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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, D₅)

Final Study Report:

Non-Regulated Study: Identification of Metabolites of
Decamethylcyclopentasiloxane in Fat Collected from Fischer 344 Rats Following
a Single Oral Dose

Dow Corning Corporation
2006-I0000-57011
December 20, 2006



303883

Manufacturer:

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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,

A handwritten signature in cursive script that reads "Kathleen P. Plotzke". The signature is written in black ink and is positioned above the printed name.

Kathleen P. Plotzke
Director, Health and Environmental Sciences
(989) 496-8046

**DOW CORNING CORPORATION
HEALTH AND ENVIRONMENTAL SCIENCES
TECHNICAL REPORT**

Report Number: 2006-I0000-57011

Title: NON-REGULATED STUDY: Identification of Metabolites of Decamethylcyclopentasiloxane in Fat Collected from Fischer 344 Rats Following a Single Oral Dose

HES Study Number: 9868-101

Test Substance: ¹⁴C-Decamethylcyclopentasiloxane (¹⁴C-D₅)

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Study Completion Date: December 20, 2006

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ABSTRACT

Decamethylcyclopentasiloxane (D₅) is a cyclic siloxane commonly used in a broad variety of consumer and industrial applications. Because of the diverse use of D₅ and the potential for human exposure, a comprehensive program was initiated to study the kinetics, metabolism, enzyme induction and toxicity of D₅ in rats after relevant routes of exposure. Two previous inhalation studies of D₅ with rats were conducted under this program where D₅ and total radioactivity were measured in various tissues following exposure.^{1,2} The results of these studies indicated that in addition to parent D₅, one or more metabolites were present in the fat. This study was conducted to confirm the presence of the metabolite(s), as well as to identify the metabolite(s). Although the previous studies were conducted following inhalation exposures, the oral route was chosen for this study to maximize the absorption of D₅ thereby maximizing the amount of radioactivity present in the fat. This would increase the probability of successful identification of metabolite(s).

Fat was collected from rats 24 hours following a single oral dose of ¹⁴C-D₅ in a corn oil carrier. The fat was then extracted with tetrahydrofuran (THF), and a metabolite profile of the fat extract was obtained using high pressure liquid chromatography with radiometric detection (HPLC/RAD). The profile indicated the presence of a metabolite as well as parent D₅ at sufficient levels of sensitivity. The metabolite was identified as nonamethylcyclopentasiloxanol (hydroxylated D₅) formed via oxidative demethylation. The structural assignment was based on GC-MS analysis of the THF fat extract by comparison to an authentic standard of hydroxylated D₅. The metabolite was also isolated using HPLC, and GC/MS analyses of the fractions were compared to the standards for conclusive identification.

APPROVAL SIGNATURES

This report consists of pages 1 through 27 including Tables 1 through 4 and Figures 1 through 7.

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20 - Dec - 2006

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Date

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20 Dec 2006

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STUDY INFORMATION

Study Initiation Date:	September 17, 2003
Experimental Starting Date (OECD):	September 23, 2003
Experimental Start Date (EPA):	September 24, 2003
Experimental Completion/Termination Date:	February 25, 2006
Study Completion Date:	December 20, 2006
Study Personnel:	Debra A. McNett Sudarsanan Varaprath Kelly McCracken

I. INTRODUCTION

In two previous inhalation studies of D₅ with rats, one or more metabolites were found to be present in the fat in addition to parent D₅.^{1,2} Oral gavage is a common and an accepted method of administration of test chemicals in pharmacokinetic and metabolism studies. The oral gavage route was chosen in this study over the inhalation route to maximize the level of absorption. The metabolites observed in the urine following inhalation exposures with D₅ and oral doses of D₅ is identical.^{1,2,7} Further, oral ingestion may also represent a potential route of exposure in the animal inhalation studies. It is possible that rats, when grooming themselves, may ingest some of the material that was deposited on the pelt during the inhalation exposure.^{1,2} This study was conducted to determine the formation of the metabolite(s) via the oral route, as well as to identify the metabolite(s).

II. OBJECTIVE

The objective of this study was to confirm the presence of a metabolite(s) and to determine the identity of any metabolite(s) present in fat following exposure to ¹⁴C-decamethylcyclopentasiloxane (¹⁴C-D₅).

III. TEST ARTICLE / SUBSTANCE / ITEM

Unlabeled

Identification:	Decamethylcyclopentasiloxane (D ₅) (supplied as Dow Corning® 1693 Fluid)
Lot Number:	LL014002
Expiration Date:	March 4, 2004 (In-life was terminated on 9-25-2003)
Source:	Dow Corning Corporation 2200 W. Salzburg Road Auburn, MI 48611
CAS Number:	541-02-6
Physical Description:	Colorless, odorless liquid
Stability:	Stable (as specified in MSDS)
Purity:	97.7%
Solubility:	Soluble in toluene, hexane, acetone, ethanol, tetrahydrofuran (THF), etc. ^{3,4}
Storage Conditions:	Room temperature (refer to MSDS)
Chemical Characterization:	HES Study No. 8824 ⁵
Archive:	An archive sample was retained

Radiolabeled

Identification: ^{14}C -Decamethylcyclopentasiloxane ($^{14}\text{C}\text{-D}_5$)

Reference Number: 001227D

Expiration Date: December 18, 2004 (In-life was terminated on 9-25-2003)

Specific activity: 5.758 mCi/g

Source: Dow Corning Corporation
2200 W. Salzburg Road
Auburn, MI 48611

Physical Description: Colorless, odorless liquid

Stability: Stable (as specified in MSDS)

Radio Chemical Purity: 99.76%

Solubility: Soluble in toluene, hexane, acetone, ethanol, tetrahydrofuran (THF), etc.^{3,4}

Storage Conditions: Stored at -80 ± 10 °C

Chemical Characterization: HES Study No. 9551⁶

Archive: An archive sample was retained.

IV. CARRIER

Identification: Corn oil
Lot No.: 86H0059
Expiration Date: 7 days after dispensing for this study.
Source: Sigma, St. Louis, MO
Physical Description: Yellow, clear liquid
Stability: Stable
Storage Conditions: Room temperature

V. TEST SYSTEM

Species: Rattus norvegicus
Strain: Fischer 344
Source: Charles River Laboratories, Inc.
P.O. Box 176
Shaver Road
Portage, MI 49081
Age: 8 weeks at dosing
Body weight: Females: a minimum of 125 g at dosing
Sex: 6 Females (nulliparous and nonpregnant)
Number used on study: 6
Number ordered: 6
Number of groups: 2
Permanent identification: Ear tags

Justification for Selection of Test System

This species and strain of animal is recognized as appropriate for toxicity studies and is recommended in EPA test guidelines. Fischer 344 female rats have previously been used in pharmacokinetic and metabolism studies of various silicone materials, and data obtained in those

studies can be used as historical data. The choice of a single sex is sufficient since the presence of unidentified metabolite(s) were demonstrated in both males and females.

Method of Randomization

After release from quarantine/acclimation, rats were assigned to test groups based on a weight stratified randomization process. Disposition of all animals not utilized in the study was maintained on file at the Testing Facility. All animals were within $\pm 20\%$ of the mean body weight for the groups.

Housing and Maintenance

Animal Receipt and Quarantine/Acclimation

Upon receipt, animal resource personnel inspected each animal. Animals were quarantined/acclimated for six days. During the quarantine period, animal resource personnel observed each animal at least once daily. The veterinarian, or designee, examined all animals. All animals were judged to be in good health and suitable as test animals and were released from quarantine/acclimation.

Animal Housing

Animals were individually housed in suspended wire-mesh cages, elevated above fecal pans containing Bed-O'Cobs[®] bedding, during quarantine/acclimation period and during the in-life phase of the study. The cages and bedding/fecal pans were routinely cleaned consistent with good husbandry practices.

Environmental Conditions

Animals were housed in an environmentally controlled animal room (12-hour fluorescent-light/dark cycle, 19.42-22.09°C, and 28-55% relative humidity), throughout the in-life phase of the study. Temperature and humidity were monitored continuously, recorded every 15 minutes using a HOBO[®] Data Logger (Onset Computer, Bourne, MA; software: BoxCar[®] Pro 4.3.1.1), and manually recorded twice daily on weekdays and at least once per day during weekends.

Basal Diet

Certified Rodent Diet #5002, PMI[®] Nutritional International Inc., St. Louis, MO, was provided *ad libitum* during the quarantine/acclimation period and throughout the study. Manufacturer's periodic analyses of the certified feed for the presence of heavy metals and pesticides, maintained on file at the testing facility, was reviewed by the Study Director to ensure that no contaminants were present in concentrations that would be expected to affect the outcome of the study.

Drinking Water

Municipal water, further purified by reverse osmosis, was available *ad libitum* via an automatic watering system. Water availability was monitored routinely and also analyzed on a semi-annual basis. To ensure that no contaminants were present at a concentration expected to interfere with the integrity of the study, the Study Director reviewed the most recent analysis results maintained on file at the testing facility.

VI. 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 Institutional Laboratory Animal Care and Use Committee (LACUC).

VII. EXPERIMENTAL DESIGN

A. Route and Rationale of Test Article Administration

1. **Route:** Test article was administered by oral gavage as a single dose.
2. **Rationale:** This route is an accepted method of administration of test article in pharmacokinetics and metabolism studies.

B. Dosing solution

1. **Preparation**

The dosing solution was prepared in corn oil to deliver a target of 0.68 mCi radioactivity/kg body weight, and nominal dose of 1000 mg D₅/kg body weight in 10 mL dosing solution/kg body weight. Radiolabeled D₅ was diluted with unlabeled D₅ to achieve a radioactivity concentration of approximately 68 µCi/mg D₅, and then added directly into corn oil and mixed to achieve a concentration of 104 mg ¹⁴C-D₅/g of dosing solution and specific activity of 71 µCi/g of dosing solution. The dosing solution was prepared two days prior to use. Stability and homogeneity for six days of storage of a dosing solution of D₅ in corn oil was demonstrated previously.⁷

2. **Analysis**

The radioactivity concentration (specific activity) and homogeneity of the dosing solution was measured by liquid scintillation analysis on the day prior to initiation of dosing by taking three aliquots from three separate locations in the dose solution and diluting in tetrahydrofuran (THF). Radiochemical purity of the ¹⁴C-D₅ in corn oil dosing solution was also evaluated the day prior to dosing by analyzing the THF dilutions by high performance liquid chromatography with radiometric detection (HPLC/RAD).

3. **Storage conditions**

The dosing solution was stored at a temperature not higher than room temperature.

C. Organization of Test Groups and Dosage Levels

Group ID	Number of animals /Sex/ Group	Treatment	Dosage level (mg T.A./kg BW)	Volume of dosing solution (mL d.s./kg BW)	Concentration of Dosing Solution (mg T.A./mL d.s.)	Exposure duration (Sacrifice Time Points)
1	1F	Corn oil	0	10	0	24 hours
2	5F	¹⁴ C-D ₅ in Corn Oil	1000	10	100	24 hours

d.s.= dosing solution T.A. = test article BW = body weight
F = female

D. Treatment Regimen and Key Events

1. Treatment Regimen

On the day of dosing, all animals were weighed in order to calculate individual doses based on body weight. A nominal dose of 1000 mg ¹⁴C-D₅/kg body weight was administered by oral gavage. A single dose of ¹⁴C-D₅ was delivered in corn oil to animals in group 2 using a curved stainless steel feeding needle. The volume of dosing solution was targeted at 10ml/kg body weight. The control animal (group 1) received a single dose of corn oil using a curved stainless steel feeding needle. The doses were determined gravimetrically. Immediately after dosing, the animals were returned and housed in the stainless steel metabolism cages for a maximum of 24 hours.

2. Key Events/Activities

Study day 1: Randomization and eartagging
Study day 2: Dose administration
Study day 3: Sample collections

E. Method of Euthanasia/Terminal Procedure

1. Scheduled animal death

Animals were euthanized by CO₂ asphyxiation until respiration ceased.

F. Test System observation

1. Mortality/Morbidity/Moribundity

All animals were observed at least once daily in their cages for mortality, morbidity, and moribundity by study personnel throughout the completion of the in-life phase of the study. There were no animals found dead.

VIII. PARAMETERS MEASURED

1. Radioactivity content in fat and feces.
2. The radioactive metabolite profile in the extracts of fat.
3. The radioactive metabolite profile in the extracts of feces.

Sample Collection

Immediately after dose administration, the animals were individually placed in stainless steel metabolism cages for continuous collection of feces until 24 hours following dosing when the animals were sacrificed and collection of fat samples was completed. While collecting feces, each jar was maintained on dry ice. At 24 hours, the jars were removed from the cage, capped, and maintained on dry ice or in an $-80 \pm 10^\circ\text{C}$ freezer until processing. At 24 hours following dosing, the animals were euthanized as described previously and the maximum amount of peri-renal fat possible was collected into a 20 mL glass vial. The fat samples were stored on ice immediately following necropsy until all animals were necropsied. The samples were then stored in an $-80 \pm 10^\circ\text{C}$ freezer until processing.

Sample Processing and Analysis

Fat

The fat samples were extracted with tetrahydrofuran (THF) and an aliquot of the extracts were taken and added to appropriate LSC cocktail and analyzed for radioactivity content with a liquid scintillation counter. THF extractions were done according to a method previously validated in a separate study.¹ Extracts of control fat were used to determine background levels of radioactivity. A qualitative metabolite profile analysis of the THF extracts was done using HPLC with radiochemical detection (RAD) in order to evaluate the potential metabolites that may be present in fat extracts. The HPLC/RAD conditions used for metabolite profiling can be found in **Table 1**. Analysis by gas chromatography/mass spectrometry (GC/MS) was performed to further elucidate the identification of the metabolite found in the fat extracts. The GC/MS conditions utilized in determining the structural identity of the metabolite found in fat are presented in **Table 2**. In addition, metabolite identification was further confirmed by fractionation of HPLC analyses for the peaks of interest with subsequent GC/MS analysis. The HPLC fractions were pooled and concentrated prior to GC/MS analysis in order to have sufficient radioactivity.

Feces

Feces was first homogenized with Milli-Q water. Aliquots of the fecal homogenates were extracted with tetrahydrofuran (THF) in the same manner as previously described for fat. The THF extracts of the fecal homogenates were then analyzed in a manner similar to fat extracts for evaluation of potential metabolite(s) present in the feces.

Sample Identification and Storage

Samples collected were identified by study number, test system or specimen number, target time point if applicable, identity/name of sample, date of collection and storage conditions.

Samples were stored under the following conditions:

Feces	-80 ± 10°C
Fat	-80 ± 10°C
THF Extracts	5 ± 4°C

IX. RESULTS AND DISCUSSION

Dose Verification

The specific activity of the $^{14}\text{C-D}_5$ corn oil dose solution was determined on the day prior to dosing. Three aliquots of the dose solution were sampled from different locations in the dose solution container, diluted with tetrahydrofuran, and then analyzed by LSC and HPLC/RAD. The mean observed specific activity of $^{14}\text{C-D}_5$ in corn oil was determined to be 71 $\mu\text{Ci/g}$ of dose solution. The relative standard deviation between the samples was 0.20%; therefore, the dose solution was determined to be homogeneous. The results of the HPLC/RAD analysis indicated that the radiochemical purity of the dose solution was adequate at 99.9%. The dose solution analysis results are summarized in **Table 3**. The HPLC conditions utilized are presented in **Table 1**. The individual animal body weight and dosing results are presented in **Table 4**. The average dose delivered to rats in group 2 was 977 mg D_5/kg body weight and 0.67 mCi/kg.

Qualitative Metabolite Profile Analysis

Figure 1 depicts example chromatograms of a control fat extract, a fat extract from a $^{14}\text{C-D}_5$ treated rat, and a $^{14}\text{C-D}_5$ in THF solvent standard. Fat taken from rats dosed with $^{14}\text{C-D}_5$ was extracted into THF. The metabolite profile resulting from the HPLC/RAD analysis of the THF extract contained two peaks. The largest peak corresponded to parent D_5 and accounted for approximately 80% of the radioactivity. The second peak that accounted for approximately 20% of the radioactivity eluted before D_5 on the reverse phase column indicating that the metabolite was slightly more polar than D_5 . The concentration of radioactivity present in the treated fat samples averaged 0.11 $\mu\text{Ci/g}$ fat corresponding to 160 μg equivalents of D_5/g fat. The profile is consistent with preliminary metabolite identification method development performed in the inhalation studies. The level of radioactivity obtained in fat samples following the inhalation exposures was not conducive for definitive identification, however, it was determined that the metabolic radioactivity was fairly non-polar and eluted just prior to parent D_5 by HPLC.² It has been shown that the metabolites observed in the urine following inhalation exposures with D_5 and oral doses of D_5 are identical.^{1,2,7} Hence, it is a safe assumption that the metabolite in fat following the different routes of exposure is the same.

Feces collected in the first 24 hours following dosing was also subjected to THF extraction. Analysis of the fecal extracts by HPLC/RAD indicated the presence of only parent D₅ at the sensitivity levels afforded by the analytical method. **Figure 2** contains an example chromatogram of a ¹⁴C-D₅ treated feces extract.

Metabolite Identification

The fat extracts were also analyzed by GC/MS in order to obtain mass spectral structural identification of the metabolite peak present. A total ion chromatogram (TIC) of a control fat extract with comparison to a TIC of a treated fat extract is shown in **Figure 3**. The treated fat extract TIC contained four peaks that were not present in the control fat extract chromatogram. The largest peak at a retention time of 7.09 minutes had a mass spectrum matching that of a standard of D₅ (see **Figure 4**). The next largest peak at a retention time of 8.02 minutes had the mass spectrum displayed in **Figure 5**. After observation of the fragmentation pattern, it was tentatively determined that the metabolite was nonamethylcyclopentasiloxanol (hydroxylated D₅, D₄D'OH). A standard of hydroxylated D₅ was obtained and its mass spectrum and GC/MS retention time was compared to that of the peak present at 8.02 minutes in the treated fat extract. The comparison confirmed the identity of the metabolite to be hydroxylated D₅. In order to further confirm that the metabolite peak present in the HPLC/RAD chromatogram was indeed hydroxylated D₅, HPLC fractionation was performed whereby the metabolite peak was collected as well as the D₅ peak. The fractions were concentrated under a nitrogen stream and subsequently analyzed in GC/MS under the same conditions as described previously. The concentrated metabolite fraction also eluted by GC/MS at 8.02 minutes and had the same mass spectrum as the authentic standard of hydroxylated D₅ (**Figure 6**). The D₅ HPLC fraction also had a mass spectrum consistent with D₅. The presence of hydroxylated D₅ in the fat from D₅ treated rats is consistent with this metabolite identification in urine from D₅ treated rats (Varaprath, et. al., 2003). This metabolite also lends further evidence to the proposed mechanism of metabolism of D₅ whereby enzymatic oxidation occurs at a methyl group followed by rearrangement and hydrolysis to give hydroxylated D₅ (Varaprath, et. al., 2003). It is of interest to note that the other two peaks present by GC/MS analysis but not by HPLC/RAD could possibly be D₄T and hydroxymethyl D₅. The structures of these possible metabolites can be found in **Figure 7**. Standards of these metabolites could not be obtained precluding definitive confirmation of these two peaks.

X. CONCLUSIONS

A metabolite was identified in fat from ¹⁴C-D₅ dosed rats as nonamethylcyclopentasiloxanol (hydroxylated D₅). The presence of the metabolite was consistent with results from an inhalation study with D₅ showing metabolite(s) in fat. The identification of hydroxylated D₅ is also consistent with the proposed mechanism of D₅ metabolism in the rat.⁸

XI. ARCHIVE

All raw data, the protocol, amendments, deviations, correspondence, study authorization form and the final report are maintained in the HES archives, Dow Corning Corporation, 2200 W. Salzburg Road, Auburn, Michigan 48611.

XII. REFERENCES

1. HES Study No. 9105. Absorption, Distribution, Metabolism, and Excretion (ADME) Study of ¹⁴C-Decamethylcyclpentasiloxane (D₅) in the Rat Following a Single Nose-only Vapor Inhalation Exposure to ¹⁴C-D₅ at Two Dose Levels. HES Report No. 2001-I0000-50459.
2. HES Study No. 9603. Disposition of Decamethylcyclpentasiloxane (D₅) in Male and Female Fischer 344 Rats Following a Single Nose-Only Vapor Inhalation Exposure to ¹⁴C-D₅. Report in Progress.
3. Angeloti, N. C. 1991. In *The Analytical Chemistry of Silicones*; A.L. Smith, ed.; Analysis of Polymers, Mixtures and Compositions (John Wiley & Sons, Inc. New York, NY) P:49.
4. Varaprath S., K.L. Salyers, K.P. Plotzke and S. Nanavati. 1998. Extraction of Octamethylcyclotetrasiloxane and its Metabolites from Biological Matrices. *Analytical Biochemistry*, 256: 14-22.
5. HES Study No. 8824. Characterization of Decamethylcyclpentasiloxane. HES Report No. 1997-I0000-43682.
6. HES Study No. 9551. Characterization of 14C-Decamethylcyclpentasiloxane (14C-D₅, Lot No. 001227). HES Report No. 2001-I0000-50104.
7. HES Study No. 9550. Disposition of ¹⁴C-Decamethylcyclpentasiloxane (D₅), in Fischer 344 Rats when Delivered in Various Carriers Following the Administration of a Single Oral Dose. HES Report No. 2003-I0000-52391.
8. Varaprath, S., McMahon, J. and Plotzke, K.P. 2003. Metabolites of Hexamethyldisiloxane and Decamethylcyclpentasiloxane in Fischer 344 Rat Urine – a Comparison of a Linear and Cyclic Siloxane. *Drug. Metab. Dispos.* 31: 206-214.

Table 1. HPLC/RAD Conditions

Instrument:	System SYS015 Hewlett Packard 1050 High Performance Liquid Chromatograph/Packard Radiomatic FLO-ONE Detector		
Column:	Phenomenex C-18, 5 μ m, 150 x 4.6 mm		
Mobile Phase:	A: Water B: 50:50 Acetonitrile:Tetrahydrofuran		
Gradient:	Time (min)	%A	%B
	0	100	0
	20	100	0
	40	0	100
	60	0	100
	65	100	0
80	100	0	
Injection:	50 μ L injection		
Flow Rate:	HPLC at 1.0mL/min		
	Radiomatic at 3.0mL/min		
Detection:	500uL liquid cell, Liquid Scintillation Cocktail: Ultima Flo M at 3.0mL/min		

Table 2. GC/MS Conditions

Instrument:	System SYS011 Hewlett Packard 6890 Gas Chromatograph/ Hewlett Packard 5973 Mass Spectrometer
Column:	Agilent HP-5MS, 30m x 0.25 mm x 0.25µm film thickness
Carrier:	Helium, Constant flow, 8.7 psi at 70°C
Oven Temperature Program:	70°C (hold 3 minutes) to 210°C at 17°C/minute to 300°C at 30°C/minute (final hold 1.0 minute); total run time 15.24 minutes
Inlet/Injection:	Split 15:1, Temperature 250°C, 1µL injection
Mass Scan Range:	35-500 atomic mass units

Table 3. ¹⁴C-D₅ Corn Oil Dose Solution Analysis Results

¹⁴C-D₅ Corn Oil Dose Solution Radiochemical Purity Verification

	¹⁴ C-D ₅ % of Rad	Impurity 1 % of Rad
Injection 1	100.00	
Injection 2	100.00	
Injection 3	99.81	0.19
Average =	99.9	0.19
std dev. =	0.1	N/AP

¹⁴C-D₅ Corn Oil Dose Solution Specific Activity and Homogeneity

Date Prepared	Date Analyzed	Aliquot ID	Observed Radioactivity Concentration (mCi/g)	Mean	Standard Deviation	% Relative Standard Deviation
				Observed Radioactivity Concentration (mCi/g)		
9/22/2003	9/23/2003	92306-TOP	0.071	0.071	1.39E-04	0.20%
		92303-MID	0.071			
		92303-BOT	0.071			

Table 4. Individual Animal Dosing Results

Animal Number	Group Number	Sex (M/F)	Body Wt. (g)	Actual Dose Wt. (g)	Calculated Dose (mg D5/kg)	Calculated Dose (mCi/kg)
D1007	1 (Corn oil)	F	142.80	1.3535	0	0
D1008	2	F	148.30	1.3374	938	0.64
D1009	2	F	145.60	1.3824	987	0.67
D1010	2	F	143.30	1.3779	1000	0.68
D1011	2	F	147.20	1.3282	938	0.64
D1012	2	F	142.40	1.3983	1021	0.70
Average =					977	0.67

Dose Calculation (mg D5/kg):
Dose Calculation (mCi/kg):

Calculated Dose (mg D5/kg body weight) = Actual Dose Wt. (g) x 104 mg D5/g dose solution / Body Wt. (kg)
Calculated Dose (mCi/kg body weight) = Actual Dose Wt. (g) x 0.071 mCi/g dose solution / Body Wt. (kg)

Figure 1. Example HPLC Fat Radioactivity Chromatograms

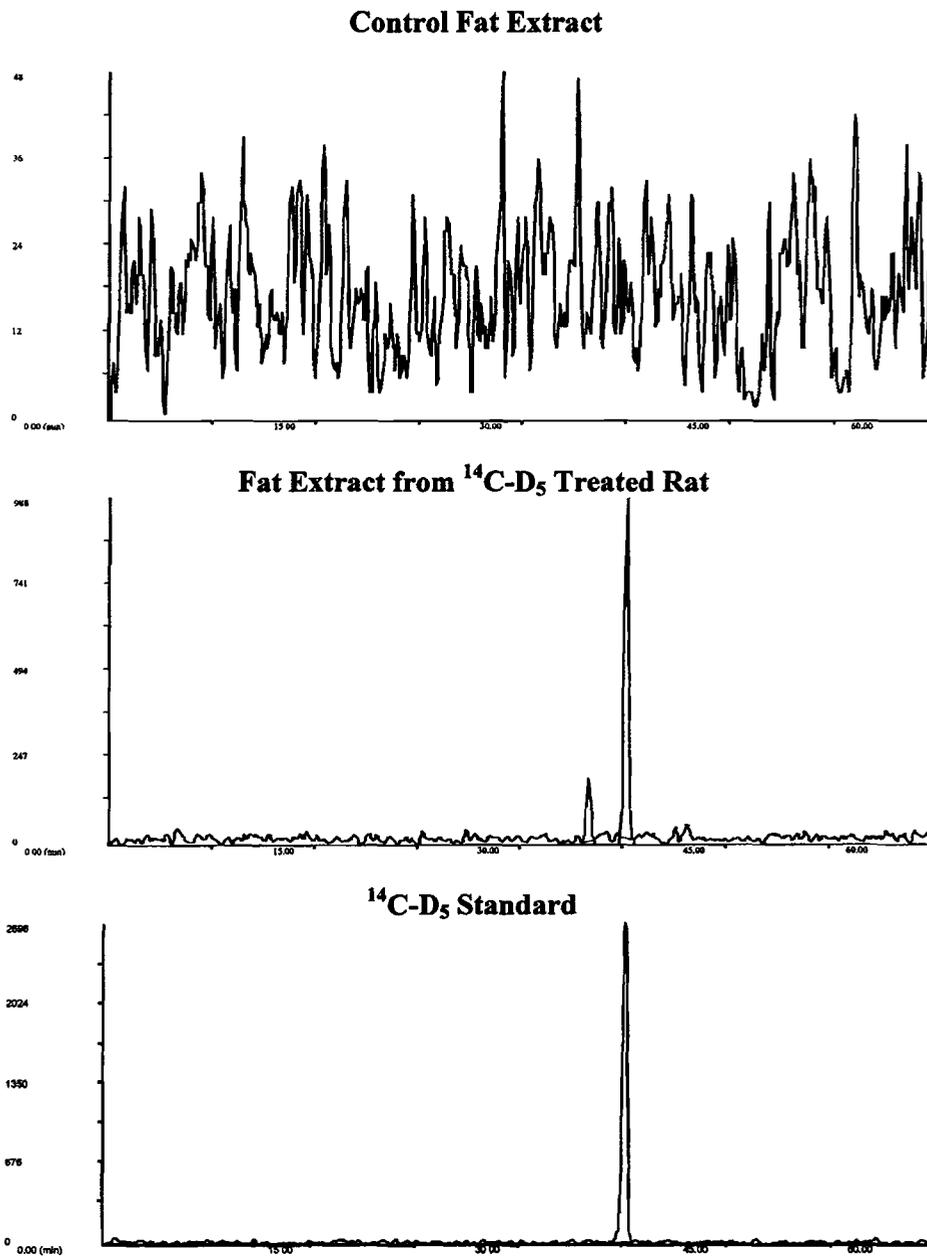


Figure 2. Example HPLC Feces Radioactivity Chromatograms

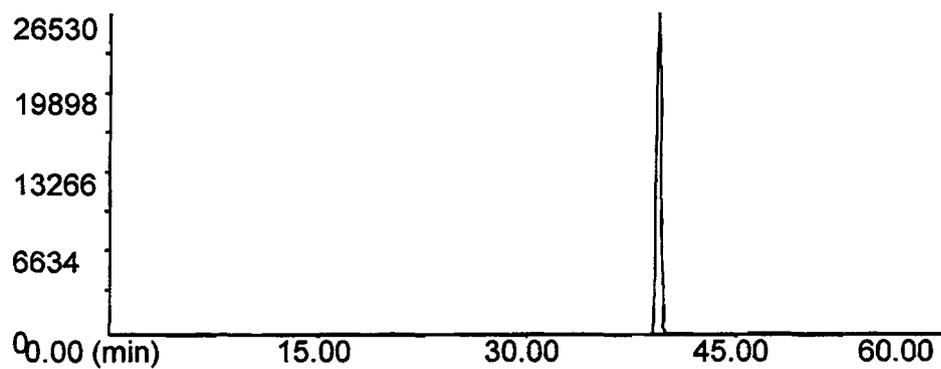
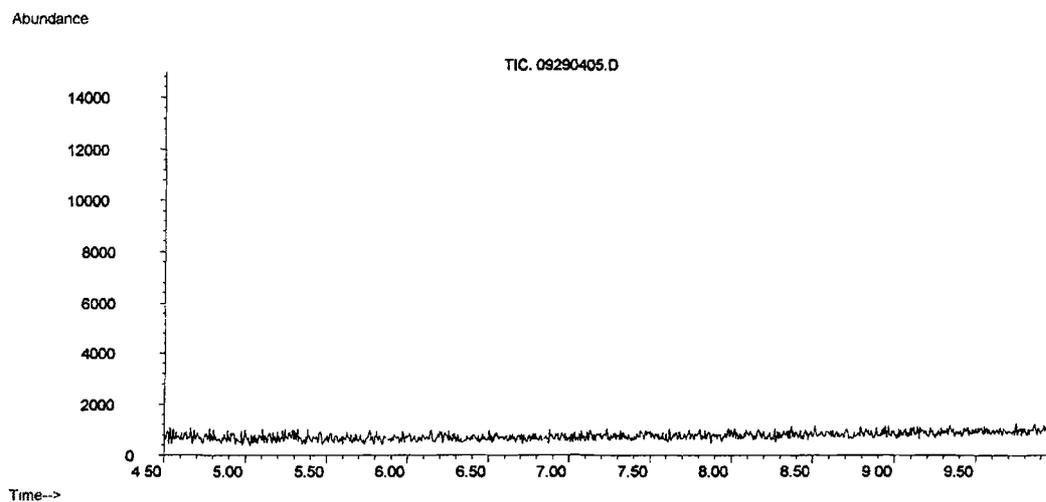


Figure 3. Example GC/MS Total Ion Chromatograms

Control Fat Extract



Fat Extract from ¹⁴C-D₅ Treated Rat

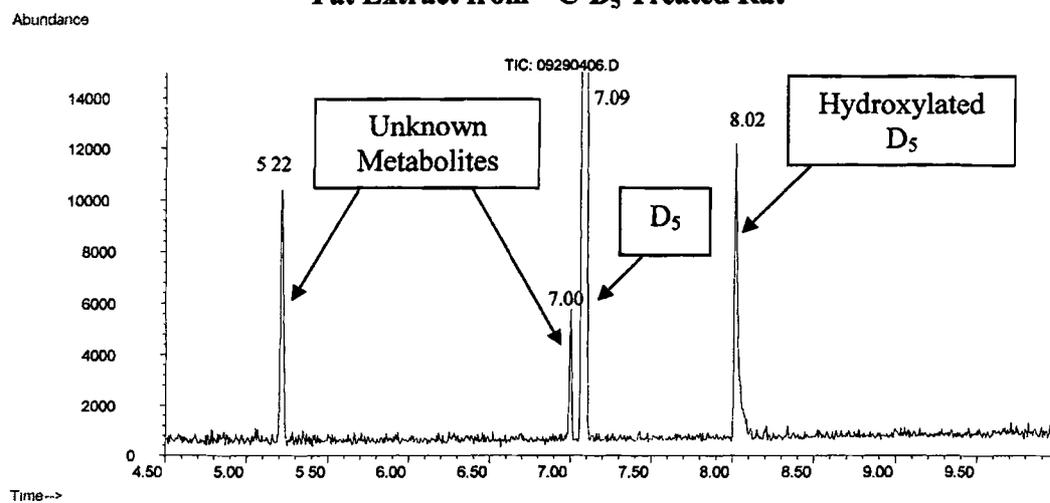


Figure 4. Mass Spectrum of D₅ in Treated Fat Extract

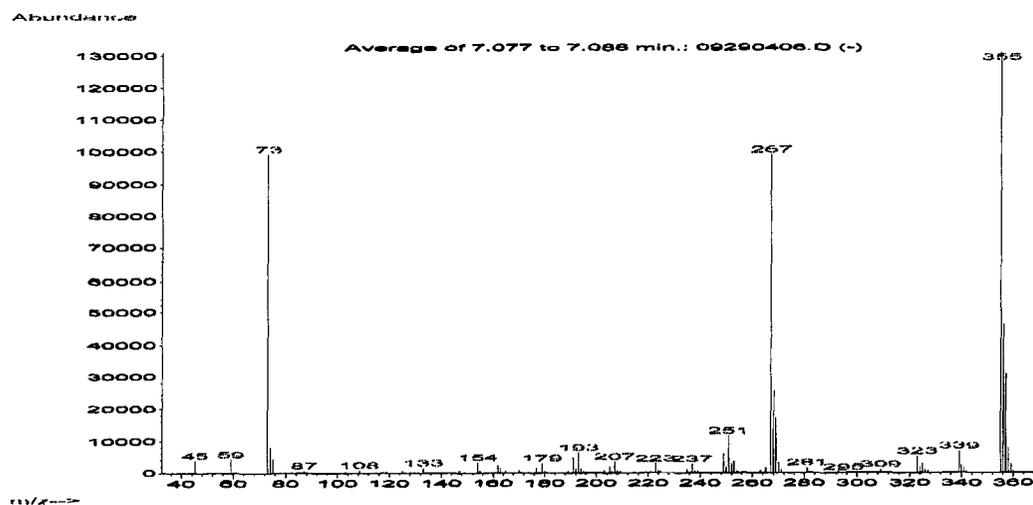


Figure 5. Mass Spectrum of Metabolite in Fat Extract from Treated Rat – Hydroxylated D₅

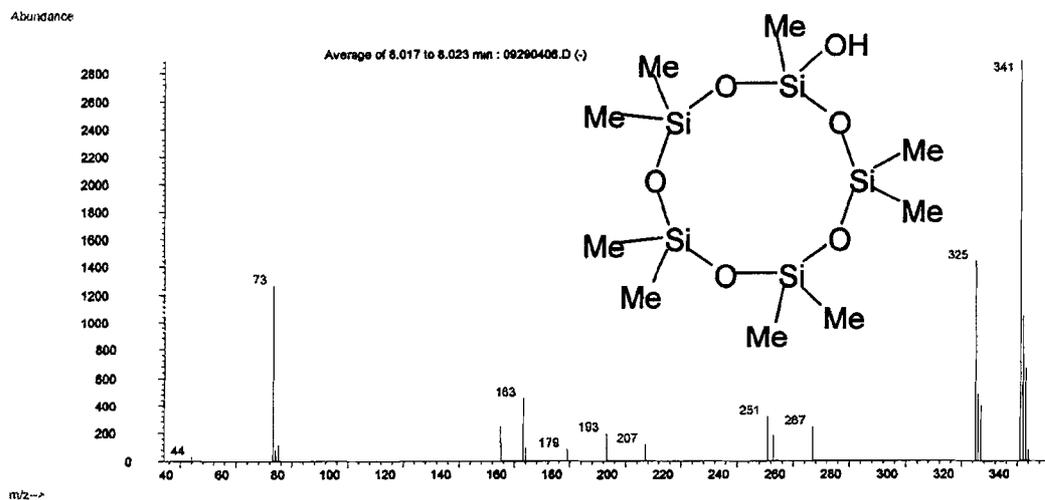


Figure 6. Total Ion Chromatogram and Mass Spectrum of Hydroxylated D₅ Standard

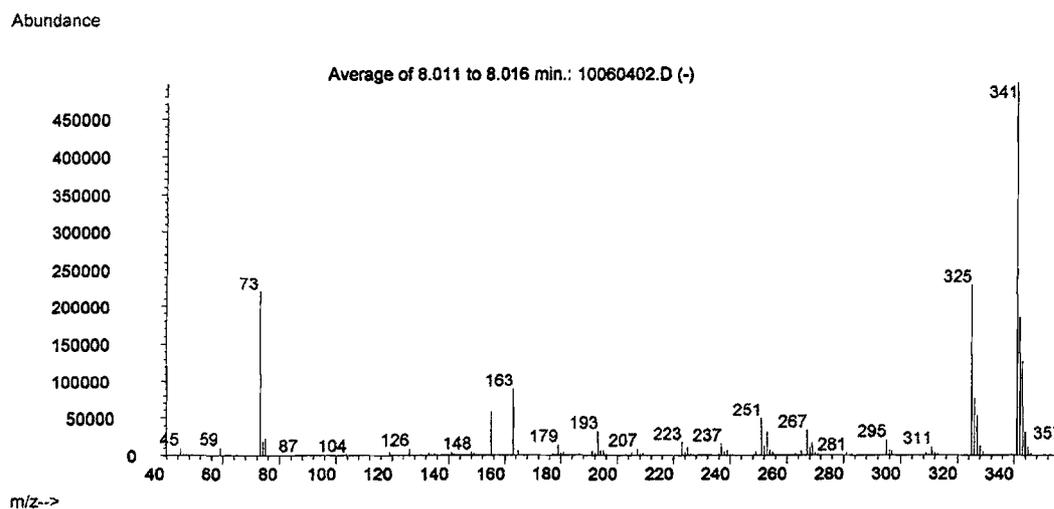
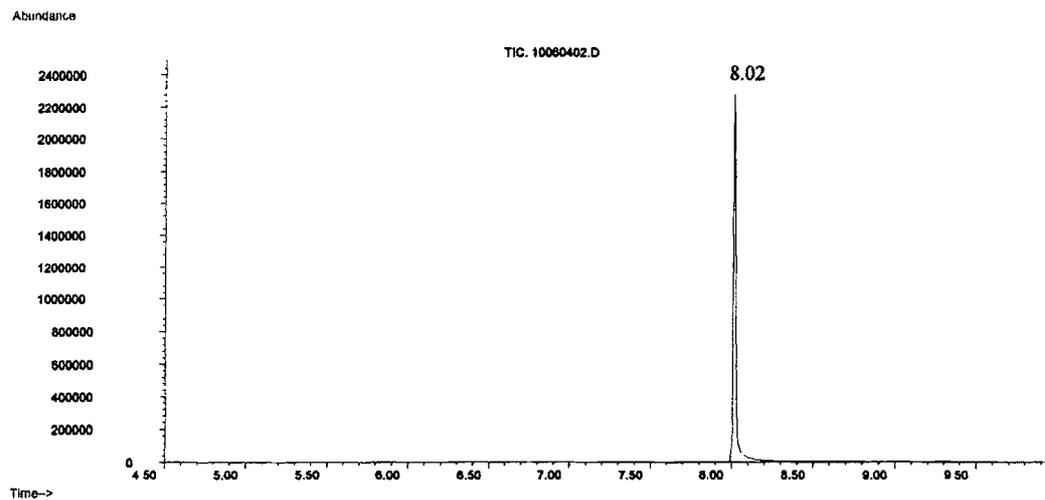
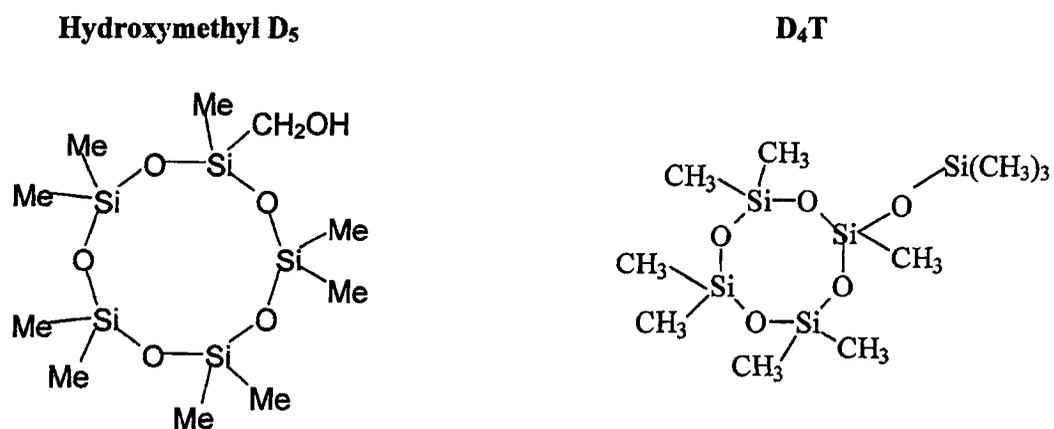


Figure 7. Structures of Additional Potential Metabolites



UPS Internet Shipping: View/Print Label

- 1. Print the label(s):** Select the Print button on the print dialog box that appears. Note: If your browser does not support this function select Print from the File menu to print the label.
- 2. Fold the printed label at the dotted line.** Place the label in a UPS Shipping Pouch. If you do not have a pouch, affix the folded label using clear plastic shipping tape over the entire label.

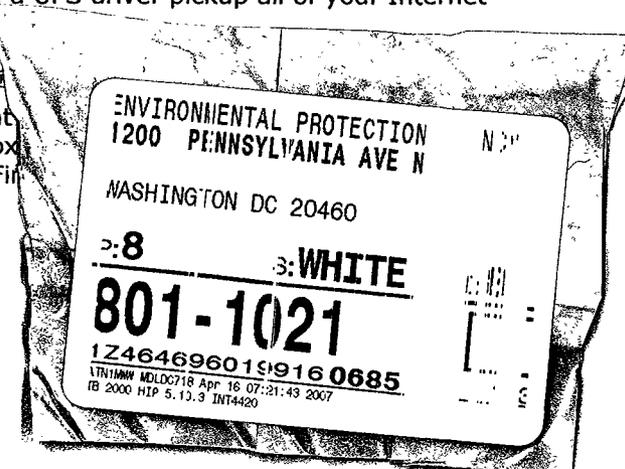
3. GETTING YOUR SHIPMENT TO UPS

Customers without a Daily Pickup

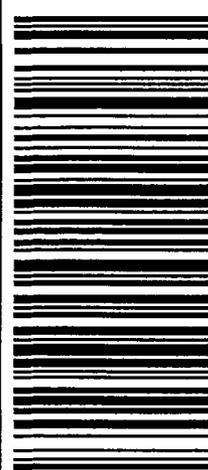
- Schedule a same day or future day Pickup to have a UPS driver pickup all of your Internet Shipping packages.
- Hand the package to any UPS driver in your area.
- Take your package to a location of The UPS Store or Authorized Shipping Outlet near you. Items sent (Ground Returns) are accepted at any UPS Drop Box.
- To find the location nearest you, please visit the 'Find a Location' page.

Customers with a Daily Pickup

- Your driver will pickup your shipment(s) as usual.



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<p>MIKE THELEN 989 4964949 DOW CORNING CORPORATE 2200 W. SALZBURG RD. MIDLAND MI 48686</p> <p>SHIP TO: DOCUMENT CONTROL OFFICE (7407) U.S. E.P.A. 1200 PENNSYLVANIA AVE. NW OFFICE OF POLLUTION PREVENTION & TO TSCA DATA PROCESSING CENTER CBIC WASHINGTON DC 20460</p>	<p>3 LBS</p> <p>1 OF 1</p> <p>MD 201 9-80</p> 	<p>UPS NEXT DAY AIR</p> <p>1</p> <p>TRACKING #: 1Z 464 696 01 9916 0685</p> 	<p>BILLING: P/P</p>  <p>US 9.0.20.0 WXP/E60 64.0A 02/2007</p>
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