	7692.90	5.69%	7406.35	7417.15	0.15%
Preparation Date	**2/9/2001**			**2/10/2001**			**2/11/2001**			**2/12/2001**		
Blood QC Name	**Amount spiked (ng)**	**Amount found (ng)**	**% Difference**	**Amount spiked (ng)**	**Amount found (ng)**	**% Difference**	**Amount spiked (ng)**	**Amount found (ng)**	**% Difference**	**Amount spiked (ng)**	**Amount found (ng)**	**% Difference**
QC-low -1-A	24.75	25.32	2.30%	23.45	24.25	3.45%	24.10	24.16	0.28%	27.35	BLQ	N/A
QC-low-1-B	27.35	27.19	-0.59%	25.40	26.90	5.92%	23.45	23.43	-0.09%	25.40	BLQ	N/A
QC-low-2-A	65.13	67.63	3.84%	64.48	65.61	1.76%	64.48	64.41	-0.11%	66.43	60.95	-8.25%
QC-low-2-B	66.43	65.51	-1.39%	65.13	65.31	0.27%	63.17	63.89	1.13%	66.43	58.64	-11.73%
QC-high-1-A	488.94	532.35	8.88%	485.09	521.83	7.57%	477.39	466.80	-2.22%	488.94	440.82	-9.84%
QC-high-1-B	481.24	465.17	-3.34%	500.49	525.68	5.03%	473.54	463.51	-2.12%	481.24	445.34	-7.46%
QC-high-2-A	7406.35	7438.81	0.44%	7278.65	7532.25	3.48%	7150.96	7259.13	1.51%	7023.26	7111.82	1.26%
QC-high-2-B	7278.65	7273.07	-0.08%	7406.35	7544.69	1.87%	7278.65	7319.20	0.56%	7406.35	7157.31	-3.36%

Table 3. Accuracy Results from the Blood Quality Control (QC) Samples (continued)

QC Samples from Part 2

Preparation Date	6/8/2001			6/9/2001			6/10/2001			6/11/2001		
Blood QC Name	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference
QC-low -1-A	23.33	23.98	2.78%	22.20	24.25	9.24%	23.33	23.18	-0.66%	22.76	24.42	7.28%
QC-low-1-B	24.47	24.05	-1.73%	23.33	23.85	2.21%	22.76	24.24	6.48%	22.20	22.39	0.86%
QC-low-2-A	56.91	56.18	-1.29%	56.34	56.34	-0.01%	56.91	55.32	-2.80%	58.05	57.09	-1.65%
QC-low-2-B	57.48	59.28	3.14%	58.05	56.48	-2.71%	56.91	54.86	-3.60%	56.91	57.32	0.72%
QC-high-1-A	464.50	485.95	4.62%	457.25	484.45	5.95%	457.25	470.80	2.96%	460.87	473.12	2.66%
QC-high-1-B	464.50	481.65	3.69%	471.76	481.92	2.15%	457.25	477.32	4.39%	457.25	466.97	2.13%
QC-high-2-A	6989.12	6898.50	-1.30%	6989.12	6897.44	-1.31%	6756.15	6843.21	1.29%	6756.15	6789.71	0.50%
QC-high-2-B	6989.12	6916.34	-1.04%	6989.12	6938.62	-0.72%	6756.15	6957.24	2.98%	6756.15	6734.48	-0.32%
Preparation Date	6/12/2001			6/13/2001			6/14/2001			6/15/2001		
Blood QC Name	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference	Amount spiked (ng)	Amount found (ng)	% Difference
QC-low -1-A	21.06	23.44	11.33%	23.33	21.83	-6.45%	23.33	26.92	15.35%	24.47	21.80	-10.92%
QC-low-1-B	22.20	22.33	0.59%	23.33	21.15	-9.35%	22.76	25.45	11.78%	23.90	20.84	-12.80%
QC-low-2-A	56.34	54.26	-3.69%	56.91	53.01	-6.86%	56.34	58.36	3.58%	56.91	54.34	-4.51%
QC-low-2-B	57.48	57.07	-0.72%	56.91	53.71	-5.63%	58.05	58.47	0.72%	56.91	56.19	-1.26%
QC-high-1-A	442.73	457.15	3.26%	453.62	463.82	2.25%	457.25	461.02	0.83%	453.62	448.21	-1.19%
QC-high-1-B	453.62	451.54	-0.46%	435.47	438.23	0.63%	449.99	461.37	2.53%	453.62	452.27	-0.30%
QC-high-2-A	6523.18	6742.38	3.36%	6523.18	6492.27	-0.47%	6872.64	6601.57	-3.94%	6639.67	6536.00	-1.56%
QC-high-2-B	6290.21	6900.73	9.71%	6756.15	6640.09	-1.72%	6523.18	6646.54	1.89%	6756.15	6678.38	-1.15%

Table 4. Accuracy Results from the Feces Quality Control (QC) Samples

QC Samples from Part 1

Preparation Date/Sequence Number	4/10/2001	9550E03b		9550E03f	
Feces QC Name	Amount spiked (ng)	Amount found (ng)	% Difference	Amount found (ng)	% Difference
QC-low -1-A	24.86	27.50	10.63%		
QC-low-1-B	26.05	23.67	-9.11%		
QC-low-2-A	59.79	56.81	-4.99%		
QC-low-2-B	59.20	55.42	-6.38%		
QC-high-1-A	479.56	461.27	-3.81%		
QC-high-1-B	471.95	462.55	-1.99%		
QC-high-2-A	7078.51	6533.44	-7.70%	6742.80	-4.74%
QC-high-2-B	6724.59	6437.48	-4.27%	6593.37	-1.95%

QC Samples from Part 2

Preparation Date/Sequence Number	7/12/2001	9550E06a		9550E06b		9550E06c	
Feces QC Name	Amount spiked (ng)	Amount found (ng)	% Difference	Amount found (ng)	% Difference	Amount found (ng)	% Difference
QC-low -1-A	24.18	22.54	-6.78%				
QC-low-1-B	24.77	22.31	-9.93%				
QC-low-2-A	58.40	56.05	-4.01%				
QC-low-2-B	58.98	57.92	-1.80%				
QC-high-1-A	478.89	459.43	-4.06%				
QC-high-1-B	478.89	482.07	0.66%				
QC-high-2-A	7376.14	6609.54	-10.39%	7301.54	-1.01%	7318.13	-0.79%
QC-high-2-B	7013.38	6678.30	-4.78%	7336.20	4.60%	7424.74	5.87%

Table 5. Accuracy Results from the Charcoal Quality Control (QC) Samples

QC Samples from Part 1

Preparation Date/Sequence Number	3/5/2001	9550E02a		9550E02b	
Charcoal Tube QC Name	Amount spiked (ng/g)	Amount found (ng/g)	% Difference	Amount found (ng/g)	% Difference
QC-2ug-a	82.92	BLQ	N/AP	92.96	12.11%
QC-2ug-b	84.68	BLQ	N/AP	86.92	2.65%
QC-50ug-a	2206.95	2225.44	0.84%	2118.50	-4.01%
QC-50ug-b	2267.06	2227.58	-1.74%	2176.93	-3.98%
QC-200ug-a	9526.08	9211.30	-3.30%	9003.86	-5.48%
QC-200ug-b	9151.93	9202.28	0.55%	8635.65	-5.64%
QC-500ug-a	23810.93	25236.66	5.99%	22166.99	-6.90%
QC-500ug-b	24256.92	24887.34	2.60%	21521.79	-11.28%
QC-2000ug-a	119908.02	115154.27	-3.96%	120073.60	0.14%
QC-2000ug-b	123282.26	113635.16	-7.83%	115666.05	-6.18%

QC Samples from Part 2

Preparation Date/Sequence Number	6/26/2001	9550E05a		9550E05b		9550E05c	
Charcoal Tube QC Name	Amount spiked (ng/g)	Amount found (ng/g)	% Difference	Amount found (ng/g)	% Difference	Amount found (ng/g)	% Difference
QC-2ug-a	93.28	88.84	-4.76%	90.89	-2.56%	97.19	4.19%
QC-2ug-b	95.17	85.90	-9.74%	92.00	-3.33%	96.10	0.99%
QC-50ug-a	2375.29	2170.14	-8.64%	2227.53	-6.22%	2174.18	-8.47%
QC-50ug-b	2434.84	2234.55	-8.23%	2254.14	-7.42%	2210.01	-9.23%
QC-200ug-a	10466.28	9350.86	-10.66%	9421.17	-9.99%	9266.47	-11.46%
QC-200ug-b	10472.66	9665.46	-7.71%	9639.03	-7.96%	9463.95	-9.63%
QC-500ug-a	25678.88	24184.81	-5.82%	23359.63	-9.03%	24257.80	-5.53%
QC-500ug-b	25678.68	24423.66	-4.89%	23193.33	-9.68%	24052.07	-6.33%
QC-2000ug-a	127972.45	122767.23	-4.07%	121899.14	-4.75%	123597.35	-3.42%
QC-2000ug-b	127713.51	120157.38	-5.92%	118553.06	-7.17%	120085.11	-5.97%

Table 6. Results from Parent D_5 Quantitation in Blood

Blood - Corn Oil Dose						
	Male			Female		
time point (hr)	D_5 Concentration (µg/g ± std error)	n	n above BLQ	D_5 Concentration (µg/g ± std error)	n	n above BLQ
0.25	0.20 ± 0.03	6	6	0.21 ± 0.04	6	6
1	6.23 ± 0.75	6	6	5.31 ± 0.41	6	6
6	62.49 ± 4.26	6	6	52.12 ± 8.97	6	6
12	44.97 ± 4.03	6	6	34.75 ± 6.15	6	6
24	11.52 ± 1.98	6	6	10.19 ± 1.40	6	6
48	0.95 ± 0.140	6	6	1.54 ± 0.30	6	6
72	0.28 ± 0.035	6	6	0.59 ± 0.06	6	6
96	0.23 ± 0.034	6	6	0.48 ± 0.06	6	6
120	0.19 ± 0.030	6	6	0.45 ± 0.06	5	5
144	0.19 ± 0.041	6	6	0.55 ± 0.11	4	4
168	0.19 ± 0.049	6	6	0.33 ± 0.11	3	3
24 control	BLQ	2	0	0.026 ± 0.03	2	1

Table 6. Results from Parent D_5 Quantitation in Blood (continued)

Blood - Females							
	Corn Oil			Neat			
time point (hr)	D_5 Concentration (µg/g ± std error)	n	n above BLQ	D_5 Concentration µg/g ± std error)	n	n above BLQ	
0.25	0.21 ± 0.04	6	6	0.09 ± 0.04	6	4	
1	5.31 ± 0.41	6	6	1.93 ± 0.47	6	6	
6	52.12 ± 8.97	6	6	7.94 ± 0.71	5	5	
12	34.75 ± 6.15	6	6	4.08 ± 1.15	5	5	
24	10.19 ± 1.40	6	6	4.02 ± 3.09	5	5	
48	1.54 ± 0.303	6	6	0.49 ± 0.18	5	5	
72	0.59 ± 0.060	6	6	0.24 ± 0.030	5	5	
96	0.48 ± 0.063	6	6	0.21 ± 0.042	5	5	
120	0.45 ± 0.060	5	5	0.15 ± 0.031	3	3	
144	0.55 ± 0.11	4	4	0.21 ± 0.011	3	3	
168	0.33 ± 0.11	3	3	0.12 ± 0.015	3	3	
24 control	0.026 ± 0.03	2	1	BLQ	2	0	

Table 7. Results from Parent D_5 Quantitation in Feces

Feces - Corn Oil Dose						
	Male			Female		
time point (hr)	D_5 Concentration (µg/g ± std error)	n	n above BLQ	D_5 Concentration (µg/g ± std error)	n	n above BLQ
6	1.48 ± 1.10	3	2	0.49	2	1
12	1911.41 ± 1894.93	3	3	1165.20 ± 1151.14	3	3
24	21818.20 ± 5517.62	4	4	19142.84 ± 5307.91	3	3
48	12075.78 ± 1409.609	4	4	11857.22 ± 4891.26	3	3
72	1319.62 ± 341.104	4	4	1410.07 ± 913.34	3	3
96	63.04 ± 30.879	4	4	17.55 ± 5.05	3	3
120	2.68 ± 1.434	4	4	1.18 ± 0.45	3	3
144	2.78 ± 2.258	4	3	0.76 ± 0.32	3	3
168	4.15 ± 3.809	4	3	23.73 ± 22.55	3	3
24 control	BLQ	2	0	0.30 ± 0.30	2	1

Table 7. Results from Parent D_5 Quantitation in Feces (continued)

Feces - Females							
	Corn Oil			Neat		[illegible]	
time point (hr)	D_5 Concentration (µg/g ± std error)	n	n above BLQ	D_5 Concentration (µg/g ± std error)	n	n above BLQ	[illegible]
6	0.49 ± 0.37	2	1	2.37 ± 3.12	3	3	
12	1165.20 ± 1151.14	3	3	9665.22 ± 5986.74	3	3	
24	19142.84 ± 5307.91	3	3	23332.70 ± 2147.07	3	3	
48	11857.22 ± 4891.261	3	3	7780.50 ± 2430.36	3	3	
72	1410.07 ± 913.340	3	3	420.94 ± 161.092	3	3	
96	17.55 ± 5.049	3	3	213.24 ± 204.006	3	3	
120	1.18 ± 0.446	3	3	0.70 ± 0.138	3	3	
144	0.76 ± 0.32	3	3	BLQ[†]	3	0	
168	23.73 ± 22.55	3	3	118.11 ± 118.108	3	1	
24 control	0.30 ± 0.30	2	1	BLQ[†]	2	0	

Table 8. Results from Parent D_5 Quantitation in Expired Volatiles

Expired Volatiles - Corn Oil Dose						
	Male			Female		
time point (hr)	D_5 Concentration (µg/hr ± std error)	n	n above BLQ	D_5 Concentration (µg/hr ± std error)	n	n above BLQ
1	98.59 ± 57 16	4	4	47.13 ± 40.12	3	3
2	6.92 ± 2.47	4	4	7.32 ± 2.03	3	3
4	21.44 ± 1.20	4	4	21.68 ± 2.71	3	3
6	44.05 ± 2.09	4	4	41.85 ± 2.16	3	3
12	199.08 ± 136 98	4	4	246.28 ± 190.29	3	3
24	2679.43 ± 1575.51	4	4	1063.34 ± 303.80	3	3
48	392.53 ± 197.690	4	4	49.40 ± 28.58	3	3
72	38.71 ± 26.286	4	4	5.14 ± 0.63	3	3
96	2.48 ± 0.177	4	4	2.21 ± 0.33	3	3
120	1.16 ± 0.179	4	4	1.04 ± 0.56	3	3
144	0.73 ± 0.165	4	4	0.81 ± 0.14	3	3
168	0.69 ± 0.102	4	4	0.83 ± 0.18	3	3
24 control	* 0.14 ± 0.01	2	2	BLQ	2	0

* Amount found in control was subtracted from all other samples

Table 8. Results from Parent D_5 Quantitation in Expired Volatiles (continued)

Expired Volatiles - Females							
	Corn Oil			Neat			
time point (hr)	D_5 Concentration (µg/hr ± std error)	n	n above BLQ	D_5 Concentration (µg/hr ± std error)	n	n above BLQ	
1	47.13 ± 40.12	3	3	279.75 ± 271.26	3	2	
2	7.32 ± 2.03	3	3	33.30 ± 25.45	3	2	
4	21.68 ± 2.71	3	3	* 266.43 ± 257.22	3	3	
6	41.85 ± 2.16	3	3	124.08 ± 103.61	3	3	
12	246.28 ± 190.29	3	3	64.56 ± 40.48	3	3	
24	1063.34 ± 303.80	3	3	112.17 ± 61.21	3	3	
48	49.40 ± 28.58	3	3	76.07 ± 40.48	3	3	
72	5.14 ± 0.63	3	3	55.67 ± 26.717	3	3	
96	2.21 ± 0.33	3	3	23.27 ± 12.293	3	3	
120	1.04 ± 0.56	3	3	5.34 ± 4.780	3	3	
144	0.81 ± 0.14	3	3	1.67 ± 1.408	3	3	
168	0.83 ± 0.18	3	3	2.15 ± 1.940	3	3	
24 control	BLQ	2	0	* 0.09 ± 0.02	2	2	

* Amount found in control was subtracted from all other samples

Table 9
Summary of Fecal Metabolites as Percentages of the Total Fecal Radioactivity

	% Unknown	% of Decamethylcyclo-pentasiloxane (D_5 parent)
12 Hour Male Corn Oil	0% N/AP	100% N/AP
12 Hour Female Corn Oil	0% N/AP	100% N/AP
12 Hour Female Neat	0% ± 0%	100% ± 0%
12 Hour Female Simethicone	0% ± 0%	100% ± 0%
24 Hour Male Corn Oil	3% ± 1%	97% ± 1%
24 Hour Female Corn Oil	1% ± 1%	99% ± 1%
24 Hour Female Neat	0% ± 0%	100% ± 0%
24 Hour Female Simethicone	0% ± 0%	100% ± 0%
48 Hour Male Corn Oil	4% ± 1%	96% ± 1%
48 Hour Female Corn Oil	2% ± 2%	98% ± 2%
48 Hour Female Neat	1% ± 1%	99% ± 1%
48 Hour Female Simethicone	0% ± 0%	100% ± 0%
72 Hour Male Corn Oil	0% ± 0%	100% ± 0%
72 Hour Female Corn Oil	0% ± 0%	100% ± 0%
72 Hour Female Neat	0% ± 0%	100% ± 0%
72 Hour Female Simethicone	0% ± 0%	100% ± 0%

Table 10
Summary of Urinary Metabolites as Percentages of the Total Urinary Radioactivity

	De-Methylated % of Methylsilanetriol	De-Methylated % of Dimethyl-disiloxane-1,3,3,3-tetrol	De-Methylated % of Dimethyl-disiloxane-1,1,3,3-tetrol	% of Dimethyl-silanediol	De-Methylated % of 1,3,3-Trimethyl-disiloxane- 1,1,3-triol	% of 1,1,3,3-Tetramethyl-disiloxane-1,3-diol	% of 1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Sum of De-methylated Peak Percentages
12 Hour Male Corn Oil	38% ± 5%	9% ± 1%	0% ± 0%	45% ± 4%	5% ± 3%	3% ± 3%	0% ± 0%	52% ± 5%
12 Hour Female Corn Oil	35% ± 3%	9% ± 8%	0% ± 0%	50% ± 11%	0% ± 0%	4% ± 7%	3% ± 5%	43% ± 6%
12 Hour Female Neat	39% ± 6%	0% ± 0%	0% ± 0%	57% ± 6%	0% ± 0%	4% ± 8%	0% ± 0%	39% ± 6%
12 Hour Female Simethicone	43% ± 5%	0% ± 0%	0% ± 0%	57% ± 5%	0% ± 0%	0% ± 0%	0% ± 0%	43% ± 5%
24 Hour Male Corn Oil	32% ± 1%	9% ± 1%	2% ± 1%	48% ± 4%	5% ± 1%	3% ± 0%	0% ± 1%	48% ± 3%
24 Hour Female Corn Oil	31% ± 1%	10% ± 0%	0% ± 1%	46% ± 11%	6% ± 0%	5% ± 1%	0% ± 0%	48% ± 1%
24 Hour Female Neat	32% ± 2%	9% ± 2%	0% ± 0%	51% ± 6%	2% ± 3%	5% ± 1%	0% ± 0%	43% ± 4%
24 Hour Female Simethicone	35% ± 4%	5% ± 6%	0% ± 0%	59% ± 5%	0% ± 0%	1% ± 3%	0% ± 0%	39% ± 3%
48 Hour Male Corn Oil	29% ± 1%	11% ± 0%	2% ± 0%	53% ± 1%	3% ± 1%	2% ± 0%	0% ± 0%	45% ± 1%
48 Hour Female Corn Oil	29% ± 2%	11% ± 2%	2% ± 1%	52% ± 3%	3% ± 2%	3% ± 2%	0% ± 0%	45% ± 1%
48 Hour Female Neat	30% ± 3%	11% ± 1%	1% ± 1%	55% ± 5%	1% ± 1%	1% ± 2%	0% ± 0%	43% ± 4%
48 Hour Female Simethicone	35% ± 3%	7% ± 8%	0% ± 0%	58% ± 6%	0% ± 0%	0% ± 0%	0% ± 0%	42% ± 6%
72 Hour Male Corn Oil	35% ± 1%	10% ± 2%	0% ± 0%	55% ± 3%	0% ± 0%	0% ± 0%	0% ± 0%	45% ± 3%
72 Hour Female Corn Oil	29% ± 2%	9% ± 1%	0% ± 1%	58% ± 5%	1% ± 2%	2% ± 2%	0% ± 0%	39% ± 4%
72 Hour Female Neat	35% ± 4%	3% ± 6%	0% ± 0%	62% ± 3%	0% ± 0%	0% ± 0%	0% ± 0%	38% ± 3%
72 Hour Female Simethicone	50% ± 34%	4% ± 7%	0% ± 0%	47% ± 31%	0% ± 0%	0% ± 0%	0% ± 0%	53% ± 31%
96 Hour Male Corn Oil	100% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	100% ± 0%
96 Hour Female Corn Oil	100% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	0% ± 0%	100% ± 0%
96 Hour Female Neat	16% ± 19%	0% ± 0%	0% ± 0%	84% ± 19%	0% ± 0%	0% ± 0%	0% ± 0%	16% ± 19%
96 Hour Female Simethicone	21% ± 29%	0% ± 0%	0% ± 0%	79% ± 29%	0% ± 0%	0% ± 0%	0% ± 0%	21% ± 29%

Figure 1. Concentration of Parent D_5 in Blood as a Function of Postexposure Time from Male and Female Rats Following Dosing with Corn Oil

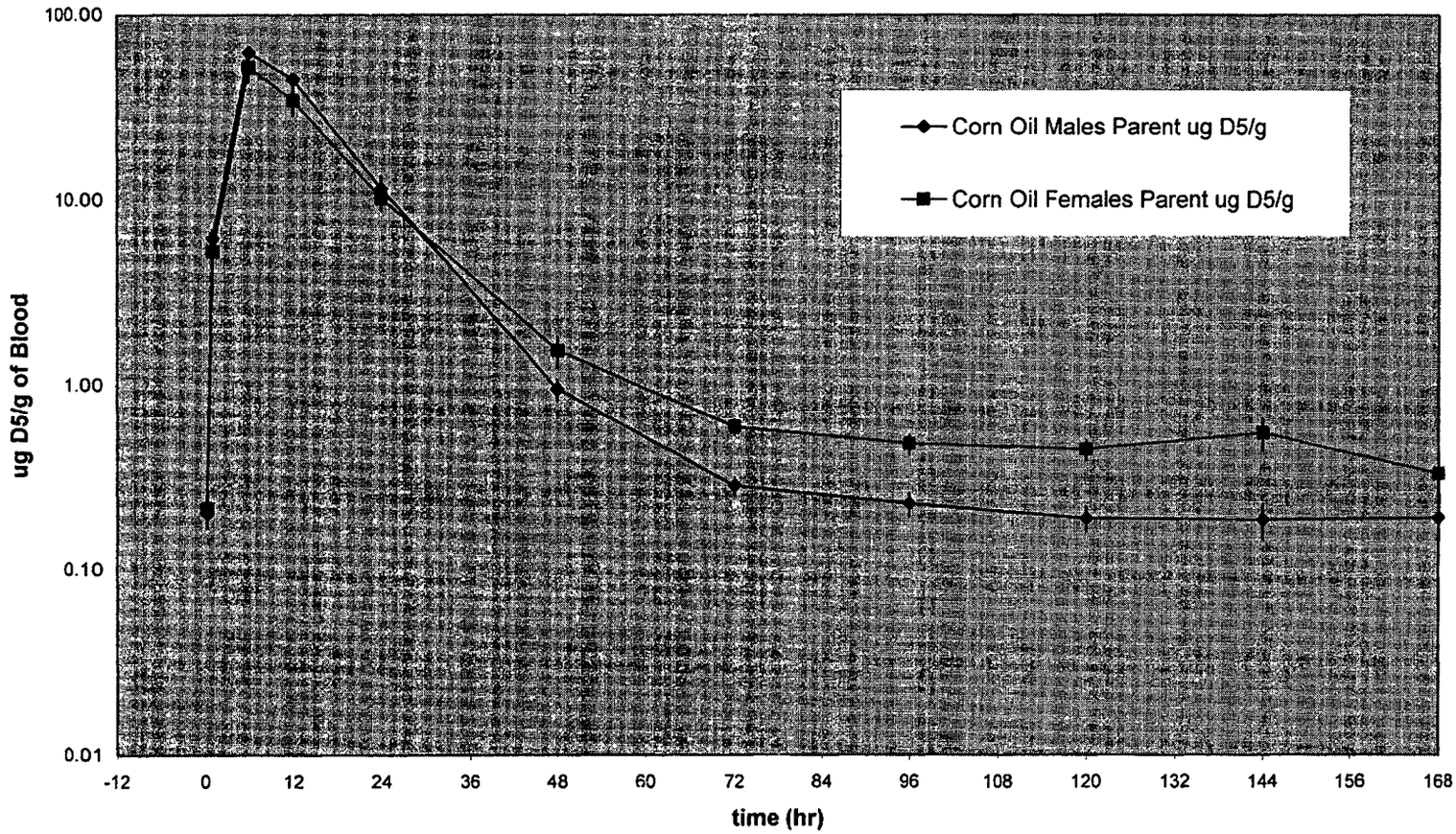


Figure 2. Concentration of Parent D_5 in Blood as a Function of Postexposure Time from Female Rats Following Dosing with Corn Oil, Simethicone or Neat

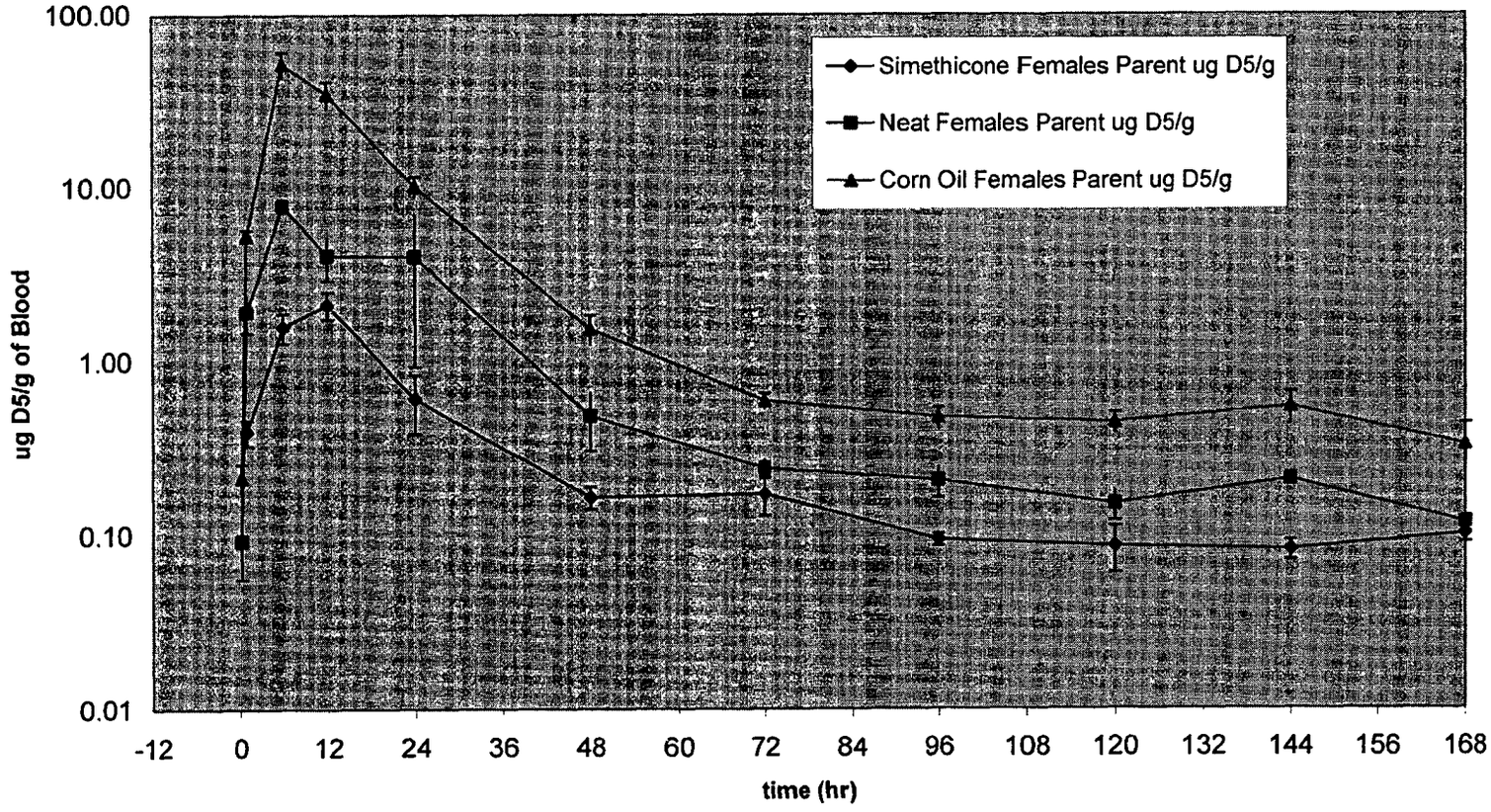


Figure 3. Concentration of Parent D_5 in Feces as a Function of Postexposure Time from Male and Female Rats Following Dosing with Corn Oil

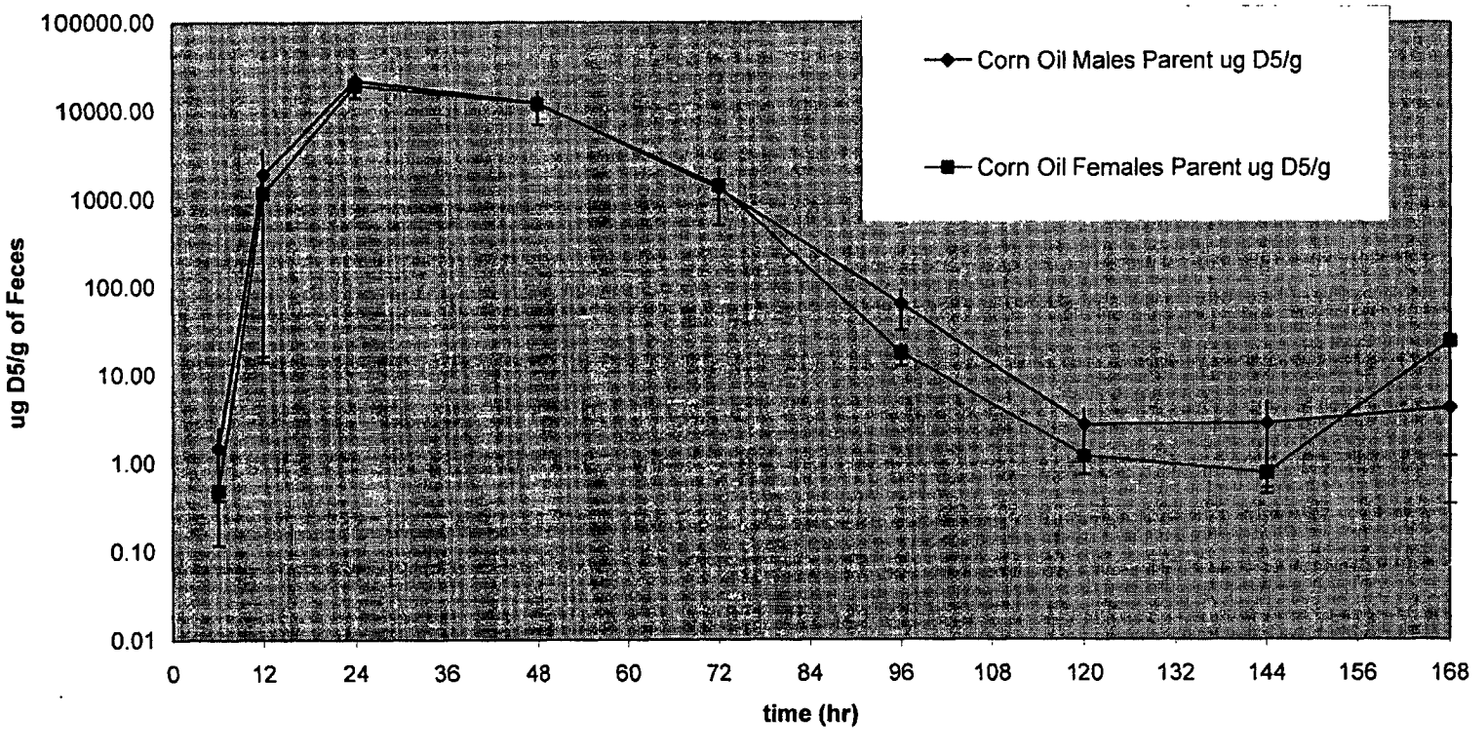


Figure 4. Concentration of Parent D_5 in Feces as a Function of Postexposure Time from Female Rats Following Dosing with Corn Oil, Simethicone or Neat

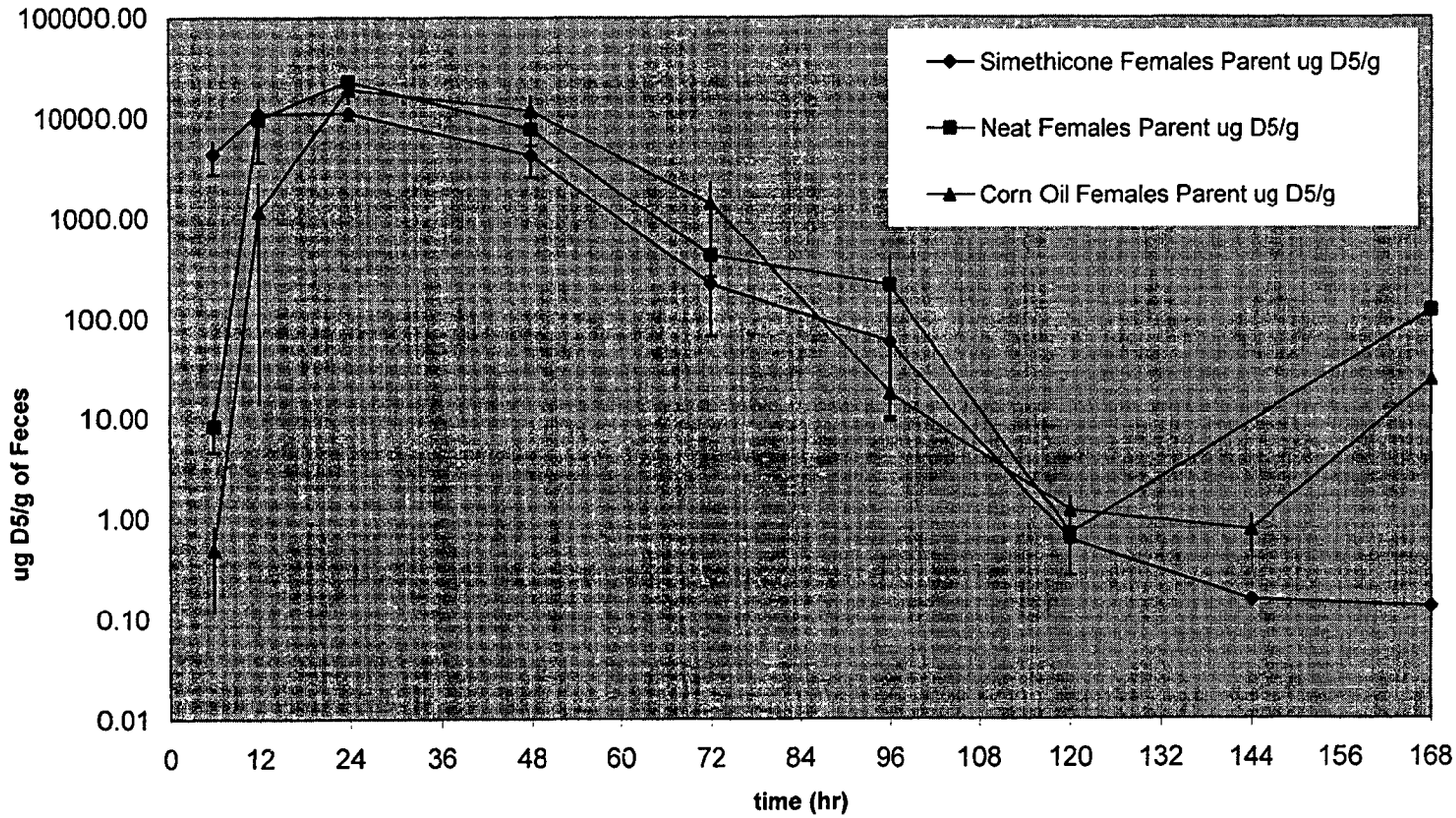


Figure 5. Concentration of Parent D_5 in Expired Volatiles as a Function of Postexposure Time from Male and Female Rats Following Dosing with Corn Oil

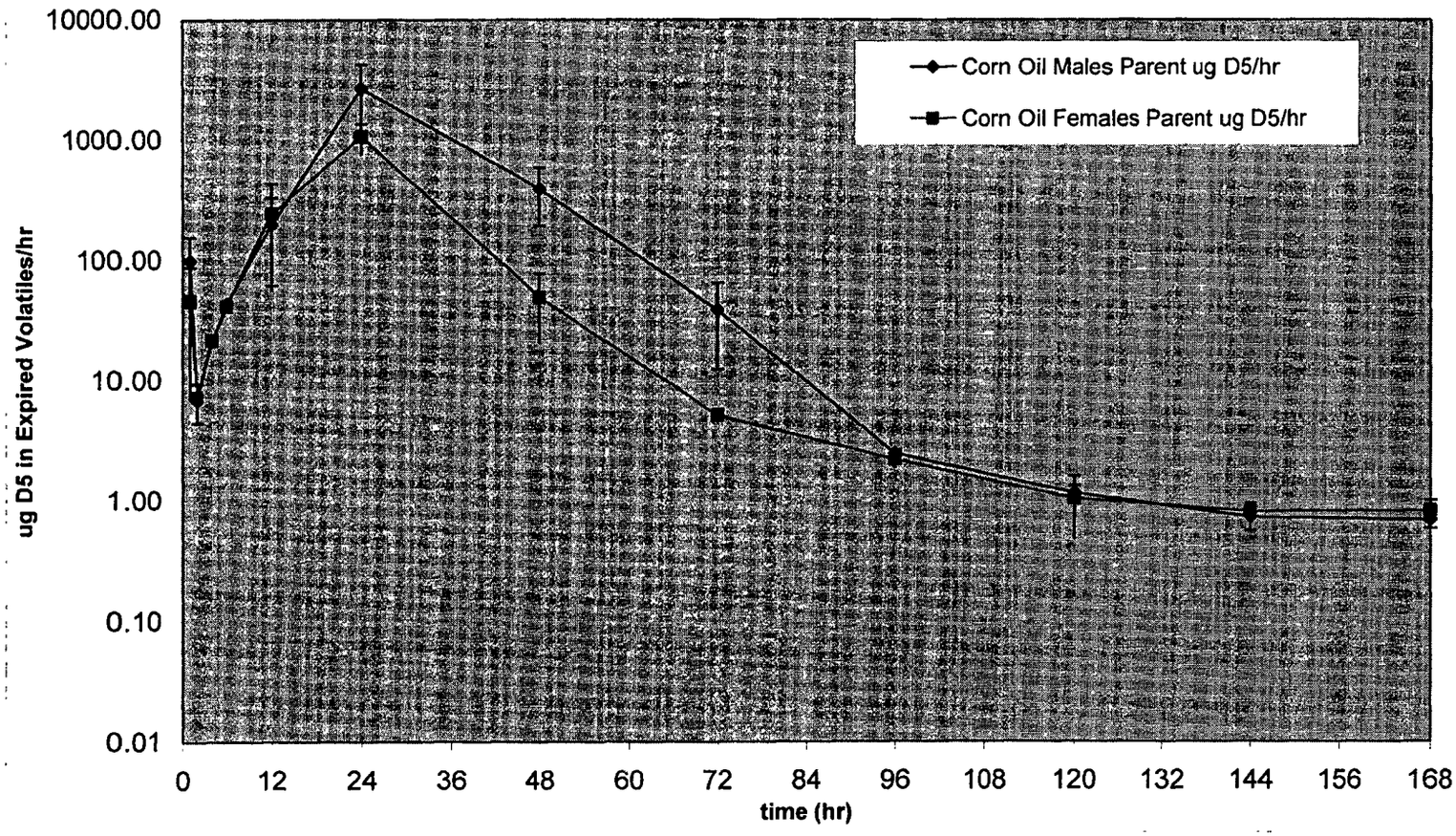


Figure 6. Concentration of Parent D_5 in Expired Volatiles as a Function of Postexposure Time from Female Rats Following Dosing with Corn Oil, Simethicone or Neat

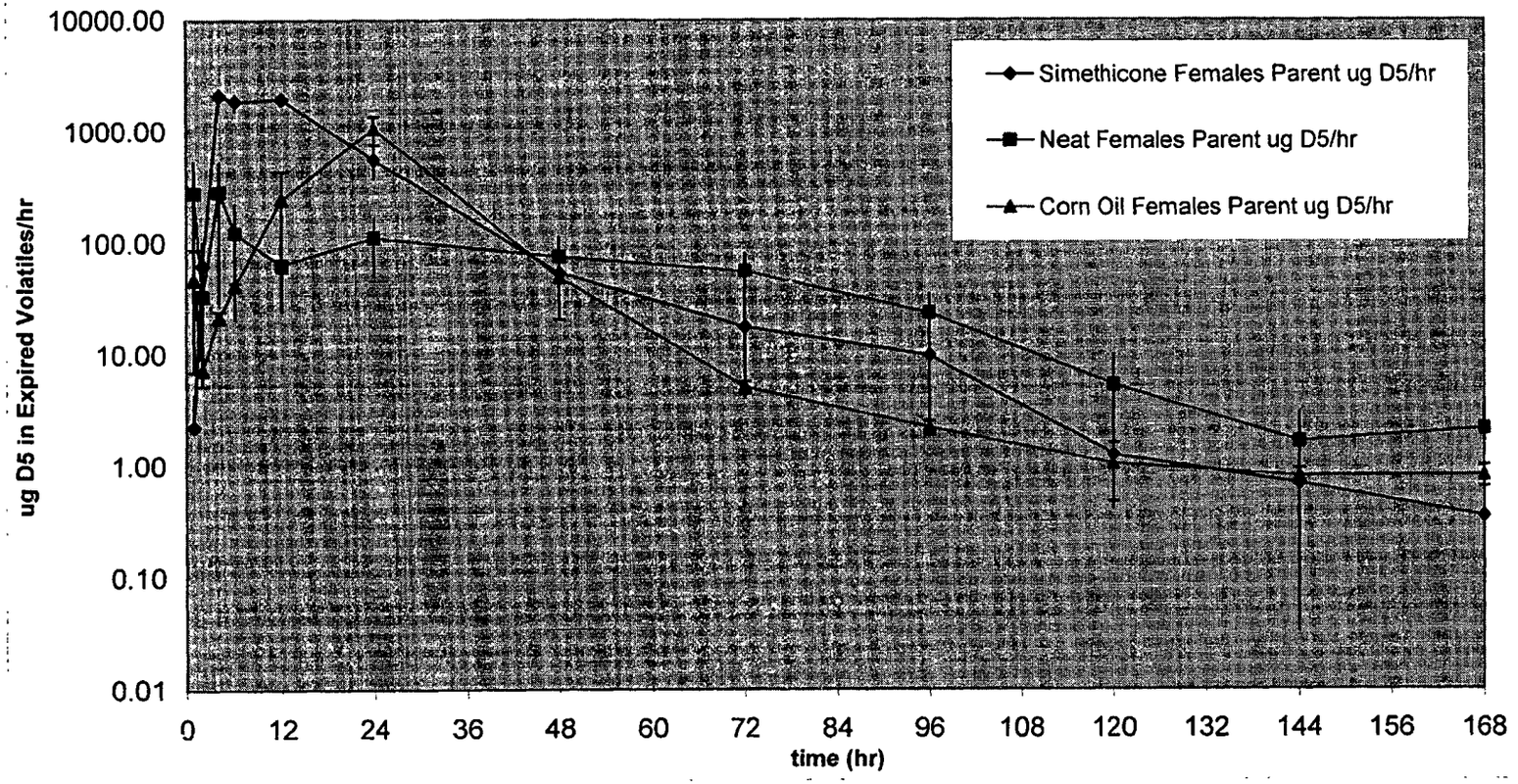


Figure 7. Example HPLC/RAD Chromatograms of a) ^{14}C-D_5 Standard and Blood Samples from b) Male and c) Female Rats at 12 Hours Following Corn Oil Dose

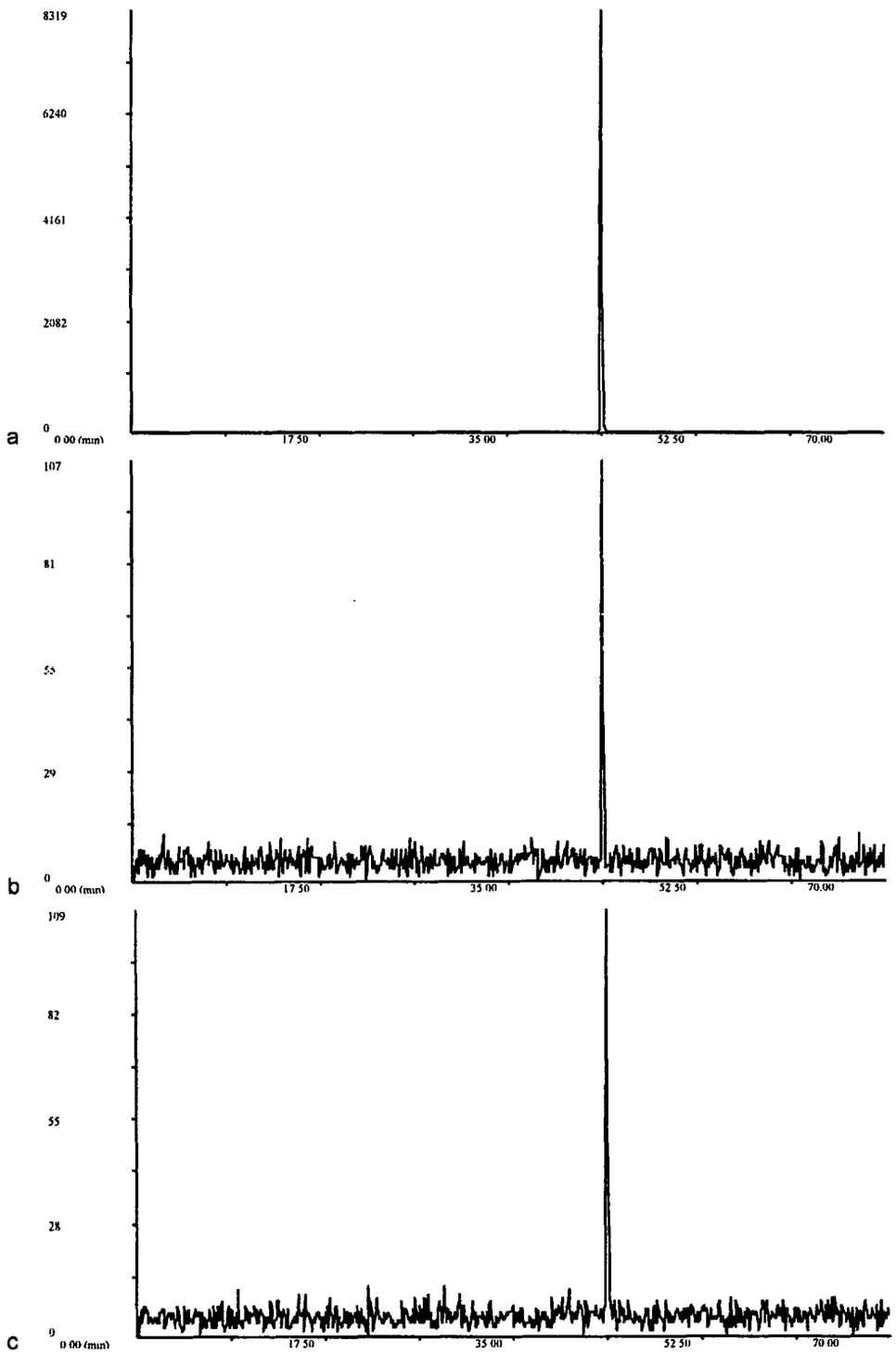


Figure 8. Example HPLC/RAD Chromatograms of a) ^{14}C-D_5 Standard and Fecal Samples from b) Male and c) Female Rats at 24 Hours Following Corn Oil Dose

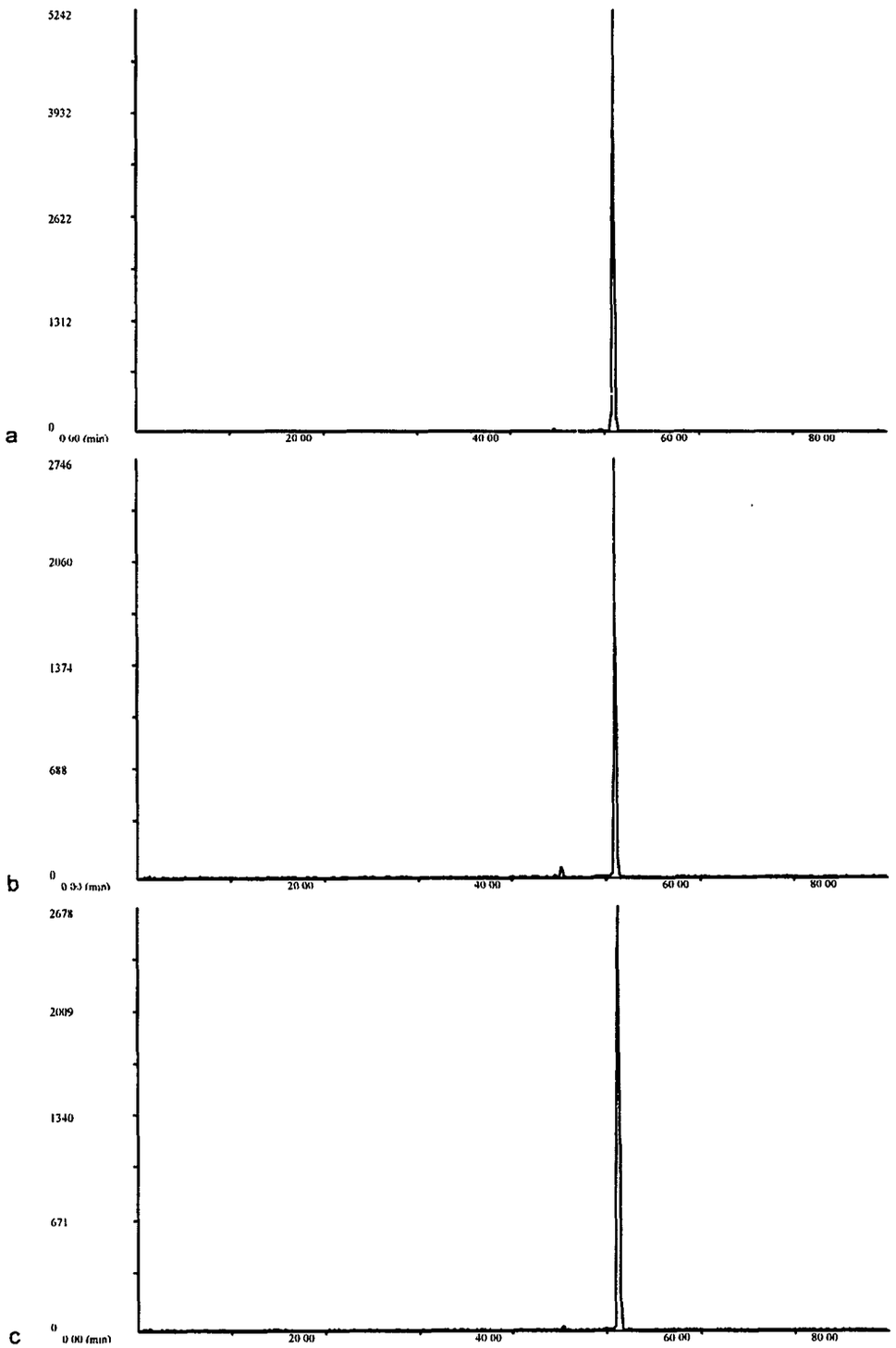


Figure 9. Example HPLC/RAD Chromatograms of a)^{14}C-D_5 Standard and Urine Samples from b) Male and c) Female Rats at 24 Hours Following Corn Oil Dose

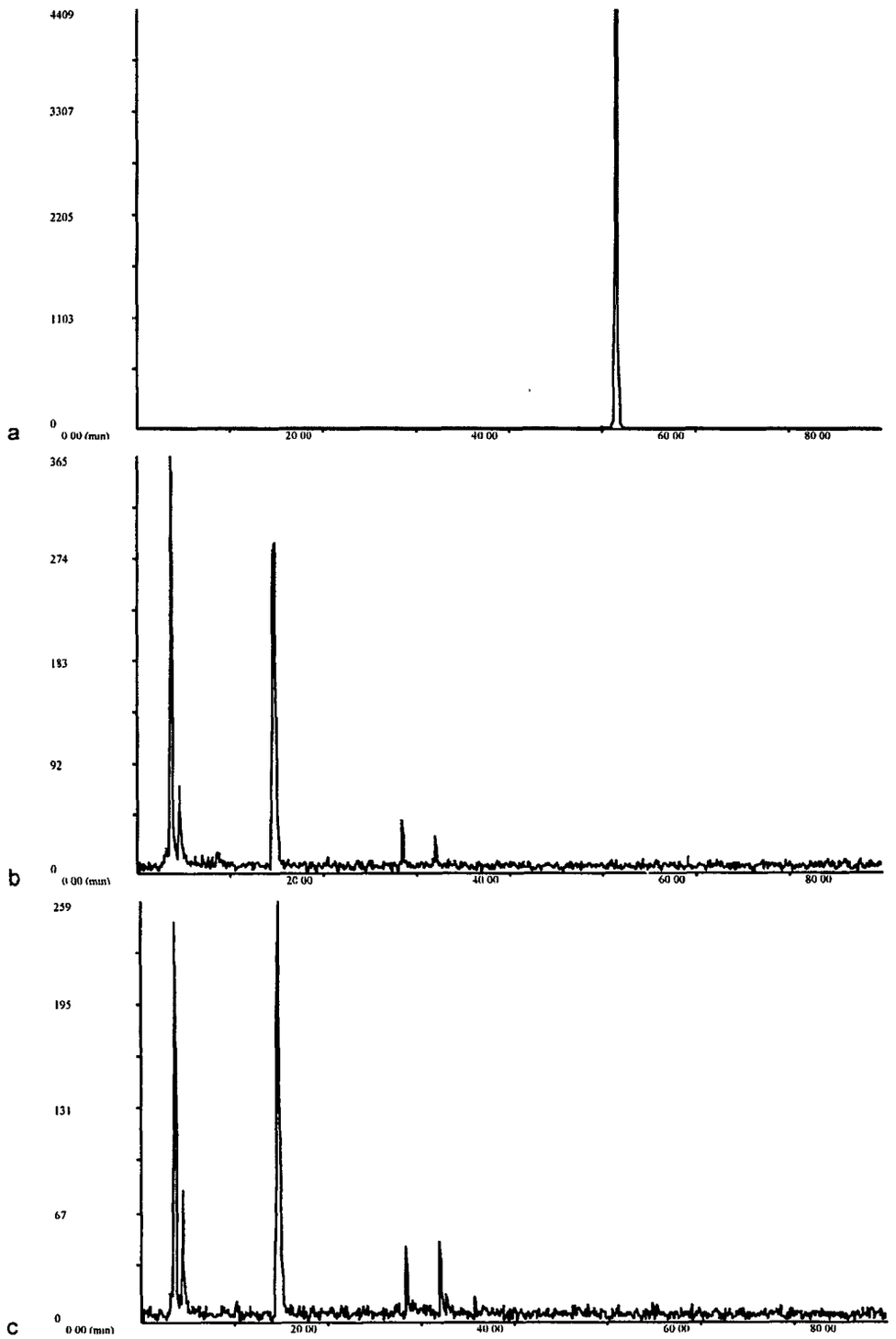
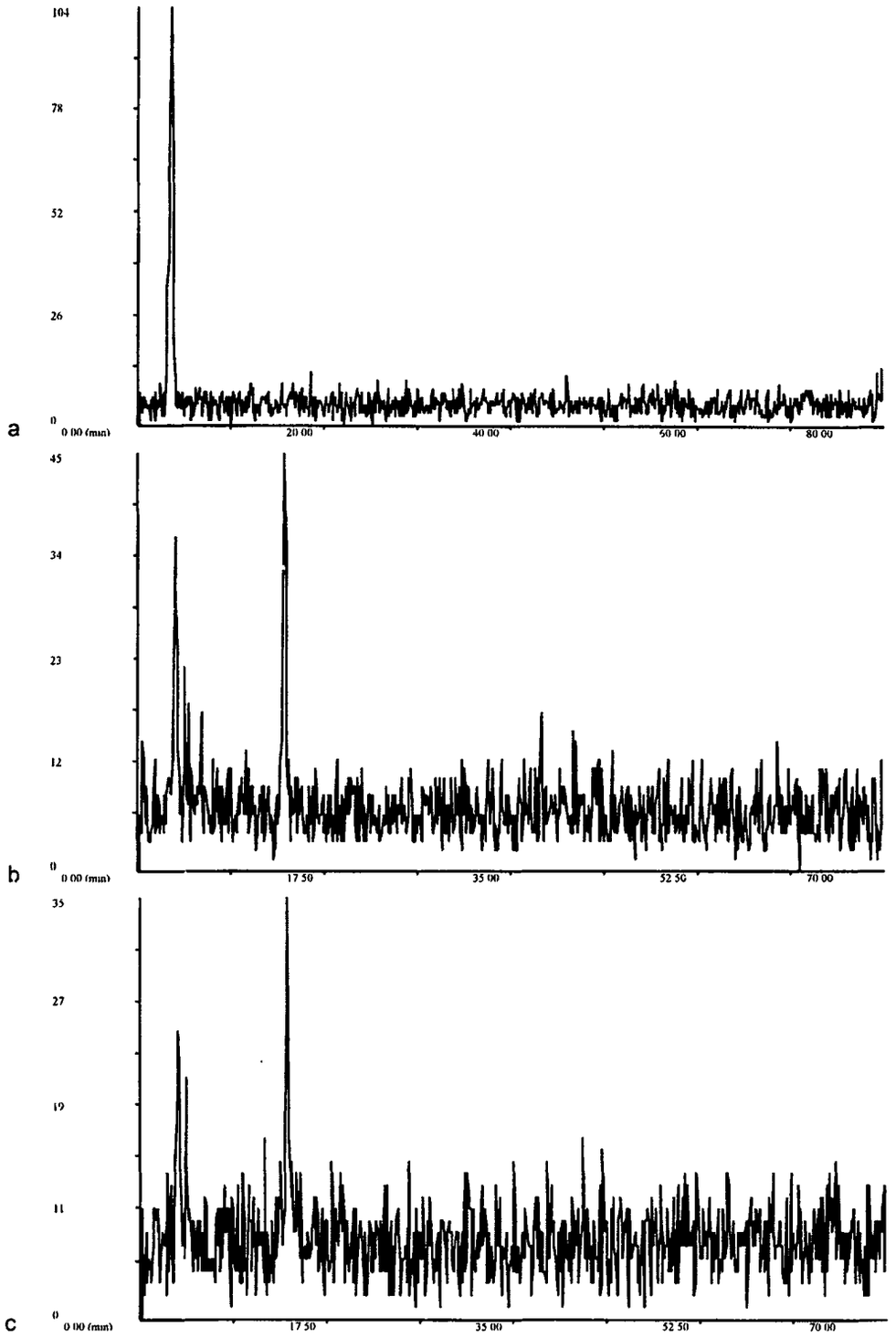


Figure 10. Example HPLC/RAD Chromatograms of Urine Samples from Female Rats at 96 Hours Following a) Corn Oil Dose b) Neat Dose and c) Simethicone Dose



ATTACHMENT A

Procedure for Determination of D_5 in Biological Matrices

(Plasma, Blood, Liver, Lung, Feces and Fat)

Procedure for Determination of D_s in Biological Matrices (Plasma, Blood, Liver, Lung, Feces, and Fat)

Debra A. McNett — Date 2-5-01

Debra A. McNett, B.S.
Bioanalytical Supervisor

Marina Jovanovic — Date 2-5-01

Marina L. Jovanovic, M.S.
Study Director

PROCEDURE FOR DETERMINATION OF D_5 IN BIOLOGICAL MATRICES (PLASMA, BLOOD, LIVER, LUNG, FECES, AND FAT)

PURPOSE

To describe a method for extraction and quantification of Decamethylcyclopentasiloxane (D_5) in biological matrices.

EQUIPMENT

1. Chemicals
   a. Decamethylcyclopentasiloxane (D_5) — supplied by DCC
   b. Tetrakis(trimethylsiloxy)silane (M_4Q) — supplied by Gelest
   c. Tetrahydrofuran anhydrous 99.9% (THF) — supplied by Aldrich
   d. Magnesium sulfate ($MgSO_4$) — supplied by Fisher

2. Equipment

GC/MS	HP 6890 HP Chemstation Software	Hewlett Packard
Column	HP-5 MS 30m x 0.25mm ID, 0.25µm film thickness	Hewlett Packard
Merlin Microseal	Microseal-221 nut Microseal-H septum	Merlin Instrument Company
Centrifuge		IEC Centra-MP4R
Vortexer		VWR Multi-Tube Vortexer
Autosampler vials	2 mL crimp top, clear glass	Hewlett Packard
Limited volume inserts	100uL glass	Alltech
Aluminum crimp caps	teflon-lined red/orange butyl rubber septa	Hewlett Packard
Extractant collection vials and caps	glass – PTFE lined	Alltech
Round bottom vial	1.7 mL crimp top, clear glass	Alltech
scissors	stainless steel surgical	

Note: equivalent equipment may be substituted for any of the above.

3. General

An analytical balance shall be used for gravimetric preparation of all standards and samples on a weight of solute per weight of solution basis.

PREPARATION OF REAGENTS

1. Internal Standard Stock Preparation

Accurately weigh and record to the nearest 0.1mg in a glass vial previously capped and tared, approximately 20.0 mg of M_4Q. Add approximately 50 mL of THF, obtain final weight of solution and mix well. (Concentration approximately 450000 ng/g).

2. Internal Standard Working Solution

The internal standard working solution (ISTD) which is added to all working solvent standards and QC matrix samples consists of THF containing M_4Q (IS). To prepare 100 mL of internal standard solution, weigh and record to the nearest 0.1 mg, approximately 0.6 mL (~0.534 g) of internal standard stock solution in a suitable glass vial. Add approximately 100 mL of THF, cap and vortex gently for 30 seconds. Obtain the final weight of the standard solution. (Concentration approximately 2700 ng/g).

3. Standard Preparation (STD)

3.1 STD STK

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg, approximately 25.0 mg of D_5. Add approximately 10 mL of THF, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and THF. (Concentration approximately 2810000 ng/g).

3.2 STD STK 1

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.1mL of STD STK (above). Add approximately 12.5 mL of THF, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and THF. (Concentration approximately 22500 ng/g)

3.3 STD STK 2

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.25mL of STD STK 1 (above). Add approximately 10 mL of THF, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and THF. (Concentration approximately 562 ng/g)

4. QC Stock Solution Preparation

4.1 QC STK

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg, approximately 10.0 mg of D_5. Add approximately 10 mL of THF, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and THF. (Concentration approximately 1120000 ng/g).

4.2 QC STK 1

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.4mL of QC STK (above). Add approximately 12.5 mL of THF, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and THF. (Concentration approximately 35800 ng/g)

4.3 QC STK 2

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.05mL of QC STK (above). Add approximately 10 mL of THF, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and THF. (Concentration approximately 5600 ng/g).

NOTE:
Record all STD STK and QC STK preparation information on an appropriate form.
Reagent volumes and weights may be scaled up or down proportionally.

STD CURVE PREPARATION

Place approximately 250 mg of $MgSO_4$ into round bottom glass vials. Prepare solvent standards with the appropriate standard stock solution and internal standard solution according to the following table. Obtain the weight of the aliquot of standard stock and the aliquot of internal standard solution placed in the vial containing $MgSO_4$ all to the nearest 0.1mg.

TABLE 1: Low STD Curve

Standard ID	Volume of STD STK (mL)	STD STK used	Volume of Internal standard solution (mL)	Total Volume (mL)	Approximate amount of IS added (ng)	Approximate amount D5 added (ng)
STD A	0	none	0.5	1.00	1350	0.00
STD B	0.04	STD STK 2	0.5	1.00	1350	22.5
STD C	0.05	STD STK 2	0.5	1.00	1350	28.1
STD D	0.06	STD STK 2	0.5	1.00	1350	33.7
STD E	0.07	STD STK 2	0.5	1.00	1350	39.3
STD F	0.09	STD STK 2	0.5	1.00	1350	50.6
STD G	0.10	STD STK 2	0.5	1.00	1350	56.2
STD H	0.13	STD STK 2	0.5	1.00	1350	73.1
STD J	0.32	STD STK 2	0.5	1.00	1350	180
STD K	0.02	STD STK 1	0.5	1.00	1350	450
STD L	0.05	STD STK 1	0.5	1.00	1350	1125
STD M	0.1	STD STK 1	0.5	1.00	1350	2250
STD N	0.25	STD STK 1	0.5	1.00	1350	5625
STD O	0.4	STD STK 1	0.5	1.00	1350	9000

STD (ng) = Concentration STD STK (1 or 2) (ng/g) X Wt. of STD (g)

Standard stock solutions and working standard solutions are stable at room temperature (18 ± 8°C) for up to 9 days.

QC SAMPLE PREPARATION

Prepare each matrix spike in duplicate according to the table below. Place approximately 250mg of matrix (plasma, liver or lung homogenate) into the appropriate vials and spike with appropriate QC stock solution as shown below. Volumes are given for comparison, but obtain weights of all aliquots for calculation purposes (to the nearest 0.1mg).

Table 2: Low QC Matrix Samples (plasma, liver and lung homogenates)

Standard ID	Volume of STD STK (mL)	STD STK used	Volume of Internal standard solution (mL) (1st extract)	Total Volume[a] (mL)	Approximate amount of IS added (ng)	Approximate amount D5 added (ng)
QC Low-0	0.000	none	0.5	1.00	1350	0.00
QC Low-1	0.005	QC STK 2	0.5	1.00	1350	28.0
QC Low-2	0.012	QC STK 2	0.5	1.00	1350	67.2

[a] Total volume is based on 1 extraction at approximately 0.5 mL of internal standard solution (weight obtained) and an additional extraction at approximately 0.5 mL of THF.

Table 3: High QC Matrix Samples (plasma, liver and lung homogenates)

Standard ID	Volume of STD STK (mL)	STD STK used	Volume of Internal standard solution (mL) (1st extract)	Total Volume[a] (mL)	Approximate amount of IS added (ng)	Approximate amount D5 added (ng)
QC High-1	0.015	QC STK 1	0.5	1.00	1350	537
QC High-2	0.007	QC STK	0.5	1.00	1350	7840

[a] Total volume is based on 1 extraction at approximately 0.5 mL of internal standard solution (weight obtained) and an additional extraction at approximately 0.5 mL of THF.

For fat QC samples, prepare each level in duplicate. Place fat sample (approximately 250mg to 1g) into an appropriate vial and spike with the appropriate QC stock solution as shown below. Volumes are given for comparison, but obtain weights of all aliquots for calculation purposes (to the nearest 0.1mg).

Table 4: Low QC Matrix Samples (fat)

Standard ID	Volume of STD STK (mL)	STD STK used	Volume of Internal standard solution added (mL)	Total Volume[a] (mL)	Approximate amount of IS added (ng)	Approximate amount D5 added (ng)
QC Low-0	0.000	none	0.5	6.00	1350	0.00
QC Low-1	0.005	QC STK 2	0.5	6.00	1350	28.0
QC Low-2	0.007	QC STK 2	0.5	6.00	1350	39.2
QC Low-3	0.012	QC STK 2	0.5	6.00	1350	67.2

[a] Total volume is based on addition of approximately 0.5 mL of internal standard solution (weight obtained) followed by addition of approximately 5.5 mL THF.

Table 5: High QC Matrix Samples (fat)

Standard ID	Volume of STD STK (mL)	STD STK used	Volume of Internal standard solution added (mL)	Total Volume[a] (mL)	Approximate amount of IS added (ng)	Approximate amount D5 added (ng)
QC High-1	0.005	QC STK 1	0.5	6.00	1350	179
QC High-2	0.030	QC STK 1	0.5	6.00	1350	1074
QC High-3	0.007	QC STK	0.5	6.00	1350	7840

[a] Total volume is based on addition of approximately 0.5 mL of internal standard solution (weight obtained) followed by addition of approximately 5.5 mL THF.

QC samples are then extracted with THF according to the Sample Preparation Section below starting with step 1.2, 2.2 (don't add blood in step 2.3), 3.2, 4.2, or 5.4 depending on the matrix used.

SAMPLE PREPARATION

1. Plasma Extraction

   1.1 Obtain vial containing approximately 250 mg plasma sample from freezer and allow to thaw on ice.

   1.2 Remove from ice, wipe water from outside of vial and obtain weight of vial (or tare balance) containing the plasma sample.

   1.3 Remove cap, add 0.5mL of internal standard solution, obtain weight, cap, and vortex at least 6 minutes.

   1.4 Centrifuge at least 15 minutes at 2800 rpm and transfer the supernatant to a new pre-weighed glass vial.

   1.5 Add 0.5mL of THF to the plasma vial for a second extraction and vortex at least 6 minutes.

   1.6 Centrifuge at least 15 minutes at 2800 rpm and transfer the supernatant to the same glass vial containing the first extract. Obtain weight of combined extracts. (note: extractant weight only needed if extractant will be used for Radiochemical analysis.)

   1.7 Add approximately 250 mg of $MgSO_4$ to glass round bottom vials. Transfer ~600uL of each of the above extracts to the glass round bottom vials, cap and vortex for approximately 15 seconds, and allow to dry at least 4 hours.

   1.8 Centrifuge the samples for at least 30 minutes at 2800 rpm.

   1.9 Transfer an aliquot of the supernatant to a low volume insert in a GC autosampler vial.

2. Blood Extraction

2.1 Add ~5 glass beads to extraction vial.

2.2 Add ~0.5 mL of internal standard solution and obtain weight.

2.3 Add approximately 150-250 mg of Blood, obtain weight, and vortex at least 6 minutes.

2.4 Centrifuge at least 15 minutes at 2800 rpm and transfer the supernatant to a new pre-weighed glass vial.

2.1 Add 0.5mL of THF to the blood vial for a second extraction and vortex at least 6 minutes.

2.2 Centrifuge at least 15 minutes at 2800 rpm and transfer the supernatant to the same glass vial containing the first extract. Obtain weight of combined extracts. (note: extractant weight only needed if extractant will be used for Radiochemical analysis.)

2.3 Add approximately 250 mg of $MgSO_4$ to glass round bottom vials. Transfer ~600uL of each of the above extracts to the glass round bottom vials, cap and vortex for approximately 15 seconds, and allow to dry at least 4 hours.

2.4 Centrifuge the samples for at least 30 minutes at 2800 rpm.

2.5 Transfer an aliquot of the supernatant to a low volume insert in a GC autosampler vial.

3. Liver or Lung Homogenate Extraction

3.1 Obtain vial containing approximately 250 mg (weight previously obtained) liver or lung homogenate sample from freezer and allow to thaw on ice.

3.2 Remove from ice, wipe water from outside of vial and obtain tare weight of vial (or tare balance) containing the homogenate sample.

3.3 Remove cap, add 0.5mL of internal standard solution, obtain weight, cap, and vortex at least 6 minutes.

3.4 Centrifuge at least 15 minutes at 2800 rpm and transfer the supernatant to a new pre-weighed glass vial.

3.5 Add 0.5mL of THF to the liver or lung homogenate vial for a second extraction and vortex at least 6 minutes.

3.6 Centrifuge at least 15 minutes at 2800 rpm and transfer the supernatant to the same glass vial containing the first extract. Obtain weight of combined extracts. (note: extractant weight only needed if extractant will be used for Radiochemical analysis.)

3.7 Add approximately 250 mg of $MgSO_4$ to glass round bottom vials. Transfer ~600uL of each of the above extracts to the glass round bottom vials, cap and vortex for approximately 15 seconds, and allow to dry at least 4 hours.

3.8 Centrifuge the samples for at least 30 minutes at 2800 rpm.

3.9 Transfer an aliquot of the supernatant to a low volume insert in a GC autosampler vial.

4. Fat Extraction

4.1 Obtain vial containing approximately 0.1 g (weight previously obtained) fat sample from freezer and allow to thaw on ice.

4.2 Remove from ice, wipe water from outside of vial and obtain tare weight of vial (or tare balance) containing the homogenate sample.

4.3 Remove cap, add 0.5mL of internal standard solution and obtain weight. Add an additional 5.5 mL of THF.

4.4 With scissors, cut fat into small pieces to improve surface area contact with THF.

4.5 Vortex at least 6 minutes.

4.6 Centrifuge at least 15 minutes at 2800 rpm and transfer the supernatant to a new pre-weighed 7 mL glass vial. Obtain weight of the extract. (note: extractant weight only needed if extractant will be used for Radiochemical analysis.)

4.7 Add approximately 250 mg of $MgSO_4$ to glass round bottom vials. Transfer an aliquot of each of the above extracts (approximately 600uL) to the glass round bottom vials, cap and vortex for approximately 15 seconds, and allow to dry at least 4 hours.

4.8 Centrifuge the samples for at least 30 minutes at 2800 rpm.

4.9 Transfer an aliquot of the supernatant to a low volume insert in a GC autosampler vial.

5. Feces or GI Content Homogenate Extraction

5.1 Obtain jar containing feces homogenate sample from freezer and allow to thaw on ice.

5.2 Vortex gently by hand.

5.3 Accurately weigh and record to the nearest 0.1 mg in an appropriate vial, approximately 0.25 g of feces homogenate. Place original container back in -80°C storage.

5.4 Remove from ice, wipe water from outside of vial and obtain tare weight of vial (or tare balance) containing the homogenate sample. Add 0.5 mL of internal standard solution, obtain weight and vortex for at least 6 minutes.

5.5 Sonicate sample for at least 5 minutes.

5.6 Centrifuge at least 15 minutes at approximately 2800rpm (until supernatent separates) and transfer the supernatant to a new pre-weighed glass vial.

5.7 Add 0.5 mL of THF to the vial containing the feces homogenate for a second extraction and vortex for at least 6 minutes.

5.8 Sonicate sample for at least 5 minutes.

5.9 Centrifuge at least 15 minutes at approximately 2800rpm (until supernatent separates) and transfer the supernatent to the vial containing the 1st extract.

5.10 Repeat steps 1.7 to 1.9 one more time and combine the supernatent with the 1st two extracts. Obtain the final weight of the vial containing the combined 3 extracts. (note: extractant weight only needed if extractant will be used for Radiochemical analysis.)

5.11 Add approximately 250 mg of $MgSO_4$ to glass round bottom vials. Transfer ~600uL of each of the above extracts to the glass round bottom vials, cap and vortex for approximately 15 seconds, and allow to dry at least 4 hours.

5.12 Centrifuge the samples for at least 30 minutes at approximately 2800 rpm.

Transfer an aliquot of the supernatant to a low volume insert in a GC autosampler vial.

Note: Once samples are in extraction solvent, samples are stable up to 17 days at 4±4 degrees C.

ANALYSIS

Samples shall be analyzed by GC/MS using the instrument parameters shown in Table 7.

Table 7. Analysis Parameters

Instrument:	Hewlett Packard 6890 Gas Chromatograph/Mass Selective Detector		
Column:	Hewlett Packard HP-5MS 30m x 0.25mm ID with 0.25um film thickness		
Carrier Gas:	Helium, initial pressure 8.5 psi, 1.0 mL/min, constant flow on		
Injection:	temperature 250°C, splitless, purge time 0.20min, 2uL injection		
Oven Ramp:	Initial 70°C for 3.0 min, ramp to 210°C at 17°C/min,		
	ramp to 250°C at 30°C/min hold for 1 min, total run time 13.57 min.		
Detection:	MSD transfer line temperature 280°C		
	Quantitation ions:	D5:	355 m/z at 100msec
		M4Q:	281 m/z at 100msec

Single injection analysis of each sample is sufficient.

Sample Analysis Order (Example)
Analyze each matrix in separate analysis runs. Separate analysis runs may occur on the same day.

Solvent Blank
Solvent Internal Standard Blank (3 injections)
Solvent Calibration Standards, (Low to High)
Solvent Blank
QC Samples (Low to High)
Solvent Blank
Solvent Standard
Sample Blank
10 Samples or Less
Solvent Standard
Sample Blank

Repeat this Solvent standard and Sample analysis pattern until all samples are analyzed.

DATA ANALYSIS

This section describes the calculations for the calibration of the GC/MS and the method to determine the amount of D_5 per gram of plasma, blood, liver, lung, fat, or feces.

All calculations for routine sample analysis shall be performed using a Microsoft Excel spreadsheet (a spreadsheet which has been prepared for a specific application and has been confirmed by an independent review to perform calculations as defined; subsequent uses of the spreadsheet require 100% check of all entered data). Non-routine calculations shall be prepared and reviewed as directed by the Study Director (or designee).

1. Instrument Calibration Calculations

   Calibration of the mass spectrometer is performed using D_5 concentrations expressed in terms of ng D_5. The nominal concentrations of calibration standards are shown in Table 1. The standard curve may be split into up to 3 ranges depending on the range of the instrument as long as at least 4 standards make up a range.

   D_5 Calibration Equation

   Calculate a linear equation, using a suitable linear regression program, for D_5 where x = concentration (ng D_5) and y = peak area response ratio for the calibration standards from the GC/MS analysis. Enter the resulting slope (m) and y-intercept (b) from each equation into the spreadsheet.

   $y = mx + b$, where y = peak area response ratio and x = ng D_5

2. Calculation of D_5 Concentrations in Samples (ng D_5)

   The concentration of D_5 in a sample extract is calculated once the slope (m) and y-intercept (b) have been entered into the spreadsheet. The concentration (ng D_5) of D_5 in a sample extract is calculated by substitution of the peak area response ratio for y into the linear equation generated from calibration standards and solving for x, ($x = (y-b)/m$).

3. Calculation of D_5 Concentrations in Samples (µg D_5/g matrix)

   Calculation of D_5 concentration (µg/g) in sample matrix is as follows:

   D_5 (µg/g) = D_5(ng) / Sample matrix weight (g) x 1µg/1000ng

   If the sample is homogenized with water (saline) prior to extraction as in the case of liver, lung or feces/GI content, the final concentration D_5 in the matrix is calculated as follows:

   D_5 (µg/g) = D_5 (µg/g homogenate) x total homogenate weight (g) / matrix weight (g)

   Note: An assumption is made that the amount of internal standard added (~0.5 mL) is the same for all samples and standards. If when obtaining the weights of these additions, it is found that the weights vary significantly (%CV > 5%), or at the discretion of the bioanalytical supervisor, then all calculations will have to be adjusted to correct for the differing amounts of internal standard added. For example, the calibration curve would be generated with x = ng D_5/ng IS. Each sample would be calculated according to the calibration curve generated by solving for x (ng D_5/ng IS). The amount of D_5 (ng) in each sample is then calculated by multiplying the ratio found (ng D_5/ng IS) by the ng IS added. The subsequent calculations for determining ug D_5/g sample would be the same as described above.

DATA ACCEPTANCE

1. Calibration Acceptance Criteria

   Agreement between the analyzed and prepared concentrations of D_5 in the calibration standards must be achieved to prove conformance to the linear calibration model. The percent relative error, calculated by the qualified spreadsheet, shall be used to prove conformance and is calculated by subtracting the analyzed concentration from the prepared concentration, and then dividing by the prepared concentration and multiplying by 100. The percent relative error shall be within 15% for every calibration standard analyzed for the calibration to be acceptable. Calibrations that do not meet these requirements shall be brought to the attention of the Study Director (or designee). Exceptions to this calibration acceptance criteria shall be made if all samples are bracketed by calibration standards that did meet the calibration acceptance criteria. The solvent standards that are run intermittently throughout the run are to be within 15% for the run to be accepted. Any samples run before a standard meeting this acceptance criteria will be accepted. If any standards do not meet this acceptance criteria, any samples run after the standard will be evaluated by the bioanalytical supervisor if they will be accepted.

REPORTING AND DATA COMPLETION

The chemistry technician shall be responsible for submission of a completed data packet to the Study Director (or designate). This data packet shall include, as a minimum:

1. Hard copies of GC/MS data (including instrument parameters and sequence)
2. The calibration curve and the data from which it was generated
3. Data reduction spreadsheet

The chemistry technician shall also be responsible for completion of the notebook:

1. Calibration Standard Form attached in notebook and completed
2. QC Sample Preparation Form attached in notebook and completed
3. One page describing which samples were analyzed and any other comments on sample workup and analysis

QUALITY CONTROL

The chemistry technician shall check the data packet for accuracy and completeness prior to forwarding to the Study Director (or designate). The Study Director (or designate) shall provide a one-over-one check for accuracy and completeness and ensure that all GLP record keeping practices were correctly performed.

ATTACHMENT B

Procedure for Determination of D_5 in Expired Volatiles (Charcoal Tubes)

Procedure for Determination of D_5 in Expired Volatiles (Charcoal Tubes)

Debra A. McNett — Date 2-2-01

Debra A. McNett, B.S.
Bioanalytical Supervisor

Marina Jovanovic — Date 02-02-2001

Marina L. Jovanovic, M.S.
Study Director

PROCEDURE FOR DETERMINATION OF D_5 EXPIRED VOLATILES (CHARCOAL TUBES)

PURPOSE

To describe a method for extraction and quantification of Decamethylcyclopentasiloxane (D_5) in expired volatiles that have been trapped on charcoal tubes.

EQUIPMENT

1. Chemicals
   a. Decamethylcyclopentasiloxane (D_5) — supplied by DCC
   b. Tetrakis(trimethylsiloxy)silane (M_4Q) — supplied by Gelest
   c. Toluene 99.9% — supplied by Fisher
   d. Magnesium sulfate ($MgSO_4$) — supplied by Fisher

2. Equipment

GC/MS	HP 6890 HP Chemstation Software	Hewlett Packard
Column	HP-5 MS 30m x 0.25mm ID, 0.25µm film thickness	Hewlett Packard
Merlin Microseal	Microseal-221 nut Microseal-H septum	Merlin Instrument Company
Centrifuge		IEC Contra-8R Centrifuge Beckman GS-6R
Vortexer		VWR Multi-Tube Vortexer
Autosampler vials	2 mL crimp top, clear glass	Hewlett Packard
Limited volume inserts	100µL glass	Alltech
Aluminum crimp caps	teflon-lined red/orange butyl rubber septa	Hewlett Packard
Desorption vials vials and caps	20 mL glass – aluminum lined	Fisher
Round bottom vial	1.7 mL crimp top, clear Glass	Alltech
Small file or glass scoring tool		Fisher
Tweezers		Fisher

Note: equivalent equipment may be substituted for any of the above.

3. General

An analytical balance shall be used for gravimetric preparation of all standards and samples on a weight of solute per weight of solution basis.

PREPARATION OF REAGENTS

1.1 Internal Standard Stock A Preparation

Accurately weigh and record to the nearest 0.1mg in a glass vial previously capped and tared, approximately 50.0 mg of M_4Q. Add approximately 12.5 mL of toluene, cap and vortex gently for 30 seconds. Obtain the final weight of the standard solution. (Concentration approximately 4000000 ng/g).

1.2 Internal Standard Stock B Preparation

Accurately weigh and record to the nearest 0.1mg in a glass vial previously capped and tared, approximately 200 mg of Internal Standard Stock A (above). Add approximately 50 mL of toluene, cap and vortex gently for 30 seconds. Obtain the final weight of the standard solution. (Concentration approximately 160000 ng/g).

1.3 Internal Standard Working Solution (toluene/ISTD)

The internal standard working solution (toluene/ISTD) which is used as the dilution/extraction solvent for all working solvent standards, QC matrix samples and study samples, consists of toluene containing M_4Q (IS). To prepare 4L of internal standard working solution, remove 40 mL of toluene from a 4L bottle of toluene and using a 10mL pipette, transfer 40 mL of Internal Standard Stock B (above) into the 4L bottle of toluene. Mix thoroughly and clearly identify the bottle with the new solution. (Concentration approximately 256 ng/g).

3. Standard Preparation (STD)

3.1 STD STK A

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg, approximately 50.0 mg of D_5. Add approximately 12.5 mL of toluene/ISTD, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and toluene/ISTD. (Concentration approximately 4000000 ng/g).

3.2 STD STK B

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.05mL of STD STK A (above). Add approximately 12.5 mL of toluene/ISTD, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and toluene/ISTD. (Concentration approximately 16000 ng/g)

3.3 STD STK 1000

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.63mL of STD STK B (above). Add approximately 10 mL of toluene/ISTD, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and toluene/ISTD. (Concentration approximately 1000 ng/g)

3.4 STD STK 100

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 1.0mL of STD STK 1000 (above). Add approximately 10 mL of toluene/ISTD, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and toluene/ISTD. (Concentration approximately 100 ng/g)

4. QC Stock Solution Preparation

4.1 QC STK 200

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg, approximately 150.0 mg of D_5. Add approximately 0.75mL of toluene, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and toluene. (Concentration approximately 200mg/g).

4.2 QC STK 50

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.25mL of QC STK 200 (above). Add approximately 1 mL of toluene, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and toluene. (Concentration approximately 50mg/g)

4.3 QC STK 5

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.1mL of QC STK 50 (above). Add approximately 1 mL of toluene, cap and vortex gently for 30 seconds at motor speed 2. Obtain the final weight of standard and toluene. (Concentration approximately 5mg/g).

4.4 QC STK 0.2

In a suitable glass vial, previously capped and tared, weigh and record to the nearest 0.1 mg approximately 0.04mL of QC STK 5 (above). Add approximately 1 mL of toluene, cap and vortex gently for 30 seconds at motor speed 2 Obtain the final weight of standard and toluene. (Concentration approximately 0.2mg/g).

NOTE:
Record all STD STK and QC STK preparation information on an appropriate form.
Reagent volumes and weights may be scaled up or down proportionally.

STD CURVE PREPARATION

Place approximately 250 mg of $MgSO_4$ into round bottom glass vials. Prepare solvent standards with the appropriate standard stock solution and toluene/ISTD solution according to the following table. Obtain the weight of the aliquot of standard stock and the final solution weight placed in the vial containing $MgSO_4$ all to the nearest 0.1mg. Vortex each standard approximately 15 seconds. Dry (with $MgSO_4$) at least 1 hour. Centrifuge each standard at a setting of 3030 rpm for approximately 30 min. Place an aliquot of each standard in a limited volume insert in an autosampler vial and analyze by GC-MS.

TABLE 1: Solvent Standards

Standard ID	Volume of STD STK (µL)	STD STK used	Volume of toluene/ISTD (µL)	Total Volume (mL)	Approximate Concentration of D5 added (ng/g)
Blank	0	none	1000	1	0
20	200	STD STK 100	800	1	20
50	500	STD STK 100	500	1	50
100	1000	STD STK 100	0	1	100
200	200	STD STK 1000	800	1	200
400	400	STD STK 1000	600	1	400
600	600	STD STK 1000	400	1	600
800	800	STD STK 1000	200	1	800
1000	1000	STD STK 1000	0	1	1000
2000	126	STD STK B	874	1	2016
4000	252	STD STK B	748	1	4032
6000	375	STD STK B	625	1	6000
8000	500	STD STK B	500	1	8000
10000	630	STD STK B	370	1	10080
12000	750	STD STK B	250	1	12000
Stock B	1000	STD STK B	0	1	16000
120000	30	STD STK A	970	1	120000
200000	50	STD STK A	950	1	200000
400000	100	STD STK A	900	1	400000

STD (ng/g) = Concentration STD STK used (ng/g) X Wt. of STD (g) / Total ~ weight (g)

Standard stock solutions and working standard solutions are stable at 2 to 8°C for up to 5 days.

QC SAMPLE PREPARATION

Prepare each matrix spike in duplicate according to the table below. Score the end of a blank charcoal tube and break the tip and remove. Fill a syringe to the mark indicated in the table below and weigh the syringe full. Spike the blank charcoal tube by placing the tip of the syringe into the level of charcoal. Weigh the empty syringe and by difference determine the weight of the spike.

Table 2: QC Charcoal Tube Samples

QC Sample ID	Volume of QC STK (uL)	QC STK used	Volume of toluene/ISTD for extraction (mL)	Total Volume (mL)	Approximate Concentration of D5 added (ng/g)
0ug	0	none	15	15	0
2ug	10	QC STK 0.2	15	15.01	133
50ug	10	QC STK 5	15	15.01	3333
200ug	4	QC STK 50	15	15.004	13333
500ug	10	QC STK 50	15	15.01	33333
2000ug	10	QC STK 200	15	15.01	133333

QC charcoal tube samples are then extracted with toluene/ISTD according to the Sample Preparation Section below starting with step 1.b.

SAMPLE PREPARATION

1. Charcoal Tube Extraction

a. Remove charcoal tube samples from –20°C frozen storage and allow to warm to 4±4°C in the walk-in refrigerator.

b. Processing of the charcoal tubes should be done in the walk-in refrigerator using chilled toluene/ISTD*. (*Due to exothermic reaction caused by the addition of the charcoal to the toluene)

c. Record information on the appropriate form.

d. Score the end of the charcoal tube containing the cotton plug with a small file or glass scoring tool. Score it back from the end far enough to allow easy access to the cotton plug with tweezers.

e. Break off the end of the charcoal tube.

f. Crack the tube and deliver entire contents to a 20 ml scintillation vial containing ~15 ml of pre-weighed appropriate solvent (e.g. toluene/ISTD). Record the solvent weight.

g. Wrap the caps of the vials with Teflon tape to prevent evaporation of solvent.

h. Allow solvent to desorb analytes from charcoal for at least overnight.

Radioactivity Analysis

1) Label caps of LSC vials.

2) Add approximately 5 ml of the scintillation cocktail to each of two 7 ml scintillation vials. If 20 ml scintillation vials are used, add approximately 15 ml of scintillation cocktail.

3) Remove two 100 - 500 µl aliquots of solvent from the vial containing the charcoal and transfer them to the two scintillation vials.

4) Record the weights of the aliquots.

5) Mix gently, and place vials in a scintillation counter tray for radioactivity analysis.

GC/MS Analysis

1) Place approximately 250mg of $MgSO_4$ in round bottom vials.

2) Transfer approximately 600µL aliquots of the solvent above each charcoal sample to the vial containing $MgSO_4$ and allow to dry for at least 1 hour.

3) Centrifuge each of the above dried samples at a setting of 3030 rpm for approximately 30 min.

4) Place an aliquot of each standard in a limited volume insert in an autosampler vial and analyze by GC-MS.

Note: Once samples are in extraction solvent, samples are stable up to 5 days at 2 to 8 degrees C.

ANALYSIS

Samples shall be analyzed by GC/MS using the instrument parameters shown in Table 7.

Table 7. Analysis Parameters

Instrument:	Hewlett Packard 6890 Gas Chromatograph/Mass Selective Detector		
Column:	Hewlett Packard HP-5MS 30m x 0.25mm ID with 0.25um film thickness		
Carrier Gas:	Helium, initial pressure 10.5 psi, 1.0 mL/min, constant flow on		
Injection:	temperature 250°C, splitless, purge time 0.20min, 2µL injection		
Oven Ramp:	Initial 100°C for 3.0 min, ramp to 210°C at 17°C/min,		
	ramp to 250°C at 30°C/min hold for 1 min, total run time 11.80 min.		
Detection:	MSD transfer line temperature 280°C		
	Quantitation ions:	D5:	355 m/z at 100msec
		M4Q:	281 m/z at 100msec

Single injection analysis of each sample is sufficient.

Sample Analysis Order (Example)
Analyze each matrix in separate analysis runs. Separate analysis runs may occur on the same day.

Solvent Blank
Solvent Internal Standard Blank (3 injections)
Solvent Calibration Standards, (Low to High)
Solvent Blank
QC Samples (Low to High)
Solvent Blank
Solvent Standard
Sample Blank
10 Samples or Less
Solvent Standard
Sample Blank

Repeat this Solvent standard and Sample analysis pattern until all samples are analyzed.

DATA ANALYSIS

This section describes the calculations for the calibration of the GC/MS and the method to determine the amount of D_5 in each charcoal tube.

All calculations for routine sample analysis shall be performed using a Microsoft Excel spreadsheet (a spreadsheet which has been prepared for a specific application and has been confirmed by an independent review to perform calculations as defined; subsequent uses of the spreadsheet require 100% check of all entered data). Non-routine calculations shall be prepared and reviewed as directed by the Study Director (or designee).

1. Instrument Calibration Calculations

   Calibration of the mass spectrometer is performed using D_5 concentrations expressed in terms of ng D_5/g toluene. The nominal concentrations of calibration standards are shown in Table 1. The standard curve may be split into up to 3 ranges depending on the range of the instrument as long as at least 4 standards make up a range.

   D_5 Calibration Equation

   Calculate a linear equation, using a suitable linear regression program, for D_5 where x = concentration (ng D_5/g) and y = peak area response ratio for the calibration standards from the GC/MS analysis. Enter the resulting slope (m) and y-intercept (b) from each equation into the spreadsheet.

   $y = mx + b$, where y = peak area response ratio and x = ng D_5/g

2. Calculation of D_5 Concentrations in Samples (µg D_5)

   The concentration of D_5 in a sample extract is calculated once the slope (m) and y-intercept (b) have been entered into the spreadsheet. The concentration (ng D_5/g toluene) of D_5 in a sample extract is calculated by substitution of the peak area response ratio for y into the linear equation generated from calibration standards and solving for x, $(x = (y-b)/m)$.

3. Calculation of D_5 Concentrations in Samples (µg D_5)
   Calculation of D_5 concentration (µg) in sample matrix is as follows:

   D_5 (µg/g) = D_5(ng)/g toluene * g toluene/ISTD used for extraction x 1µg/1000ng

DATA ACCEPTANCE

1. Calibration Acceptance Criteria

   Agreement between the analyzed and prepared concentrations of D_5 in the calibration standards must be achieved to prove conformance to the linear calibration model. The percent relative error, calculated by the qualified spreadsheet, shall be used to prove conformance and is calculated by subtracting the analyzed concentration from the prepared concentration, and then dividing by the prepared concentration and multiplying by 100. The percent relative error shall be within 15% for every calibration standard analyzed for the calibration to be acceptable. Calibrations that do not meet these requirements shall be brought to the attention of the Study Director (or designee). Exceptions to this calibration acceptance criteria shall be made if all samples are bracketed by calibration standards that did meet the calibration acceptance criteria. The solvent standards that are run intermittently

throughout the run are to be within 15% for the run to be accepted. Any samples run before a standard meeting this acceptance criteria will be accepted. If any standards do not meet this acceptance criteria, any samples run after the standard will be evaluated by the bioanalytical supervisor if they will be accepted.

REPORTING AND DATA COMPLETION

The chemistry technician shall be responsible for submission of a completed data packet to the Study Director (or designate). This data packet shall include, as a minimum:

1. Hard copies of GC/MS data (including instrument parameters and sequence)
2. The calibration curve and the data from which it was generated
3. Data reduction spreadsheet

The chemistry technician shall also be responsible for completion of the notebook:

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QUALITY CONTROL

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ATTACHMENT C

Individual Animal Results for Quantitation of D_5 in Blood, Feces and Charcoal Tubes

And the Qualitative Analysis of Blood, Feces and Urine

Definition of Abbreviations	
BLQ	Below the lower limit of quantitation
ALQ	Above the upper limit of quantitation
NS	No Sample
NA	Not Applicable
N/AP	Not Applicable
ND	None Detected
N	Neat
S or SF	Simethicone
F	Female
M	Male

Blood Results

Sample Name	Group (CORN OIL)	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9182 24hr Control	Grp 7 Female	BLQ	0.026	0.026
Q0041 24hr Control	Grp 7 Female	0.053		
C9184 24hr Control	Grp 8 Male	BLQ	BLQ	
C9185 24hr Control	Grp 8 Male	BLQ		
C9186 15min	Grp 9 Female	0.109	0.215	0.042
C9187 15min	Grp 9 Female	0.333		
C9188 15min	Grp 9 Female	0.205		
C9189 15min	Grp 9 Female	0.172		
C9190 15min	Grp 9 Female	0.346		
C9191 15min	Grp 9 Female	0.124		
C9192 15min	Grp 10 Male	0.329	0.202	0.035
C9193 15min	Grp 10 Male	0.252		
C9194 15min	Grp 10 Male	0.231		
C9195 15min	Grp 10 Male	0.090		
C9196 15min	Grp 10 Male	0.155		
Q0037 15min	Grp 10 Male	0.152		
C9186 60 min	Grp 9 Female	3.467	5.310	0.407
C9187 60 min	Grp 9 Female	5.735		
C9188 60 min	Grp 9 Female	5.415		
C9189 60 min	Grp 9 Female	6.457		
C9190 60 min	Grp 9 Female	5.230		
C9191 60 min	Grp 9 Female	5.554		
C9192 60min	Grp 10 Male	5.933	6.226	0.754
C9193 60min	Grp 10 Male	4.660		
C9194 60min	Grp 10 Male	3.888		
C9195 60min	Grp 10 Male	8.141		
C9196 60min	Grp 10 Male	8.543		
Q0037 60min	Grp 10 Male	6.192		
C9186 6hr	Grp 9 Female	93.922	52.121	8.972
C9187 6hr	Grp 9 Female	50.704		
C9188 6hr	Grp 9 Female	47.502		
C9189 6hr	Grp 9 Female	49.461		
C9190 6hr	Grp 9 Female	28.900		
C9191 6hr	Grp 9 Female	42.237		
C9192 6hr	Grp 10 Male	61.853	62.490	4.261
C9193 6hr	Grp 10 Male	66.277		
C9194 6hr	Grp 10 Male	63.418		
C9195 6hr	Grp 10 Male	71.237		
C9196 6hr	Grp 10 Male	42.470		
Q0037 6hr	Grp 10 Male	69.682		
C9186 12hr	Grp 9 Female	50.271	34.753	6.148
C9187 12hr	Grp 9 Female	25.587		
C9188 12hr	Grp 9 Female	18.551		

Blood Results

Sample Name	Group (CORN OIL)	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9189 12hr	Grp 9 Female	40.823		
C9190 12hr	Grp 9 Female	20.794		
C9191 12hr	Grp 9 Female	52.495		
C9192 12hr	Grp 10 Male	50.183	44.975	4.032
C9193 12hr	Grp 10 Male	41.453		
C9194 12hr	Grp 10 Male	59.849		
C9195 12hr	Grp 10 Male	32.360		
C9196 12hr	Grp 10 Male	48.486		
Q0037 12hr	Grp 10 Male	37.518		
C9186 24hr	Grp 9 Female	9.632	10.185	1.396
C9187 24hr	Grp 9 Female	10.015		
C9188 24hr	Grp 9 Female	6.204		
C9189 24hr	Grp 9 Female	13.589		
C9190 24hr	Grp 9 Female	6.970		
C9191 24hr	Grp 9 Female	14.701		
C9192 24hr	Grp 10 Male	11.842	11.517	1.980
C9193 24hr	Grp 10 Male	5.323		
C9194 24hr	Grp 10 Male	11.383		
C9195 24hr	Grp 10 Male	9.353		
C9196 24hr	Grp 10 Male	20.132		
Q0037 24hr	Grp 10 Male	11.066		
C9186 48hr	Grp 9 Female	1.134	1.541	0.303
C9187 48hr	Grp 9 Female	1.331		
C9188 48hr	Grp 9 Female	0.921		
C9189 48hr	Grp 9 Female	2.168		
C9190 48hr	Grp 9 Female	0.960		
C9191 48hr	Grp 9 Female	2.734		
C9192 48hr	Grp 10 Male	0.664	0.952	0.140
C9193 48hr	Grp 10 Male	0.591		
C9194 48hr	Grp 10 Male	1.020		
C9195 48hr	Grp 10 Male	0.811		
C9196 48hr	Grp 10 Male	1.094		
Q0037 48hr	Grp 10 Male	1.529		
C9186 72hr	Grp 9 Female	0.514	0.593	0.060
C9187 72hr	Grp 9 Female	0.630		
C9188 72hr	Grp 9 Female	0.460		
C9189 72hr	Grp 9 Female	0.726		
C9190 72hr	Grp 9 Female	0.434		
C9191 72hr	Grp 9 Female	0.796		
C9192 72hr	Grp 10 Male	0.227	0.285	0.035
C9193 72hr	Grp 10 Male	0.233		
C9194 72hr	Grp 10 Male	0.323		
C9195 72hr	Grp 10 Male	0.241		
C9196 72hr	Grp 10 Male	0.442		
Q0037 72hr	Grp 10 Male	0.242		

Blood Results

Sample Name	Group (CORN OIL)	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9186 96hr	Grp 9 Female	0.415	0.479	0.063
C9187 96hr	Grp 9 Female	0.560		
C9188 96hr	Grp 9 Female	0.414		
C9189 96hr	Grp 9 Female	0.752		
C9190 96hr	Grp 9 Female	0.318		
C9191 96hr	Grp 9 Female	0.414		
C9192 96hr	Grp 10 Male	0.205	0.227	0.034
C9193 96hr	Grp 10 Male	0.162		
C9194 96hr	Grp 10 Male	0.231		
C9195 96hr	Grp 10 Male	0.207		
C9196 96hr	Grp 10 Male	0.391		
Q0037 96hr	Grp 10 Male	0.168		
C9186 120hr	Grp 9 Female	0.346	0.447	0.060
C9187 120hr	Grp 9 Female	0.503		
C9188 120hr	Grp 9 Female	0.300		
C9189 120hr	Grp 9 Female	0.638		
C9190 120hr	Grp 9 Female	NS		
C9191 120hr	Grp 9 Female	0.450		
C9192 120hr	Grp 10 Male	0.147	0.190	0.030
C9193 120hr	Grp 10 Male	0.145		
C9194 120hr	Grp 10 Male	0.176		
C9195 120hr	Grp 10 Male	0.152		
C9196 120hr	Grp 10 Male	0.337		
Q0037 120hr	Grp 10 Male	0.183		
C9186 144hr	Grp 9 Female	0.538	0.549	0.115
C9187 144hr	Grp 9 Female	0.637		
C9188 144hr	Grp 9 Female	0.239		
C9189 144hr	Grp 9 Female	0.780		
C9190 144hr	Grp 9 Female	NS		
C9191 144hr	Grp 9 Female	NS		
C9192 144hr	Grp 10 Male	0.156	0.186	0.041
C9193 144hr	Grp 10 Male	0.124		
C9194 144hr	Grp 10 Male	0.166		
C9195 144hr	Grp 10 Male	0.138		
C9196 144hr	Grp 10 Male	0.389		
Q0037 144hr	Grp 10 Male	0.145		
C9186 168hr	Grp 9 Female	NS	0.331	0.109
C9187 168hr	Grp 9 Female	NS		
C9188 168hr	Grp 9 Female	0.209		
C9189 168hr	Grp 9 Female	0.549		
C9190 168hr	Grp 9 Female	0.234		

Blood Results

Sample Name	Group (CORN OIL)	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9191 168hr	Grp 9 Female	NS		
C9192 168hr	Grp 10 Male	0.138	0.191	0.049
C9193 168hr	Grp 10 Male	0.139		
C9194 168hr	Grp 10 Male	0.132		
C9195 168hr	Grp 10 Male	0.127		
C9196 168hr	Grp 10 Male	0.434		
Q0037 168hr	Grp 10 Male	0.176		

Blood Results

Sample Name	Group	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9210 24hr Control	Grp 15 Female	BLQ	BLQ	
Q9211 24hr Control	Grp 15 Female	BLQ		
C9218 24hr Control	Grp 16 Female	BLQ	BLQ	
C9219 24hr Control	Grp 16 Female	BLQ		
C9212 15min	Grp 17 Female **NEAT**	0.000	0.093	0.037
C9213 15min	Grp 17 Female	0.000		
C9214 15min	Grp 17 Female	0.102		
C9215 15min	Grp 17 Female	0.064		
C9216 15min	Grp 17 Female	0.167		
C9217 15min	Grp 17 Female	0.225		
C9220 15min	Grp 18 Female **SF**	0.000	BLQ	N/AP
C9221 15min	Grp 18 Female	0.000		
C9222 15min	Grp 18 Female	0.000		
C9223 15min	Grp 18 Female	0.000		
C9224 15min	Grp 18 Female	0.000		
C9225 15min	Grp 18 Female	0.000		
C9212 60 min	Grp 17 Female **NEAT**	0.988	1.928	0.470
C9213 60 min	Grp 17 Female	0.701		
C9214 60 min	Grp 17 Female	1.829		
C9215 60 min	Grp 17 Female	1.773		
C9216 60 min	Grp 17 Female	2.338		
C9217 60 min	Grp 17 Female	3.938		
C9220 60min	Grp 18 Female **SF**	0.434	0.395	0.065
C9221 60min	Grp 18 Female	0.142		
C9222 60min	Grp 18 Female	0.631		
C9223 60min	Grp 18 Female	0.439		
C9224 60min	Grp 18 Female	0.321		
C9225 60min	Grp 18 Female	0.403		
C9212 6hr	Grp 17 Female **NEAT**	5.336	7.943	0.708
C9213 6hr	Grp 17 Female	NS		
C9214 6hr	Grp 17 Female	8.668		
C9215 6hr	Grp 17 Female	8.043		
C9216 6hr	Grp 17 Female	8.095		
C9217 6hr	Grp 17 Female	9.575		
C9220 6hr	Grp 18 Female **SF**	2.711	1.578	0.308
C9221 6hr	Grp 18 Female	0.513		
C9222 6hr	Grp 18 Female	1.214		
C9223 6hr	Grp 18 Female	1.259		
C9224 6hr	Grp 18 Female	1.914		
C9225 6hr	Grp 18 Female	1.857		
C9212 12hr	Grp 17 Female **NEAT**	3.461	4.080	1.149
C9213 12hr	Grp 17 Female	NS		
C9214 12hr	Grp 17 Female	3.603		
C9215 12hr	Grp 17 Female	8.528		
C9216 12hr	Grp 17 Female	2.848		
C9217 12hr	Grp 17 Female	1.960		

Blood Results

Sample Name	Group	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9220 12hr	Grp 18 Female **SF**	3.240	2.134	0.385
C9221 12hr	Grp 18 Female	0.828		
C9222 12hr	Grp 18 Female	2.567		
C9223 12hr	Grp 18 Female	1.168		
C9224 12hr	Grp 18 Female	2.243		
C9225 12hr	Grp 18 Female	2.757		
C9212 24hr	Grp 17 Female **NEAT**	0.644	4.023	3.088
C9213 24hr	Grp 17 Female	NS		
C9214 24hr	Grp 17 Female	0.832		
C9215 24hr	Grp 17 Female	1.488		
C9216 24hr	Grp 17 Female	16.360		
C9217 24hr	Grp 17 Female	0.790		
C9220 24hr	Grp 18 Female **SF**	0.455	0.612	0.227
C9221 24hr	Grp 18 Female	0.287		
C9222 24hr	Grp 18 Female	0.545		
C9223 24hr	Grp 18 Female	0.319		
C9224 24hr	Grp 18 Female	0.335		
C9225 24hr	Grp 18 Female	1.731		
C9212 48hr	Grp 17 Female **NEAT**	0.263	0.487	0.180
C9213 48hr	Grp 17 Female	NS		
C9214 48hr	Grp 17 Female	0.393		
C9215 48hr	Grp 17 Female	0.369		
C9216 48hr	Grp 17 Female	1.196		
C9217 48hr	Grp 17 Female	0.214		
C9220 48hr	Grp 18 Female **SF**	0.211	0.165	0.024
C9221 48hr	Grp 18 Female	0.099		
C9222 48hr	Grp 18 Female	0.237		
C9223 48hr	Grp 18 Female	0.121		
C9224 48hr	Grp 18 Female	0.118		
C9225 48hr	Grp 18 Female	0.205		
C9212 72hr	Grp 17 Female **NEAT**	0.180	0.242	0.030
C9213 72hr	Grp 17 Female	NS		
C9214 72hr	Grp 17 Female	0.256		
C9215 72hr	Grp 17 Female	0.247		
C9216 72hr	Grp 17 Female	0.345		
C9217 72hr	Grp 17 Female	0.182		
C9220 72hr	Grp 18 Female **SF**	0.203	0.173	0.043
C9221 72hr	Grp 18 Female	0.089		
C9222 72hr	Grp 18 Female	0.107		
C9223 72hr	Grp 18 Female	0.106		
C9224 72hr	Grp 18 Female	0.372		
C9225 72hr	Grp 18 Female	0.160		
C9212 96hr	Grp 17 Female **NEAT**	0.133	0.206	0.042
C9213 96hr	Grp 17 Female	NS		
C9214 96hr	Grp 17 Female	0.303		
C9215 96hr	Grp 17 Female	0.154		

Blood Results

Sample Name	Group	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9216 96hr	Grp 17 Female	0.312		
C9217 96hr	Grp 17 Female	0.130		
C9220 96hr	Grp 18 Female **SF**	0.120	0.094	0.007
C9221 96hr	Grp 18 Female	0.075		
C9222 96hr	Grp 18 Female	0.104		
C9223 96hr	Grp 18 Female	0.077		
C9224 96hr	Grp 18 Female	0.085		
C9225 96hr	Grp 18 Female	0.105		
C9212 120hr	Grp 17 Female **NEAT**	0.191	0.152	0.031
C9213 120hr	Grp 17 Female	NS		
C9214 120hr	Grp 17 Female	NS		
C9215 120hr	***Grp 17 Female***	***0.175***	***excluded based on Q-test***	
C9216 120hr	Grp 17 Female	0.174		
C9217 120hr	Grp 17 Female	0.091		
C9220 120hr	Grp 18 Female **SF**	0.060	0.087	0.026
C9221 120hr	Grp 18 Female	0.000		
C9222 120hr	Grp 18 Female	0.136		
C9223 120hr	Grp 18 Female	0.180		
C9224 120hr	Grp 18 Female	0.063		
C9225 120hr	Grp 18 Female	0.081		
C9212 144hr	Grp 17 Female **NEAT**	0.230	0.209	0.011
C9213 144hr	Grp 17 Female	NS		
C9214 144hr	Grp 17 Female	NS		
C9215 144hr	Grp 17 Female	0.198		
C9216 144hr	Grp 17 Female	0.198		
C9217 144hr	Grp 17 Female	NS		
C9220 144hr	Grp 18 Female **SF**	0.087	0.082	0.011
C9221 144hr	Grp 18 Female	0.050		
C9222 144hr	***Grp 18 Female***	***0.115***	***excluded based on Q-test***	
C9223 144hr	Grp 18 Female	0.088		
C9224 144hr	Grp 18 Female	0.115		
C9225 144hr	Grp 18 Female	0.072		
C9212 168hr	Grp 17 Female **NEAT**	0.101	0.118	0.015
C9213 168hr	Grp 17 Female	NS		
C9214 168hr	Grp 17 Female	NS		
C9215 168hr	Grp 17 Female	0.105		
C9216 168hr	Grp 17 Female	0.148		
C9217 168hr	Grp 17 Female	NS		
C9220 168hr	Grp 18 Female **SF**	0.077	0.101	0.011
C9221 168hr	Grp 18 Female	0.131		
C9222 168hr	Grp 18 Female	0.119		
C9223 168hr	Grp 18 Female	0.118		
C9224 168hr	Grp 18 Female	0.060		
C9225 168hr	Grp 18 Female	0.103		

Feces Results

Sample Name	Group (CORN OIL)	timepoint (hr)	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9158	Grp 1 Female	24hr	0.61	0.30	0.30
C9159	Grp 1 Female	24hr	BLQ		
C9160	Grp 2 Male	24hr	BLQ	BLQ	
C9161	Grp 2 Male	24hr	BLQ		
C9162	Grp 3 Female	6hr	2.87		excluded
C9163	Grp 3 Female	6hr	NS	0.49	0.37
C9164	Grp 3 Female	6hr	0.00		
C9165	Grp 3 Female	6hr	0.97		
C9166	Grp 4 Male	6hr	0.81	1.48	1.10
C9167	Grp 4 Male	6hr	3.62		
C9168	Grp 4 Male	6hr	NS		
C9169	Grp 4 Male	6hr	0.00		
C9162	Grp 3 Female	12hr	NS		excluded
C9163	Grp 3 Female	12hr	21.11	1165.20	1151.14
C9164	Grp 3 Female	12hr	7.02		
C9165	Grp 3 Female	12hr	3467.47		
C9166	Grp 4 Male	12hr	16.36	1911.41	1894.93
C9167	Grp 4 Male	12hr	16.61		
C9168	Grp 4 Male	12hr	5701.26		
C9169	Grp 4 Male	12hr	NS		
C9162	Grp 3 Female	24hr	NS		excluded
C9163	Grp 3 Female	24hr	20351.38	19142.84	5307.91
C9164	Grp 3 Female	24hr	27672.37		
C9165	Grp 3 Female	24hr	9404.76		
C9166	Grp 4 Male	24hr	28383.34	21818.20	5517.62
C9167	Grp 4 Male	24hr	25329.06		
C9168	Grp 4 Male	24hr	28163.06		
C9169	Grp 4 Male	24hr	5397.34		
C9162	Grp 3 Female	48hr	14502.36		excluded
C9163	Grp 3 Female	48hr	9065.20	11857.22	4891.26
C9164	Grp 3 Female	48hr	21372.76		
C9165	Grp 3 Female	48hr	5133.70		
C9166	Grp 4 Male	48hr	9776.88	12075.78	1409.61
C9167	Grp 4 Male	48hr	9499.84		
C9168	Grp 4 Male	48hr	14657.40		
C9169	Grp 4 Male	48hr	14368.98		
C9162	Grp 3 Female	72hr	2918.10		excluded
C9163	Grp 3 Female	72hr	560.92	1410.07	913.34
C9164	Grp 3 Female	72hr	3235.27		
C9165	Grp 3 Female	72hr	434.01		
C9166	Grp 4 Male	72hr	521.42	1319.62	341.10
C9167	Grp 4 Male	72hr	1192.89		
C9168	Grp 4 Male	72hr	2179.13		
C9169	Grp 4 Male	72hr	1385.04		
C9162	Grp 3 Female	96hr	100.99		excluded
C9163	Grp 3 Female	96hr	8.05	17.55	5.05

Feces Results

Sample Name	Group (CORN OIL)	timepoint (hr)	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9164	Grp 3 Female	96hr	25.27		
C9165	Grp 3 Female	96hr	19.32		
C9166	Grp 4 Male	96hr	36.86	63.04	30.88
C9167	Grp 4 Male	96hr	41.72		
C9168	Grp 4 Male	96hr	154.52		
C9169	Grp 4 Male	96hr	19.06		
C9162	Grp 3 Female	120hr	3.28		excluded
C9163	Grp 3 Female	120hr	0.74	1.18	0.45
C9164	Grp 3 Female	120hr	2.07		
C9165	Grp 3 Female	120hr	0.74		
C9166	Grp 4 Male	120hr	1.38	2.68	1.43
C9167	Grp 4 Male	120hr	1.56		
C9168	Grp 4 Male	120hr	6.96		
C9169	Grp 4 Male	120hr	0.83		
C9162	Grp 3 Female	144hr	0.91		excluded
C9163	Grp 3 Female	144hr	0.42	0.76	0.32
C9164	Grp 3 Female	144hr	1.39		
C9165	Grp 3 Female	144hr	0.48		
C9166	Grp 4 Male	144hr	9.52	2.78	2.26
C9167	Grp 4 Male	144hr	0.66		
C9168	Grp 4 Male	144hr	0.92		
C9169	Grp 4 Male	144hr	0.00		
C9162	Grp 3 Female	168hr	0.91		excluded
C9163	Grp 3 Female	168hr	0.55	23.73	22.55
C9164	Grp 3 Female	168hr	68.83		
C9165	Grp 3 Female	168hr	1.81		
C9166	Grp 4 Male	168hr	15.58	4.15	3.81
C9167	Grp 4 Male	168hr	0.58		
C9168	Grp 4 Male	168hr	0.45		
C9169	Grp 4 Male	168hr	0.00		

Feces Results

Sample Name	Group	timepoint (hr)	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
C9198	Grp 11 Neat	24	BLQ	BLQ	
C9199	Grp 11 Neat	24	BLQ		
C9204	Grp 12 Simethicone	24	0.95	1.00	0.047
C9205	Grp 12 Simethicone	24	1.04		
C9200	Grp 13 Neat	6	2.48	8.37	3.72
C9201	Grp 13 Neat	6	5.56		excluded
Q0004	Grp 13 Neat	6	7.39		
C9203	Grp 13 Neat	6	15.25		
C9206	Grp 14 Simethicone	6	6928.59	4397.60	1627.61
C9207	Grp 14 Simethicone	6	32.58		excluded
C9208	Grp 14 Simethicone	6	4904.92		
C9209	Grp 14 Simethicone	6	1359.28		
C9200	Grp 13 Neat	12	20625.84	9665.22	5986.74
C9201	Grp 13 Neat	12	7.61		excluded
Q0004	Grp 13 Neat	12	10.96		
C9203	Grp 13 Neat	12	8358.86		
C9206	Grp 14 Simethicone	12	7654.10	11067.66	1710.20
C9207	Grp 14 Simethicone	12	16265.65		excluded
C9208	Grp 14 Simethicone	12	12587.27		
C9209	Grp 14 Simethicone	12	12961.62		
C9200	Grp 13 Neat	24	23428.93	23332.70	2147.07
C9201	Grp 13 Neat	24	3974.38		excluded
Q0004	Grp 13 Neat	24	19566.69		
C9203	Grp 13 Neat	24	27002.48		
C9206	Grp 14 Simethicone	24	10698.94	11133.75	1560.52
C9207	Grp 14 Simethicone	24	15692.22		excluded
C9208	Grp 14 Simethicone	24	8674.61		
C9209	Grp 14 Simethicone	24	14027.69		
C9200	Grp 13 Neat	48	3001.88	7780.50	2430.36
C9201	Grp 13 Neat	48	16741.71		excluded
Q0004	Grp 13 Neat	48	10940.19		
C9203	Grp 13 Neat	48	9399.43		
C9206	Grp 14 Simethicone	48	2014.08	4283.65	1697.24
C9207	Grp 14 Simethicone	48	10660.30		excluded
C9208	Grp 14 Simethicone	48	3232.40		
C9209	Grp 14 Simethicone	48	7604.46		
C9200	Grp 13 Neat	72	121.76	420.94	161.09
C9201	Grp 13 Neat	72	949.56		excluded
Q0004	Grp 13 Neat	72	466.98		
C9203	Grp 13 Neat	72	674.07		
C9206	Grp 14 Simethicone	72	55.87	218.07	151.51
C9207	Grp 14 Simethicone	72	1530.97		excluded
C9208	Grp 14 Simethicone	72	77.49		
C9209	Grp 14 Simethicone	72	520.84		
C9200	Grp 13 Neat	96	2.66	213.24	204.01
C9201	Grp 13 Neat	96	257.46		excluded

Feces Results

Sample Name	Group	timepoint (hr)	Parent µg D5/g	Parent µg D5/g Averages/sex/ timepoint	std error of the mean
Q0004	Grp 13 Neat	96	621.18		
C9203	Grp 13 Neat	96	15.89		
C9206	Grp 14 Simethicone	96	0.73	57.19	47.11
C9207	Grp 14 Simethicone	96	79.53		excluded
C9208	Grp 14 Simethicone	96	150.74		
C9209	Grp 14 Simethicone	96	20.10		
C9200	Grp 13 Neat	120	0.96	0.70	0.14
C9201	Grp 13 Neat	120	0.51		excluded
Q0004	Grp 13 Neat	120	0.50		
C9203	Grp 13 Neat	120	0.64		
C9206	Grp 14 Simethicone	120	1.16	0.61	0.34
C9207	Grp 14 Simethicone	120	2.06		excluded
C9208	Grp 14 Simethicone	120	0.00		
C9209	Grp 14 Simethicone	120	0.66		
C9200	Grp 13 Neat	144	0.00	0.00	
C9201	Grp 13 Neat	144	BLQ		excluded
Q0004	Grp 13 Neat	144	0.00		
C9203	Grp 13 Neat	144	0.00		
C9206	Grp 14 Simethicone	144	0.46	0.15	0.15
C9207	Grp 14 Simethicone	144	BLQ		excluded
C9208	Grp 14 Simethicone	144	0.00		
C9209	Grp 14 Simethicone	144	0.00		
C9200	Grp 13 Neat	168	0.00	118.11	118.11
C9201	Grp 13 Neat	168	BLQ		excluded
Q0004	Grp 13 Neat	168	0.00		
C9203	Grp 13 Neat	168	354.32		
C9206	Grp 14 Simethicone	168	0.39	0.13	0.13
C9207	Grp 14 Simethicone	168	0.89		excluded
C9208	Grp 14 Simethicone	168	0.00		
C9209	Grp 14 Simethicone	168	0.00		

Charcoal Results

Sample Name	Group (CORN OIL)	timepoint (hr)	Parent µg/hr	Parent µg D5/hr Averages/sex /timepoint	std error of the mean
C9158	Grp 1 Female	24	BLQ	BLQ	
C9159	Grp 1 Female	24	BLQ		
C9160	Grp 2 Male	24	0.14	0.14	0.01
C9161	Grp 2 Male	24	0.15		
C9162	Grp 3 Female	1	24789.66		excluded
C9163	Grp 3 Female	1	127.36	47.13	40.12
C9164	Grp 3 Female	1	5.93		
C9165	Grp 3 Female	1	8.09		
C9166	Grp 4 Male	1	16.85	98.59	57.16
C9167	Grp 4 Male	1	98.04		
C9168	Grp 4 Male	1	19.03		
C9169	Grp 4 Male	1	260.44		
C9162	Grp 3 Female	2	4400.09		excluded
C9163	Grp 3 Female	2	11.37	7.32	2.03
C9164	Grp 3 Female	2	5.05		
C9165	Grp 3 Female	2	5.52		
C9166	Grp 4 Male	2	3.00	6.92	2.47
C9167	Grp 4 Male	2	5.67		
C9168	Grp 4 Male	2	4.86		
C9169	Grp 4 Male	2	14.14		
C9162	Grp 3 Female	4	1178.83		excluded
C9163	Grp 3 Female	4	26.72	21.68	2.71
C9164	Grp 3 Female	4	20.89		
C9165	Grp 3 Female	4	17.44		
C9166	Grp 4 Male	4	19.43	21.44	1.20
C9167	Grp 4 Male	4	24.73		
C9168	Grp 4 Male	4	21.71		
C9169	Grp 4 Male	4	19.88		
C9162	Grp 3 Female	6	239.31		excluded
C9163	Grp 3 Female	6	42.22	41.85	2.16
C9164	Grp 3 Female	6	37.94		
C9165	Grp 3 Female	6	45.38		
C9166	Grp 4 Male	6	41.16	44.05	2.09
C9167	Grp 4 Male	6	45.95		
C9168	Grp 4 Male	6	49.02		
C9169	Grp 4 Male	6	40.05		
C9162	Grp 3 Female	12	79.98		excluded
C9163	Grp 3 Female	12	60.15	246.28	190.29
C9164	Grp 3 Female	12	51.86		
C9165	Grp 3 Female	12	626.84		
C9166	Grp 4 Male	12	67.71	199.08	136.98
C9167	Grp 4 Male	12	61.89		
C9168	Grp 4 Male	12	609.97		
C9169	Grp 4 Male	12	56.75		
C9162	Grp 3 Female	24	31.36		excluded
C9163	Grp 3 Female	24	918.74	1063.34	303.80

Charcoal Results

Sample Name	Group (CORN OIL)	timepoint (hr)	Parent µg/hr	Parent µg D5/hr Averages/sex /timepoint	std error of the mean
C9164	Grp 3 Female	24	624.56		
C9165	Grp 3 Female	24	1646.71		
C9166	Grp 4 Male	24	7238.62	2679.43	1575.51
C9167	Grp 4 Male	24	968.81		
C9168	Grp 4 Male	24	2259.41		
C9169	Grp 4 Male	24	250.90		
C9162	Grp 3 Female	48	10.11		excluded
C9163	Grp 3 Female	48	18.46	49.40	28.58
C9164	Grp 3 Female	48	23.25		
C9165	Grp 3 Female	48	106.49		
C9166	Grp 4 Male	48	764.48	392.53	197.69
C9167	Grp 4 Male	48	28.30		
C9168	Grp 4 Male	48	74.08		
C9169	Grp 4 Male	48	703.25		
C9162	Grp 3 Female	72	3.86		excluded
C9163	Grp 3 Female	72	4.48	5.14	0.63
C9164	Grp 3 Female	72	4.52		
C9165	Grp 3 Female	72	6.41		
C9166	Grp 4 Male	72	19.93	38.71	26.29
C9167	Grp 4 Male	72	7.61		
C9168	Grp 4 Male	72	10.13		
C9169	Grp 4 Male	72	117.16		
C9162	Grp 3 Female	96	2.29		excluded
C9163	Grp 3 Female	96	1.78	2.21	0.33
C9164	Grp 3 Female	96	1.99		
C9165	Grp 3 Female	96	2.85		
C9166	Grp 4 Male	96	2.93	2.48	0.18
C9167	Grp 4 Male	96	2.07		
C9168	Grp 4 Male	96	2.40		
C9169	Grp 4 Male	96	2.51		
C9162	Grp 3 Female	120	1.28		excluded
C9163	Grp 3 Female	120	1.20	1.04	0.56
C9164	Grp 3 Female	120	0.00		
C9165	Grp 3 Female	120	1.92		
C9166	Grp 4 Male	120	1.58	1.16	0.18
C9167	Grp 4 Male	120	1.10		
C9168	Grp 4 Male	120	1.23		
C9169	Grp 4 Male	120	0.72		
C9162	Grp 3 Female	144	0.99		excluded
C9163	Grp 3 Female	144	0.75	0.81	0.14
C9164	Grp 3 Female	144	0.61		
C9165	Grp 3 Female	144	1.08		
C9166	Grp 4 Male	144	1.19	0.73	0.16
C9167	Grp 4 Male	144	0.66		
C9168	Grp 4 Male	144	0.64		
C9169	Grp 4 Male	144	0.42		

Charcoal Results

Sample Name	Group (CORN OIL)	timepoint (hr)	Parent µg/hr	Parent µg D5/hr Averages/sex /timepoint	std error of the mean
C9162	Grp 3 Female	168	0.96		excluded
C9163	Grp 3 Female	168	0.80	0.83	0.18
C9164	Grp 3 Female	168	0.53		
C9165	Grp 3 Female	168	1.15		
C9166	Grp 4 Male	168	0.97	0.69	0.10
C9167	Grp 4 Male	168	0.70		
C9168	Grp 4 Male	168	0.59		
C9169	Grp 4 Male	168	0.50		

Charcoal Results

Sample Name	Group	timepoint (hr)	Parent µg/hr	Parent µg D5/hr Averages/sex /timepoint	std error of the mean
C9198	Grp 11 Neat	24hr	0.11	0.09	0.02
C9199	Grp 11 Neat	24hr	0.07		
C9204	Grp 12 Simethicone	24hr	0.24	0.19	0.05
C9205	Grp 12 Simethicone	24hr	0.14		
C9200	Grp 13 Neat	1hr	0.00	279.75	271.26
C9201	Grp 13 Neat	1hr	ALQ		excluded
Q0004	Grp 13 Neat	1hr	822.18		
C9203	Grp 13 Neat	1hr	17.06		
C9206	Grp 14 Simethicone	1hr	0.00	2.27	2.27
C9207	Grp 14 Simethicone	1hr	2361.82		excluded
C9208	Grp 14 Simethicone	1hr	6.80		
C9209	Grp 14 Simethicone	1hr	0.00		
C9200	Grp 13 Neat	2hr	0.00	33.30	25.45
C9201	Grp 13 Neat	2hr	ALQ		excluded
Q0004	Grp 13 Neat	2hr	83.29		
C9203	Grp 13 Neat	2hr	16.60		
C9206	Grp 14 Simethicone	2hr	0.00	63.50	41.86
C9207	Grp 14 Simethicone	2hr	224.25		excluded
C9208	Grp 14 Simethicone	2hr	142.50		
C9209	Grp 14 Simethicone	2hr	48.01		
C9200	Grp 13 Neat	4hr	800.55	286.43	257.22
C9201	Grp 13 Neat	4hr	2288.05		excluded
Q0004	Grp 13 Neat	4hr	45.02		
C9203	Grp 13 Neat	4hr	13.70		
C9206	Grp 14 Simethicone	4hr	2670.86	2102.69	385.99
C9207	Grp 14 Simethicone	4hr	284.51		excluded
C9208	Grp 14 Simethicone	4hr	1366.01		
C9209	Grp 14 Simethicone	4hr	2271.20		
C9200	Grp 13 Neat	6hr	331.22	124.08	103.61
C9201	Grp 13 Neat	6hr	220.60		excluded
Q0004	Grp 13 Neat	6hr	25.32		
C9203	Grp 13 Neat	6hr	15.69		
C9206	Grp 14 Simethicone	6hr	2273.22	1868.02	336.84
C9207	Grp 14 Simethicone	6hr	781.94		excluded
C9208	Grp 14 Simethicone	6hr	2131.52		
C9209	Grp 14 Simethicone	6hr	1199.31		
C9200	Grp 13 Neat	12hr	145.45	64.59	40.49
C9201	Grp 13 Neat	12hr	63.52		excluded
Q0004	Grp 13 Neat	12hr	20.58		
C9203	Grp 13 Neat	12hr	27.73		
C9206	Grp 14 Simethicone	12hr	2139.49	1957.67	142.03
C9207	Grp 14 Simethicone	12hr	372.80		excluded
C9208	Grp 14 Simethicone	12hr	2055.76		
C9209	Grp 14 Simethicone	12hr	1677.76		
C9200	Grp 13 Neat	24hr	36.62	112.17	61.21
C9201	Grp 13 Neat	24hr	32.50		excluded

Charcoal Results

Sample Name	Group	timepoint (hr)	Parent µg/hr	Parent µg D5/hr Averages/sex /timepoint	std error of the mean
Q0004	Grp 13 Neat	24hr	233.37		
C9203	Grp 13 Neat	24hr	66.53		
C9206	Grp 14 Simethicone	24hr	224.67	560.69	185.98
C9207	Grp 14 Simethicone	24hr	176.75		excluded
C9208	Grp 14 Simethicone	24hr	866.84		
C9209	Grp 14 Simethicone	24hr	590.55		
C9200	Grp 13 Neat	48hr	12.19	76.07	40.48
C9201	Grp 13 Neat	48hr	232.70		excluded
Q0004	Grp 13 Neat	48hr	151.10		
C9203	Grp 13 Neat	48hr	64.93		
C9206	Grp 14 Simethicone	48hr	30.05	54.43	34.04
C9207	Grp 14 Simethicone	48hr	57.48		excluded
C9208	Grp 14 Simethicone	48hr	121.66		
C9209	Grp 14 Simethicone	48hr	11.58		
C9200	Grp 13 Neat	72hr	2.24	55.67	26.72
C9201	Grp 13 Neat	72hr	16.28		excluded
Q0004	Grp 13 Neat	72hr	82.81		
C9203	Grp 13 Neat	72hr	81.97		
C9206	Grp 14 Simethicone	72hr	1.49	17.59	13.56
C9207	Grp 14 Simethicone	72hr	3.44		excluded
C9208	Grp 14 Simethicone	72hr	44.53		
C9209	Grp 14 Simethicone	72hr	6.75		
C9200	Grp 13 Neat	96hr	0.66	23.27	12.29
C9201	Grp 13 Neat	96hr	11.09		excluded
Q0004	Grp 13 Neat	96hr	42.95		
C9203	Grp 13 Neat	96hr	26.19		
C9206	Grp 14 Simethicone	96hr	0.22	9.78	7.80
C9207	Grp 14 Simethicone	96hr	1.18		excluded
C9208	Grp 14 Simethicone	96hr	25.24		
C9209	Grp 14 Simethicone	96hr	3.89		
C9200	Grp 13 Neat	120hr	0.40	5.34	4.78
C9201	Grp 13 Neat	120hr	0.55		excluded
Q0004	Grp 13 Neat	120hr	0.71		
C9203	Grp 13 Neat	120hr	14.89		
C9206	Grp 14 Simethicone	120hr	0.05	1.26	0.85
C9207	Grp 14 Simethicone	120hr	0.62		excluded
C9208	Grp 14 Simethicone	120hr	0.82		
C9209	Grp 14 Simethicone	120hr	2.89		
C9200	Grp 13 Neat	144hr	0.27	1.67	1.41
C9201	Grp 13 Neat	144hr	0.44		excluded
Q0004	Grp 13 Neat	144hr	0.25		
C9203	Grp 13 Neat	144hr	4.48		
C9206	Grp 14 Simethicone	144hr	0.00	0.69	0.66
C9207	Grp 14 Simethicone	144hr	0.47		excluded
C9208	Grp 14 Simethicone	144hr	0.07		
C9209	Grp 14 Simethicone	144hr	2.02		

Charcoal Results

Sample Name	Group	timepoint (hr)	Parent µg/hr	Parent µg D5/hr Averages/sex /timepoint	std error of the mean
C9200	Grp 13 Neat	168hr	0.19	2.15	1.94
C9201	Grp 13 Neat	168hr	0.46		excluded
Q0004	Grp 13 Neat	168hr	0.23		
C9203	Grp 13 Neat	168hr	6.03		
C9206	Grp 14 Simethicone	168hr	0.08	0.35	0.30
C9207	Grp 14 Simethicone	168hr	0.49		excluded
C9208	Grp 14 Simethicone	168hr	0.03		
C9209	Grp 14 Simethicone	168hr	0.95		

STUDY 9550 Part 1 HPLC FECES ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Sex	NET AREA CPM		Total CPMs Detected
			Unknown **45.3min.** Retention time metabolite	Decamethyl-cyclopenta-siloxane **51.2min.** Retention time metabolite	
C9162	12	3/F	NS	NS	NS
C9163	12	3/F	NA	NA	NA
C9164	12	3/F	NA	NA	NA
C9165	12	3/F	0 *0%*	8265 *61%*	8265
C9166	12	4/M	NA	NA	NA
C9167	12	4/M	NA	NA	NA
C9168	12	4/M	0 *0%*	13649 *100%*	13649
C9169	12	4/M	NS	NS	NS

Retention times listed are approximate

STUDY 9550 Part 1 HPLC FECES ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Sex	NET AREA CPM		Total CPMs Detected
			Unknown **45.3min.** Retention time metabolite	Decamethyl-cyclopenta-siloxane **51.2min.** Retention time metabolite	
C9162	24	3/F	NS	NS	NS
C9163	24	3/F	350 *1%*	57528 *99%*	57878
C9164	24	3/F	556 *1%*	49566 *99%*	50122
C9165	24	3/F	 *0%*	21273 *100%*	21273
C9166	24	4/M	1759 *3%*	52525 *97%*	54284
C9167	24	4/M	1280 *2%*	55264 *98%*	56544
C9168	24	4/M	1170 *2%*	54651 *98%*	55821
C9169	24	4/M	463 *3%*	15172 *97%*	15635

Retention times listed are approximate

STUDY 9550 Part 1 HPLC FECES ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Sex	NET AREA CPM		Total CPMs Detected
			Unknown	Decamethyl-cyclopenta-siloxane	
			45.3min. Retention time metabolite	**51.2min.** Retention time metabolite	
C9162	48	3/F	996	34365	35361
			3%	*97%*	
C9163	48	3/F	844	23273	24117
			3%	*97%*	
C9164	48	3/F	553	27057	27610
			2%	*98%*	
C9165	48	3/F		8968	8968
			0%	*100%*	
C9166	48	4/M	680	15269	15949
			4%	*96%*	
C9167	48	4/M	1118	18253	19371
			6%	*94%*	
C9168	48	4/M	1122	30911	32033
			4%	*96%*	
C9169	48	4/M	1071	31348	32419
			3%	*97%*	

Retention times listed are approximate

STUDY 9550 Part 1 HPLC FECES ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Sex	NET AREA CPM		Total CPMs Detected
			Unknown	Decamethyl-cyclopenta-siloxane	
			45.3min. Retention time metabolite	**51.2min.** Retention time metabolite	
C9162	72	3/F		5954	5954
			0%	*100%*	
C9163	72	3/F		1073	1073
			0%	*100%*	
C9164	72	3/F		5935	5935
			0%	*100%*	
C9165	72	3/F	ND	ND	ND
C9166	72	4/M		903	903
			0%	*100%*	
C9167	72	4/M		4229	4229
			0%	*100%*	
C9168	72	4/M		6115	6115
			0%	*100%*	
C9169	72	4/M		3651	3651
			0%	*100%*	

Retention times listed are approximate

STUDY 9550 Part 2 HPLC FECES ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Dose	NET AREA CPM		Total CPMs Detected
			Unknown	Decamethyl-cyclopenta-siloxane	
			45.1min. Retention time metabolite	**50.5min.** Retention time metabolite	
C9200	12	13/N		43369	43369
			0%	*100%*	
C9201	12	13/N	ND	ND	ND
Q0004	12	13/N	ND	ND	ND
C9203	12	13/N		16358	16358
			0%	*100%*	
C9206	12	14/S		20506	20506
			0%	*100%*	
C9207	12	14/S		33997	33997
			0%	*100%*	
C9208	12	14/S		37251	37251
			0%	*100%*	
C9209	12	14/S		39732	39732
			0%	*100%*	

Retention times listed are approximate

STUDY 9550 Part 2 HPLC FECES ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Dose	NET AREA CPM		Total CPMs Detected
			Unknown **45.1min.** Retention time metabolite	Decamethyl-cyclopenta-siloxane **50.5min.** Retention time metabolite	
C9200	24	13/N	695	87409	88104
			1%	*99%*	
C9201	24	13/N	0	8304	8304
			0%	*100%*	
Q0004	24	13/N	0	66669	66669
			0%	*100%*	
C9203	24	13/N	0	90301	90301
			0%	*100%*	
C9206	24	14/S	0	27185	27185
			0%	*100%*	
C9207	24	14/S	0	29451	29451
			0%	*100%*	
C9208	24	14/S	0	23693	23693
			0%	*100%*	
C9209	24	14/S	0	39575	39575
			0%	*100%*	

Retention times listed are approximate

STUDY 9550 Part 2 HPLC FECES ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Dose	NET AREA CPM: Unknown 45.1min. Retention time metabolite	NET AREA CPM: Decamethyl-cyclopenta-siloxane 50.5min. Retention time metabolite	Total CPMs Detected
C9200	48	13/N	NA	NA	NA
C9201	48	13/N	719 *2%*	37358 *98%*	38077
Q0004	48	13/N	0 *0%*	27678 *100%*	27678
C9203	48	13/N	0 *0%*	24105 *100%*	24105
C9206	48	14/S	0 *0%*	5316 *100%*	5316
C9207	48	14/S	0 *0%*	32252 *100%*	32252
C9208	48	14/S	0 *0%*	7723 *100%*	7723
C9209	48	14/S	0 *0%*	19462 *100%*	19462

Retention times listed are approximate

STUDY 9550 Part 2 HPLC FECES ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Dose	NET AREA CPM		Total CPMs Detected
			Unknown	Decamethyl-cyclopenta-siloxane	
			45.1min. Retention time metabolite	**50.5min.** Retention time metabolite	
C9200	72	13/N		619	619
			0%	*100%*	
C9201	72	13/N		2309	2309
			0%	*100%*	
Q0004	72	13/N		1211	1211
			0%	*100%*	
C9203	72	13/N		2136	2136
			0%	*100%*	
C9206	72	14/S	ND	ND	ND
C9207	72	14/S		4094	4094
			0%	*100%*	
C9208	72	14/S	ND	ND	ND
C9209	72	14/S		1682	1682
			0%	*100%*	

Retention times listed are approximate

STUDY 9550 Part 1 HPLC URINE ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Sex	NET AREA CPM													Total CPMs Detected	Sum of percentage of (2) most abundant peaks
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3 tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
			3.5min. Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite		
C9162	12	3/F	713					1201								1914	
			37%					*63%*									100%
C9163	12	3/F	1477	564				2232				544				4817	
			31%	*12%*				*46%*				11%					77%
C9164	12	3/F	1434	578				1701						316		4029	
			36%	*14%*				*42%*						*8%*			78%
C9165	12	3/F	NO SAMPLE														
																	N/A
C9166	12	4/M	2526	791				3423		476		321				7537	
			34%	*10%*				*45%*		*6%*		*4%*					79%
C9167	12	4/M	1713	398				2213								4324	
			40%	*9%*				*51%*									91%
C9168	12	4/M	2541	664				3281		427		473				7386	
			34%	*9%*				*44%*		*6%*		*6%*					79%
C9169	12	4/M	2767	538				2584		432						6321	
			44%	*9%*				*41%*		*7%*							85%

Retention times listed are approximate

STUDY 9550 Part 1 HPLC URINE ANALYSIS

			NET AREA CPM														
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3 tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3 tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
Sample ID	Time Point (hours post dosing)	Group/ Sex	**3.5min.** Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite	Total CPMs Detected	Sum of percentage of (2) most abundant peaks
C9162	24	3/F	3721	1212				5068	449	629		550				11629	
			32%	*10%*				*44%*	*4%*	*5%*		*5%*					76%
C9163	24	3/F	4875	1492				6812		858		983				15020	
			32%	*10%*				*45%*		*6%*		*7%*					78%
C9164	24	3/F	6947	2428		347	451	10271		1365		945				22754	
			31%	*11%*		*2%*	*2%*	*45%*		*6%*		*4%*					76%
C9165	24	3/F	5242	1804				8474		853		806				17179	
			31%	*11%*				*49%*		*5%*		*5%*					80%
C9166	24	4/M	9113	2406		738		14042		1596	411	870		336		29512	
			31%	*8%*		*3%*		*48%*		*5%*	*1%*	*3%*		*1%*			78%
C9167	24	4/M	6370	1643				10338		672		494				19517	
			33%	*8%*				*53%*		*3%*		*3%*					86%
C9168	24	4/M	10421	3484		795		14513		1536		806				31555	
			33%	*11%*		*3%*		*46%*		*5%*		*3%*					79%
C9169	24	4/M	9814	2840		712	382	14365		1361		937				30411	
			32%	*9%*		*2%*	*1%*	*47%*		*4%*		*3%*					42%

Retention times listed are approximate

STUDY 9550 Part 1 HPLC URINE ANALYSIS

			NET AREA CPM														
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3-tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
Sample ID	Time Point (hours post dosing)	Group/ Sex	**3.5min.** Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite	Total CPMs Detected	Sum of percentage of (2) most abundant peaks
C9162	48	3/F	11670	4058	356	1054		20392		1674		1552				40756	
			29%	*10%*	*1%*	*3%*		*50%*		*4%*		*4%*					*79%*
C9163	48	3/F	8484	3093		519		15273		784		944				29097	
			29%	*11%*		*2%*		*52%*		*3%*		*3%*					*82%*
C9164	48	3/F	1610	715				2894								5219	
			31%	*14%*				*55%*									*86%*
C9165	48	3/F	11300	4070		844	406	20520	502	2475		1983	446			42546	
			27%	*10%*		*2%*	*1%*	*48%*	*1%*	*6%*		*5%*	*1%*				*75%*
C9166	48	4/M	9977	3450		402		17123		957		628	350			32887	
			30%	*10%*		*1%*		*52%*		*3%*		*2%*	*1%*				*82%*
C9167	48	4/M	11048	3866		596		19868		1304		751				37433	
			30%	*10%*		*2%*		*53%*		*3%*		*2%*					*83%*
C9168	48	4/M	14787	5637		1175		27520		2512		1286				52917	
			28%	*11%*		*2%*		*52%*		*5%*		*2%*					*80%*
C9169	48	4/M	9994	3663		550		18846		815		508				34376	
			29%	*11%*		*2%*		*55%*		*2%*		*1%*					*84%*

Retention times listed are approximate

STUDY 9550 Part 1 HPLC URINE ANALYSIS

			NET AREA CPM														
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3 tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3 tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-tnol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
Sample ID	Time Point (hours post dosing)	Group/ Sex	**3.5min.** Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite	Total CPMs Detected	Sum of percentage of (2) most abundant peaks
C9162	72	3/F	3517	971				8091								12579	
			28%	*8%*				*64%*									92%
C9163	72	3/F	2216	610	302			4729								7857	
			28%	*8%*	*4%*			*60%*									88%
C9164	72	3/F	9155	2656	364	427		17341		982		935				31860	
			29%	*8%*	*1%*	*1%*		*54%*		*3%*		*3%*					83%
C9165	72	3/F	3725	1263				6178				451				11617	
			32%	*11%*				*53%*				4%					85%
C9166	72	4/M	2801	992				3901								7694	
			36%	*13%*				*51%*									87%
C9167	72	4/M	2845	819				4741								8405	
			34%	*10%*				*56%*									90%
C9168	72	4/M	5440	1537				8583								15560	
			35%	*10%*				*55%*									90%
C9169	72	4/M	2745	668				4325								7738	
			35%	*9%*				*56%*									91%

Retention times listed are approximate

STUDY 9550 Part 1 HPLC URINE ANALYSIS

			NET AREA CPM														
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3-tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
Sample ID	Time Point (hours post dosing)	Group/ Sex	**3.5min.** Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite	Total CPMs Detected	Sum of percentage of (2) most abundant peaks
C9162	96	3/F	7621													7621	
			100%														100%
C9163	96	3/F	529													529	
			100%														100%
C9164	96	3/F	1999													1999	
			100%														100%
C9165	96	3/F	3825													3825	
			100%														100%
C9166	96	4/M	2465													2465	
			100%														100%
C9167	96	4/M	3535													3535	
			100%														100%
C9168	96	4/M	4403													4403	
			100%														100%
C9169	96	4/M	2800													2800	
			100%														100%

Retention times listed are approximate

STUDY 9550 Part 1 HPLC URINE ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Sex	NET AREA CPM													Total CPMs Detected	Sum of percentage of (2) most abundant peaks
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3 tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
			3.5min. Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite		
C9162	120	3/F	2941													2941	
			100%														100%
C9163	120	3/F	1717													1717	
			100%														100%
C9164	120	3/F	983													983	
			100%														100%
C9165	120	3/F	2029													2029	
			100%														100%
C9166	120	4/M	1865													1865	
			100%														100%
C9167	120	4/M	2407													2407	
			100%														100%
C9168	120	4/M	3237													3237	
			100%														100%
C9169	120	4/M	2470													2470	
			100%														100%

Retention times listed are approximate

STUDY 9550 Part 2 HPLC URINE ANALYSIS

			NET AREA CPM														
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3-tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
Sample ID	Time Point (hours post dosing)	Group/ Sex	3.5min. Retention time metabolite	4.4min. Retention time metabolite	7.0min. Retention time metabolite	8.5min. Retention time metabolite	10.1min. Retention time metabolite	14.6min. Retention time metabolite	16.5min. Retention time metabolite	28.4min. Retention time metabolite	29.6min. Retention time metabolite	32.1min. Retention time metabolite	32.8min. Retention time metabolite	40.1min. Retention time metabolite	50.9min. Retention time metabolite	Total CPMs Detected	Sum of percentage of (2) most abundant peaks
C9200	12	3/F	946					1493				465				2904	
			33%					*51%*				*16%*					84%
C9201	12	3/F	1307					1810								3117	
			42%					*58%*									100%
Q0004	12	3/F	1205					2233								3438	
			35%					*65%*									100%
C9203	12	3/F	957					1121								2078	
			46%					*54%*									100%
C9206	12	4/M	1132					1799								2931	
			39%					*61%*									100%
C9207	12	4/M	612					730								1342	
			46%					*54%*									100%
C9208	12	4/M	832					1254								2086	
			40%					*60%*									100%
C9209	12	4/M	1303					1353								2656	
			49%					*51%*									100%

Retention times listed are approximate

STUDY 9550 Part 2 HPLC URINE ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Sex	NET AREA CPM														
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3-tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane	Total CPMs Detected	Sum of percentage of (2) most abundant peaks
			3.5min. Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.3min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite		
C9200	24	3/F	2801	726				4861				458				8846	
			32%	*8%*				*55%*				5%					87%
C9201	24	3/F	4499	1443				5965		570		713				13190	
			34%	*11%*				*45%*		*4%*		5%					79%
Q0004	24	3/F	3610	903				5966		551	401	602				12033	
			30%	*8%*				*50%*		*5%*	*3%*	5%					80%
C9203	24	3/F	2169	647				3573				429				6818	
			32%	*9%*				*52%*				6%					84%
C9206	24	4/M	1745					2805								4550	
			38%					*62%*									100%
C9207	24	4/M	1048					1852								2900	
			36%					*64%*									100%
C9208	24	4/M	2708	1035				4856				456				9055	
			30%	*11%*				*54%*				*5%*					84%
C9209	24	4/M	2045	421				3413								5879	
			35%	*7%*				*58%*									93%

Retention times listed are approximate

STUDY 9550 Part 2 HPLC URINE ANALYSIS

			NET AREA CPM														
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3-tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
Sample ID	Time Point (hours post dosing)	Group/ Sex	**3.5min.** Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite	Total CPMs Detected	Sum of percentage of (2) most abundant peaks
C9200	48	3/F	4288	1514				8547				435				14784	
			29%	*10%*				*58%*				3%					87%
C9201	48	3/F	12370	4554		1125	754	21268		1246		1228				42545	
			29%	*11%*		*3%*	*2%*	*50%*		*3%*		3%					79%
Q0004	48	3/F	2154	761				3403								6318	
			34%	*12%*				*54%*									88%
C9203	48	3/F	1853	769				3982								6604	
			28%	*12%*				*60%*									88%
C9206	48	4/M	1292					2381								3673	
			35%					*65%*									100%
C9207	48	4/M	2034	692				3247								5973	
			34%	*12%*				*54%*									88%
C9208	48	4/M	1183					1843								3026	
			39%					*61%*									100%
C9209	48	4/M	1361	652				2217								4230	
			32%	*15%*				*52%*									85%

Retention times listed are approximate

STUDY 9550 Part 2 HPLC URINE ANALYSIS

			NET AREA CPM														
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3-tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
Sample ID	Time Point (hours post dosing)	Group/ Sex	**3.5min.** Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite	Total CPMs Detected	Sum of percentage of (2) most abundant peaks
C9200	72	3/F	1183					2065								3248	
			36%					*64%*									100%
C9201	72	3/F	3445	1268				6812								11525	
			30%	*11%*				*59%*									89%
Q0004	72	3/F	627					950								1577	
			40%					*60%*									100%
C9203	72	3/F	546					985								1531	
			36%					*64%*									100%
C9206	72	4/M	568					875								1443	
			39%					*61%*									100%
C9207	72	4/M	1464	822				3329								5615	
			26%	*15%*				*59%*									85%
C9208	72	4/M	461													461	
			100%														100%
C9209	72	4/M	709					1403								2112	
			34%					*66%*									100%

Retention times listed are approximate

STUDY 9550 Part 2 HPLC URINE ANALYSIS

Sample ID	Time Point (hours post dosing)	Group/ Sex	NET AREA CPM													Total CPMs Detected	Sum of percentage of (2) most abundant peaks
			Methyl-silanetriol	Dimethyl-disiloxane-1,3,3,3-tetrol	unknown	1,3-Dimethyl-disiloxane-1,1,3,3-tetrol	Unknown	Dimethyl-silanediol	Unknown	1,3,3-Trimethyl-disiloxane-1,1,3-triol	Unknown	1,1,3,3-Tetramethyl-disiloxane-1,3-diol	Unknown	1,1,3,3,5,5-Hexamethyl-trisiloxane-1,5-diol	Decamethyl-cyclopenta-siloxane		
			3.5min. Retention time metabolite	**4.4min.** Retention time metabolite	**7.0min.** Retention time metabolite	**8.5min.** Retention time metabolite	**10.1min.** Retention time metabolite	**14.6min.** Retention time metabolite	**16.5min.** Retention time metabolite	**28.4min.** Retention time metabolite	**29.6min.** Retention time metabolite	**32.1min.** Retention time metabolite	**32.8min.** Retention time metabolite	**40.1min.** Retention time metabolite	**50.9min.** Retention time metabolite		
C9200	96	3/F	631					1355								1986	
			32%					*68%*									100%
C9201	96	3/F	641					1305								1946	
			33%					*67%*									100%
Q0004	96	3/F						659								659	
								100%									100%
C9203	96	3/F						518								518	
								100%									100%
C9206	96	4/M														0	
																	0%
C9207	96	4/M	442					627								1069	
			41%					*59%*									100%
C9208	96	4/M														0	
																	0%
C9209	96	4/M						492								492	
								100%									100%

Retention times listed are approximate

APPENDIX B
Radioactivity Spreadsheets

Calculations and Abbreviations

Calculations

1. Dosing Solution

Targeted dose : 1g D_5/ 1000 g B.W.

Neat D_5: Calculated dose (g) = Body Weight (g) *1g/1000g

D_5 in carrier: Calculated dose (g) = $\frac{\text{Body Weight (g)/1000}}{\text{D}_5 \text{ concentration (mg D}_5\text{/g d.s.)/1000mg/g}}$

2. Radioactivity
1 μCi = 2.22 x 10^6 DPMs

3. Specific activity of dosing solution:
DPM/mg of dosing solution / 2.22 x 10^6 (DPM/μCi) = μCi/mg of dosing solution

4. D_5 Specific activity (DPM/ mg D_5)
DPM/mg of dosing solution*1000 (mg/g)/D_5 concentration (mg D_5)/ g of dosing solution

5. Dose (DPMs):
S.A. of dosing solution (DPMs/mg) * dose (mg) = DPMs

6. Dose (μCi)
S.A. of dosing solution (μCi/mg) * dose (mg) = μCi

7. Matrix Background
Average DPM/g of control samples

8. Radioactivity concentration in the sample aliquots (Corrected DPM/g)
Aliquot DPM/Aliquot Wt.(g) - matrix background (DPM/g)

9. Total DPMs in the sample:
Radioactivity conc. (DPM/g) * Sample wt.[a] (g) = DPM

[a]Sample wt. = homogenate wt.(e.g. feces), extract wt. (e.g. charcoal) or direct sample wt. (e.g. urine)

10. Percent of Administered Dose:
$\frac{\text{Total DPMs in sample}}{\text{Dose (DPMs)}}$ * 100 = % Dose

11. Average Percent Dose
Percent dose for the group of test systems.

12. Percent Dose eliminated through GI Tract
Percent of administered dose excreted in feces over 168 hours.

13. Correction for solubilization processing efficiency
Percent of administered dose recovered in feces *100/ processing efficiency

14. Percent of the total recovery
Percent of administered dose recovered in the sample (e.g. excreta) *100/Total % dose recovered in all the samples.

15. Equivalent μg D_5/g of specimen

$$\frac{\text{Total DPM in the sample}^a \text{ / specimen}^b \text{ weight (g)} * 1000\ \mu g/mg}{\text{Specific activity of } D_5 \text{ in dosing solution (DPM/mg } D_5)}$$

[a]Sample = homogenate (e.g. feces, solubilized tissues) or direct sample (e.g. urine, KOH)
[b]Specimen = tissue, carcass or excreta (e.g. feces, urine)

16. Reanalysis Criteria is defined by the percent relative range (%RR)
The %RR is derived by calculating the difference between two values (DPM/g) and expressing this difference as a percentage of the mean for the two values (aliquots). Samples which failed to meet the following criteria were re-analyzed in duplicate:

Note: F1, F2, and F3 are flags on Excel data sheets; the flags F1, F2 and F3 are used if criteria defined below are not met:

A) For DPM/g between 0 and 299 the %RR must be less than or equal to 20%. (*i.e.*F1 if %RR>20%)
B) For DPM/g between 300 and 999 the %RR must be less than or equal to 15%. (*i.e.*F2 if %RR>15%)
C) For DPM/g greater than 1000, the %RR must be less than 10%.(*i.e.*F3 if %RR>10%)

An exception to the above criteria is when the % dose recovered in the sample is less than or equal to 0.1%, then no re-analysis of a sample is required.

17. BLQ
Values below limits of quantification (BLQ) are considered to equal zero.

18. Q-Test Used to identify statistical outliers in data (Mitschele J. 1991. Small sample Statistics. J. Chem. Ed. 68: 470-473; ASTM Standard E 178-94. Standard practice for dealing with outlying observations. American Society for Testing Materials.)

Abbreviations:

DPM = Disintegrations per minute	Bkg. = Background
Avg. = Average	N.S. = No sample
Sol'n. = Solution	N.A. = Not applicable
S.A.= Specific Activity	B.W. = Body weight
d.s. = dosing solution	N.D. = Not determined
Cum. = cumulative	LOQ = Limit of quantification
Conc. = concentration	BLQ = Below limit of quantification
Rep. = Replicate	ALQ= Above limit of quantification
WBA = Whole Body Autoradiography	Hr. = hour
LSC = Liquid Scintillation Counter	F = flag indicating non-uniformity of the sampling
GI tract =Gastrointestinal Tract	Homog., Homogen. = Homogenate
Wt. = Weight	SF = Simethicone
St.Dev. = SD = Standard Deviation	CO = Corn Oil
Eq./Equiv. = Equivalent	No. = number
SEM = Standard error of the mean	%RR = Percent Relative Range
THF = Tetrahydrofuran	
TEAH = Tetraethylammonium hydroxide	

Animal ID/ Timepoint	Group ID and Sex (CORN OIL)	Parent µg D_5/g blood	Parent µg D_5/g of blood Averages/Sex/ Timepoint	SEM	Radioactivity µg Eq. D_5/g blood	Radioactivity µg Eq. D_5/g of blood/ Averages/ Sex/ Timepoint	SEM
C9182 24hr Control	Grp 7 Female	BLQ					
Q0041 24hr Control	Grp 7 Female	0.053					
C9184 24hr Control	Grp 8 Male	BLQ					
C9185 24hr Control	Grp 8 Male	BLQ					
C9186 15min	Grp 9 Female	0.109	0.215	0.042	0.103	0.241	0.081
C9187 15min	Grp 9 Female	0.333			0.617		
C9188 15min	Grp 9 Female	0.205			0.200		
C9189 15min	Grp 9 Female	0.172			0.062		
C9190 15min	Grp 9 Female	0.346			0.186		
C9191 15min	Grp 9 Female	0.124			0.279		
C9192 15min	Grp 10 Male	0.329	0.202	0.035	0.255	0.129	0.039
C9193 15min	Grp 10 Male	0.252			0.190		
C9194 15min	Grp 10 Male	0.231			0.180		
C9195 15min	Grp 10 Male	0.090			0.000		
C9196 15min	Grp 10 Male	0.155			0.066		
Q0037 15min	Grp 10 Male	0.152			0.082		
C9186 60 min	Grp 9 Female	3.467	5.310	0.407	2.708	4.784	0.478
C9187 60 min	Grp 9 Female	5.735			4.574		
C9188 60 min	Grp 9 Female	5.415			5.076		
C9189 60 min	Grp 9 Female	6.457			6.078		
C9190 60 min	Grp 9 Female	5.230			5.636		
C9191 60 min	Grp 9 Female	5.554			4.633		
C9192 60min	Grp 10 Male	5.933	6.226	0.754	4.953	5.222	0.577
C9193 60min	Grp 10 Male	4.660			3.708		
C9194 60min	Grp 10 Male	3.888			3.713		
C9195 60min	Grp 10 Male	8.141			6.760		
C9196 60min	Grp 10 Male	8.543			6.949		
Q0037 60min	Grp 10 Male	6.192			5.250		
C9186 6hr	Grp 9 Female	93.922	52.121	8.972	94.415	46.936	9.783
C9187 6hr	Grp 9 Female	50.704			37.979		
C9188 6hr	Grp 9 Female	47.502			41.501		
C9189 6hr	Grp 9 Female	49.461			44.839		
C9190 6hr	Grp 9 Female	28.900			28.067		
C9191 6hr	Grp 9 Female	42.237			34.814		
C9192 6hr	Grp 10 Male	61.853	62.490	4.261	54.054	51.149	2.930
C9193 6hr	Grp 10 Male	66.277			55.336		
C9194 6hr	Grp 10 Male	63.418			47.782		
C9195 6hr	Grp 10 Male	71.237			52.989		
C9196 6hr	Grp 10 Male	42.470			38.331		
Q0037 6hr	Grp 10 Male	69.682			58.403		
C9186 12hr	Grp 9 Female	50.271	34.753	6.148	43.996	30.809	4.039
C9187 12hr	Grp 9 Female	25.587			23.936		
C9188 12hr	Grp 9 Female	18.551			22.424		
C9189 12hr	Grp 9 Female	40.823			34.399		
C9190 12hr	Grp 9 Female	20.794			20.461		
C9191 12hr	Grp 9 Female	52.495			39.637		
C9192 12hr	Grp 10 Male	50.183	44.975	4.032	42.902	40.176	2.315
C9193 12hr	Grp 10 Male	41.453			36.220		
C9194 12hr	Grp 10 Male	59.849			49.529		
C9195 12hr	Grp 10 Male	32.360			33.729		
C9196 12hr	Grp 10 Male	48.486			41.251		
Q0037 12hr	Grp 10 Male	37.518			37.425		
C9186 24hr	Grp 9 Female	9.632	10.185	1.396	14.081	13.718	1.489
C9187 24hr	Grp 9 Female	10.015			12.954		
C9188 24hr	Grp 9 Female	6.204			9.404		
C9189 24hr	Grp 9 Female	13.589			16.701		
C9190 24hr	Grp 9 Female	6.970			10.292		

Rounding errors may occur due to electronic handling of numbers

Animal ID/ Timepoint	Group ID and Sex (CORN OIL)	Parent µg D_5/g blood	Parent µg D_5/g of blood Averages/Sex/ Timepoint	SEM	Radioactivity µg Eq. D_5/g blood	Radioactivity µg Eq. D_5/g of blood/ Averages/ Sex/ Timepoint	SEM
C9191 24hr	Grp 9 Female	14.701			18.876		
C9192 24hr	Grp 10 Male	11.842	11.517	1.980	17.086	16.815	2.000
C9193 24hr	Grp 10 Male	5.323			10.328		
C9194 24hr	Grp 10 Male	11.383			16.628		
C9195 24hr	Grp 10 Male	9.353			15.055		
C9196 24hr	Grp 10 Male	20.132			25.446		
Q0037 24hr	Grp 10 Male	11.066			16.349		
C9186 48hr	Grp 9 Female	1.134	1.541	0.303	3.491	4.114	0.690
C9187 48hr	Grp 9 Female	1.331			3.448		
C9188 48hr	Grp 9 Female	0.921			2.436		
C9189 48hr	Grp 9 Female	2.168			6.507		
C9190 48hr	Grp 9 Female	0.960			2.857		
C9191 48hr	Grp 9 Female	2.734			5.943		
C9192 48hr	Grp 10 Male	0.664	0.952	0.140	2.200	2.867	0.335
C9193 48hr	Grp 10 Male	0.591			1.727		
C9194 48hr	Grp 10 Male	1.020			3.259		
C9195 48hr	Grp 10 Male	0.811			2.776		
C9196 48hr	Grp 10 Male	1.094			4.025		
Q0037 48hr	Grp 10 Male	1.529			3.215		
C9186 72hr	Grp 9 Female	0.514	0.593	0.060	1.571	1.611	0.155
C9187 72hr	Grp 9 Female	0.630			1.445		
C9188 72hr	Grp 9 Female	0.460			0.995		
C9189 72hr	Grp 9 Female	0.726			1.900		
C9190 72hr	Grp 9 Female	0.434			1.665		
C9191 72hr	Grp 9 Female	0.796			2.090		
C9192 72hr	Grp 10 Male	0.227	0.285	0.035	0.929	1.038	0.142
C9193 72hr	Grp 10 Male	0.233			0.736		
C9194 72hr	Grp 10 Male	0.323			1.067		
C9195 72hr	Grp 10 Male	0.241			0.933		
C9196 72hr	Grp 10 Male	0.442			1.714		
Q0037 72hr	Grp 10 Male	0.242			0.852		
C9186 96hr	Grp 9 Female	0.415	0.479	0.063	0.938	1.485	0.304
C9187 96hr	Grp 9 Female	0.560			1.134		
C9188 96hr	Grp 9 Female	0.414			0.789		
C9189 96hr	Grp 9 Female	0.752			2.716		
C9190 96hr	Grp 9 Female	0.318			2.046		
C9191 96hr	Grp 9 Female	0.414			1.286		
C9192 96hr	Grp 10 Male	0.205	0.227	0.034	0.686	1.918	1.121
C9193 96hr	Grp 10 Male	0.162			0.556		
C9194 96hr	Grp 10 Male	0.231			7.487		
C9195 96hr	Grp 10 Male	0.207			0.778		
C9196 96hr	Grp 10 Male	0.391			1.389		
Q0037 96hr	Grp 10 Male	0.168			0.612		
C9186 120hr	Grp 9 Female	0.346	0.447	0.060	0.673	0.793	0.214
C9187 120hr	Grp 9 Female	0.503			0.887		
C9188 120hr	Grp 9 Female	0.300			0.557		
C9189 120hr	Grp 9 Female	0.638			1.556		
C9190 120hr	Grp 9 Female	NS			NS		
C9191 120hr	Grp 9 Female	0.450			0.290		
C9192 120hr	Grp 10 Male	0.147	0.190	0.030	0.395	0.579	0.097
C9193 120hr	Grp 10 Male	0.145			0.342		
C9194 120hr	Grp 10 Male	0.176			0.489		
C9195 120hr	Grp 10 Male	0.152			0.532		
C9196 120hr	Grp 10 Male	0.337			0.972		
Q0037 120hr	Grp 10 Male	0.183			0.743		
C9186 144hr	Grp 9 Female	0.538	0.549	0.115	1.151	2.561	1.333
C9187 144hr	Grp 9 Female	0.637			1.311		

Rounding errors may occur due to electronic handling of numbers

Animal ID/ Timepoint	Group ID and Sex (CORN OIL)	Parent µg D_5/g blood	Parent µg D_5/g of blood Averages/Sex/ Timepoint	SEM	Radioactivity µg Eq. D_5/g blood	Radioactivity µg Eq. D_5/g of blood/ Averages/ Sex/ Timepoint	SEM
C9188 144hr	Grp 9 Female	0.239			6.557		
C9189 144hr	Grp 9 Female	0.780			1.224		
C9190 144hr	Grp 9 Female	NS			NS		
C9191 144hr	Grp 9 Female	NS			NS		
C9192 144hr	Grp 10 Male	0.156	0.186	0.041	0.581	0.709	0.130
C9193 144hr	Grp 10 Male	0.124			0.484		
C9194 144hr	Grp 10 Male	0.166			1.139		
C9195 144hr	Grp 10 Male	0.138			0.539		
C9196 144hr	Grp 10 Male	0.389			1.088		
Q0037 144hr	Grp 10 Male	0.145			0.422		
C9186 168hr	Grp 9 Female	NS	0.331	0.109	NS	0.868	0.278
C9187 168hr	Grp 9 Female	NS			NS		
C9188 168hr	Grp 9 Female	0.209			0.513		
C9189 168hr	Grp 9 Female	0.549			1.416		
C9190 168hr	Grp 9 Female	0.234			0.675		
C9191 168hr	Grp 9 Female	NS			NS		
C9192 168hr	Grp 10 Male	0.138	0.191	0.049	0.585	0.613	0.116
C9193 168hr	Grp 10 Male	0.139			0.371		
C9194 168hr	Grp 10 Male	0.132			0.655		
C9195 168hr	Grp 10 Male	0.127			0.284		
C9196 168hr	Grp 10 Male	0.434			1.091		
Q0037 168hr	Grp 10 Male	0.176			0.693		

Rounding errors may occur due to electronic handling of numbers

Animal ID/ Timepoint	Group ID and Carrier	Parent µg D_5/g blood	Parent µg D_5/g of blood Averages/ Carrier / Timepoint	Std error of the mean	Radioactivity µg Eq. D_5/g blood	Radioactivity µg Eq. D_5/g of blood Averages/ Carrier/ Timepoint	Std error of the mean
C9210 24hr Control	Grp 15 Female	BLQ	BLQ		NA		
C9211 24hr Control	Grp 15 Female	BLQ			NA		
C9218 24hr Control	Grp 16 Female	BLQ	BLQ		NA		
C9219 24hr Control	Grp 16 Female	BLQ			NA		
C9212 15min	Grp 17/ **NEAT D_5**	0.000	0.093	0.037	0.082	0.133	0.044
C9213 15min	Grp 17/ **NEAT D_5**	0.000			0.026		
C9214 15min	Grp 17/ **NEAT D_5**	0.102			0.153		
C9215 15min	Grp 17/ **NEAT D_5**	0.064			0.022		
C9216 15min	Grp 17/ **NEAT D_5**	0.167			0.273		
C9217 15min	Grp 17/ **NEAT D_5**	0.225			0.244		
C9220 15min	Grp 18/ **SF**	0.000	0.000	0.000	0.000	0.025	0.016
C9221 15min	Grp 18/ **SF**	0.000			0.000		
C9222 15min	Grp 18/ **SF**	0.000			0.083		
C9223 15min	Grp 18/ **SF**	0.000			0.066		
C9224 15min	Grp 18/ **SF**	0.000			0.000		
C9225 15min	Grp 18/ **SF**	0.000			0.001		
C9212 60 min	Grp 17/ **NEAT D_5**	0.988	1.928	0.470	1.546	2.185	0.475
C9213 60 min	Grp 17/ **NEAT D_5**	0.701			0.773		
C9214 60 min	Grp 17/ **NEAT D_5**	1.829			2.048		
C9215 60 min	Grp 17/ **NEAT D_5**	1.773			1.941		
C9216 60 min	Grp 17/ **NEAT D_5**	2.338			2.582		
C9217 60 min	Grp 17/ **NEAT D_5**	3.938			4.221		
C9220 60min	Grp 18/ **SF**	0.434	0.395	0.065	0.226	0.434	0.098
C9221 60min	Grp 18/ **SF**	0.142			0.131		
C9222 60min	Grp 18/ **SF**	0.631			0.733		
C9223 60min	Grp 18/ **SF**	0.439			0.630		
C9224 60min	Grp 18/ **SF**	0.321			0.332		
C9225 60min	Grp 18/ **SF**	0.403			0.553		
C9212 6hr	Grp 17/ **NEAT D_5**	5.336	7.943	0.708	6.172	9.328	0.846
C9213 6hr	Grp 17/ **NEAT D_5**	NS			NS		
C9214 6hr	Grp 17/ **NEAT D_5**	8.668			10.351		
C9215 6hr	Grp 17/ **NEAT D_5**	8.043			9.222		
C9216 6hr	Grp 17/ **NEAT D_5**	8.095			9.821		
C9217 6hr	Grp 17/ **NEAT D_5**	9.575			11.075		
C9220 6hr	Grp 18/ **SF**	2.711	1.578	0.308	3.655	2.168	0.392
C9221 6hr	Grp 18/ **SF**	0.513			0.826		
C9222 6hr	Grp 18/ **SF**	1.214			1.672		
C9223 6hr	Grp 18/ **SF**	1.259			1.838		
C9224 6hr	Grp 18/ **SF**	1.914			2.517		
C9225 6hr	Grp 18/ **SF**	1.857			2.500		
C9212 12hr	Grp 17/ **NEAT D_5**	3.461	4.080	1.149	4.945	5.585	1.224
C9213 12hr	Grp 17/ **NEAT D_5**	NS			NS		
C9214 12hr	Grp 17/ **NEAT D_5**	3.603			5.060		
C9215 12hr	Grp 17/ **NEAT D_5**	8.528			10.355		
C9216 12hr	Grp 17/ **NEAT D_5**	2.848			3.890		
C9217 12hr	Grp 17/ **NEAT D_5**	1.960			3.672		
C9220 12hr	Grp 18/ **SF**	3.240	2.134	0.385	4.442	3.097	0.479
C9221 12hr	Grp 18/ **SF**	0.828			1.535		

Rounding errors may occur due to electronic handling of numbers

Animal ID/ Timepoint	Group ID and Carrier	Parent µg D_5/g blood	Parent µg D_5/g of blood Averages/ Carrier / Timepoint	Std error of the mean	Radioactivity µg Eq. D_5/g blood	Radioactivity µg Eq. D_5/g of blood Averages/ Carrier/ Timepoint	Std error of the mean
C9222 12hr	Grp 18/ SF	2.567			3.147		
C9223 12hr	Grp 18/ SF	1.168			1.987		
C9224 12hr	Grp 18/ SF	2.243			3.195		
C9225 12hr	Grp 18/ SF	2.757			4.277		
C9212 24hr	Grp 17/ NEAT D_5	0.644	4.023	3.088	1.918	5.790	3.547
C9213 24hr	Grp 17/ NEAT D_5	NS			NS		
C9214 24hr	Grp 17/ NEAT D_5	0.832			2.006		
C9215 24hr	Grp 17/ NEAT D_5	1.488			3.501		
C9216 24hr	Grp 17/ NEAT D_5	16.360			19.918		
C9217 24hr	Grp 17/ NEAT D_5	0.790			1.606		
C9220 24hr	Grp 18/ SF	0.455	0.612	0.227	1.274	1.393	0.311
C9221 24hr	Grp 18/ SF	0.287			0.940		
C9222 24hr	Grp 18/ SF	0.545			1.309		
C9223 24hr	Grp 18/ SF	0.319			0.812		
C9224 24hr	Grp 18/ SF	0.335			1.121		
C9225 24hr	Grp 18/ SF	1.731			2.898		
C9212 48hr	Grp 17/ NEAT D_5	0.263	0.487	0.180	0.569	1.292	0.611
C9213 48hr	Grp 17/ NEAT D_5	NS			NS		
C9214 48hr	Grp 17/ NEAT D_5	0.393			0.657		
C9215 48hr	Grp 17/ NEAT D_5	0.369			0.971		
C9216 48hr	Grp 17/ NEAT D_5	1.196			3.718		
C9217 48hr	Grp 17/ NEAT D_5	0.214			0.548		
C9220 48hr	Grp 18/ SF	0.211	0.165	0.024	0.379	0.348	0.070
C9221 48hr	Grp 18/ SF	0.099			0.209		
C9222 48hr	Grp 18/ SF	0.237			0.505		
C9223 48hr	Grp 18/ SF	0.121			0.221		
C9224 48hr	Grp 18/ SF	0.118			0.186		
C9225 48hr	Grp 18/ SF	0.205			0.590		
C9212 72hr	Grp 17/ NEAT D_5	0.180	0.242	0.030	0.482	0.481	0.179
C9213 72hr	Grp 17/ NEAT D_5	NS			NS		
C9214 72hr	Grp 17/ NEAT D_5	0.256			0.512		
C9215 72hr	Grp 17/ NEAT D_5	0.247			0.084		
C9216 72hr	Grp 17/ NEAT D_5	0.345			1.120		
C9217 72hr	Grp 17/ NEAT D_5	0.182			0.206		
C9220 72hr	Grp 18/ SF	0.203	0.173	0.043	0.362	0.205	0.046
C9221 72hr	Grp 18/ SF	0.089			0.080		
C9222 72hr	Grp 18/ SF	0.107			0.194		
C9223 72hr	Grp 18/ SF	0.106			0.178		
C9224 72hr	Grp 18/ SF	0.372			0.104		
C9225 72hr	Grp 18/ SF	0.160			0.312		
C9212 96hr	Grp 17/ NEAT D_5	0.133	0.206	0.042	0.390	0.409	0.103
C9213 96hr	Grp 17/ NEAT D_5	NS			NS		
C9214 96hr	Grp 17/ NEAT D_5	0.303			0.297		
C9215 96hr	Grp 17/ NEAT D_5	0.154			0.192		
C9216 96hr	Grp 17/ NEAT D_5	0.312			0.795		
C9217 96hr	Grp 17/ NEAT D_5	0.130			0.371		
C9220 96hr	Grp 18/ SF	0.120	0.094	0.007	0.125	0.108	0.018

Animal ID/ Timepoint	Group ID and Carrier	Parent µg D_5/g blood	Parent µg D_5/g of blood Averages/ Carrier / Timepoint	Std error of the mean	Radioactivity µg Eq. D_5/g blood	Radioactivity µg Eq. D_5/g of blood Averages/ Carrier/ Timepoint	Std error of the mean
C9221 96hr	Grp 18/ SF	0.075			0.124		
C9222 96hr	Grp 18/ SF	0.104			0.164		
C9223 96hr	Grp 18/ SF	0.077			0.034		
C9224 96hr	Grp 18/ SF	0.085			0.085		
C9225 96hr	Grp 18/ SF	0.105			0.118		
C9212 120hr	Grp 17/ NEAT D_5	0.191	0.152	0.031	0.126	0.243	0.163
C9213 120hr	Grp 17/ NEAT D_5	NS			NS		
C9214 120hr	Grp 17/ NEAT D_5	NS			NS		
C9215 120hr	*Grp 17/ NEAT D_5*	*0.175*			*13.246*	*excluded based on Q-test*	
C9216 120hr	Grp 17/ NEAT D_5	0.174			0.565		
C9217 120hr	Grp 17/ NEAT D_5	0.091			0.039		
C9220 120hr	Grp 18/ SF	0.060	0.087	0.026	0.193	0.115	0.046
C9221 120hr	Grp 18/ SF	0.000			0.000		
C9222 120hr	Grp 18/ SF	0.136			0.286		
C9223 120hr	Grp 18/ SF	0.180			0.140		
C9224 120hr	Grp 18/ SF	0.063			0.018		
C9225 120hr	Grp 18/ SF	0.081			0.052		
C9212 144hr	Grp 17/ NEAT D_5	0.230	0.209	0.011	0.093	0.252	0.100
C9213 144hr	Grp 17/ NEAT D_5	NS			NS		
C9214 144hr	Grp 17/ NEAT D_5	NS			NS		
C9215 144hr	Grp 17/ NEAT D_5	0.198			0.227		
C9216 144hr	Grp 17/ NEAT D_5	0.198			0.436		
C9217 144hr	Grp 17/ NEAT D_5	NS			NS		
C9220 144hr	Grp 18/ SF	0.087	0.082	0.011	0.139	0.112	0.012
C9221 144hr	Grp 18/ SF	0.050			0.069		
C9222 144hr	*Grp 18/ SF*	*0.115*			*0.914*	*excluded based on Q-test*	
C9223 144hr	Grp 18/ SF	0.088			0.125		
C9224 144hr	Grp 18/ SF	0.115			0.104		
C9225 144hr	Grp 18/ SF	0.072			0.123		
C9212 168hr	Grp 17/ NEAT D_5	0.101	0.118	0.015	0.025	0.152	0.104
C9213 168hr	Grp 17/ NEAT D_5	NS			NS		
C9214 168hr	Grp 17/ NEAT D_5	NS			NS		
C9215 168hr	Grp 17/ NEAT D_5	0.105			0.073		
C9216 168hr	Grp 17/ NEAT D_5	0.148			0.357		
C9217 168hr	Grp 17/ NEAT D_5	NS			NS		
C9220 168hr	Grp 18/ SF	0.077	0.101	0.011	0.192	0.032	0.032
C9221 168hr	Grp 18/ SF	0.131			0.000		
C9222 168hr	Grp 18/ SF	0.119			0.000		
C9223 168hr	Grp 18/ SF	0.118			0.000		
C9224 168hr	Grp 18/ SF	0.060			0.001		
C9225 168hr	Grp 18/ SF	0.103			0.000		

Rounding errors may occur due to electronic handling of numbers

Dosing Solution : ^{14}C-D_5 in corn oil
Dosing Solution Specific Activity= 0.036 µCi/mg and 79920 DPM/mg
D_5 Concentration = 125.26 mg D_5/g dosing solution and 638033 DPM/mg D_5 in dosing solution

Animal ID	Time Point	Group ID, Sex	Radioactivity µg Eq. D_5/hr	Average Radioactivity µg Eq. D_5/hr	SD	SEM	Parent µg D_5/hr	Parent µg D_5/hr Average/ sex/ timepoint	SD	SEM	% Dose Recovered in Expired Volatiles	Cumulative % Dose Recovered in Expired Volatiles	Average Cumulative % Dose Recovered per Group	SD	SEM
C9162	*1hr*	*3/F*	*27300.369*				*24789.663*				*20.318*	*20.318*			
C9163	1hr	3/F	124.648				127.358				0.089	0.089			
C9164	1hr	3/F	3.743				5.926				0.003	0.003			
C9165	1hr	3/F	7.512	45.301	68.743	39.689	8.094	47.126	69.492	40.121	0.005	0.005	0.032	0.049	0.028
C9166	1hr	4/M	19.264				16.851								
C9167	1hr	4/M	103.447				98.037				0.043	0.043			
C9168	1hr	4/M	22.764				19.028				0.009	0.009			
C9169	1hr	4/M	249.223	98.674	107.635	53.818	260.443	98.590	114.321	57.161	0.103	0.103	0.052	0.047	0.024
C9162	*2hr*	*3/F*	*4532.010*				*4400.092*				*3.373*	*23.691*			
C9163	2hr	3/F	11.778				11.369				0.008	0.097			
C9164	2hr	3/F	6.167				5.055				0.004	0.007			
C9165	2hr	3/F	5.623	7.856	3.408	1.967	5.524	7.316	3.518	2.031	0.004	0.009	0.038	0.051	0.030
C9166	2hr	4/M	6.081				3.005				0.003	0.011			
C9167	2hr	4/M	9.130				5.674				0.004	0.047			
C9168	2hr	4/M	8.098				4.860				0.003	0.013			
C9169	2hr	4/M	*19.062*	10.593	5.787	2.893	14.135	6.918	4.939	2.470	0.008	0.111	0.045	0.047	0.023
C9162	*4hr*	*3/F*	*1309.816*				*1178.834*				*1.950*	*25.640*			
C9163	4hr	3/F	29.577				26.719				0.042	0.139			
C9164	4hr	3/F	24.385				20.889				0.035	0.042			
C9165	4hr	3/F	21.077	25.013	4.285	2.474	17.442	21.683	4.689	2.707	0.030	0.039	0.074	0.057	0.033
C9166	4hr	4/M	23.873				19.426				0.020	0.031			
C9167	4hr	4/M	29.705				24.728				0.025	0.072			
C9168	4hr	4/M	25.057				21.707				0.021	0.034			

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Sex	Radioactivity µg Eq. D_5/hr	Average Radioactivity µg Eq. D_5/hr	SD	SEM	Parent µg D_5/hr	Parent µg D_5/hr Average/ sex/ timepoint	SD	SEM	% Dose Recovered in Expired Volatiles	Cumulative % Dose Recovered in Expired Volatiles	Average Cumulative % Dose Recovered per Group	SD	SEM
C9169	4hr	4/M	24.358	25.749	2.682	1.341	19.881	21.436	2.406	1.203	0.020	0.131	0.067	0.047	0.023
C9162	*6hr*	*3/F*	*248.030*				*238.315*				*0.369*	*26.010*			
C9163	6hr	3/F	45.534				42.224				0.065	0.204			
C9164	6hr	3/F	46.425				37.940				0.067	0.109			
C9165	6hr	3/F	53.011	48.323	4.084	2.358	45.381	41.848	3.735	2.156	0.076	0.115	0.143	0.053	0.031
C9166	6hr	4/M	46.665				41.165				0.039	0.070			
C9167	6hr	4/M	52.463				45.945				0.044	0.115			
C9168	6hr	4/M	55.079				49.022				0.046	0.079			
C9169	6hr	4/M	46.890	50.274	4.178	2.089	40.048	44.045	4.189	2.095	0.039	0.169	0.108	0.045	0.023
C9162	*12hr*	*3/F*	*187.514*				*79.978*				*0.391*	*26.400*			
C9163	12hr	3/F	65.825				60.155				0.280	0.484			
C9164	12hr	3/F	54.180				51.858				0.234	0.343			
C9165	12hr	3/F	673.003	264.336	353.964	204.361	626.841	246.284	329.597	190.293	2.877	2.992	1.273	1.490	0.860
C9166	12hr	4/M	59.801				67.714				0.150	0.220			
C9167	12hr	4/M	64.512				61.893				0.161	0.277			
C9168	12hr	4/M	669.052				609.974				1.663	1.742			
C9169	12hr	4/M	60.157	213.380	303.788	151.894	56.751	199.083	273.964	136.982	0.149	0.318	0.639	0.736	0.368
C9162	*24hr*	*3/F*	*34.819*				*31.356*				*0.311*	*26.711*			
C9163	24hr	3/F	801.560				918.743				6.830	7.314			
C9164	24hr	3/F	729.729				624.557				6.303	6.646			
C9165	24hr	3/F	1289.048	940.113	304.314	175.696	1646.714	1063.338	526.196	303.799	11.020	14.012	9.324	4.073	2.352
C9166	24hr	4/M	4063.784				7238.617				20.446	20.666			
C9167	24hr	4/M	1147.496				968.807				5.735	6.012			
C9168	24hr	4/M	1714.739				2259.409				8.523	10.266			
C9169	24hr	4/M	258.929	1796.237	1626.099	813.049	250.896	2679.432	3151.011	1575.505	1.280	1.598	9.635	8.161	4.081

Italicized data for rat No. C9162 were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Sex	Radioactivity µg Eq. D_5/hr	Average Radioactivity µg Eq. D_5/hr	SD	SEM	Parent µg D_5/hr	Parent µg D_5/hr Average/ sex/ timepoint	SD	SEM	% Dose Recovered in Expired Volatiles	Cumulative % Dose Recovered in Expired Volatiles	Average Cumulative % Dose Recovered per Group	SD	SEM
C9162	*48hr*	*3/F*	*15.061*				*10.110*				*0.233*	*26.945*			
C9163	48hr	3/F	13.028				18.455				0.222	7.536			
C9164	48hr	3/F	26.303				23.247				0.454	7.101			
C9165	48hr	3/F	111.389	50.240	53.371	30.814	106.489	49.397	49.501	28.579	1.905	15.916	10.184	4.969	2.869
C9166	48hr	4/M	628.838				764.484				6.328	26.994			
C9167	48hr	4/M	33.098				28.298				0.331	6.343			
C9168	48hr	4/M	87.111				74.078				0.866	11.132			
C9169	48hr	4/M	561.639	327.672	310.958	155.479	703.254	392.529	395.380	197.690	5.552	7.149	12.904	9.624	4.812
C9162	*72hr*	*3/F*	*54.222*				*3.861*				*0.076*	*27.021*			
C9163	72hr	3/F	4.559				4.484				0.078	7.614			
C9164	72hr	3/F	4.823				4.522				0.083	7.184			
C9165	72hr	3/F	7.827	5.736	1.816	1.048	6.405	5.137	1.098	0.634	0.134	16.050	10.283	4.999	2.886
C9166	72hr	4/M	23.123				19.934				0.233	27.227			
C9167	72hr	4/M	8.404				7.614				0.084	6.427			
C9168	72hr	4/M	11.256				10.126				0.112	11.243			
C9169	72hr	4/M	116.405	39.797	51.469	25.734	117.164	38.709	52.573	26.286	1.151	8.300	13.299	9.494	4.747
C9162	*96hr*	*3/F*	*2.623*				*2.288*				*0.047*	*27.068*			
C9163	96hr	3/F	1.955				1.785				0.033	7.647			
C9164	96hr	3/F	2.119				1.989				0.037	7.221			
C9165	96hr	3/F	3.064	2.379	0.598	0.345	2.851	2.208	0.566	0.327	0.052	16.103	10.323	5.009	2.892
C9166	96hr	4/M	4.267				2.928				0.043	27.270			
C9167	96hr	4/M	2.376				2.072				0.024	6.450			
C9168	96hr	4/M	2.682				2.395				0.027	11.270			
C9169	96hr	4/M	2.731	3.014	0.850	0.425	2.513	2.477	0.354	0.177	0.027	8.327	13.329	9.503	4.751
C9162	*120hr*	*3/F*	*1.035*				*1.277*				*0.024*	*27.092*			

Italicized data for rat No. C9162 were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Sex	Radioactivity µg Eq. D_5/hr	Average Radioactivity µg Eq. D_5/hr	SD	SEM	Parent µg D_5/hr	Parent µg D_5/hr Average/ sex/ timepoint	SD	SEM	% Dose Recovered in Expired Volatiles	Cumulative % Dose Recovered in Expired Volatiles	Average Cumulative % Dose Recovered per Group	SD	SEM
C9163	120hr	3/F	1.106				1.204				0.019	7.666			
C9164	120hr	3/F	0.017				0.000				0.000	7.221			
C9165	120hr	3/F	2.002	1.041	0.994	0.574	1.921	1.042	0.971	0.561	0.034	16.137	10.341	5.024	2.901
C9166	120hr	4/M	2.164				1.584				0.022	27.291			
C9167	120hr	4/M	1.105				1.096				0.011	6.461			
C9168	120hr	4/M	1.325				1.233				0.013	11.283			
C9169	120hr	4/M	0.691	1.321	0.620	0.310	0.716	1.157	0.359	0.179	0.007	8.334	13.342	9.509	4.754
C9162	*144hr*	*3/F*	*1.044*				*0.990*				*0.019*	*27.110*			
C9163	144hr	3/F	0.767				0.746				0.013	7.679			
C9164	144hr	3/F	0.700				0.606				0.012	7.233			
C9165	144hr	3/F	1.165	0.878	0.251	0.145	1.075	0.809	0.241	0.139	0.020	16.157	10.356	5.028	2.903
C9166	144hr	4/M	1.689				1.194				0.017	27.308			
C9167	144hr	4/M	0.689				0.656				0.007	6.468			
C9168	144hr	4/M	0.763				0.644				0.008	11.291			
C9169	144hr	4/M	0.488	0.907	0.534	0.267	0.419	0.728	0.329	0.165	0.005	8.339	13.352	9.514	4.757
C9162	*168hr*	*3/F*	*0.961*				*0.959*				*0.017*	*27.127*			
C9163	168hr	3/F	0.709				0.797				0.012	7.691			
C9164	168hr	3/F	0.609				0.533				0.011	7.243			
C9165	168hr	3/F	1.126	0.814	0.274	0.158	1.149	0.827	0.309	0.178	0.019	16.176	10.370	5.033	2.906
C9166	168hr	4/M	1.088				0.972				0.011	27.319			
C9167	168hr	4/M	0.695				0.696				0.007	6.475			
C9168	168hr	4/M	0.665				0.594				0.007	11.297			
C9169	168hr	4/M	0.352	0.700	0.301	0.151	0.499	0.690	0.204	0.102	0.003	8.342	13.359	9.517	4.758

Italicized data for rat No. C9162 were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Dosing Solutions : ^{14}C-D_5 Neat and ^{14}C-D_5 in Simethicone

^{14}C-D_5 Neat (Group 13) Dosing Solution Specific Activity= 0.302 µCi/mg and 670440 DPM/mg

^{14}C-D_5 in Simethicone (Group 14) Dosing Solution Specific Activity= 0.029 µCi/mg and 64380 DPM/mg

D_5 Concentration = 97.47 mg D_5/g SFdosing solution and 660511 DPM/mg D_5 in SF dosing solution

Animal ID	Time Point	Group ID, Carrier	Radioactivity µg Eq D_5/hr	Average Radioactivity µg Eq D_5/hr	SD	SEM	Parent µg D_5/hr	Parent µg D_5/hr Avg/ carrier/ timepoint	SD	SEM	% Dose Recovered in Expired Volatiles	Cumulative % Dose Recovered in Expired Volatiles	Average Cumulative % Dose Recovered per Group	SD	SEM
C9200	1hr	13/Neat	1.252				0.000				0.001	0.001			
C9201	*1hr*	*13/Neat*	*3610.124*				*2410.1*				*22.612*	*22.612*			
Q0004	1hr	13/Neat	873.482				822.180				0.578	0.578			
C9203	1hr	13/Neat	20.667	298.467	498.072	287.562	17.065	279.748	469.837	271.261	0.014	0.014	0.198	0.329	0.190
C9206	1hr	14/SF	0.236				0.000				0.000	0.000			
C9207	*1hr*	*14/SF*	*2790.672*				*1860.823*				*1.830*	*1.830*			
C9208	1hr	14/SF	10.163				6.801				0.007	0.007			
C9209	1hr	14/SF	0.000	3.466	5.800	3.349	0.000	2.267	3.926	2.267	0.000	0.000	0.002	0.004	0.002
C9200	2hr	13/Neat	0.000				0.000				0.000	0.001			
C9201	*2hr*	*13/Neat*	*2708.225*				*2010.1*				*12.692*	*35.174*			
Q0004	2hr	13/Neat	99.531				83.286				0.066	0.644			
C9203	2hr	13/Neat	21.361	40.298	52.398	30.252	16.603	33.296	44.081	25.450	0.015	0.029	0.225	0.363	0.210
C9206	2hr	14/SF	0.000				0.000				0.000	0.000			
C9207	*2hr*	*14/SF*	*2511.778*				*1674.238*				*0.768*	*2.598*			
C9208	2hr	14/SF	161.107				142.505				0.115	0.122			
C9209	2hr	14/SF	56.939	72.682	81.699	47.169	48.007	63.504	72.505	41.861	0.039	0.039	0.054	0.062	0.036
C9200	4hr	13/Neat	921.340				800.554				1.660	1.661			
C9201	*4hr*	*13/Neat*	*2577.221*				*2288.752*				*3.066*	*38.070*			
Q0004	4hr	13/Neat	51.179				45.024				0.068	0.711			
C9203	4hr	13/Neat	19.425	330.648	511.800	295.488	13.698	286.425	445.524	257.223	0.027	0.056	0.809	0.807	0.466
C9206	4hr	14/SF	3173.407				2670.857				5.472	5.473			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

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Rounding errors may occur due to electronic handling of numbers

Expired Volatiles
(D_5 Neat and D_6 in Simethicone)

Animal ID	Time Point	Group ID, Carrier	Radioactivity µg Eq D_5/hr	Average Radioactivity µg Eq D_5/hr	SD	SEM	Parent µg D_5/hr	Parent µg D_5/hr Avg/ carrier/ timepoint	SD	SEM	% Dose Recovered in Expired Volatiles	Cumulative % Dose Recovered in Expired Volatiles	Average Cumulative % Dose Recovered per Group	SD	SEM
C9207	*4hr*	*14/SF*	*918.605*				*784.514*				*0.418*	*2.416*			
C9208	4hr	14/SF	1555.539				1366.006				2.221	2.343			
C9209	4hr	14/SF	2649.850	2459.599	825.543	476.627	2271.203	2102.689	668.548	385.987	3.590	3.628	3.815	1.573	0.908
C9200	6hr	13/Neat	366.232				331.223				0.660	2.321			
C9201	*6hr*	*13/Neat*	*246.229*				*220.804*				*0.292*	*0.468*			
Q0004	6hr	13/Neat	32.386				25.325				0.043	0.754			
C9203	6hr	13/Neat	23.060	140.559	195.494	112.868	15.693	124.080	179.455	103.609	0.032	0.087	1.054	1.147	0.662
C9206	6hr	14/SF	2702.545				2273.218				4.660	10.133			
C9207	*6hr*	*14/SF*	*986.000*				*784.514*				*0.418*	*2.834*			
C9208	6hr	14/SF	2450.441				2131.516				3.498	5.841			
C9209	6hr	14/SF	1304.058	2152.348	745.376	430.343	1199.312	1868.015	583.432	336.845	1.767	5.395	7.123	2.616	1.510
C9200	12hr	13/Neat	90.478				145.453				0.489	2.810			
C9201	*12hr*	*13/Neat*	*172.058*				*63.018*				*0.077*	*0.780*			
Q0004	12hr	13/Neat	25.244				20.579				0.100	0.854			
C9203	12hr	13/Neat	33.489	49.737	35.523	20.509	27.726	64.586	70.124	40.486	0.138	0.225	1.296	1.348	0.778
C9206	12hr	14/SF	2248.846				2139.490				11.634	21.767			
C9207	*12hr*	*14/SF*	*1745.027*				*1677.757*				*1.503*	*5.003*			
C9208	12hr	14/SF	2252.698				2055.764				9.648	15.489			
C9209	12hr	14/SF	2194.927	2232.157	32.300	18.648	1677.757	1957.670	246.001	142.028	8.920	14.315	17.190	4.007	2.313
C9200	24hr	13/Neat	42.459				36.617				0.459	3.269			
C9201	*24hr*	*13/Neat*	*97.245*				*82.805*				*0.273*	*0.913*			
Q0004	24hr	13/Neat	254.907				233.371				2.023	2.877			
C9203	24hr	13/Neat	67.958	121.775	115.998	66.972	66.528	112.172	106.022	61.212	0.560	0.785	2.310	1.336	0.771
C9206	24hr	14/SF	245.527				224.667				2.540	24.307			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing
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Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Carrier	Radioactivity µg Eq D_5/hr	Average Radioactivity µg Eq D_5/hr	SD	SEM	Parent µg D_5/hr	Parent µg D_5/hr Avg/ carrier/ timepoint	SD	SEM	% Dose Recovered in Expired Volatiles	Cumulative % Dose Recovered in Expired Volatiles	Average Cumulative % Dose Recovered per Group	SD	SEM
C9207	24hr	14/SF	192.891				176.763				1.546	6.649			
C9208	24hr	14/SF	948.717				866.840				8.126	23.616			
C9209	24hr	14/SF	625.401	606.548	351.974	203.212	590.550	560.686	322.127	185.980	5.083	19.398	22.440	2.657	1.534
C9200	48hr	13/Neat	14.157				12.192				0.306	3.575			
C9201	48hr	13/Neat	38.561				32.695				0.549	39.562			
Q0004	48hr	13/Neat	158.003				151.096				2.508	5.385			
C9203	48hr	13/Neat	69.245	80.468	72.577	41.902	64.931	76.073	70.119	40.483	1.141	1.925	3.629	1.731	0.999
C9206	48hr	14/SF	33.016				30.051				0.683	24.991			
C9207	48hr	14/SF	62.083				57.481				0.995	7.644			
C9208	48hr	14/SF	130.012				121.660				2.227	25.843			
C9209	48hr	14/SF	13.395	58.808	62.440	36.050	11.578	54.430	58.951	34.035	0.218	19.616	23.483	3.376	1.949
C9200	72hr	13/Neat	2.489				2.239				0.054	3.629			
C9201	72hr	13/Neat	16.149				16.281				0.259	39.821			
Q0004	72hr	13/Neat	86.612				82.806				1.375	6.760			
C9203	72hr	13/Neat	85.382	58.161	48.217	27.838	81.966	55.670	46.275	26.717	1.406	3.332	4.574	1.899	1.097
C9206	72hr	14/SF	1.729				1.486				0.036	25.026			
C9207	72hr	14/SF	3.996				3.436				0.064	7.708			
C9208	72hr	14/SF	47.556				44.534				0.815	26.658			
C9209	72hr	14/SF	7.908	19.064	24.867	14.357	6.746	17.588	23.483	13.558	0.129	19.745	23.809	3.614	2.086
C9200	96hr	13/Neat	0.869				0.664				0.019	3.648			
C9201	96hr	13/Neat	12.828				11.090				0.183	40.004			
Q0004	96hr	13/Neat	47.084				42.946				0.747	7.507			
C9203	96hr	13/Neat	28.146	25.366	23.232	13.413	26.194	23.268	21.292	12.293	0.464	3.795	4.984	2.187	1.263
C9206	96hr	14/SF	0.384				0.216				0.008	25.034			
C9207	96hr	14/SF	1.469				1.177				0.024	7.732			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

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Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Carrier	Radioactivity µg Eq D_5/hr	Average Radioactivity µg Eq D_5/hr	SD	SEM	Parent µg D_5/hr	Parent µg D_5/hr Avg/ carrier/ timepoint	SD	SEM	% Dose Recovered in Expired Volatiles	Cumulative % Dose Recovered in Expired Volatiles	Average Cumulative % Dose Recovered per Group	SD	SEM
C9208	96hr	14/SF	27.427				25.242				0.470	27.128			
C9209	96hr	14/SF	4.475	10.762	14.576	8.416	3.885	9.781	13.515	7.803	0.073	19.817	23.993	3.765	2.174
C9200	120hr	13/Neat	0.575				0.402				0.012	3.660			
C9201	120hr	13/Neat	0.777				0.551				0.011	40.018			
Q0004	120hr	13/Neat	0.817				0.712				0.013	7.520			
C9203	120hr	13/Neat	16.686	6.026	9.232	5.330	14.894	5.336	8.279	4.780	0.275	4.070	5.084	2.120	1.224
C9206	120hr	14/SF	0.178				0.053				0.004	25.038			
C9207	120hr	14/SF	0.726				0.520				0.012	7.744			
C9208	120hr	14/SF	1.058				0.824				0.018	27.146			
C9209	120hr	14/SF	3.382	1.539	1.655	0.956	2.891	1.256	1.467	0.847	0.055	19.872	24.019	3.742	2.161
C9200	144hr	13/Neat	0.394				0.265				0.009	3.669			
C9201	144hr	13/Neat	0.593				0.441				0.008	40.023			
Q0004	144hr	13/Neat	0.330				0.252				0.005	7.526			
C9203	144hr	13/Neat	4.980	1.901	2.667	1.540	4.481	1.666	2.438	1.408	0.082	4.152	5.116	2.101	1.213
C9206	144hr	14/SF	0.056				0.000				0.001	25.039			
C9207	144hr	14/SF	0.690				0.474				0.011	7.765			
C9208	144hr	14/SF	0.249				0.066				0.004	27.150			
C9209	144hr	14/SF	2.334	0.880	1.263	0.729	2.018	0.695	1.147	0.662	0.038	19.910	24.033	3.723	2.150
C9200	168hr	13/Neat	0.322				0.190				0.007	3.676			
C9201	168hr	13/Neat	0.579				0.464				0.008	40.031			
Q0004	168hr	13/Neat	0.263				0.232				0.004	7.530			
C9203	168hr	13/Neat	6.991	2.525	3.867	2.233	6.030	2.151	3.360	1.940	0.115	4.267	5.158	2.076	1.198
C9206	168hr	14/SF	0.046				0.079				0.001	25.040			
C9207	168hr	14/SF	0.675				0.490				0.011	7.765			
C9208	168hr	14/SF	0.166				0.027				0.003	27.153			
C9209	168hr	14/SF	1.207	0.473	0.639	0.369	0.952	0.353	0.519	0.300	0.020	19.930	24.041	3.714	2.144

Italicized data for rats No C9201 and C9207 were excluded because of inaccuracy in dosing

Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Urine
(D_5 in Corn Oil)

Dosing Solution : ^{14}C-D_5 in corn oil
Dosing Solution Specific Activity= 0.036 µCi/mg and 79920 DPM/mg
D_5 Concentration = 125.26 mg D_5/g dosing solution and 638033 DPM/mg D_5 in dosing solution

Animal ID	Time Point	Group ID, Sex	Concentration µg Eq D_5/g of Urine	Average Concentration µg Eq D_5/g of Urine	SD	SEM	% Dose Recovered in Urine	Cumulative % Dose Recovered in Urine	Average Cumulative % Dose Recovered per Group	SD	SEM
C9162	*6hr*	*3/F*	*12.371*				*0.019*	*0.019*			
C9163	6hr	3/F	13.106				0.022	0.022			
C9164	6hr	3/F	0.053				0.000	0.000			
C9165	6hr	3/F	19.822	10.994	10.053	5.804	0.017	0.017	0.013	0.012	0.007
C9166	6hr	4/M	25.237				0.033	0.033			
C9167	6hr	4/M	17.225				0.024	0.024			
C9168	6hr	4/M	16.241				0.017	0.017			
C9169	6hr	4/M	16.739	18.860	4.270	2.135	0.015	0.015	0.022	0.008	0.004
C9162	*12hr*	*3/F*	*141.858*				*0.065*	*0.084*			
C9163	12hr	3/F	85.360				0.126	0.148			
C9164	12hr	3/F	71.550				0.135	0.135			
C9165	12hr	3/F	105.267	87.392	16.950	9.786	0.047	0.064	0.116	0.045	0.026
C9166	12hr	4/M	131.726				0.130	0.163			
C9167	12hr	4/M	85.161				0.064	0.088			
C9168	12hr	4/M	119.297				0.122	0.138			
C9169	12hr	4/M	108.339	111.131	19.774	9.887	0.108	0.123	0.128	0.032	0.016
C9162	*24hr*	*3/F*	*195.528*				*0.763*	*0.807*			
C9163	24hr	3/F	268.753				0.643	0.791			
C9164	24hr	3/F	372.321				0.554	0.689			
C9165	24hr	3/F	294.958	312.011	53.849	31.089	0.656	0.720	0.733	0.052	0.030

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Sex	Concentration µg Eq D_5/g of Urine	Average Concentration µg Eq D_5/g of Urine	SD	SEM	% Dose Recovered in Urine	Cumulative % Dose Recovered in Urine	Average Cumulative % Dose Recovered per Group	SD	SEM
C9166	24hr	4/M	517.653				0.889	1.052			
C9167	24hr	4/M	352.395				0.850	0.938			
C9168	24hr	4/M	550.604				0.884	1.023			
C9169	24hr	4/M	534.756	488.852	91.961	45.980	0.925	1.048	1.015	0.053	0.027
C9162	*48hr*	*3/F*	*710.105*				*2.384*	*3.192*			
C9163	48hr	3/F	462.759				2.802	3.593			
C9164	48hr	3/F	81.923				0.678	1.367			
C9165	48hr	3/F	682.461	409.048	303.851	175.428	2.383	3 103	2.688	1.170	0.675
C9166	48hr	4/M	564.917				1.801	2.853			
C9167	48hr	4/M	627.948				2.617	3.555			
C9168	48hr	4/M	947.394				2.505	3.528			
C9169	48hr	4/M	624.852	691.278	173.191	86.596	1.974	3.022	3.240	0.355	0.178
C9162	*72hr*	*3/F*	*248.126*				*0.951*	*4.143*			
C9163	72hr	3/F	137.782				1.016	4.609			
C9164	72hr	3/F	550.444				0.389	1.756			
C9165	72hr	3/F	193.258	293.828	223.960	129.303	1.399	4.501	3.622	1.617	0.934

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Sex	Concentration µg Eq D_5/g of Urine	Average Concentration µg Eq D_5/g of Urine	SD	SEM	% Dose Recovered in Urine	Cumulative % Dose Recovered in Urine	Average Cumulative % Dose Recovered per Group	SD	SEM
C9166	72hr	4/M	133.486				0.54	3.40			
			153.276				0.71	4.27			
C9167	72hr	4/M									
			310.966				1.15	4.68			
C9168	72hr	4/M									
			134.408				0.57	3.60			
C9169	72hr	4/M		183.034	85.774	42.887			3.985	0.595	0.298
C9162	*96hr*	*3/F*	*136.906*				*0.378*	*4.514*			
C9163	96hr	3/F	48.136				0.35	4.95			
C9164	96hr	3/F	26.899				0.17	1.93			
C9165	96hr	3/F	62.714	45.917	18.010	10.398	0.41	4.92	3.932	1.737	1.003
C9166	96hr	4/M	45.607				0.23	3.63			
C9167	96hr	4/M	58.856				0.32	4.59			
C9168	96hr	4/M	85.627				0.41	5.09			
C9169	96hr	4/M	50.265	60.089	17.888	8.944	0.26	3.85	4.289	0.675	0.337
C9162	*120hr*	*3/F*	*50.103*				*0.241*	*4.726*			
C9163	120hr	3/F	25.245				0.22	5.17			
C9164	120hr	3/F	18.334				0.12	2.04			
C9165	120hr	3/F	35.808	26.463	8.800	5.081	0.21	5.13	4.113	1.793	1.035
C9166	120hr	4/M	27.988				0.14	3.77			
C9167	120hr	4/M	34.800				0.18	4.77			
C9168	120hr	4/M	55.968				0.23	5.32			
C9169	120hr	4/M	35.443	38.550	12.092	6.046	0.13	3.98	4.460	0.716	0.358

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Sex	Concentration µg Eq D_5/g of Urine	Average Concentration µg Eq D_5/g of Urine	SD	SEM	% Dose Recovered in Urine	Cumulative % Dose Recovered in Urine	Average Cumulative % Dose Recovered per Group	SD	SEM
C9162	*144hr*	*3/F*	*30.235*				*0.150*	*4.876*			
C9163	144hr	3/F	22.341				0.16	5.33			
C9164	144hr	3/F	13.612				0.08	2.13			
C9165	144hr	3/F	26.776	20.910	6.698	3.867	0.15	5.28	4.244	1.833	1.058
C9166	144hr	4/M	20.841				0.09	3.86			
C9167	144hr	4/M	27.251				0.14	4.90			
C9168	144hr	4/M	35.371				0.16	5.48			
C9169	144hr	4/M	24.649	27.028	6.153	3.077	0.11	4.10	4.585	0.747	0.373
C9162	*168hr*	*3/F*	*28.713*				*0.129*	*5.003*			
C9163	168hr	3/F	12.742				0.11	5.44			
C9164	168hr	3/F	9.320				0.09	2.22			
C9165	168hr	3/F	12.343	11.468	1.871	1.080	0.16	5.44	4.365	1.859	1.073
C9166	168hr	4/M	22.794				0.12	3.97			
C9167	168hr	4/M	23.288				0.12	5.03			
C9168	168hr	4/M	28.457				0.13	5.61			
C9169	168hr	4/M	17.930	23.117	4.303	2.152	0.08	4.18	4.698	0.760	0.380

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Dosing Solutions : ^{14}C-D_5 Neat and ^{14}C-D_5 in Simethicone

^{14}C-D_5 Neat (Group 13) Dosing Solution Specific Activity= 0.302 µCi/mg and 670440 DPM/mg

^{14}C-D_5 in Simethicone (Group 14) Dosing Solution Specific Activity= 0.029 µCi/mg and 64380 DPM/mg

D_5 Concentration = 97.47 mg D_5/g SFdosing solution and 660511 DPM/mg D_5 in SF dosing solution

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g of Urine	Average Concentration µg Eq D_5/g of Urine	SD	SEM	% Dose Recovered in Urine	Cumulative % Dose Recovered in Urine	Average Cumulative % Dose Recovered per Group	SD	SEM
C9200	6hr	13/Neat D_5	10.264				0.022	0.022			
C9201	*6hr*	*13/Neat D_5*	*27.112*				*0.025*	*0.025*			
Q0004	6hr	13/Neat D_5	35.116				0.036	0.036			
C9203	6hr	13/Neat D_5	8.177	17.852	14.987	8.653	0.023	0.023	0.027	0.008	0.005
C9206	6hr	14/SF	13.307				0.034	0.034			
C9207	*6hr*	*14/SF*	*10.429*				*0.020*	*0.020*			
C9208	6hr	14/SF	16.289				0.023	0.023			
C9209	6hr	14/SF	16.754	15.450	1.870	1.080	0.017	0.017	0.025	0.008	0.005
C9200	12hr	13/Neat D_5	63.302				0.117	0.139			
C9201	*12hr*	*13/Neat D_5*	*68.825*				*0.063*	*0.088*			
Q0004	12hr	13/Neat D_5	60.943				0.069	0.106			
C9203	12hr	13/Neat D_5	58.704	60.983	2.300	1.328	0.083	0.106	0.117	0.019	0.011
C9206	12hr	14/SF	72.780				0.114	0.148			
C9207	*12hr*	*14/SF*	*29.121*				*0.028*	*0.048*			
C9208	12hr	14/SF	62.883				0.095	0.118			
C9209	12hr	14/SF	62.823	66.162	5.731	3.309	0.062	0.079	0.115	0.034	0.020

Italicized data for rats No. C9201 and C9207 were excluded because of inaccuracy in dosing

Urine
(D_5 Neat and D_5 In Simethicone)

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g of Urine	Average Concentration µg Eq D_5/g of Urine	SD	SEM	% Dose Recovered in Urine	Cumulative % Dose Recovered in Urine	Average Cumulative % Dose Recovered per Group	SD	SEM
C9200	24hr	13/Neat D_5	147.393				0.650	0.788			
C9201	*24hr*	*13/Neat D_5*	*246.730*				*0.782*	*0.870*			
Q0004	24hr	13/Neat D_5	175.195				0.390	0.495			
C9203	24hr	13/Neat D_5	108.451	143.680	33.527	19.357	0 361	0.467	0.583	0.178	0.103
C9206	24hr	14/SF	103.338				0.299	0.446			
C9207	*24hr*	*14/SF*	*60.138*				*0.079*	*0.127*			
C9208	24hr	14/SF	156.825				0.303	0.420			
C9209	24hr	14/SF	109.562	123.242	29.250	16.888	0.194	0.274	0.380	0.093	0.054
C9200	48hr	13/Neat D_5	256.694				1.542	2.330			
C9201	*48hr*	*13/Neat D_5*	*758.030*				*1.698*	*2.767*			
Q0004	48hr	13/Neat D_5	113.959				0.836	1.331			
C9203	48hr	13/Neat D_5	124.121	164.924	79.637	45.978	0.867	1.334	1.665	0.576	0.333
C9206	48hr	14/SF	86.473				0.530	0.976			
C9207	*48hr*	*14/SF*	*104.685*				*0.331*	*0.459*			
C9208	48hr	14/SF	69.938				0.368	0.789			
C9209	48hr	14/SF	75.298	77.236	8.436	4.871	0.261	0.534	0.766	0.222	0.128

Italicized data for rats No. C9201 and C9207 were excluded because of inaccuracy in dosing

Urine
(D_5 Neat and D_5 in Simethicone)

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g of Urine	Average Concentration µg Eq D_5/g of Urine	SD	SEM	% Dose Recovered in Urine	Cumulative % Dose Recovered in Urine	Average Cumulative % Dose Recovered per Group	SD	SEM
C9200	72hr	13/Neat D_5	80.111				0.596	2.926			
C9201	*72hr*	*13/Neat D_5*	*203.242*				*0.936*	*3.703*			
Q0004	72hr	13/Neat D_5	37.541				0.194	1.525			
C9203	72hr	13/Neat D_5	33.454	50.369	25.838	14.918	0.289	1.623	2.025	0.782	0.452
C9206	72hr	14/SF	23.618				0.174	1.151			
C9207	*72hr*	*14/SF*	*87.788*				*0.259*	*0.717*			
C9208	72hr	14/SF	17.688				0.113	0.901			
C9209	72hr	14/SF	41.234	27.513	12.247	7.071	0.161	0.696	0.916	0.228	0.132
C9200	96hr	13/Neat D_5	33.058				0.253	3.179			
C9201	*96hr*	*13/Neat D_5*	*36.416*				*0.216*	*3.919*			
Q0004	96hr	13/Neat D_5	16.403				0.099	1.624			
C9203	96hr	13/Neat D_5	14.938	21.466	10.065	5.811	0.120	1.742	2.182	0.866	0.500
C9206	96hr	14/SF	6.959				0.053	1.203			
C9207	*96hr*	*14/SF*	*21.921*				*0.164*	*0.881*			
C9208	96hr	14/SF	6.935				0.051	0.953			
C9209	96hr	14/SF	14.011	9.302	4.078	2.355	0.066	0.761	0.972	0.222	0.128
C9200	120hr	13/Neat D_5	17.716				0.137	3.316			
C9201	*120hr*	*13/Neat D_5*	*21.242*				*0.111*	*4.030*			
Q0004	120hr	13/Neat D_5	11.350				0.055	1.679			
C9203	120hr	13/Neat D_5	11.318	13.461	3.685	2.127	0.068	1.810	2.268	0.910	0.525

Italicized data for rats No. C9201 and C9207 were excluded because of inaccuracy in dosing

Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Urine
(D_5 Neat and D_5 In Simethicone)

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g of Urine	Average Concentration µg Eq D_5/g of Urine	SD	SEM	% Dose Recovered in Urine	Cumulative % Dose Recovered in Urine	Average Cumulative % Dose Recovered per Group	SD	SEM
C9206	120hr	14/SF	4.546				0.030	1.234			
C9207	*120hr*	*14/SF*	*12.576*				*0.078*	*0.959*			
C9208	120hr	14/SF	4.529				0.025	0.978			
C9209	120hr	14/SF	6.743	5.273	1.274	0.735	0.028	0.789	1.000	0.223	0.129
C9200	144hr	13/Neat D_5	11.921				0.100	3.416			
C9201	*144hr*	*13/Neat D_5*	*14.637*				*0.087*	*4.117*			
Q0004	144hr	13/Neat D_5	5.520				0.043	1.722			
C9203	144hr	13/Neat D_5	4.701	7.381	3.953	2.282	0.056	1.866	2.335	0.939	0.542
C9206	144hr	14/SF	2.729				0.023	1.257			
C9207	*144hr*	*14/SF*	*8.259*				*0.060*	*1.018*			
C9208	144hr	14/SF	3.389				0.020	0.998			
C9209	144hr	14/SF	4.512	3.543	0.902	0.521	0.020	0.809	1.021	0.225	0.130
C9200	168hr	13/Neat D_5	7.596				0.072	3.488			
C9201	*168hr*	*13/Neat D_5*	*11.251*				*0.064*	*4.181*			
Q0004	168hr	13/Neat D_5	4.007				0.036	1.759			
C9203	168hr	13/Neat D_5	4.194	5.266	2.021	1.167	0.042	1.908	2.385	0.958	0.553
C9206	168hr	14/SF	1.639				0.018	1.275			
C9207	*168hr*	*14/SF*	*9.997*				*0.058*	*1.076*			
C9208	168hr	14/SF	1.852				0.017	1.015			
C9209	168hr	14/SF	2.842	2.111	0.642	0.370	0.016	0.825	1.038	0.226	0.130

Italicized data for rats No. C9201 and C9207 were excluded because of inaccuracy in dosing

Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Feces
(D_5 in Corn Oil)

Dosing Solution : ^{14}C-D_5 in corn oil
Dosing Solution Specific Activity= 0.036 µCi/mg and 79920 DPM/mg
D_5 Concentration = 125.26 mg D_5/g dosing solution and 638033 DPM/mg D_5 in dosing solution

Animal ID	Time Point	Group ID, Sex	Radioactivity µg Eq D_5/g of Feces	Average radioactivity µg Eq D_5/g of Feces	SD	SEM	Parent µg D_5/g feces	Parent µg D_5/g Average/ sex/ timepoint	SD	SEM	% Dose Recovered in Feces	Cumulative % Dose Recovered in Feces	Average Cumulative % Dose Recovered per Group	SD	SEM
C9162	*6hr*	*3/F*	*2.550*				*2.866*				*0.003*	*0.003*			
C9163	6hr	3/F	N.S.				NS				NS	0.000			
C9164	6hr	3/F	0.118				0.000				0.000	0.000			
C9165	6hr	3/F	1.670	0.894	1.098	0.634	0.972	0.486	0.687	0.486	0.002	0.002	0.001	0.001	0.001
C9166	6hr	4/M	1.175				0.81				0.000	0.000			
C9167	6hr	4/M	3.245				3.62				0.002	0.002			
C9168	6hr	4/M	N.S.				NS				NS	0.000			
C9169	6hr	4/M	0.004	1.475	1.641	0.821	0.000	1.476	1.897	1.095	0.000	0.000	0.001	0.001	0.000
C9162	*12hr*	*3/F*	*NS*				*NS*				*0.000*	*0.003*			
C9163	12hr	3/F	19.020				21.11				0.007	0 007			
C9164	12hr	3/F	7.224				7.02				0.005	0 005			
C9165	12hr	3/F	2057.876	694 707	1180.554	681.593	3467.469	1165.199	1993.837	1151.142	3.840	3.842	1.285	2.215	1.279
C9166	12hr	4/M	19.415				16.36				0.011	0.011			
C9167	12hr	4/M	14.443				16.61				0.004	0.007			
C9168	12hr	4/M	5409.395				5701.26				3.723	3.723			
C9169	12hr	4/M	N S.	1814.418	3113.343	1556.671	NS	1911.412	3282.107	1894.925	NS	0.000	0.935	1.859	0.929
C9162	*24hr*	*3/F*	*N S.*				*NS*				*0.000*	*0.003*			
C9163	24hr	3/F	23384.347				20351.38				39.416	39.423			
C9164	24hr	3/F	25431.704				27672.37				27.737	27.742			
C9165	24hr	3/F	9758.653	19524.902	8519.544	4918.761	9404.762	19142.838	9193.574	5307.912	30 844	34 686	33.950	5.875	3.392
C9166	24hr	4/M	21233 252				28383.34				27.127	27.138			
C9167	24hr	4/M	23930.435				25329.06				39.347	39.354			
C9168	24hr	4/M	26815.307				28163.06				25.428	29.151			
C9169	24hr	4/M	7906.920	19971.479	8359.764	4179.882	5397.341	21818.200	11035.232	5517.616	17.090	17.090	28.183	9.126	4.563
C9162	*48hr*	*3/F*	*12885.158*				*14502.358*				*34.369*	*34.392*			
C9163	48hr	3/F	8438.827				9065.20				32.282	71.705			
C9164	48hr	3/F	15304.126				21372.76				43.605	71.347			

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Feces
(D_5 in Corn Oil)

Animal ID	Time Point	Group ID, Sex	Radioactivity µg Eq D_5/g of Feces	Average radioactivity µg Eq D_5/g of Feces	SD	SEM	Parent µg D_5/g feces	Parent µg D_5/g Average/ sex/ timepoint	SD	SEM	% Dose Recovered in Feces	Cumulative % Dose Recovered in Feces	Average Cumulative % Dose Recovered per Group	SD	SEM
C9165	48hr	3/F	4788.459	9510.471	5339 113	3082.538	5133.705	11857 223	8471.912	4891.261	20.977	55.663	66.238	9.160	5 289
C9166	48hr	4/M	8546.136				9776.88				27.487	54.625			
C9167	48hr	4/M	9660.095				9499.84				30 306	69 660			
C9168	48hr	4/M	13786.129				14657.40				34.483	63.634			
C9169	48hr	4/M	13138.184	11282.636	2571 096	1285.548	14368 979	12075 775	2819.218	1409.609	58.905	75.995	65 978	9.097	4 549
C9162	*72hr*	*3/F*	*3124.970*				*2818.702*				*10.088*	*44.481*			
C9163	72hr	3/F	728 968				560.92				2.999	74.705			
C9164	72hr	3/F	1208.719				3235.27				3 899	75.246			
C9165	72hr	3/F	469.456	802.381	375 059	216.541	434.005	1410 065	1581.951	913.340	3.154	58.817	69.589	9.333	5 388
C9166	72hr	4/M	565.765				521.42				2.015	56.639			
C9167	72hr	4/M	1474 090				1192.89				5.224	74.884			
C9168	72hr	4/M	2224 834				2179.13				7.135	70.769			
C9169	72hr	4/M	1211.247	1368.984	686.432	343.216	1385.043	1319.623	682.209	341.104	5.597	81.592	70.971	10.545	5.272
C9162	*96hr*	*3/F*	*212.205*				*100.987*				*0.573*	*45.053*			
C9163	96hr	3/F	74.177				8 05				0.244	74.949			
C9164	96hr	3/F	22.505				25.27				0.054	75 301			
C9165	96hr	3/F	66 609	54 430	27.906	16.111	19.316	17.545	8 745	5.049	0 380	59.198	69.816	9.197	5.310
C9166	96hr	4/M	78.699				36.86				0.309	56.949			
C9167	96hr	4/M	93 314				41.72				0.323	75 207			
C9168	96hr	4/M	277.286				154.52				0.878	71.647			
C9169	96hr	4/M	55.229	126.132	101.983	50.992	19.064	63 042	61.758	30 879	0.173	81.765	71.392	10.501	5.251
C9162	*120hr*	*3/F*	*52.595*				*3.279*				*0.168*	*45.222*			
C9163	120hr	3/F	38.922				0.74				0.172	75.121			
C9164	120hr	3/F	67.699				2.07				0.258	75.559			
C9165	120hr	3/F	24.222	43.614	22.115	12.768	0.736	1.183	0.772	0 446	0.151	59.349	70.010	9.235	5.332
C9166	120hr	4/M	20.952				1.38				0.069	57.017			
C9167	120hr	4/M	27.409				1.56				0.096	75.303			
C9168	120hr	4/M	39.102				6.96				0.144	71.791			
C9169	120hr	4/M	N.S.	29 154	9.200	4.600	0 829	2.680	2.869	1.434	NS	81.765	71 469	10.483	5.241

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Feces
(D_5 in Corn Oil)

Animal ID	Time Point	Group ID, Sex	Radioactivity µg Eq D_5/g of Feces	Average radioactivity µg Eq D_5/g of Feces	SD	SEM	Parent µg D_5/g feces	Parent µg D_5/g Average/ sex/ timepoint	SD	SEM	% Dose Recovered in Feces	Cumulative % Dose Recovered in Feces	Average Cumulative % Dose Recovered per Group	SD	SEM
C9162	*144hr*	*3/F*	*15.969*				*0.910*				*0.061*	*45.283*			
C9163	144hr	3/F	17.318				0.42				0.101	75.222			
C9164	144hr	3/F	26.659				1.39				0.052	75.611			
C9165	144hr	3/F	21.910	21.962	4.670	2.696	0.478	0.762	0.547	0.316	0.080	59.429	70 087	9 233	5.330
C9166	144hr	4/M	14.483				9.52				0.047	57.065			
C9167	144hr	4/M	21.653				0.66				0.053	75.357			
C9168	144hr	4/M	24.984				0.92				0.045	71.836			
C9169	144hr	4/M	14 917	19 009	5.161	2.581	0 000	2.775	4.515	2.258	0.049	81.814	71.518	10.484	5.242
C9162	*168hr*	*3/F*	*25.213*				*0.905*				*0.098*	*45.381*			
C9163	168hr	3/F	23.969				0.55				0.120	75.341			
C9164	168hr	3/F	91.153				68 83				0.663	76 274			
C9165	168hr	3/F	15.290	43.470	41.522	23.973	1.813	23.730	39.059	22 551	0.065	59.493	70 370	9.431	5.445
C9166	168hr	4/M	47.225				15.58				0.175	57.239			
C9167	168hr	4/M	16.627				0.58				0.056	75.412			
C9168	168hr	4/M	17.177				0.45				0.063	71.899			
C9169	168hr	4/M	9 595	22.656	16 739	8.370	0.000	4.153	7.619	3.809	0.033	81.846	71.599	10.422	5.211

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Feces
(D_5 Neat and D_5 in Simethicone)

Dosing Solutions : ^{14}C-D_5 Neat and ^{14}C-D_5 in Simethicone
^{14}C-D_5 Neat (Group 13) Dosing Solution Specific Activity= 0.302 µCi/mg and 670440 DPM/mg
^{14}C-D_5 in Simethicone (Group 14) Dosing Solution Specific Activity= 0.029 µCi/mg and 64380 DPM/mg
D_5 Concentration = 97.47 mg D_5/g SFdosing solution and 660511 DPM/mg D_5 in SF dosing solution

Animal ID	Time Point	Group ID, Carrier	Radioactivity µg Eq D_5/g of feces	Average radioactivity µg Eq D_5/g of Feces	SD	SEM	Parent µg D_5/g feces	Parent µg D_5/g Average/ carrier/ timepoint	SD	SEM	% Dose Recovered in Feces	Cumulative % Dose Recovered in Feces	Average Cumulative % Dose Recovered per Group	SD	SEM
C9200	6hr	13/Neat D5	2.394				2.476				0.003	0.003			
C9201	*6hr*	*13/Neat D5*	*5.016*				*5.564*				*0.003*	*0.003*			
Q0004	6hr	13/Neat D5	9.671				7.389				0.006	0.006			
C9203	6hr	13/Neat D5	14.386	8.817	6.041	3.488	15.254	8.373	6.445	3.721	0.014	0.014	0.008	0.006	0.003
C9206	6hr	14/SF	6329.720				6928.593				12.339	12.339			
C9207	*6hr*	*14/SF*	*35.910*				*32.583*				*0.053*	*0.053*			
C9208	6hr	14/SF	4638.294				4904.918				4.935	4.935			
C9209	6hr	14/SF	1198.827	4055.614	2614.603	1509.542	1359.278	4397.597	2819.104	1627.611	0.311	0.311	5.862	6.067	3.503
C9200	12hr	13/Neat D5	21849.623				20625.843				11.726	11.729			
C9201	*12hr*	*13/Neat D5*	*12.645*				*7.610*				*0.001*	*0.004*			
Q0004	12hr	13/Neat D5	17.373				10.960				0.005	0.011			
C9203	12hr	13/Neat D5	8183.068	10016.688	11031.020	6368.762	8358.864	9665.222	10369.343	5986.743	2.718	2.732	4.824	6.133	3.541
C9206	12hr	14/SF	6501.561				7654.099				20.032	32.371			
C9207	*12hr*	*14/SF*	*10357.278*				*10265.653*				*3.252*	*3.305*			
C9208	12hr	14/SF	10865.078				12587.267				12.925	17.861			
C9209	12hr	14/SF	16004.567	11123.735	4756.780	2746.328	12961.621	11067.662	2962.152	1710.199	15.087	15.397	21.876	9.172	5.295
C9200	24hr	13/Neat D5	24014.292				23428.928				50.235	61.965			
C9201	*24hr*	*13/Neat D5*	*4214.841*				*3974.377*				*1.826*	*1.830*			
Q0004	24hr	13/Neat D5	27952.395				19566.686				41.047	41.058			
C9203	24hr	13/Neat D5	32843.429	28270.039	4423.131	2553.696	27002.478	23332.697	3718.830	2147.068	38.677	41.409	48.144	11.970	6.911
C9206	24hr	14/SF	11016.358				10698.940				19.082	51.452			
C9207	*24hr*	*14/SF*	*15207.894*				*15692.221*				*5.471*	*8.776*			
C9208	24hr	14/SF	9848.384				8674.611				21.135	38.996			
C9209	24hr	14/SF	15448.135	12104.292	2954.150	1705.579	14027.692	11133.748	2702.899	1560.520	26.398	41.796	44.081	6.535	3.773

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Feces
(D_5 Neat and D_5 in Simethicone)

Animal ID	Time Point	Group ID, Carrier	Radioactivity µg Eq D_5/g of feces	Average radioactivity µg Eq D_5/g of Feces	SD	SEM	Parent µg D_5/g feces	Parent µg D_5/g Average/ carrier/ timepoint	SD	SEM	% Dose Recovered in Feces	Cumulative % Dose Recovered in Feces	Average Cumulative % Dose Recovered per Group	SD	SEM
C9200	48hr	13/Neat D5	3175.062				3001.878				15.481	77.446			
C9201	*48hr*	*13/Neat D5*	*18104.262*				*16741.707*				*34.576*	*36.406*			
Q0004	48hr	13/Neat D5	10610.207				10940.192				35.209	76.267			
C9203	48hr	13/Neat D5	9933.188	7906.152	4111.204	2373.605	9399.435	7780.501	4209.503	2430.358	32.592	74.001	75.904	1.751	1.011
C9206	48hr	14/SF	2056.254				2014.085				9.598	61.051			
C9207	*48hr*	*14/SF*	*10644.676*				*10660.296*				*27.005*	*35.781*			
C9208	48hr	14/SF	3254.512				3232.398				13.280	52.276			
C9209	48hr	14/SF	7538.332	4283.033	2882.132	1664.000	7604.458	4283.647	2939.713	1697.244	23.770	65.566	59.631	6.758	3.902
C9200	72hr	13/Neat D5	213.597				121.762				1.012	78.458			
C9201	*72hr*	*13/Neat D5*	*1196.096*				*949.558*				*3.824*	*40.230*			
Q0004	72hr	13/Neat D5	552.653				466.978				1.916	78.183			
C9203	72hr	13/Neat D5	738.441	501.563	266.126	153.648	674.073	420.938	279.019	161.092	3.033	77.034	77.892	0.755	0.436
C9206	72hr	14/SF	83.159				55.867				0.386	61.436			
C9207	*72hr*	*14/SF*	*1658.513*				*1530.975*				*3.827*	*39.607*			
C9208	72hr	14/SF	107.042				77.492				0.320	52.595			
C9209	72hr	14/SF	661.528	283.910	327.245	188.935	520.837	218.066	262.431	151.515	1.841	67.407	60.480	7.452	4.303
C9200	96hr	13/Neat D5	39.056				2.657				0.176	78.634			
C9201	*96hr*	*13/Neat D5*	*302.905*				*257.459*				*0.894*	*41.124*			
Q0004	96hr	13/Neat D5	689.038				621.184				3.929	82.112			
C9203	96hr	13/Neat D5	32.381	253.491	377.209	217.782	15.890	213.243	353.349	204.006	0.148	77.182	79.309	2.533	1.463
C9206	96hr	14/SF	7.866				0.734				0.036	61.472			
C9207	*96hr*	*14/SF*	*145.253*				*79.530*				*0.455*	*40.062*			
C9208	96hr	14/SF	184.917				150.744				0.615	53.210			
C9209	96hr	14/SF	35.291	76.025	95.296	55.019	20.104	57.194	81.594	47.108	0.121	67.528	60.737	7.187	4.150
C9200	120hr	13/Neat D5	23.986				0.962				0.101	78.735			
C9201	*120hr*	*13/Neat D5*	*29.537*				*0.510*				*0.085*	*41.209*			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

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Rounding errors may occur due to electronic handling of numbers

Feces
(D_5 Neat and D_5 in Simethicone)

Animal ID	Time Point	Group ID, Carrier	Radioactivity µg Eq D_5/g of feces	Average radioactivity µg Eq D_5/g of Feces	SD	SEM	Parent µg D_5/g feces	Parent µg D_5/g Average/ carrier/ timepoint	SD	SEM	% Dose Recovered in Feces	Cumulative % Dose Recovered in Feces	Average Cumulative % Dose Recovered per Group	SD	SEM
Q0004	120hr	13/Neat D5	10.556				0.496				0.050	82.162			
C9203	120hr	13/Neat D5	7.769	14.103	8.671	5.006	0.638	0.698	0.239	0.138	0.053	77.235	79.377	2.526	1.458
C9206	120hr	14/SF	7.049				1.158				0.040	61.512			
C9207	*120hr*	*14/SF*	*16.885*				*2.057*				*0.076*	*40.136*			
C9208	120hr	14/SF	5.276				0.000				0.019	53.230			
C9209	120hr	14/SF	6.821	6.382	0.965	0.557	0.658	0.605	0.581	0.335	0.023	67.551	60.764	7.190	4.151
C9200	144hr	13/Neat D5	7.986				0.000				0.074	78.809			
C9201	*144hr*	*13/Neat D5*	*18.891*				*BLQ*				*0.062*	*41.271*			
Q0004	144hr	13/Neat D5	5.624				0.000				0.022	82.184			
C9203	144hr	13/Neat D5	7.593	7.068	1.265	0.730	0.000	0.000	0.000	0.000	0.030	77.265	79.419	2.516	1.452
C9206	144hr	14/SF	2.736				0.462				0.012	61.524			
C9207	*144hr*	*14/SF*	*9.260*				*BLQ*				*0.028*	*40.166*			
C9208	144hr	14/SF	2.960				0.000				0.012	53.241			
C9209	144hr	14/SF	2.783	2.826	0.118	0.068	0.000	0.154	0.267	0.154	0.013	67.564	60.776	7.191	4.151
C9200	168hr	13/Neat D5	11.999				0.000				0.054	78.863			
C9201	*168hr*	*13/Neat D5*	*19.309*				*BLQ*				*0.048*	*41.319*			
Q0004	168hr	13/Neat D5	5.820				0.000				0.030	82.214			
C9203	168hr	13/Neat D5	382.234	133.351	215.561	124.454	354.325	118.108	204.570	118.108	1.043	78.308	79.795	2.113	1.220
C9206	168hr	14/SF	3.853				0.393				0.019	61.543			
C9207	*168hr*	*14/SF*	*17.952*				*0.889*				*0.049*	*40.215*			
C9208	168hr	14/SF	3.053				0.000				0.011	53.252			
C9209	168hr	14/SF	1.940	2.949	0.961	0.555	0.000	0.131	0.227	0.131	0.009	67.573	60.789	7.190	4.151

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Cage Rinses

Animal ID	Time Point	Group ID, Sex	Concentration µg Eq D_5/g Rinse	Average Conc. µg Eq D_5/g Rinse	SD	SEM	% Dose Recovered in Cage Rinses	Average % Dose Recovered per Group	SD	SEM
C9162	*168hr*	*3/F*	*0.895*				*0.036*			
C9163	168hr	3/F	0.404				0.016			
C9164	168hr	3/F	0.300				0.012			
C9165	168hr	3/F	0.776	0.493	0.250	0.145	0.043	0.024	0.017	0.010
C9166	168hr	4/M	2.354				0.052			
C9167	168hr	4/M	1.077				0.029			
C9168	168hr	4/M	1.327				0.034			
C9169	168hr	4/M	0.791	1.387	0.681	0.340	0.021	0.034	0.013	0.006

Contents of GI Tract

Animal ID	Time Point	Group ID, Sex	Concentration µg Eq D_5/g of GI Contents	Average Conc. µg Eq D_5/g of GI contents	SD	SEM	% Dose Recovered in Contents of GI Tract	Average % Dose Recovered per Group	SD	SEM
C9162	*168hr*	*3/F*	*8.556*				*0.038*			
C9163	168hr	3/F	5.060				0.040			
C9164	168hr	3/F	4.693				0.033			
C9165	168hr	3/F	6.423	5.392	0.911	0.526	0.039	0.038	0.004	0.002
C9166	168hr	4/M	5.743				0.033			
C9167	168hr	4/M	5.898				0.035			
C9168	168hr	4/M	6.027				0.028			
C9169	168hr	4/M	4.120	5.447	0.892	0.446	0.022	0.030	0.006	0.003

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Cage Rinse and Contents of GI Tract
(D_5 neat and D_5 in Simethicone)

Cage Rinses

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g Rinse	Average Conc. µg Eq D_5/g Rinse	SD	SEM	% Dose Recovered in Cage Rinses	Average % Dose Recovered per Group	SD	SEM
C9200	168hr	13/Neat D_5	0.840				0.018			
C9201	*168hr*	*13/Neat D_5*	*0.632*				*0.016*			
Q0004	168hr	13/Neat D_5	0.481				0.011			
C9203	168hr	13/Neat D_5	2.552	1.291	1.107	0.639	0.082	0.037	0.039	0.022
C9206	168hr	14/SF	0.253				0.007			
C9207	*168hr*	*14/SF*	*0.340*				*0.012*			
C9208	168hr	14/SF	0.136				0.005			
C9209	168hr	14/SF	0.132	0.174	0.069	0.040	0.004	0.005	0.002	0.001

Contents of GI Tract

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g of GI Contents	Average Conc. µg Eq D_5/g of GI contents	SD	SEM	% Dose Recovered in Contents of GI Tract	Average % Dose Recovered per Group	SD	SEM
C9200	168hr	13/Neat D_5	3.192				0.029			
C9201	*168hr*	*13/Neat D_5*	*2.719*				*0.029*			
Q0004	168hr	13/Neat D_5	1.745				0.011			
C9203	168hr	13/Neat D_5	2.837	2.591	0.754	0.435	0.019	0.020	0.009	0.005
C9206	168hr	14/SF	0.802				0.005			
C9207	*168hr*	*14/SF*	*4.313*				*0.026*			
C9208	168hr	14/SF	0.797				0.004			
C9209	168hr	14/SF	0.625	0.741	0.101	0.058	0.004	0.004	0.000	0.000

Italicized data for rats No. C9201 and C9207 were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Dosing Solution : ^{14}C-D_5 in corn oil
Dosing Solution Specific Activity= 0.036 μCi/mg and 79920 DPM/mg
D_5 Concentration = 125.26 mg D_5/g dosing solution and 638033 DPM/mg D_5 in dosing solution

Animal ID	Time Point	Group ID, Sex	Concentration μg Eq D_5/g of KOH	Average Conc. μg Eq D_5/g of KOH	SD	SEM	% Dose Recovered in KOH	Cumulative % Dose Recovered in KOH	Average Cumulative % Dose Recovered per Group	SD	SEM
C9162	*24hr*	*3/F*	*2.345*				*0.28*	*0.28*			
C9163	24hr	3/F	2.505				0.31	0.31			
C9164	24hr	3/F	1.381				0.17	0.17			
C9165	24hr	3/F	2.282	2.056	0.595	0.343	0.27	0.27	0 251	0.075	0.043
C9166	24hr	4/M	3.987				0.27	0.27			
C9167	24hr	4/M	4.285				0.30	0.30			
C9168	24hr	4/M	5.237				0.39	0.39			
C9169	24hr	4/M	5.038	4.637	0.596	0.298	0.27	0.27	0.308	0.059	0.030
C9162	*48hr*	*3/F*	*3.744*				*0.44*	*0.72*			
C9163	48hr	3/F	3.474				0.44	0.75			
C9164	48hr	3/F	2.145				0.28	0.45			
C9165	48hr	3/F	3.827	3.149	0.887	0.512	0.47	0.74	0.649	0.174	0.100
C9166	48hr	4/M	3.784				0.28	0.55			
C9167	48hr	4/M	5.628				0.43	0.74			
C9168	48hr	4/M	6.064				0.47	0.86			
C9169	48hr	4/M	4.383	4.965	1.062	0.531	0.30	0.57	0.678	0.148	0.074

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Sex	Concentration µg Eq D_5/g of KOH	Average Conc. µg Eq D_5/g of KOH	SD	SEM	% Dose Recovered in KOH	Cumulative % Dose Recovered in KOH	Average Cumulative % Dose Recovered per Group	SD	SEM
C9162	*72hr*	*3/F*	*1.159*				*0.17*	*0.89*			
C9163	72hr	3/F	1.147				0.15	0.91			
C9164	72hr	3/F	0.637				0.09	0.54			
C9165	72hr	3/F	1.398	1.060	0.388	0.224	0.19	0.93	0.792	0.220	0.127
C9166	72hr	4/M	1.011				0.08	0.63			
C9167	72hr	4/M	1.612				0.12	0.86			
C9168	72hr	4/M	2.201				0.19	1.05			
C9169	72hr	4/M	1.124	1.487	0.543	0.271	0.08	0.65	0.796	0.196	0.098
C9162	*96hr*	*3/F*	*0.512*				*0.07*	*0.96*			
C9163	96hr	3/F	0.521				0.07	0.98			
C9164	96hr	3/F	0.324				0.04	0.58			
C9165	96hr	3/F	0.697	0.514	0.186	0.108	0.09	1.02	0.860	0.241	0.139
C9166	96hr	4/M	0.482				0.03	0.66			
C9167	96hr	4/M	0.750				0.05	0.91			
C9168	96hr	4/M	1.099				0.07	1.11			
C9169	96hr	4/M	0.673	0.751	0.258	0.129	0.04	0.69	0.842	0.212	0.106
C9162	*120hr*	*3/F*	*0.389*				*0.06*	*1.01*			
C9163	120hr	3/F	0.375				0.05	1.03			
C9164	120hr	3/F	0.213				0.03	0.61			
C9165	120hr	3/F	0.375	0.321	0.094	0.054	0.05	1.07	0.902	0.252	0.146

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Sex	Concentration µg Eq D_5/g of KOH	Average Conc. µg Eq D_5/g of KOH	SD	SEM	% Dose Recovered in KOH	Cumulative % Dose Recovered in KOH	Average Cumulative % Dose Recovered per Group	SD	SEM
C9166	120hr	4/M	0.349				0.02	0.68			
C9167	120hr	4/M	0.481				0.04	0.95			
C9168	120hr	4/M	0.604				0.05	1.16			
C9169	120hr	4/M	0.382	0.454	0.115	0.057	0.03	0.72	0.876	0.223	0.111
C9162	*144hr*	*3/F*	*0.307*				*0.04*	*1.05*			
C9163	144hr	3/F	0.351				0.04	1.07			
C9164	144hr	3/F	0.233				0.03	0.64			
C9165	144hr	3/F	0.358	0.314	0.070	0.041	0.05	1.11	0.939	0.262	0.151
C9166	144hr	4/M	0.266				0.02	0.70			
C9167	144hr	4/M	0.375				0.03	0.98			
C9168	144hr	4/M	0.461				0.03	1.19			
C9169	144hr	4/M	0.347	0.362	0.080	0.040	0.02	0.74	0.900	0.228	0.114
C9162	*168hr*	*3/F*	*0.253*				*0.03*	*1.09*			
C9163	168hr	3/F	0.229				0.03	1.09			
C9164	168hr	3/F	0.197				0.02	0.66			
C9165	168hr	3/F	0.288	0.238	0.047	0.027	0.03	1.15	0.968	0.266	0.153
C9166	168hr	4/M	0.229				0.01	0.71			
C9167	168hr	4/M	0.312				0.02	1.00			
C9168	168hr	4/M	0.357				0.02	1.21			
C9169	168hr	4/M	0.240	0.284	0.061	0.030	0.02	0.75	0.920	0.233	0.116

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing

Carbon Dioxide trapped in KOH
(D_5 Neat and D_5 in Simethicone)

Dosing Solutions : ^{14}C-D_5 Neat and ^{14}C-D_5 in Simethicone
^{14}C-D_5 Neat (Group 13) Dosing Solution Specific Activity= 0.302 µCi/mg and 670440 DPM/mg
^{14}C-D_5 in Simethicone (Group 14) Dosing Solution Specific Activity= 0.029 µCi/mg and 64380 DPM/mg
D_5 Concentration = 97.47 mg D_5/g SFdosing solution and 660511 DPM/mg D_5 in SF dosing solution

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g of KOH	Average Conc. µg Eq D5/g of KOH	SD	SEM	% Dose Recovered in KOH	Cumulative % Dose Recovered in KOH	Average Cumulative % Dose Recovered per Group	SD	SEM
C9198	24hr	11/F (Controls)									
C9199	24hr	11/F (Controls)									
C9204	24hr	12/F (Controls)									
C9205	24hr	12/F (Controls)									
C9200	24hr	13/Neat D_5	1.719				0.267	0.267			
C9201	*24hr*	*13/Neat D_5*	*1.959*				*0.199*	*0.199*			
Q0004	24hr	13/Neat D_5	1.607				0.157	0.157			
C9203	24hr	13/Neat D_5	1.375	1.567	0.175	0.101	0.155	0.155	0.193	0.064	0.037
C9206	24hr	14/SF	0.791				0.117	0.117			
C9207	*24hr*	*14/SF*	*0.340*				*0.036*	*0.036*			
C9208	24hr	14/SF	0.861				0.111	0.111			
C9209	24hr	14/SF	0.667	0.773	0.098	0.057	0.078	0.078	0.102	0.021	0.012
C9200	48hr	13/Neat D_5	2.290				0.356	0.623			
C9201	*48hr*	*13/Neat D_5*	*2.662*				*0.401*	*0.601*			
Q0004	48hr	13/Neat D_5	1.149				0.136	0.292			
C9203	48hr	13/Neat D_5	1.476	1.638	0.588	0.339	0.175	0.330	0.415	0.181	0.104
C9206	48hr	14/SF	0.759				0.097	0.214			
C9207	*48hr*	*14/SF*	*0.515*				*0.061*	*0.097*			
C9208	48hr	14/SF	0.510				0.067	0.178			
C9209	48hr	14/SF	0.442	0.571	0.167	0.096	0.046	0.124	0.172	0.046	0.026
C9200	72hr	13/Neat D_5	0.759				0.116	0.739			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

Rounding errors may occur due to electronic handling of numbers

Carbon Dioxide trapped in KOH
(D_5 Neat and D_5 in Simethicone)

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g of KOH	Average Conc. µg Eq D5/g of KOH	SD	SEM	% Dose Recovered in KOH	Cumulative % Dose Recovered in KOH	Average Cumulative % Dose Recovered per Group	SD	SEM
C9201	*72hr*	*13/Neat D_5*	*1.383*				*0.133*	*0.734*			
Q0004	72hr	13/Neat D_5	0.335				0.036	0.329			
C9203	72hr	13/Neat D_5	0.440	0.512	0.221	0.128	0.049	0.379	0.482	0.224	0.129
C9206	72hr	14/SF	0.235				0.031	0.245			
C9207	*72hr*	*14/SF*	*0.415*				*0.044*	*0.141*			
C9208	72hr	14/SF	0.188				0.022	0.200			
C9209	72hr	14/SF	0.297	0.240	0.054	0.031	0.033	0.156	0.201	0.044	0.026
C9200	96hr	13/Neat D_5	0.342				0.052	0.791			
C9201	*96hr*	*13/Neat D_5*	*0.416*				*0.042*	*0.776*			
Q0004	96hr	13/Neat D_5	0.193				0.023	0.352			
C9203	96hr	13/Neat D_5	0.196	0.244	0.085	0.049	0.026	0.404	0.516	0.240	0.138
C9206	96hr	14/SF	0.076				0.012	0.257			
C9207	*96hr*	*14/SF*	*0.192*				*0.023*	*0.164*			
C9208	96hr	14/SF	0.080				0.011	0.211			
C9209	96hr	14/SF	0.146	0.101	0.039	0.023	0.021	0.177	0.215	0.040	0.023
C9200	120hr	13/Neat D_5	0.191				0.030	0.822			
C9201	*120hr*	*13/Neat D_5*	*0.238*				*0.026*	*0.803*			
Q0004	120hr	13/Neat D_5	0.109				0.012	0.365			
C9203	120hr	13/Neat D_5	0.115	0.139	0.046	0.026	0.014	0.418	0.535	0.250	0.144

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

Rounding errors may occur due to electronic handling of numbers

Animal ID	Time Point	Group ID, Carrier	Concentration µg Eq D_5/g of KOH	Average Conc. µg Eq D5/g of KOH	SD	SEM	% Dose Recovered in KOH	Cumulative % Dose Recovered in KOH	Average Cumulative % Dose Recovered per Group	SD	SEM
C9206	120hr	14/SF	0.069				0.010	0.267			
C9207	*120hr*	*14/SF*	*0.125*				*0.018*	*0.179*			
C9208	120hr	14/SF	0.057				0.007	0.218			
C9209	120hr	14/SF	0.053	0.059	0.008	0.005	0.007	0.184	0.223	0.042	0.024
C9200	144hr	13/Neat D_5	0.133				0.022	0.843			
C9201	*144hr*	*13/Neat D_5*	*0.170*				*0.028*	*0.821*			
Q0004	144hr	13/Neat D_5	0.080				0.010	0.375			
C9203	144hr	13/Neat D_5	0.089	0.101	0.028	0.016	0.011	0.429	0.549	0.256	0.148
C9206	144hr	14/SF	0.027				0.004	0.272			
C9207	*144hr*	*14/SF*	*0.082*				*0.011*	*0.190*			
C9208	144hr	14/SF	0.041				0.005	0.224			
C9209	144hr	14/SF	0.034	0.034	0.007	0.004	0.004	0.188	0.228	0.042	0.024
C9200	168hr	13/Neat D_5	0.113				0.018	0.861			
C9201	*168hr*	*13/Neat D_5*	*0.140*				*0.023*	*0.838*			
Q0004	168hr	13/Neat D_5	0.069				0.008	0.383			
C9203	168hr	13/Neat D_5	0.081	0.088	0.023	0.013	0.010	0.439	0.561	0.261	0.151
C9206	168hr	14/SF	0.034				0.005	0.277			
C9207	*168hr*	*14/SF*	*0.104*				*0.015*	*0.202*			
C9208	168hr	14/SF	0.033				0.004	0.228			
C9209	168hr	14/SF	0.043	0.037	0.006	0.003	0.005	0.193	0.233	0.042	0.024

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Dosing Solution : ^{14}C-D_5 in corn oil
Dosing Solution Specific Activity= 0.036 µCi/mg and 79920 DPM/mg
D_5 Concentration = 125.26 mg D_5/g dosing solution and 638033 DPM/mg D_5 in dosing solution

	Group 3, Females				Group 4, Males			
Tissues	*C9162*	C9163	C9164	C9165	C9166	C9167	C9168	C9169
LUNGS								
Concentration µg Eq D_5/g lungs	*1199.590*	14.068	8.588	12.839	9.521	10.729	15.645	10.408
Average/Sex		11.832				11.576		
SD		2.876				2.760		
SEM		1.660				1.380		
% Dose Recovered in lungs	*0.792*	0.008	0.004	0.006	0.004	0.004	0.006	0.004
Average/Sex		0.006				0.004		
SD		0.002				0.001		
SEM		0.001				0.000		
SPLEEN								
Concentration µg Eq D_5/g spleen	*14.842*	16.375	6.922	15.206	13.482	19.452	18.166	12.546
Average/Sex		12.835				15.912		
SD		5.154				3.408		
SEM		2.975				1.704		
% Dose Recovered in spleen	*0.004*	0.005	0.002	0.004	0.003	0.004	0.004	0.003
Average/Sex		0.004				0.003		
SD		0.002				0.001		
SEM		0.001				0.000		

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Tissues	Group 3, Females				Group 4, Males			
	C9162	C9163	C9164	C9165	C9166	C9167	C9168	C9169
LIVER								
Concentration µg Eq D_5/g liver	*62.795*	89.297	30.731	66.803	33.121	65.574	93.218	38.647
Average/Sex	62.277				57.640			
SD	29.544				27.633			
SEM	17.057				13.816			
% Dose Recovered in liver	*0.262*	0.420	0.128	0.292	0.142	0.280	0.385	0.168
Average/Sex	0.280				0.244			
SD	0.146				0.112			
SEM	0.084				0.056			
PERIRENAL FAT								
Concentration µg Eq D_5/g fat	*275.846*	240.91	153.29	211.30	92.68	124.68	155.83	87.38
Average/Sex	201.832				115.146			
SD	44.569				31.737			
SEM	25.732				15.868			
% Dose Recovered in fat	*0.060*	0.045	0.048	0.062	0.014	0.021	0.044	0.015
Average/Sex	0.052				0.024			
SD	0.009				0.014			
SEM	0.005				0.007			
ADRENALS								
Concentration µg Eq D_5/g adrenals	*731.591*	94.440	36.879	97.154	39.198	28.691	93.997	20.668
Average/Sex	76.157				45.638			
SD	34.043				33.120			
SEM	19.655				16.560			
% Dose Recovered in adrenals	*0.006*	0.004	0.001	0.004	0.001	0.001	0.002	0.000
Average/Sex	0.003				0.001			
SD	0.002				0.001			
SEM	0.001				0.000			

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

	Group 3, Females				Group 4, Males			
Tissues	*C9162*	C9163	C9164	C9165	C9166	C9167	C9168	C9169
KIDNEYS								
Concentration µg Eq D_5/g kidneys	*19.292*	21.949	8.973	16.311	10.917	11.478	19.004	9.905
Average/Sex	15.745				12.826			
SD	6.507				4.170			
SEM	3.757				2.085			
% Dose Recovered in kidneys	*0.011*	0.020	0.008	0.014	0.008	0.009	0.015	0.007
Average/Sex	0.014				0.010			
SD	0.006				0.003			
SEM	0.003				0.002			
TESTES or OVARIES	Ovaries				Testes			
Concentration µg Eq D_5/g ovaries or testes	*62.439*	42.445	26.894	41.206	5.559	6.665	8.775	5.907
Average/Sex	36.848				6.726			
SD	8.643				1.442			
SEM	4.990				0.721			
% Dose Recovered in ovaries or testes	*0.002*	0.003	0.001	0.002	0.007	0.008	0.011	0.007
Average/Sex	0.002				0.008			
SD	0.001				0.002			
SEM	0.001				0.001			
EMPTIED GI TRACT								
Concentration µg Eq D_5/g GI tract	*29.862*	30.193	13.180	29.348	16.979	25.541	35.029	19.391
Average/Sex	24.240				24.235			
SD	9.588				8.048			
SEM	5.536				4.024			
% Dose Recovered in GI tract	*0.134*	0.158	0.053	0.175	0.063	0.082	0.150	0.057
Average/Sex	0.129				0.088			
SD	0.066				0.043			
SEM	0.038				0.021			

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

	Group 3, Females				Group 4, Males			
Tissues	***C9162***	**C9163**	**C9164**	**C9165**	**C9166**	**C9167**	**C9168**	**C9169**
REMAINING CARCASS								
Concentration µg Eq D_5/g carcass	*55.604*	42.088	29.684	45.462	25.394	34.092	33.726	27.645
Average/Sex	39.078				30.214			
SD	8.309				4.367			
SEM	4.797				2.183			
% Dose Recovered in carcass	*4.835*	3.697	2.551	4.043	2.057	2.818	2.707	2.252
Average/Sex	3.430				2.459			
SD	0.781				0.363			
SEM	0.451				0.181			

Italicized data for rat No. C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Dosing Solutions : ^{14}C-D_5 Neat and ^{14}C-D_5 in Simethicone
^{14}C-D_5 Neat (Group 13) Dosing Solution Specific Activity= 0.302 µCi/mg and 670440 DPM/mg

^{14}C-D_5 in Simethicone (Group 14) Dosing Solution Specific Activity= 0.029 µCi/mg and 64380 DPM/mg
D_5 Concentration = 97.47 mg D_5/g SFdosing solution and 660511 DPM/mg D_5 in SF dosing solution

	Group 13, ^{14}C-D_5 Neat				Group 14, ^{14}C-D_5 in Simethicone			
Tissues	C9200	*C9201*	Q0004	C9203	C9206	*C9207*	C9208	C9209
LUNGS								
Concentration µg Eq D_5/g lungs	7.930	*8.162*	4.582	5.463	2.403	*3175.171*	3.112	2.177
Average/Carrier	5.991				2.564			
SD	1.736				0.488			
SEM	1.002				0.282			
% Dose Recovered in lungs	0.005	*0.004*	0.002	0.003	0.001	*1.999*	0.002	0.001
Average/Carrier	0.003				0.001			
SD	0.002				0.000			
SEM	0.001				0.000			
SPLEEN								
Concentration µg Eq D_5/g spleen	5.570	*13.664*	4.426	3.808	1.855	*9.372*	1.360	1.951
Average/Carrier	4.601				1.722			
SD	0.894				0.317			
SEM	0.516				0.183			
% Dose Recovered in spleen	0.002	*0.003*	0.001	0.001	0.001	*0.002*	0.000	0.000
Average/Carrier	0.001				0.000			
SD	0.000				0.000			
SEM	0.000				0.000			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

Tissues	Group 13, ^{14}C-D_5 Neat				Group 14, ^{14}C-D_5 in Simethicone			
	C9200	C9201	Q0004	C9203	C9206	C9207	C9208	C9209
LIVER								
Concentration µg Eq D_5/g liver	33.765	*75.772*	19.171	22.279	10.478	*97.263*	8.950	8.420
Average/Carrier	25.072				9.282			
SD	7.687				1.069			
SEM	4.438				0.617			
% Dose Recovered in liver	0.176	*0.276*	0.086	0.087	0.048	*0.363*	0.034	0.032
Average/Carrier	0.116				0.038			
SD	0.052				0.009			
SEM	0.030				0.005			
PERIRENAL FAT								
Concentration µg Eq D_5/g fat	103.656	*109.494*	36.673	63.177	16.206	*25.930*	21.484	15.532
Average/Carrier	67.835				17.741			
SD	33.733				3.260			
SEM	19.476				1.882			
% Dose Recovered in fat	0.050	*0.023*	0.017	0.024	0.007	*0.006*	0.008	0.006
Average/Carrier	0.030				0.007			
SD	0.018				0.001			
SEM	0.010				0.001			
ADRENALS								
Concentration µg Eq D_5/g adrenals	22.909	*50.264*	20.550	14.583	8.455	*26.734*	5.981	5.735
Average/Carrier	19.347				6.724			
SD	4.292				1.505			
SEM	2.478				0.869			
% Dose Recovered in adrenals	0.001	*0.002*	0.001	0.001	0.000	*0.001*	0.000	0.000
Average/Carrier	0.001				0.000			
SD	0.000				0.000			
SEM	0.000				0.000			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

Tissues	Group 13, ^{14}C-D_5 Neat				Group 14, ^{14}C-D_5 in Simethicone			
	C9200	C9201	Q0004	C9203	C9206	C9207	C9208	C9209
KIDNEYS								
Concentration µg Eq D_5/g kidneys	6.943	*9.748*	5.375	4.411	1.527	*8.084*	1.855	1.357
Average/Carrier	5.576				1.580			
SD	1.278				0.253			
SEM	0.738				0.146			
% Dose Recovered in kidneys	0.007	*0.007*	0.004	0.004	0.002	*0.006*	0.002	0.001
Average/Carrier	0.005				0.001			
SD	0.002				0.000			
SEM	0.001				0.000			
OVARIES								
Concentration µg Eq D_5/g ovaries	22.690	*39.305*	16.194	12.283	5.185	*16.771*	7.014	4.065
Average/Carrier	17.056				5.422			
SD	5.257				1.489			
SEM	3.035				0.859			
% Dose Recovered in ovaries	0.001	*0.002*	0.001	0.001	0.000	*0.001*	0.000	0.000
Average/Carrier	0.001				0.000			
SD	0.000				0.000			
SEM	0.000				0.000			
EMPTIED GI TRACT								
Concentration µg Eq D_5/g GI tract	11.685	*16.086*	6.876	6.811	0.014	*9.751*	2.796	2.269
Average/Carrier	8.457				1.693			
SD	2.796				1.478			
SEM	1.614				0.853			
% Dose Recovered in GI tract	0.057	*0.065*	0.031	0.025	0.000	*0.092*	0.010	0.010
Average/Carrier	0.038				0.007			
SD	0.017				0.006			
SEM	0.010				0.003			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

Tissues	Group 13, ^{14}C-D_5 Neat				Group 14, ^{14}C-D_5 in Simethicone			
	C9200	C9201	Q0004	C9203	C9206	C9207	C9208	C9209
REMAINING CARCASS								
Concentration µg Eq D_5/g carcass	21.999	22.827	13.327	13.373	5.040	68.360	4.600	4.469
Average/Carrier	16.233				4.703			
SD	4.994				0.299			
SEM	2.883				0.173			
% Dose Recovered in carcass	2.490	1.676	1.225	1.192	0.534	13.657	0.413	0.393
Average/Carrier	1.636				0.447			
SD	0.740				0.077			
SEM	0.427				0.044			

Italicized data for rats No.C9201 and C9207 were excluded because of inaccuracy in dosing

Percent of administered dose recovered in urine, expired volatiles, expired CO_2, tissues and remaining carcasses
(% Dose absorbed)

Fischer 344, Females

		% of administered dose													
Animal ID	Group	Urine	Expired air	CO2 (KOH)	Carcass	Adrenal	Lung	Ovaries	Fat	Spleen	Kidneys	Liver	GI tract	Tissues	% Dose absorbed
C9162	*3*	*5.002*	*27.127*	*1.088*	*4.835*	*0.006*	*0.792*	*0.002*	*0.060*	*0.004*	*0.011*	*0.262*	*0.134*	*1.271*	*39.325*
C9163	3	5.438	7.691	1.091	3.697	0.004	0.008	0.003	0.045	0.005	0.020	0.420	0.158	0.662	18.579
C9164	3	2.218	7.243	0.663	2.551	0.001	0.004	0.001	0.048	0.002	0.008	0.128	0.053	0.246	12.922
C9165	3	5.439	16.176	1.149	4.043	0.004	0.006	0.002	0.062	0.004	0.014	0.292	0.175	0.560	27.367
	Avg.	**4.365**	**10.370**	**0.968**	**3.430**	**0.003**	**0.006**	**0.002**	**0.052**	**0.004**	**0.014**	**0.280**	**0.129**	**0.489**	**19.622**
	SD	**1.859**	**5.033**	**0.266**	**0.781**	**0.002**	**0.002**	**0.001**	**0.009**	**0.002**	**0.006**	**0.146**	**0.066**	**0.217**	**7.279**
	SEM	**1.073**	**2.906**	**0.153**	**0.451**	**0.001**	**0.001**	**0.001**	**0.005**	**0.001**	**0.003**	**0.084**	**0.038**	**0.125**	**4.202**

Fischer 344, Males

		% of administered dose													
Animal ID	Group	Urine	Expired air	CO2 (KOH)	Carcass	Adrenal	Lung	Testes	Fat	Spleen	Kidneys	Liver	GI tract	Tissues	% Dose absorbed
C9166	4	3.973	27.319	0.713	2.057	0.001	0.004	0.007	0.014	0.003	0.008	0.142	0.063	0.241	34.302
C9167	4	5.027	6.475	0.998	2.818	0.001	0.004	0.008	0.021	0.004	0.009	0.280	0.082	0.409	15.728
C9168	4	5.609	11.297	1.213	2.707	0.002	0.006	0.011	0.044	0.004	0.015	0.385	0.150	0.616	21.443
C9169	4	4.182	8.342	0.755	2.252	0.000	0.004	0.007	0.015	0.003	0.007	0.168	0.057	0.260	15.791
	Avg.	**4.698**	**13.359**	**0.920**	**2.459**	**0.001**	**0.004**	**0.008**	**0.024**	**0.003**	**0.010**	**0.244**	**0.088**	**0.382**	**21.816**
	SD	**0.760**	**9.517**	**0.233**	**0.363**	**0.001**	**0.001**	**0.002**	**0.014**	**0.001**	**0.003**	**0.112**	**0.043**	**0.173**	**8.745**
	SEM	**0.380**	**4.758**	**0.116**	**0.181**	**0.000**	**0.000**	**0.001**	**0.007**	**0.000**	**0.002**	**0.056**	**0.021**	**0.087**	**4.372**

Percent of administered dose recovered in feces (eliminated through GI tract)

Fischer 344, Females

		% of administered dose			
Animal ID	Group	Feces[1)]	Contents of GI tract	Cage rinse	Eliminated through GI Tract
C9162	*3*	*51.569*	*0.038*	*0.036*	*51.643*
C9163	3	85.615	0.040	0.016	85.671
C9164	3	86.675	0.033	0.012	86.721
C9165	3	67.606	0.039	0.043	67.687
	Avg.	**79.965**	**0.038**	**0.024**	**80.027**
	SD	**10.717**	**0.004**	**0.017**	**10.699**
	SEM	**6.187**	**0.002**	**0.010**	**6.177**

Fischer 344, Males

		% of administered dose			
Animal ID	Group	Feces[1)]	Contents of GI tract	Cage rinse	Eliminated through GI Tract
C9166	4	65.045	0.033	0.052	65.129
C9167	4	85.696	0.035	0.029	85.759
C9168	4	81.703	0.028	0.034	81.765
C9169	4	93.007	0.022	0.021	93.051
	Avg.	**81.363**	**0.030**	**0.034**	**81.426**
	SD	**11.843**	**0.006**	**0.013**	**11.827**
	SEM	**5.921**	**0.003**	**0.006**	**5.913**

[1)] Percent dose recovered in feces was corrected for the sample processing efficiency (88%)

Italicized data for Rat No.C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Mass balance as a percent of administered dose

Fischer 344, Females

		% of administered dose						
Animal ID	Group	% Dose eliminated through GI Tract[1)]	% Dose recovered in urine	% Dose recovered in expired air	% Dose recovered in KOH (%)	%Dose recovered in tissues and carcass	% Dose absorbed	Total Recovery[1)] (%)
C9162	*3*	*51.643*	*5.003*	*27.127*	*1.088*	*6.106*	*39.825*	*90.969*
C9163	3	85.671	5.438	7.691	1.091	4.359	18.579	104.250
C9164	3	86.721	2.218	7.243	0.663	2.797	12.922	99.643
C9165	3	67.687	5.439	16.176	1.149	4.603	27.367	95.054
	Avg.	**80.027**	**4.365**	**10.370**	**0.968**	**3.920**	**19.622**	**99.649**
	SDEV	**10.699**	**1.859**	**5.033**	**0.266**	**0.980**	**7.279**	**4.598**
	SEM	**6.177**	**1.073**	**2.906**	**0.153**	**0.566**	**4.202**	**2.655**

[1)] Percent dose recovered in feces was corrected for the sample processing efficiency (88%)

Fischer 344, Males

		% of administered dose						
Animal ID	Group	% Dose eliminated through GI Tract[1)]	% Dose recovered in urine	% Dose recovered in expired air	% Dose recovered in KOH (%)	%Dose recovered in tissues and carcass	% Dose absorbed	Total Recovery[1)] (%)
C9166	4	65.129	3.973	27.319	0.713	2.298	34.302	99.431
C9167	4	85.759	5.027	6.475	0.998	3.227	15.728	101.487
C9168	4	81.765	5.609	11.297	1.213	3.323	21.443	103.208
C9169	4	93.051	4.182	8.342	0.755	2.513	15.791	108.842
	Avg.	**81.426**	**4.698**	**13.359**	**0.920**	**2.840**	**21.816**	**103.242**
	SDEV	**11.827**	**0.760**	**9.517**	**0.233**	**0.511**	**8.745**	**4.040**
	SEM	**5.913**	**0.380**	**4.758**	**0.116**	**0.256**	**4.372**	**2.020**

[1)] Percent dose recovered in feces was corrected for the sample processing efficiency (88%)

Italicized data for Rat No.C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Mass balance as a percent of the total recovered dose

Fischer 344, Females

			% of Total Recovered Dose					
Animal ID	Group	Total Recovery[1] (% of administered dose)	Eliminated through GI Tract [1]	Urine	Expired air	KOH	Tissues, carcass	% of Total Recovery Absorbed
C9162	*3*	*90.969*	*56.771*	*5.500*	*29.821*	*1.796*	*6.713*	*43.229*
C9163	3	104.250	82.179	5.216	7.378	1.047	4.181	17.821
C9164	3	99.643	87.032	2.226	7.269	0.665	2.807	12.968
C9165	3	95.054	71.209	5.722	17.018	1.209	4.843	28.791
	Average	**99.649**	**80.140**	**4.388**	**10.555**	**0.974**	**3.944**	**19.860**
	SD	**4.598**	**8.106**	**1.889**	**5.597**	**0.279**	**1.038**	**8.106**
	SEM	**2.655**	**4.680**	**1.091**	**3.232**	**0.161**	**0.599**	**4.680**

[1] Percent dose recovered in feces was corrected for the sample processing efficiency (88%)

Fischer 344, Males

			% of Total Recovered Dose					
Animal ID	Group	Total Recovery[1] (% of administered dose)	Eliminated through GI Tract [1]	Urine	Expired air	KOH	Tissues, carcass	% of Total Recovery Absorbed
C9166	4	99.431	65.502	3.995	27.476	0.717	2.311	34.498
C9167	4	101.487	84.503	4.953	6.380	0.984	3.180	15.497
C9168	4	103.208	79.224	5.435	10.946	1.175	3.220	20.776
C9169	4	108.842	85.491	3.842	7.665	0.694	2.309	14.509
	Average	**103.242**	**78.680**	**4.556**	**13.117**	**0.892**	**2.755**	**21.320**
	SD	**4.040**	**9.206**	**0.765**	**9.764**	**0.230**	**0.514**	**9.206**
	SEM	**2.020**	**4.603**	**0.382**	**4.882**	**0.115**	**0.257**	**4.603**

[1] Percent dose recovered in feces was corrected for the sample processing efficiency (88%)

Italicized data for Rat No.C9162
were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

Percent of administered dose recovered in urine, expired air, expired CO_2, tissues and carcasses (% Dose absorbed)

Fischer 344, Females - Neat D_5

		% of administered dose													
Animal ID	Group	Urine	Expired air	CO2 (KOH)	Carcass	Adrenal	Lung	Ovaries	Fat	Spleen	Kidneys	Liver	GI tract	Tissues	% Dose absorbed
C9200	13	3.488	3.676	0.861	2.490	0.001	0.005	0.001	0 050	0.002	0.007	0.176	0.057	0.300	10.815
C9201	*13*	*4.181*	*40.031*	*0.836*	*1.676*	*0.002*	*0.004*	*0.002*	*0.023*	*0.003*	*0.007*	*0.276*	*0.065*	*0.383*	*47.107*
Q0004	13	1.759	7.530	0.383	1.225	0.001	0.002	0.001	0.017	0.001	0.004	0.086	0 031	0.143	11.040
C9203	13	1.908	4.267	0.439	1.192	0 001	0.003	0.001	0.024	0.001	0.004	0.087	0.025	0.144	7.951
	Average	**2.385**	**5.158**	**0.561**	**1.636**	**0.001**	**0.003**	**0.001**	**0.030**	**0.001**	**0.005**	**0.116**	**0.038**	**0.196**	**9.935**
	SD	**0.958**	**2.076**	**0.261**	**0.740**	**0.000**	**0.002**	**0.000**	**0.018**	**0.000**	**0.002**	**0.052**	**0.017**	**0.090**	**1.722**
	SEM	**0.553**	**1.198**	**0.151**	**0.427**	**0.000**	**0.001**	**0.000**	**0.010**	**0.000**	**0.001**	**0.030**	**0.010**	**0.052**	**0.994**

Fischer 344, Females - D_5 in Simethicone dosing solution

		% of administered dose													
Animal ID	Group	Urine	Expired air	CO2 (KOH)	Carcass	Adrenal	Lung	Ovaries	Fat	Spleen	Kidneys	Liver	GI tract	Tissues	% Dose absorbed
C9206	14	1.275	25.040	0.277	0.534	0.000	0.001	0.000	0.007	0.001	0.002	0.048	0.000	0.059	27.185
C9207	*14*	*1.076*	*7.765*	*0.202*	*13.857*	*0.001*	*1.999*	*0.001*	*0.006*	*0.002*	*0.006*	*0.363*	*0.042*	*2.421*	*25.122*
C9208	14	1.015	27.153	0.228	0.413	0.000	0.002	0.000	0 008	0.000	0.002	0.034	0 010	0.055	28 864
C9209	14	0.825	19.930	0.193	0.393	0.000	0.001	0.000	0.006	0 000	0.001	0.032	0 010	0.052	21.393
	Average	**1.038**	**24.041**	**0.233**	**0.447**	**0.000**	**0.001**	**0.000**	**0.007**	**0.000**	**0.001**	**0.038**	**0.007**	**0.055**	**25.814**
	SD	**0.226**	**3.714**	**0.042**	**0.077**	**0.000**	**0.000**	**0.000**	**0.001**	**0.000**	**0.000**	**0.009**	**0.006**	**0.004**	**3.920**
	SEM	**0.130**	**2.144**	**0.024**	**0.044**	**0.000**	**0.000**	**0.000**	**0.001**	**0.000**	**0.000**	**0.005**	**0.003**	**0.002**	**2.263**

Percent of administered dose excreted in feces (eliminated through GI tract)

Fischer 344, Females - Neat D_5 dosing solution

		% of administered dose			
Animal ID	Group	Feces[1)]	Contents of GI tract	Cage rinse	Eliminated through GI Tract
C9200	13	83.896	0.029	0.018	83.944
C9201	*13*	*43.956*	*0.029*	*0.016*	*44.001*
Q0004	13	87.462	0.011	0 011	87 483
C9203	13	83 307	0 019	0.082	83.407
	Average	**84.888**	**0.020**	**0.037**	**84.945**
	SD	**2.248**	**0.009**	**0.039**	**2.215**
	SEM	**1.298**	**0.005**	**0.022**	**1.279**

[1)] % Radioactivity recovered in feces was corrected for sample processing efficiency (94%)

Fischer 344, Females - D_5 in Simethicone dosing solution

		% of administered dose			
Animal ID	Group	Feces[1)]	Contents of GI tract	Cage rinse	Eliminated through GI Tract
C9206	14	69.149	0.005	0.007	69.161
C9207	*14*	*45.185*	*0.026*	*0.012*	*45.223*
C9208	14	59.834	0.004	0.005	59.843
C9209	14	75.924	0.004	0.004	75 933
	Average	**68.303**	**0.004**	**0.005**	**68.312**
	SD	**8.079**	**0.000**	**0.002**	**8.078**
	SEM	**4.664**	**0.000**	**0.001**	**4.664**

[1)] %Radioactivity recovered in feces was corrected for sample processing efficiency (89%)

Italicized data for rats No. C9201 and C9207 were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

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Mass balance as a percent of administered dose

Fischer 344, Females - Neat D_5

		% of administered dose						
Animal ID	Group	% Dose eliminated through GI Tract[1)]	% Dose recovered in urine	% Dose recovered in expired air	% Dose recovered in KOH (%)	%Dose recovered in tissues and carcass	% Dose absorbed	Total Recovery[1)] (%)
C9200	13	83.944	3.488	3.676	0.861	2.791	10.815	94.759
C9201	*13*	*44.001*	*3.161*	*40.031*	*0.836*	*2.059*	*47.407*	*91.408*
Q0004	13	87.483	1.759	7.530	0.383	1.368	11.040	98.523
C9203	13	83.407	1.908	4.267	0.439	1.336	7.951	91.358
	Average	**84.945**	**2.385**	**5.158**	**0.561**	**1.832**	**9.935**	**94.880**
	SDEV	**2.215**	**0.958**	**2.076**	**0.261**	**0.831**	**1.722**	**3.584**
	SEM	**1.279**	**0.553**	**1.198**	**0.151**	**0.480**	**0.994**	**2.069**

[1)] % Radioactivity recovered in feces was corrected for sample processing efficiency (94%)

Fischer 344, Females - D_5 in Simethicone dosing solution

		% of administered dose						
Animal ID	Group	% Dose eliminated through GI Tract[1)]	% Dose recovered in urine	% Dose recovered in expired air	% Dose recovered in KOH (%)	%Dose recovered in tissues and carcass	% Dose absorbed	Total Recovery[1)] (%)
C9206	14	69.161	1.275	25.040	0.277	0.593	27.185	96.346
C9207	*14*	*45.023*	*1.076*	*7.765*	*0.202*	*0.078*	*25.122*	*70.145*
C9208	14	59.843	1.015	27.153	0.228	0.468	28.864	88.707
C9209	14	75.933	0.825	19.930	0.193	0.444	21.393	97.325
	Average	**68.312**	**1.038**	**24.041**	**0.233**	**0.502**	**25.814**	**94.126**
	SDEV	**8.078**	**0.226**	**3.714**	**0.042**	**0.080**	**3.920**	**4.719**
	SEM	**4.664**	**0.130**	**2.144**	**0.024**	**0.046**	**2.263**	**2.724**

[1)] %Radioactivity recovered in feces was corrected for sample processing efficiency (89%)

Italicized data for rats No. C9201 and C9207 were excluded because of inaccuracy in dosing

Mass balance as a percent of the total recovered dose

Fischer 344, Females - Neat D_5

			% of Total Recovered Dose					
Animal ID	Group	Total Dose Recovery[1] (%)	Eliminated through GI Tract[1]	Urine	Expired air	KOH	Tissues, carcass	% of Total Recovery Absorbed
C9200	13	94.759	88.587	3.681	3.879	0.909	2.945	11.413
C9201	*13*	*91.706*	*48.296*	*4.589*	*43.938*	*0.918*	*2.260*	*51.704*
Q0004	13	98.523	88.795	1.785	7.643	0 389	1.389	11.205
C9203	13	91 358	91 296	2.089	4.671	0 481	1 463	8.704
	Average	**94.880**	**89.559**	**2.518**	**5.398**	**0.593**	**1.932**	**10.441**
	SDEV	**3.584**	**1.508**	**1.018**	**1.984**	**0.277**	**0.878**	**1.508**
	SEM	**2.069**	**0.871**	**0.588**	**1.146**	**0.160**	**0.507**	**0.871**

[1] % Radioactivity recovered in feces was corrected for sample processing efficiency (94%)

Fischer 344, Females- D_5 in Simethicone dosing solution

			% of Total Recovered Dose					
Animal ID	Group	Total Dose Recovery[1] (%)	Eliminated through GI Tract[1]	Urine	Expired air	KOH	Tissues, carcass	% of Total Recovery Absorbed
C9206	14	96.346	71.784	1.323	25.990	0.287	0.616	28.216
C9207	*14*	*70.345*	*64.288*	*1.530*	*17.039*	*0.287*	*22.856*	*35.712*
C9208	14	88.707	67.461	1.144	30.609	0.257	0.528	32.539
C9209	14	97.325	78 020	0.848	20.478	0.199	0.457	21.980
	Average	**94.126**	**72.422**	**1.105**	**25.692**	**0.248**	**0.533**	**27.578**
	SDEV	**4.719**	**5.308**	**0.240**	**5.073**	**0.045**	**0.080**	**5.308**
	SEM	**2.724**	**3.065**	**0.139**	**2.929**	**0.026**	**0.046**	**3.065**

[1] %Radioactivity recovered in feces was corrected for sample processing efficiency (89%)

Italicized data for rats No. C9201 and C9207 were excluded because of inaccuracy in dosing
Microsoft™ Excel 2000

Rounding errors may occur due to electronic handling of numbers

APPENDIX C
Statistical Analysis

Date: September 18, 2002
To: Marina Jovanovic
Subject: Contributing Scientist Report: Statistical Analysis of the Data from Study No. 9550 Submitted by Trevor Newhook, biostatistician specialist on January 29, 2003

Summary

The objectives of this study were to determine the amount of ^{14}C-decamethylcyclopentasiloxane (D5) absorbed through the gastrointestinal (GI) tract of Fischer 344 rats and to determine if there were any differences in absorption or distribution between males and females when D5 was delivered in corn oil and to evaluate any effects that the carriers may have on the absorption and disposition of D5 following oral administration, when the D5 was delivered in corn oil, simethicone and neat. A dose of 1000 mg/kg of D5 was administered by oral gavage.

In blood, the radiolabeled area under the curve (AUC) is significantly larger than the parent area under the curve for males and females, (1121.48 vs. 1014.50) for males and (1035.47 vs. 879.50) for females and the mean parent area under the curve in blood was significantly larger for males compared to females, (1014.50 vs. 879.50). The radioactivity area under the curve in blood was also significantly larger than the parent area under the curve when D5 was delivered in simethicone (85.76 vs. 54.70). Also, the parent and radioactivity areas under the curve in blood were significantly different among the three carriers with corn oil having the largest area under the curve followed by neat and then simethicone, (879.50 vs. 188.00 vs. 54.70 and 1035.47 vs. 270.46 vs. 85.46) for parent and radioactivity, respectively.

In feces, the radioactivity area under the curve did not significantly differ from the parent area under the curve and there was no significant difference in the radioactivity area under the curve between sexes. When comparing the AUCs between carriers, the AUC was significantly larger in neat when compared to corn oil, (761599.77 vs. 551553.00) and when compared to simethicone, (761599.77 vs. 426286.15).

In expired air, the radioactivity area under the curve did not significantly differ from the parent area under the curve and there was no significant difference in the radioactivity area under the curve between sexes. When comparing the AUCs between carriers, the AUC was significantly different between each carrier with simethicone having the largest area under the curve, followed by corn oil and neat D5 (44693.37 vs. 20852.14 vs. 7944.34).

When comparing the mean % level of endpoints of the administered dose among carrier, there were significant differences between the mean % level of administered dose between corn oil and simethicone in urine, expired air, CO_2, carcass, adrenals, lungs, ovaries, fat, spleen, kidneys, liver, GI tract, GI tract contents, overall tissues and tissues + remaining carcass. There were also significant differences between neat and simethicone in expired air, GI tract contents and percent dose absorbed. There were significant differences between neat and corn oil in carcass, tissues + remaining carcass and GI tract contents. When comparing endpoint means between males and females, there was a significantly higher mean fat level in females.

Introduction

The objectives of this study were to determine the amount of D5 absorbed through the gastrointestinal tract of Fischer 344 rats and to determine if there were any differences in absorption or distribution between males and females when D5 was delivered in corn oil and to evaluate any effect that the carrier may have on the absorption and disposition of D5 following oral administration, when D5 was delivered in corn oil, simethicone and neat.

Methods

The responses in each analysis were percent of administered parent or radioactivity recovered in a given sample. All statistical analyses were carried out using SAS®, version 8.2. The probability of Type I error (α) was 5 %. Comparisons were made using area under the curves (AUC). The AUCs were calculated for parent and radioactive content and the areas were compared between males and females as well as among carriers. Differences in the AUC between sexes were determined by constructing a 95% confidence interval for the difference ($AUC_{male} - AUC_{female}$) using the method of Nedelman and Jia (1998). Confidence intervals for the area under the curve were constructed using the method of Nedelman, Gibansky and Lau (1995). If the confidence interval did not contain the value zero, then the mean AUCs were considered to be statistically significant. The AUCs for parent and radioactive were calculated by the methods mentioned above and the areas were compared between the parent and radioactivity content in corn oil, neat and simethicone carriers for blood, feces and expired air. Half lives were calculated using the method of Gibaldi and Perrier (1982). The mean % levels of all endpoints of the administered dose were analyzed using Analysis of Variance. When comparing mean endpoints between the sexes, no further multiple comparison tests were used but when comparing mean endpoints among the carriers, the Analysis of Variance was followed by Tukey's multiple comparison technique.

Results

Blood

Parent vs. Radioactivity AUC Comparison (Tables 1 & 2)

There were significant differences between the parent area under the curves in blood when compared to the radioactivity area under the curve when D5 was administered in corn oil to females, (879.50 vs. 1035.47, p=0.0431) and to males, (1014.50 vs. 1121.48, p=0.0439). There was no significant difference in the mean parent and radiolabeled areas under the curve when D5 was administered in neat to females, (188.00 vs. 270.46, p=0.0925) but the radioactivity area under the curve in blood was significant larger than the parent area under the curve when D5 was delivered in simethicone to females, (85.76 vs. 54.70, p=0.00090). Since there was a significant difference between the parent and radioactivity AUCs in simethicone and corn oil, the AUCs between sexes and among carriers will be compared using both the parent and radioactivity data.

AUC Comparison between Sexes (Table 1)

The parent area under the curve in blood was significant larger for males compared to females, (1014.50 vs. 879.50, p=0.0439) but there was no significant difference in the radioactivity area under the curves in blood between females and males, (1035.47 vs. 1121.48, p=0.0931).

AUC Comparison among Carriers (Table 2)

The parent areas under the curve were significantly different among the three carriers. When corn oil was compared to simethicone, (879.50 vs. 54.70, p<0.0001), when corn oil was compared to neat, (879.50 vs. 188.00, p<0.0001) and when neat was compared to simethicone, (188.00 vs. 54.70, p=0.0183). The radioactivity areas under the curve were also significantly different among the three carriers. When neat was compared to simethicone, (270.46 vs. 85.76, p=0.0104), when corn oil was compared to neat, (1035.47 vs. 270.46, p<0.0001) and when corn oil was compared to simethicone, (1035.47 vs. 85.76, p<0.0001).

Feces

Parent vs. Radioactivity AUC Comparison (Tables 3 & 4)

There was no significant difference between the parent area under the curves in feces when compared to the radioactivity area under the curve when D5 was administered in corn oil to females, (603084.69 vs. 551553.00, p=0.1921) or to males, (660667.01 vs. 616222.51, p=0.1865). There was also no difference between parent and radioactivity AUCs when D5 was administered in simethicone to females, (407934.79 vs. 426286.15, p=0.1978) or when D5 was delivered in neat to females, (663725.03 vs. 761599.77, p=0.1047). Since there were no significant differences between parent and radioactivity area under the curves, the AUC comparisons between sexes and among carriers will only be performed on the radioactivity data.

AUC Comparison between Sexes (Table 3)

There were no significant differences in the radioactivity area under the curve in feces between females and males, (551553.00 vs. 616222.51, p=0.1602).

AUC Comparison among Carriers (Table 4)

The radioactivity area under the curve for feces was not significantly different when D5 was administered by corn oil compared to simethicone, (551553.00 vs. 426286.15, p=0.0826) but there were significant differences between corn oil and neat, (551553.00 vs. 761599.77, p=0.0404) and between simethicone and neat, (426286.15 vs. 761599.77, p=0.0019).

Expired Air

Parent vs. Radioactivity AUC Comparison (Tables 5 & 6)

There was no significant difference between the parent areas under the curve in expired air when compared to the radioactivity areas under the curve when D5 was administered in corn oil to females, (22842.10 vs. 20852.14, p=0.1962) or to males, (58654.70 vs. 41800.33, p=0.1563). There was also no significant difference between parent and radioactivity AUCS when D5 was administered by simethicone to females, (39679.74 vs. 44693.37, p=0.1078) or when D5 was delivered in neat to females, (7544.77 vs. 7944.34, p=0.2205). Since there were no significant difference in the AUCs for either carrier between the parent and radioactivity curves, the AUCs between sexes and among carriers will be will be compared only on the radioactivity data.

AUC Comparison between Sexes (Table 5)

There were no significant differences between sexes in the radioactivity area under the curve in expired air (20852.14 vs. 41800.33, p=0.0629).

AUC Comparison among Carriers (Table 6)

The radioactivity areas under the curves in expired air were significantly different between corn oil and simethicone, (20852.14 vs. 44693.37, p=0.0011), between neat and simethicone, (7944.34 vs. 44693.37, p=0.0001) and between corn oil and neat, (20852.14 vs. 7944.34, p=0.0063).

Endpoints (*Tables 7 and 8*)

When comparing the mean % level of endpoints of the administered dose among carrier, there were significant differences between the mean % level of administered dose between corn oil and simethicone in urine, (p=0.0353), expired air, (p=0.0108), CO_2, (p=0.0140), carcass, (p=0.0026), adrenals, (p=0.0208), lungs, (0.0140), ovaries, (p=0.0250), fat, (p=0.0075), spleen, (p=0.0181), kidneys, (p=0.0137), liver, (p=0.0372), GI tract, (p=0.0213), overall tissues, (p=0.0183), percent dose recovered in tissues, which consists of carcass + tissues, (p=0.0032) and GI tract contents, (p=0.0010).

There were significant differences between neat and simethicone in expired air, (p=0.0022), percent dose absorbed, (0.0170) and GI tract contents, (p=0.0404).

There were significant differences between neat and corn oil in carcass, (p=0.0287), percent dose recovered, which consists of carcass + tissues, (p=0.0318) and GI tract contents, (p=0.0199).

When comparing endpoint means between males and females there was a significant higher mean level of fat in females, (p=0.0282).

D5 Half-lives in Blood

Corn Oil

In males, under the parent curve, the half-life for the distribution phase ($T_{1/2}'$) was 6.78 and 166.80 for the elimination phase ($T_{1/2}'$). Under the radiolabeled curve, the half-life for the distribution phase was 9.88, and 81.15 for the elimination phase.

In females, under the parent curve, the half-life for the distribution phase ($T_{1/2}'$) was 8.15, and 160.91 for the elimination phase ($T_{1/2}'$). Under the radiolabeled curve, the half-life for the distribution phase was 12.05, and 240.36 for the elimination phase.

Simethicone

In females, under the parent curve, the half-life for the distribution phase ($T_{1/2}'$) was 17.16, and 242.21 for the elimination phase. Under the radiolabeled curve, the half-life for the distribution phase was 16.54, and 45.45 for the elimination phase ($T_{1/2}''$).

Neat

In females, under the parent curve, the half-life for the distribution phase ($T_{1/2}'$) was 11.00, and 116.77 for the elimination phase. Under the radiolabeled curve, the half-life for the distribution phase was 15.68, and 59.62 for the elimination phase ($T_{1/2}''$).

Tables

Table 1. Summary Table for Area Under the Curves between Sexes in Blood

	Sex	Mean Area Under the Curve (μgXhr/g)	Standard Error
Parent	Female *+	879.50	78.58
	Male *+	1014.50	56.13
Radioactivity	Female +	1035.47	78.86
	Male +	1121.48	52.74

* - Statistically significant difference between sexes at α=0.05.
+ - Statistically significant difference between parent and radioactivity curves for sexes at α=0.05.

Table 2. Summary Table for Area Under the Curves, by Carrier in Blood

	Carrier	Mean Area Under the Curve (μgXhr/g)	Standard Error
Parent	Corn oil *+	879.498	78.5789
	Simethicone *+	54.695	5.7812
	neat *	188.001	56.7938
Radioactivity	Corn oil *+	1035.47	78.8618
	Simethicone *+	85.76	7.6849
	neat *	270.46	66.2548

* - Statistically significant difference between carriers at α=0.05.
+ - Statistically significant difference in carrier between parent and radioactivity at α=0.05.

Table 3. Summary Table for Area Under the Curves between Sexes in Feces

	Sex	Mean Area Under the Curve (μgXhr/g)	Standard Error
Parent	Female	603084.69	132165.76
	Male	660667.01	104240.57
Radioactivity	Female	551553.00	104797.70
	Male	616222.51	80791.59

Table 4. Summary Table for Area Under the Curves, by Carrier in Feces

	Carrier	Mean Area Under the Curve (μgXhr/g)	Standard Error
Parent	Corn oil	603084.69	132165.76
	Neat	663725.03	79695.74
	Simethicone	407934.79	45319.79
Radioactivity	Corn oil +	551553.00	104797.70
	Neat	761599.77	85246.42
	Simethicone +	426286.15	50416.29

+ - Statistically significant difference from neat in radioactivity at α=0.05.

Table 5. Summary Table for Area Under the Curves between Sexes in Expired Air

	Sex	Mean Area Under the Curve (µg)	Standard Error
Parent	Female	22842.10	5754.53
	Male	58654.70	28615.48
Radioactivity	Female	20852.14	3702.19
	Male	41800.33	14976.19

Table 6. Summary Table for Area Under the Curves, by Carrier in Expired Air

	Carrier	Mean Area Under the Curve (µg)	Standard Error
Parent	Corn oil	22842.10	5754.53
	Neat	7544.77	1823.12
	Simethicone	39679.74	4097.53
Radioactivity	Corn oil •	20852.14	3702.19
	Neat •	7944.34	1921.83
	Simethicone •	44693.37	4426.23

• - Statistically significant difference between carriers at α=0.05.

Table 7. Summary Statistics for Endpoints by Carrier

Carrier	Variable	N	Mean	Std Dev	Std Error
Corn oil	Urine•	3	4.364801	1.859052	1.073324
	Expair•	3	10.370173	5.032968	2.905786
	CO_2•	3	0.967634	0.265510	0.153292
	Carcass•+	3	3.430222	0.780748	0.450765
	Adrenal•	3	0.003137	0.001537	0.000887
	Lung•	3	0.006050	0.001751	0.001011
	Ovaries•	3	0.001886	0.000873	0.000504
	Fat•	3	0.051869	0.009196	0.005310
	Spleen•	3	0.003712	0.001693	0.000977
	Kidneys•	3	0.013802	0.006028	0.003480
	Liver•	3	0.280279	0.146250	0.084437
	Gitract•	3	0.128754	0.066024	0.038119
	Gitract content•+	3	0.037535	0.003703	0.002138
	Tissues•	3	0.489487	0.216960	0.125262
	perDoseabs	3	19.622318	7.278926	4.202490
	Feces	3	79.965363	10.716745	6.187316
	Cagerinse	3	0.023625	0.016581	0.009573
	perDoserecfeces	3	80.026523	10.698941	6.177036
	perDoserectissues•+	3	3.919709	0.979815	0.565696
	TotalRec	3	99.648841	4.597854	2.654572
Neat	Urine	3	2.384843	0.958157	0.553192
	Expair†	3	5.157687	2.075516	1.198300
	CO_2	3	0.561205	0.261211	0.150810
	Carcass+	3	1.635629	0.740182	0.427344
	Adrenal	3	0.000950	0.000341	0.000197
	Lung	3	0.003463	0.001602	0.000925
	Ovaries	3	0.000886	0.000344	0.000199
	Fat	3	0.030303	0.017737	0.010240
	Spleen	3	0.001425	0.000460	0.000265
	Kidneys	3	0.005046	0.001840	0.001063

	Liver	3	0.116291	0.051673	0.029834
	GItract	3	0.037766	0.017086	0.009865
	GItract content+†	3	0.019555	0.009190	0.005306
	Tissues	3	0.196129	0.090368	0.052174
	perDoseabs†	3	9.935494	1.721940	0.994162
	Feces	3	84.888277	2.248120	1.297953
	Cagerinse	3	0.036840	0.038863	0.022438
	perDoserecfeces	3	84.944672	2.214908	1.278778
	perDoserectissues+	3	1.831758	0.830518	0.479500
	TotalRec	3	94.880166	3.583929	2.069182
Simethicone	Urine*	3	1.038289	0.225929	0.130440
	Expair*†	3	24.040874	3.713685	2.144097
	CO_2*	3	0.232693	0.041796	0.024131
	Carcass*	3	0.446660	0.076554	0.044199
	Adrenal*	3	0.000307	0.000080	0.000046
	Lung*	3	0.001362	0.000279	0.000161
	Ovaries*	3	0.000266	0.000078	0.000045
	Fat*	3	0.007072	0.000950	0.000549
	Spleen*	3	0.000458	0.000094	0.000054
	Kidneys*	3	0.001371	0.000255	0.000147
	Liver*	3	0.037846	0.008908	0.005143
	Gitract*	3	0.006663	0.005712	0.003298
	Gitract content*†	3	0.004396	0.000468	0.000270
	Tissues*	3	0.055345	0.003698	0.002135
	perDoseabs†	3	25.813862	3.919929	2.263172
	Feces	3	68.302515	8.078625	4.664196
	Cagerinse	3	0.005385	0.001572	0.000908
	perDoserecfeces	3	68.312296	8.078475	4.664110
	perDoserectissues*	3	0.502006	0.079962	0.046166
	TotalRec	3	94.126058	4.718550	2.724256

- perdoserecfeces=Feces+Cagerinse+GI tract contents.
- Perdoserectissues=Carcass+tissues.
- PerDoseabs=Percent dose absorbed.

*- Statistically significant difference between corn oil and simethicone at α=0.05.

+- Statistically significant difference between corn oil and neat at α=0.05.

†- Statistically significant difference between neat and simethicone at α=0.05.

Table 8. Summary Statistics for Endpoints by Sexes

Sex	Variable	N	Mean	Std Dev	Std Error
Female	Urine	3	4.364801	1.859052	1.073324
	Expair	3	10.370173	5.032968	2.905786
	CO_2	3	0.967634	0.265510	0.153292
	Carcass	3	3.430222	0.780748	0.450765
	Adrenal	3	0.003137	0.001537	0.000887
	Lung	3	0.006050	0.001751	0.001011
	Ovaries	3	0.001886	0.000873	0.000504
	Fat *	3	0.051869	0.009196	0.005310
	Spleen	3	0.003712	0.001693	0.000977
	Kidneys	3	0.013802	0.006028	0.003480
	Liver	3	0.280279	0.146250	0.084437
	GItract	3	0.128754	0.066024	0.038119
	Tissues	3	0.489487	0.216960	0.125262
	perDoseabs	3	19.622318	7.278926	4.202490
	Feces	3	79.965363	10.716745	6.187316
	Cagerinse	3	0.023625	0.016581	0.009573
	perDoserecfeces	3	80.026523	10.698941	6.177036
	Tiscar	3	3.919709	0.979815	0.565696
	TotalRec	3	99.648841	4.597854	2.654572

Male	Urine	4	4.697593	0.759752	0.379876
	Expair	4	13.358537	9.516582	4.758291
	CO_2	4	0.919759	0.232602	0.116301
	Carcass	4	2.458543	0.362922	0.181461
	Adrenal	4	0.000949	0.000784	0.000392
	Lung	4	0.004297	0.000982	0.000491
	Testes	4	0.008040	0.001914	0.000957
	Fat *	4	0.023502	0.013769	0.006885
	Spleen	4	0.003437	0.000734	0.000367
	Kidneys	4	0.009653	0.003409	0.001705
	Liver	4	0.243763	0.111908	0.055954
	GItract	4	0.088007	0.042661	0.021330
	Tissues	4	0.381650	0.173402	0.086701
	perDoseabs	4	21.816083	8.744617	4.372308
	Feces	4	81.362760	11.842987	5.921494
	Cagerinse	4	0.033752	0.012982	0.006491
	perDoserecfeces	4	81.426026	11.826764	5.913382
	tiscar	4	2.840193	0.511327	0.255664
	TotalRec	4	103.242108	4.039973	2.019986

- perdoserecfeces=Feces+Cagerinse+GI tract contents.
- Perdoserectissues=tiscar=Carcass+tissues.
- PerDoseabs=Percent dose absorbed.

*- Statistically significant difference between sexes at α=0.05.

References

1. Gibaldi, M. and Perrier, D. Pharmacokinetics. Second Edition: 5, 1982

2. Nedelman J.R. and Jia, X. An Extension of Satterthwaite's Approximation to Pharmacekinetics. J. Biopharm. Stat. 8: 317-328, 1998

3. Nedelman, J.R., Gibiansky, E., and Lau, D.T.W. Applying Biler's Method for AUC Confidence Intervals to Sparse Sampling. Pharmaceutical Research, 12: 124-128, 1995

4. SAS/Lab® Software: User's Guide. Version 6. First Edition. SAS Institute Inc. Cary, N.C.

5. SAS/Stat® User's Guide. Version 8. First Edition. Volume 2. SAS Institute Inc. Cary, N.C.

Documentation

A copy of the SAS® output for this analysis is filed with the raw data in the study file.

Roy A Campbell For Trevor Nowlock 25-Nov-2003

Roy A. Campbell
Manager, HES Operations
Health and Environmental Sciences

Date

APPENDIX D
Whole Body Autoradiography

Memorandum

To: Marina Jovanovic

From: J.M. Regan

Date: January 13, 2003

Re: Study 9550- Part 1 Whole-body Autoradiography

Title: Disposition of ^{14}C-Decamethylcyclopentasiloxane (D5) in Fischer 344 Rats when Delivered in Various Carriers Following the Administration of a Single Oral Dose

Introduction

The objective of this study was to determine absorption, distribution, metabolism, and elimination of the test article, ^{14}C- decamethylcyclopentasiloxane (^{14}C-D5), in Fischer 344 rats. The ^{14}C-D5 was mixed with corn oil as a carrier and delivered as a single exposure by oral gavage. The whole-body autoradiography (WBA) portion of this study was performed concurrently with the mass balance and blood kinetic analysis. WBA is a method used for the *in vivo* determination of the distribution and disposition of radioactivity in tissues. Experimental design and specific information regarding the test system, test article, and dosing may be found in the study protocol and in the main body of the final report.

Methods

One animal from Groups 5 (females) and 6 (males) was sacrificed at selected time points (3, 12, 24, 48, 96, and 168 hours) by CO_2 asphyxiation following a single exposure by oral gavage of ^{14}C-D5 mixed with corn oil. The dosing solution was prepared to deliver a targeted radioactivity of 25µCi/100g body weight and a nominal dose of 1000 mg D5/ kg of body weight for each animal. Immediately following euthanasia, each animal was rapidly frozen in a hexane/dry ice mixture at approximately -75°C and stored at -80°C. The frozen carcasses were embedded in a 4% aqueous solution of carboxymethylcellulose (Sigma Chemical Company, St. Louis, MO) which, when frozen, supported the carcass for sectioning on the CryoMacrocut® cryomicrotome (Leica, Deerfield, IL) with temperature maintained at approximately -25°C ± 5°. Parasagittal sections of approximately 40 microns in thickness were collected at various levels to include major organs and tissues of interest. The non-dehydrated sections were then placed immediately onto Kodak BioMax MR film (Eastman Kodak Company, Rochester, NY) and exposed at -80°C for 1, 2, and 4 weeks. One representative section from each level was dehydrated within the cryochamber for 48 to 72 hours and retained as a reference for comparison with the film. At the end of the exposure periods, films were developed on a Cordell™ MXR-14 automatic

film processor (Cordell, Peabody, MA). The reported images were digitally acquired from the original autoradiographs with a Hewlett-Packard ScanJet Pro (Palo Alto, CA) with output in grayscale at a resolution of 200 PPI (pixels per inch).

Results

Film exposure times at -80°C were determined empirically as one, two, and four weeks after developing films from the first animal in Group 5 (#C9170). There appeared to be no discernable difference in the intensity of the radioactivity between films developed at two and four weeks. All original films were reviewed and evaluated visually for the intensity of radioactivity as compared to background. Individual animal results are listed in Tables 1 and 2. It should be noted that at the earlier time points (3 through 24 hours) the high intensity of radioactivity in the gastrointestinal tract tended to obscure adjacent organs rendering difficulty in visualization.

Three hours following dosing, radioactivity was distributed throughout the rats of both sexes (Figures 1 and 2). In the female rat the highest concentration of radioactivity was found in the contents of the stomach, cecum, and small intestines and the ethmoturbinates. Moderate levels were found in the liver, fat, brown fat, skin, and bone marrow. Low levels (slightly above the background of the film) were present in the lung and myocardium. In the male the highest concentrations were also found in the contents of the stomach, cecum, and small intestines, as well as the contents of the urinary bladder. Moderate amounts were found in the skin, fat, and brown fat with lower levels in the liver, seminal vesicles, skeletal muscle, and bone marrow.

At twelve hours, the female (Figure 3) had high to moderate amounts in the contents of the stomach, cecum and small intestines, liver, fat, brown fat, skin, bone marrow, ethmoturbinates, esophagus, and tongue. It was noted that this animal (#C9171) had test article around the mouth area after dosing. There were low levels seen in the myocardium, cortex of the kidney, skeletal muscle, lens of the eye, and the Harderian gland. The male rat (Figure 4) also exhibited high to moderate amounts in the contents of the stomach, cecum, and small intestines, liver, fat, brown fat, skin, bone marrow, as well as the Harderian gland, and contents of the bladder. Low levels could be seen in the lens of the eye, seminal vesicle, skeletal muscle, and the region of the epiglottis and soft palette.

Twenty-four hours after dose both the female and male (Figures 5 and 6) had high levels in the contents of the cecum and colon and in the brown fat and moderate amounts in the liver, fat, skin, bone marrow, and contents of the small intestine. The female had low levels in the contents of the stomach, Harderian gland, myocardium, cortex of the kidney, and the esophagus. The male had low levels in the preputial gland, red pulp of the spleen, Harderian gland, myocardium, cortex of the kidney, contents of the urinary bladder, and the hard palette.

Forty-eight hours post dose the highest concentration for both female and male (Figures 7 and 8) was seen in the contents of the cecum and colon and brown fat. Moderate amounts for both were in the liver, fat, and bone marrow. The female had low levels in the cortex of the kidney, adrenal cortex, Harderian gland, skin, myocardium, red pulp of the spleen, tongue, and structures within the ovary related to the rat's cycling pattern. The male had low levels observed in the skin, preputial gland, Harderian gland, pulp of the spleen, myocardium, cortex of the kidney, tongue, and some speckling effect within the lung.

The highest level of radioactivity observed at 96 hours for both female and male (Figures 9 and 10) was in the brown fat. In the female moderate amounts were observed in the liver, fat, bone marrow, and contents of the colon with lower levels seen in the contents of the cecum, skin, myocardium, red pulp of spleen, tongue, and structures within the ovary related to the rat's cycling pattern. The male had low levels in the contents of the cecum and colon, preputial gland, Harderian gland, red pulp of the spleen, and myocardium.

At 168 hours, the last time point, both female and male (Figures 11 and 12) had high levels found only in the brown fat. Both sexes had moderate amounts in the liver, fat, and bone marrow. In addition, the male also had moderate amounts in the skin and preputial gland. Low levels were observed in the red pulp of the spleen and myocardium of both sexes and, in addition, the female had low levels in the contents of the cecum, skin, and structures within the ovary.

Both sexes showed comparatively similar patterns of disposition at each time point (Figures 13 and 14) with differences in intensities of some organs and in sex specific organs.

Records To Be Archived

Frozen carcasses, as well as the non-dehydrated sections will be disposed after authorization and finalization of the study. Films, dehydrated reference sections, and processing records will be maintained in HES archives of Dow Corning Corporation, Midland, MI.

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11/18/03

Jane M. Regan, HT/MLT (ASCP) Date
Technologist

Table 1

Individual Animal Qualitative Radioactivity Concentrations- Females

Animal ID	Time point	highest	moderate	low (slightly above background)
C9170	3 hour	stomach/contents cecum/contents small intestine/contents ethmoturbinates	liver fat brown fat skin bone marrow	lung myocardium
C9171	12 hour	stomach/contents cecum/contents brown fat	liver fat skin bone marrow tongue esophagus ethmoturbinates	myocardium kidney (cortex) skeletal muscle eye (lens) Harderian gland
C9172	24 hour	cecum/contents colon/feces brown fat	liver fat skin bone marrow small intestine/contents	stomach/contents Harderian gland myocardium kidney (cortex) esophagus
C9173	48 hour	cecum/contents colon/feces brown fat	liver fat bone marrow	kidney (cortex) adrenal (cortex) Harderian gland skin myocardium spleen (red pulp) ovarian structures(cyclical) tongue
C9174	96 hour	brown fat	liver fat bone marrow colon/feces	cecum/contents skin myocardium spleen (red pulp) ovarian structures(cyclical) tongue
C9175	168 hour	brown fat	fat liver bone marrow	cecum/contents skin myocardium spleen (red pulp) ovarian structures (cyclical)

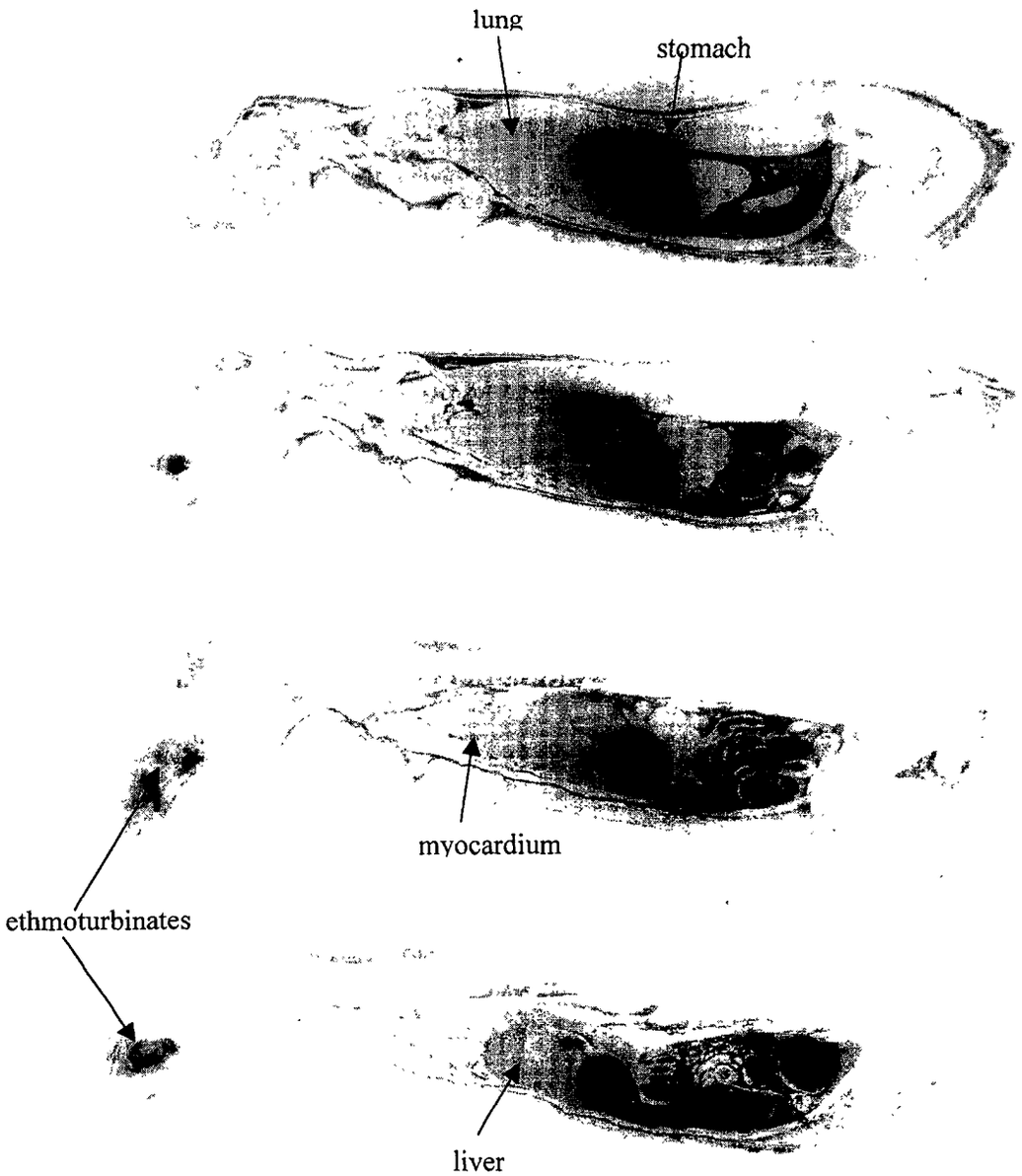
Table 2

Individual Animal Qualitative Radioactivity Concentrations- Males

Animal	Time point	highest	moderate	low (slightly above background)
C9176	3 hour	stomach/contents	skin	liver
		cecum/contents	fat	seminal vesicle
		small intestine/contents	brown fat	skeletal muscle
		bladder/contents		bone marrow
C9177	12 hour	stomach/contents	bladder/contents	eye (lens)
		cecum/contents	liver	seminal vesicle
		small intestine/contents	fat	skeletal muscle
			brown fat	epiglottis/soft palette
			skin	
			bone marrow	
			harderian gland	
C9178	24 hour	cecum/contents	liver	preputial gland
		colon/feces	fat	Harderian gland
		brown fat	skin	spleen (red pulp)
			bone marrow	myocardium
			small intestine/contents	kidney (cortex)
				bladder/contents
				hard palette
C9179	48 hour	cecum/contents	liver	preputial gland
		colon/feces	fat	skin
		brown fat	bone marrow	Harderian gland
				spleen (red pulp)
				myocardium
				kidney (cortex)
				tongue
				lungs (speckled)
C9180	96 hour	brown fat	liver	cecum/contents
			bone marrow	colon/feces
			skin	preputial gland
			fat	harderian gland
				spleen (red pulp)
				myocardium
C9181	168 hour	brown fat	liver	spleen (red pulp)
			bone marrow	myocardium
			fat	
			skin	
			preputial gland	

Figure 1

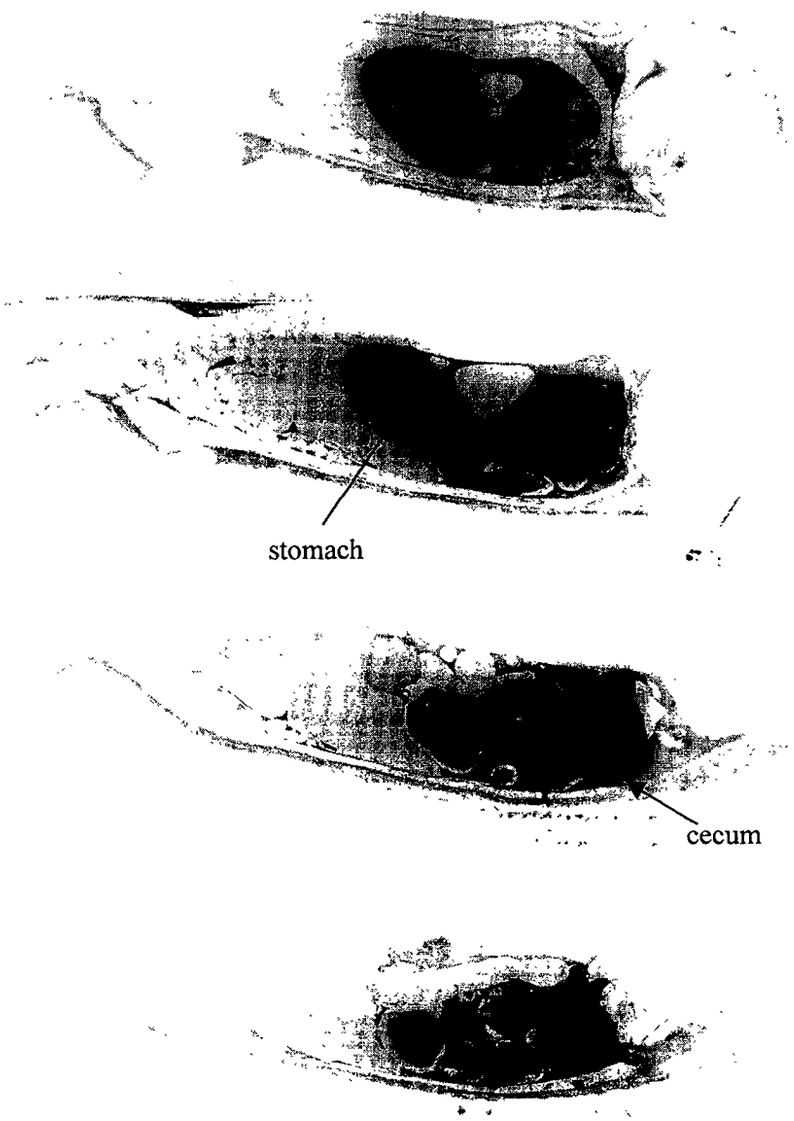
Whole Body Autoradiograph of Female Fischer 344 Rat 3 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9170 Female 3 hour

Figure 2

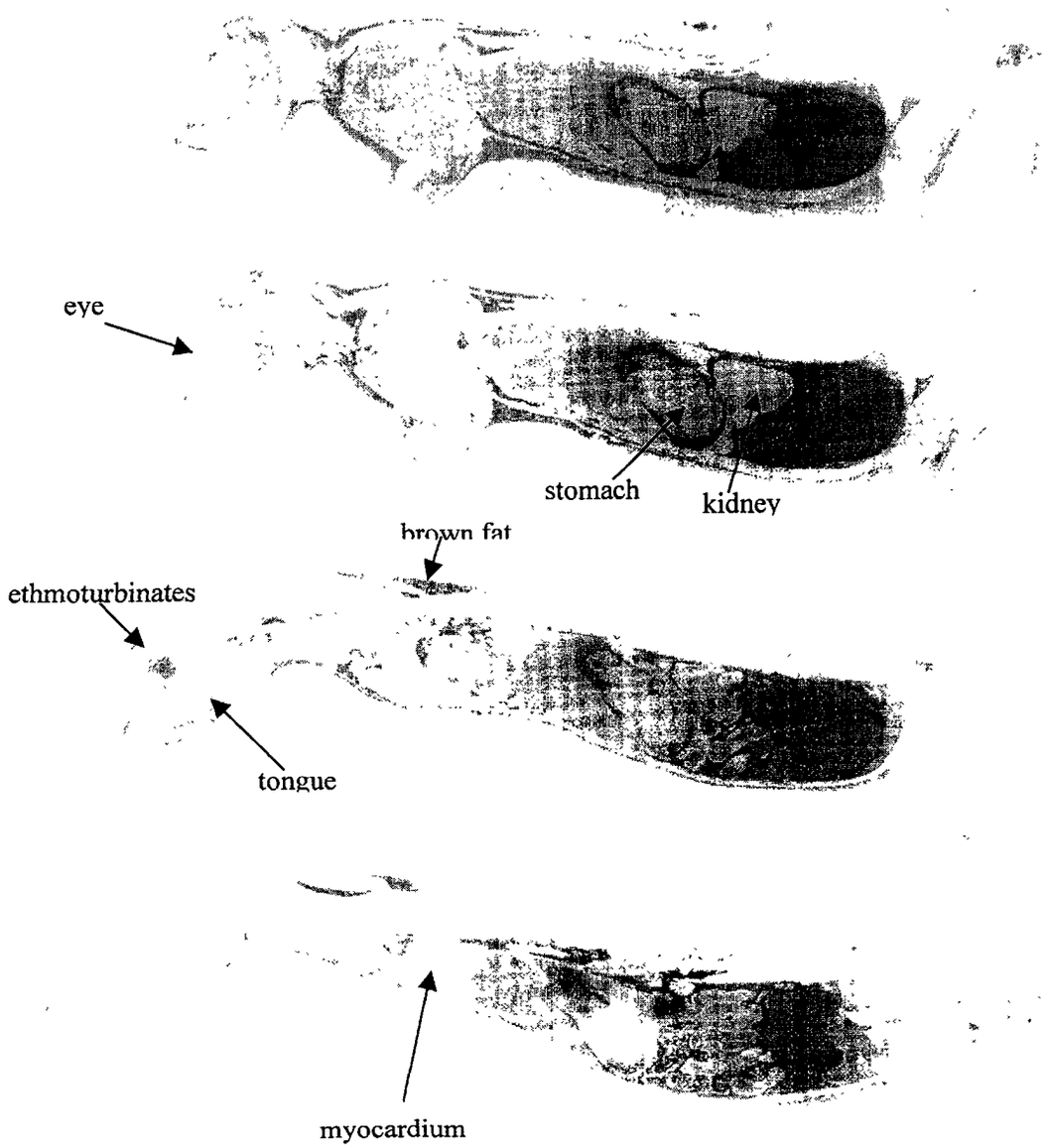
Whole Body Autoradiograph of Male Fischer 344 Rat 3 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9176 Male 3 hour

Figure 3

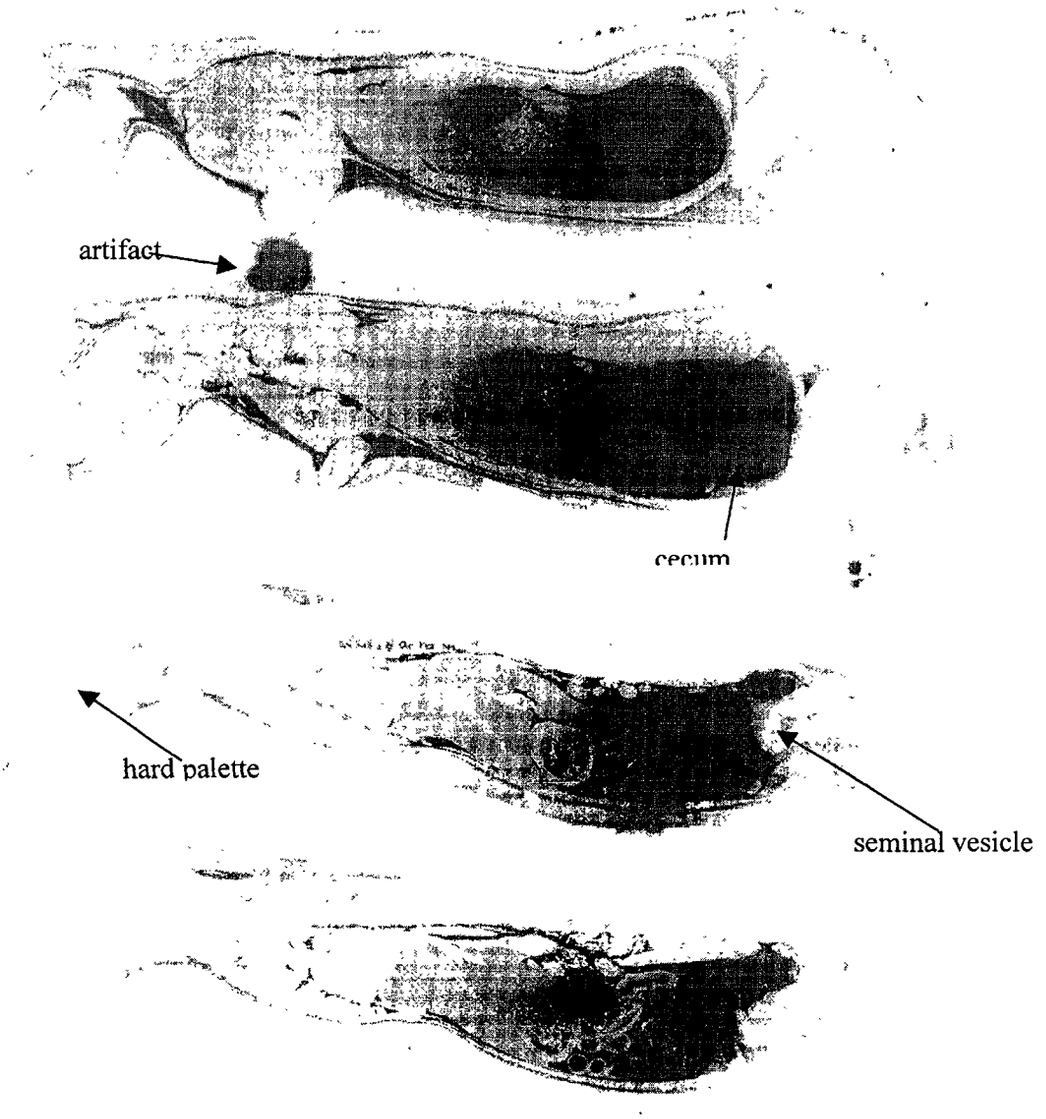
Whole Body Autoradiograph of Female Fischer 344 Rat 12 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9171 Female 12 hour

Figure 4

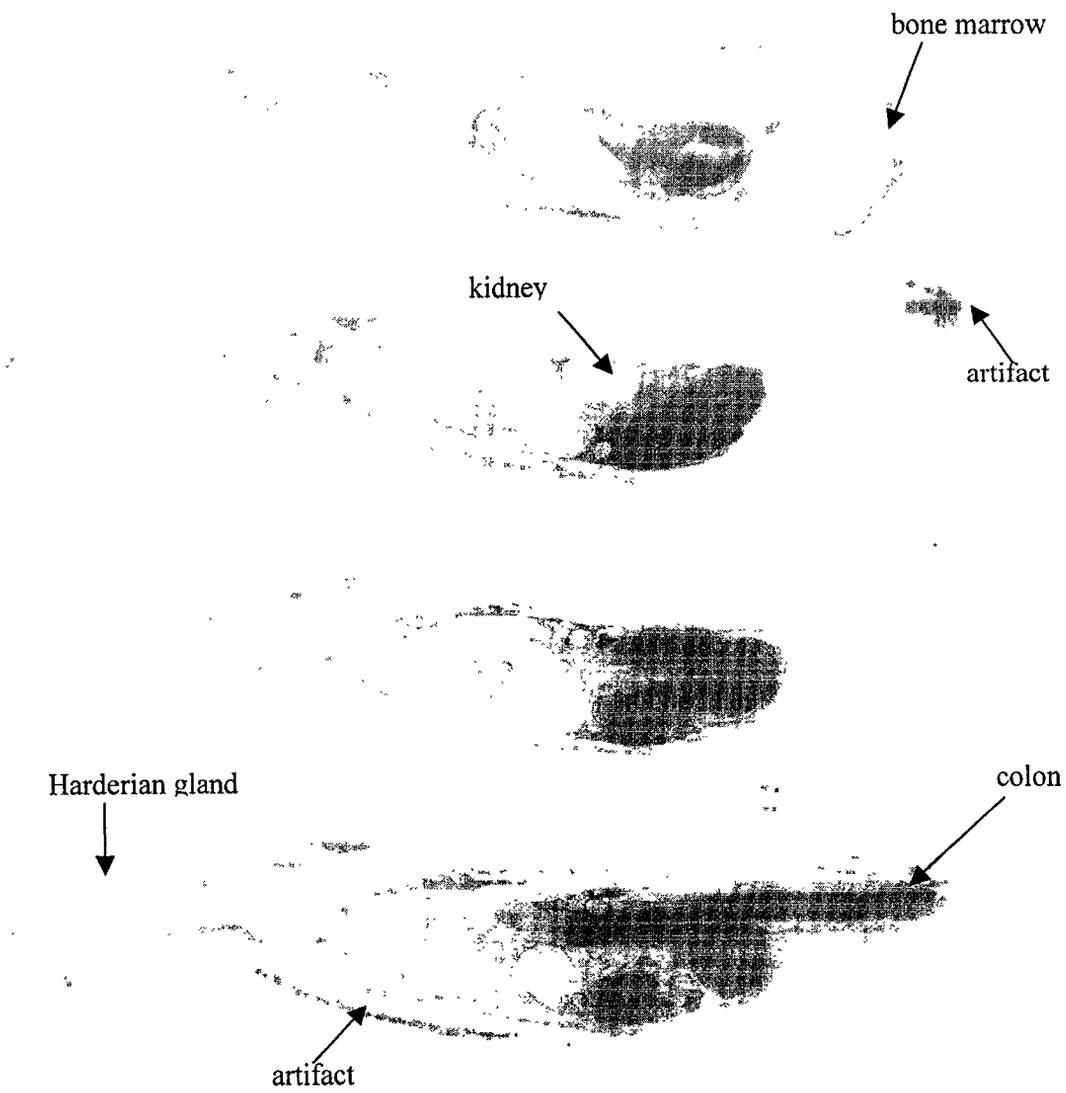
Whole Body Autoradiograph of Male Fischer 344 Rat 12 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9177 Male 12 hour

Figure 5

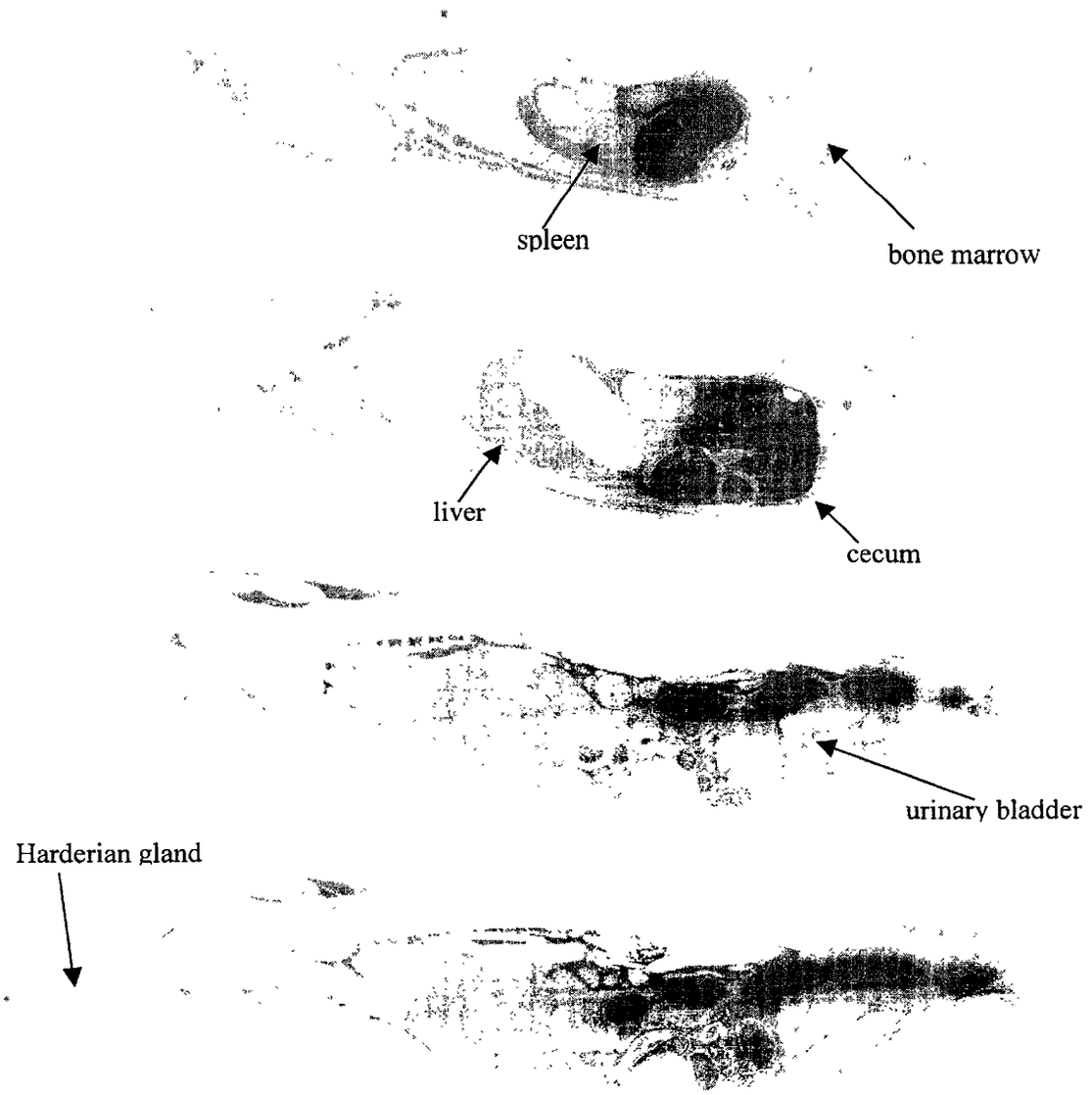
Whole Body Autoradiograph of Female Fischer 344 Rat 24 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9172 Female 24 hour

Figure 6

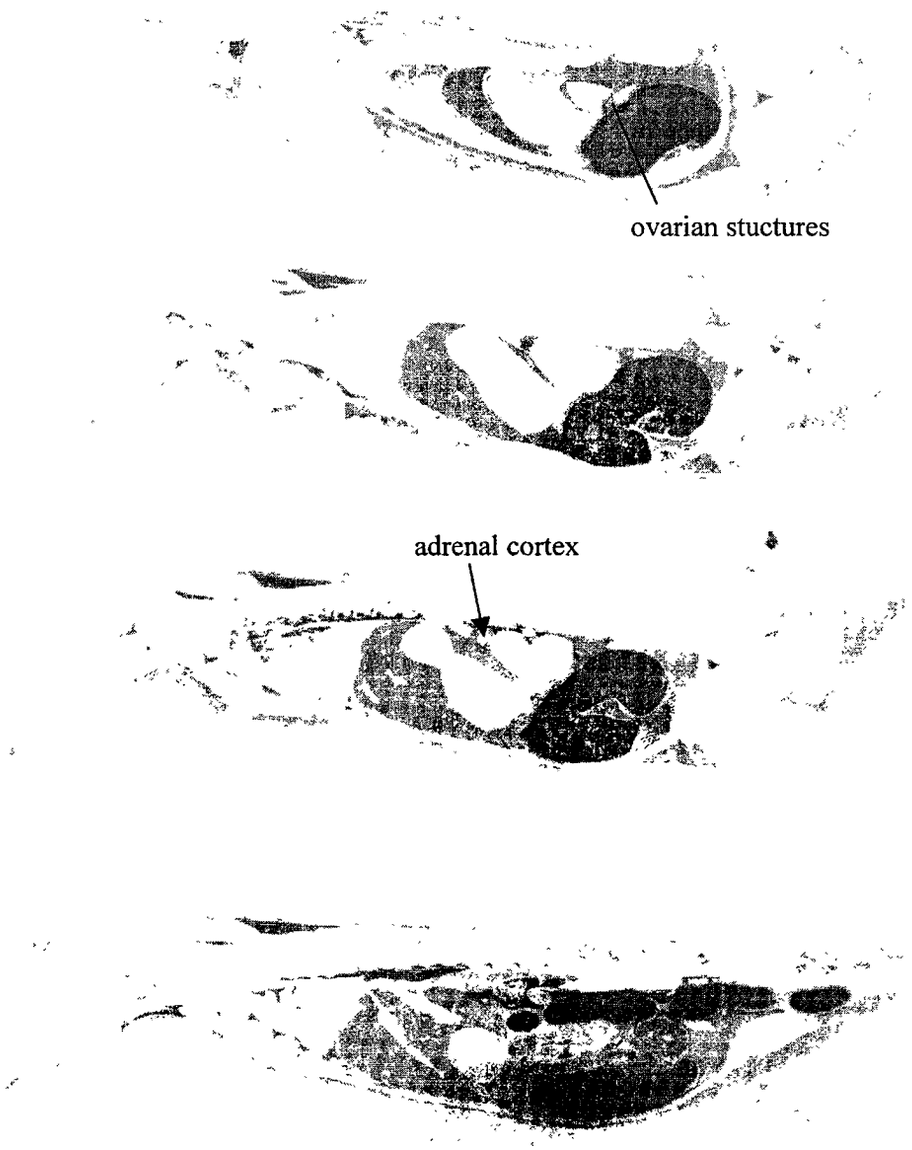
Whole Body Autoradiograph of Male Fischer 344 Rat 24 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9178 Male 24 hour

Figure 7

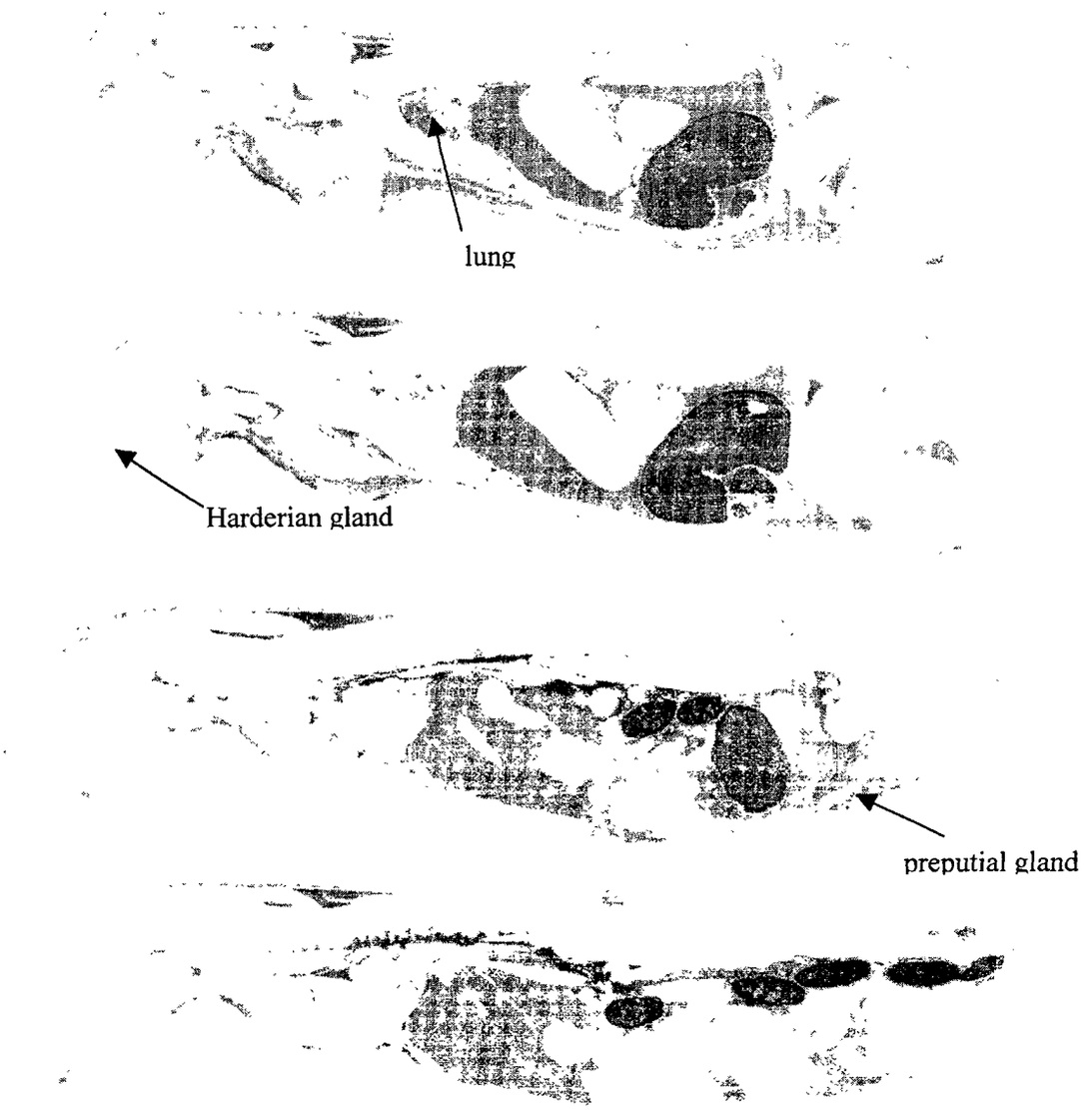
Whole Body Autoradiograph of Female Fischer 344 Rat 48 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9173 Female 48 hour

Figure 8

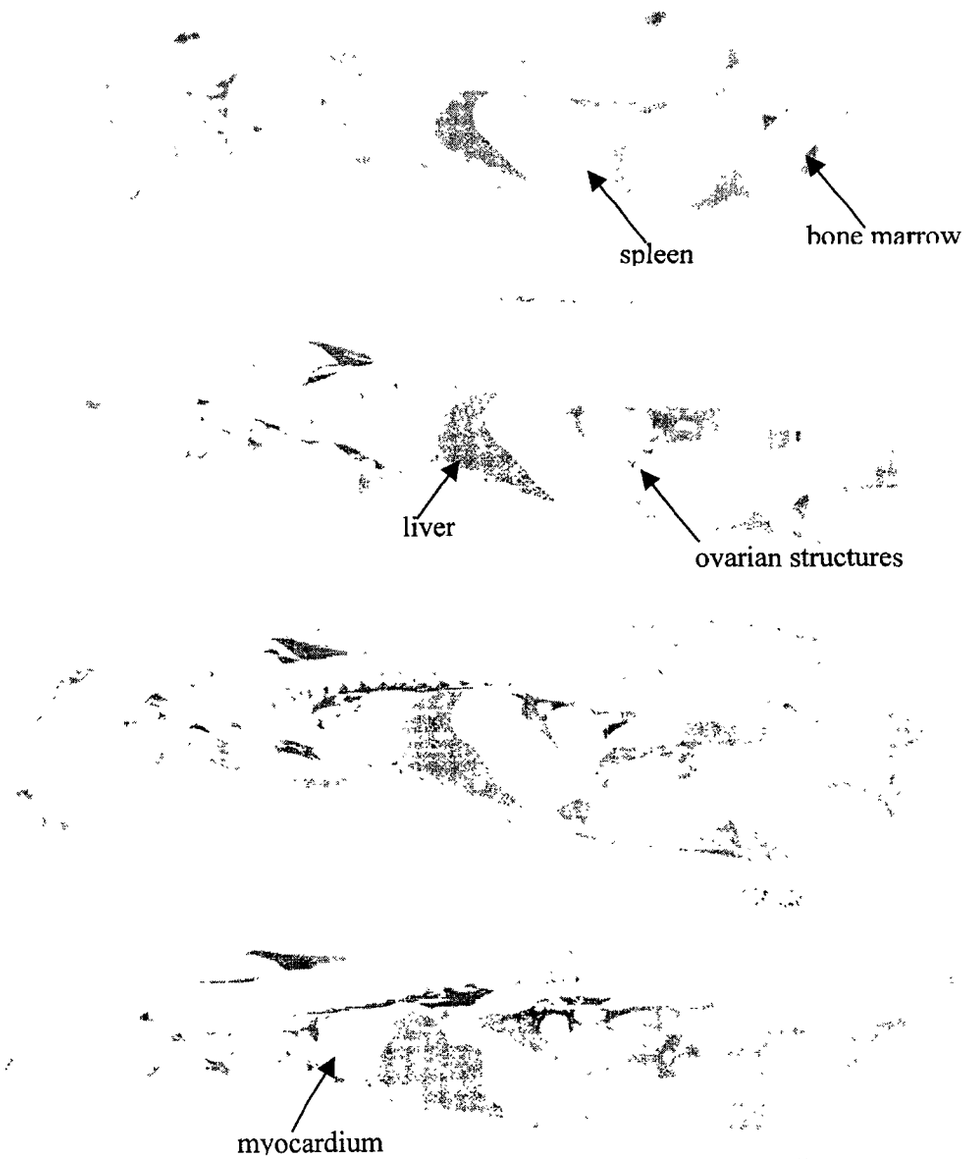
Whole Body Autoradiograph of Male Fischer 344 Rat 48 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9179 Male 48 hour

Figure 9

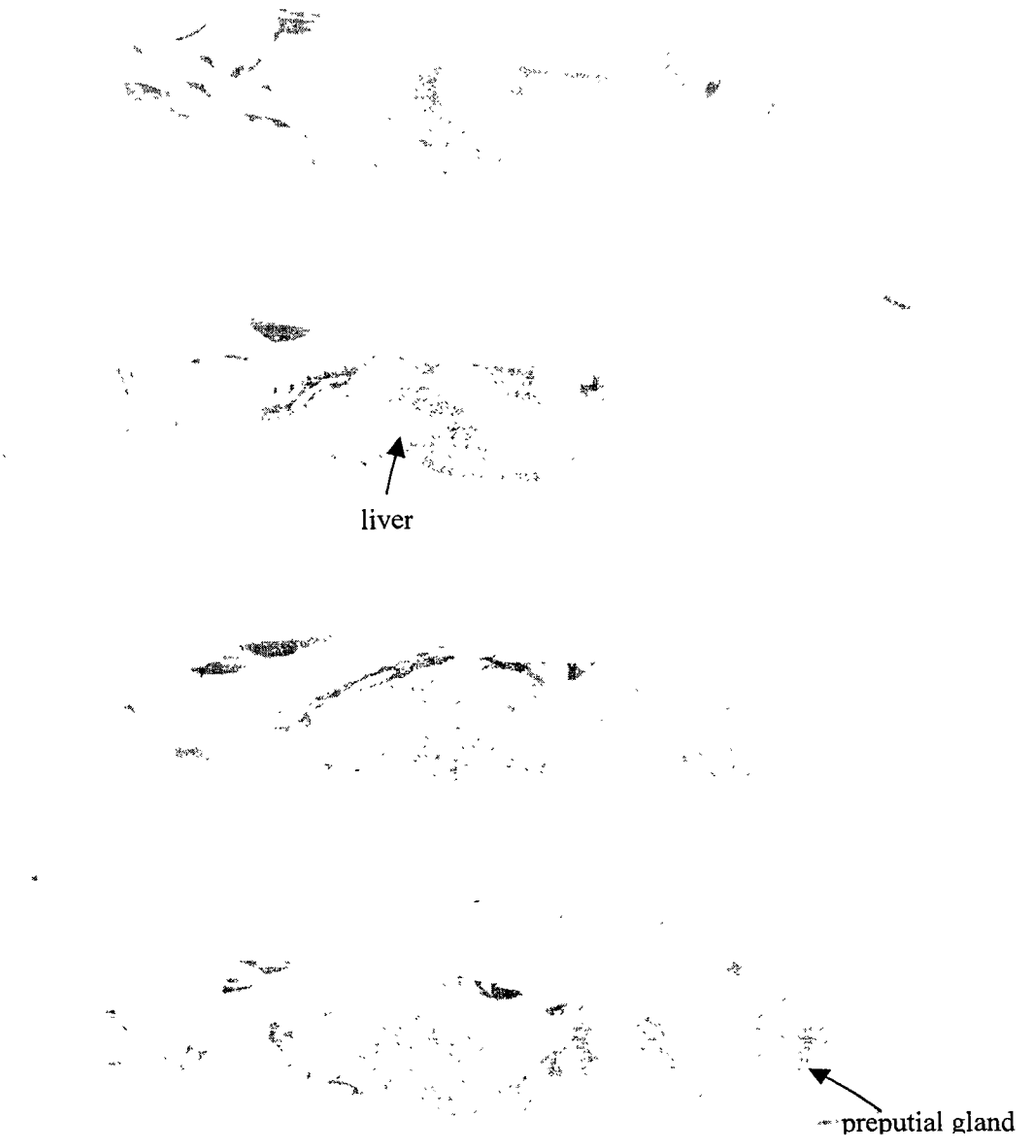
Whole Body Autoradiograph of Female Fischer 344 Rat 96 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9174 Female 96 hour

Figure 10

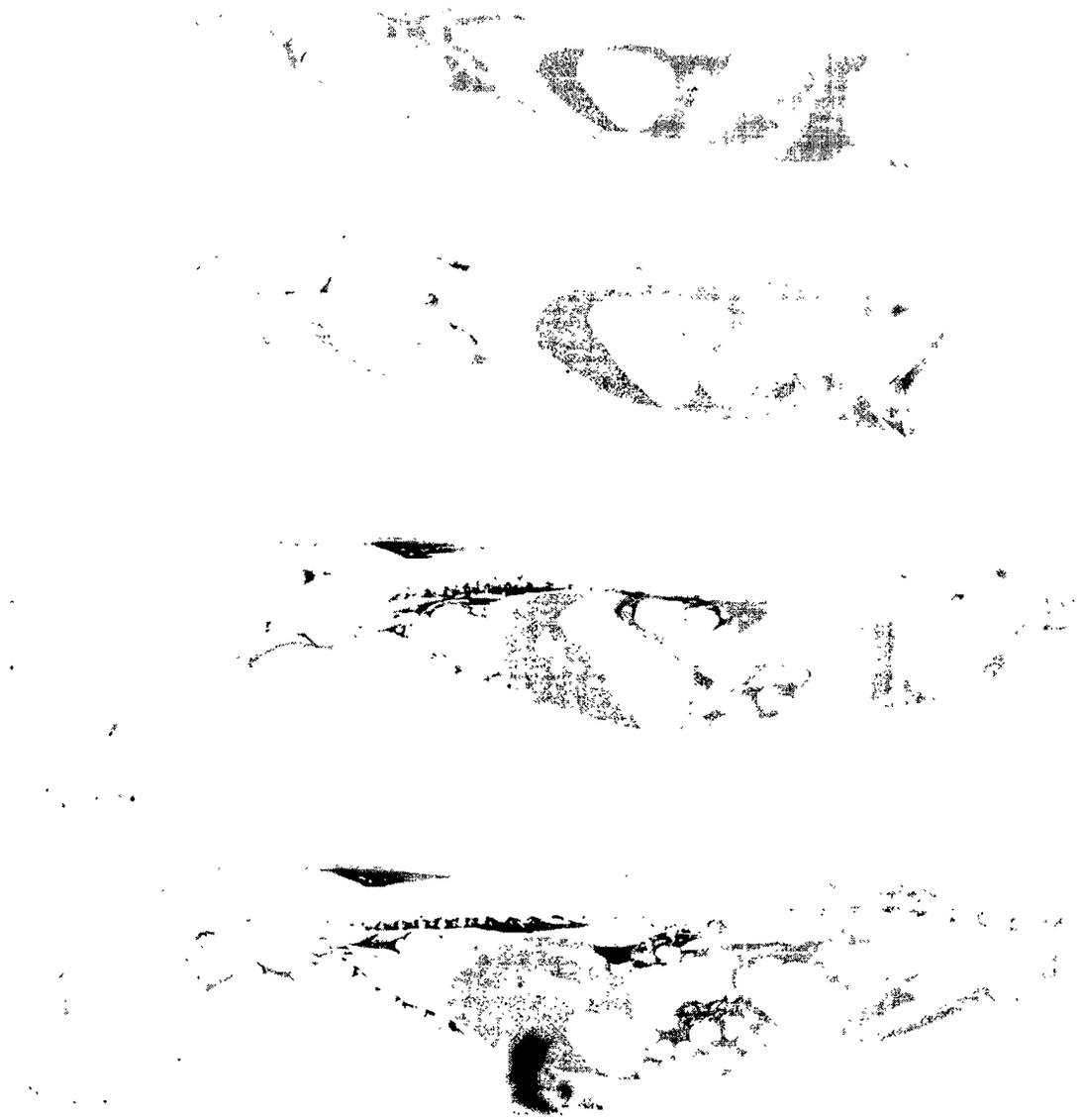
Whole Body Autoradiograph of Male Fischer 344 Rat 96 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9180 Male 96 hour

Figure 11

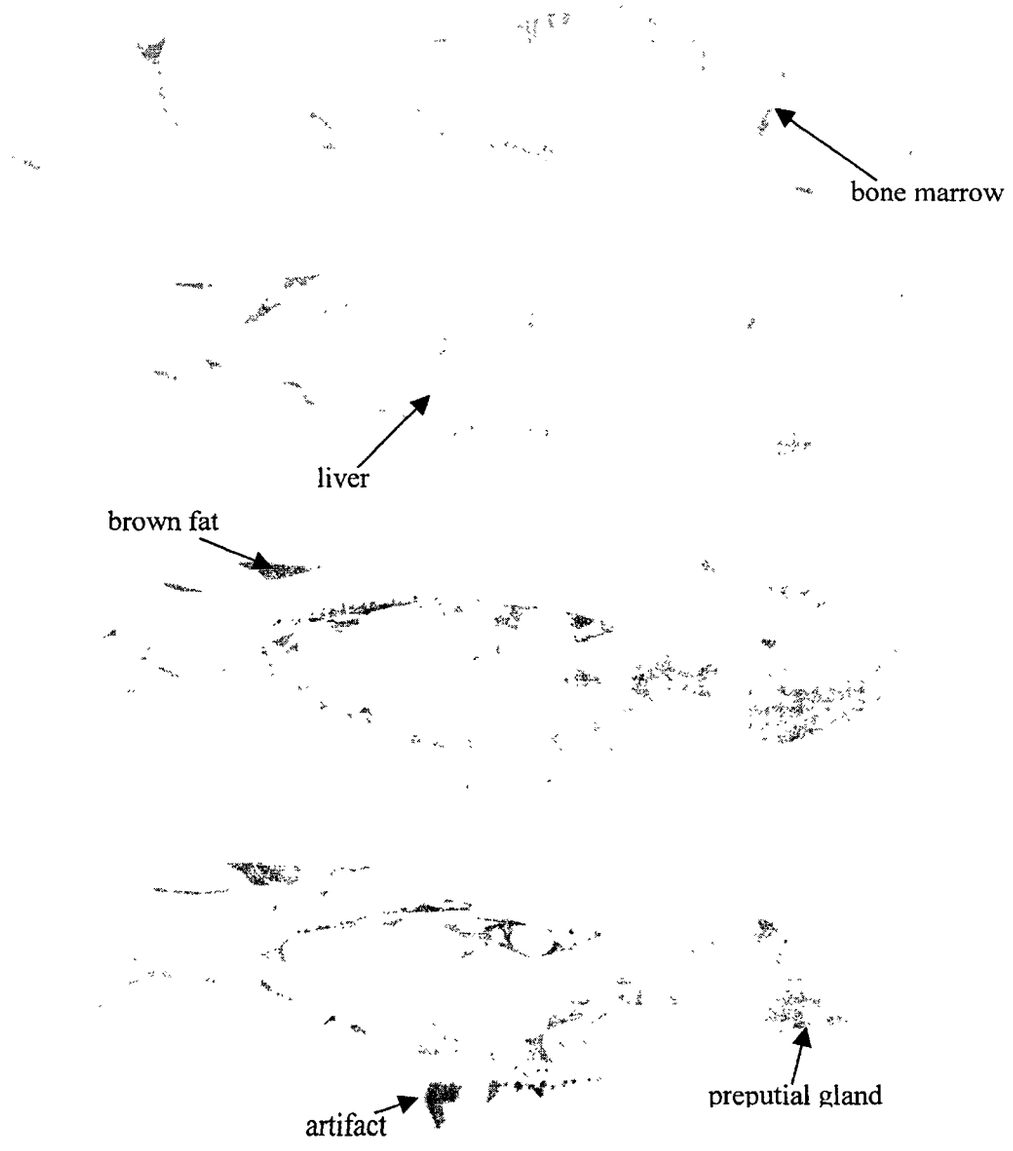
Whole Body Autoradiograph of Female Fischer 344 Rat 168 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



C9175 Female 168 hour

Figure 12

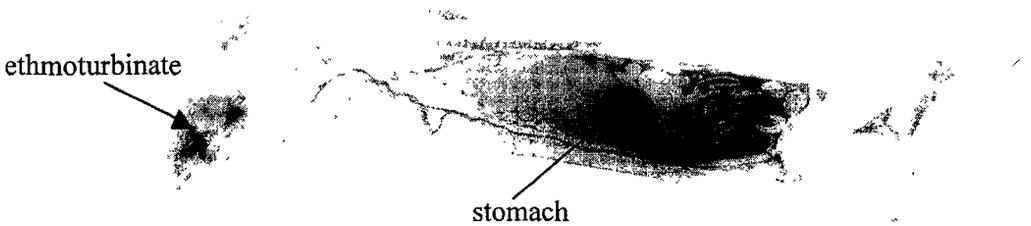
Whole Body Autoradiograph of Male Fischer 344 Rat 168 Hours Following Administration of a Single Oral Dose of D5 in Corn Oil



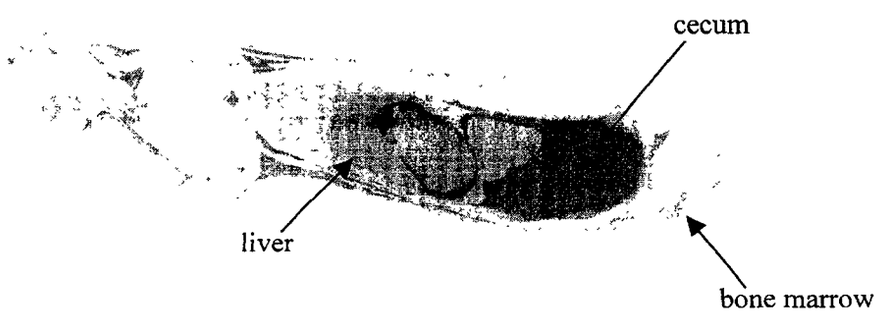
C9181 Male 168 hr

Figure 13

Representative Autoradiographs by Time Point of Female Fischer 344 Rats
Following Administration of a Single Oral Dose of D5 in Corn Oil



3 hours

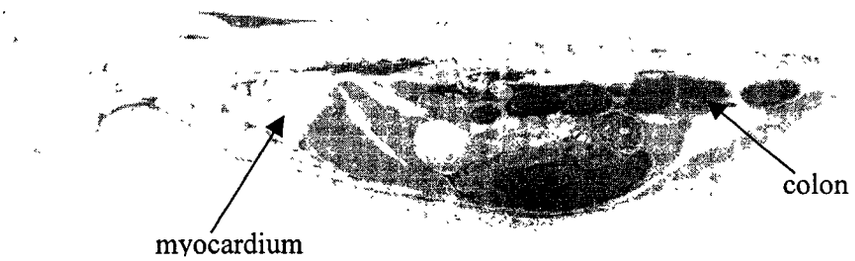


12 hours

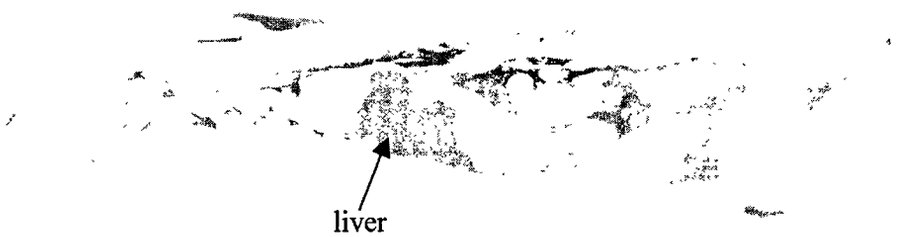
24 hours

Figure 13 (continued)

Representative Autoradiographs by Time Point of Female Fischer 344 Rats
Following Administration of a Single Oral Dose of D5 in Corn Oil



48 hours



96 hours

168 hours

Figure 14

Representative Autoradiographs by Time Point of Male Fischer 344 Rats Following Administration of a Single Oral Dose of D5 in Corn Oil

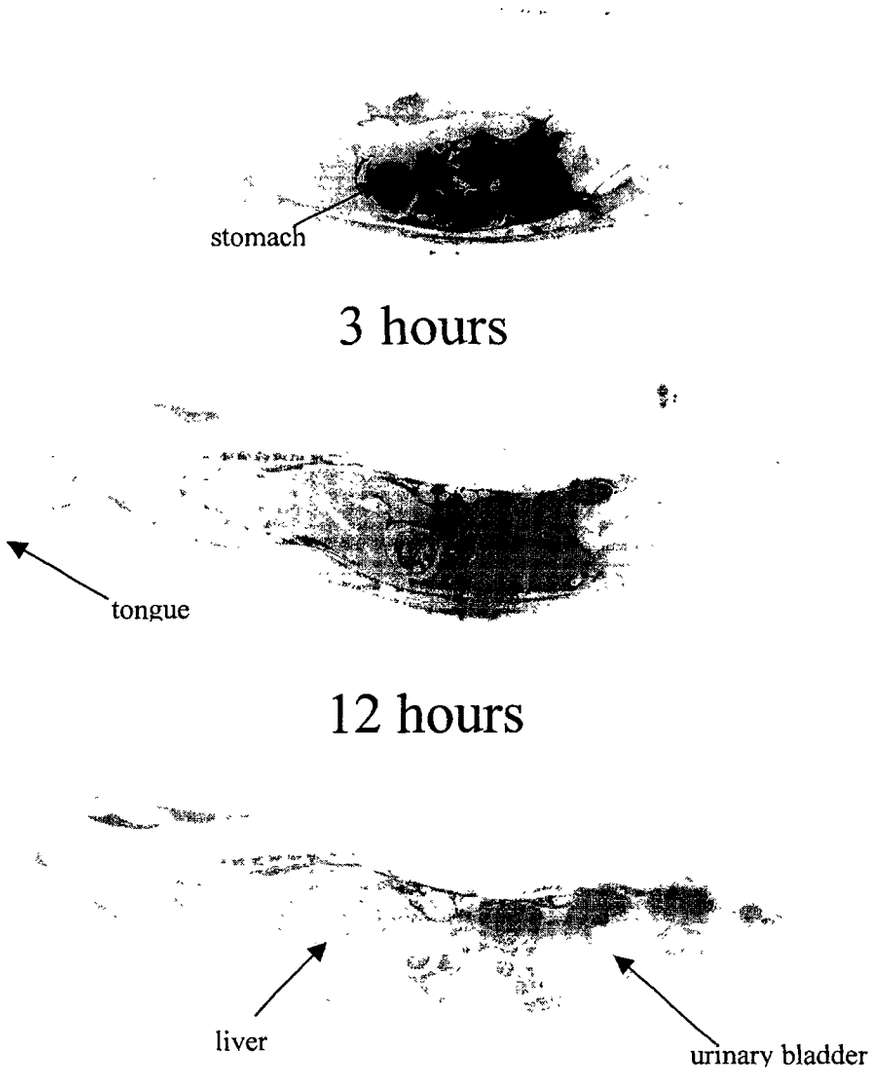
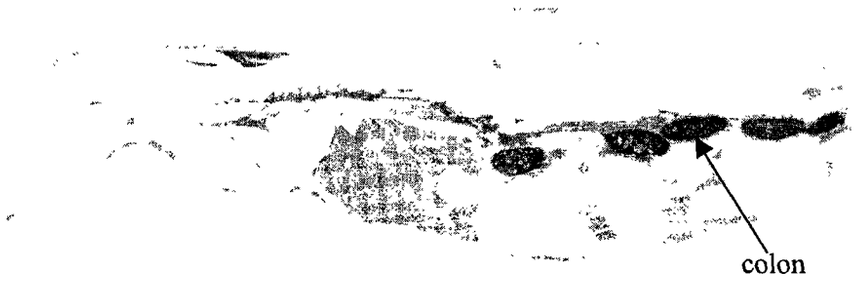


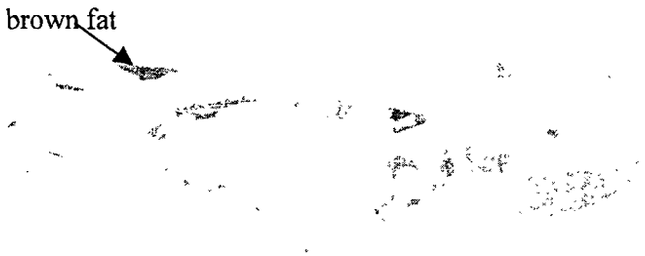
Figure 14 (continued)

Representative Autoradiographs by Time Point of Male Fischer 344 Rats
Following Administration of a Single Oral Dose of D5 in Corn Oil



48 hours

96 hours



168 hours

Manufacturer:

Dow Corning Corporation
PO Box 994
2200 West Salzburg Road
Midland, Michigan 48686-0994

For purposes of this TSCA For-Your-Information (FYI) submission, the general INTERNAL designation on the attached health and safety report is waived by Dow Corning.

If you require further information regarding this submission, please contact Michael Thelen, Manager of U.S. EPA Regulatory Affairs, at 989-496-4168 or at the address provided herein.

Sincerely,

Kathleen P. Plotzke

Kathleen P. Plotzke
Director, Health and Environmental Sciences
(989) 496-8046