

MR# 302741

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February 14, 2007

Re: *In vivo* Dermal Absorption Study – TSCA Section 8(e)

This letter is filed on behalf of the companies listed below<sup>1</sup> to inform the agency of findings from a rat *in vivo* dermal absorption study conducted with creosote (CAS number 8001-58-9) and is intended to comply with the reporting requirements of TSCA section 8(e) and the agency' implementing regulations. The study is sponsored by Creosote Council III, a FIFRA § 3(c)(2)(B) joint data development group, and was conducted at the E. I. du Pont de Nemours and Company Haskell Laboratory for Health and Environmental Sciences in conjunction with the FIFRA re-registration of creosote. Creosote is a complex coal tar-derived liquid used as a restricted-use wood preservative for pressure-treatment of industrial wood products such as railway ties, utility poles, and marine piling. Creosote is applied to wood via pressure treatment in a closed system. The companies filing this notification first possessed or knew about the findings within the past 30 days and are filing this TSCA section 8(e) report because they believe that no dermal absorption data for creosote or similar substances have ever been available to EPA. This notice is being submitted under section 8(e) of TSCA because there are physical and chemical similarities between creosote and a non-pesticidal coal tar product known as Coal Tar Distillate (CAS 65996-92-1).

<sup>1</sup> Coopers Creek Chemical Corporation, W. Conshohocken, PA  
KMG-Bernuth, Inc, Houston, TX  
Koppers, Inc, Pittsburgh, PA  
Rutgers Chemicals Ag, Houston, TX  
Tangent Rail Corporation, Pittsburgh, PA.



The dermal absorption study was conducted in conjunction with the ongoing creosote FIFRA reregistration review to estimate a dermal penetration rate of whole creosote. Eight <sup>14</sup>C-labeled polyaromatic hydrocarbon components of creosote were added to creosote and 10µL/cm<sup>2</sup> of the spiked creosote was applied to a 10.5 cm<sup>2</sup> area of shaved skin on the dorso-lumbar region of eight rats. <sup>14</sup>C-spiked creosote was allowed to remain on the skin for 8 hours. At the end of the application period 4 rats were sacrificed and the remaining rats were held for 21 days then sacrificed. Expired air, excreta, blood and selected tissues were collected for each animal and analyzed for radioactivity. Initial study findings include:

- 1.0) The majority of the applied dose was removed by washing the skin (56%)
- 2.0) Total radioactivity recovered at the end of the 8-hour exposure (0 hours post-exposure) and at 496 hours post-exposure were 95.009% and 96.609%, respectively;
- 3.0) Creosote components moved through rat skin effectively with about 6.3% of the applied radioactivity absorbed at the end of the 8-hour dosing with most of that (~34%) entering urine. Less than 0.3% of the applied radioactivity remained in blood and internal organs at the end of the 8-hour dosing suggesting fast clearance;
- 4.0) At 496 hours-post dose about 34% of the applied dose was absorbed. The majority of this (about 93% ) was in the urine and feces. Less than 0.01% remained in the carcass and, blood and internal organs, combined;
- 5.0) Dosed skin never retained more than 1.55% of the applied dose (0 hours post-exposure) and diminished to 0.005% at termination;

These findings along with others detailed in the draft report suggest that creosote components move through the skin, are rapidly metabolized and clear the blood.

The Creosote Council asked Haskell Laboratory to conduct a companion *in vitro* study comparing <sup>14</sup>C-creosote absorption in human and rat skin. This study used the same <sup>14</sup>C -PAH/creosote test material as the *in vivo* rat study. A draft report for that work is not yet available, but summary data tables (QC'd but unaudited) are enclosed. These data show that the *in vivo* rat absorption and the *in vitro* rat absorption are equivalent (about 34% of the applied dose) and that human skin absorption is about 4% of the applied dose, or about 8-fold lower than the rat.

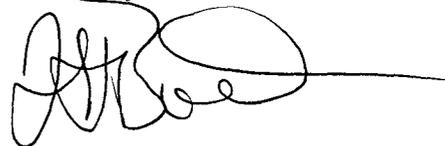
The acute and subchronic dermal toxicity of creosote have been assessed and are rather low. The acute dermal LD50 of creosote in rabbits is greater than 2000mg/kg. No pharmacotoxic signs were observed in any animal nor were body weight changes or postmortem findings associated with acute dermal treatment. A 90-day dermal study was conducted in rats in which daily (five days/week) creosote applications of 4, 40 or 400 mg/kg were administered to groups of ten males and ten females. One high-dose male animal died during the study. Surviving animals developed dermal irritation (slight

erythema and desquamation) but no test article-related effects on body weight, food consumption or clinical pathology were reported. There were no test article-related macroscopic or microscopic findings in dosed animals and no organ-weight variations.

More recently, Wong and Harris<sup>2</sup> have shown that employment in the creosote wood treating industry is not associated with any significant mortality increase from site-specific cancers or non-malignant diseases. Employees who may come into contact with Coal Tar Distillate are currently instructed to avoid prolonged or repeated exposure of the material to their skin or eyes, to wear appropriate clothing and gloves, and to remove Coal Tar Distillate-soaked clothing immediately. If skin contact occurs, employees are instructed to remove contaminated clothing and shoes and to thoroughly wash skin with soap and water or waterless hand cleaner.

The audited draft of the *in vivo* study report (copy enclosed) is currently under review by the sponsors and a draft of the *in vitro* study report is expected soon. To assist in the agency's evaluation of the *in vivo* results, a copy of the draft study report for *in vitro* absorption will be sent to the agency upon receipt from the laboratory. Final reports for both studies will be submitted to the agency when they become available. If there are questions about this letter or the studies, please do not hesitate to contact me directly. I can be contacted at [butala@jhbutala.com](mailto:butala@jhbutala.com) or phoned at 724-443-0097.

Sincerely,

A handwritten signature in black ink, appearing to read 'JH Butala', with a long horizontal line extending to the right.

John H. Butala, DABT

cc w/o att: Coopers Creek Chemical Corporation  
KMG-Bernuth, Inc.  
Koppers, Inc.  
Rutgers Chemicals Ag.  
Tangent Rail Corporation.

---

<sup>2</sup> Wong, O and F. Harris. 2005. Retrospective Cohort Mortality Study and Nested Case-Control Study of Workers Exposed to Creosote at 11 Wood-Treating Plants in the United States. *JOEM*, 47:7, 683-697.

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PENETRATION KINETICS AND RECOVERY VALUES  
FROM 8-HOUR *IN VITRO* DERMAL ABSORPTION STUDY  
IN HUMAN CADAVER AND RAT SKIN

Draft study report not yet available. The enclosed data have been quality controlled but have not yet been through GLP Quality assurance review.

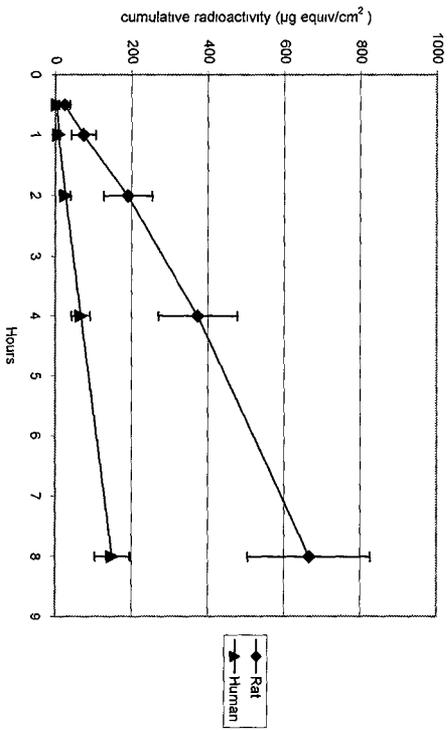
Results indicate that the 8-hour rat *in vitro* absorption (34.3% absorbable) is equivalent to the rat *in vivo* absorbable dose at 496-hours post exposure (~34%). This suggest that the human *in vitro* absorbable dose (~4%) would be equivalent to human *in vivo* absorption, about 4%.

Penetration kinetics of [<sup>14</sup>C]AVP A. B. H. 3. Creosote, 0.0000 mg Creosolent, 0.8 hours

Data expressed in cumulative µg equiv/cm<sup>2</sup>

Time (hr)	Rat		Human	
	Mean	SD	Mean	SD
0.5	24.0	14.1	5.11	1.85
1	74.0	31.9	8.38	4.56
2	189.9	63.4	27.1	12.5
4	373.6	103.4	66.9	24.6
8	655.8	161.0	149.7	45.7
Penetration rate, 0.5-8 h <sup>a</sup> (µg equiv/cm <sup>2</sup> /h)	85.3		19.7	

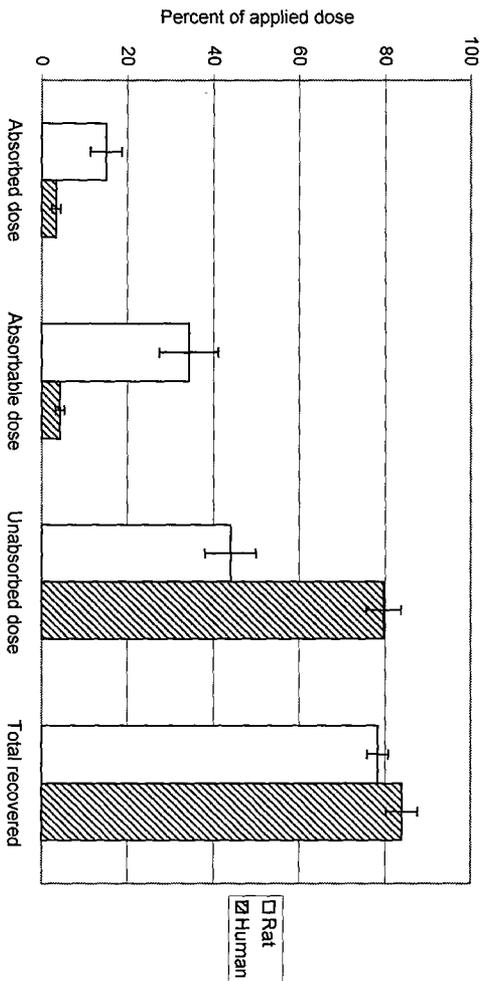
<sup>a</sup> Slope of mean data, 0.5-8 hours



Recovery of applied dose following a 6-hour topical exposure

Data expressed as a percent of applied dose

	Rat		Human	
	Mean	SD	Mean	SD
Absorbed dose				
Receptor fluid	15.1	3.64	3.38	1.03
Total absorbed	15.1	3.64	3.38	1.03
Absorbable dose				
Receptor fluid	15.1	3.64	3.38	1.03
Tape-stripped skin	19.2	6.82	0.86	0.26
Total absorbable	34.3	6.84	4.24	1.07
Unabsorbed dose				
Skin wash	12.8	2.33	70.3	7.52
Donor chamber	7.52	2.44	1.89	0.75
Tape strips	23.6	4.60	5.33	0.98
Total unabsorbed	44.0	5.98	79.7	4.08
Total recovered	78.3	2.44	83.9	3.68



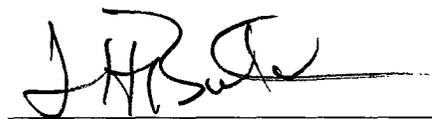
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*IN VIVO* DERMAL ABSORPTION STUDY  
OF CREOSOTE IN RATS

This study is the property of the Creosote Council III. The submission does not contain Confidential Business Information.



14 February 07

John H. Butala  
Technical Advisor  
Creosote Council III

**Study Title**

AWPA P1-P13 Creosote:  
In Vivo Dermal Absorption in the Rat

**TEST GUIDELINES:** OECD Guideline for the Testing of Chemicals. Guideline 427: Skin Absorption: in vivo Method (2004).

OECD Guidance Document for the Conduct of Skin Absorption Studies. OECD Environmental Health and Safety Publication Series on Testing and Assessment No. 28. (2004).

European Commission Guidance Document on Dermal Absorption. Sanco/222/2000 rev 7 (2004).

**AUTHOR:** William J. Fasano, Sr., B.S.

**STUDY COMPLETED ON:** 

**PERFORMING LABORATORY:** E.I. du Pont de Nemours and Company  
Haskell<sup>SM</sup> Laboratory for Health and Environmental Sciences  
Elkton Road, P.O. Box 50  
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U.S.A.

**LABORATORY PROJECT ID:** DuPont-19622

**WORK REQUEST NUMBER:** 16308

**SERVICE CODE NUMBER:** 1378

**SPONSOR:** The Creosote Council III  
P.O. Box 160  
Valencia, Pennsylvania 16059  
U.S.A.

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3. leave the page as is, issue report, and replace it with their own page prior to submission.



**QUALITY ASSURANCE STATEMENT**

Work Request Number: 16308  
Study Code Number: 1378

<i>Phase Audited</i>	<i>Audit Dates</i>	<i>Date Reported to Study Director</i>	<i>Date Reported to Management</i>
Protocol:	April 19-20, 2006	April 20, 2006	April 20, 2006
Conduct:	November 3, 2006	November 3, 2006	November 3, 2006
Report/Records:	January 15-18, 2007	January 18, 2007	January 29, 2007

Reported by: \_\_\_\_\_  
Joseph C. Hamill  
Quality Assurance Auditor

\_\_\_\_\_ Date

**CERTIFICATION**

We, the undersigned, declare that this report provides an accurate evaluation of data obtained from this study.

**Analytical  
Evaluation by:** \_\_\_\_\_  
Timothy A. Snow, Ph.D.  
Senior Research Chemist  
Date

**Reviewed and Approved by:** \_\_\_\_\_  
John C. O'Connor, M.S.  
Research Manager  
Date

**Issued by Study Director:** \_\_\_\_\_  
William J. Fasano, Sr., B.S.  
Senior Research Toxicologist  
Date

This report is approved by the sponsor.

**Approved by:** \_\_\_\_\_  
John H. Butala  
Sponsor Representative  
Date

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### STUDY INFORMATION

Substance Tested: • AWPA P1-P13 Creosote  
• CASN 8001-58-9

Haskell Number: 27413

Composition: See Appendix A

Purity: 98.5%

Physical Characteristics: Dark, amber colored liquid

Study Initiated/Completed: April 19, 2006 / (see report cover page)

Experimental Start/Termination: November 3, 2006 / November 27, 2006

## SUMMARY

Creosote (AWPA P1-P13) is a coal tar-based pesticide that is used primarily as a wood preservative on railroad ties, utility poles, and pilings found in tidal and non-tidal applications. Creosote is a complex mixture containing numerous polycyclic aromatic hydrocarbons and other hetero-nuclear aromatic chemicals. Owing to potential dermal exposure based on its use pattern, creosote's dermal bioavailability has been determined in vivo using the laboratory rat as the exposure model.

Initially, creosote was screened by GC-MS to establish an understanding of the variety of chemicals (abundance response). Subsequently, the GC-MS method was used as the primary tool for assessing the quantitative recovery of twelve creosote marker chemicals from spiked rat plasma. Following these preliminary evaluations, a dermal assessment experiment was conducted using the rat in vivo model to determine the dermal bioavailability of the twelve marker chemicals. In the plasma kinetic experiment, the creosote test substance was applied to a 10.5 cm<sup>2</sup> shaved area on the dorso-lumbar region to four male rats at a rate of 10 µL/cm<sup>2</sup>. The applied dose remained in contact with the skin for 8 hours. At the end of the 8-hour exposure, the skin surface was washed to remove excess creosote and each rat was maintained until 168 hours, post-dose. Whole blood samples were collected pre-dose and post-dose at 0.5, 1, 2, 4, 6, 8 (end of exposure), 10, 12, and 24 hours, and every 24 hours thereafter for 7 days (168 hours). Whole blood was held on wet ice and plasma isolated from the red cell fraction by centrifugation. Plasma was then processed for quantification of the twelve creosote marker chemicals by GC-MS.

In a final experiment, the dermal absorption of creosote containing selected radiolabeled marker chemicals was determined in vivo in the rat. For this experiment, the creosote test substance was spiked with eight radiolabeled chemicals, which represented approximately 43% of chemicals in creosote, and then was applied to a 10.5 cm<sup>2</sup> shaved area on the dorso-lumbar region to two groups of four rats at a rate of 10 µL/cm<sup>2</sup>. The applied dose remained in contact with the skin for 8 hours. At 8 hours, the skin surface of all rats was washed, and one group of four rats sacrificed to determine the distribution of the applied radioactive dose at the end of the exposure phase (0 hours post-exposure). The remaining four rats were maintained until 504 hours post-dose (21 days) and then sacrificed to determine maximum absorption, based on total radioactivity (496 hours post-exposure). At sacrifice, the application skin site was tape-stripped to remove the stratum corneum and total distribution of the applied radioactivity was determined for each post-exposure group. The exposure time and application rates were designed to mimic potential exposures to neat creosote.

### A. Abundance of Creosote Test Substance by GC-MS

In all cases, the twelve individual chemicals of interest were well resolved by GC-MS.

**B. Recovery from Spiked Plasma**

The average recoveries for the twelve target chemicals from spiked rat plasma ranged from approximately 66% to 106%, with the exception of benzo(a)pyrene (~54%). When extracted from frozen plasma, the average recovery was >80%.

**C. Assessment Experiment – Plasma Kinetics of Selected Creosote Chemicals following a Single Dermal Application**

The concentration of the twelve selected chemicals was found to be below the limit of detection in all serial plasma samples from all collection time points during and following an 8-hour exposure to a single finite application of the creosote test substance. These results suggest that all twelve target chemicals were metabolized upon first pass through the skin and likely have negligible bioavailability.

**D. Distribution and Recovery of a Single Dermal Application of Creosote Spiked with Selected Radiolabeled Chemicals**

Following an 8-hour dermal exposure to the spiked creosote test substance, the majority of the dose was removed by washing the skin (>56%). Following the 8-hour exposure and a 21-day collection period, the total absorbable dose was determined to be 34%. A negligible portion of the applied dose (0.04%) remained in the skin following removal of the stratum corneum by tape stripping at the end the 21-day period.

Overall, these results demonstrate that the radiolabeled creosote target chemicals readily penetrated rat skin. Indirectly, the results also confirm that the target chemicals were metabolized upon first pass through the skin, and that systemic exposure following dermal application of creosote is essentially to its metabolites.

## INTRODUCTION

The dermal absorption potential of American Wood Preserves Association (AWPA) P1-P13 Creosote (creosote) is currently under investigation by the sponsor. Creosote is a mixture of aromatic hydrocarbons and is used as a wood preservative. This study was designed to achieve the following objectives.

1. Confirm and optimize a gas-chromatography mass spectrometry (GC-MS) analysis method for individual chemicals in the creosote test substance.
2. Develop a quantitative extraction method for creosote chemicals from rat plasma and determine the limit of detection (LOD) and limit of quantitation (LOQ).
3. Conduct an in vivo dermal assessment experiment to identify and establish the concentration (bioavailability) of selected creosote chemicals in rat plasma.
4. Conduct a main study in vivo dermal experiment, with key creosote chemicals added in radiolabeled form to the creosote test substance, at near-equivalent specific activities, to determine total absorption, distribution, and recovery of the applied dose.

Objectives #1 and #2 established a foundation for the dermal assessment experiment (#3), which provided the identity and rationale for selection of key creosote chemicals to be obtained in radiolabeled form for use in the main in vivo dermal experiment (#4).

## MATERIALS AND METHODS

### A. Test Guidelines

The study design complied with the following test guidelines:

- OECD Guideline for the Testing of Chemicals. Guideline 427: Skin Absorption: in vivo Method (2004).
- OECD Guidance Document for the Conduct of Skin Absorption Studies. OECD Environmental Health and Safety Publication Series on Testing and Assessment No. 28. (2004).
- European Commission Guidance Document on Dermal Absorption. Sanco/222/2000 rev 7 (2004).

## B. Test Substances

### 1. Test Substance

The creosote test substance (CASN 8001-58-9) was supplied by the sponsor and assigned Haskell Laboratory Number 27413 upon receipt. Additional information regarding the test substance is located on the study information page of this report and in Appendix A.

### 2. Selected Radiolabeled Chemicals

The selected radiolabeled test substances listed below (for use in the final in vivo dermal experiment, objective #4) were purchased by Haskell Laboratory for the sponsor from the Sigma-Aldrich Company (St. Louis, MO) and each was assigned a Haskell Laboratory Number upon receipt. Documentation provided by Sigma-Aldrich is presented in Appendix B.

Radiolabeled Chemical	Haskell Number	MW	Specific Activity (mCi/mmol)	Specific Activity (µCi/mg)
Benzo(a)pyrene - 7 - <sup>14</sup> C	22705-130	252	26.6	105.6
2-methylnaphthalene - 8 - <sup>14</sup> C	22705-131	142	8.5	59.9
Fluoranthene - 3 - <sup>14</sup> C	22705-132	202	45	222.8
Anthracene - 1,2,3,4,4A,9A- <sup>14</sup> C	22705-133	178	20.6	115.7
Naphthalene - Benzene - UL - <sup>14</sup> C	22705-134	128	31.3	244.5
Phenanthrene - 9 - <sup>14</sup> C	22705-135	178	8.2	46.1
Biphenyl - UL - <sup>14</sup> C	22705-136	154	7.6	49.4
Pyrene - 4,5,9,10 - <sup>14</sup> C	22705-137	202	55	272.3

## C. Gas Chromatograph - Mass Spectrometry (GC-MS) Analysis of the Creosote Test Substance - General Abundance

The relative concentration of twelve selected creosote target chemicals (i.e., 1-methylnaphthalene, 2-methylnaphthalene, acenaphthalene, benzo(a)pyrene, benzo(b)fluoranthene, cabazole, dibenzofuran, fluoranthene, fluorene, naphthalene, phenanthrene, and pyrene) was measured by gas chromatography (GC) with mass spectrometry detection (MS) using the following equipment and methods.

### Method 1

GC Instrument: Agilent Model 6890  
MS Instrument: Agilent Model 5973  
Software: ChemStation Version D.01.02.16  
GC Parameters:  
Column: Agilent DB5-MS 0.25mm x 30 m, 1 µm film thickness  
Oven:  
Initial Temp: 40°C  
Maximum Temperature: 300°C  
Initial Time: 2.00 min

Temperature Ramp:	Time (min)	Temperature (°C)	Rate (°C/min)
	0.00	40	0.0
	2.00	40	6.0
	45.33	300	0.0
	60.00	300	0.0

Inlet:  
Mode: Split  
Split ratio: 20:1 (1.0 µL injection)  
Pressure: 7.28 psi  
Inlet Temp: 280°C

MS Parameters:  
Electron Multiplier Voltage: ~1.4 kV  
Source Temperature: 230°C  
MS Quad Temperature: 150°C  
Aux Temperature: 280°C  
Data Acquisition Function:  
Mass Scan Range: 35 to 450 daltons  
Scans/second: 1.00 scans/sec

The abundance of each creosote chemical of interest was estimated by total mass spectral area response and was compared to the certificate of analysis provided by the sponsor. The identification of each chemical was confirmed by automatic spectral comparison with the Wiley Registry of Mass Spectral Data.

#### D. Recovery of Selected Creosote Chemicals from Rat Plasma

Recovery of the twelve chemicals of interest was determined by fortification of rat plasma with the creosote test substance in dimethylsulfoxide at four concentrations. Rat plasma was then spiked with 500 µL of acetonitrile and vortexed to precipitate out plasma proteins. Following protein precipitation, 200 mg of anhydrous sodium sulfate, 990 µL of toluene, and 10 µL of 150 µg/mL phenanthrene-d<sub>10</sub> in-toluene internal standard solution was added, vortexed, and centrifuged. The organic layer was withdrawn and analyzed by GC-MS using the following equipment and methods.

##### Method 2

GC Instrument:	Agilent Model 6890		
MS Instrument:	Agilent Model 5973		
Software:	ChemStation Version D.01.02.16		
GC Parameters:			
Column:	Agilent DB5-MS 0.25mm x 30 m, 1 µm film thickness		
Oven:			
Initial Temp:	40°C		
Maximum Temperature:	300°C		
Initial Time:	2.00 min		
Temperature Ramp:	Time (min)	Temperature (°C)	Rate (°C/min)
	0.00	40	0.0
	2.00	40	6.0
	45.33	300	0.0
	60.00	300	0.0

Inlet:  
Mode: Split  
Split ratio: 3:1 (1.0 µL injection)  
Pressure: 7.26 psi  
Inlet Temp: 280°C  
MS Parameters:  
Electron Multiplier Voltage: ~1.4 kV  
Source Temperature: 230°C  
MS Quad Temperature: 150°C  
Aux Temperature: 280°C  
Data Acquisition Function:  
SIM of Masses: 128, 142, 154, 166, 167, 168, 178, 188, 202, 252  
Dwell Time: 200 msec/ion

#### **E. Test System For In Vivo Dermal Plasma Kinetic (Assessment) and Material Balance Experiments**

Male Sprague-Dawley Crl:CD(SD) rats approximately 8-10 weeks of age were used and were supplied by Charles River Laboratories (Raleigh, NC). Rats identified for the plasma kinetic assessment experiment were obtained from the supplier with a cannula inserted in the jugular vein for serial blood sampling. Upon release from quarantine, each rat was identified by a tail mark with the Haskell animal number. The rat, a species common to most toxicity studies, is the practical test system for assessing in vivo dermal absorption. In general, chemicals pass more rapidly through rat skin than through human skin and thus determination of the dermal penetration in the rat is a conservative model for assessing dermal penetration in humans.

On the day prior to dermal dosing, rats were anesthetized with Isoflurane<sup>®</sup>, the back and shoulders clipped free of hair, and the clipped area washed with an aqueous 2% Ivory<sup>®</sup> Soap solution. Following shaving and washing, a glass O-ring with an internal area of 10.5 cm<sup>2</sup>, was glued to the clipped area on the back using Instant Crazy Glue Gel adhesive. The O-ring appliance then was covered with Coban<sup>™</sup> body wrap and rats were acclimatized (overnight) in all-glass metabolism units prior to and following dermal application of the creosote test substance.

#### **F. Animal Husbandry**

##### **1. Environmental Conditions**

Animal rooms were maintained at a temperature of 18-26°C and a relative humidity of 30-70%. Animal rooms were artificially illuminated (fluorescent light) on an approximate 12-hour light/dark cycle. Unless judged by the study director or the laboratory veterinarian to have significantly affected the results of the study, the relative humidity and temperature ranges in the housing rooms were recorded but will not be included in the final report.

##### **2. Feed and Water**

All animals were provided tap water ad libitum and fed PMI<sup>®</sup> Nutrition International, LLC Certified Rodent LabDiet<sup>®</sup> 5002 ad libitum. Animals were not fasted before dosing with test substance.

### 3. Animal Health and Environmental Monitoring Program

As specified in the Haskell Laboratory animal health and environmental monitoring program, the following procedures are performed periodically to ensure that contaminant levels are below those that would be expected to impact the scientific integrity of the study:

- Water samples are analyzed for total bacterial counts, and the presence of coliforms, lead, and other contaminants.
- Samples from freshly washed cages and cage racks are analyzed to ensure adequate sanitation by the cagewashers.

Certified animal feed is used, guaranteed by the manufacturer to meet specified nutritional requirements and not to exceed stated maximum concentrations of key contaminants, including specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The presence of these contaminants below the maximum concentration stated by the manufacturer would not be expected to impact the integrity of the study.

The animal health and environmental monitoring program is administered by the attending laboratory animal veterinarian. Evaluation of these data did not indicate any conditions that affected the validity of the study.

#### G. In Vivo Dermal Assessment – Identifying Key Creosote Chemicals in Plasma

On the day of dosing, the protective Coban™ body wrap was removed and the test substance was applied as a finite dose at a rate of 10- $\mu\text{L}/\text{cm}^2$  to the shaved dorsal area of 4 male rats. Following dose administration, each animal was housed separately in an all-glass, metabolism cage.

Rats were exposed to the test substance for 8 hours. At the end of the exposure period, the application site was cleansed with at least 3 cycles of one natural sponge soaked in a 2% Ivory® Soap (wash), followed by one natural sponge soaked with water (rinse), followed by one dry natural sponge (dry). Following washing, rats were returned to their metabolism cages until sacrifice at 168 hours post-dose.

Serial whole blood samples (100  $\mu\text{L}$ ) were collected pre-dose, and post-dose at 0.5, 1, 2, 4, 6, 8, 10, 12, 24 hours, and every 24 hours thereafter until 168 hours (7 days). Whole blood for each of 2 rats was pooled ( $n = 2$  plasma samples per time point), and plasma separated from the red cell fraction by centrifugation. Plasma was analyzed for creosote chemicals using the following equipment and methods.

Plasma samples from the assessment experiment (100  $\mu\text{L}$ ) were immediately prepared for extraction by adding 500  $\mu\text{L}$  of acetonitrile and vortexing to precipitate out the plasma proteins. Following protein precipitation, 200 mg of anhydrous sodium sulfate, 990  $\mu\text{L}$  toluene and 10  $\mu\text{L}$  of 150  $\mu\text{g}/\text{mL}$  phenanthrene- $\text{d}_{10}$  in-toluene internal standard solution was added, vortexed and centrifuged. The organic layer was withdrawn and the sample analyzed by GC-MS using analytical Method 2.

**H. Creosote Test Substance Preparation – Addition of Key Radiolabeled Chemicals**

Initially, toluene was added to each of the eight radiolabeled materials selected for spiking into the creosote test substance and the amount of radioactivity per volume was verified by taking representative aliquots followed by analysis using liquid scintillation counting (LSC). Based on these evaluations, and the following target level of activity scheme below, aliquots of each were removed and combined into a vial. The sample was evaporated to dryness by nitrogen convection (with an isopropyl alcohol trap) and approximately 5 mL of the creosote substance was added, mixed, and sonicated.

Radiolabeled Chemical	Concentration In Creosote (%) <sup>a</sup>	Amount of Chemical in 5 mL (mg)	Specific Activity of Neat Sample (µCi/mg)	Amount of Activity Required (µCi)
Phenanthrene (solid)	12.2	653	46.1	250
Naphthalene (solid)	9.0	482	244.5	184
Fluoranthene (MeOH solution)	6.8	364	222.8	139
Pyrene (solid)	6.0	321	272.3	123
2-methynaphthalene (solid)	5.1	273	59.9	105
Anthracene (toluene solution)	2.2	118	115.7	45
Biphenyl (toluene solution)	1.2	64	49.4	25
Benzo(a)pyrene (toluene solution)	0.5	27	105.6	10

<sup>a</sup>Based on COA provided by sponsor.

The sample was evaporated to dryness by nitrogen convection (with an isopropyl alcohol trap) and approximately 5 mL of the creosote substance was added, mixed, and sonicated.

**I. Radiochemical Homogeneity and Dose Determination**

The amount and distribution (homogeneity) of radioactivity per volume in the final spiked test substance was determined by taking 3 x 105 µL aliquots (volume of applied dose for in vivo study) followed by LSC.

The final specific activity of each radiolabeled chemical in the creosote test substance was based on the specific activity of each (neat) radiolabeled chemical (vendor's COA), the amount of radioactivity of each added to creosote, and the nominal concentration of each chemical in the creosote test substance (sponsor's COA). Based on the preparation scheme, the calculated (nominal) specific activity target for each chemical was 0.39-µCi/mg, which provided equivalent radiochemical sensitivity for the each of the eight radiochemicals.

## J. In Vivo Dermal Absorption with Creosote Test Substance spike with <sup>14</sup>C-Labeled Chemicals

On the day of dosing, the protective porous bandage was removed and the test substance was applied as a finite dose to the shaved dorsal area of 8 male rats at a rate of 10- $\mu$ L/cm<sup>2</sup>. The exposure area was 10.5 cm<sup>2</sup>, which required a target dose of 105  $\mu$ L.

Following dose administration, a glass cap containing Anasorb<sup>®</sup> 747 trapping media (SKC Inc., Eighty Four, PA) was fitted onto the top of the glass O-ring. The entire glass appliance was further secured with Coban<sup>™</sup> body wrap, and each animal was then housed separately in an all-glass, closed metabolism cage, suitable for the collection of <sup>14</sup>CO<sub>2</sub> (2N NaOH), <sup>14</sup>C-organic volatiles (ethylene glycol), urine, and feces.

### 1. Exposure Period

All rats were exposed topically to the creosote test substance for 8 hours. At 8 hours, the rats were removed from the metabolism cage, the organic trapping contents was removed and placed into acetonitrile, and the application site was then washed using a 2% Ivory<sup>®</sup> Soap solution.

Following washing at 8 hours post-dose, one group of 4 rats was euthanized. The remaining group of 4 rats was euthanized at 504 hours (21 days) post-dose (496 hours post-exposure).

### 2. Sample Collection, Post-Dose

The charcoal trap media was collected at 8 hours for the 0 hour post-exposure group, and at 216 hours for the 496 hour post-exposure group. Due to evidence of stress (decline in bodyweight), the glass cap of the charcoal trap was removed from the 496 hour post-exposure rats at 216 hours post exposure instead of remaining in-place until 496 hours post-exposure. Although this deviated from the protocol it had no impact on the results or interpretation.

Urine and feces was collected in vessels cooled by solid carbon dioxide during the 0-8 hour exposure period, and for surviving rats 8-12, 12-24, and every 24 hours thereafter until sacrifice.

The closed system chamber air was drawn through a 2N NaOH trap (<sup>14</sup>CO<sub>2</sub>) and an ethylene glycol trap (<sup>14</sup>C-volatiles) in series during the 0-8 hour exposure period, and for surviving rats 8-12, 12-24, and every 24 hours thereafter until radioactivity in sample aliquots was  $\leq$ LOD.

Residual feed and cage washings were collected as needed. At the end of the in-life phase, the metabolism cages were rinsed with a dilute soap solution followed by an acetone rinse. The rinse was placed in a suitable container and retained for analysis.

### 3. Animal Processing, Washing of the Application Skin Site

At 8 hours post-dose, rats were anesthetized using Isoflurane<sup>®</sup>, the body wrap and organic volatile trapping media were removed and retained for extraction and analysis.

The dose application site was then cleansed with at least 3 cycles of one natural sponge soaked in a 2% Ivory<sup>®</sup> Soap (wash), followed by one natural sponge soaked with water (rinse), followed by

one dry natural sponge (dry). All sponge pieces were combined as a single sample for solubilization and analysis.

Rats forming the 8-hour group (0 hours post-exposure) were sacrificed following washing of the application site. Rats forming the 504-hour group (496 hours post-exposure) had a fresh organic volatile trap and body wrap applied, and were then returned to their metabolism cages until sacrifice.

#### 4. Animal Sacrifice

Rats were anesthetized using Isofluorane<sup>®</sup>, the body wrap, organic volatile trapping media (collected at 8- and 192 hours post-exposure), and glass O-ring appliance were removed, and each was placed into a separate container for solvent extraction and analysis. Animals were then exsanguinated via cardiac puncture.

Whole blood was centrifuged to obtain separate fractions of plasma and red blood cells. The application skin site was excised and then tape-stripped to remove the stratum corneum using Leukotape<sup>®</sup> P (BSN Medical, Ltd., Pinetown, South Africa). The individual tape strips were each placed into a separate glass vial and extracted with acetonitrile.

The application skin site was placed into a glass container for solubilization and analysis. The lungs, heart, kidney, and liver were excised, held briefly on wet ice, and then stored frozen at  $\leq 10^{\circ}\text{C}$  prior to processing.

#### 5. Sample Storage

Samples not immediately processed for analysis were stored frozen at  $\leq 10^{\circ}\text{C}$  (i.e., plasma, carcasses, urine, feces, application skin site, tissues) or refrigerated at approximately  $0-10^{\circ}\text{C}$  (i.e., cage wash, residual feed, whole blood, red blood cells, sponge pieces, body wrap, O-rings, and tape strips).

#### 6. Determination of Radioactivity

- Aliquots of whole blood were combusted.
- Aliquots of plasma were added directly to a liquid scintillant (e.g., Ultima Gold<sup>™</sup> XR).
- Aliquots of red blood cells were combusted.
- Feces were homogenized in water. Aliquots were combusted.
- Residual feed was homogenized in water. Aliquots were combusted.
- Carcasses were homogenized with water. Aliquots were combusted.
- Tissues were minced. Aliquots were combusted.

- Urine, cage wash, sodium hydroxide ( $^{14}\text{CO}_2$ ), and ethylene glycol ( $^{14}\text{C}$ ) were not processed further. Aliquots were added directly to a liquid scintillant (e.g., Ultima Gold<sup>TM</sup> XR).
- The application skin site and sponge pieces were digested in Soluene<sup>®</sup>-350. Aliquots were added directly to Hionic-Fluor<sup>TM</sup> liquid scintillant.
- The organic volatile trapping media, body wrap, O-rings, and tape strips were extracted with acetonitrile. Aliquots were added directly to Ultima Gold<sup>TM</sup> XR liquid scintillant.

#### 7. Combustion Method

Aliquots of whole blood, red blood cells, feces, residual feed, carcass homogenate, and tissues were combusted using a Packard Tri-Carb Automatic Sample Oxidizer. The resultant  $^{14}\text{CO}_2$  generated was collected in a suitable absorbent scintillation system.

#### 8. Liquid Scintillation Counting

All samples were analyzed in a Packard liquid scintillation counter for total radioactivity. Samples were counted for 10 minutes or until 160,000 disintegrations were accumulated (0.5%,  $2\sigma$ ), whichever came first.

The limit of detection (LOD) and the limit of quantitation (LOQ) for the analysis of each sample were taken as twice and three times the background disintegration rate obtained from analysis of appropriate blank samples, respectively.

#### 9. Data Presentation and Statistical Analyses

Group data is represented as Mean  $\pm$  SD.

The total absorbed dose (as a percent of applied dose) was defined as a sum of the applied radioactive dose detected in urine, feces, cage wash, residual feed, carcass, tissues, whole blood, RBC, plasma, expired air (2N NaOH;  $^{14}\text{CO}_2$ ), and  $^{14}\text{C}$ -organic volatile traps (ethylene glycol).

Total absorbable dose was the sum of the absorbed dose plus any residual radioactivity that remained in the tape-stripped skin (epidermis, dermis).

The unabsorbed dose was the sum of the applied radioactive dose detected in the body wrap, charcoal (volatile) trapping media, skin wash, O-ring, and tape-strips (stratum corneum).

Calculated values in tables and appendices were generated by computer and by Debra (V.5.1a), a protocol-driven GLP-compliant laboratory information system (LabLogic Systems Ltd., Sheffield, England) and were rounded appropriately for inclusion in the report. As a consequence, calculation of mean data will, in some instances, yield a value that is not precisely the same due to rounding.

## RESULTS AND DISCUSSION

### A. Gas Chromatograph – Mass Spectrometry (GC-MS) Analysis of the Creosote Test Substance – General Abundance

(Table 2, Figure 1)

A representative total ion chromatogram (TIC) of the twelve target chemicals in the creosote test substance is presented in Figure 1. In all cases, the individual chemicals of interest were well resolved. Retention times and quantification masses are given in Table 2.

### B. Recovery of Selected Creosote Chemicals from Rat Plasma

The average recoveries for the twelve target chemicals from spiked rat plasma ranged from approximately 66% to 106%, with the exception of benzo(a)pyrene (~54%). When extracted from frozen plasma recovery of the chemicals of interest was >80%.

### C. Assessment experiment – plasma kinetics of selected creosote chemicals following a single dermal application of creosote

(Table 3)

In all serial plasma samples from all time points the concentration of the target chemicals were found to be below the limit of detection (<LOD). The LOD and limit of quantification (LOQ) for each of the twelve creosote target chemicals is presented in Table 3. These findings suggest that the chemicals were (essentially) metabolized upon first pass through the skin and therefore have negligible bioavailability.

### D. In Vivo Dermal Absorption of Creosote Spiked with <sup>14</sup>C-Labeled Chemicals

(Tables 4-9, Figures 2-6, Appendix C)

#### 1. Verification of Radioactivity

The spiked creosote test substance was verified to be homogeneous and contained approximately 16.7  $\mu\text{Ci}$  per 105  $\mu\text{L}$ , the volume of the applied dose. The calculated specific activity for each of the eight radiolabeled chemicals was 0.37  $\mu\text{Ci}/\text{mg}$ , which provided equivalent sensitivity for each radiolabeled chemical spiked into the creosote test substance.

#### 2. 0-Hour Post-Exposure Group

Key observations of mean data:

- During an 8-hour dermal exposure, only a small portion of the applied dose was absorbed (6.34%). An additional 1.55% of the applied dose remained in the skin following tape stripping. The total absorbable dose after an 8-hour exposure was 7.90%.

- Washing of the application skin site at the end of the exposure phase removed 59.3% of the applied dose, which made up a significant portion of the total unabsorbed material (87.1%); a minor portion of the applied dose (6.89%) was removed by tape-stripping the skin (stratum corneum).
- Total recovery of the applied dose was 95%.

3. 496-Hour Post-Exposure Group

Key observations of mean data:

- Following an 8-hour dermal exposure and a 496-hour post-exposure period, approximately 34% of the applied dose had been absorbed; a negligible amount of the applied dose (0.005%) remained in the tape-stripped skin yielding a total absorbable dose of 34%.
- As was observed for the 0-hour post-exposure group, washing of the application skin site at the end of the exposure phase removed 56.8% of the applied dose, which made up a significant portion of the total unabsorbed material (62.6%); only a minor portion of the applied dose (0.04%) was removed by tape-stripping the skin (stratum corneum).
- Recovery of the applied dose was >96%.
- Evaluation of the cumulative (total) excretion graphs confirms that elimination of the systemically available dose was essentially complete by 496-hours post-exposure.

## CONCLUSIONS

### A. Abundance of Creosote Test Substance by GC-MS

In all cases, the twelve individual chemicals of interest were well resolved by GC-MS.

### B. Recovery from Spiked Plasma

The average recoveries for the twelve target chemicals from spiked rat plasma ranged from approximately 66% to 106%, with the exception of benzo(a)pyrene (~54%). When extracted from frozen plasma, the average recovery was >80%.

### C. Assessment Experiment – Plasma Kinetics of Selected Creosote Chemicals following a Single Dermal Application

The concentration of the twelve selected chemicals was found to be below the limit of detection in all serial plasma samples from all collection time points during and following an 8-hour exposure to a single finite application of the creosote test substance. These results suggest that all twelve target chemicals were metabolized upon first pass through the skin and likely have negligible bioavailability.

**D. Distribution and Recovery of a Single Dermal Application of Creosote Spiked with Selected Radiolabeled Chemicals**

Following an 8-hour dermal exposure to the spiked creosote test substance, the majority of the dose was removed by washing the skin (>56%). Following the 8-hour exposure and a 21-day collection period, the total absorbable dose was determined to be 34%. A negligible portion of the applied dose (0.04%) remained in the skin following removal of the stratum corneum by tape stripping at the end the 21-day period.

Overall, these results demonstrate that the radiolabeled creosote target chemicals readily penetrated rat skin. Indirectly, the results also confirm that the target chemicals were metabolized upon first pass through the skin, and that systemic exposure following dermal application of creosote is essentially to its metabolites.

**RECORDS AND SAMPLE STORAGE**

Specimens (if applicable), raw data, the protocol, amendments (if any), and the final report will be retained at Haskell Laboratory, Newark, Delaware, and will be returned to John H. Butala (No. 7 Glasgow Road, Gibsonsia, PA 10544) 6 months after the final report issues, unless arrangements are made for further archiving.

Data recorded and archived electronically, and laboratory-specific raw data such as personnel files, instrument, equipment, refrigerator and/or freezer raw data will be retained at the facility where the work was done.

**TABLES**

TABLES

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**EXPLANATORY NOTES**

ABBREVIATIONS:

LOD	limit of detection
LOQ	limit of quantitation
MS	mass spectrometry
NA	not applicable
NS	no sample
SD	standard deviation

**Table 1: Preparation of the creosote calibration standards**

Calibration (Target Level) ( $\mu\text{g}/\text{mL}$ )	Target Concentration in Spiked Plasma ( $\mu\text{g}/\text{mL}$ ) <sup>a</sup>	Target Stock Concentration in DMSO ( $\mu\text{g}/\text{mL}$ )	Actual Stock Concentration ( $\mu\text{g}/\text{mL}$ )	Actual Concentration ( $\mu\text{g}/\text{mL}$ )
50	750	75,000	77,940	51.960
10	150	15,000	15,588	10.392
5	75	7,500	7,794	5.196
1.0	15	1,500	1,559	1.039
0.5	7.5	750	779.4	0.0520

<sup>a</sup>Dilution factor from extraction is 15 (1500  $\mu\text{L}/100 \mu\text{L}$ )

**Table 2: Retention times, MS quantification mass employed, and COA concentrations of the 12 creosote target chemicals**

Target Analyte	Retention Time (minutes)	Quantification Mass	% Concentration in Creosote <sup>a</sup>
Naphthalene	21.1	128	9.0
2-Methylnaphthalene	23.9	142	5.1
1-Methylnaphthalene	24.3	142	2.3
Acenaphthene	28.3	154	6.1
Dibenzofuran	29.0	168	3.1
Fluorene	30.4	166	4.2
Phenanthrene	34.4	178	12.2
Fluoranthene	39.3	202	6.8
Pyrene	40.2	202	6.0
Carbazole	35.3	167	1.2
Benzo[b]fluoranthene	50.5	252	0.8
Benz[a]pyrene	52.5	252	0.5

<sup>a</sup>From COA provided by sponsor.

**Table 3: Detection limits for the 12 creosote target chemicals**

Target Analyte	Peak Height in Fortified Plasma	Peak Height in Blank	LOD (ppm)	LOQ (ppm)
Naphthalene	657	39	0.120	0.400
2-Methylnaphthalene	172	4	0.027	0.090
1-Methylnaphthalene	77	3	0.020	0.067
Acenaphthene	177	2	0.016	0.053
Dibenzofuran	161	2	0.009	0.030
Fluorene	132	6	0.043	0.143
Phenanthrene	793	39	0.135	0.450
Fluoranthene	313	37	0.181	0.603
Pyrene	202	26	0.174	0.508
Carbazole	12	1	0.022	0.073
Benzo[b]fluoranthene	10	5	0.090	0.300
Benz[a]pyrene	4	2	0.056	0.187

**Table 4: Summary of dosing information for rats exposed to a single topical application of <sup>14</sup>C-spiked creosote test substance, 0 and 496 hours post-dose groups**

Sample	Hours Post-Exposure			
	0		496	
	Mean	SD	Mean	SD
Body weight (g)	340.9	19.1	340.0	17.9
Weight of formulation (g)	0.1124	0.00	0.1124	0.00
Total radioactivity applied (μCi)	16.7	0.00	16.7	0.00
Total Creosote applied (μg)	112350	0.00	112350	0.00
Application Rate (μg/cm <sup>2</sup> ) <sup>a</sup>	10700	0.00	10700	0.00

<sup>a</sup>Application rate = total Creosote applied (112350 μg) ÷ 10.5 cm<sup>2</sup>

**Table 5: Summary of percent of applied dose following an 8-hour exposure to a single topical application of creosote, recovered 0 and 496 hours post-exposure**

	Data expressed as a percent of applied dose			
	Hours Post-Exposure			
	0		496	
	Mean	SD	Mean	SD
<b>Absorbed Dose</b>				
Urine	2 129	0 360	18 967	4 973
Feces	0 026	0 026	12 604	4 105
Cage wash	0 697	0 272	1 670	1 131
CO <sub>2</sub>	N A	N A	0 000	0 000
Residual feed	0 005	0 001	0 241	0 174
Volatile organics	0 049	N A	0 233	0 224
Non-dosed skin	0 020	0 004	0 039	0 014
Carcass	3 144	0 524	0 195	0 211
Whole blood	0 027	0 006	0 003	0 001
RBC (terminal)	0 011	0 004	0 002	0 001
Heart	0 002	0 000	N A	N A
Lungs	0 006	0 002	N A	N A
Liver	0 185	0 015	0 005	0 002
Kidney	0 073	0 009	0 002	0 001
Plasma (terminal)	0 011	0 002	N A	N A
<b>Total Dose Absorbed</b>	<b>6 342</b>	<b>0 808</b>	<b>33 959</b>	<b>8 445</b>
<b>Absorbable Dose</b>				
Absorbed Dose	6 342	0 808	33 959	8 445
Dosed skin	1 553	0 299	0 005	0 003
<b>Total Dose Absorbable</b>	<b>7 895</b>	<b>1 081</b>	<b>33 964</b>	<b>8 447</b>
<b>Unabsorbed Dose</b>				
Body wrap	2 097	2 186	2 443	1 437
Skin wash - sponges	59 283	12 547	56 822	8 294
Charcoal trap	0 490	0 152	0 451	0 108
O-ring	18 357	8 177	2 889	0 511
Tape strips	6 886	2 744	0 041	0 040
<b>Total Dose Unabsorbed</b>	<b>87 113</b>	<b>3 545</b>	<b>62 645</b>	<b>8 404</b>
<b>Total Dose Recovered</b>	<b>95 009</b>	<b>2 569</b>	<b>96 609</b>	<b>3 628</b>

\*Samples were below the limit of detection (<LOD) or limit of quantitation (LOQ)

**Table 6: Cumulative percent of dose recovered in urine following an 8-hour topical exposure to creosote, 496 hours post-exposure**

Post-dose Timepoint (hours)	Cumulative Percent	
	Mean	SD
8	2.76	0.32
12	4.06	0.64
24	7.46	1.48
48	11.52	2.62
72	14.19	3.57
96	15.75	4.02
120	16.82	4.39
144	17.44	4.53
168	17.83	4.64
192	18.09	4.70
216	18.24	4.72
240	18.38	4.76
264	18.49	4.79
288	18.58	4.83
312	18.66	4.86
336	18.72	4.88
360	18.77	4.90
384	18.82	4.92
408	18.86	4.93
432	18.89	4.95
456	18.92	4.96
480	18.95	4.97
504	18.97	4.97

**Table 7: Cumulative percent of dose recovered in feces following an 8-hour topical exposure to creosote, 496 hours post-exposure**

Post-dose Timepoint (hours)	Cumulative Percent	
	Mean	SD
8	0.02	0.02
12	0.25	0.21
24	1.76	1.47
48	4.80	2.31
72	7.14	2.63
96	8.59	3.00
120	9.59	3.24
144	10.30	3.49
168	10.76	3.66
192	11.15	3.76
216	11.42	3.84
240	11.64	3.92
264	11.78	3.96
288	11.91	4.00
312	12.03	4.03
336	12.11	4.05
360	12.18	4.06
384	12.24	4.09
408	12.30	4.10
432	12.34	4.12
456	12.43	4.11
480	12.57	4.09
504	12.60	4.11

**Table 8: Cumulative percent of dose recovered in volatile organics following an 8-hour topical exposure to creosote, 496 hours post-exposure**

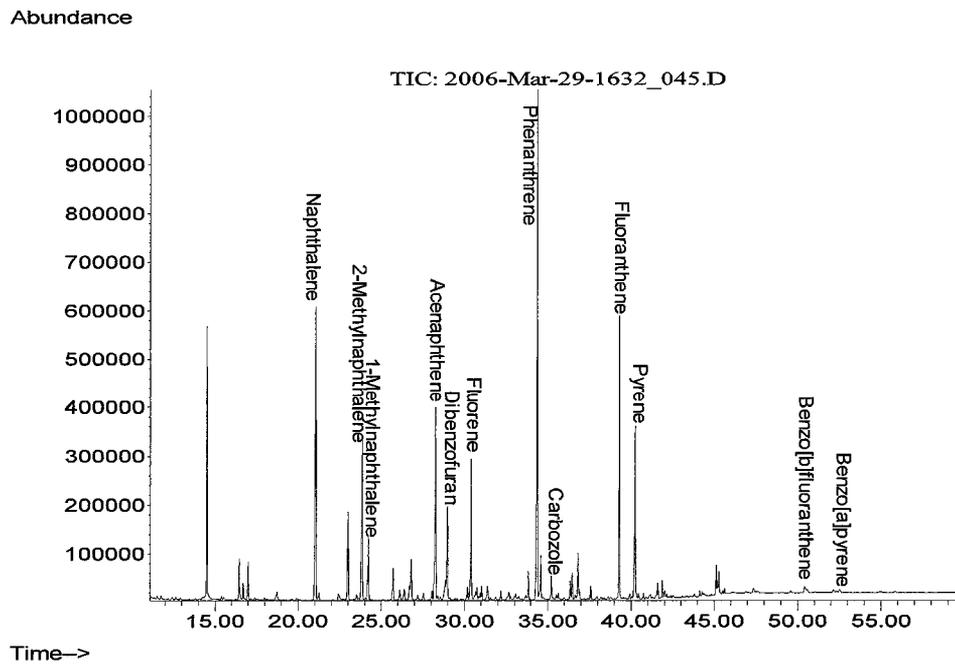
Post-dose Timepoint (hours)	Cumulative Percent	
	Mean	SD
8	<LOD	NA
12	<LOD	NA
24	0.082	0.036
48	0.144	0.096
72	0.226	0.130
96	0.280	0.147
120	0.296	0.174
144	0.311	0.198
168	0.311	0.198
192	0.311	0.198
216	NS	NA
240	NS	NA
264	NS	NA
288	NS	NA
312	NS	NA
336	NS	NA
360	NS	NA
384	NS	NA
408	NS	NA
432	NS	NA
456	NS	NA
480	NS	NA
504	NS	NA

**Table 9: Cumulative percent of dose recovered in total excreta following an 8-hour topical exposure to creosote, 496 hours post-exposure**

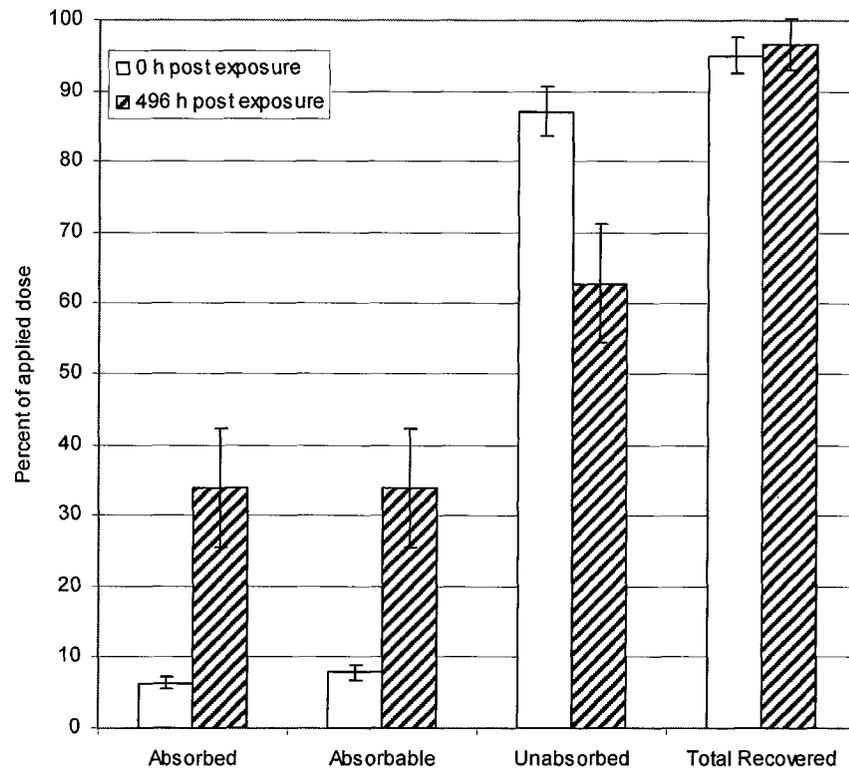
Post-dose Timepoint (hours)	Cumulative Percent	
	Mean	SD
8	2.78	0.30
12	4.31	0.55
24	9.26	1.68
48	16.42	3.65
72	21.50	4.88
96	24.55	5.85
120	26.63	6.43
144	27.97	6.78
168	28.82	7.04
192	29.48	7.24
216	29.66	7.20
240	30.03	7.32
264	30.28	7.39
288	30.50	7.47
312	30.68	7.54
336	30.84	7.59
360	30.95	7.63
384	31.06	7.67
408	31.15	7.70
432	31.23	7.73
456	31.35	7.76
480	31.52	7.81
504	31.57	7.82

**FIGURES**

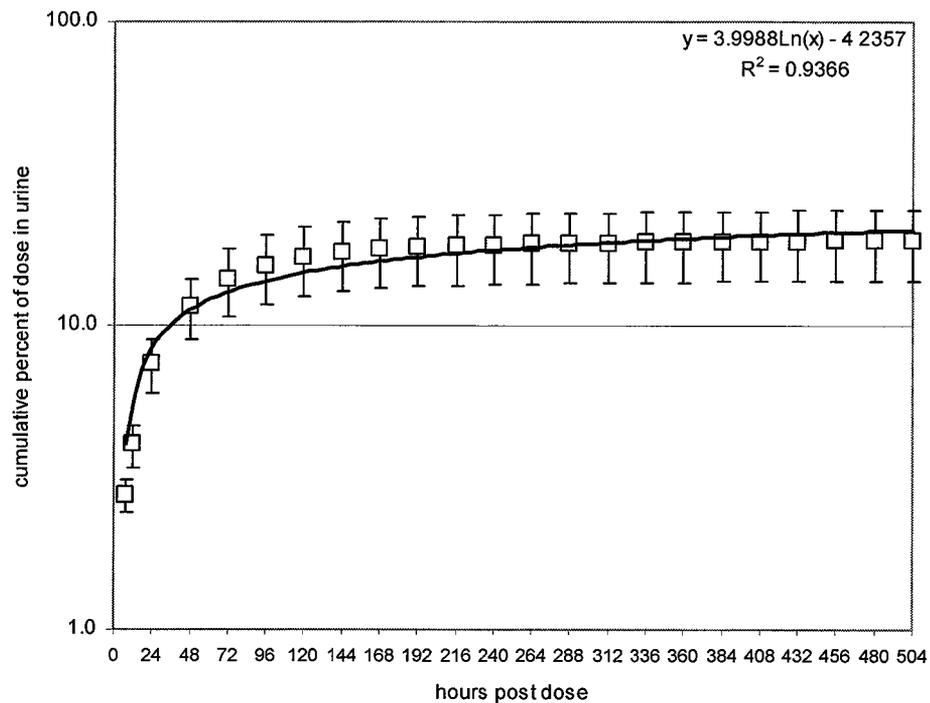
Figure 1: Total ion chromatogram for creosote test material



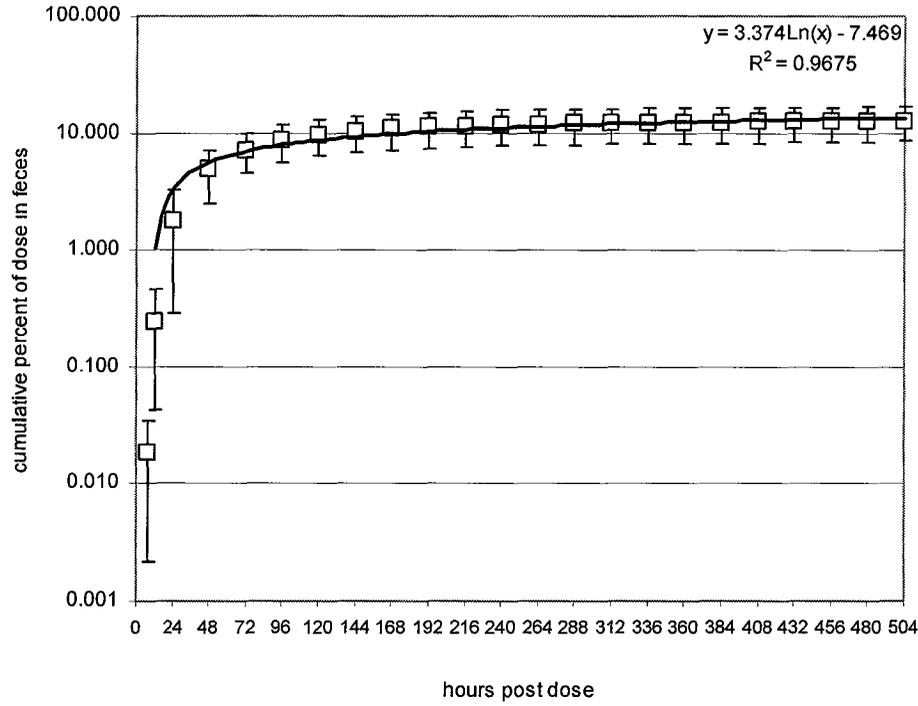
**Figure 2: Summary of percent of applied dose following an 8-hour exposure to a single topical application of creosote recovered 0 and 496 hours post-exposure**



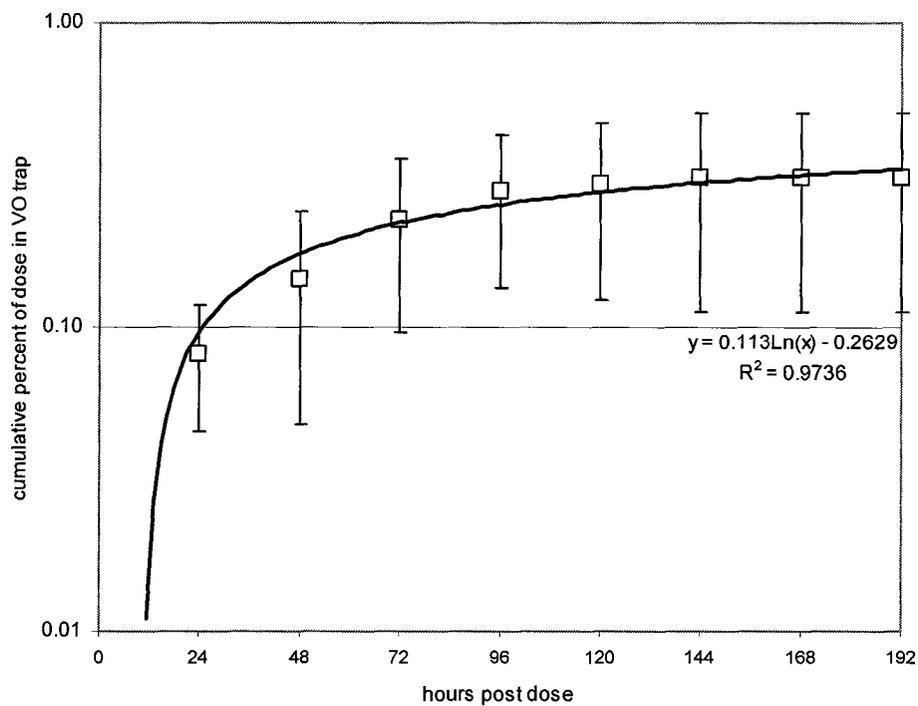
**Figure 3: Cumulative percent of dose recovered in urine following an 8-hour topical exposure to creosote, 496 hours post-exposure**



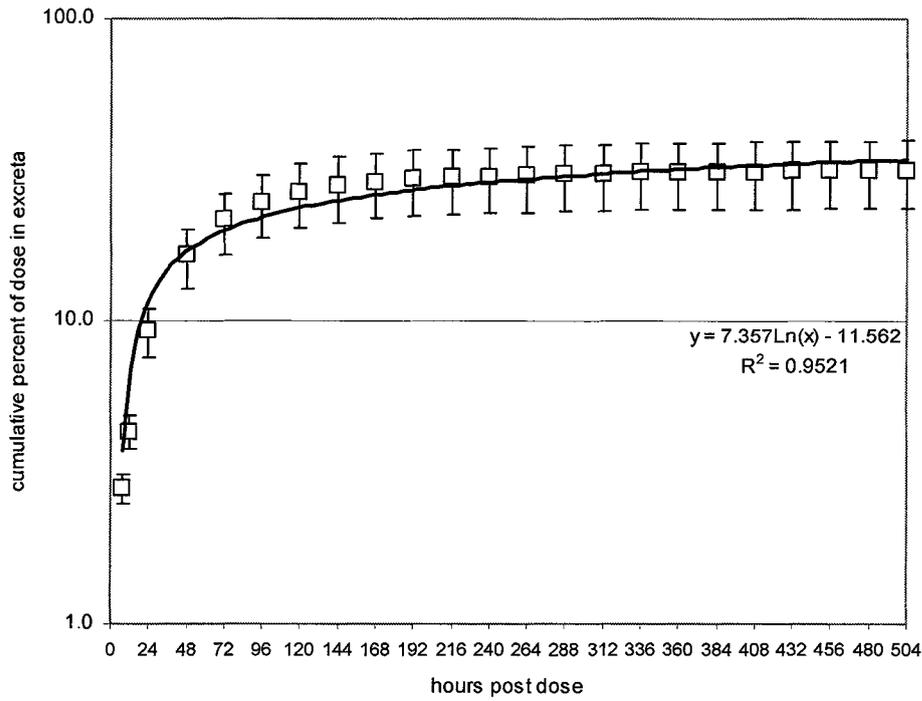
**Figure 4: Cumulative percent of dose recovered in feces following an 8-hour topical exposure to creosote, 496 hours post-exposure**



**Figure 5: Cumulative percent of dose recovered in volatile organic (VO) trap following an 8-hour topical exposure to creosote, 496 hours post-exposure**



**Figure 6: Cumulative percent of dose recovered in total excreta following an 8-hour topical exposure to creosote, 496 hours post-exposure**



**APPENDICES**

APPENDICES

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**EXPLANATORY NOTES**

ABBREVIATIONS:

Hr, hr, or h	hour(s)
LOD	limit of detection
LOQ	limit of quantitation
min	minute(s)
NA	not applicable
NS	no sample
SD	standard deviation

**Appendix A:**  
**Creosote Test Substance Information**

**JOHN H. BUTALA**

Diplomate - American Board of Toxicology

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William J. Fasano, Sr.  
E. I. du Pont de Nemours and Company  
Haskell Laboratory for Health and Environmental Sciences  
1090 Elkton Road  
Newark, DE 19714-0050

April 20, 2006

Re: Work Request Number 16308  
AWPA P1/P13 Creosote: *In Vivo* Dermal Absorption in the Rat

Dear Bill:

Enclosed are copies of the American Wood Preservers' Association (AWPA) Standard for P1/P13 creosote and results of creosote product chemistry testing for conformance with the AWPA standards. These documents are the certification that North American Creosote P1/P13 Composite Test Material is a *bona fide* P1/P13 creosote sample and is at least 98.5% pure. Because coal tar creosote is a complex mixture of variable composition, the commercial specifications for it (and for P2 creosote) are based on chemical and physical properties. Those properties are specified in the AWPA Standard, and the Research Triangle Institute report (70C-6939-001) establishes that North American Creosote P1/P13 Composite Test Material meets those specifications. Note that the Research Triangle Institute report is fully EPA GLP compliant.

The creosote test material supplied to Haskell Laboratory for dermal testing is an aliquot of the North American Creosote P1/P13 Composite Test Material assayed at RTI. Under the conditions of storage used for these samples, creosote is stable for at least four years.

This letter and the enclosures are intended to meet the need for documentation of creosote test material identity, strength and purity. Please contact me if you have questions or require additional information.

Best regards,



John H. Butala,  
Technical Advisor  
Creosote Council III

cc w/enc: Ken Branner

**AMERICAN  
WOOD-PRESERVERS'  
ASSOCIATION**

**STANDARDS  
1995**

RESEARCH TRIANGLE INSTITUTE



Analytical and Chemical Sciences

RTI/6939-North American 1 F

February 19, 1999

**FINAL REPORT**

**STUDY TITLE**

Preliminary Analysis for North American CTM Creosote P1/P13

**DATA REQUIREMENT**

Guideline 62-1

**AUTHOR**

Charles M. Sparacino

**STUDY COMPLETION DATE**

October 15, 1998

**PERFORMING LABORATORY**

Research Triangle Institute  
3040 Cornwallis Road  
Research Triangle Park, NC 27709

**LABORATORY PROJECT ID**

70C-6939-001

  
Charles M. Sparacino, Study Director

2-17-99  
Date

Page 1 of 31

3040 Cornwallis Road • Post Office Box 12194 • Research Triangle Park, North Carolina 27709-2194 USA  
Telephone 919 541-6507 • Fax 919 541-7208

North American P1/P13  
Series G2 Preliminary Analysis  
RTI Study No. 6229

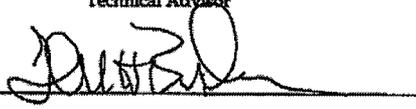
**STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS**

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA section 10 (d) (1) (A), (B) or (C).

Company: Creosote Council II

Company Agent: J. H. Butala

Title: Technical Advisor

Signature: 

Date: 3-1-99

North American P1/P13  
Series G2 Preliminary Analysis  
K11 Study No. 6939

**GOOD LABORATORY PRACTICE STATEMENT**

This study meets the requirements of 40 CFR Part 160.

Submitter: J. H. Butala Date: 3-1-99  
Sponsor: Permate Power II Date: 3-1-99  
Study Director: Cliff Johnson Date: 2-17-99



North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 6939

**SPONSOR AND TEST FACILITY**

**The study was sponsored by:**

Creosote Council II  
7 Glasgow Road  
Gibsonia, PA 15044

**The sponsor representative was:**

J. H. Butala  
Creosote Council II  
7 Glasgow Road  
Gibsonia, PA 15044

**The study was conducted at:**

Research Triangle Institute  
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Research Triangle Park, NC 27709

**The Study Director was:**

Charles M. Sparacino, Ph.D.  
Senior Program Director  
Research Triangle Institute  
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North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 6939

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10.0 APPENDX ..... 31

- SP CC-001 Preliminary Analysis Testing: North American Composite P1/P13 USEPA  
Pesticide Assessment Guidelines Subdivision D, Series 62
- SOP PCA-110 Receipt, Storage and Recordkeeping for FIFRA Product Chemistry and  
Pesticide Registration Samples Received at RTI
- SOP PCA-112 Procedures for Handling Numerical Data
- AP CC-001A Quantitative Analysis of Creosote Using the HP 5988A Gas  
Chromatograph/Mass Spectrometer
- AP CC-001B Qualitative Analysis of Creosote Samples by GC/MS Using the Hewlett-  
Packard 5988A System

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## SECTION 1.0

### ABSTRACT

To comply with the Product Chemistry data requirements of the EPA Re-registration Standard and Data Call-In Notice issued for pesticide products containing coal tar creosote, product identity data were generated. Pursuant to requirements described in Pesticide Assessment Guidelines, Subdivision D, Series 62 (ref. 1), Preliminary Analysis work was performed. Preliminary Analysis involved determination of component identity and quantitation of all components present at levels equal to or greater than 0.1 % by weight. For samples provided by North American, more than 100 components were detected at levels greater than or equal to 0.1 % by gas chromatography/mass spectrometry. The components were identified by use of published mass spectral libraries and/or by manual interpretation of individual component spectra. The samples were shown to consist predominantly of polycyclic aromatic hydrocarbons, with lesser numbers and amounts of saturated hydrocarbons, and nitrogen/sulfur/oxygen heterocyclic aromatics. All components were quantitated using an internal standard procedure.

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**SECTION 2.0**  
**INTRODUCTION**

The U.S. EPA has issued a pesticide data call-in notice for coal tar creosote (CAS # 8001-58-9). These initiatives required development of product identity and purity data. The requirements for such testing have been issued by EPA as per 40 CFR 158.150. This includes testing as described in Pesticide Assessment Guidelines, Subdivision D, Series 62-1 (Preliminary Analysis of Product Samples)(ref. 1). For Preliminary Analysis, three representative samples were provided for analysis. Analyses were conducted using a validated gas chromatographic/mass spectrometric (GC/MS) procedure that allowed for tentative identification of all components and provided quantitative data for all components present at levels equal to or greater than 0.1 % by weight. The work reported herein was conducted as described in RTI Study Protocol No. CC-001.

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**SECTION 3.0**  
**TEST MATERIAL**

Name of Test Material: North American CFM Creosote P1/P13  
Source of Test Material: Creosote Council II, Ontario, Canada  
Test Material CAS Registry No.: 8001-58-9  
Date of Receipt of Test Material: June 17, 1997

All samples were received and logged in according to RTI SOP PCA-110, rev. 0, "Receipt, Storage and Recordkeeping for FIFRA Product Chemistry and Pesticide Registration Samples Received at RTI". Each sample was shipped to RTI under proper seal at ambient temperatures, and was received in good condition with no evidence of leakage. Following log-in operations, the samples were stored at room temperature until used. Sample identification information includes: According to the sponsor, this test material was collected from a commercial or research facility and is representative of the P1/P13 creosote used to treat wood. Test material receipt and labeling information are shown in Table 1.

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#### SECTION 4.0 PRELIMINARY ANALYSIS

Subdivision D Guidelines require that manufacturing-use and certain end-use materials be analyzed for each active ingredient and for all impurities for which a certified limit is required. For creosote, there are numerous components, each of which (at levels equal to or greater than 0.1 %) was identified and quantitated by GC/MS. Identification was based on comparison of individual component mass spectra with spectra from published libraries, or by manual interpretation of the spectra by an individual skilled in such interpretations. Reference materials, when available, were used to confirm the identities of identified components. Components were quantitated using an internal standard method that was validated prior to sample analysis. Details of the procedures used are provided in the appropriate Standard Operating Procedures (SOPs) or Analytical Protocols (APs). All SOPs and APs used for this study are included in the Appendix. All raw data, reports, notebooks and other supporting documentation for this study are stored in the RTI ACS QA Archive facility.

##### 4.1 COMPONENT IDENTIFICATION

To determine the identity of each creosote sample component, analysis of each lot was conducted by GC/MS. Prior to GC/MS analysis, separation of the components of creosote was optimized using gas chromatography with flame ionization detection with a nonpolar, fused silica capillary column. This provided high resolution separation of all components that were amenable to GC assay. As described in AP CC-001B, each creosote sample was dissolved in methylene chloride and full scan data (35-350 daltons) were obtained for each eluting component. The spectra associated with the components were searched by computer against two libraries of spectra: the NIH/EPA/MSDC Mass Spectral Data Base (NIST Library) (ref. 2) and the Registry of Mass Spectral Data (Wiley Library) (ref. 3) containing more than 100,000 compounds. The spectra were also interpreted manually. In most cases, the identification of each component was unambiguous. For many substances, reference standards were available

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which were used for comparison of both spectra and component retention values in order to confirm identity. For those substances for which reference standards were not available, the identification by mass spectral interpretation alone must be regarded as tentative. The identified components for each of the three North American samples are shown in Table 2. A reconstructed ion chromatogram for a representative lot (RTI 8889-2C) is shown in Figure 1. All North American P1/P13 samples yielded virtually identical RICs, as is indicated by the relative amounts of components quantitated (see Table 2).

Identification was achieved by examination of the mass spectra and the results of the computer search against the library of spectra mentioned earlier. If the goodness of fit parameter was very high, and if the identification was consistent with other parameters (such as elution time, or inherent chemical properties), then the library identification was adopted. If a reference standard was available for a tentatively identified compound, its mass spectrum and retention value were compared to confirm or refute the identification. If a library spectrum did not match, or there was no library "hit", a spectrum was interpreted manually by a skilled interpreter. As noted earlier, identifications should be considered firm only when a reference standard was available (noted in Table 2) that produced both a spectral match and a retention time match. All other identifications should be considered tentative, although the mass spectral evidence is very strong in most cases. Some substances showed characteristic fragmentation patterns, but with no indication of which of several isomers might be responsible for the observed spectrum. For example, methylbenzothiophene can exist in six isomeric forms, which, unless all six forms are available as standards, cannot be readily distinguished by mass spectrometry. In such cases, only the generic denotation was given. In other instances, spectra were of sufficiently high quality to provide a molecular ion and limited fragmentation, but with insufficient information to identify the substance. For these compounds, empirical formulas were noted as the identified component. Finally, some spectra could be identified only with a significantly lower level of certainty than others. These spectra typically showed ions that could indicate the presence of a certain compound, but lacked the necessary number of ions for more certain identification, or had interfering ions that also

rendered the identification uncertain. These compounds are indicated in the table with a parenthetical question mark.

#### 4.2 COMPONENT QUANTITATION

To meet EPA pesticide registration requirements, registrants must determine the levels of all components of the pesticide that are present at levels equal to or greater than 0.1 % by weight. It is further required that the analytical methodology be validated over the appropriate concentration range. Creosote, a complex mixture of more than 100 components, is an atypical pesticide, and thus required a different and more specialized approach to the determination of overall composition. Many of the components of the substance have not been unambiguously identified, and reference standards for most of the components are therefore not available. However, since the great majority of creosote components belong to a single class of compounds (polycyclic aromatic hydrocarbons - PAHs) that span a range of molecular weights (two to six condensed rings), an assay method was developed that employed a selection of PAHs that served as markers or surrogates for the entire range of creosote components. Four creosote markers were selected: a 2-ring compound (naphthalene), a 3-ring compound (phenanthrene), and two 4-ring compounds (pyrene and chrysene). These markers spanned the elution range of the creosote components, and were used to quantitate components that eluted in a window centered on a specific marker.

Calibration curves were generated for each substance (in methylene chloride) over a concentration range of 2-1000 µg/mL. The lowest concentration corresponds, for the 8-g sample of each creosote lot that was analyzed, to 0.05 % by weight of that marker, and, by extension, to 0.05 % for the other (related) substances which were quantitated using the marker compounds. Each calibration curve consisted of nine concentration points (2, 4, 10, 40, 100, 200, 500, 750 and 1000 µg/mL). Each curve was based on the ratio of the marker substance response to an internal standard (tetalin) response. Tetalin (using ion 132 for quantitation) was chosen as an internal standard since it is structurally similar to the creosote PAH components, but was not present in any of the samples analyzed. The calibration curve data

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(response ratio vs. concentration) was best fitted to a logarithmic regression equation of the form  $\ln y = a + b \ln x$ , where  $y$  represents response ratio,  $x$  equals concentration, and  $b$  equals slope.

Four calibration curves were thus generated for quantitation of the components in each lot of creosote. Each curve equation met linearity requirements ( $r \geq 0.99$ ); none had any point with more than 13.7 % error (as determined by comparison of equation-generated concentration values with nominal values). Each concentration point was required to yield % error values of less than 25 %. Each curve for the four marker compounds is shown in Figures 2-5. Included with each plot is the regression equation and correlation coefficient. Check standards were injected at the beginning of analysis of each lot and confirmed that the calibration curve initially generated was still valid. For system suitability determinations, one concentration point was analyzed in replicate (six injections); area ratios (naphthalene response : internal standard response) were precise, with a % relative standard deviation (%RSD) of 2.61.

With a validated method, described in AP CC-001A, analysis was conducted for each lot of creosote. As noted above, full mass spectral scans were obtained for each component. The area of each component was also determined, and all component areas were transferred from the mass spectrometer output file to a spreadsheet program that produced the information shown in Table 2. The program calculated concentrations of each component using the appropriate calibration curve. Each concentration value, in units of  $\mu\text{g}/\text{mL}$ , was converted to a percentage value based on the weight of creosote drawn from each lot. As shown in Table 2, for each of the three creosote lots, a mean percentage and relative standard deviation were calculated.

The table shows concentration values only for those components that were quantitated at levels equal to or greater than the specified lower limit of 0.1 %. For compounds that were not detected, the compound was recorded as "NF" (Not Found). Substances that were detected at values less than 0.1 % are designated as "< 0.1 %". In some cases, one or two of the three lots showed quantifiable levels of a given component, and < 0.1 % or "NF" for the other lot(s). In these cases, a mean was not calculated and "NC" (Not Calculated) was reported.

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To illustrate the method of determination of the concentration of each creosote component, the following example is provided for the compound identified as 2-methylnaphthalene in sample 8889-2C. The peak corresponding to this compound was integrated yielding an area of 2,633,924 counts. Integrated area for the internal standard was 135,657 counts, giving a ratio (compound : internal standard) of 19.41605667. Solving the regression equation ( $\ln y = a + b \ln x$ ) for  $\ln x$  yields  $\ln x = (\ln y - a)/b$ . From Figure 1, the coefficients for the equation used for quantization of 2-methylnaphthalene are:  $a = -1.93087245$ ;  $b = 0.913900056$ .

Thus,

$$\ln x = (\ln 19.41605667 + 1.93087245)/0.913900056$$

$$\ln x = (2.966100387 + 1.93087245)/0.913900056$$

$$\ln x = 4.896972837/0.913900056$$

$$\ln x = 5.358324255.$$

The value of  $x$  is obtained by exponentiation of the natural logarithm yielding a value of  $x = 212.37$ . The calibration curve was prepared from standards with concentration units of  $\mu\text{g/mL}$ , and thus the calculated concentration is 212.37  $\mu\text{g/mL}$  for this component. To convert to units of percent, the amount of creosote drawn for analysis must be known as well as any dilution factors used in sample preparation prior to analysis. In this case, the amount of creosote sample was 8.052 g, and the dilution factor was 2,000. To convert g to  $\mu\text{g}$  requires division by 1,000,000, and to convert from  $\mu\text{g}$  to percent requires multiplication by 100. Thus, the formula for converting the found concentration of  $\mu\text{g/mL}$  to percent is:

$$\text{wt \%} = [(\text{component conc}) * (\text{dil. factor}) * 10^4] / \text{wt. of creosote sample}$$

Substituting the values given above:

$$\text{wt \%} = [(212.37)(2000)(10^4)]/8.052, \text{ or}$$

$$\text{wt \%} = 42.474/8.052 = 5.3 \text{ (rounded).}$$

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**SECTION 3.0  
CONCLUSIONS**

All required activities for Preliminary Analysis (Guideline 62-1) were addressed in this study. Analysis by GC/MS of each of three creosote lots provided identity and concentration values for all substances detected at levels greater than or equal to 0.1 % by weight.

North American P1/P13  
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RTI Study No. 6939

**SECTION 6.0**  
**ACKNOWLEDGMENTS**

Laboratory support for the work described in this report was provided by Nora  
Castillo, Scott Clifton, Ivy Igwe, Jeff Keever, and Marlene Clifton.

North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 6939

**SECTION 7.0**  
**REFERENCES**

1. Pesticide Assessment Guidelines, Subdivision D, Product Chemistry, EPA-540/9-82-018, OPTS, Washington, DC, October, 1982.
2. S. Stein, A. Levitsky and O. Fateev, NIST/EPA/NIH Mass Spectral Library, Version 1.0, Copyright 1994, U. S. Secretary of Commerce.
3. F. McLafferty, Registry of Mass Spectral Data: CD ROM, 5<sup>th</sup> Ed., John Wiley and Sons, New York, 1989.

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Series 62 Preliminary Analyte  
RTI Study No. 6209

**SECTION 8.0**  
**TABLES**

North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 6939

Table 1. North American CTM Creosote P1/P13 Samples - Receiving Information

Lot Number	Date of Collection	RTI Log Number
P1/13-14	6/13/97	8889-2C
P1/13-10	6/13/97	8889-2D
P1/13-13	6/13/97	8889-2F

North American P1/P13  
Series G2 Preliminary Analysis  
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Table 2. Components Identified by GC/MS in North American P1/P13 Creosote

Ref. Std. <sup>a</sup>	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889-2C <sup>b</sup>	8889-2D <sup>b</sup>	8889-2E <sup>b</sup>		
		1P	1M	2M		
	1,2,3-Trinitrobenzene	ND	ND	ND	ND	NA
	1,3-Dinitrobenzene	<0.1	<0.1	<0.1	<0.1	NA
	2,4-Dinitrobenzene	ND	ND	<0.1	ND	NA
	2,6-Dinitrobenzene	<0.1	<0.1	<0.1	<0.1	NA
	2,4,6-Trinitrobenzene	0.1	0.1	0.1	0.1	2.6
	Indan	0.3	0.3	0.4	0.3	19
	Indene	0.9	0.9	0.9	0.9	0
	2-Methylphenol	0.1	0.1	0.1	0.1	0
	Methylbenzofuran (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Methylindan (isomer) + Dimethylphenol (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	1,2,3-Trinitrobenzene (continued)					
	Naphthalene	0.4	0.4	0.4	0.4	0
	1-Methylindole	0.1	0.1	0.1	0.1	0
	2-Methylindole	0.1	0.1	0.1	0.1	0
	1-Methylindole	0.1	0.1	0.1	0.1	0
	Methylbenzothiophene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	1H-Indole	0.5	0.4	0.4	0.4	14
	2-Methylnaphthalene	5.3	5	5	5.1	3.4
	Methylbenzothiophene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Methylquinoline (isomer)	0.1	0.2	0.2	0.2	29
	1-Methylnaphthalene	2.2	2.2	2.2	2.2	6.6
	6-Methylindole	<0.1	<0.1	<0.1	<0.1	NA
	4-Methylindole	<0.1	<0.1	<0.1	<0.1	NA
	1-Indolyl	1.3	1.2	1.2	1.2	8.8
	2-Methylnaphthalene	0.5	0.5	0.5	0.5	2.8
	2,6-Dimethylnaphthalene	0.4	0.4	0.4	0.4	0
	Dimethylnaphthalene (isomer)	0.3	0.3	0.3	0.3	0
	1,3-Dimethylnaphthalene	0.7	0.6	0.6	0.6	9.6
	Dimethylnaphthalene (isomer)	0.3	0.3	0.3	0.3	0
	Dimethylnaphthalene (isomer)	0.3	0.3	0.3	0.3	0
	Acenaphthylene	0.1	0.1	0.1	0.1	0
	Dimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Acenaphthene	0.4	0.4	0.4	0.4	0
	1-Naphthylacetone	0.2	0.2	0.2	0.2	0
	Acenaphthene	0.1	0.1	0.1	0.1	0
	Isopropylindole (isomer) + n-Pentadecane	<0.1	<0.1	<0.1	<0.1	NA
	C <sub>15</sub> H <sub>32</sub> (isomer)	0.3	0.3	0.3	0.3	0
	Dibenzofuran	3.2	3	3	3.1	3.7
	Naphthalenecarbonitrile (isomer)	ND	<0.1	0.1	NC	NA
	Trimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Dimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Dimethylnaphthalene (isomer)	0.1	<0.1	<0.1	<0.1	NA
	Dimethylnaphthalene (isomer)	0.1	<0.1	<0.1	<0.1	NA
	2,5-Dimethylnaphthalene	<0.1	<0.1	<0.1	<0.1	NA

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K11 Study No. 6939

Table 2. (continued)

Ref. Std. <sup>a</sup>	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889- 2C <sup>b</sup>	8889- 2D <sup>b</sup>	8889- 2F <sup>b</sup>		
	Methylbenzothiothiophene (isomer)	<0.1	NF	NE	NC	NA
■	9H-Fluorene	4.5	4.0	4.2	4.2	6.0
	Allylnaphthalene (isomer)	0.3	0.2	0.4	0.3	33
■	Diphenylmethane	0.4	0.4	0.4	0.4	0
	Methylfluorene (isomer)	0.1	0.1	0.1	0.1	0
	2-Methylbiphenyl	0.2	0.2	0.2	0.2	0
	4-Methylbiphenyl	0.3	0.4	0.3	0.3	14
	Diphenylmethane (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Methylbenzofuran (isomer)	0.7	0.7	0.7	0.7	0
	Methylbenzofuran (isomer)	<0.1	<0.1	<0.1	<0.1	NA
■	1,10-Dihydroquinoline	0.5	0.5	0.5	0.5	0
	1,2-Dihydrophenanthrene	0.1	0.1	0.1	0.1	0
	Methylfluorene (isomer)	0.4	0.4	0.4	0.4	0
■	1-Methyl-9H-fluorene	0.3	0.2	0.2	0.2	29
	Methylfluorene (isomer)	0.3	0.2	0.2	0.2	29
	Dimethylbiphenyl (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	2-Fluorene (isomer)	0.7	0.7	0.7	0.7	0
	6-Fluorene (isomer)	0.1	NF	NF	NC	NA
	8-Fluorene (isomer)	0.1	<0.1	<0.1	<0.1	NA
■	Dibenzofuran	1.4	1.4	1.4	1.4	0
■	Fluorene	17.9	17.9	17.0	17.2	0
■	Anthracene	2.3	2.1	2.1	2.2	5.2
■	Acridine	0.2	0.2	0.2	0.2	0
■	5,6-benzoquinoline or phenanthridine	0.3	0.3	0.3	0.3	0
■	9H-Carbazole	1.3	1.2	1.2	1.2	4.8
	Methylbenzothiothiophene (isomer)	0.3	0.2	0.2	0.2	29
■	1-Phenylpiperazine	0.2	0.2	0.1	0.2	7
	1-Benzopyrrolone (isomer)	0.1	<0.1	<0.1	<0.1	NA
	Methylbenzothiothiophene (isomer)	0.1	0.1	0.2	0.1	NA
	Methylphenanthrene (isomer)	0.2	0.6	0.7	0.2	62
■	2-Methylphenanthrene	0.5	0.7	0.6	0.6	14
■	4H-Cyclopenta[def]phenanthrene	1.9	1.7	1.8	1.8	5.6
■	1-Methylphenanthrene	0.5	0.4	0.5	0.5	12
	Methylcarbazole (isomer)	NF	<0.1	NF	NC	NA
	Methylcarbazole (isomer)	<0.1	<0.1	0.2	NC	NA
	Methylcarbazole (isomer)	<0.1	NF	<0.1	NC	NA
	2-Methylphenanthrene	0.5	0.5	0.5	0.5	0
	3H-Fluorene (isomer)	<0.1	NF	<0.1	NC	NA
	5-Methylfluorene (isomer)	NF	<0.1	NF	NC	NA
	6-Methylfluorene (isomer)	0.3	0.3	0.3	0.3	0
	8-Methylfluorene (isomer)	<0.1	<0.1	<0.1	<0.1	NA

North American P1/P13  
Series 02 Preliminary Analysis  
KTI Study No. 0939

Table 2. (continued)

Ref. Std.	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889-2C <sup>a</sup>	8889-2D <sup>a</sup>	8889-2E <sup>a</sup>		
	Dimethylphenanthrene (isomer)	<0.1	<0.1	<0.1	0.0	NA
	Dimethylphenanthrene or anthracene (isomer)	0.4	0.3	0.2	0.3	33
■	Fluoranthene	7.2	6.5	6.6	6.8	5.6
■	9-Anthracenecarbonitrile	<0.1	<0.1	<0.1	NA	NA
	Benzylphthalene + C <sub>12</sub> H <sub>10</sub> (isomer)	<0.1	<0.1	<0.1	NA	NA
	Chrysene (isomer)	0.2	0.1	0.2	0.2	19
	Azanthrene (isomer)	NF	0.1	0.1	NC	NA
	Pyrene	6.1	5.8	5.7	6.0	4.8
	Vanilanthracene (isomer)	0.1	0.2	0.2	0.2	19
	Benzonaphthofuran (isomer)	0.1	0.1	0.1	0.1	0
	Benzonaphthofuran (isomer) + Azapyrene	0.7	0.5	0.5	0.6	17
	Benzonaphthofuran (isomer)	0.1	0.1	0.1	0.1	0
	Benzofluorene (isomer) or methylpyrene	0.3	0.3	0.3	0.3	0
	Pyrrrolocazole or 9H-fluorencarbonitrile	0.3	0.3	0.3	0.3	0
	Benzofluorene (isomer)	0.3	0.2	0.3	0.3	19
	Benzo[a]fluorene	0.1	0.2	0.2	0.2	0
■	2,3-Benzofluorene	0.2	0.1	0.1	0.1	0
	Methylpyrene (isomer)	0.3	0.2	0.2	0.2	0
	Phenylmethylphthalene (isomer)	0.5	0.4	0.5	0.5	17
	Methylpyrene (isomer)	0.4	0.3	0.4	0.4	17
	Methylpyrene or benzofluorene (isomer)	0.2	0.2	0.2	0.2	0
	Methylpyrene (isomer)	NF	<0.1	NF	NC	NA
	5,12-Dihydronaphthalene	0.3	0.3	0.3	0.3	0
	Dimethylpyrene (isomer)	0.1	0.1	0.1	0.1	0
	o-Turpene	0.3	0.2	0.2	0.2	29
	Dimethylpyrene (isomer)	0.2	0.2	0.2	0.2	0
	Dimethylpyrene (isomer)	0.1	<0.1	NF	NC	NA
■	1,2-Benzocyclopentadiene	0.4	0.3	0.3	0.3	17
	Acenaphthene	0.5	0.5	0.5	0.5	0
	Benzo[a]acridine	0.2	0.2	0.2	0.2	0
	Benzonaphthothiophene (isomer)	0.1	0.2	0.1	0.1	58
	Dicyanonaphthalene (isomer)	0.1	0.1	0.1	0.1	0
■	2,3-Benzanthracene	1.6	1.5	1.5	1.5	3.8
■	Chrysene	1.6	1.4	1.5	1.5	6.7
■	Benz[a]anthracene	0.5	0.5	0.5	0.5	0
	Methylbenzanthracene (isomer)	0.1	<0.1	0.1	0.1	0
	Benzofluorene (isomer)	0.1	0.1	0.1	0.1	0
	C <sub>12</sub> H <sub>10</sub> (isomer)	0.2	0.2	0.2	0.2	0
	C <sub>12</sub> H <sub>10</sub> (isomer)	0.1	0.1	0.1	0.1	0
	Methylchrysene (isomer)	0.2	0.2	0.2	0.2	0
	Methylchrysene or methylbenzanthracene (isomer)	0.1	0.1	0.1	0.1	0

North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 6939

Table 2. (continued)

Ref. Std. <sup>a</sup>	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889- 2C <sup>b</sup>	8889- 2D <sup>b</sup>	8889- 2F <sup>b</sup>		
	Methanochrysenes or 2,8-bis formylidibenzothiophene (isomer)	0.1	0.1	0.1	0.1	0
	Methanochrysenes or 2,8-bis formylidibenzothiophene (isomer)	0.1	NF	0.1	NC	NA
	Methanochrysenes or 2,8-bis formylidibenzothiophene (isomer)	0.2	0.2	0.2	0.2	0
	Methanochrysenes or 2,8-bis formylidibenzothiophene (isomer)	NF	NF	<0.1	NC	NA
	Benzo[a]fluoranthene	0.1	0.1	0.1	0.1	0
	Benzo[b]fluoranthene	0.1	0.1	0.1	0.1	0
	Chrysene	0.2	0.2	0.2	0.2	0
	Fluorene	0.1	0.1	0.1	0.1	0
	Benzo[a]pyrene	0.1	0.1	0.1	0.1	0
	Benzo[a]pyrene	0.5	0.4	0.5	0.5	12
	Pyrene	0.1	0.1	0.1	0.1	0
	C <sub>21</sub> H <sub>14</sub> (isomer)	NF	NF	<0.1	NC	NA
	Indeno(1,2,3-c,d)pyrene	0.2	0.1	0.1	0.1	58
	C <sub>21</sub> H <sub>14</sub> (isomer) (tent)	0.2	0.2	0.2	0.2	0
	Hexo[2,3]perylene	0.1	<0.1	0.1	<0.1	0
	C <sub>21</sub> H <sub>14</sub> (isomer)	NF	NF	<0.1	NC	NA

<sup>a</sup>Authentic material used where indicated (\*).

<sup>b</sup>See Table 1 for additional sample information.

NF = Not Found.

NC = Not Calculated.

NA = Not Applicable.

58  
144

North American P1/P13  
Series G2 Preliminary Analysis  
RTI Study No. 6999

**SECTION 9.0**

**FIGURES**

North American F1/P13  
Series 62 Preliminary Analysis  
K11 Study No. 8939

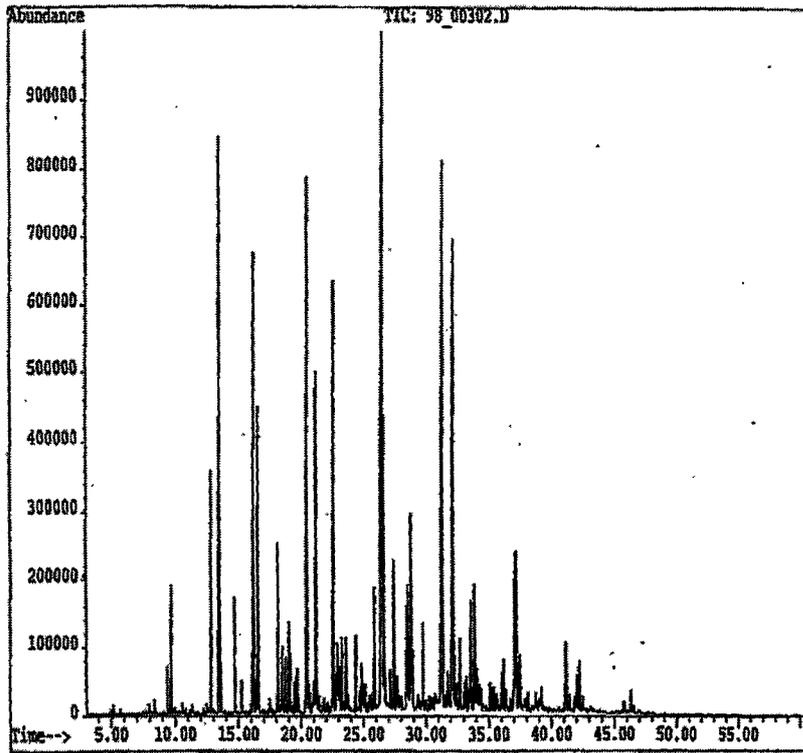


Figure 1. Reconstructed ion chromatogram of North American Composite sample 8889-2C

North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 6909

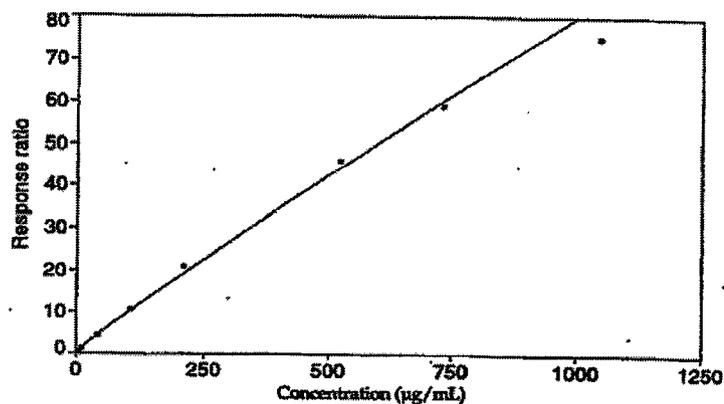


Figure 2. Naphthalene Calibration Curve  
Weighted (1/x) Regression Equation:  $\ln y = -1.931 + 0.9139 \ln x$   
Correlation Coefficient (r) = 0.99998

North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 4939

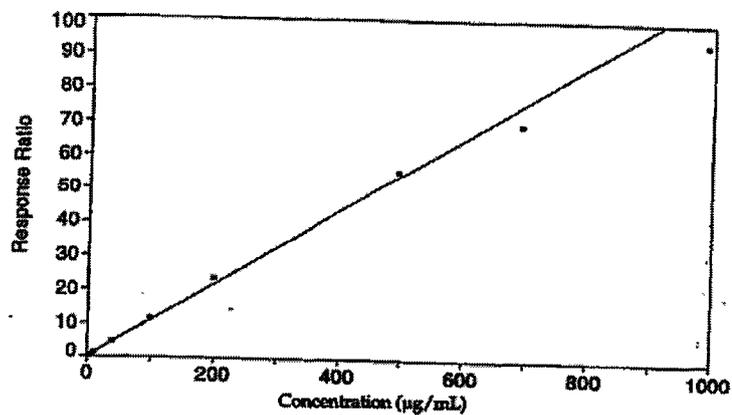


Figure 3. Phenanthrene Calibration Curve  
Weighted (1/x) Regression Equation:  $\ln y = -2.166 + 0.9925 \ln x$   
Correlation Coefficient (r) = 0.99998

North American P1/P13  
Series 62 Preliminary Analysis  
RT11Seady No. 6909

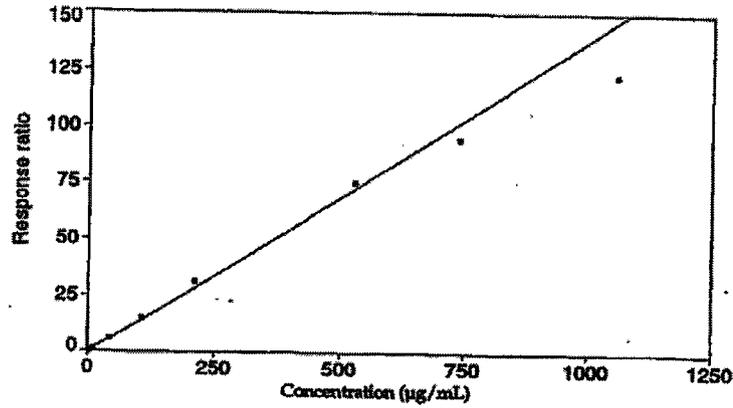


Figure 4. Pyrene Calibration Curve  
Weighted (1/x) Regression Equation:  $\ln y = -2.130 + 1.022 \ln x$   
Correlation Coefficient ( $r$ ) = 0.99990

North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 6939

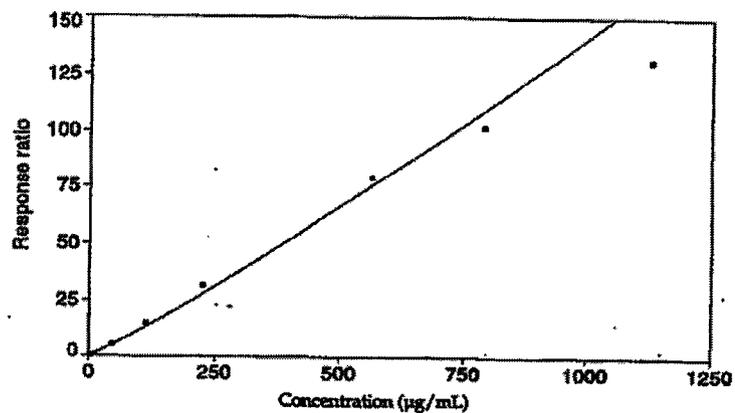


Figure 5. Chrysene Calibration Curve  
Weighted (1/x) Regression Equation:  $\ln y = -2.580 + 1.090 \ln x$   
Correlation Coefficient (r) = 0.9980

North American P1/P13  
Series 62 Preliminary Analysis  
RTI Study No. 6609

**SECTION 10.0**

**APPENDIX**

**Appendix B:**  
**Radiolabeled Test Substance Information**



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### Product Information

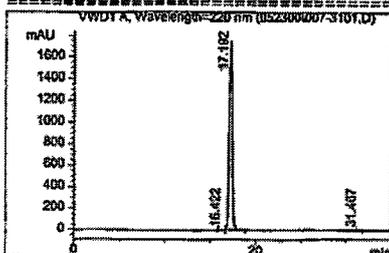
PROD NAME: 2-METHYLNAPHTHALENE-8-14C  
LOT NUMBER: 050K9424/25  
PROD NUMBER: M6146-14C  
ANALYST: 027BD  
DATE: 5/24/00 9:57:19 AM Inj Volume: 0.10ul

\*\*\*\*\*METHOD FOR M6146 2-METHYLNAPHTHALENE-8-14C\*\*\*\*\*

Column: Supelco Discovery C18, 250 x 2.1 mm, 5 micron  
Column Temp: 35°C  
Flow Rate: 0.3 ml/min  
Mobile Phase: A=0.1% Phosphoric Acid (V/V) in Water  
B=Acetonitrile  
50% A for 10 minutes to 0% A over 15 minutes, hold  
for 10 minutes  
Detection: UV Absorbance at 220NM

\*\*\*\*\*PRODUCT INFORMATION\*\*\*\*\*

Specific Activity : 8.5 mCi/mmol Storage Temp : 2-8°C  
Molecular Weight : 142.2 Packaging : Combi-vial  
Concentration : Solid



Peak #	RetTime [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.422	0.359	80.238	3.678	0.194
2	17.192	0.380	4.133e4	1.751e3	99.707
3	31.467	0.197	41.189	3.201	0.099

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### Product Information

PROD NAME: ANTHRACENE-1,2,3,4,4A,9A-14C  
LOT NUMBER: 018H9432/33  
PROD NUMBER: A9081-14C  
ANALYST: Quality Control  
DATE: 3/7/06 6:27:34 PM

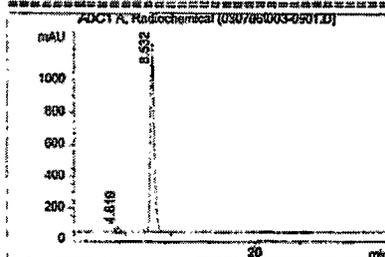
Inj Volume: 1.00ul

\*\*\*\*\*METHOD FOR A9081 ANTHRACENE-(1,2,3,4,4A,9A-14C)\*\*\*\*\*

Column: Supelco Ascentis C18, 250 x 2.1 mm, 5 micron  
Column Temp: 35°C  
Flow Rate: 0.3 ml/min  
Mobil Phase: A=0.1% Phosphoric Acid (V/V) in Water  
B=Acetonitrile  
25% A For 10 minutes to 0% A over 15 minutes, hold  
for 10 minutes  
Detection: Radiochemical

#### \*\*\*\*\*PRODUCT INFORMATION\*\*\*\*\*

Specific Activity : 20.6 mCi/mmol Storage Temp : 2-8°C  
Molecular Weight : 178.2 Packaging : Sealed Ampule  
Concentration : 0.9 mCi/ml in Toluene



Peak #	RetTime [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.819	0.373	839.250	33.443	2.476
2	8.532	0.428	3.306e4	1.163e3	97.524



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### Product Information

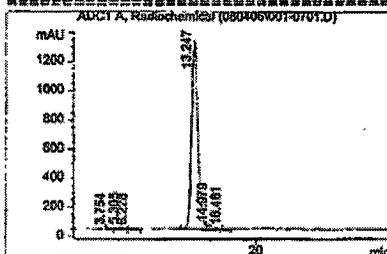
PROD NAME: BENZO-A-PYRENE-7-14C  
LOT NUMBER: 033H9241  
PROD NUMBER: B4642-14C  
ANALYST: Quality Control  
DATE: 8/4/06 3:42:01 PM Inj Volume: 3.00ul

\*\*\*\*\*METHOD FOR B4642 BENZO(A)PYRENE-7-14C\*\*\*\*\*

Column: Supelco Discovery C18, 250 x 2.1 mm, 5 micron  
Column Temp: 35°C  
Flow Rate: 0.3 ml/min  
Mobil Phase: A=0.1% Phosphoric Acid (V/V) in Water  
B=Acetonitrile  
25% A For 10 minutes to 0% A over 15 minutes, hold  
for 10 minutes  
Detection: Radiochemical

#### \*\*\*\*\*PRODUCT INFORMATION\*\*\*\*\*

Specific Activity : 26.6 mCi/nmol Storage Temp : 2-8°C  
Molecular Weight : 252.3 Packaging : Sealed Ampule  
Concentration : 1.0 mCi/ml in toluene



Peak #	RetTime [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.754	0.632	315.785	6.486	0.483
2	5.305	0.931	691.370	10.255	1.057
3	6.228	0.862	340.668	5.085	0.521
4	13.247	0.789	6.197e4	1.309e3	94.781
5	14.979	0.969	1.745e3	30.048	2.671
6	16.461	0.489	317.751	8.411	0.486

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### Product Information

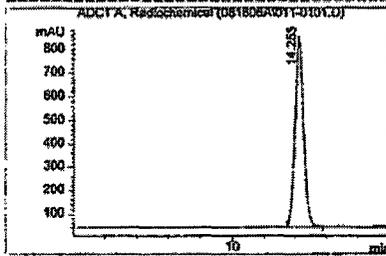
PROD NAME: BIPHENYL-UL-14C  
LOT NUMBER: 115F9247  
PROD NUMBER: B5892-14C  
ANALYST: Quality Control  
DATE: 8/16/06 2:04:10 PM Inj Volume: 1.00ul

\*\*\*\*\*METHOD FOR B5892 BIPHENYL-UL-14C\*\*\*\*\*

Column: Supelco Discovery C18, 250 x 2.1 mm, 5 micron  
Column Temp: 35°C  
Flow Rate: 0.3 ml/min  
Mobil Phase: A=0.1% Phosphoric Acid (V/V) in Water  
B=Acetonitrile  
50% A For 5 minutes to 25% A over 10 minutes, hold  
for 5 minutes  
Detection: Radiochemical

#### \*\*\*\*\*PRODUCT INFORMATION\*\*\*\*\*

Specific Activity : 7.6 mCi/mmol Storage Temp : 2-8°C  
Molecular Weight : 154.2 Packaging : Sealed ampule  
Concentration : 1.0 mCi/ml in Toluene



Peak #	RetTime [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.255	0.585	3.014e4	797.905	100.000

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### Product Information

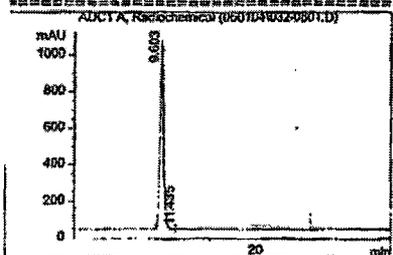
ROD NAME: FLUORANTHENE-3-14C  
JT NUMBER: 054K9630  
ROD NUMBER: F6147-14C  
ANALYST: Quality Control  
ATE: 6/1/04 9:18:17 PM Inj Volume: 7.00ul

\*\*\*\*\*METHOD FOR F6147 FLUORANTHENE-3-14C\*\*\*\*\*

column: Supelco Discovery HS C18, 250 x 2.1 mm, Sum  
column Temp: 35°C  
flow Rate: 0.3 ml/min  
mobile Phase: A=0.1% Phosphoric Acid (V/V) in Water  
B=Acetonitrile  
25% A For 10 minutes to 0% A over 15 minutes, hold  
for 10 minutes  
detection: Radiochemical

\*\*\*\*\*PRODUCT INFORMATION\*\*\*\*\*

Specific Activity : 45 mCi/mmol Storage Temp : 2-8°C  
Molecular Weight : 202.3 Packaging : Combi Vial  
Concentration : 1.0 mCi/ml in Methanol



Peak #	RetTime [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.603	0.403	2.863e4	1.022e3	99.523
2	11.435	0.529	137.120	3.116	0.477

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### Product Information

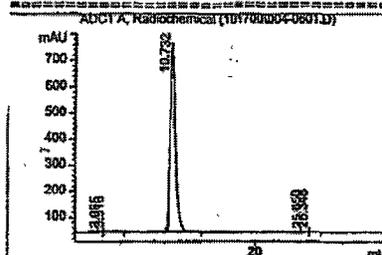
ROD NAME: NAPHTHLENE-BENZENE-UL-14C  
LOT NUMBER: 068H9600/01  
ROD NUMBER: N3145-14C  
ANALYST: 027BD  
DATE: 10/17/00 7:44:35 PM Inj Volume: 1.50ul

\*\*\*\*\*METHOD FOR N3145 NAPHTHLENE-BENZENE-UL-14C\*\*\*\*\*

Column: Supelco Discovery C18, 250 x 2.1 mm, 5 micron  
Column Temp: 35°C  
Flow Rate: 0.3 ml/min  
Mobile Phase: A=0.1% Phosphoric Acid (V/V) in Water  
B=Acetonitrile  
50% A For 10 minutes to 0% A over 15 minutes, hold  
for 10 minutes  
Detection: Radiochemical

\*\*\*\*\*PRODUCT INFORMATION\*\*\*\*\*

Specific Activity : 31.3 mCi/mmol Storage Temp : 2-8°C  
Molecular Weight : 128.2 Packaging : Combi Vial  
Concentration : Solid



Peak #	RetTime [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.085	0.357	25.711	1.201	0.084
2	3.516	0.951	170.614	2.990	0.559
3	10.732	0.596	3.027e4	716.960	99.119
4	25.650	0.395	21.919	0.926	0.072
5	26.348	0.614	50.758	1.377	0.166

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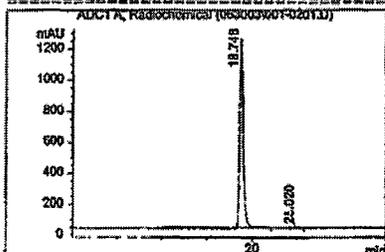
### Product Information

PROD NAME: PHENANTHRENE-9-14C  
LOT NUMBER: 111K9412/13  
PROD NUMBER: P0785-14C  
ANALYST: Quality Control  
DATE: 6/30/03 3:42:26 PM Inj Volume: 1.50ul  
\*\*\*\*\*METHOD FOR P0785 PHENANTHRENE-9-14C\*\*\*\*\*

Column: Supelco Discovery C18, 250 x 2.1 mm, 5 micron  
Column Temp: 35°C  
Flow Rate: 0.4 ml/min  
Mobil Phase: A=0.1% Phosphoric Acid (V/V) in Water  
B=Acetonitrile  
50% A for 10 minutes to 0% A over 15 minutes, hold  
for 10 minutes  
Detection: Radiochemical

#### \*\*\*\*\*PRODUCT INFORMATION\*\*\*\*\*

Specific Activity : 8.2 mCi/mmol Storage Temp : 2-8°C  
Molecular Weight : 178.2 Packaging : Combi Vial  
Concentration : Solid



Peak #	RetTime [min]	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.748	0.452	3.324e4	1.225e3	99.623
2	25.020	0.539	125.823	3.889	0.377

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### Product Information

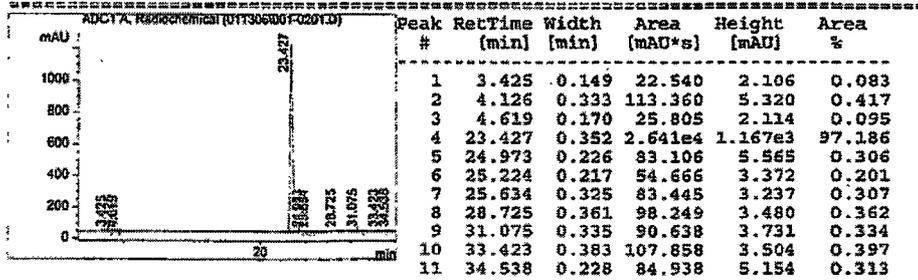
PROD NAME: PYRENE-4,5,9,10-14C  
LOT NUMBER: 079H9662/63  
PROD NUMBER: P6805-14C  
ANALYST: Quality Control  
DATE: 1/13/06 2:03:13 PM Inj Volume: 1.00ul

\*\*\*\*\*METHOD FOR P6805 PYRENE(4,5,9,10-14C)\*\*\*\*\*

Column: Supelco Ascentis C18, 250 x 2.1 mm, 5 micron  
Column Temp: 35°C  
Flow Rate: 0.4 ml/min  
Mobil Phase: A=0.1% Phosphoric Acid (V/V) in Water  
B=Acetonitrile  
50% A For 10 minutes to 0% A over 15 minutes, hold  
for 10 minutes  
Detection: Radiochemical

\*\*\*\*\*PRODUCT INFORMATION\*\*\*\*\*

Specific Activity : 55 mCi/mmol Storage Temp : 2-8°C  
Molecular Weight : 202.3 Packaging : Combi Vial  
Concentration : Solid



Accelerating Customers' success through leadership in Life Science, High Technology and Service.

**Appendix C:**  
**Individual Animal Data**

Application Amounts and Rates

0 Hour Post-Exposure Group

Rat Number	Body Weight (g)	Weight of Formulation (g) <sup>a</sup>	Total Radioactivity Applied (μCi)	Total Creosote Applied (μg) <sup>b</sup>	Application Rate (μg/cm <sup>2</sup> ) <sup>c</sup>
001M	345.4	0.11235	16.7	112350	10700
002M	313.4	0.11235	16.7	112350	10700
003M	357.5	0.11235	16.7	112350	10700
004M	347.1	0.11235	16.7	112350	10700
Mean	340.9	0.1124	16.7	112350	10700
SD	19.1	0.000	0.00	0.00	0.00

496 Hour Post-Exposure Group

Rat Number	Body Weight (g)	Weight of Formulation (g) <sup>a</sup>	Total Radioactivity Applied (μCi)	Total Creosote Applied (μg) <sup>b</sup>	Application Rate (μg/cm <sup>2</sup> ) <sup>c</sup>
005M	329.3	0.11235	16.7	112350	10700
006M	362.4	0.11235	16.7	112350	10700
007M	345.9	0.11235	16.7	112350	10700
008M	322.3	0.11235	16.7	112350	10700
Mean	340.0	0.1124	16.7	112350	10700
SD	17.9	0.000	0.00	0.00	0.00

<sup>a</sup> An application volume of 105 μL x density of 1.07 g/mL = 0.11235 g applied

<sup>b</sup> Based on weight applied x 1,000,000 μg/g

<sup>c</sup> Application rate = total Creosote applied (112350 μg)/10.5 cm<sup>2</sup>

Percent of applied dose - 0 hours post-exposure

Absorbed		001M	002M	003M	004M	Mean	SD
urine	8 h	1 913	1 936	2 002	2 666	2 129	0 36
feces	8 h	0 007	<LOQ	0 015	0 055	0 026	0 026
cage wash	8 h	0 988	0 787	0 338	0 675	0 697	0 272
CO2	8 h	<LOD	<LOD	<LOD	<LOD	N A	N A
residual feed	8 h	0 005	0 006	0 004	<LOQ	0 005	0 001
Volatile organics	8 h	0 049	<LOD	<LOD	<LOD	0 049	N A
non-dosed skin	8 h	0 016	0 025	0 023	0 017	0 02	0 004
Carcass	8 h	3 706	3 391	2 496	2 984	3 144	0 524
whole blood	8 h	0 031	0 019	0 028	0 031	0 027	0 006
rbc (terminal)	8 h	0 012	0 015	0 006	0 011	0 011	0 004
Heart	8 h	0 002	0 003	0 002	0 002	0 002	0
Lungs	8 h	0 007	0 007	0 004	0 007	0 006	0 002
Liver	8 h	0 187	0 204	0 169	0 181	0 185	0 015
Kidney	8 h	0 06	0 079	0 075	0 078	0 073	0 009
plasma (terminal)	8 h	0 013	0 011	0 009	0 012	0 011	0 002
Total		6 996	6 483	5 171	6 719	6 342	0 808
Absorbable		001M	002M	003M	004M	Mean	SD
Urine	8 h	1 913	1 936	2 002	2 666	2 129	0 36
Feces	8 h	0 007	<LOQ	0 015	0 055	0 026	0 026
cage wash	8 h	0 988	0 787	0 338	0 675	0 697	0 272
CO2	8 h	<LOD	<LOD	<LOD	<LOD	N A	N A
residual feed	8 h	0 005	0 006	0 004	<LOQ	0 005	0 001
Volatile organics	8 h	0 049	<LOD	<LOD	<LOD	0 049	N A
dosed skin	8 h	1 72	1 805	1 132	1 555	1 553	0 299
non-dosed skin	8 h	0 016	0 025	0 023	0 017	0 02	0 004
Carcass	8 h	3 706	3 391	2 496	2 984	3 144	0 524
whole blood	8 h	0 031	0 019	0 028	0 031	0 027	0 006
rbc (terminal)	8 h	0 012	0 015	0 006	0 011	0 011	0 004
Heart	8 h	0 002	0 003	0 002	0 002	0 002	0
Lungs	8 h	0 007	0 007	0 004	0 007	0 006	0 002
Liver	8 h	0 187	0 204	0 169	0 181	0 185	0 015
Kidney	8 h	0 06	0 079	0 075	0 078	0 073	0 009
plasma (terminal)	8 h	0 013	0 011	0 009	0 012	0 011	0 002
Total		8 716	8 288	6 303	8 274	7 895	1 081
Unabsorbed		001M	002M	003M	004M	Mean	SD
body wrap	8 h	5 229	1 541	1 479	0 14	2 097	2 186
skin wash -- sponges	8 h	45 803	51 827	66 939	72 563	59 283	12 547
charcoal (trap)	8 h	0 704	0 394	0 371	0 49	0 49	0 152
O-ring	8 h	24 952	23 46	18 105	6 911	18 357	8 177
tape strip 1	8 h	2 488	2 364	1 077	1 943	1 968	0 638
tape strip 2	8 h	1 132	2 257	0 742	0 721	1 213	0 721
tape strip 3	8 h	1 234	1 354	0 754	0 577	0 98	0 373
tape strip 4	8 h	0 927	1 259	0 334	0 346	0 717	0 455
tape strip 5	8 h	0 709	0 69	0 342	0 297	0 51	0 22
tape strip 6	8 h	0 467	0 83	0 259	0 166	0 431	0 295
tape strip 7	8 h	0 521	0 431	1 188	0 15	0 573	0 44
tape strip 8	8 h	0 223	0 472	0 29	0 067	0 263	0 168
tape strip 9	8 h	0 067	0 55	0 073	0 045	0 184	0 244
tape strip 10	8 h	0 053	0 122	0 011	0 013	0 05	0 052
tape sub total		7 821	10 329	5 070	4 325	6 886	2 744
Total		84 509	87 551	91 964	84 429	87 113	3 545
Total Recovered		93 225	95 839	98 267	92 703	95 009	2 569

Percent of applied dose - 496 hours post-exposure

Absorbed		005M	006M	007M	008M	Mean	SD
urine	8 h	2.341	3.001	2.691	3.019	2.763	0.319
urine	12 h	0.833	1.5	1.289	1.547	1.292	0.326
urine	24 h	2.198	3.424	3.692	4.303	3.404	0.884
urine	48 h	2.259	4.783	4.759	4.426	4.057	1.21
urine	72 h	1.276	2.428	3.895	3.087	2.672	1.107
urine	96 h	0.883	1.735	1.875	1.766	1.565	0.458
urine	120 h	0.552	1.06	1.143	1.522	1.069	0.399
urine	144 h	0.402	0.645	0.651	0.761	0.615	0.152
urine	168 h	0.23	0.482	0.386	0.473	0.393	0.117
urine	192 h	0.158	0.345	0.233	0.305	0.26	0.082
urine	216 h	0.129	0.176	0.111	0.203	0.155	0.042
urine	240 h	0.086	0.166	0.077	0.232	0.14	0.073
urine	264 h	0.065	0.109	0.06	0.207	0.11	0.068
urine	288 h	0.041	0.104	0.051	0.157	0.088	0.054
urine	312 h	0.037	0.084	0.037	0.142	0.075	0.05
urine	336 h	0.035	0.063	0.047	0.112	0.064	0.034
urine	360 h	0.025	0.048	0.039	0.097	0.052	0.031
urine	384 h	0.023	0.039	0.037	0.074	0.043	0.022
urine	408 h	0.018	0.026	0.028	0.081	0.038	0.029
urine	432 h	0.016	0.03	0.023	0.062	0.033	0.02
urine	456 h	0.016	0.028	0.035	0.053	0.033	0.015
urine	480 h	0.021	0.03	0.029	0.045	0.031	0.01
urine	504 h	0.008	0.017	0.015	0.014	0.014	0.004
sub total urine		11.652	20.323	21.203	22.688	18.967	4.973
feces	8 h	0.038	0.007	0.027	0.003	0.019	0.017
feces	12 h	0.437	0.368	0.079	0.041	0.231	0.2
feces	24 h	1.878	3.187	0.457	0.512	1.509	1.298
feces	48 h	2.04	4.572	3.228	2.319	3.04	1.14
feces	72 h	1.471	2.851	2.775	2.275	2.343	0.635
feces	96 h	0.715	1.904	1.833	1.339	1.448	0.549
feces	120 h	0.562	1.353	0.949	1.132	0.999	0.335
feces	144 h	0.459	1.085	0.595	0.7	0.71	0.269
feces	168 h	0.276	0.701	0.437	0.433	0.462	0.176
feces	192 h	0.22	0.546	0.293	0.514	0.393	0.161
feces	216 h	0.161	0.379	0.214	0.308	0.266	0.097
feces	240 h	0.129	0.348	0.129	0.289	0.224	0.112
feces	264 h	0.08	0.196	0.093	0.195	0.141	0.063
feces	288 h	0.049	0.175	0.084	0.21	0.13	0.076
feces	312 h	0.055	0.152	0.068	0.179	0.114	0.061
feces	336 h	0.04	0.11	0.065	0.132	0.087	0.042
feces	360 h	0.025	0.083	0.06	0.093	0.065	0.03
feces	384 h	0.024	0.094	0.059	0.074	0.063	0.03
feces	408 h	0.021	0.073	0.043	0.082	0.055	0.028
feces	432 h	0.016	0.056	0.033	0.065	0.043	0.022
feces	456 h	0.016	0.042	0.21	0.08	0.087	0.086
feces	480 h	0.044	0.071	0.291	0.179	0.146	0.113
feces	504 h	0.019	0.05	0.006	0.057	0.033	0.024
sub total feces		8.775	18.403	12.028	11.211	12.604	4.105

Percent of applied dose - 496 hours post-exposure (continued)

Absorbed (cont'd)		005M	006M	007M	008M	Mean	SD
cage wash	504 h	0.49	0.917	2.723	2.549	1.67	1.131
CO2	8 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	12 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	24 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	48 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	72 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	96 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	120 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	144 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	168 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	192 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	216 h	NS	NS	NS	NS	NA	NA
CO2	240 h	NS	NS	NS	NS	NA	NA
CO2	264 h	NS	NS	NS	NS	NA	NA
CO2	288 h	NS	NS	NS	NS	NA	NA
CO2	312 h	NS	NS	NS	NS	NA	NA
CO2	336 h	NS	NS	NS	NS	NA	NA
CO2	360 h	NS	NS	NS	NS	NA	NA
CO2	384 h	NS	NS	NS	NS	NA	NA
CO2	408 h	NS	NS	NS	NS	NA	NA
CO2	432 h	NS	NS	NS	NS	NA	NA
CO2	456 h	NS	NS	NS	NS	NA	NA
CO2	480 h	NS	NS	NS	NS	NA	NA
CO2	504 h	NS	NS	NS	NS	NA	NA
sub total CO2		0.000	0.000	0.000	0.000	0.000	0.000
residual feed	504 h	0.041	0.403	0.37	0.151	0.241	0.174
Volatile organics (VO)	8 h	<LOD	<LOD	<LOD	<LOD	NA	NA
VO	12 h	<LOD	<LOD	<LOD	<LOD	NA	NA
VO	24 h	<LOQ	0.056	0.107	<LOQ	0.082	0.036
VO	48 h	<LOQ	0.07	0.141	0.058	0.09	0.045
VO	72 h	<LOQ	0.065	0.121	0.059	0.082	0.034
VO	96 h	<LOD	0.041	0.076	0.047	0.055	0.019
VO	120 h	<LOD	<LOQ	0.048	<LOQ	0.048	NA
VO	144 h	<LOD	<LOD	0.043	<LOQ	0.043	NA
VO	168 h	<LOD	<LOD	<LOQ	<LOD	NA	NA
VO	192 h	<LOD	<LOD	<LOQ	<LOD	NA	NA
VO	216 h	NS	NS	NS	NS	NA	NA
VO	240 h	NS	NS	NS	NS	NA	NA
VO	264 h	NS	NS	NS	NS	NA	NA
VO	288 h	NS	NS	NS	NS	NA	NA
VO	312 h	NS	NS	NS	NS	NA	NA
VO	336 h	NS	NS	NS	NS	NA	NA
VO	360 h	NS	NS	NS	NS	NA	NA
VO	384 h	NS	NS	NS	NS	NA	NA
VO	408 h	NS	NS	NS	NS	NA	NA
VO	432 h	NS	NS	NS	NS	NA	NA
VO	456 h	NS	NS	NS	NS	NA	NA
VO	480 h	NS	NS	NS	NS	NA	NA
VO	504 h	NS	NS	NS	NS	NA	NA
sub total VO		0.000	0.232	0.536	0.164	0.233	0.224
non-dosed skin	504 h	0.053	0.034	0.046	0.021	0.039	0.014
Carcass	504 h	0.511	0.077	0.099	0.091	0.195	0.211
whole blood	504 h	0.001	0.003	0.003	0.003	0.003	0.001
rbc (terminal)	504 h	0.001	0.002	0.002	0.002	0.002	0.001
Heart	504 h	<LOD	<LOD	<LOD	<LOD	NA	NA
Lungs	504 h	<LOD	<LOD	<LOQ	<LOQ	NA	NA
Liver	504 h	0.003	0.006	0.006	0.006	0.005	0.002
Kidney	504 h	0.001	0.002	0.002	0.002	0.002	0.001
plasma (terminal)	504 h	<LOD	<LOD	<LOD	<LOD	NA	NA
Total		21.528	40.402	37.018	36.888	33.959	8.445

Percent of applied dose - 496 hours post-exposure (continued)

Absorbable		005M	006M	007M	008M	Mean	SD
Urine	8 h	2 341	3 001	2 691	3 019	2 763	0 319
Urine	12 h	0 833	1 5	1 289	1 547	1 292	0 326
Urine	24 h	2 198	3 424	3 692	4 303	3 404	0 884
Urine	48 h	2 259	4 783	4 759	4 426	4 057	1 21
Urine	72 h	1 276	2 428	3 895	3 087	2 672	1 107
Urine	96 h	0 883	1 735	1 875	1 766	1 565	0 458
Urine	120 h	0 552	1 06	1 143	1 522	1 069	0 399
Urine	144 h	0 402	0 645	0 651	0 761	0 615	0 152
Urine	168 h	0 23	0 482	0 386	0 473	0 393	0 117
Urine	192 h	0 158	0 345	0 233	0 305	0 26	0 082
Urine	216 h	0 129	0 176	0 111	0 203	0 155	0 042
Urine	240 h	0 086	0 166	0 077	0 232	0 14	0 073
Urine	264 h	0 065	0 109	0 06	0 207	0 11	0 068
Urine	288 h	0 041	0 104	0 051	0 157	0 088	0 054
Urine	312 h	0 037	0 084	0 037	0 142	0 075	0 05
Urine	336 h	0 035	0 063	0 047	0 112	0 064	0 034
Urine	360 h	0 025	0 048	0 039	0 097	0 052	0 031
Urine	384 h	0 023	0 039	0 037	0 074	0 043	0 022
Urine	408 h	0 018	0 026	0 028	0 081	0 038	0 029
Urine	432 h	0 016	0 03	0 023	0 062	0 033	0 02
Urine	456 h	0 016	0 028	0 035	0 053	0 033	0 015
Urine	480 h	0 021	0 03	0 029	0 045	0 031	0 01
Urine	504 h	0 008	0 017	0 015	0 014	0 014	0 004
sub total urine		11 652	20 323	21 203	22 688	18 967	4 973
Feces	8 h	0 038	0 007	0 027	0 003	0 019	0 017
Feces	12 h	0 437	0 368	0 079	0 041	0 231	0 2
Feces	24 h	1 878	3 187	0 457	0 512	1 509	1 298
Feces	48 h	2 04	4 572	3 228	2 319	3 04	1 14
Feces	72 h	1 471	2 851	2 775	2 275	2 343	0 635
Feces	96 h	0 715	1 904	1 833	1 339	1 448	0 549
Feces	120 h	0 562	1 353	0 949	1 132	0 999	0 335
Feces	144 h	0 459	1 085	0 595	0 7	0 71	0 269
Feces	168 h	0 276	0 701	0 437	0 433	0 462	0 176
Feces	192 h	0 22	0 546	0 293	0 514	0 393	0 161
Feces	216 h	0 161	0 379	0 214	0 308	0 266	0 097
Feces	240 h	0 129	0 348	0 129	0 289	0 224	0 112
Feces	264 h	0 08	0 196	0 093	0 195	0 141	0 063
Feces	288 h	0 049	0 175	0 084	0 21	0 13	0 076
Feces	312 h	0 055	0 152	0 068	0 179	0 114	0 061
Feces	336 h	0 04	0 11	0 065	0 132	0 087	0 042
Feces	360 h	0 025	0 083	0 06	0 093	0 065	0 03
Feces	384 h	0 024	0 094	0 059	0 074	0 063	0 03
Feces	408 h	0 021	0 073	0 043	0 082	0 055	0 028
Feces	432 h	0 016	0 056	0 033	0 065	0 043	0 022
Feces	456 h	0 016	0 042	0 21	0 08	0 087	0 086
Feces	480 h	0 044	0 071	0 291	0 179	0 146	0 113
Feces	504 h	0 019	0 05	0 006	0 057	0 033	0 024
sub total feces		8 775	18 403	12 028	11 211	12 604	4 105
cage wash	504 h	0 49	0 917	2 723	2 549	1 67	1 131

Percent of applied dose - 496 hours post-exposure (continued)

Absorbable (cont'd)		005M	006M	007M	008M	Mean	SD
CO2	8 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	12 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	24 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	48 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	72 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	96 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	120 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	144 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	168 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	192 h	<LOD	<LOD	<LOD	<LOD	NA	NA
CO2	216 h	NS	NS	NS	NS	NA	NA
CO2	240 h	NS	NS	NS	NS	NA	NA
CO2	264 h	NS	NS	NS	NS	NA	NA
CO2	288 h	NS	NS	NS	NS	NA	NA
CO2	312 h	NS	NS	NS	NS	NA	NA
CO2	336 h	NS	NS	NS	NS	NA	NA
CO2	360 h	NS	NS	NS	NS	NA	NA
CO2	384 h	NS	NS	NS	NS	NA	NA
CO2	408 h	NS	NS	NS	NS	NA	NA
CO2	432 h	NS	NS	NS	NS	NA	NA
CO2	456 h	NS	NS	NS	NS	NA	NA
CO2	480 h	NS	NS	NS	NS	NA	NA
CO2	504 h	NS	NS	NS	NS	NA	NA
sub total CO2		0 000	0 000	0 000	0 000	0 000	0 000
residual feed	504 h	0 041	0 403	0 37	0 151	0 241	0 174
Volatile organics (VO)	8 h	<LOD	<LOD	<LOD	<LOD	NA	NA
VO	12 h	<LOD	<LOD	<LOD	<LOD	NA	NA
VO	24 h	<LOQ	0 056	0 107	<LOQ	0 082	0 036
VO	48 h	<LOQ	0 07	0 141	0 058	0 09	0 045
VO	72 h	<LOQ	0 065	0 121	0 059	0 082	0 034
VO	96 h	<LOD	0 041	0 076	0 047	0 055	0 019
VO	120 h	<LOD	<LOQ	0 048	<LOQ	0 048	NA
VO	144 h	<LOD	<LOD	0 043	<LOQ	0 043	NA
VO	168 h	<LOD	<LOD	<LOQ	<LOD	NA	NA
VO	192 h	<LOD	<LOD	<LOQ	<LOD	NA	NA
VO	216 h	NS	NS	NS	NS	NA	NA
VO	240 h	NS	NS	NS	NS	NA	NA
VO	264 h	NS	NS	NS	NS	NA	NA
VO	288 h	NS	NS	NS	NS	NA	NA
VO	312 h	NS	NS	NS	NS	NA	NA
VO	336 h	NS	NS	NS	NS	NA	NA
VO	360 h	NS	NS	NS	NS	NA	NA
VO	384 h	NS	NS	NS	NS	NA	NA
VO	408 h	NS	NS	NS	NS	NA	NA
VO	432 h	NS	NS	NS	NS	NA	NA
VO	456 h	NS	NS	NS	NS	NA	NA
VO	480 h	NS	NS	NS	NS	NA	NA
VO	504 h	NS	NS	NS	NS	NA	NA
sub total VO		0 000	0 232	0 536	0 164	0 233	0 224
dosed skin	504 h	0 002	0 005	0 008	0 003	0 005	0 003
non-dosed skin	504 h	0 053	0 034	0 046	0 021	0 039	0 014
Carcass	504 h	0 511	0 077	0 099	0 091	0 195	0 211
whole blood	504 h	0 001	0 003	0 003	0 003	0 003	0 001
rbc (terminal)	504 h	0 001	0 002	0 002	0 002	0 002	0 001
Heart	504 h	<LOD	<LOD	<LOD	<LOD	NA	NA
Lungs	504 h	<LOD	<LOD	<LOQ	<LOQ	NA	NA
Liver	504 h	0 003	0 006	0 006	0 006	0 005	0 002
Kidney	504 h	0 001	0 002	0 002	0 002	0 002	0 001
plasma (terminal)	504 h	<LOD	<LOD	<LOD	<LOD	NA	NA
Total		21 530	40 407	37 026	36 891	33 964	8 447

Percent of applied dose - 496 hours post-exposure (continued)

Unabsorbed		005M	006M	007M	008M	Mean	SD
body wrap	8 h	0 311	0 474	0 657	0 308	0 438	0 166
body wrap	504 h	0 908	1 903	3 82	1 391	2 006	1 276
bw sub total		1 219	2 377	4 477	1 699	2 443	1 437
skin wash - sponges	8 h	68 328	49 149	56 875	52 935	56 822	8 294
charcoal (trap)	8 h	0 49	0 292	0 391	0 461	0 409	0 088
charcoal (trap)	216 h	0 016	0 017	0 04	0 097	0 043	0 038
charcoal trap sub total		0 506	0 309	0 431	0 558	0 451	0 108
O-ring	504 h	3 197	2 125	3 128	3 104	2 889	0 511
tape strip 1	504 h	0 014	0 035	0 083	0 002	0 034	0 036
tape strip 2	504 h	0 002	0 013	0 007	<LOQ	0 007	0 006
tape strip 3	504 h	0 001	0 002	0 002	<LOD	0 002	0 001
tape strip 4	504 h	0 001	<LOQ	0 001	<LOD	0 001	0
tape strip 5	504 h	<LOQ	<LOD	<LOD	<LOD	NA	NA
tape strip 6	504 h	<LOQ	<LOD	NS	<LOD	NA	NA
tape strip 7	504 h	<LOD	NS	NS	<LOD	NA	NA
tape strip 8	504 h	<LOD	NS	NS	NS	NA	NA
tape strip 9	504 h	<LOD	NS	NS	NS	NA	NA
tape sub total		0 018	0 050	0 093	0 002	0 041	0 040
	Total	73 268	54 010	65 004	58 296	62 645	8 404
<b>Total Recovered</b>		94 798	94 417	102 030	95 189	96 609	3 628

Cumulative Percent of Dose Recovered in Urine, 496 hours post-exposure

Timepoint (hours)	005M			006M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	2.341	2.34	20.1	3.001	3.00	14.8
12 h	0.833	3.17	27.2	1.5	4.50	22.1
24 h	2.198	5.37	46.1	3.424	7.93	39.0
48 h	2.259	7.63	65.5	4.783	12.7	62.5
72 h	1.276	8.91	76.4	2.428	15.1	74.5
96 h	0.883	9.79	84.0	1.735	16.9	83.0
120 h	0.552	10.34	88.8	1.06	17.9	88.2
144 h	0.402	10.74	92.2	0.645	18.6	91.4
168 h	0.23	10.97	94.2	0.482	19.1	93.8
192 h	0.158	11.13	95.5	0.345	19.4	95.5
216 h	0.129	11.26	96.6	0.176	19.6	96.3
240 h	0.086	11.35	97.4	0.166	19.7	97.2
264 h	0.065	11.41	97.9	0.109	19.9	97.7
288 h	0.041	11.45	98.3	0.104	20.0	98.2
312 h	0.037	11.49	98.6	0.084	20.0	98.6
336 h	0.035	11.53	98.9	0.063	20.1	98.9
360 h	0.025	11.55	99.1	0.048	20.2	99.2
384 h	0.023	11.57	99.3	0.039	20.2	99.4
408 h	0.018	11.59	99.5	0.026	20.2	99.5
432 h	0.016	11.61	99.6	0.03	20.2	99.6
456 h	0.016	11.62	99.8	0.028	20.3	99.8
480 h	0.021	11.64	99.9	0.03	20.3	99.9
504 h	0.008	11.65	100.0	0.017	20.3	100.0
Total	11.652			20.323		

Timepoint (hours)	007M			008M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	2.691	2.69	12.7	3.019	3.02	13.3
12 h	1.289	3.98	18.8	1.547	4.57	20.1
24 h	3.692	7.67	36.2	4.303	8.87	39.1
48 h	4.759	12.4	58.6	4.426	13.3	58.6
72 h	3.895	16.3	77.0	3.087	16.4	72.2
96 h	1.875	18.2	85.8	1.766	18.1	80.0
120 h	1.143	19.3	91.2	1.522	19.7	86.7
144 h	0.651	20.0	94.3	0.761	20.4	90.1
168 h	0.386	20.4	96.1	0.473	20.9	92.1
192 h	0.233	20.6	97.2	0.305	21.2	93.5
216 h	0.111	20.7	97.7	0.203	21.4	94.4
240 h	0.077	20.8	98.1	0.232	21.6	95.4
264 h	0.06	20.9	98.4	0.207	21.9	96.3
288 h	0.051	20.9	98.6	0.157	22.0	97.0
312 h	0.037	21.0	98.8	0.142	22.2	97.6
336 h	0.047	21.0	99.0	0.112	22.3	98.1
360 h	0.039	21.0	99.2	0.097	22.4	98.5
384 h	0.037	21.1	99.4	0.074	22.4	98.9
408 h	0.028	21.1	99.5	0.081	22.5	99.2
432 h	0.023	21.1	99.6	0.062	22.6	99.5
456 h	0.035	21.2	99.8	0.053	22.6	99.7
480 h	0.029	21.2	99.9	0.045	22.7	99.9
504 h	0.015	21.2	100.0	0.014	22.7	100.0
Total	21.203			22.69		

Timepoint (hours)	Cumulative	
	Mean	SD
8 h	2.763	0.319
12 h	4.055	0.643
24 h	7.460	1.484
48 h	11.516	2.615
72 h	14.188	3.567
96 h	15.753	4.022
120 h	16.822	4.385
144 h	17.437	4.531
168 h	17.829	4.636
192 h	18.090	4.699
216 h	18.244	4.716
240 h	18.385	4.756
264 h	18.495	4.792
288 h	18.583	4.827
312 h	18.658	4.856
336 h	18.722	4.879
360 h	18.775	4.901
384 h	18.818	4.917
408 h	18.856	4.935
432 h	18.889	4.949
456 h	18.922	4.962
480 h	18.953	4.970
504 h	18.967	4.973

Cumulative Percent of Dose Recovered in Feces, 496 hours post-exposure

Timepoint (hours)	005M			006M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	0.038	0.038	0.4	0.007	0.007	0.0
12 h	0.437	0.475	5.4	0.368	0.375	2.0
24 h	1.878	2.353	26.8	3.187	3.562	19.4
48 h	2.04	4.393	50.1	4.572	8.134	44.2
72 h	1.471	5.864	66.8	2.851	10.985	59.7
96 h	0.715	6.579	75.0	1.904	12.889	70.0
120 h	0.562	7.141	81.4	1.353	14.242	77.4
144 h	0.459	7.600	86.6	1.085	15.327	83.3
168 h	0.276	7.876	89.8	0.701	16.028	87.1
192 h	0.22	8.096	92.3	0.546	16.574	90.1
216 h	0.161	8.257	94.1	0.379	16.953	92.1
240 h	0.129	8.386	95.6	0.348	17.301	94.0
264 h	0.08	8.466	96.5	0.196	17.497	95.1
288 h	0.049	8.515	97.0	0.175	17.672	96.0
312 h	0.055	8.570	97.7	0.152	17.824	96.9
336 h	0.04	8.610	98.1	0.11	17.934	97.5
360 h	0.025	8.635	98.4	0.083	18.017	97.9
384 h	0.024	8.659	98.7	0.094	18.111	98.4
408 h	0.021	8.680	98.9	0.073	18.184	98.8
432 h	0.016	8.696	99.1	0.056	18.240	99.1
456 h	0.016	8.712	99.3	0.042	18.282	99.3
480 h	0.044	8.756	99.8	0.071	18.353	99.7
504 h	0.019	8.775	100.0	0.05	18.403	100.0
Total	8.775			18.403		

Timepoint (hours)	007M			008M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	0.027	0.027	0.2	0.003	0.003	0.0
12 h	0.079	0.106	0.9	0.041	0.044	0.4
24 h	0.457	0.563	4.7	0.512	0.556	5.0
48 h	3.228	3.791	31.5	2.319	2.875	25.6
72 h	2.775	6.566	54.6	2.275	5.150	45.9
96 h	1.833	8.399	69.8	1.339	6.489	57.9
120 h	0.949	9.348	77.7	1.132	7.621	68.0
144 h	0.595	9.943	82.7	0.7	8.321	74.2
168 h	0.437	10.380	86.3	0.433	8.754	78.1
192 h	0.293	10.673	88.7	0.514	9.268	82.7
216 h	0.214	10.887	90.5	0.308	9.576	85.4
240 h	0.129	11.016	91.6	0.289	9.865	88.0
264 h	0.093	11.109	92.4	0.195	10.060	89.7
288 h	0.084	11.193	93.1	0.21	10.270	91.6
312 h	0.068	11.261	93.6	0.179	10.449	93.2
336 h	0.065	11.326	94.2	0.132	10.581	94.4
360 h	0.06	11.386	94.7	0.093	10.674	95.2
384 h	0.059	11.445	95.2	0.074	10.748	95.9
408 h	0.043	11.488	95.5	0.082	10.830	96.6
432 h	0.033	11.521	95.8	0.065	10.895	97.2
456 h	0.21	11.731	97.5	0.08	10.975	97.9
480 h	0.291	12.022	100.0	0.179	11.154	99.5
504 h	0.006	12.028	100.0	0.057	11.211	100.0
Total	12.028			11.211		

Timepoint (hours)	Cumulative	
	Mean	SD
8 h	0.019	0.017
12 h	0.250	0.208
24 h	1.759	1.470
48 h	4.798	2.310
72 h	7.141	2.627
96 h	8.589	2.999
120 h	9.588	3.244
144 h	10.298	3.493
168 h	10.760	3.662
192 h	11.153	3.765
216 h	11.418	3.843
240 h	11.642	3.923
264 h	11.783	3.961
288 h	11.913	3.997
312 h	12.026	4.026
336 h	12.113	4.046
360 h	12.178	4.063
384 h	12.241	4.089
408 h	12.296	4.105
432 h	12.338	4.117
456 h	12.425	4.110
480 h	12.571	4.095
504 h	12.604	4.105

Cumulative Percent of Dose Recovered in Volatile Organic Trap, 496 hours post-exposure

Timepoint (hours)	005M			006M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
12 h	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
24 h	<LOQ	<LOQ	<LOQ	0.056	0.056	24.1
48 h	<LOQ	<LOQ	<LOQ	0.07	0.126	54.3
72 h	<LOQ	<LOQ	<LOQ	0.065	0.191	82.3
96 h	<LOD	<LOD	<LOD	0.041	0.232	100.0
120 h	<LOD	<LOD	<LOD	<LOQ	0.232	100.0
144 h	<LOD	<LOD	<LOD	<LOD	0.232	100.0
168 h	<LOD	<LOD	<LOD	<LOD	0.232	100.0
192 h	<LOD	<LOD	<LOD	<LOD	0.232	100.0
216 h	NS			NS		
240 h	NS			NS		
264 h	NS			NS		
288 h	NS			NS		
312 h	NS			NS		
336 h	NS			NS		
360 h	NS			NS		
384 h	NS			NS		
408 h	NS			NS		
432 h	NS			NS		
456 h	NS			NS		
480 h	NS			NS		
504 h	NS			NS		
Total	0			0.232		

Timepoint (hours)	007M			008M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
12 h	<LOD	<LOD	<LOD	<LOD	<LOD	<LOD
24 h	0.107	0.107	20.0	<LOQ	<LOQ	<LOQ
48 h	0.141	0.248	46.3	0.058	0.058	35.4
72 h	0.121	0.369	68.8	0.059	0.117	71.3
96 h	0.076	0.445	83.0	0.047	0.164	100.0
120 h	0.048	0.493	92.0	<LOQ	0.164	100.0
144 h	0.043	0.536	100.0	<LOQ	0.164	100.0
168 h	<LOQ	0.536	100.0	<LOD	0.164	100.0
192 h	<LOQ	0.536	100.0	<LOD	0.164	100.0
216 h	NS			NS		
240 h	NS			NS		
264 h	NS			NS		
288 h	NS			NS		
312 h	NS			NS		
336 h	NS			NS		
360 h	NS			NS		
384 h	NS			NS		
408 h	NS			NS		
432 h	NS			NS		
456 h	NS			NS		
480 h	NS			NS		
504 h	NS			NS		
Total	0.536			0.164		

Timepoint (hours)	Cumulative	
	Mean	SD
8 h	<LOD	NA
12 h	<LOD	NA
24 h	0.082	0.036
48 h	0.144	0.096
72 h	0.226	0.130
96 h	0.280	0.147
120 h	0.296	0.174
144 h	0.311	0.198
168 h	0.311	0.198
192 h	0.311	0.198
216 h	NS	NA
240 h	NS	NA
264 h	NS	NA
288 h	NS	NA
312 h	NS	NA
336 h	NS	NA
360 h	NS	NA
384 h	NS	NA
408 h	NS	NA
432 h	NS	NA
456 h	NS	NA
480 h	NS	NA
504 h	NS	NA

Cumulative Percent of Dose Recovered in Total Excreta, 496 hours post-exposure

005M					006M				
Timepoint (hours)	Urine	Feces	VO	cumulative %	Timepoint (hours)	Urine	Feces	VO	cumulative %
8 h	2.34	0.04	<LOD	2.38	8 h	3.00	0.01	<LOD	3.01
12 h	3.17	0.48	<LOD	3.65	12 h	4.50	0.38	<LOD	4.88
24 h	5.37	2.35	<LOQ	7.73	24 h	7.93	3.56	0.06	11.54
48 h	7.63	4.39	<LOQ	12.02	48 h	12.71	8.13	0.13	20.97
72 h	8.91	5.86	<LOQ	14.77	72 h	15.14	10.99	0.19	26.31
96 h	9.79	6.58	<LOD	16.37	96 h	16.87	12.89	0.23	29.99
120 h	10.34	7.14	<LOD	17.48	120 h	17.93	14.24	0.23	32.41
144 h	10.74	7.60	<LOD	18.34	144 h	18.58	15.33	0.23	34.14
168 h	10.97	7.88	<LOD	18.85	168 h	19.06	16.03	0.23	35.32
192 h	11.13	8.10	<LOD	19.23	192 h	19.40	16.57	0.23	36.21
216 h	11.26	8.26	0.00	19.52	216 h	19.58	16.95	0.00	36.53
240 h	11.35	8.39	0.00	19.73	240 h	19.75	17.30	0.00	37.05
264 h	11.41	8.47	0.00	19.88	264 h	19.85	17.50	0.00	37.35
288 h	11.45	8.52	0.00	19.97	288 h	19.96	17.67	0.00	37.63
312 h	11.49	8.57	0.00	20.06	312 h	20.04	17.82	0.00	37.87
336 h	11.53	8.61	0.00	20.14	336 h	20.11	17.93	0.00	38.04
360 h	11.55	8.64	0.00	20.19	360 h	20.15	18.02	0.00	38.17
384 h	11.57	8.66	0.00	20.23	384 h	20.19	18.11	0.00	38.30
408 h	11.59	8.68	0.00	20.27	408 h	20.22	18.18	0.00	38.40
432 h	11.61	8.70	0.00	20.30	432 h	20.25	18.24	0.00	38.49
456 h	11.62	8.71	0.00	20.34	456 h	20.28	18.28	0.00	38.56
480 h	11.64	8.76	0.00	20.40	480 h	20.31	18.35	0.00	38.66
504 h	11.65	8.78	0.00	20.43	504 h	20.32	18.40	0.00	38.73

007M					008M				
Timepoint (hours)	Urine	Feces	VO	cumulative %	Timepoint (hours)	Urine	Feces	VO	cumulative %
8 h	2.69	0.03	<LOD	2.72	8 h	3.02	0.00	<LOD	3.02
12 h	3.98	0.11	<LOD	4.09	12 h	4.57	0.04	<LOD	4.61
24 h	7.67	0.56	0.11	8.34	24 h	8.87	0.56	<LOQ	9.43
48 h	12.43	3.79	0.25	16.47	48 h	13.30	2.88	0.06	16.23
72 h	16.33	6.57	0.37	23.26	72 h	16.38	5.15	0.12	21.65
96 h	18.20	8.40	0.45	27.05	96 h	18.15	6.49	0.16	24.80
120 h	19.34	9.35	0.49	29.19	120 h	19.67	7.62	0.16	27.46
144 h	20.00	9.94	0.54	30.47	144 h	20.43	8.32	0.16	28.92
168 h	20.38	10.38	0.54	31.30	168 h	20.90	8.75	0.16	29.82
192 h	20.61	10.67	0.54	31.82	192 h	21.21	9.27	0.16	30.64
216 h	20.73	10.89	0.00	31.61	216 h	21.41	9.58	0.00	30.99
240 h	20.80	11.02	0.00	31.82	240 h	21.64	9.87	0.00	31.51
264 h	20.86	11.11	0.00	31.97	264 h	21.85	10.06	0.00	31.91
288 h	20.91	11.19	0.00	32.11	288 h	22.01	10.27	0.00	32.28
312 h	20.95	11.26	0.00	32.21	312 h	22.15	10.45	0.00	32.60
336 h	21.00	11.33	0.00	32.32	336 h	22.26	10.58	0.00	32.84
360 h	21.04	11.39	0.00	32.42	360 h	22.36	10.67	0.00	33.03
384 h	21.07	11.45	0.00	32.52	384 h	22.43	10.75	0.00	33.18
408 h	21.10	11.49	0.00	32.59	408 h	22.51	10.83	0.00	33.34
432 h	21.12	11.52	0.00	32.65	432 h	22.58	10.90	0.00	33.47
456 h	21.16	11.73	0.00	32.89	456 h	22.63	10.98	0.00	33.60
480 h	21.19	12.02	0.00	33.21	480 h	22.67	11.15	0.00	33.83
504 h	21.20	12.03	0.00	33.23	504 h	22.69	11.21	0.00	33.90

Timepoint (hours)	Mean	SD
8 h	2.782	0.303
12 h	4.305	0.547
24 h	9.259	1.677
48 h	16.423	3.654
72 h	21.498	4.884
96 h	24.552	5.855
120 h	26.632	6.435
144 h	27.967	6.778
168 h	28.822	7.042
192 h	29.475	7.239
216 h	29.663	7.203
240 h	30.027	7.317
264 h	30.278	7.387
288 h	30.496	7.472
312 h	30.684	7.538
336 h	30.835	7.586
360 h	30.953	7.627
384 h	31.059	7.667
408 h	31.152	7.699
432 h	31.227	7.727
456 h	31.347	7.762
480 h	31.524	7.806
504 h	31.571	7.822