

MR# 305890

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SECTION 8(e)
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July 13, 2007

Re: 8EHQ ML-34673
Dermal Absorption Studies – TSCA Section 8(e)

This letter is a follow-up to the February 14, 2007 submission regarding findings from a rat *in vivo* dermal absorption study conducted with creosote (CAS number 8001-58-9). The study was sponsored by Creosote Council III, a FIFRA § 3(c)(2)(B) joint data development group,¹ and was conducted at the E. I. du Pont de Nemours and Company Haskell Laboratory for Health and Environmental Sciences. A final report for that study is now available and a copy is enclosed. The final study report shows that when in direct contact with the skin of a rat liquid creosote can be absorbed systemically but not as rapidly or completely as initially thought. Following 8 hours of dermal exposure, about 9% (8.85%) of the applied dose was absorbed during a three week period, not 34% as initially thought. The higher value provided to EPA (in the February submission) was shown to result from excess creosote test material retained on or under the dosing appliance which remained on the animal skin after washing but throughout the 21-day observation period. A supplemental study, fully described in the report, provides empirical data which support this explanation.

¹ The members of the Creosote Council III are:

- 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.



Findings from the *in vivo* rat study include:

- 1.0) The majority of the applied dose was unabsorbed (83.9%);
- 2.0) Total radioactivity recovered at the end of the 21-day post-exposure was 92.775%;
- 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 (2.1%) 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 8.85% of the applied dose was absorbed. The majority of this (about 8.2%) was in the urine and feces. Less than 0.1% 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.

In addition to the *in vivo* study, an *in vitro* study using rat and human cadaver skin was completed with creosote. The purpose of that study was to compare ¹⁴C-creosote absorption in identical test systems using skin of each species. This study used the same ¹⁴C-PAH/creosote test material as the *in vivo* rat study. A final report for that work is included with this letter. These data show that over 8 hours creosote penetrated rat skin about 4.3 times faster than human skin and that more creosote (about 4.4 times more) penetrated rat skin than human skin. Washing the skin at the termination of the exposure period removed 70.3% of the applied dose from human skin and 12.8% of the applied dose from rat skin. The total absorbable creosote dose was 4.24% for human skin and 34.3% for rat skin meaning that rat skin is about 8-times more permeable to creosote than human skin.

Taken together, the results of the *in vitro* and *in vivo* studies suggest that transdermal absorption of creosote on human skin is about 1.1%.

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 or phoned at 724-443-0097.

Sincerely,

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

John H. Butala, DABT

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

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).

MAFF Japan, Agricultural Chemicals Laws and Regulations, Japan (II), (59 Nousan Number 4200) (1985).

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

STUDY COMPLETED ON: July 2, 2007

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
HaskellSM Laboratory for Health and Environmental Sciences
Elkton Road, P.O. Box 50
Newark, Delaware 19714-0050
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
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PAGE RESERVED

GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with U.S. EPA FIFRA (40 CFR part 160) Good Laboratory Practice Standards, which are compatible with current OECD and MAFF (Japan) Good Laboratory Practices, except for the item documented below. The item listed did not impact the validity of the study.

The chemical and radiochemical concentration and the radiochemical purity of the selected chemicals of the creosote test substance that was spiked with radiolabeled chemicals, was based on the certificates of analyses provided by the sponsor and vendors and the verified radioactivity per volume.

Applicant/Sponsor The Creosote Council III
P.O. Box 160
Valencia, Pennsylvania 16059
U.S.A.

Study Director:



William J. Fasano, Sr., B.S.
Senior Research Toxicologist

2-JUL-2007

Date

Applicant/Sponsor:



Applicant/Sponsor Representative

11-July-2007

Date

QUALITY ASSURANCE STATEMENT

Work Request Number: 16308
Study Code Number: 1378

Key inspections for DuPont work request 16308, service code 1378 were performed for the tasks completed at DuPont by the Quality Assurance Unit of DuPont and the findings were submitted on the following dates.

<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, 2007	April 20, 2007	April 20, 2007
Conduct:	November 3, 2006	November 3, 2006	November 3, 2006
Report/Records:	January 15-18, 2007	January 18, 2007	January 29, 2007
Supplemental Report:	June 8 & 11, 2007	June 11, 2007	June 15, 2007
Sponsor Edits	June 28, 2007	June 28, 2007	June 28, 2007

Reported by:

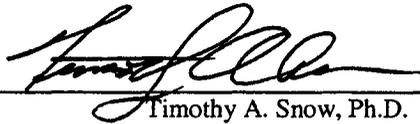

Molly A. Butler
Quality Assurance Auditor

28 June 2007
Date

CERTIFICATION

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

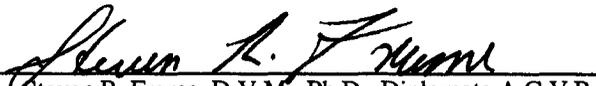
Analytical
Evaluation by:



Timothy A. Snow, Ph.D.
Senior Research Chemist

28-Jun-2007
Date

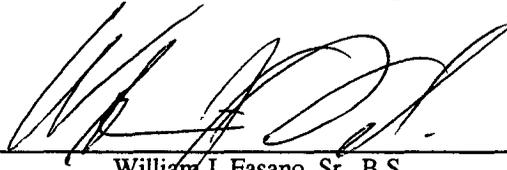
Reviewed and Approved by:



Steven R. Frame, D.V.M., Ph.D., Diplomate A.C.V.P.
Research Fellow and Manager

2-Jul-2007
Date

Issued by Study Director:



William J. Fasano, Sr., B.S.
Senior Research Toxicologist

2-Jul-2007
Date

This report is approved by the sponsor.

Approved by:



John H. Butala
Sponsor Representative

6-29-07
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 / April 26, 2007

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 12 marker chemicals. In the plasma kinetic (assessment) experiment, the creosote test substance was applied neat to a 10.5 cm² shaved area on the dorso-lumbar region to 4 male rats at a rate of 10 µL/cm². 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.

The dermal absorption of creosote containing selected radiolabeled marker chemicals was also determined in vivo in the rat. For this experiment, the creosote test substance was spiked with 8 radiolabeled chemicals, which represented approximately 43% of chemicals in creosote, and then was applied to a 10.5 cm² shaved area on the dorso-lumbar region to 2 groups of 4 rats at a rate of 10 µL/cm². 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 4 rats sacrificed to determine the distribution of the applied radioactive dose at the end of the exposure phase (0 hours post-exposure). The remaining 4 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.

To clarify the results of the initial 496 hour post-exposure group, a supplemental experiment was conducted, since it was hypothesized that the reported absorbed dose for the first set of rats was erroneously high due to retention of a portion of the applied dose with either the underside of the O-ring, which demarcated the 10.5 cm² exposure area, or the glue used to secure the O-ring to the dorsal area of the rats. This portion of the applied dose was not removed by washing at the end of the 8-hour exposure period and subsequently became systemically available, yielding an erroneously high absorption.

The supplemental experiment was composed of 4 rats. On the day prior to dosing, the dorsal area was shaved and an area (10.5 cm²) demarcated within the shaved area using indelible ink. Isofluorane[®] anesthesia was used during this procedure. The shaved and demarcated area was then protected with Coban[™] body wrap and rats were maintained overnight in glass metabolism units. On the day of dosing, the Coban[™] body wrap was removed and discarded and the creosote (radioactive) dose applied within the demarcated area at a rate of 10- μ L/cm². Isofluorane[®] anesthesia was used during the application of the dose. Following dose application, O-ring spacers were placed over the dose site and wrapped securely with Coban[™]. At 8 hours, the Coban[™] body wrap and O-ring spacers were removed, the skin washed with a 2% soap solution, and the rats wrapped with a fresh Coban[™] body wrap to protect the dose site. The rats were returned to their metabolism cages for a 21 day recovery-collection phase. Urine and feces were collected 0-8 hours, 8-24 hours and at 24 hour intervals until sacrifice. At the end of the 21-day recovery-collection phase, the rats were processed for a complete material balance of the applied dose.

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%.

The limit of detection (LOD) for the 12 creosote marker chemicals in rat plasma ranged from 0.009 ppm (dibenzofuran) to 0.181 ppm (fluoranthene). The limit of quantitation (LOQ) ranged from 0.030 ppm (dibenzofuran) to 0.603 ppm (fluoranthene).

Target Analyte	LOD (ppm)	LOQ (ppm)
Naphthalene	0.120	0.400
2-Methylnaphthalene	0.027	0.090
1-Methylnaphthalene	0.020	0.067
Acenaphthene	0.016	0.053
Dibenzofuran	0.009	0.030
Fluorene	0.043	0.143
Phenanthrene	0.135	0.450
Fluoranthene	0.181	0.603
Pyrene	0.174	0.508
Carbazole	0.022	0.073
Benzo[b]fluoranthene	0.090	0.300
Benzo[a]pyrene	0.056	0.187

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 LOD 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 (Initial Experiment)

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 (496 hours post-exposure), 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.

E. Supplemental Experiment, 496-hour post-exposure group

To clarify the results of the 496-hour post-exposure group (initial experiment), a supplemental experiment was conducted, since it was hypothesized that the reported absorbed dose for the first set of rats (34%) was erroneously high due to retention of a portion of the applied dose with either the underside of the O-ring, which demarcated the 10.5 cm² exposure area, or the glue used to secure the O-ring to the dorsal area of the rats. Following an 8-hour dermal exposure and a 496-hour post-exposure period, approximately 8.85% of the applied dose was absorbed; a negligible amount of the applied dose (0.005%) remained in the tape-stripped skin yielding a total absorbable dose of 8.86%. Washing of the application skin site at the end of the exposure phase removed 22.2% of the applied dose, which made up approximately one third of the unabsorbed dose (83.9%). The remaining unabsorbed dose was found to be associated with the body wrap (34.2%) and O-ring (27.5%) with only a minor portion being removed by tape-stripping the skin (0.001%).

The results of this supplemental experiment confirm that the absorbed dose value from the initial 496 hour post-exposure group was erroneously high do to retention of dose, likely associated with the O-ring appliance, which was not removed by washing at the end of the 8-hour exposure and that was subsequently absorbed.

Overall, these results demonstrate that maximum absorption of creosote was 8.86% following an 8-hour exposure to a single finite dose. Indirectly, the in vivo dermal experiment, based on total radioactivity and when compared to the plasma kinetic experiment, also confirms that the target chemicals were metabolized upon first pass through the skin and that systemic exposure following dermal application of creosote was 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).
- MAFF Japan, Agricultural Chemicals Laws and Regulations, Japan (II), (59 Nousan Number 4200) (1985).

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, Missouri, U.S.A.) 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 - ¹⁴ C	22705-130	252	26.6	105.6
2-methylnaphthalene - 8 - ¹⁴ C	22705-131	142	8.5	59.9
Fluoranthene - 3 - ¹⁴ C	22705-132	202	45	222.8
Anthracene - 1,2,3,4,4A,9A- ¹⁴ C	22705-133	178	20.6	115.7
Naphthalene - Benzene - UL - ¹⁴ C	22705-134	128	31.3	244.5
Phenanthrene - 9 - ¹⁴ C	22705-135	178	8.2	46.1
Biphenyl - UL - ¹⁴ C	22705-136	154	7.6	49.4
Pyrene - 4,5,9,10 - ¹⁴ 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 μ m 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 μ L 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 5 concentrations. Rat plasma was then spiked with 500 μ L of acetonitrile and vortexed to precipitate out plasma proteins. Following protein precipitation, 200 mg of anhydrous sodium sulfate, 990 μ L of toluene, and 10 μ L of 150 μ g/mL phenanthrene- d_{10} 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 the In Vivo Dermal Plasma Kinetic Experiment (Non-Radiolabeled) and the In Vivo Dermal Absorption Experiment (Radiolabeled)

Male Sprague-Dawley Crl:CD(SD) rats approximately 8-10 weeks of age were used and were supplied by Charles River Laboratories (Raleigh, North Carolina, U.S.A.). 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[®], the back and shoulders clipped free of hair, and the clipped area washed with an aqueous 2% Ivory[®] Soap solution. Following shaving and washing, a glass O-ring appliance with an internal area of

10.5 cm², was glued to the clipped area on the back using Instant Krazy Glue Gel adhesive. The O-ring then was covered with Coban™ 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® Nutrition International, LLC Certified Rodent LabDiet® 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-µL/cm² 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 μ 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 μ L) were immediately prepared for extraction by adding 500 μ L of acetonitrile and vortexing to precipitate out the plasma proteins. Following protein precipitation, 200 mg of anhydrous sodium sulfate, 990 μ L toluene and 10 μ L of 150 μ g/mL phenanthrene-d₁₀ 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 8 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.

Radiolabeled Chemical	Concentration In Creosote (%) ^a	Amount of Chemical in 5 mL (mg)	Specific Activity of Neat Sample ($\mu\text{Ci}/\text{mg}$)	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

a 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 liquid scintillation counting (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- $\mu\text{Ci}/\text{mg}$, which provided equivalent radiochemical sensitivity for the each of the 8 radiochemicals.

J. In Vivo Dermal Absorption with Creosote Test Substance spike with ¹⁴C-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- $\mu\text{L}/\text{cm}^2$. The exposure area was 10.5 cm^2 , which required a target dose of 105 μL .

Following dose administration, a glass cap containing Anasorb[®] 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[™] body wrap, and each animal was then housed separately in an all-glass, closed metabolism cage, suitable for the collection of ¹⁴CO₂ (2N NaOH), ¹⁴C-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[®] Soap solution.

Following washing at 8 hours post-dose, one group of 4 rats was euthanized (0 hours post-exposure). 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 (¹⁴CO₂) and an ethylene glycol trap (¹⁴C-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 ≤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[®], 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[®] 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 Isoflurane[®], 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[®] P (BSN Medical, Ltd., Charlotte, NC, USA). 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 $1-10^{\circ}\text{C}$ (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 Ultima Gold[™] XR liquid scintillant.
- 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}C) were not processed further. Aliquots were added directly to Ultima Gold[™] XR liquid scintillant.
- The application skin site and sponge pieces were digested in Soluene[®]-350. Aliquots were added directly to Hionic-Fluor[™] 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™ 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%, 2σ), whichever came first.

The LOD and the 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}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.

10. Supplemental Experiment

Additionally, a supplemental experiment was conducted to clarify total absorption reported for the 21-day test group (496-hours post-dose), from the main in vivo dermal experiment. It was hypothesized that a portion of the applied dose for this group became associated with either the underside of the glass O-ring or the glue used to secure the glass O-ring to the dorsal area of the rats. This portion of the applied dose was not removed by washing at the end of the 8-hour exposure period and subsequently became systemically available, yielding an erroneously high absorption (~34%).

The supplemental experiment was composed of 4 rats. On the day prior to dosing, the dorsal area was shaved and an area (10.5 cm²) demarcated within the shaved area using indelible ink. Although the protocol amendment describing the supplemental experiment indicated an area of 10 cm², the correct area was 10.5 cm², which was consistent with the original exposure groups. Isoflurane[®] anesthesia was used during this procedure. The shaved and demarcated area was protected with Coban[™] body wrap while rats were maintained overnight in glass metabolism units. On the day of dosing, the Coban[™] body wrap was removed and discarded and the creosote (radioactive) dose applied within the demarcated area at a rate of 10-μL/cm²; an organic volatile trap was not used since <0.5% of the applied dose (on average) evolved from the dose site of rats in main study experiment. Isoflurane[®] anesthesia was used during the application of the dose. Following dose application, silicone O-ring spacers were placed over the dose site without glue and wrapped securely with Coban[™]. At 8 hours, the Coban[™] body wrap and silicone O-ring spacers were removed, the skin washed with a 2% soap solution, and the rats wrapped with a fresh Coban[™] body wrap to protect the dose site. The rats were then returned to their metabolism cages for a 21-day recovery-collection phase.

Urine and feces were collected 0-8 hours, 8-24 hours and at 24-hour intervals until sacrifice. ¹⁴CO₂ and ¹⁴C-organic volatiles were not collected since <0.3% of the applied dose (on average) was collected in these samples from rats in the main study experiment. At the discretion of the Study Director, the Coban[™] body wrap was changed periodically over the course of the 21 days (496-hours post-exposure).

At the end of the 21-day recovery-collection phase, the rats were processed for a complete material balance of the applied dose as previously described for the rats in the initial, main in vivo dermal study.

RESULTS AND DISCUSSION

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

(Table 1, 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

(Table 2)

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%.

The limit of detection (LOD) for the 12 creosote marker chemicals in rat plasma ranged from 0.009 ppm (dibenzofuran) to 0.181 ppm (fluoranthene). The limit of quantitation (LOQ) ranged from 0.030 ppm (dibenzofuran) to 0.603 ppm (fluoranthene).

Target Analyte	LOD (ppm)	LOQ (ppm)
Naphthalene	0.120	0.400
2-Methylnaphthalene	0.027	0.090
1-Methylnaphthalene	0.020	0.067
Acenaphthene	0.016	0.053
Dibenzofuran	0.009	0.030
Fluorene	0.043	0.143
Phenanthrene	0.135	0.450
Fluoranthene	0.181	0.603
Pyrene	0.174	0.508
Carbazole	0.022	0.073
Benzo[b]fluoranthene	0.090	0.300
Benzo[a]pyrene	0.056	0.187

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

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). 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 ¹⁴C-Labeled Chemicals

(Tables 3-11, Figures 2-9, Appendix C)

1. Verification of Radioactivity

The spiked creosote test substance was verified to be homogeneous and contained approximately 16.7 μCi per 105 μL , the volume of the applied dose. The calculated specific activity for each of the 8 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.

4. Supplemental 496-Hour Post-Exposure Group

Key observations of mean data:

- Following an 8-hour dermal exposure and a 496-hour post-exposure period, approximately 8.85% 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 8.86%.
- At the end of the 8-hour exposure, the total unabsorbed dose (83.9%) was comparable to the 0-hour post exposure group (87.1%).
- Although a larger portion of the applied dose was associated with the body wrap in the supplemental group compared to the 0-hour post exposure group at the end of the 8-hour exposure [~32% of the total recovered dose, with the balance (~2%) collected from the end of the exposure period until 496 hours post exposure], washing of the application skin site at 8 hours, confirmed that excess creosote was still available for absorption (22.2%).
- The remaining unabsorbed dose was found to be associated with the silicone O-ring (27.5%), which was removed at the end of the 8-hour exposure (note: the 0-hour post exposure group O-ring was glued to the back skin, and remained in-place until 496 hours post exposure); only a minor portion of the applied dose was removed by tape-stripping the skin at 496 hours post exposure (0.001%).
- Recovery of the applied dose was >92%.
- Evaluation of the cumulative (total) excretion (urine and feces) confirms that elimination of the systemically available dose was essentially complete by 360-hours post-exposure.
- The results of this supplemental experiment confirm that the absorbed dose value from the first 496-hour post-exposure group was erroneously high do to retention of dose, likely associated with the O-ring appliance, which was not removed by washing at the end of the 8-hour exposure and that was subsequently absorbed.

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%.

The limit of detection (LOD) for the 12 creosote marker chemicals in rat plasma ranged from 0.009 ppm (dibenzofuran) to 0.181 ppm (fluoranthene). The limit of quantitation (LOQ) ranged from 0.030 ppm (dibenzofuran) to 0.603 ppm (fluoranthene).

Target Analyte	LOD (ppm)	LOQ (ppm)
Naphthalene	0.120	0.400
2-Methylnaphthalene	0.027	0.090
1-Methylnaphthalene	0.020	0.067
Acenaphthene	0.016	0.053
Dibenzofuran	0.009	0.030
Fluorene	0.043	0.143
Phenanthrene	0.135	0.450
Fluoranthene	0.181	0.603
Pyrene	0.174	0.508
Carbazole	0.022	0.073
Benzo[b]fluoranthene	0.090	0.300
Benzo[a]pyrene	0.056	0.187

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 (Initial Experiment)

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 (496 hours post-exposure), 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.

E. Supplemental Experiment, 496-hour post-exposure group

To clarify the results of the 496-hour post-exposure group (initial experiment), a supplemental experiment was conducted, since it was hypothesized that the reported absorbed dose for the first set of rats (34%) was erroneously high due to retention of a portion of the applied dose with either the underside of the O-ring, which demarcated the 10.5 cm² exposure area, or the glue used to secure the O-ring to the dorsal area of the rats. Following an 8-hour dermal exposure and

a 496-hour post-exposure period, approximately 8.85% of the applied dose was absorbed; a negligible amount of the applied dose (0.005%) remained in the tape-stripped skin yielding a total absorbable dose of 8.86%. Washing of the application skin site at the end of the exposure phase removed 22.2% of the applied dose, which made up approximately one third of the unabsorbed dose (83.9%). The remaining unabsorbed dose was found to be associated with the body wrap (34.2%) and O-ring (27.5%) with only a minor portion being removed by tape-stripping the skin (0.001%).

The results of this supplemental experiment confirm that the absorbed dose value from the initial 496 hour post-exposure group was erroneously high do to retention of dose, likely associated with the O-ring appliance, which was not removed by washing at the end of the 8-hour exposure and that was subsequently absorbed.

Overall, these results demonstrate that maximum absorption of creosote was 8.86% following an 8-hour exposure to a single finite dose. Indirectly, the in vivo dermal experiment, based on total radioactivity and when compared to the plasma kinetic experiment, also confirms that the target chemicals were metabolized upon first pass through the skin and that systemic exposure following dermal application of creosote was 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, Gibsonia, Pennsylvania 10544, U.S.A.) 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

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
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 ^a
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
Benzo[a]pyrene	52.5	252	0.5

^aFrom COA provided by sponsor.

Table 2
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
Benzo[a]pyrene	4	2	0.056	0.187

Table 3
Summary of dosing information for rats exposed to a single topical application of ¹⁴C-spiked creosote test substance, 0 and 496 hours post-dose, (initial) and supplemental (S-496) experiments

Sample	Hours Post-Exposure					
	0		496		S-496	
	Mean	SD	Mean	SD	Mean	SD
Body weight (g)	340.9	19.1	340.0	17.9	330.1	3.20
Weight of formulation (g)	0.1124	0.00	0.1124	0.00	0.1124	0.00
Total radioactivity applied (μCi)	16.7	0.00	16.7	0.00	18.9	0.14
Total Creosote applied (μg)	112350	0.00	112350	0.00	112350	0.00
Application Rate (μg/cm ²) ^a	10700	0.00	10700	0.00	10700	0.00

^aApplication rate = total Creosote applied (112350 μg) ÷ 10.5 cm²

Table 4
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, initial and supplemental (S-496) experiments

	Data expressed as a percent of applied dose					
	Hours Post-Exposure					
	0		496		S-496	
	Mean	SD	Mean	SD	Mean	SD
Absorbed Dose						
Urine	2.129	0.360	18.967	4.973	4.812	0.862
Feces	0.026	0.026	12.604	4.105	3.423	0.939
Cage wash	0.697	0.272	1.670	1.131	0.551	0.137
CO ₂	N.A.	N.A.	0.000	0.000	N.S.	N.S.
Residual feed	0.005	0.001	0.241	0.174	0.066	0.076
Volatile organics	0.049	N.A.	0.233	0.224	N.S.	N.S.
Non-dosed skin	0.020	0.004	0.039	0.014	0.001	N.A.
Carcass	3.144	0.524	0.195	0.211	N.A.	N.A.
Whole blood	0.027	0.006	0.003	0.001	0.001	N.A.
RBC (terminal)	0.011	0.004	0.002	0.001	0.001	0.001
Heart	0.002	0.000	N.A.	N.A.	N.A.	N.A.
Lungs	0.006	0.002	N.A.	N.A.	N.A.	N.A.
Liver	0.185	0.015	0.005	0.002	N.A.	N.A.
Kidney	0.073	0.009	0.002	0.001	<0.001	N.A.
Plasma (terminal)	0.011	0.002	N.A.	N.A.	N.A.	N.A.
Total Dose Absorbed	6.342	0.808	33.959	8.445	8.853	1.570
Absorbable Dose						
Absorbed Dose	6.342	0.808	33.959	8.445	8.853	1.570
Dosed skin	1.553	0.299	0.005	0.003	0.005	N.A.
Total Dose Absorbable	7.895	1.081	33.964	8.447	8.855	1.570
Unabsorbed Dose						
Body wrap	2.097	2.186	2.443	1.437	34.228 ^b	6.328
Skin wash - sponges	59.283	12.547	56.822	8.294	22.240	7.818
Charcoal trap	0.490	0.152	0.451	0.108	N.S.	N.S.
O-ring	18.357	8.177	2.889	0.511	27.452	3.680
Tape strips	6.886	2.744	0.041	0.040	0.001	0.002
Total Dose Unabsorbed	87.113	3.545	62.645	8.404	83.920	2.308
Total Dose Recovered	95.009	2.569	96.609	3.628	92.775	2.700

^aSamples were below the limit of detection (<LOD) or limit of quantitation (LOQ)

^bApproximately 32% of the applied dose was collected at the end of the 8-hour period and the balance (approximately 2%) was collected post-exposure.

Table 5
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 6
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 7
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 8
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

Table 9
Cumulative percent of dose recovered in urine following an 8-hour topical exposure to creosote,
496 hours post-exposure - Supplemental Experiment

Post-dose Timepoint (hours)	Cumulative Percent	
	Mean	SD
8	2.01	0.36
24	3.82	0.67
48	4.42	0.80
72	4.62	0.85
96	4.72	0.85
120	4.75	0.85
144	4.78	0.85
168	4.79	0.85
192	4.79	0.86
216	4.79	0.86
240	4.80	0.86
264	4.80	0.86
288	4.80	0.86
312	4.80	0.86
336	4.80	0.86
360	4.81	0.86
384	4.81	0.86
408	4.81	0.86
432	4.81	0.86
456	4.81	0.86
480	4.81	0.86
504	4.81	0.86

Table 10
Cumulative percent of dose recovered in feces following an 8-hour topical exposure to creosote,
496 hours post-exposure - Supplemental Experiment

Post-dose Timepoint (hours)	Cumulative Percent	
	Mean	SD
8	0.02	0.01
24	1.94	0.76
48	2.91	0.93
72	3.22	0.90
96	3.31	0.92
120	3.36	0.93
144	3.39	0.93
168	3.40	0.93
192	3.41	0.93
216	3.42	0.94
240	3.42	0.94
264	3.42	0.94
288	3.42	0.94
312	3.42	0.94
336	3.42	0.94
360	3.42	0.94
384	3.42	0.94
408	3.42	0.94
432	3.42	0.94
456	3.42	0.94
480	3.42	0.94
504	3.42	0.94

Table 11
Cumulative percent of dose recovered in total excreta following an 8-hour topical exposure to
creosote, 496 hours post-exposure - Supplemental Experiment

Post-dose Timepoint (hours)	Cumulative Percent	
	Mean	SD
8	2.03	0.35
24	5.76	1.10
48	7.33	1.53
72	7.84	1.58
96	8.02	1.59
120	8.11	1.59
144	8.16	1.59
168	8.19	1.59
192	8.20	1.60
216	8.21	1.60
240	8.22	1.60
264	8.22	1.60
288	8.22	1.61
312	8.22	1.61
336	8.23	1.60
360	8.23	1.61
384	8.23	1.61
408	8.23	1.61
432	8.23	1.61
456	8.23	1.61
480	8.23	1.61
504	8.24	1.61

FIGURES

Figure 1
Total ion chromatogram for creosote test material

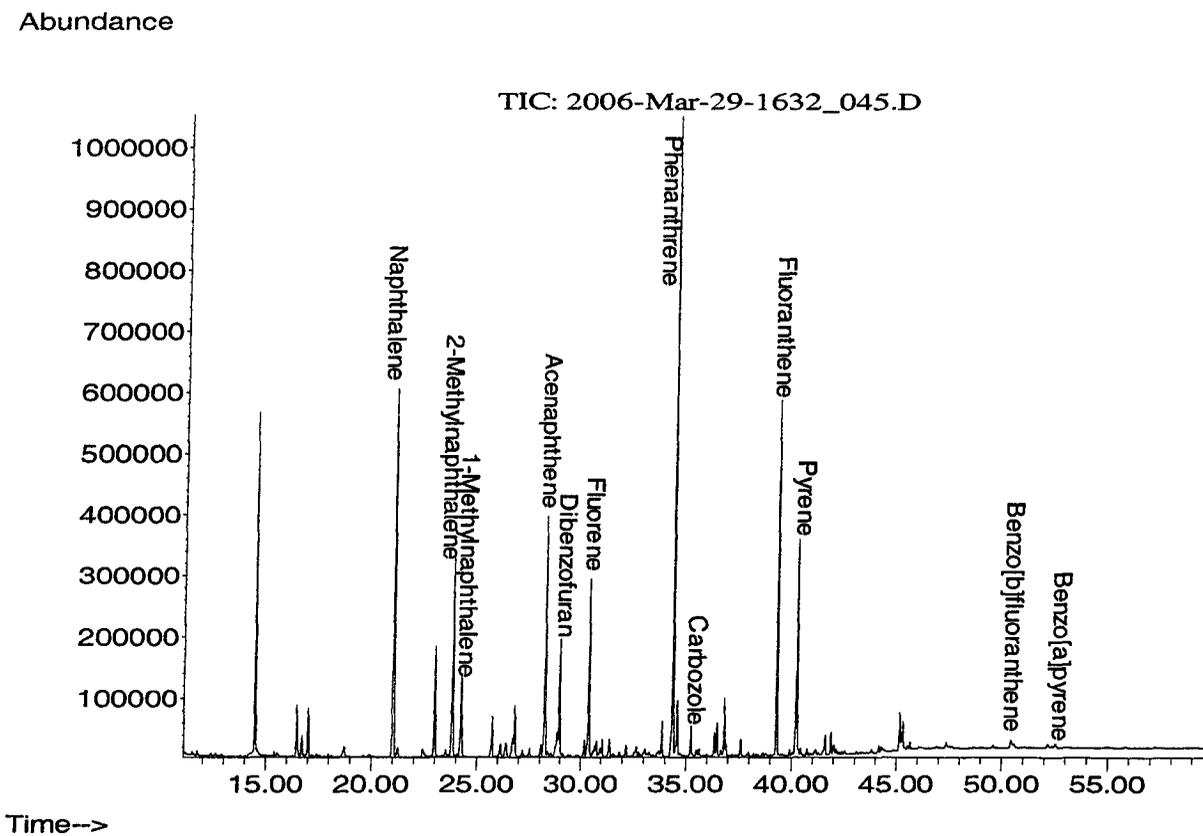


Figure 2
Summary of percent of applied dose following an 8-hour exposure to a single topical application
of creosote recovered 0 and 496 hours post-exposure

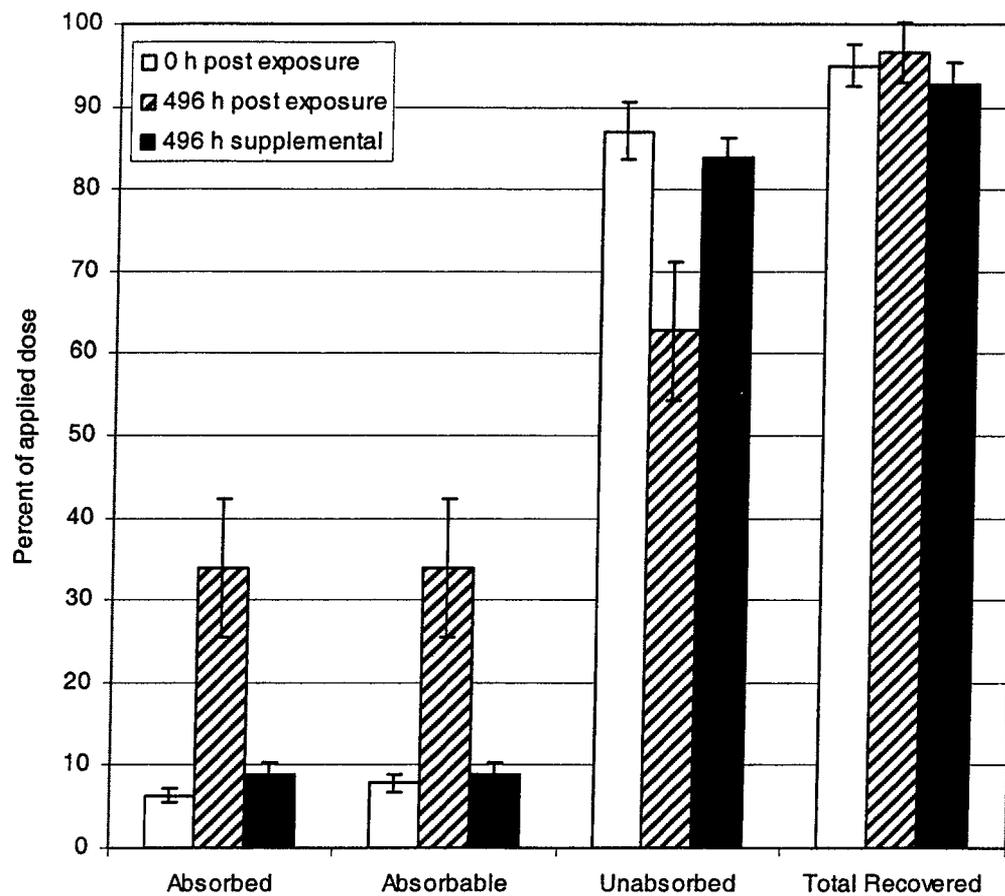


Figure 3
Cumulative percent of dose recovered in urine following an 8-hour topical exposure to creosote,
496 hours post-exposure

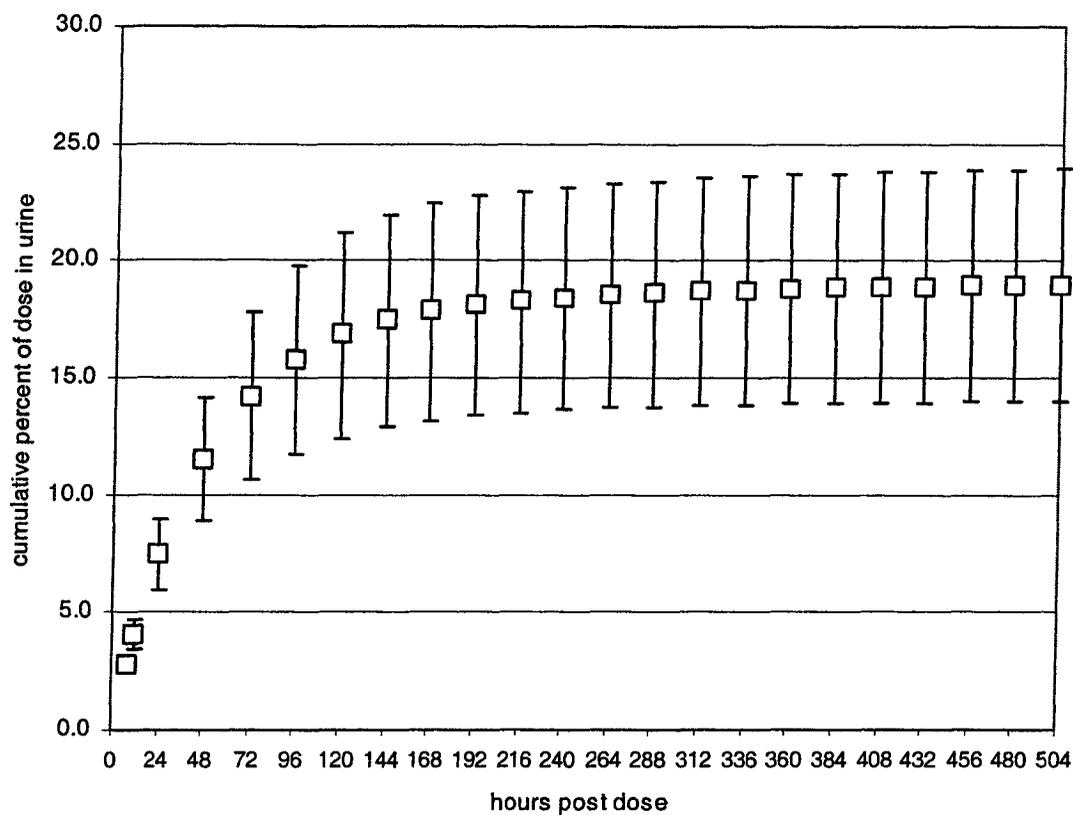


Figure 4
Cumulative percent of dose recovered in feces following an 8-hour topical exposure to creosote,
496 hours post-exposure

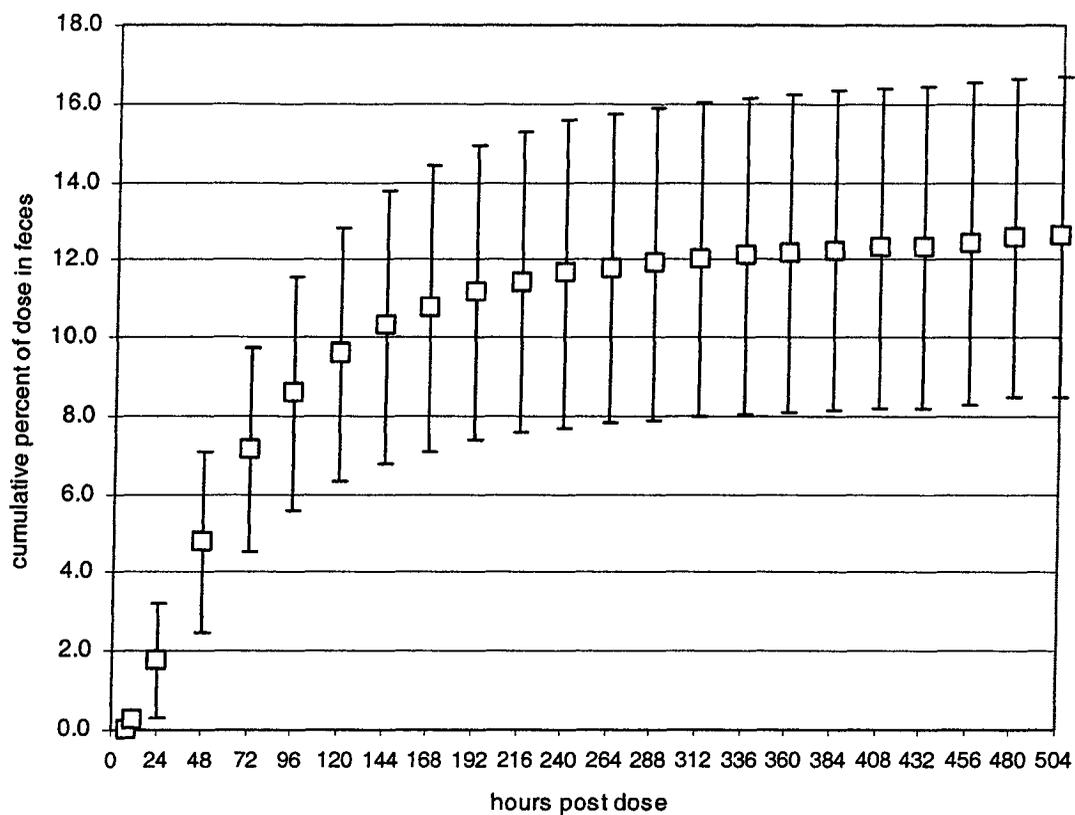


Figure 5
Cumulative percent of dose recovered in volatile organic (VO) trap following an 8-hour topical exposure to creosote, 496 hours post-exposure

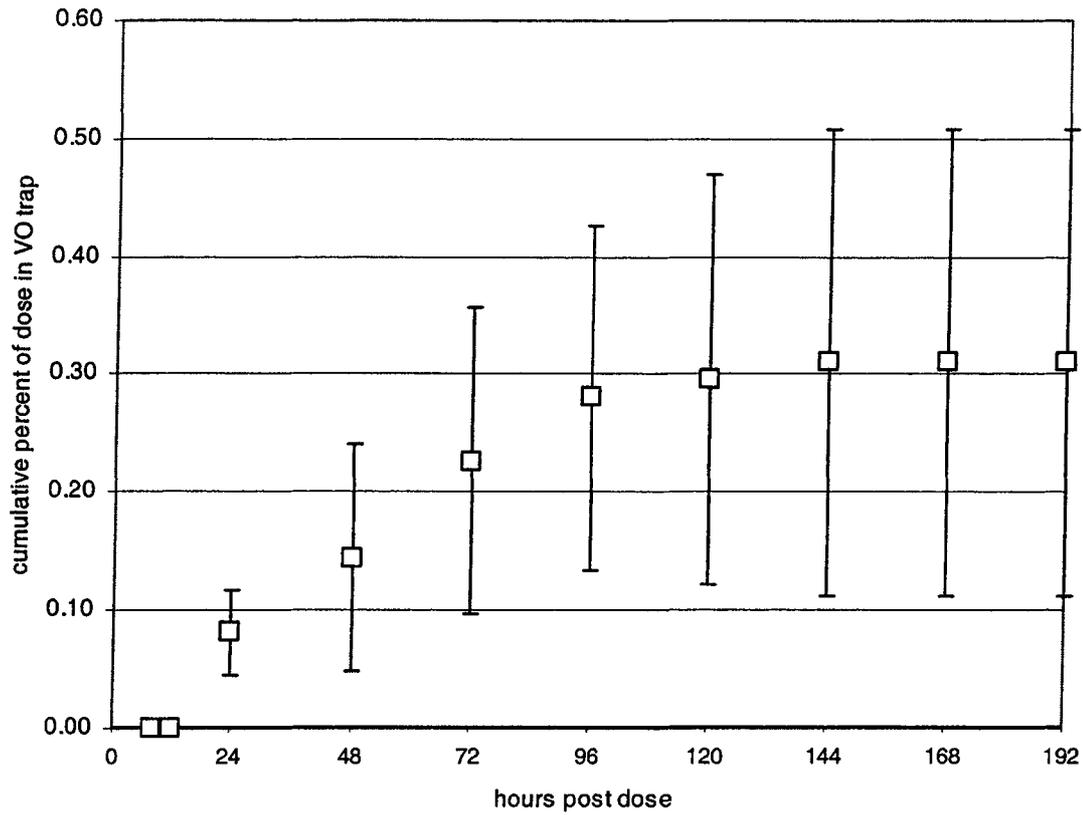


Figure 6
Cumulative percent of dose recovered in total excreta following an 8-hour topical exposure to
creosote, 496 hours post-exposure

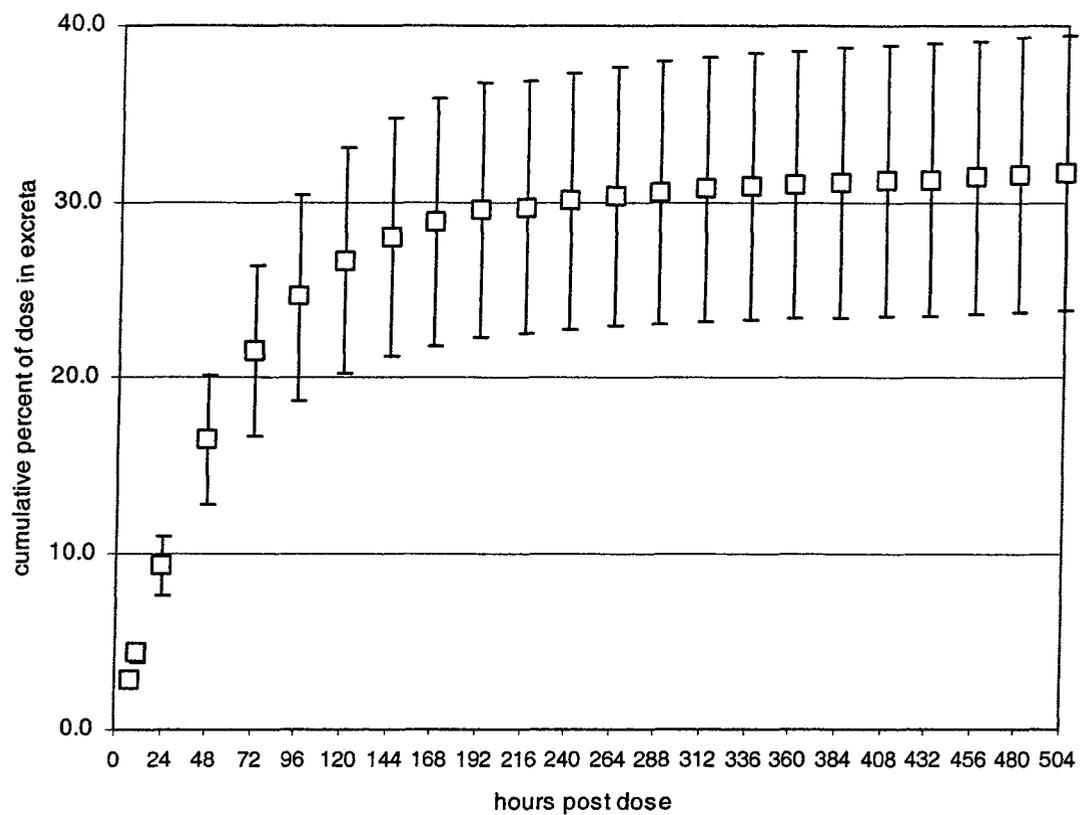


Figure 7
Cumulative percent of dose recovered in urine following an 8-hour topical exposure to creosote,
496 hours post-exposure - Supplemental Experiment

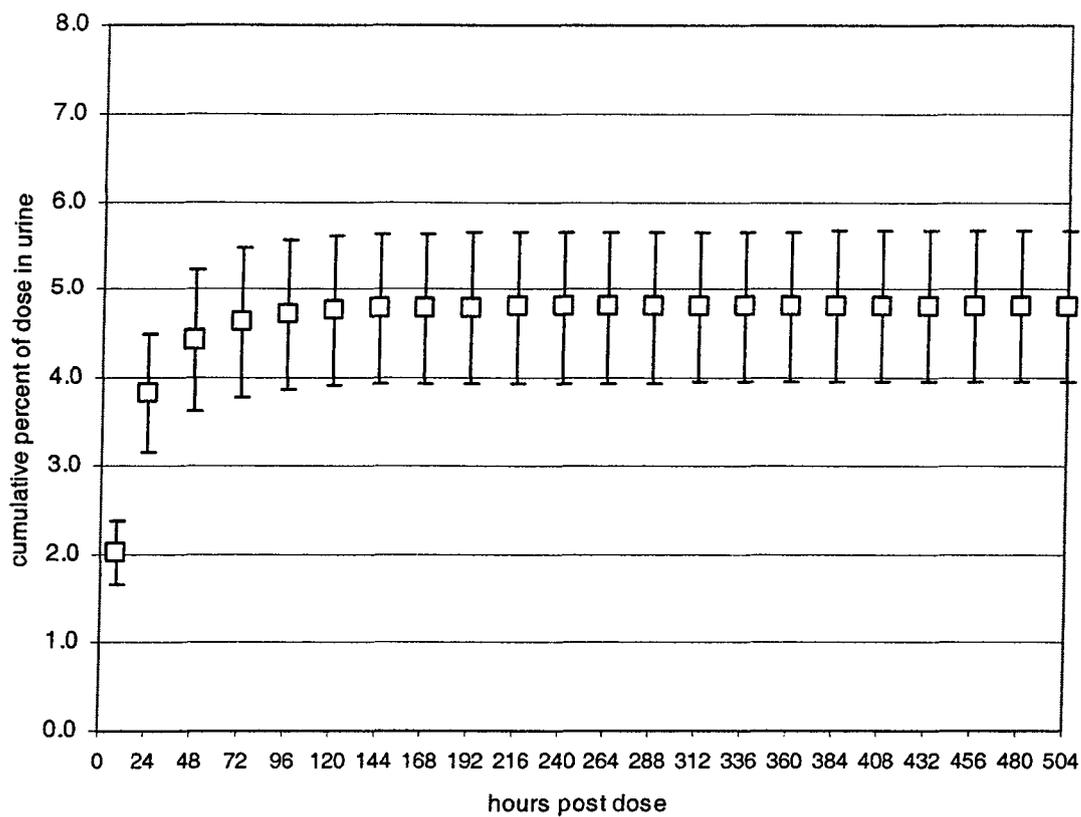


Figure 8
Cumulative percent of dose recovered in feces following an 8-hour topical exposure to creosote,
496 hours post-exposure - Supplemental Experiment

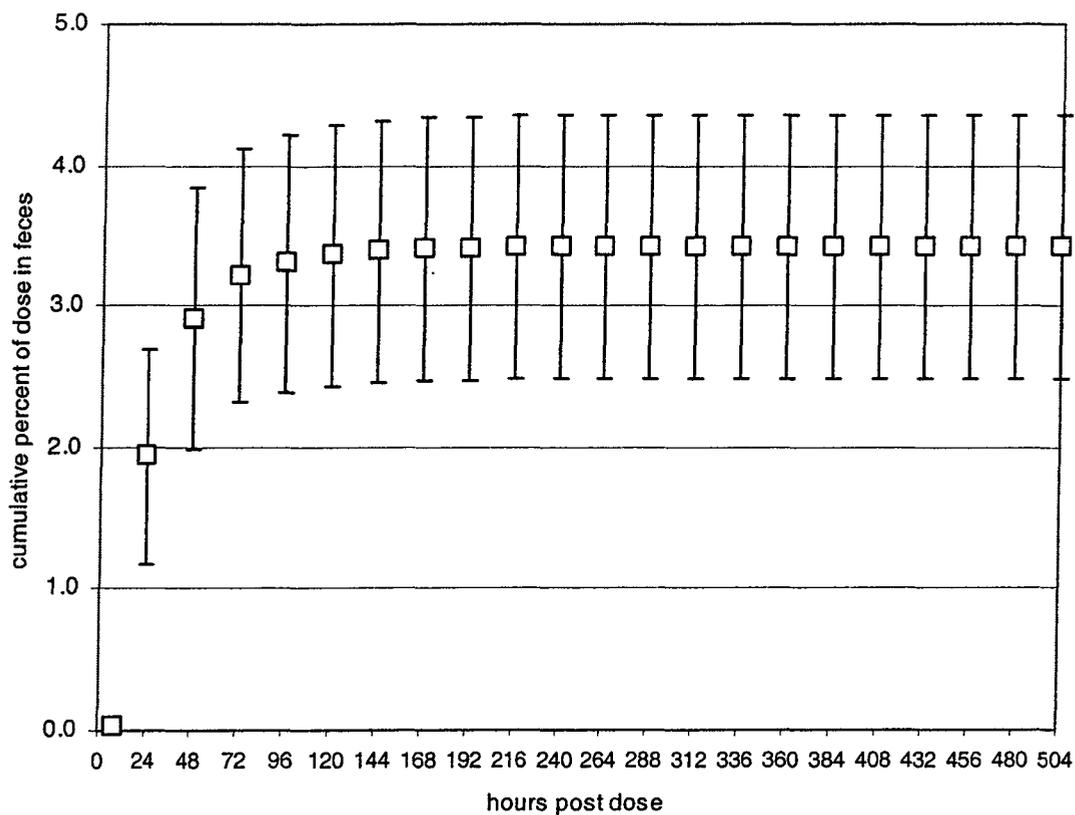
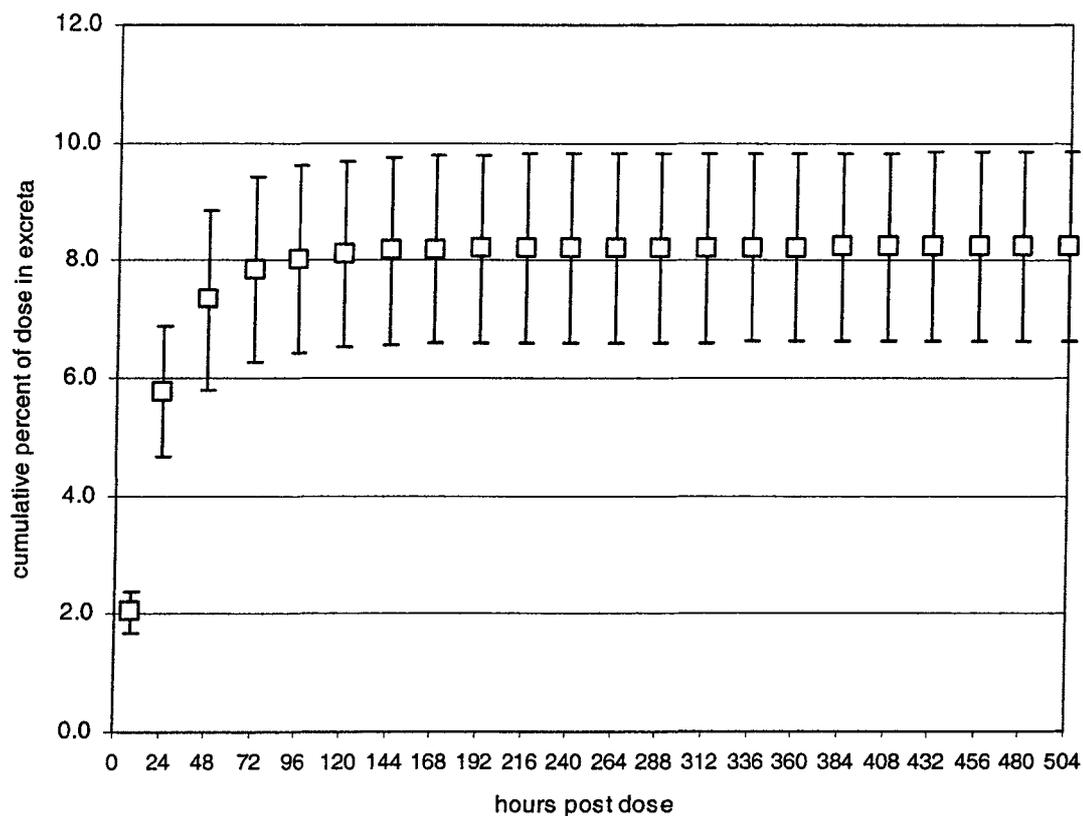


Figure 9
Cumulative percent of dose recovered in total excreta following an 8-hour topical exposure to
creosote, 496 hours post-exposure - Supplemental Experiment



APPENDICES

APPENDICES

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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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/encl: 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

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North American P1/P13
Series 62 Preliminary Analysis
RTI Study No. 6699

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 62 Preliminary Analysis
RTI 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: PREOSOTE Power II Date: 3-1-99
Study Director: Cliff Gamm Date: 2-17-99

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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
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The study was conducted at:

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The Study Director was:

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RTI Study No. 6939

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10.0 APPENDIX 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 CTM 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

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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 (tetralin) response. Tetralin (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 2.81.

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 $\mu\text{g/mL}$, 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.

North American P1/P13
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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 μg requires division by $1,000,000$, and to convert from μg 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 5.0
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.

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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.

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SECTION 7.0
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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, 5th Ed., John Wiley and Sons, New York, 1989.

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SECTION 8.0
TABLES

North American P1/P13
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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

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Table 2. Components Identified by GC/MS in North American P1/P13 Creosote

Ref. Std. ^a	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889- 2C ^b	8889- 2D ^b	8889- 2F ^b		
	Toluene	NC	NC	NC	NC	NA
	Ethylbenzene	<0.1	<0.1	<0.1	<0.1	NA
	p-Xylene + Styrene	NC	NC	<0.1	NC	NA
	Benzene	<0.1	<0.1	<0.1	<0.1	NA
	2,3-Dibenzofuran + 2,7-Dimethylbenzene	0.1	0.1	0.1	0.1	0
	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
	1,2,3,4-Tetrahydronaphthalene (isomer)	0.0	0.0	0.0	0.0	0
	Naphthalene	9.0	9.0	9.0	9.0	0
	Benzo[1,2,3-cd]pyrene	0.3	0.3	0.3	0.3	0
	Quinoline	0.3	0.3	0.3	0.3	0
	Acridone	0.3	0.2	0.2	0.2	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	2.1	2.1	2.1	2.1	66
	6-Methylquinoline	<0.1	<0.1	<0.1	<0.1	NA
	Methylindole	<0.1	<0.1	<0.1	<0.1	NA
	1-Methylbenzothiophene	<0.1	<0.1	<0.1	<0.1	NA
	1-Methylnaphthalene	0.5	0.5	0.5	0.5	0
	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	0.3	0.3	0.3	0.3	0
	Dimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Acenaphthene	4.4	5.0	5.0	4.8	77
	1-Naphthalenecarbonitrile	0.2	0.2	0.2	0.2	0
	1-Methylphenyl	0.1	0.1	0.1	0.1	0
	Isopropylphenyl (isomer) + n-Pentadecane	<0.1	<0.1	<0.1	<0.1	NA
	C ₁₅ H ₃₂ (isomer)	0.3	0.3	0.3	0.3	0
	Dibenzofuran	3.2	3	3	3.1	3.7
	Naphthalenecarbonitrile (isomer)	NC	<0.1	0.1	NC	NA
	Trimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Trimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Trimethylnaphthalene (isomer)	0.1	<0.1	<0.1	<0.1	NA
	Trimethylnaphthalene (isomer)	0.1	<0.1	<0.1	<0.1	NA
	2,3,5-Trimethylnaphthalene	<0.1	<0.1	<0.1	<0.1	NA

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Table 2. (continued)

Ref. Std. ^a	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889-2C ^b	8889-2D ^b	8889-2F ^b		
	Methylacetylphthalene (isomer)	<0.1	NF	NF	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
	1-Methylbenzofuran	0.3	0.3	0.3	0.3	0
	Diphenylene methane	<0.1	<0.1	<0.1	<0.1	NA
	Methylbenzofuran (isomer)	0.7	0.6	0.7	0.7	0
	Methylbenzofuran (isomer)	<0.1	<0.1	<0.1	<0.1	NA
■	9,10-Dihydroanthracene	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
	C ₂ H ₅ (isomer)	0.2	0.1	0.1	0.1	58
	C ₂ H ₅ (isomer)	0.1	NF	NF	NC	NA
	C ₂ H ₅ (isomer)	0.1	<0.1	<0.1	<0.1	NA
	Dibenzothiophene	1.4	1.2	1.2	1.2	0
	Phenanthrene	12.8	11.7	12.0	12.2	4.7
■	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
	Methylbenzothiophene (isomer)	0.3	0.2	0.2	0.2	29
■	1-Phenylaphthalene	0.2	0.2	0.2	0.2	0
	Dibenzo-p-dioxin (7)	0.1	<0.1	<0.1	<0.1	NA
	Methylbenzothiophene (isomer)	0.1	0.1	0.1	0.1	NA
	Methylphenanthrene (isomer)	0.2	0.6	0.7	0.5	57
■	2-Methylphenanthrene	0.3	0.7	0.8	0.6	12
■	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-Phenylaphthalene	0.2	0.5	0.5	0.5	12
	9H-Fluorene-carbonitrile	<0.1	NF	<0.1	NC	NA
	Ethylanthracene (isomer)	NF	<0.1	NF	NC	NA
	Ethylanthracene or dimethylphenanthrene (isomer)	0.1	0.1	0.1	0.1	0
	Dimethylphenanthrene (isomer)	<0.1	<0.1	<0.1	<0.1	NA

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Table 2. (continued)

Ref. Std. ^a	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889- 2C ^b	8889- 2D ^b	8889- 2F ^b		
	Dimethylphenanthrene (isomer)	<0.1	<0.1	<0.1	<0.1	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
	Benzylanthracene + C ₁₄ H ₁₀ (isomers)	<0.1	<0.1	<0.1	NA	NA
	C ₁₄ H ₁₀ (isomer)	0.2	0.2	0.2	0.2	0
	Anthracene (isomer)	NF	NF	NF	NC	NA
■	Pyrene	5.5	5.1	5.5	5.4	4.8
	Vinylanthracene (isomer)	0.3	0.2	0.3	0.3	0
	Benzonaphthofuran (isomer)	0.1	0.1	0.1	0.1	0
	Benzonaphthofuran (isomer) + Azapyrene	0.7	0.5	0.6	0.6	17
	Benzonaphthofuran (isomer)	0.1	0.1	0.1	0.1	0
	Benzo[fluorene] (isomer) or methylpyrene	0.3	0.3	0.3	0.3	0
	Pyrolocarbazole or 9Fl-fluorene carbonitrile	0.3	0.3	0.3	0.3	0
	Benzo[fluorene] (isomer)	0.3	0.2	0.3	0.3	19
■	Benzo[fluorene]	1.0	0.9	0.9	0.9	6.4
	2,3-Benzofluorene	1.2	1.1	1.1	1.1	5.2
	Methylpyrene (isomer)	0.5	0.5	0.5	0.5	0
	Phenylmethylanthracene (isomer)	0.5	0.4	0.5	0.5	12
	Methylpyrene (isomer)	0.4	0.3	0.4	0.4	16
	Methylpyrene or benzo[fluorene] (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-Terphenyl	0.3	0.2	0.2	0.2	29
	Dimethylpyrene (isomer)	0.4	0.3	0.3	0.3	0
	Dimethylpyrene (isomer)	<0.1	<0.1	NF	NC	NA
■	1,2-Benzodiphenylene sulfide	0.4	0.3	0.3	0.3	13
	Acenaphthene	0.5	0.5	0.5	0.5	0
	Benzo[c]acridine	0.3	0.3	0.3	0.3	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
	Methylbenz[a]anthracene (isomer)	<0.1	<0.1	0.1	<0.1	NA
	Benzo[carbazole] (isomer)	0.1	0.1	0.1	0.1	0
	C ₁₅ H ₁₀ N (isomer)	0.2	0.2	0.2	0.2	0
	C ₁₅ H ₁₀ N (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

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Table 2. (continued)

Ref. Std. ^a	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889- 2C ^b	8889- 2D ^b	8889- 2F ^b		
	Methanochrysene or 2,8-bis formyl dibenzothiophene (isomer)	0.1	0.1	0.1	0.1	0
	Methanochrysene or 2,8-bis formyl dibenzothiophene (isomer)	0.1	NF	0.1	NC	NA
	Methanochrysene or 2,8-bis formyl dibenzothiophene (isomer)	0.2	0.2	0.2	0.2	0
	Methylchrysene (isomer)	NF	NF	<0.1	NC	NA
	Benzo[b]fluoranthene	0.1	0.1	0.1	0.1	0
	Benzo[k]fluoranthene	0.1	0.1	0.1	0.1	0
	Chrysene (isomer)	0.2	0.2	0.2	0.2	0
	Unknown	0.2	0.2	0.2	0.2	0
	Benzo[a]pyrene	0.4	0.4	0.4	0.4	0
	Benzo[a]pyrene	0.5	0.4	0.5	0.5	12
	Perylene	0.1	0.1	0.1	0.1	0
	C ₂₁ H ₁₄ (isomer)	NF	NF	<0.1	NC	NA
	Indeno(1,2,3-c,d)pyrene	0.2	0.1	0.1	0.1	58
	C ₂₁ H ₁₄ S ₂ (isomer) (tent)	0.2	0.2	0.2	0.2	0
	Benzo[ghi]perylene	0.1	<0.1	0.1	<0.1	0
	C ₂₁ H ₁₄ (isomer)	NF	NF	<0.1	NC	NA

^aAuthentic material used where indicated (■).

^bSee Table 1 for additional sample information.

^cNF = Not Found.

^dNC = Not Calculated.

^eNA = Not Applicable.

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Series 62 Preliminary Analysis
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SECTION 9.0

FIGURES

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

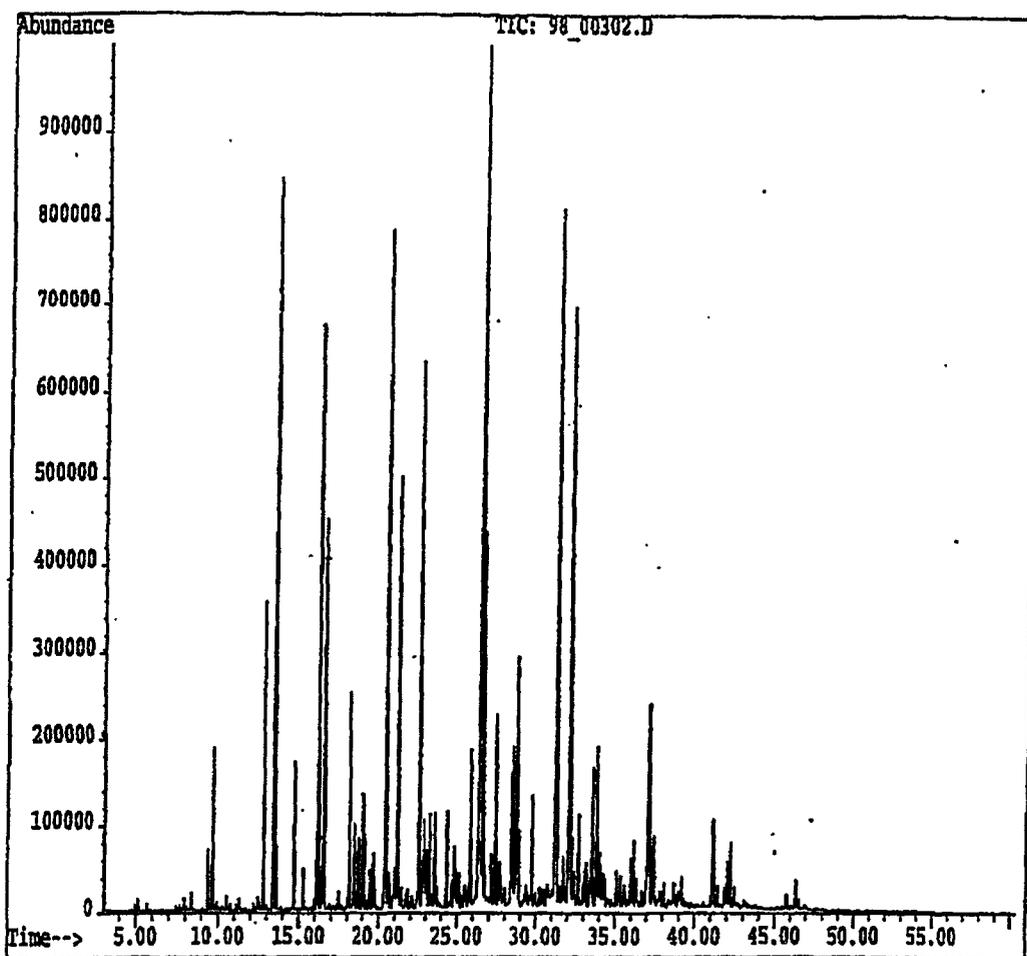


Figure 1. Reconstructed ion chromatogram of North American Composite sample 8889-2C

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

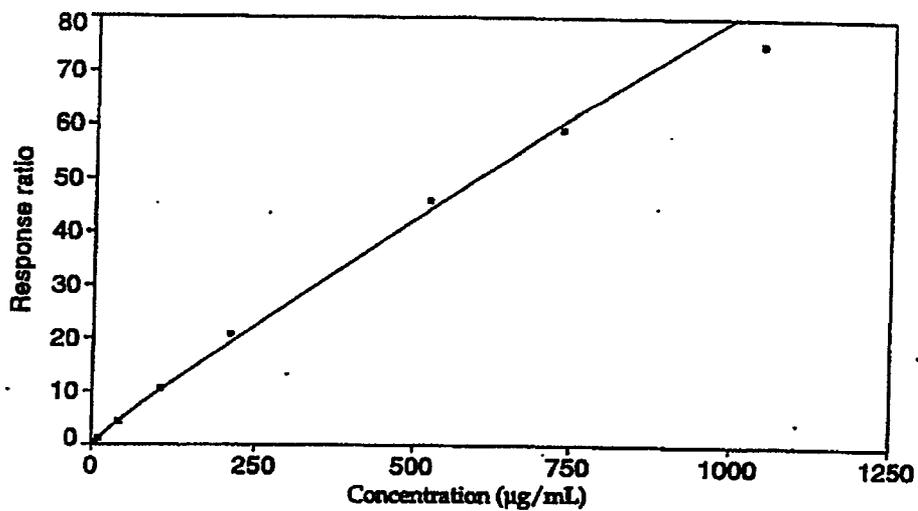


Figure 2. Naphthalene Calibration Curve
Weighted (1/x) Regression Equation: $\ln y = -1.931 + 0.9139 \ln x$
Correlation Coefficient (r) = 0.99998

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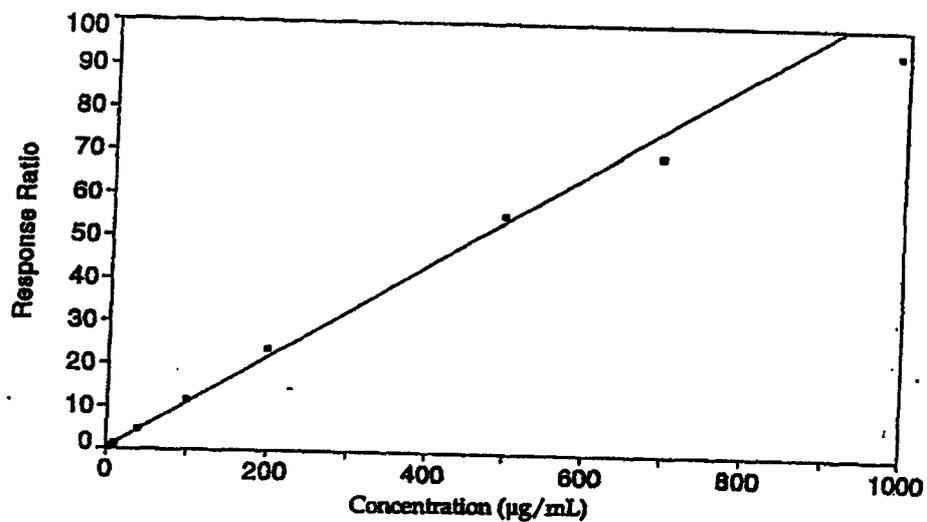


Figure 3. Phenanthrene Calibration Curve
Weighted (1/x) Regression Equation: $\ln y = -2.166 + 0.9925 \ln x$
Correlation Coefficient (r) = 0.99998

North American P1/P13
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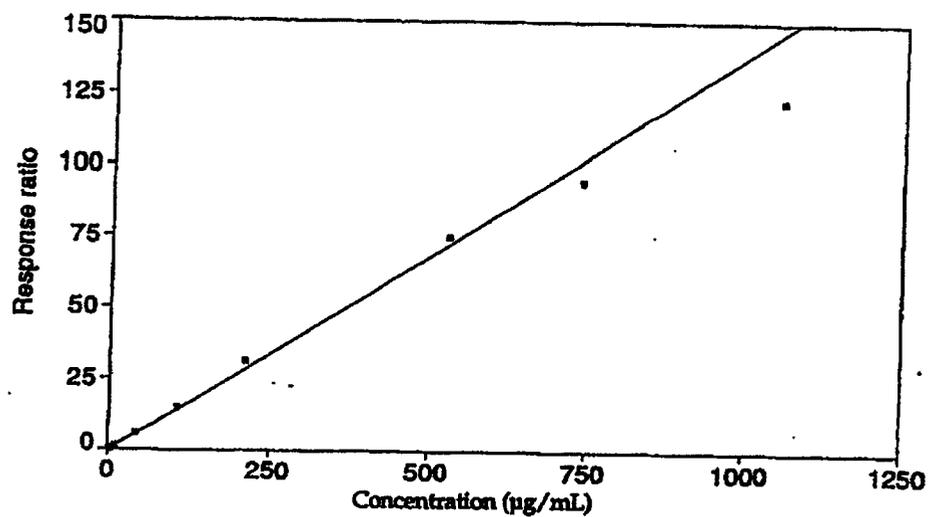


Figure 4. Pyrene Calibration Curve
Weighted (1/x) Regression Equation: $\ln y = -2.130 + 1.022 \ln x$
Correlation Coefficient (r) = 0.99990

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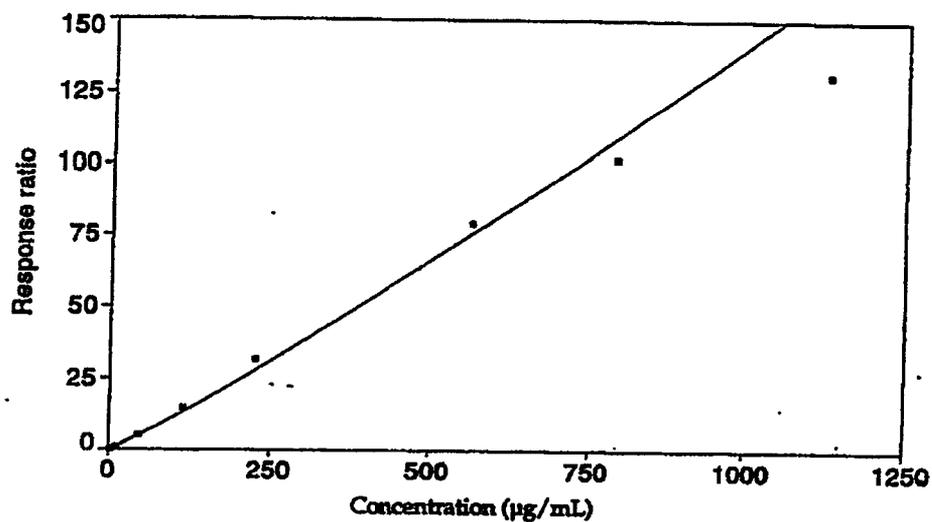


Figure 5. Chrysene Calibration Curve
Weighted (1/x) Regression Equation: $\ln y = -2.580 + 1.090 \ln x$
Correlation Coefficient (r) = 0.9980

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SECTION 10.0

APPENDIX

Appendix B
Radiolabeled Test Substance Information



11542 Fort Mims Dr.
Saint Louis, Missouri 63146 USA
Telephone 800-325-4581 • (314) 771-5765
Fax (314) 569-0682
www.sigma-aldrich.com

Product Information

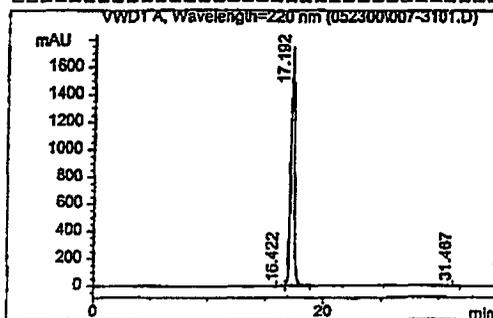
PROD NAME: 2-METHYLNAPHTHALENE-8-14C
LOT NUMBER: 050K9424/25
PROD NUMBER: M6146-14C
ANALYST: 027BD
DATE: 5/24/00 9:57:19 AM Inj Volume: 0.10ul

*****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
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: 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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sigma-aldrich.com

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

Product Information ->

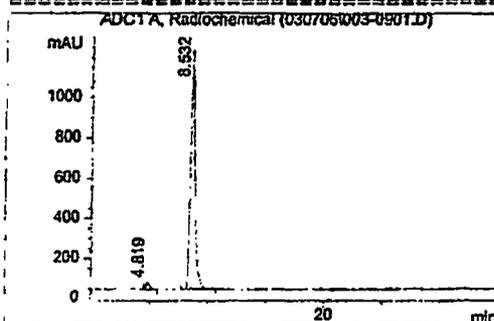
Inj Volume: 1.00ul

*****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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sigma-aldrich.com

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

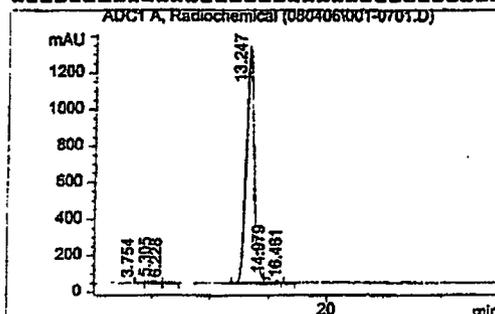
Inj Volume: 3.00ul

*****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/mmol 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	1.746e3	30.048	2.671
6	16.461	0.489	317.751	8.411	0.486



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Product Information

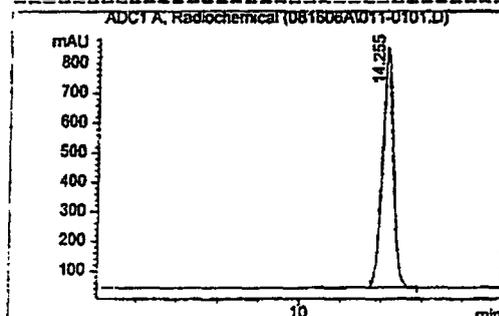
PROD NAME: BIPHENYL-UL-14C
LOT NUMBER: 115F9247
PROD NUMBER: B5892-14C
ANALYST: Quality Control
DATE: 8/16/06 2:04:10 PM Inj Volume: 1.00ul

*****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
DATE: 6/1/04 9:18:17 PM

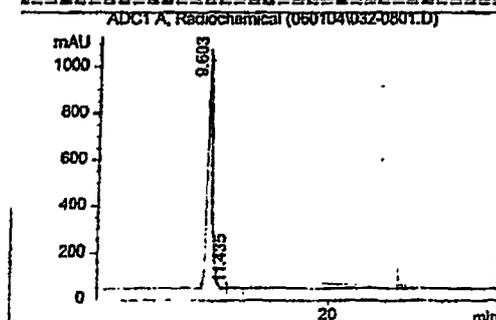
Inj Volume: 7.00ul

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

column: Supelco Discovery HS C18, 250 x 2.1 mm, 5um
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

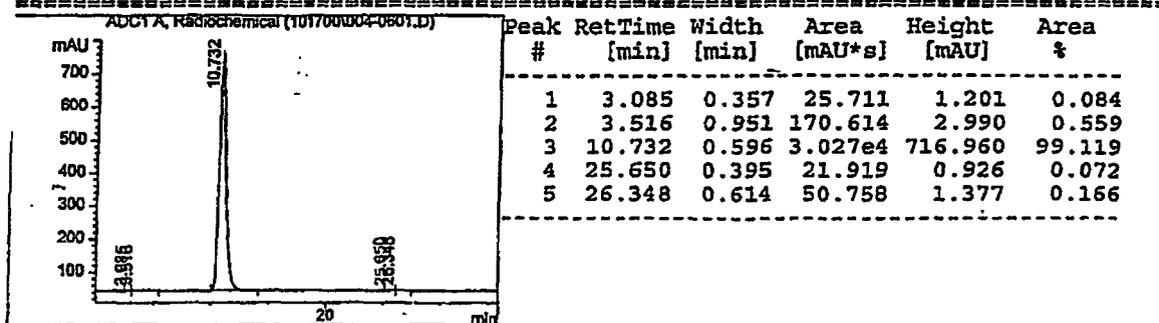
ROD NAME: NAPHTHLENE-BENZENE-UL-14C
LOT NUMBER: 068H9600/01
ROD NUMBER: N3145-14C
ANALYST: 027BD
DATE: 10/17/00 7:44:35 PM Inj Volume: 1.50ul

*****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





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Product Information

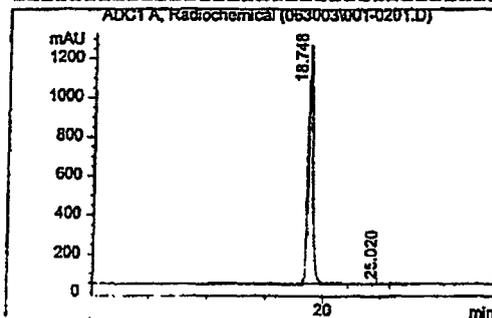
PROD NAME: PHENANTHRENE-9-14C
LOT NUMBER: 111K9412/13
PROD NUMBER: P0785-14C
ANALYST: Quality Control
DATE: 6/30/03 3:42:26 PM Inj Volume: 1.50ul

*****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

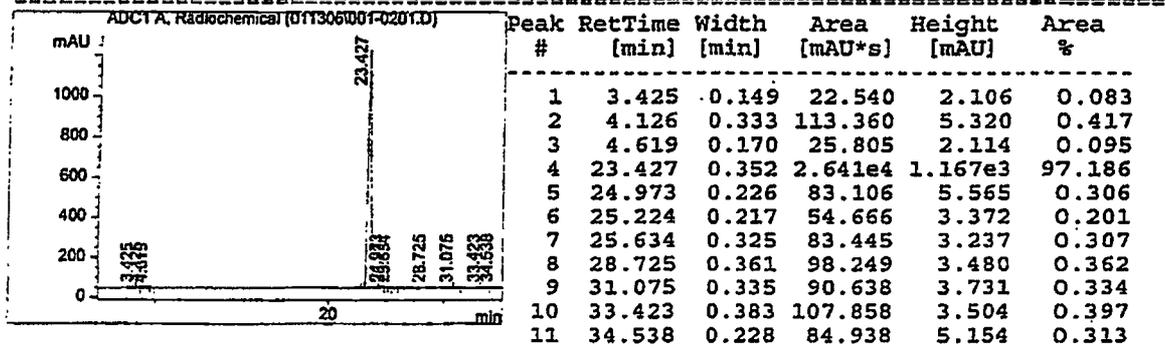
PROD NAME: PYRENE-4,5,9,10-14C
LOT NUMBER: 079H9662/63
PROD NUMBER: P6805-14C
ANALYST: Quality Control
DATE: 1/13/06 2:03:13 PM Inj Volume: 1.00ul

*****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



Appendix C
Individual Animal Data

Application Amounts and Rates

0 Hour Post-Exposure Group

Rat Number	Body Weight (g)	Weight of Formulation (g) ^a	Total Radioactivity Applied (μCi)	Total Creosote Applied (μg) ^b	Application Rate (μg/cm ²) ^c
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) ^a	Total Radioactivity Applied (μCi)	Total Creosote Applied (μg) ^b	Application Rate (μg/cm ²) ^c
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

Supplemental Experiment - 496 Hour Post-Exposure Group

Rat Number	Body Weight (g)	Weight of Formulation (g) ^a	Total Radioactivity Applied (μCi)	Total Creosote Applied (μg) ^b	Application Rate (μg/cm ²) ^c
001M	331.7	0.11235	19.0	112350	10700
002M	333.6	0.11235	18.9	112350	10700
003M	326.6	0.11235	19.0	112350	10700
004M	328.4	0.11235	18.7	112350	10700
Mean	330.1	0.1124	18.9	112350	10700
SD	3.16	0.000	0.14	0.00	0.00

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

^b Based on weight applied x 1,000,000 μg/g

^c Application rate = total Creosote applied (112350 μg)/10.5 cm²

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 non-dosed skin	8 h	0.049	<LOD	<LOD	<LOD	0.049	N.A.
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 dosed skin	8 h	0.049	<LOD	<LOD	<LOD	0.049	N.A.
non-dosed skin	8 h	1.72	1.805	1.132	1.555	1.553	0.299
Carcass	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	001M	002M	003M	004M	Mean	SD
	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	N.A.	N.A.
CO2	12 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	24 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	48 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	72 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	96 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	120 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	144 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	168 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	192 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	216 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	240 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	264 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	288 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	312 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	336 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	360 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	384 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	408 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	432 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	456 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	480 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	504 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
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	N.A.	N.A.
VO	12 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
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	N.A.
VO	144 h	<LOD	<LOD	0.043	<LOQ	0.043	N.A.
VO	168 h	<LOD	<LOD	<LOQ	<LOD	N.A.	N.A.
VO	192 h	<LOD	<LOD	<LOQ	<LOD	N.A.	N.A.
VO	216 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	240 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	264 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	288 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	312 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	336 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	360 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	384 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	408 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	432 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	456 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	480 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	504 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
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	N.A.	N.A.
Lungs	504 h	<LOD	<LOD	<LOQ	<LOQ	N.A.	N.A.
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	N.A.	N.A.
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	N.A.	N.A.
CO2	12 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	24 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	48 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	72 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	96 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	120 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	144 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	168 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	192 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
CO2	216 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	240 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	264 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	288 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	312 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	336 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	360 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	384 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	408 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	432 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	456 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	480 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
CO2	504 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
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	N.A.	N.A.
VO	12 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
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	N.A.
VO	144 h	<LOD	<LOD	0.043	<LOQ	0.043	N.A.
VO	168 h	<LOD	<LOD	<LOQ	<LOD	N.A.	N.A.
VO	192 h	<LOD	<LOD	<LOQ	<LOD	N.A.	N.A.
VO	216 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	240 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	264 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	288 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	312 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	336 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	360 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	384 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	408 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	432 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	456 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	480 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
VO	504 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
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	N.A.	N.A.
Lungs	504 h	<LOD	<LOD	<LOQ	<LOQ	N.A.	N.A.
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	N.A.	N.A.
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	N.A.	N.A.
tape strip 6	504 h	<LOQ	<LOD	N.S.	<LOD	N.A.	N.A.
tape strip 7	504 h	<LOD	N.S.	N.S.	<LOD	N.A.	N.A.
tape strip 8	504 h	<LOD	N.S.	N.S.	N.S.	N.A.	N.A.
tape strip 9	504 h	<LOD	N.S.	N.S.	N.S.	N.A.	N.A.
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
Total Recovered		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	N.S.			N.S.		
240 h	N.S.			N.S.		
264 h	N.S.			N.S.		
288 h	N.S.			N.S.		
312 h	N.S.			N.S.		
336 h	N.S.			N.S.		
360 h	N.S.			N.S.		
384 h	N.S.			N.S.		
408 h	N.S.			N.S.		
432 h	N.S.			N.S.		
456 h	N.S.			N.S.		
480 h	N.S.			N.S.		
504 h	N.S.			N.S.		
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	N.S.			N.S.		
240 h	N.S.			N.S.		
264 h	N.S.			N.S.		
288 h	N.S.			N.S.		
312 h	N.S.			N.S.		
336 h	N.S.			N.S.		
360 h	N.S.			N.S.		
384 h	N.S.			N.S.		
408 h	N.S.			N.S.		
432 h	N.S.			N.S.		
456 h	N.S.			N.S.		
480 h	N.S.			N.S.		
504 h	N.S.			N.S.		
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				
Timepoint (hours)	Urine	Feces	VO	cumulative %
8 h	2.34	0.04	<LOD	2.38
12 h	3.17	0.48	<LOD	3.65
24 h	5.37	2.35	<LOQ	7.73
48 h	7.63	4.39	<LOQ	12.02
72 h	8.91	5.86	<LOQ	14.77
96 h	9.79	6.58	<LOD	16.37
120 h	10.34	7.14	<LOD	17.48
144 h	10.74	7.60	<LOD	18.34
168 h	10.97	7.88	<LOD	18.85
192 h	11.13	8.10	<LOD	19.23
216 h	11.26	8.26	0.00	19.52
240 h	11.35	8.39	0.00	19.73
264 h	11.41	8.47	0.00	19.88
288 h	11.45	8.52	0.00	19.97
312 h	11.49	8.57	0.00	20.06
336 h	11.53	8.61	0.00	20.14
360 h	11.55	8.64	0.00	20.19
384 h	11.57	8.66	0.00	20.23
408 h	11.59	8.68	0.00	20.27
432 h	11.61	8.70	0.00	20.30
456 h	11.62	8.71	0.00	20.34
480 h	11.64	8.76	0.00	20.40
504 h	11.65	8.78	0.00	20.43

006M				
Timepoint (hours)	Urine	Feces	VO	cumulative %
8 h	3.00	0.01	<LOD	3.01
12 h	4.50	0.38	<LOD	4.88
24 h	7.93	3.56	0.06	11.54
48 h	12.71	8.13	0.13	20.97
72 h	15.14	10.99	0.19	26.31
96 h	16.87	12.89	0.23	29.99
120 h	17.93	14.24	0.23	32.41
144 h	18.58	15.33	0.23	34.14
168 h	19.06	16.03	0.23	35.32
192 h	19.40	16.57	0.23	36.21
216 h	19.58	16.95	0.00	36.53
240 h	19.75	17.30	0.00	37.05
264 h	19.85	17.50	0.00	37.35
288 h	19.96	17.67	0.00	37.63
312 h	20.04	17.82	0.00	37.87
336 h	20.11	17.93	0.00	38.04
360 h	20.15	18.02	0.00	38.17
384 h	20.19	18.11	0.00	38.30
408 h	20.22	18.18	0.00	38.40
432 h	20.25	18.24	0.00	38.49
456 h	20.28	18.28	0.00	38.56
480 h	20.31	18.35	0.00	38.66
504 h	20.32	18.40	0.00	38.73

007M				
Timepoint (hours)	Urine	Feces	VO	cumulative %
8 h	2.69	0.03	<LOD	2.72
12 h	3.98	0.11	<LOD	4.09
24 h	7.67	0.56	0.11	8.34
48 h	12.43	3.79	0.25	16.47
72 h	16.33	6.57	0.37	23.26
96 h	18.20	8.40	0.45	27.05
120 h	19.34	9.35	0.49	29.19
144 h	20.00	9.94	0.54	30.47
168 h	20.38	10.38	0.54	31.30
192 h	20.61	10.67	0.54	31.82
216 h	20.73	10.89	0.00	31.61
240 h	20.80	11.02	0.00	31.82
264 h	20.86	11.11	0.00	31.97
288 h	20.91	11.19	0.00	32.11
312 h	20.95	11.26	0.00	32.21
336 h	21.00	11.33	0.00	32.32
360 h	21.04	11.39	0.00	32.42
384 h	21.07	11.45	0.00	32.52
408 h	21.10	11.49	0.00	32.59
432 h	21.12	11.52	0.00	32.65
456 h	21.16	11.73	0.00	32.89
480 h	21.19	12.02	0.00	33.21
504 h	21.20	12.03	0.00	33.23

008M				
Timepoint (hours)	Urine	Feces	VO	cumulative %
8 h	3.02	0.00	<LOD	3.02
12 h	4.57	0.04	<LOD	4.61
24 h	8.87	0.56	<LOQ	9.43
48 h	13.30	2.88	0.06	16.23
72 h	16.38	5.15	0.12	21.65
96 h	18.15	6.49	0.16	24.80
120 h	19.67	7.62	0.16	27.46
144 h	20.43	8.32	0.16	28.92
168 h	20.90	8.75	0.16	29.82
192 h	21.21	9.27	0.16	30.64
216 h	21.41	9.58	0.00	30.99
240 h	21.64	9.87	0.00	31.51
264 h	21.85	10.06	0.00	31.91
288 h	22.01	10.27	0.00	32.28
312 h	22.15	10.45	0.00	32.60
336 h	22.26	10.58	0.00	32.84
360 h	22.36	10.67	0.00	33.03
384 h	22.43	10.75	0.00	33.18
408 h	22.51	10.83	0.00	33.34
432 h	22.58	10.90	0.00	33.47
456 h	22.63	10.98	0.00	33.60
480 h	22.67	11.15	0.00	33.83
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

Percent of applied dose - 496 hours post-exposure - Supplemental Experiment

Absorbed		001M	002M	003M	004M	Mean	SD
urine	8 h	1.657	2.488	1.832	2.052	2.007	0.359
urine	12 h	NS	NS	NS	NS	NA	NA
urine	24 h	1.823	2.34	1.626	1.465	1.814	0.38
urine	48 h	0.752	0.757	0.304	0.584	0.599	0.213
urine	72 h	0.25	0.265	0.138	0.166	0.205	0.062
urine	96 h	0.105	0.086	0.079	0.094	0.091	0.011
urine	120 h	0.064	0.032	0.028	0.031	0.039	0.017
urine	144 h	0.025	0.02	0.012	0.028	0.021	0.007
urine	168 h	0.018	0.012	0.005	0.007	0.011	0.006
urine	192 h	0.005	0.006	0.004	0.005	0.005	0.001
urine	216 h	0.004	0.004	0.002	0.003	0.003	0.001
urine	240 h	0.002	0.003	0.002	0.003	0.003	0.001
urine	264 h	0.002	0.003	0.001	0.002	0.002	0.001
urine	288 h	0.003	0.002	0.001	0.002	0.002	0.001
urine	312 h	0.002	0.002	0.001	0.002	0.002	0.001
urine	336 h	0.002	0.002	0.001	0.002	0.002	0.001
urine	360 h	0.001	0.002	0.001	0.001	0.001	0.001
urine	384 h	0.001	0.001	0.001	0.001	0.001	0
urine	408 h	0	0.003	0.001	0.001	0.001	0.001
urine	432 h	<LOQ	0.004	0.001	0.001	0.002	0.002
urine	456 h	0.001	0.002	0.001	0.001	0.001	0.001
urine	480 h	<LOQ	0.001	0.001	0.001	0.001	0
urine	504 h	<LOQ	0.001	0.001	0.001	0.001	0
sub total urine		4.717	6.036	4.043	4.453	4.812	0.862
feces	8 h	0.027	0.009	0.024	0.033	0.023	0.01
feces	12 h	NS	NS	NS	NS		
feces	24 h	0.922	2.135	2.764	1.841	1.916	0.766
feces	48 h	0.976	1.8	0.609	0.495	0.97	0.59
feces	72 h	0.467	0.368	0.199	0.196	0.308	0.133
feces	96 h	0.101	0.122	0.076	0.072	0.093	0.023
feces	120 h	0.041	0.053	0.077	0.032	0.051	0.02
feces	144 h	0.025	0.034	0.027	0.025	0.028	0.004
feces	168 h	0.014	0.02	0.014	0.019	0.017	0.003
feces	192 h	0.008	0.01	0.008	0.005	0.008	0.002
feces	216 h	0.007	0.007	0.005	<LOQ	0.006	0.001
feces	240 h	0.004	0.006	<LOQ	<LOQ	0.005	0.001
feces	264 h	<LOQ	0.005	<LOQ	<LOQ	0.005	N.A.
feces	288 h	<LOQ	0.004	<LOQ	<LOQ	0.004	N.A.
feces	312 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
feces	336 h	0.005	<LOQ	<LOQ	<LOQ	0.005	N.A.
feces	360 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
feces	384 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
feces	408 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
feces	432 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
feces	456 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
feces	480 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
feces	504 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
sub total feces		2.597	4.573	3.803	2.718	3.423	0.939
cage wash	192 h	0.697	0.457	0.441	0.496	0.523	0.118
cage wash	504 h	0.054	0.06	<LOQ	<LOQ	0.057	0.004
sub total cagewash		0.751	0.517	0.441	0.496	0.55125	0.137
residual feed	504 h	0.036	0.031	0.18	0.018	0.066	0.076
non-dosed skin	504 h	<LOQ	<LOQ	0.001	<LOQ	0.001	N.A.
carcass	504 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
whole blood	504 h	<LOQ	0.001	<LOQ	<LOQ	0.001	NA
rbc (terminal)	504 h	<LOQ	0.001	<LOQ	0	0.001	0.001
heart	504 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
lungs	504 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
liver	504 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
kidney	504 h	<LOQ	0	<LOQ	<LOQ	0	N.A.
plasma (terminal)	504 h	<LOQ	<LOQ	<LOQ	<LOQ	N.A.	N.A.
Total		8.101	11.159	8.468	7.685	8.853	1.570

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

Absorbable		001M	002M	003M	004M	Mean	SD
Absorbed dose		8.101	11.159	8.468	7.685	8.853	1.570
dosed skin		<LOD	<LOQ	0.005	<LOQ	0.005	N.A.
	Total	8.101	11.159	8.473	7.685	8.855	1.570
Unabsorbed		001M	002M	003M	004M	Mean	SD
body wrap	8 h	30.147	23.691	38.545	37.617	32.5	6.973
body wrap	24 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	48 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	72 h	1.372	2.552	1.416	1.056	1.599	0.655
body wrap	96 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	120 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	144 h	0.082	0.174	0.049	0.048	0.088	0.059
body wrap	168 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	192 h	0.013	0.033	0.006	0.006	0.015	0.013
body wrap	216 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	240 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	264 h	0.009	0.025	0.004	0.003	0.01	0.01
body wrap	288 h	N.S.	N.S.	N.S.	<LOQ	N.A.	N.A.
body wrap	312 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	336 h	0.006	0.018	0.003	0.001	0.007	0.008
body wrap	360 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	384 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	408 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	432 h	0.003	0.016	0.002	0.002	0.006	0.007
body wrap	456 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	480 h	N.S.	N.S.	N.S.	N.S.	N.A.	N.A.
body wrap	504 h	0.002	0.007	0.001	0.001	0.003	0.003
subtotal bodywrap		31.634	26.516	40.026	38.734	34.2275	6.328
skin wash - sponges	8 h	22.621	33.081	15.456	17.803	22.24	7.818
O-ring	504 h	32.746	24.298	25.957	26.805	27.452	3.68
tape strip 1	504 h	<LOQ	0.001	<LOQ	<LOD	0.001	N.A.
tape strip 2	504 h	<LOD	0.001	<LOQ	<LOD	0.001	N.A.
tape strip 3	504 h	<LOD	0.001	<LOD	<LOD	0.001	N.A.
tape strip 4	504 h	<LOD	<LOQ	<LOD	<LOD	N.A.	N.A.
tape strip 5	504 h	<LOD	<LOQ	<LOD	<LOD	N.A.	N.A.
tape strip 6	504 h	<LOD	<LOQ	<LOD	<LOD	N.A.	N.A.
tape strip 7	504 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
tape strip 8	504 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
tape strip 9	504 h	<LOD	<LOD	<LOD	<LOD	N.A.	N.A.
tape strip 10	504 h	N.S.	<LOD	N.S.	<LOD	N.A.	N.A.
tape strip 11	504 h	N.S.	<LOD	N.S.	<LOD	N.A.	N.A.
tape sub total		0.000	0.003	0.000	0.000	0.001	0.002
	Total	87.001	83.898	81.439	83.342	83.920	2.308
Total Recovered		95.102	95.057	89.912	91.027	92.775	2.700

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

Timepoint (hours)	001M			002M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	1.657	1.66	35.1	2.488	2.49	41.2
24 h	1.823	3.48	73.8	2.34	4.83	80.0
48 h	0.752	4.23	89.7	0.757	5.59	92.5
72 h	0.25	4.48	95.0	0.265	5.85	96.9
96 h	0.105	4.59	97.2	0.086	5.94	98.3
120 h	0.064	4.65	98.6	0.032	5.97	98.9
144 h	0.025	4.68	99.1	0.02	5.99	99.2
168 h	0.018	4.69	99.5	0.012	6.00	99.4
192 h	0.005	4.70	99.6	0.006	6.01	99.5
216 h	0.004	4.70	99.7	0.004	6.01	99.6
240 h	0.002	4.71	99.7	0.003	6.01	99.6
264 h	0.002	4.71	99.8	0.003	6.02	99.7
288 h	0.003	4.71	99.9	0.002	6.02	99.7
312 h	0.002	4.71	99.9	0.002	6.02	99.7
336 h	0.002	4.71	99.9	0.002	6.02	99.8
360 h	0.001	4.72	100.0	0.002	6.02	99.8
384 h	0.001	4.72	100.0	0.001	6.03	99.8
408 h	0.000	4.72	100.0	0.003	6.03	99.9
432 h	<LOQ	4.72	100.0	0.004	6.03	99.9
456 h	0.001	4.72	100.0	0.002	6.03	100.0
480 h	<LOQ	4.72	100.0	0.001	6.04	100.0
504 h	<LOQ	4.72	100.0	0.001	6.04	100.0
Total	4.717			6.036		

Timepoint (hours)	003M			004M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	1.832	1.83	45.3	2.052	2.05	46.1
24 h	1.626	3.46	85.5	1.465	3.52	79.0
48 h	0.304	3.76	93.0	0.584	4.10	92.1
72 h	0.138	3.90	96.5	0.166	4.27	95.8
96 h	0.079	3.98	98.4	0.094	4.36	97.9
120 h	0.028	4.01	99.1	0.031	4.39	98.6
144 h	0.012	4.02	99.4	0.028	4.42	99.3
168 h	0.005	4.02	99.5	0.007	4.43	99.4
192 h	0.004	4.03	99.6	0.005	4.43	99.5
216 h	0.002	4.03	99.7	0.003	4.44	99.6
240 h	0.002	4.03	99.7	0.003	4.44	99.7
264 h	0.001	4.03	99.8	0.002	4.44	99.7
288 h	0.001	4.03	99.8	0.002	4.44	99.8
312 h	0.001	4.04	99.8	0.002	4.44	99.8
336 h	0.001	4.04	99.8	0.002	4.45	99.8
360 h	0.001	4.04	99.9	0.001	4.45	99.9
384 h	0.001	4.04	99.9	0.001	4.45	99.9
408 h	0.001	4.04	99.9	0.001	4.45	99.9
432 h	0.001	4.04	99.9	0.001	4.45	99.9
456 h	0.001	4.04	100.0	0.001	4.45	100.0
480 h	0.001	4.04	100.0	0.001	4.45	100.0
504 h	0.001	4.04	100.0	0.001	4.45	100.0
Total	4.043			4.45		

Timepoint (hours)	Cumulative	
	Mean	SD
8 h	2.007	0.359
24 h	3.821	0.672
48 h	4.420	0.802
72 h	4.625	0.851
96 h	4.716	0.851
120 h	4.755	0.851
144 h	4.776	0.852
168 h	4.786	0.855
192 h	4.791	0.856
216 h	4.795	0.856
240 h	4.797	0.857
264 h	4.799	0.857
288 h	4.801	0.858
312 h	4.803	0.858
336 h	4.805	0.858
360 h	4.806	0.859
384 h	4.807	0.859
408 h	4.808	0.860
432 h	4.810	0.861
456 h	4.811	0.862
480 h	4.812	0.862
504 h	4.812	0.862

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

Timepoint (hours)	001M			002M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	0.027	0.027	1.0	0.009	0.009	0.2
24 h	0.922	0.949	36.5	2.135	2.144	46.9
48 h	0.976	1.925	74.1	1.8	3.944	86.2
72 h	0.467	2.392	92.1	0.368	4.312	94.3
96 h	0.101	2.493	96.0	0.122	4.434	97.0
120 h	0.041	2.534	97.6	0.053	4.487	98.1
144 h	0.025	2.559	98.5	0.034	4.521	98.9
168 h	0.014	2.573	99.1	0.02	4.541	99.3
192 h	0.008	2.581	99.4	0.01	4.551	99.5
216 h	0.007	2.588	99.7	0.007	4.558	99.7
240 h	0.004	2.592	99.8	0.006	4.564	99.8
264 h	<LOQ	2.592	99.8	0.005	4.569	99.9
288 h	<LOQ	2.592	99.8	0.004	4.573	100.0
312 h	<LOQ	2.592	99.8	<LOQ	4.573	100.0
336 h	0.005	2.597	100.0	<LOQ	4.573	100.0
360 h	<LOQ	2.597	100.0	<LOQ	4.573	100.0
384 h	<LOQ	2.597	100.0	<LOQ	4.573	100.0
408 h	<LOQ	2.597	100.0	<LOQ	4.573	100.0
432 h	<LOQ	2.597	100.0	<LOQ	4.573	100.0
456 h	<LOQ	2.597	100.0	<LOQ	4.573	100.0
480 h	<LOQ	2.597	100.0	<LOQ	4.573	100.0
504 h	<LOQ	2.597	100.0	<LOQ	4.573	100.0
Total	2.597			4.573		

Timepoint (hours)	003M			004M		
	Percent	cumulative %	interval % of total	Percent	cumulative %	interval % of total
8 h	0.024	0.024	0.6	0.033	0.033	1.2
24 h	2.764	2.788	73.3	1.841	1.874	68.9
48 h	0.609	3.397	89.3	0.495	2.369	87.2
72 h	0.199	3.596	94.6	0.196	2.565	94.4
96 h	0.076	3.672	96.6	0.072	2.637	97.0
120 h	0.077	3.749	98.6	0.032	2.669	98.2
144 h	0.027	3.776	99.3	0.025	2.694	99.1
168 h	0.014	3.790	99.7	0.019	2.713	99.8
192 h	0.008	3.798	99.9	0.005	2.718	100.0
216 h	0.005	3.803	100.0	<LOQ	2.718	100.0
240 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
264 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
288 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
312 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
336 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
360 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
384 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
408 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
432 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
456 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
480 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
504 h	<LOQ	3.803	100.0	<LOQ	2.718	100.0
Total	3.803			2.718		

Timepoint (hours)	Cumulative	
	Mean	SD
8 h	0.023	0.010
24 h	1.939	0.763
48 h	2.909	0.925
72 h	3.216	0.903
96 h	3.309	0.916
120 h	3.360	0.928
144 h	3.388	0.932
168 h	3.404	0.933
192 h	3.412	0.934
216 h	3.417	0.936
240 h	3.419	0.937
264 h	3.421	0.939
288 h	3.422	0.941
312 h	3.422	0.941
336 h	3.423	0.939
360 h	3.423	0.939
384 h	3.423	0.939
408 h	3.423	0.939
432 h	3.423	0.939
456 h	3.423	0.939
480 h	3.423	0.939
504 h	3.423	0.939

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

001M

Timepoint (hours)	Urine	Feces	cumulative %
8 h	1.66	0.03	1.68
24 h	3.48	0.95	4.43
48 h	4.23	1.93	6.16
72 h	4.48	2.39	6.87
96 h	4.59	2.49	7.08
120 h	4.65	2.53	7.19
144 h	4.68	2.56	7.24
168 h	4.69	2.57	7.27
192 h	4.70	2.58	7.28
216 h	4.70	2.59	7.29
240 h	4.71	2.59	7.30
264 h	4.71	2.59	7.30
288 h	4.71	2.59	7.30
312 h	4.71	2.59	7.30
336 h	4.71	2.60	7.31
360 h	4.72	2.60	7.31
384 h	4.72	2.60	7.31
408 h	4.72	2.60	7.31
432 h	4.72	2.60	7.31
456 h	4.72	2.60	7.31
480 h	4.72	2.60	7.31
504 h	4.72	2.60	7.31

002M

Timepoint (hours)	Urine	Feces	cumulative %
8 h	2.49	0.01	2.50
24 h	4.83	2.14	6.97
48 h	5.59	3.94	9.53
72 h	5.85	4.31	10.16
96 h	5.94	4.43	10.37
120 h	5.97	4.49	10.46
144 h	5.99	4.52	10.51
168 h	6.00	4.54	10.54
192 h	6.01	4.55	10.56
216 h	6.01	4.56	10.57
240 h	6.01	4.56	10.58
264 h	6.02	4.57	10.59
288 h	6.02	4.57	10.59
312 h	6.02	4.57	10.59
336 h	6.02	4.57	10.60
360 h	6.02	4.57	10.60
384 h	6.03	4.57	10.60
408 h	6.03	4.57	10.60
432 h	6.03	4.57	10.61
456 h	6.03	4.57	10.61
480 h	6.04	4.57	10.61
504 h	6.04	4.57	10.61

003M

Timepoint (hours)	Urine	Feces	cumulative %
8 h	1.83	0.02	1.86
24 h	3.46	2.79	6.25
48 h	3.76	3.40	7.16
72 h	3.90	3.60	7.50
96 h	3.98	3.67	7.65
120 h	4.01	3.75	7.76
144 h	4.02	3.78	7.80
168 h	4.02	3.79	7.81
192 h	4.03	3.80	7.83
216 h	4.03	3.80	7.83
240 h	4.03	3.80	7.84
264 h	4.03	3.80	7.84
288 h	4.03	3.80	7.84
312 h	4.04	3.80	7.84
336 h	4.04	3.80	7.84
360 h	4.04	3.80	7.84
384 h	4.04	3.80	7.84
408 h	4.04	3.80	7.84
432 h	4.04	3.80	7.84
456 h	4.04	3.80	7.84
480 h	4.04	3.80	7.85
504 h	4.04	3.80	7.85

004M

Timepoint (hours)	Urine	Feces	cumulative %
8 h	2.05	0.03	2.09
24 h	3.52	1.87	5.39
48 h	4.10	2.37	6.47
72 h	4.27	2.57	6.83
96 h	4.36	2.64	7.00
120 h	4.39	2.67	7.06
144 h	4.42	2.69	7.11
168 h	4.43	2.71	7.14
192 h	4.43	2.72	7.15
216 h	4.44	2.72	7.15
240 h	4.44	2.72	7.16
264 h	4.44	2.72	7.16
288 h	4.44	2.72	7.16
312 h	4.44	2.72	7.16
336 h	4.45	2.72	7.16
360 h	4.45	2.72	7.17
384 h	4.45	2.72	7.17
408 h	4.45	2.72	7.17
432 h	4.45	2.72	7.17
456 h	4.45	2.72	7.17
480 h	4.45	2.72	7.17
504 h	4.45	2.72	7.17

Timepoint (hours)	Mean	SD
8 h	2.031	0.352
24 h	5.760	1.097
48 h	7.329	1.525
72 h	7.841	1.577
96 h	8.025	1.590
120 h	8.114	1.590
144 h	8.163	1.592
168 h	8.191	1.594
192 h	8.203	1.596
216 h	8.211	1.598
240 h	8.216	1.601
264 h	8.220	1.604
288 h	8.223	1.606
312 h	8.224	1.606
336 h	8.227	1.605
360 h	8.229	1.605
384 h	8.230	1.605
408 h	8.231	1.607
432 h	8.232	1.608
456 h	8.234	1.609
480 h	8.234	1.609
504 h	8.235	1.609

Study Title

AWPA P1-P13 Creosote:
In Vitro Kinetics in Rat and Human Skin

TEST GUIDELINES: OECD Guideline for the Testing of Chemicals. Guideline 428: Skin Absorption: in vitro 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).

MAFF Japan, Agricultural Chemicals Laws and Regulations, Japan (II), (59 Nousan Number 4200) (1985).

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

STUDY COMPLETED ON: April 30, 2007

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
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LABORATORY PROJECT ID: DuPont-21647

WORK REQUEST NUMBER: 16308

SERVICE CODE NUMBER: 1377

SPONSOR: The Creosote Council III
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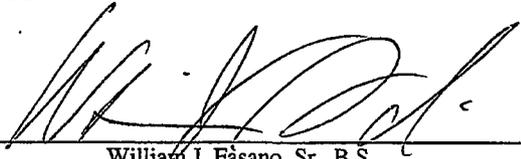
GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

This study was conducted in compliance with U.S. EPA FIFRA (40 CFR part 160) Good Laboratory Practice Standards, which are compatible with current OECD and MAFF (Japan) Good Laboratory Practices, except for the item documented below. The item listed did not impact the validity of the study.

- The chemical and radiochemical concentration and the radiochemical purity of the selected chemicals, which were spiked into the creosote test substance, were based on the certificates of analyses provided by the sponsor and vendors and the verified radioactivity per volume.

Applicant/Sponsor The Creosote Council III
P.O. Box 160
Valencia, Pennsylvania 16059
U.S.A.

Study Director:



William J. Fasano, Sr., B.S.
Senior Research Toxicologist

30-APR-2007

Date

Applicant/Sponsor:



Applicant/Sponsor Representative

4-25-07

Date

QUALITY ASSURANCE STATEMENT

Work Request Number: 16308
Study Code Number: 1377

<i>Phase Audited</i>	<i>Audit Dates</i>	<i>Date Reported to Study Director</i>	<i>Date Reported to Management</i>
Protocol:	January 15, 2007	January 15, 2007	January 17, 2007
Conduct:	January 17, 2007	January 17, 2007	January 17, 2007
Report/Records:	April 4, 2007	April 4, 2007	April 11, 2007

Reported by: Pauline N. Weiner for JCH 30-APR-2007
Joseph C. Hamilton
Quality Assurance Auditor
Date

CERTIFICATION

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

Reviewed and Approved by:  26-Apr-2007
John C. O'Connor, M.S. Date
Research Manager

Issued by Study Director:  30-APR-2007
William J. Fasano, Sr., B.S. Date
Senior Research Toxicologist

This report is approved by the sponsor.

Approved by:  4/25/07
John H. Butala Date
Sponsor Representative

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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: January 11, 2007 / (see report cover page)

Experimental Start/Termination: January 18, 2007 / January 19, 2007

SUMMARY

The dermal penetration and absorption of AWPA P1-P13 creosote has been measured for rat and human skin using an in vitro static diffusion cell model. The creosote test substance was spiked with selected radiolabeled chemicals and applied at a rate of 10 $\mu\text{L}/\text{cm}^2$ to 6 skin replicates per species. The applied test substance remained in contact with the skins for 8 hours, and over the course the exposure, serial receptor fluid samples were taken and analyzed for total radioactivity to determine the rate and extent of penetration. At the end of the 8 hour exposure, the skin surface was washed to remove excess creosote and then tape-stripped to remove the stratum corneum. Distribution and recovery of the applied material was determined.

- Over the course of the 8-hour exposure period, radioactivity penetrated through rat skin approximately 4.3-times faster ($85.3 \mu\text{g equiv}/\text{cm}^2/\text{h}$) than through human skin ($19.7 \mu\text{g equiv}/\text{cm}^2/\text{h}$).
- Total penetration of radioactivity at the end of the exposure was 4.4-fold greater for rat skin ($665.8 \mu\text{g equiv}/\text{cm}^2$) than for human skin ($149.7 \mu\text{g equiv}/\text{cm}^2$).
- Washing of the skin at the end of the exposure removed 12.8% and 70.3% of the applied creosote test substance from rat and human skin, respectively, which reflected the greater rate and extent of total penetration for rat skin.
- A significant portion of the unabsorbed dose for rat skin (44%) had penetrated into the stratum corneum (23.6%); a minor portion of the unabsorbed dose for human skin (79.7%) was contained in the stratum corneum (5.33%).
- The total absorbable dose, receptor fluid plus any dose remaining in the tape-stripped skin, was 34.3% and 4.24% for rat and human skin, respectively.

Overall, the results confirm that creosote penetrated through rat skin at a faster rate and to a greater extent than for human skin, and that the total absorbable dose was 8-fold greater for rat skin than for human skin.

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 is designed to determine the penetration kinetics and the distribution of creosote, spiked with selected radiolabeled chemicals found in the test substance, in rat and human skin following a single, finite application of creosote over an 8-hour exposure period.

MATERIALS AND METHODS

A. Test Guidelines

The study design complied with the following test guidelines:

- OECD Guideline for the Testing of Chemicals. Guideline 428: Skin Absorption: in vitro 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).
- MAFF Japan, Agricultural Chemicals Laws and Regulations, Japan (II), (59 Nousan Number 4200) (1985).

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 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 - ¹⁴ C	22705-130	252	26.6	105.6
2-methynaphthalene - 8 - ¹⁴ C	22705-131	142	8.5	59.9
Fluoranthene - 3 - ¹⁴ C	22705-132	202	45	222.8
Anthracene - 1,2,3,4,4A,9A- ¹⁴ C	22705-133	178	20.6	115.7
Naphthalene - Benzene - UL - ¹⁴ C	22705-134	128	31.3	244.5
Phenanthrene - 9 - ¹⁴ C	22705-135	178	8.2	46.1
Biphenyl - UL - ¹⁴ C	22705-136	154	7.6	49.4
Pyrene - 4,5,9,10 - ¹⁴ C	22705-137	202	55	272.3

C. Test System

1. Justification for Selection of Test System

Dermal contact is a potential route of human exposure.

The rat was the species of choice for use in the in vitro test system as this species has been used in toxicological evaluations of creosote. Human skin was the comparative species of choice in order to aid in the extrapolation of in vitro data to the human in vivo situation.

In vitro dermal techniques employing glass (static) diffusion cells (Figure 1) have been shown to predict percutaneous absorption of various chemicals in vivo.⁽¹⁻²⁾

2. Rat Skin

Skin harvested from young adult male rats of the Sprague-Dawley strain, Crl:CD(SD), approximately 6-8 weeks of age were utilized in this comparative study. Rats were supplied by Charles River Laboratories, Inc. (Raleigh, NC). Following a required quarantine period, rats were removed from stock and uniquely identified by tail markings. Rats were sacrificed by carbon dioxide asphyxiation and the fur from the dorsal region carefully shaved using clippers. Any animals showing obvious abrasion within the region of the test skin area were considered unsuitable and discarded. The shaved area was excised, placed on an aluminum pan with the ID written on the pan, held briefly on wet ice, and then frozen at approximately -20°C until prepared for use. Skin specimens were identified using the Haskell animal number.

3. Human Skin

Samples of human cadaver skin from the National Disease Research Interchange (NDRI, Philadelphia, PA), were stored frozen at approximately -20°C until prepared for use. The source and identity of the skin sample (sex, anatomical locale, and approximate age of donor) was documented in the study records. Skin specimens selected for use were identified using a unique code (e.g., HCFA-26A = Human, Caucasian, Female, Abdomen sample 26-A).

D. Dose Groups

This study was composed of the following dose groups and target parameters.

Species	Group	Creosote Concentration ($\mu\text{g total creosote/mL}$) ^a	Volume of Creosote Applied to the Skin (μL)	Skin Dose Level ($\mu\text{g creosote/cm}^2$) ^b	Number of Skin Preparations ^a	$\mu\text{Ci/skin}$
Rat	A	1,070,000	6.4	10,700	6	1.0
Human	B	1,070,000	6.4	10,700	6	1.0

^a Based on a density of 1.07 g total creosote/mL

^b Exposure area 0.64 cm²

E. Preparation of Skin Membranes

Samples of rat and human skin that were stored frozen were allowed to thaw at room temperature. Full thickness skin was dermatomed to approximately 450 μm using a Padgett Electro Dermatome[®] (Padgett Instruments, Inc., Kansas City, MO). The skin sample was then placed onto an aluminum pan, with its code embossed or written on the pan, and stored refrigerated at 1-10°C until readied for use.

F. In Vitro Diffusion Cells Assembly

Glass [static] diffusion cells (Figure 1) were used in this study. The skin membrane was first mounted, stratum corneum uppermost, onto the top of the receptor chamber, which was filled with receptor fluid (e.g., saline). The donor (top) chamber was then placed over the skin section and clamped in place. The in vitro diffusion cells had an exposure area of 0.64 cm². The receptor fluid was continuously stirred throughout the exposure using a magnetic stir bar.

G. Assessment of Membrane Integrity and Membrane Equilibration

The integrity of each membrane was assessed by measurement of electrical impedance prior to application of test substance.⁽³⁻⁴⁾

Membranes were removed from refrigeration storage and hydrated in 0.9% saline for approximately 15 minutes. Following hydration, the membrane was mounted onto the top of the receptor chamber, which was filled with 0.9% saline. The donor chamber was then clamped in place and filled with 0.9% saline. The membrane was then allowed to equilibrate for approximately 30 minutes. During equilibration, the water-jacketed cells were maintained at approximately 32°C using a re-circulating water bath system. Following equilibration, an impedance measurement of each skin membrane was taken.

Membranes with an impedance of ≥ 6 k Ω (rat) and ≥ 17 k Ω (human) were considered intact and retained for use on study. Membranes not meeting these criteria were replaced, and electrical impedance confirmed following equilibration. This procedure was followed until a minimum of 6 skin preparations represented by at least 3 individuals per species was achieved.

Following electrical impedance measurement, saline in the donor chamber was removed and discarded. Saline in the receptor chamber was reduced to approximately half of the total volume,

and cells with acceptable membranes maintained at approximately 32°C overnight, without occlusion of the donor chamber, prior to dose application. The receptor chamber sampling arm remained occluded with Parafilm[®].

H. In Vitro Percutaneous Absorption of Radiolabeled Creosote

1. Pretreatment Procedures

Following overnight equilibration, the contents of the receptor chamber were removed and discarded and refilled with a 50% (v/v) ethanol in deionized water solution. Prior to application of the formulated test substance, a single 50 µL (pre-treatment background) receptor fluid sample was collected and replaced with an equal volume of fresh receptor fluid.

2. Application of the Formulated Test Substance

The prepared creosote test substance spiked with radiolabeled materials was applied to the skin surface (0.64 cm²), via the donor chamber, as a single application distributed evenly over the exposure area at a rate of 10 µL/cm². Following dosing, the donor chamber opening was occluded with Parafilm[®] for the duration of the exposure period.

3. Dose Determination

The homogeneity of the radioactivity in the creosote test substance and the amount of radioactivity administered to the skin was determined by counting replicate aliquots (mock doses) and using the mean value as the amount of radioactivity applied. The total amount of creosote applied to the skin (expressed in total µg equivalents) was based on the amount of radioactivity applied (mock dose) and the calculated specific activity (0.37 µCi/mg).

4. Exposure Period

The exposure period was 8 hours for all skin preparations.

5. Serial Sampling of Receptor Fluid, Post-Exposure

Following dose application, duplicate 50 µL samples of receptor fluid, were taken from the receptor chambers at 0.5, 1, 2, 4, and 8 hours for all preparations.

Receptor fluid samples were placed directly into liquid scintillation vials. The volume of receptor fluid in the receptor chamber was maintained by the replacement of a volume of fresh receptor fluid, equal to the sample volume, after both duplicate 50 µL samples had been taken. The receptor chamber arm remained occluded with Parafilm[®] at all times other than at sampling.

6. Washing of the Application Skin Site

At end of the 8-hour exposure, the surface of each skin replicate was washed using 3 x 1 mL of a 2% Ivory[®] soap solution, followed by 1 x 1 mL rinse with deionized water. The wash-rinse was collected into a liquid scintillation vial. The donor chamber remained clamped in-place during washing-rinsing procedure.

7. Terminal Procedures

Following washing and rinsing of the skin surface to remove excess creosote test substance, the donor chamber was removed and rinsed with approximately 5 mL of acetonitrile directly into a liquid scintillation vial.

The skin membrane was removed from the receptor chamber and tape-stripped five times to remove the stratum corneum using Leukotape[®] P (BSN Medical, Ltd., Pinetown, South Africa). Each piece of tape was placed into an individual glass vial and extracted with acetonitrile. The remaining skin piece was placed into a glass vial for digestion.

I. Determination of Radioactivity

1. Sample handling and processing

The serial receptor fluid samples, donor chamber rinse, skin wash samples, and tape strips were not processed further. Ultima Gold[™] XR liquid scintillation cocktail was added to each vial and the samples analyzed for total radioactivity.

Each skin piece was digested using Soluene[®]-350. Heating at approximately 60°C accompanied by constant shaking was used to facilitate sample digestion. Hionic-Fluor[™] liquid scintillation cocktail was added to each vial and the samples analyzed for total radioactivity.

2. Liquid Scintillation Counting

Samples were analyzed in a Packard liquid scintillation counter. Samples were counted for 10 minutes or until 160,000 disintegrations are accumulated (0.5%, 2σ), whichever came first.

The limit of detection (LOD) for the analysis of each sample was taken as twice the background disintegration rate obtained from analysis of appropriate blank samples.

J. Statistical Analyses and Data Presentation

Group data is represented as Mean \pm SD. Statistical evaluations was performed using Grubb's outlier test.⁽⁵⁾ Significance was judged at $p \leq 0.05$.

The cumulative amount of [¹⁴C]creosote equivalents detected in the receptor compartment at each serial collection timepoint, and adjusted for total receptor chamber volume, was plotted against time (in hours) to produce an absorption profile.

Total recovery of the applied dose is a sum of the receptor fluid samples, the amount washed and rinsed from the skin, the amount from the donor chamber rinse, the amount in the individual tape strips, and the amount in/on the skin not removed by washing.

RESULTS AND DISCUSSION

A. Verification of Radioactivity

The spiked creosote test substance was verified to be homogeneous by LSC and contained approximately 1.05 μCi per 6.4 μL , 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 that was spiked into the creosote test substance.

B. In Vitro Kinetics in Rat and Human Skin

(Tables 1-2, Figures 2-3, Appendix C)

Key observation of mean data:

- Over the course of the 8-hour exposure period, radioactivity penetrated through rat skin approximately 4.3-times faster ($85.3 \mu\text{g equiv}/\text{cm}^2/\text{h}$) than through human skin ($19.7 \mu\text{g equiv}/\text{cm}^2/\text{h}$).
- Total penetration of radioactivity at the end of the exposure was 4.4-fold greater for rat skin ($665.8 \mu\text{g equiv}/\text{cm}^2$) than for human skin ($149.7 \mu\text{g equiv}/\text{cm}^2$).
- Washing of the skin removed 12.8% and 70.3% of the applied creosote test substance from rat and human skin, respectively, which reflected the greater rate and extent of total penetration for rat skin.
- A significant portion of the unabsorbed dose for rat skin (44%) was contained in the stratum corneum (23.6%); a minor portion of the unabsorbed dose for human skin (79.7%) was contained in the stratum corneum (5.33%).
- The total absorbable dose, receptor fluid plus any dose remaining in the tape-stripped skin, was 8-fold greater for rat skin (34.3%) than for human skin (4.24%).
- Recovery of the applied dose ranged from 78.3% (rat) to 83.9% (human). Although this was outside of the target boundary ($100\% \pm 10\%$), it's plausible that chemical instability and subsequent volatilization from the wash, from the skin section during tape-stripping, and/or from the tape strip sections prior to solvent extraction may have occurred, which has been previously observed in our laboratory for water-insoluble (radiolabeled) chemicals.

CONCLUSIONS

- Over the course of the 8-hour exposure period, radioactivity penetrated through rat skin approximately 4.3-times faster ($85.3 \mu\text{g equiv}/\text{cm}^2/\text{h}$) than through human skin ($19.7 \mu\text{g equiv}/\text{cm}^2/\text{h}$).

- Total penetration of radioactivity at the end of the exposure was 4.4-fold greater for rat skin (665.8 $\mu\text{g equiv}/\text{cm}^2$) than for human skin (149.7 $\mu\text{g equiv}/\text{cm}^2$).
- Washing of the skin at the end of the exposure removed 12.8% and 70.3% of the applied creosote test substance from rat and human skin, respectively, which reflected the greater rate and extent of total penetration for rat skin.
- A significant portion of the unabsorbed dose for rat skin (44%) had penetrated into the stratum corneum (23.6%); a minor portion of the unabsorbed dose for human skin (79.7%) was contained in the stratum corneum (5.33%).
- The total absorbable dose, receptor fluid plus any dose remaining in the tape-stripped skin, was 34.3% and 4.24% for rat and human skin, respectively.

Overall, the results confirm that creosote penetrated through rat skin at a faster rate and to a greater extent than for human skin, and that the total absorbable dose was 8-fold greater for rat skin than for human skin.

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.

REFERENCES

1. Ramsey JD, Woollen BH, Auton TR and Scott RC (1994). The Predictive Accuracy of In Vitro Measurements for Dermal Absorption of a Lipophilic Penetrant (Fluazifop-Butyl) through Rat and Human Skin. *Fundamental and Applied Toxicology* 23, 230-236.
2. Scott RC, Walker M and Dugard PH (1986). A comparison of the in vitro permeability properties of human and some laboratory animal skins. *International Journal of Cosmetic Science* 8, 189-194.
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5. Grubbs, Frank (1969). Procedures for Detecting Outlying Observations in Samples. Technometrics 11, 1-21.

TABLES

TABLES

EXPLANATORY NOTES

ABBREVIATIONS:

Hr, hr, or h	hour(s)
SD	standard deviation

Table 1: Penetration kinetics of [¹⁴C]creosote, 0-8 hours (0-hour post-exposure group)

Data expressed in cumulative $\mu\text{g equiv/cm}^2$				
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 (end exposure)	665.8	161.0	149.7	45.7
Penetration rate, 0.5-8 h ^a ($\mu\text{g equiv/cm}^2/\text{h}$)	85.3		19.7	

^a Slope of mean data, 0.5-8 hours

Table 2: Recovery of total radioactivity at 8 hours following a 8-hour topical exposure to creosote (0-hour post-exposure group)

	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

FIGURES

EXPLANATORY NOTES

ABBREVIATIONS:

equiv equivalent

Figure 1: Static diffusion cell

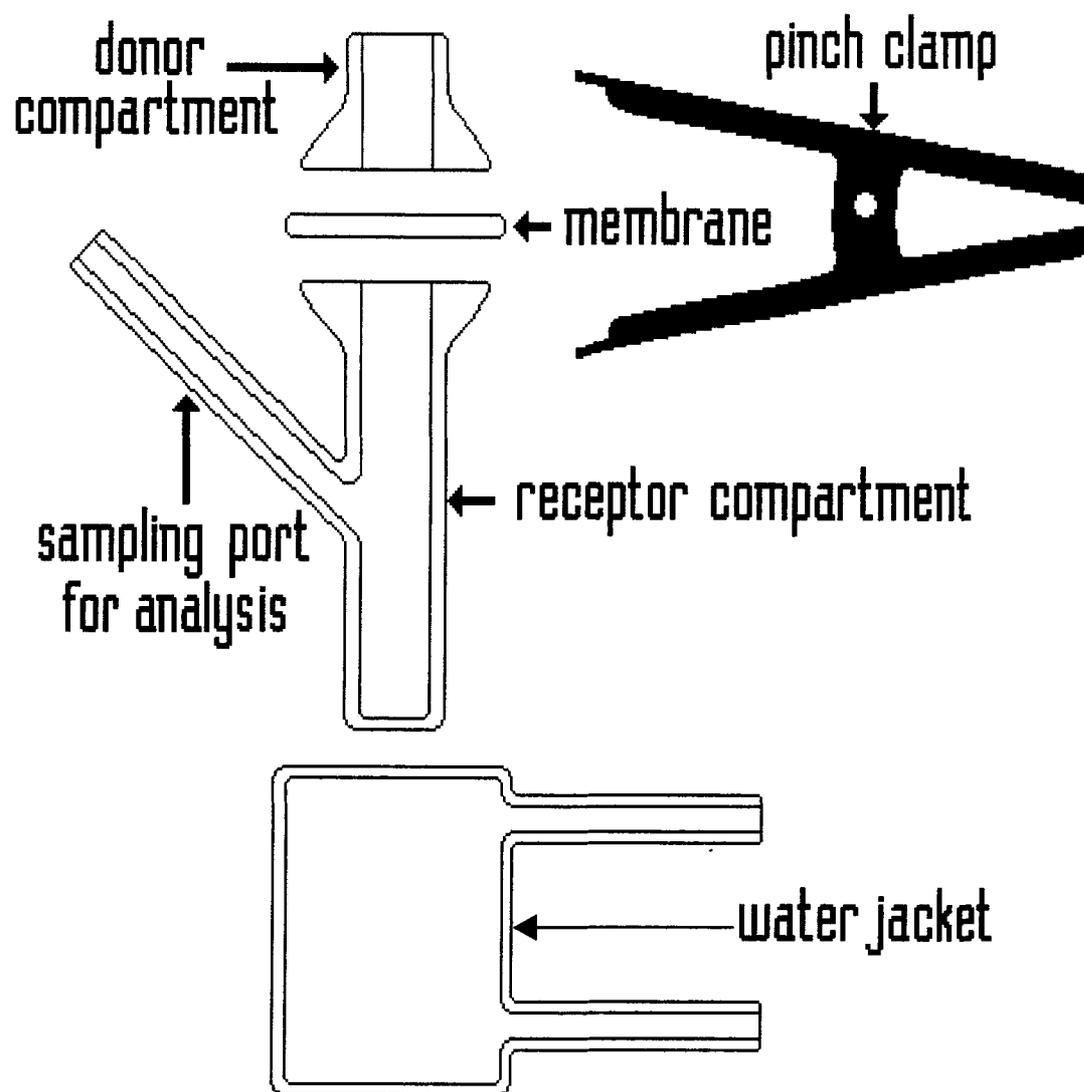


Figure 2: Penetration kinetics of [^{14}C]creosote, 0 8 hours

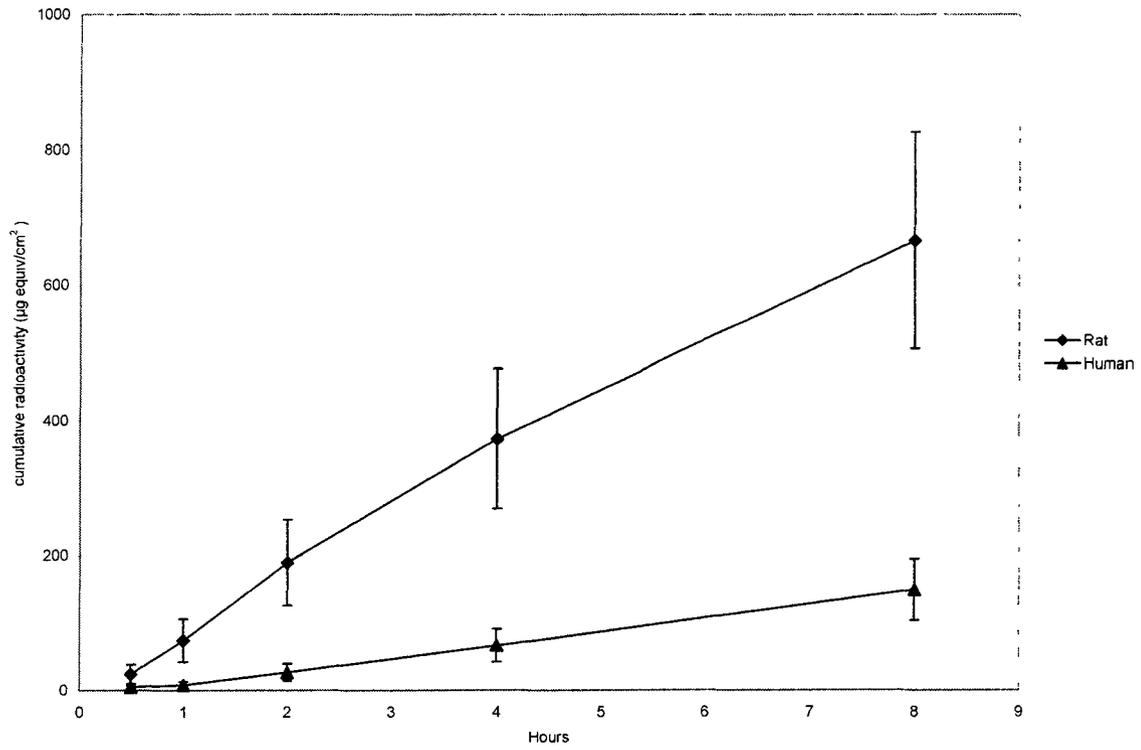
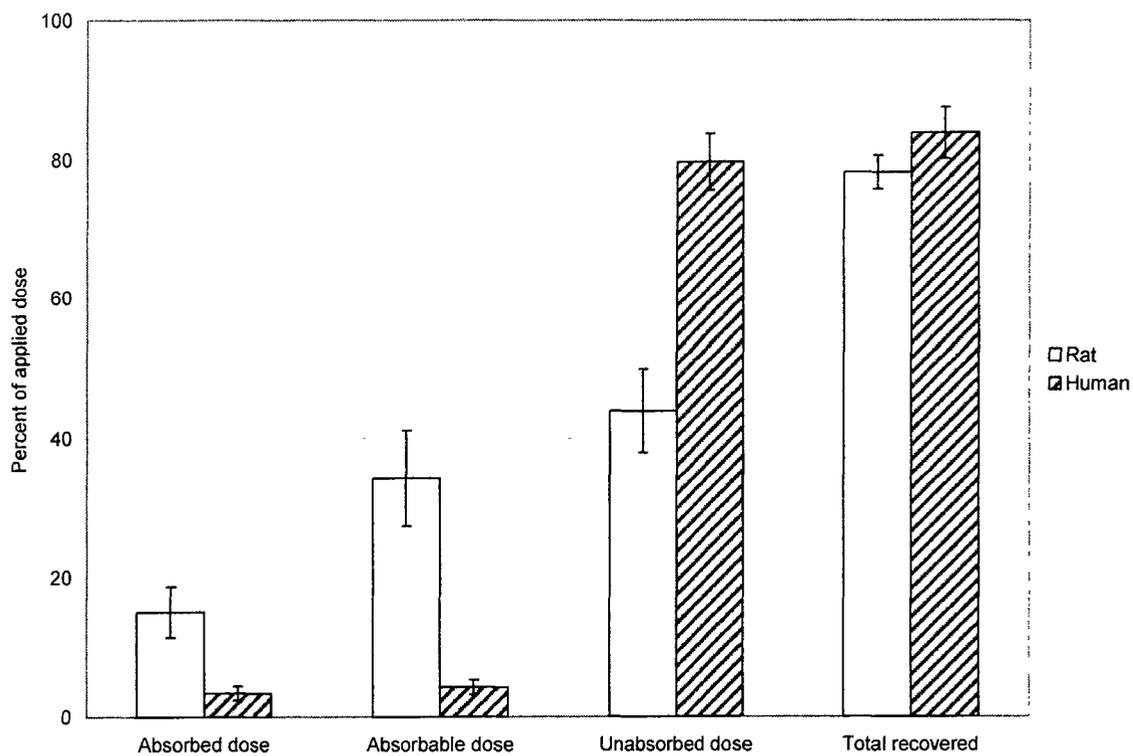


Figure 3: Recovery of total radioactivity at 8 hours following a 8 hour topical exposure to creosote



APPENDICES

APPENDICES

EXPLANATORY NOTES

ABBREVIATIONS:

equiv	equivalent
Hr, hr, or h	hour(s)
NA	not applicable
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/encl: 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

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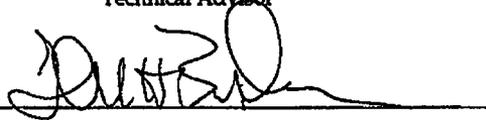
STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

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

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GOOD LABORATORY PRACTICE STATEMENT

This study meets the requirements of 40 CFR Part 160.

Submitter: J. H. Butala Date: 3-1-99

Sponsor: CREOSOTE Council II Date: 3-1-99

Study Director: Cliff Juman Date: 2-17-99

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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
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The study was conducted at:

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

The Study Director was:

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10.0 APPENDIX 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 CTM 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.

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 2.81.

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 $\mu\text{g/mL}$, 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 μg requires division by $1,000,000$, and to convert from μg 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 5.0
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.

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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.

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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, 5th Ed., John Wiley and Sons, New York, 1989.

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SECTION 8.0
TABLES

North American P1/P13
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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

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Table 2. Components Identified by GC/MS in North American P1/P13 Creosote

Ref. Std. ^A	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889-2C ^B	8889-2D ^B	8889-2F ^B		
	Toluene	NE	NE	<0.1	NC	NA
	Ethylbenzene	<0.1	<0.1	<0.1	<0.1	NA
	p-Xylene + Styrene	NE	NE	<0.1	NC	NA
	Phenol	<0.1	<0.1	<0.1	<0.1	NA
	2,3-Benzofuran + 1,2,4-Trimethylbenzene	0.1	0.1	0.1	0.1	0
	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
	1,2,3,4-Tetrahydrophthalene (int. Std)					
	Naphthalene	9.0	9.0	9.0	9.0	0
	Benzofluorene	0.5	0.5	0.5	0.5	0
	Quinoline	0.6	0.6	0.6	0.6	0
	Isoquinoline	0.3	0.2	0.2	0.2	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	7.5	7.3	7.3	7.3	6.6
	6-Methylquinoline	<0.1	<0.1	<0.1	<0.1	NA
	4-Methylquinoline	<0.1	<0.1	<0.1	<0.1	NA
	1,1'-Bi-phenyl	1.3	1.2	1.2	1.2	4.9
	1-Methylnaphthalene	0.5	0.5	0.5	0.5	0
	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	0.3	0.3	0.3	0.3	0
	Dimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Acenaphthene	6.4	5.9	5.9	6.1	6.7
	1-Naphthalenecarbonitrile	0.2	0.2	0.2	0.2	0
	2-Methylbiphenyl	0.1	0.1	<0.1	0.1	0
	Isopropylnaphthalene (isomer) + n-Pentadecane	<0.1	<0.1	<0.1	<0.1	NA
	C ₁₅ H ₁₂ (isomer)	0.3	0.3	0.3	0.3	0
	Dibenzofuran	3.2	3	3	3.1	3.7
	Naphthalenecarbonitrile (isomer)	NE	<0.1	0.1	NC	NA
	Trimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Trimethylnaphthalene (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Trimethylnaphthalene (isomer)	0.1	<0.1	<0.1	<0.1	NA
	Trimethylnaphthalene (isomer)	0.1	<0.1	<0.1	<0.1	NA
	2,3,5-Trimethylnaphthalene	<0.1	<0.1	<0.1	<0.1	NA

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Table 2. (continued)

Ref. Std. ^a	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889- 2C ^b	8889- 2D ^b	8889- 2F ^b		
	Methylacenaphthylene (monomer)	<0.1	NF	NF	NC	NA
■	9H-Fluorene	4.5	4.0	4.2	4.2	6.0
■	Allynaphthalene (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-Methylbenzofuran	0.5	0.4	0.4	0.4	14
	Diphenylmethane	<0.1	<0.1	<0.1	<0.1	NA
	Methylbenzofuran (isomer)	0.7	0.6	0.7	0.7	8.7
	Methylbenzofuran (isomer)	<0.1	<0.1	<0.1	<0.1	NA
■	9,10-Dihydroanthracene	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
	C ₁₀ H ₈ (isomer)	0.7	0.6	0.6	0.6	5.8
	C ₁₀ H ₈ (isomer)	<0.1	NF	NF	NC	NA
	C ₁₀ H ₈ (isomer)	<0.1	<0.1	<0.1	<0.1	NA
	Dibenzofuran	1.4	1.2	1.1	1.3	8.9
	Phenanthrene	12.5	11.7	12.0	12.2	4.7
■	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
	Methylbenzothiophene (isomer)	0.3	0.2	0.2	0.2	29
■	1-Phenylaphthalene	0.2	0.2	0.2	0.2	0
	Dibenzo-p-dioxin (C ₁₂)	0.1	<0.1	<0.1	<0.1	NA
	Methylbenzothiophene (isomer)	0.1	0.1	<0.1	<0.1	NA
	Methylphenanthrene (isomer)	0.2	0.6	0.7	0.7	6.2
■	2-Methylphenanthrene	0.9	0.7	0.8	0.8	12
■	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-Phenylphenanthrene	0.6	0.5	0.5	0.5	12
	9H-Fluorene-carbazole	<0.1	NF	<0.1	NC	NA
	Ethylanthracene (isomer)	NF	<0.1	NF	NC	NA
	Ethylanthracene or dimethylphenanthrene (isomer)	0.1	0.1	0.1	0.1	0
	Dimethylphenanthrene (isomer)	<0.1	<0.1	<0.1	<0.1	NA

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Table 2. (continued)

Ref. Std.*	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889- 2C*	8889- 2D*	8889- 2F*		
	Dimethylphenanthrene (isomer)	<0.1	<0.1	<0.1	0.3	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-Anthracene carbonitrile	<0.1	<0.1	<0.1	NA	NA
	Benzyl naphthalene + C ₁₀ H ₁₀ (isomers)	<0.1	<0.1	<0.1	NA	NA
	C ₁₂ H ₈ (isomer)	0.2	0.2	0.2	0.2	19
	Azanthracene (isomer)	NE	0.1	0.1	NC	NA
■	Pyrene	6.3	5.6	5.8	6.0	4.1
	Vinylanthracene (isomer)	0.3	0.2	0.2	0.3	19
	Benzonaphthofuran (isomer)	0.1	0.1	0.1	0.1	0
	Benzonaphthofuran (isomer) + Azapyrene	0.7	0.5	0.6	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
	Pyrolocarbazole or 9H-fluorene carbonitrile	0.3	0.3	0.3	0.3	0
	Benzofluorene (isomer)	0.3	0.2	0.3	0.3	19
■	Benzo[a]fluorene	1.0	0.9	0.9	0.9	6.1
■	2,3-Benzofluorene	1.2	1.1	1.1	1.1	5.2
	Methylpyrene (isomer)	0.3	0.3	0.3	0.3	0
	Phenylmethyl naphthalene (isomer)	0.5	0.4	0.5	0.5	12
	Methylpyrene (isomer)	0.4	0.3	0.4	0.4	14
	Methylpyrene or benzofluorene (isomer)	0.2	0.2	0.2	0.2	0
	Methylpyrene (isomer)	NE	<0.1	NE	NC	NA
	5,12-Dihydronaphthacene	0.3	0.3	0.3	0.3	0
	Dimethylpyrene (isomer)	0.1	0.1	0.1	0.1	0
	o-Terphenyl	0.3	0.2	0.2	0.2	29
	Dimethylpyrene (isomer)	0.3	0.3	0.3	0.3	0
	Dimethylpyrene (isomer)	<0.1	<0.1	NE	NE	NA
■	1,2-Benzodiphenylene sulfide	0.2	0.3	0.3	0.3	19
	Acapyrene	0.5	0.5	0.5	0.5	0
	Benzo[c]acridine	0.3	0.3	0.3	0.3	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
	Methylbenz[a]anthracene (isomer)	<0.1	<0.1	0.1	<0.1	NA
	Benzo[carbazole (isomer)	0.3	0.1	0.1	0.1	0
	C ₁₂ H ₈ N (isomer)	0.2	0.2	0.2	0.2	0.5
	C ₁₂ H ₈ N (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

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Table 2. (continued)

Ref. Std. ^a	Identified Components	Found Concentration (weight percent)			Mean	%RSD
		8889- 2C ^b	8889- 2D ^b	8889- 2F ^b		
	Methanochrysen ^c or 2,8-bis formyl dibenzothiophene (isomer)	0.1	0.1	0.1	0.1	0
	Methanochrysen ^c or 2,8-bis formyl dibenzothiophene (isomer)	0.1	NF	0.1	NC	NA
	Methanochrysen ^c or 2,8-bis formyl dibenzothiophene (isomer)	0.2	0.2	0.2	0.2	0
	Methylichrysen ^c (isomer)	NF	NF	<0.1	NC	NA
■	Benzo(b)fluoranthene	0.4	0.4	0.4	0.4	0
■	Benzo(k)fluoranthene	0.1	0.3	0.3	0.3	0
■	C ₂₁ H ₁₂ (isomer)	0.2	0.2	0.2	0.2	0
■	Unknown	0.2	0.2	0.2	0.2	79
■	Benzo(e)pyrene	0.4	0.4	0.4	0.4	0
■	Benzo(a)pyrene	0.5	0.4	0.5	0.5	12
■	Perylene	0.1	0.1	0.1	0.1	0
■	C ₂₁ H ₁₄ (isomer)	NF	NF	<0.1	NC	NA
■	Indeno(1,2,3-cd)pyrene	0.2	0.1	0.1	0.1	58
■	C ₂₁ H ₁₆ S ₂ (isomer) (tent)	0.2	0.2	0.2	0.2	0
■	Benzo(g)hperylene	0.1	<0.1	0.1	<0.1	0
■	C ₂₁ H ₁₆ (isomer)	NF	NF	<0.1	NC	NA

^aAuthentic material used where indicated (■).

^bSee Table 1 for additional sample information.

^cNF = Not Found.

^dNC = Not Calculated.

^eNA = Not Applicable.

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SECTION 9.0

FIGURES

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

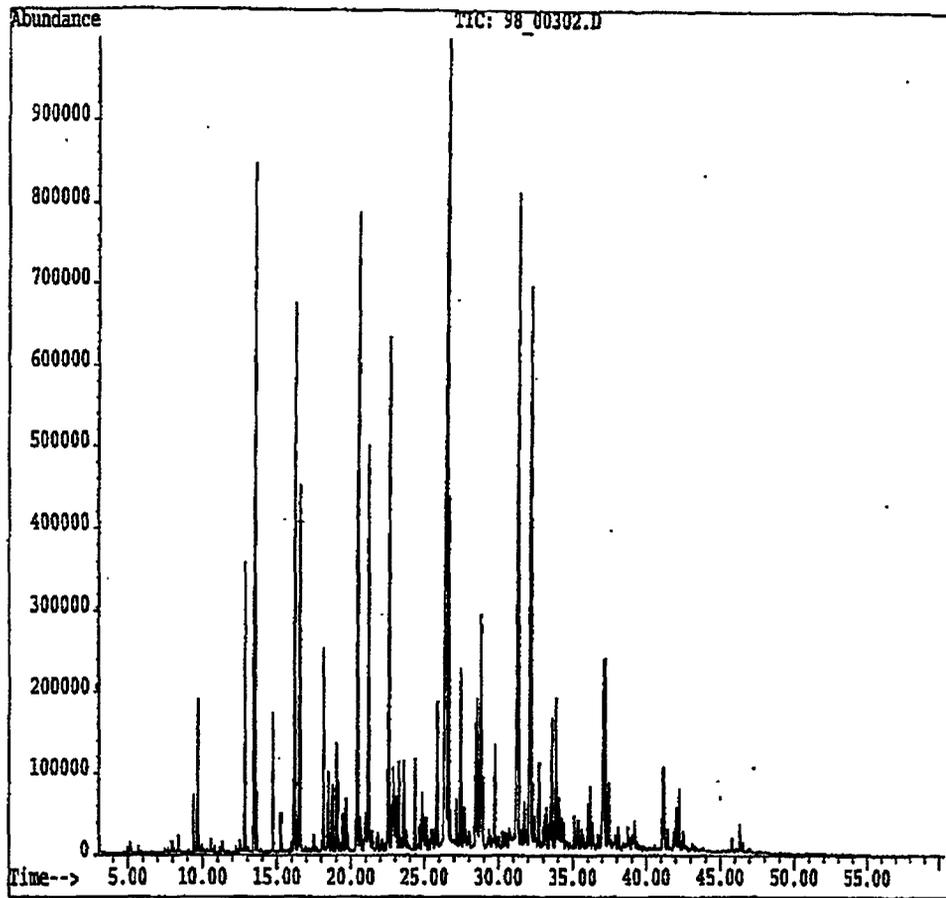


Figure 1. Reconstructed ion chromatogram of North American Composite sample 8889-2C

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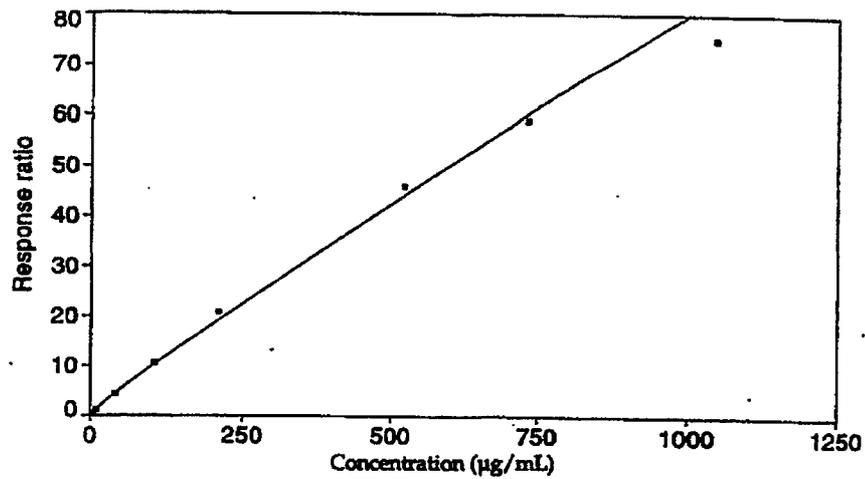


Figure 2. Naphthalene Calibration Curve
Weighted (1/x) Regression Equation: $\ln y = -1.931 + 0.9139 \ln x$
Correlation Coefficient (r) = 0.99998

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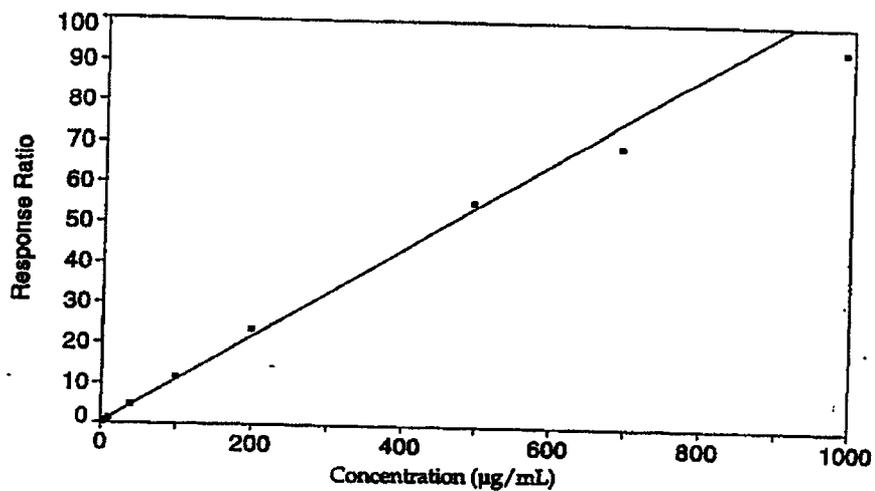


Figure 3. Phenanthrene Calibration Curve
Weighted (1/x) Regression Equation: $\ln y = -2.166 + 0.9925 \ln x$
Correlation Coefficient (r) = 0.99998

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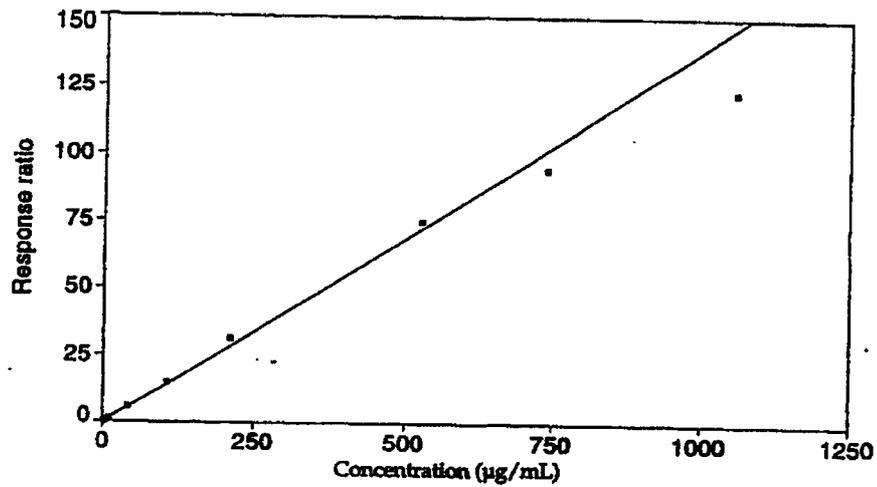


Figure 4. Pyrene Calibration Curve
Weighted (1/x) Regression Equation: $\ln y = -2.130 + 1.022 \ln x$
Correlation Coefficient (r) = 0.99990

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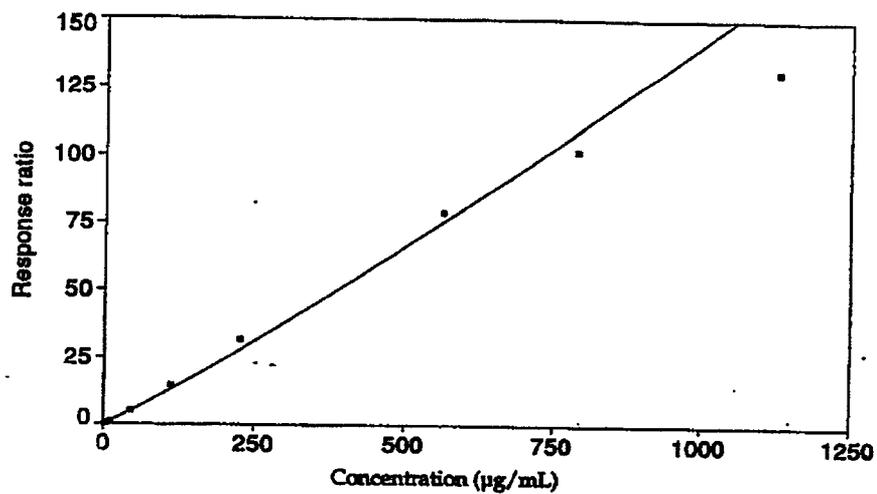


Figure 5. Chrysene Calibration Curve
Weighted (1/x) Regression Equation: $\ln y = -2.580 + 1.090 \ln x$
Correlation Coefficient (r) = 0.9980

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SECTION 10.0

APPENDIX

Appendix B:
Radiolabeled Test Substance Information



11542 Fort Mims Dr.
Saint Louis, Missouri 63146 USA
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Fax (314) 569-0682
www.sigma-aldrich.com

Product Information

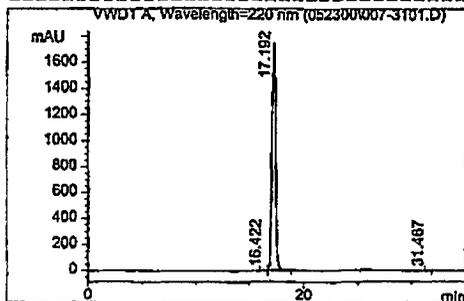
PROD NAME: 2-METHYLNAPHTHALENE-8-14C
LOT NUMBER: 050K9424/25
PROD NUMBER: M6146-14C
ANALYST: 027BD
DATE: 5/24/00 9:57:19 AM Inj Volume: 0.10ul

*****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
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: 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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email: techservice@sigma.com
sigma-aldrich.com

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

Product Information

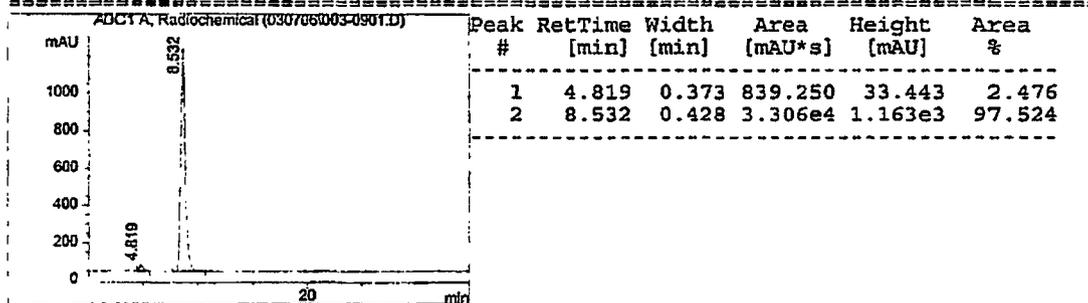
Inj Volume: 1.00ul

*****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





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email: techservice@sls.com
sigma-aldrich.com

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

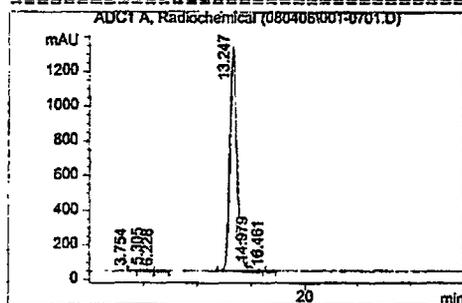
Inj Volume: 3.00ul

*****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/μmol 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	1.746e3	30.048	2.671
6	16.461	0.489	317.751	8.411	0.486



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Product Information

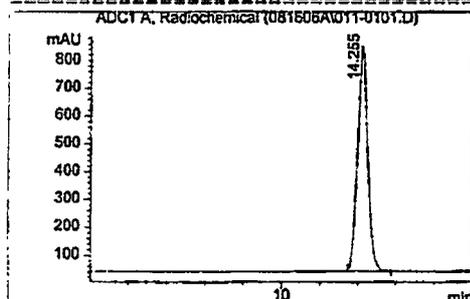
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LOT NUMBER: 115F9247
PROD NUMBER: B5892-14C
ANALYST: Quality Control
DATE: 8/16/06 2:04:10 PM Inj Volume: 1.00ul

*****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

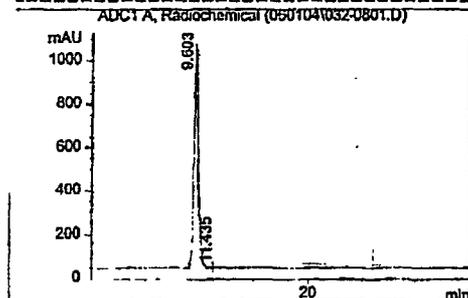
ROD NAME: FLUORANTHENE-3-14C
LOT NUMBER: 054K9630
ROD NUMBER: F6147-14C
ANALYST: Quality Control
DATE: 6/1/04 9:18:17 PM Inj Volume: 7.00ul

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

column: Supelco Discovery HS C18, 250 x 2.1 mm, 5um
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

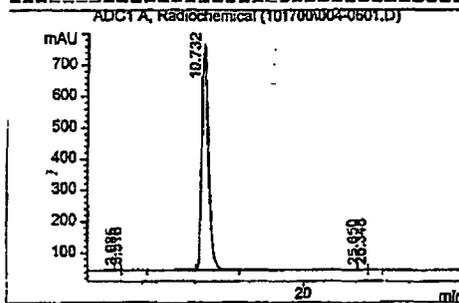
PROD NAME: NAPHTHLENE-BENZENE-UL-14C
LOT NUMBER: 068H9600/01
PROD NUMBER: N3145-14C
ANALYST: 027BD
DATE: 10/17/00 7:44:35 PM Inj Volume: 1.50ul

*****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 : 51.3 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

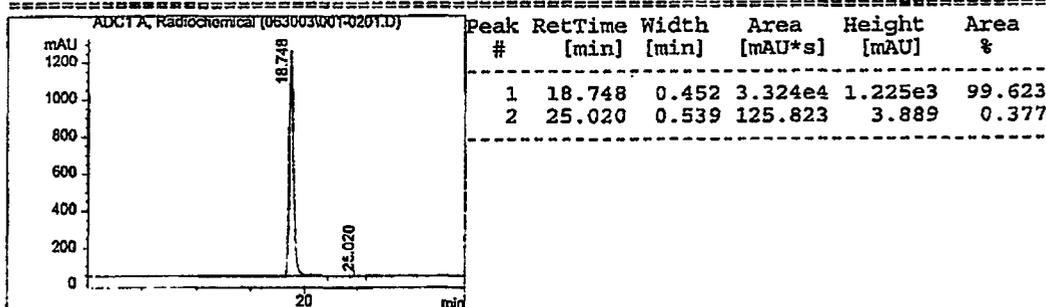
PROD NAME: PHENANTHRENE-9-14C
LOT NUMBER: 111K9412/13
PROD NUMBER: P0785-14C
ANALYST: Quality Control
DATE: 6/30/03 3:42:26 PM Inj Volume: 1.50ul

*****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



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Product Information

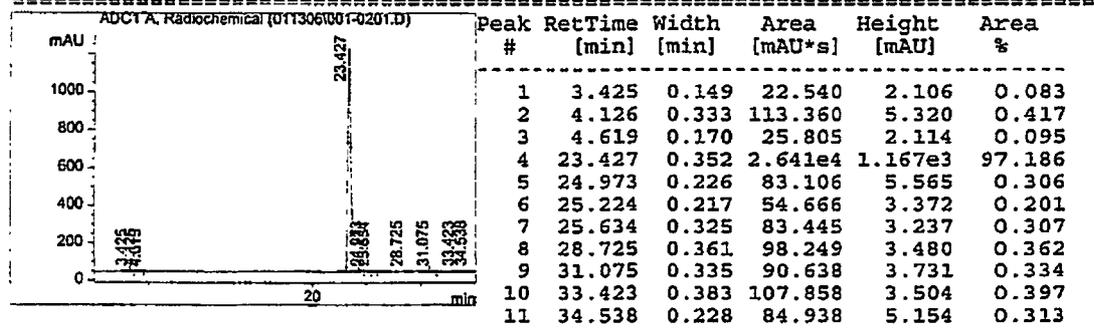
PROD NAME: PYRENE-4,5,9,10-14C
LOT NUMBER: 079H9662/63
PROD NUMBER: P6805-14C
ANALYST: Quality Control
DATE: 1/13/06 2:03:13 PM Inj Volume: 1.00ul

*****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



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6

Appendix C:

Dose Determination, Replicate Aliquots of Creosote

AWPA P1-P13 Creosote:
In Vitro Kinetics in Rat and Human Skin

DuPont-21647

Replicate	Aliquot (μL)	Dilution (mL)	Aliquot (mL)	Radioactivity in aliquot (dpm)	Radioactivity in aliquot (dpm) - background
1	6.4	10	0.1	22768	22739
				23495	23466
				23633	23604
2	6.4	10	0.1	22962	22933
				23461	23432
				23527	23498
3	6.4	10	0.1	22922	22893
				23371	23342
				23418	23389
Background sample					29
Sum (dpm)					209296
Average (dpm)					23255
Amount in mock (dpm)					2325511

A - Radioactivity applied (dpm)	2325511	
B - Radioactivity applied (μCi)	1.05	(=A/2.22 x 10 ⁶ dpm/μCi)
C - Verified specific activity (μCi/mg)	0.37	
D - Specific activity (dpm/μg)	821	(=[C*2.22 x 10 ⁶ dpm/μCi]/1000 μg/mg)
E - Total compound applied (μg)	2831.2	(=A/D)
F - Application rate (μg/cm ²)	4423.7	(=E/0.64 cm ²)

Appendix D:
Penetration and Recovery Data

Rat, Summary Penetration Data, 0 Hours Post-Exposure

Cumulative amount absorbed ($\mu\text{g equiv/cm}^2$)

Cell ID	Time after dosing (hr)				
	0.5	1	2	4	8
A	14.2	64.1	193.8	391.8	696.2
B	5.02	24.4	99.2	252.8	476.2
C	30.8	97.6	247.1	476.8	868.0
D	25.0	76.2	190.4	368.6	641.6
E	22.9	64.5	140.5	257.6	496.7
F	46.1	117.2	268.5	493.7	816.1
MEAN	24.0	74.0	189.9	373.6	665.8
SD	14.1	31.9	63.4	103.4	161.0

Human, Summary Penetration Data, 0 Hours Post-Exposure

Cumulative amount absorbed ($\mu\text{g equiv/cm}^2$)

Cell ID	Time after dosing (hr)				
	0.5	1	2	4	8
G	3.23	11.0	25.7	61.5	128.5
H	5.14	11.3	35.3	80.7	177.7
I	NA	4.27	16.4	47.6	128.2
J	NA	4.38	14.5	38.3	85.4
K	6.94	14.8	47.6	106.9	216.3
L	NA	4.57	22.8	66.6	162.4
MEAN	5.11	8.38	27.1	66.9	149.7
SD	1.85	4.56	12.5	24.6	45.7

Rat. Recovery Data (percent of applied dose)

Cell ID	Receptor Fluid	Skin Washes	Donor Chamber	Tape-Stripped Skin
A	15.7	13.3	4.18	28.4
B	10.8	14.5	6.34	25.5
C	19.6	16.2	8.33	15.2
D	14.5	10.8	10.2	9.62
E	11.2	10.1	10.2	18.3
F	18.4	11.9	5.94	18.5
MEAN	15.1	12.8	7.52	19.2
SD	3.64	2.33	2.44	6.82

Cell ID	Tape Strips	Total Unabsorbed	Total Absorbable	Total Recovery
A	17.3	34.7	44.1	78.9
B	21.1	41.9	36.2	78.1
C	22.9	47.5	34.8	82.3
D	29.7	50.6	24.1	74.8
E	28.2	48.5	29.5	78.0
F	22.6	40.5	36.9	77.4
MEAN	23.6	44.0	34.3	78.3
SD	4.60	5.98	6.84	2.44

Human, Recovery Data (percent of applied dose)

Cell ID	Receptor fluid	Skin Washes	Donor Chamber	Tape-Stripped Skin
G	2.90	58.2	6.57	0.75
H	4.02	75.0	3.14	0.66
I	2.90	73.2	1.77	0.56
J	1.93	74.8	1.25	0.99
K	4.89	63.7	1.92	0.89
L	3.67	76.8	1.39	1.29
MEAN	3.38	70.3	1.89	0.86
SD	1.03	7.52	0.75	0.26

Cell ID	Tape Strips	Total Unabsorbed	Total Absorbable	Total Recovery
G	13.7	78.5	3.65	82.2
H	4.08	82.2	4.67	86.9
I	6.30	81.3	3.46	84.7
J	5.00	81.1	2.92	84.0
K	6.36	72.0	5.78	77.8
L	4.89	83.1	4.96	88.1
MEAN	5.33	79.7	4.24	83.9
SD	0.98	4.08	1.07	3.68

Note: **Bolded** values are excluded from Mean and SD as outliers by Grubb's Test