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Re: For Your Information Submission:

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

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Listed Chemical Substance:

540-97-6 Dodecamethylcyclohexasiloxane (DDMCHS, D_6)

Final Study Report:

In Vitro Dermal Absorption of ^{14}C- Dodecamethylcyclohexasiloxane (D_6) in Human Skin

Dow Corning Corporation
2002-I0000-51728
January 15, 2003

Dow Corning Corporation
Midland, Michigan 48686-0994
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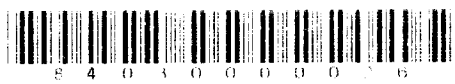

Manufacturer:

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For purposes of this TSCA For-Your-Information (FYI) submission, the general INTERNAL designation on the attached health and safety report is waived by Dow Corning.

If you require further information regarding this submission, please contact Michael Thelen, Manager of U.S. EPA Regulatory Affairs, at 989-496-4168 or at the address provided herein.

Sincerely,

Kathleen P. Plotzke
Director, Health and Environmental Sciences
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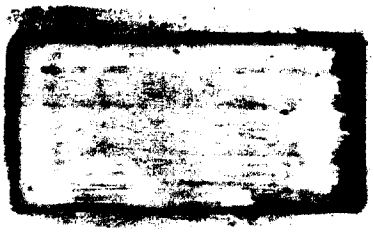

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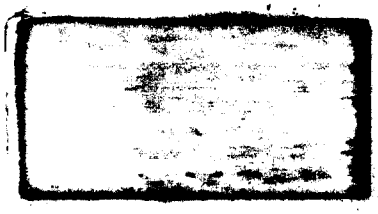

DOW CORNING CORPORATION
HEALTH & ENVIRONMENTAL SCIENCES
TECHNICAL REPORT

Report No.:	2002-I0000-51728
Title:	*In Vitro* Dermal Absorption of ^{14}C-Dodecamethylcyclohexasiloxane (D_6) in Human Skin
Study No:	9613
Test Article:	^{14}C- Dodecamethylcyclohexasiloxane (^{14}C- D_6)
Study Director:	Marina L. Jovanovic, M.S. Associate Toxicology Specialist
Sponsor:	Dow Corning Corporation
HES Management:	Steven D. Crofoot, M.S. Team Leader, Toxicology Health and Environmental Sciences
Testing Facility:	Dow Corning Corporation Health and Environmental Sciences 2200 West Salzburg Road Midland, MI 48686
Study Completion Date:	01/15/2003
Security Statement:	**Dow Corning Internal.** This report may be reproduced and shared with any Dow Corning employee. Distribution outside the Corporation must be approved by the Director of Health and Environmental Sciences. When this INTERNAL report is no longer needed, it may be placed in office waste baskets for destruction.

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ABSTRACT

This study was done to evaluate the percutaneous absorption of neat dodecamethylcyclohexasiloxane (D_6) radiolabeled with ^{14}C, when applied to human skin in an *in vitro* assay, under semi-occluded conditions using a flow-through diffusion cell system. Human epidermis was prepared from intact abdominal skin obtained frozen from the Ohio Valley Tissue and Skin Center. The epidermis with the top layer of dermis was separated from the rest of the skin by dermatoming. Skin samples were prepared from six donors and mounted in replicate in the Teflon flow-through cells. A physiological receptor fluid was pumped beneath the skin samples and collected in a fraction collector at predetermined time points. The barrier integrity of each piece of skin was evaluated prior to dosing using ^{3}H-H_2O. In this experiment, skin samples from each of the six donors were dosed with neat ^{14}C-D_6 at a targeted dose of 6 mg/cm^2. Immediately after dosing, a charcoal basket was placed above each of the skin samples and secured into a custom designed holder to capture any volatilized material. At the end of 24 hours of exposure, the charcoal baskets were removed and extracted, skin was washed, tape stripped and solubilized. The receptor fluid was collected over 24 hours. The radioactivity content in each sample was measured by liquid scintillation analysis. Penetration of applied dose through the skin was determined by analyzing the receptor fluid. The amount of ^{14}C-D_6 that remained in the skin after washing and tape stripping was determined by analyzing skin samples and the Saran® wrap the skin was placed on prior to tape stripping.

Skin from three donors passed the barrier integrity test. At the end of the assay (T = 24 hr), the majority of the applied dose was found on the skin surface (46.407% of applied dose) or volatilized from the dosing site and collected in the charcoal traps (40.057% of applied dose). Virtually no ^{14}C-D_6 penetrated through the skin into the receptor fluid in this assay. The percent of applied neat ^{14}C-D_6 recovered from all analyzed samples was 89.542% ± 4.154% including 3.075% of the applied neat ^{14}C- D_6 (standard error of the mean = 0.852% of applied dose) that was found in the skin. Additional method development experiment indicated that after a wash at 24 hours, the portion of ^{14}C-D_6 that appeared in the skin did not penetrate through the skin but continued to evaporate. Therefore, under conditions of this assay no percutaneous absorption of D_6 was demonstrated.

GLP COMPLIANCE STATEMENT

The study was conducted in compliance with Environmental Protection Agency Toxic Substances Control Act Good Laboratory Practice Regulations 40 CFR part 792 with the exception of the method development experiments. Deviations to the Protocol are listed on the page 17. There were no circumstances that would negatively impact or bias the results of this study.

Marina Jovanovic January 15, 2003

Marina L. Jovanovic, M.S. Date

Study Director
Associate Toxicology Specialist
Dow Corning Corporation

Steven D. Crofoot 1/15/2003

Steven D. Crofoot, M.S. Date

Team Leader, Toxicology
Health and Environmental Sciences
Dow Corning Corporation

QUALITY ASSURANCE STATEMENT

Title: In Vitro Dermal Absorption of ^{14}C-Dodecamethylcyclohexasiloxane (D_6) in Human Skin

Study Number: 9613

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

Dates of Inspection	Phase Inspected	Findings Reported to Study Director	Findings Reported to Management
25 Jul 01	Draft Protocol Review	31 Jul 01	28 Aug 01
02 Apr 02	Skin Preparation, System Set-Up and Dosing	03 Apr 02	09 Apr 02
03 Apr 02	Sample Collection	03 Apr 02	08 Apr 02
02-10 Dec 02	Draft Final Report and Associated Raw Data Review	10 Dec 02	16 Dec 02
23 Dec 02	Wet Specimen Verification	23 Dec 02	06 Jan 03

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

14 Jan 03
Date

APPROVAL SIGNATURES

This report consists of pages 1 through 57 including Tables 1 through 3, Figures 1 and 2, and Appendices A, B and C.

Marina Jovanovic January 15, 2003

Marina L. Jovanovic, M.S. Date

Study Director
Associate Toxicology Specialist
Dow Corning Corporation

Steven D. Crofoot 1/15/2003

Steven D. Crofoot, M.S. Date

Team Leader, Toxicology
Health and Environmental Sciences
Dow Corning Corporation

STUDY INFORMATION

Study Initiation Date:	03/12/2002
Experimental Start Date:	04/02/2002
Experimental Termination Date: (GLP study)	04/29/2002
Experimental Termination Date: (Method Development)	09/26/2002
Study Completion Date:	01/15/2003
Study Director:	Marina L. Jovanovic, M.S. Associate Toxicology Specialist
Sponsor:	Dow Corning Corporation 2200 W. Salzburg Road Midland, MI 48686
HES Management:	Steven D. Crofoot, M.S. Team Leader, Toxicology Health and Environmental Sciences (HES) Roy A. Campbell Team Leader, Analytical Chemistry Health and Environmental Sciences (HES)
Study Personnel:	Joan McMahon S&T Technologist
Testing Facility:	Dow Corning Corporation Health and Environmental Sciences 2200 West Salzburg Road Midland, MI 48686

OBJECTIVE

The objective of this study was to evaluate the absorption of neat ^{14}C-D_6 when applied to human skin, under semi-occluded conditions using the Bronaugh Flow-Through Diffusion Cell System (Bronaugh, 1985).

TEST SYSTEM

Model: Human cadaver skin obtained within approximately 24 hours of death, as required by the Standards of the American Association of Tissue Banks (AATB), was purchased from the Ohio Valley tissue and Skin Center, Cincinnati, OH. This documentation is retained at the Tissue Bank from which the skin is acquired. The skin was shipped on dry ice, and stored at -80°C until used in the percutaneous absorption assays. Abdominal skin was used from six individuals, 5 males, 60-70 years of age and 1 female, 65 years of age. Specific information obtained on the donors is documented in the study records.

RANDOMIZATION

No randomization was used in this study.

PREPARATION AND MAINTENANCE OF TEST SYSTEM

On the day of dosing, prior to use in percutaneous absorption assay, the skin samples were cleaned of underlying fat where needed, and thawed at the room temperature. Once thawed, all skin samples, except skin from donor No. 4869, were dermatomed with a mini-dermatome (Vincent Willey, Tyne & Wear England) to separate epidermis from most of the dermis. The thickness of the epidermal sections ranged from 220-380 microns. Dermatomed skin samples were placed into petri dishes containing Minimum Essential Medium (HMEM, Biowhittaker, Lot No. 013707) to keep it hydrated while the other skin sections were being cleaned, thawed and dermatomed. Each petri dish was labeled with the donor number associated with that piece of skin, study number, and dated. Blemish free sections of the skin of the appropriate thickness were chosen, and two circular pieces measuring approximately 2 cm in diameter (approximate surface area 3 cm^2) were cut from each skin sample and placed epidermis side up in the Teflon diffusion cell.

TEST, CONTROL, REFERENCE ARTICLE INFORMATION

Results of test article characterizations were reviewed by the study director and are maintained in the HES Archive.

A. Unlabeled Test Article

• Identification:	Dodecamethylcyclohexasiloxane (supplied as Dow Corning® 246 Fluid)
• Lot No:	LL114030
• CAS Number:	540-97-6
• Physical Description:	Colorless liquid (as specified in MSDS)
• Source:	Dow Corning Corporation 2200 W. Salzburg Road Midland, MI 48686
• Chemical stability:	Stable (as specified in MSDS)
• Storage Conditions:	Room temperature (as specified MDMS)
• Expiration Date:	March 04, 2004
• Purity:	99.6%
• Solubility:	Soluble in tetrahydrofuran (THF), hexane, acetone, toluene, ethanol (based on references by Angelloti, 1991, Varaprath *et al.*, 1998 and information provided by the developmental chemist)
• Chemical characterization:	HES Study No. 8825, TIS Report No. 1997-I0000-43804
• Archive:	A sample is retained in the HES Test Article Archives, Dow Corning Corporation Midland, MI 48686-0994

B. Labeled Test Article

• Identification:	^{14}C-Dodecamethylcyclohexasiloxane
• Lot No.:	17521-88D
• Physical Description:	Colorless liquid (MDMS)
• Source:	Dow Corning Corporation

2200 West Salzburg Rd.
Midland, MI 48686

• Chemical stability:	Material degrades in contact with strong acids or bases. Radiolysis may occur in prolonged storage at high specific activity (information provided by developmental chemist)
• Storage Conditions:	Freezer (as recommended by developmental chemist)
• Expiration Date:	March 04, 2004
• Specific Activity:	5.172 mCi/g
• Radiochemical Purity:	100%
• Solubility:	Soluble in THF, toluene, hexane, acetone, ethanol (based on Angelloti, 1991, Varaprath *et al.*, 1998 and information provided by developmental chemist)
• Chemical characterization:	HES Study No. 9676 TIS Report No. 2002-I0000-51536
• Archive:	A sample is retained in the HES Test Article Archives, Dow Corning Corporation Midland, MI 48686-0994

C. Intra-assay Control

• Identification:	Tritiated Water (^3H-H_2O)
• Lot No.:	3249-336
• Physical Description:	Clear liquid
• Source:	NEN™ Life Science Products, Inc. (previously Dupont NEN™) 549 Albany Street Boston, MA 02118
• Storage Conditions:	Refrigerator
• Expiration date:	10/31/2002
• Specific Activity:	0.938 mCi/g
• Purity:	Intra-assay control is representative of tritiated water and is considered pure

D. Carrier for Tritiated Water

- Identification: Sterile water
- Lot No.: 9774
- Expiration date: October, 2003
- Physical Description: Clear liquid
- Source: American Regent Laboratories Shirley, NY 11967
- Storage Conditions: Room temperature

EXPERIMENTAL DESIGN

A. Route of exposure

The dermal route is a potential route of human exposure to products containing D_6. Excised human skin from cadavers is a commonly used and accepted model for assessment of the percutaneous absorption of test materials *in vitro* (Federal register, 1996). The test material was applied as a single application for a 24-hour exposure period.

B. Dosing Solution Preparation and Analysis

The neat dosing solution was prepared by mixing ^{14}C-D_6 (Ref. No. 17521-88D) and unlabeled D_6 (Lot No. LL114030) to achieve the target specific activity. Specific activity of the dosing test article was determined by liquid scintillation analysis on the day of preparation and the day of dosing. On the day of dosing it was determined to be 1.29 mCi/g. The actual percent relative range (%RR) between the two sampling time points was determined to be 0.39%. Acceptance criteria of the stability of the ^{14}C- D_6 was a %RR between the two analyses for the time of dosing and time of preparation of no more than 10%. The radiochemical purity for the dosing test article was verified on the day of dosing using HPLC with radiometric detection and was determined to be 100%. Dosing solution was stored in the freezer at -20°C.

C. Dose Groups

The study consisted of six different human skin samples evaluated on the same day. On the day of dosing, skin samples from the six human subjects were dermatomed, placed in diffusion

cells in duplicate, and dosed with neat dosing solution. The target application level of D_6 was 6 mg/cm^2 of skin and the target radioactivity for each piece of skin was 6 μCi.

D. Treatment Regimen and Key Events

Apparatus Preparation

A Bronaugh flow-through apparatus was set-up with the skin area available for dosing after mounting into the diffusion cell of 0.64 cm^2. Specially designed holders were used to hold charcoal baskets, and to secure the skin in place confining the application site (Figure 1). The receptor fluid, Hank's Balanced Salt Solution with 0.6% HEPES, 0.005% Geneticin (Gibco BRL, Gaithersburg, MD), and 4% Bovine Serum Albumin (Sigma, St. Louis, MO) was mixed, the pH was adjusted to 7.35 with 2N NaOH and then filtered through 0.45 micron filter. The receptor fluid was pumped beneath the skin samples through the receptor compartment for 24 hours at a flow rate of 2.0 and 2.4 ml/hr and collected using a fraction collector.

Pre-dosing barrier integrity evaluation

Each skin piece received a finite dose of ^{3}H-H_2O (~200μl, exact dose was determined gravimetrically) for 20 minutes in order to determine if the barrier integrity of the skin had been compromised (Appendix A). ^{3}H-H_2O was diluted to the specific activity of 0.0009 mCi/g using sterile water.

The applied dose of ^{3}H-H_2O was removed after 20 minutes of exposure, skin was washed with reverse osmosis water and aliquots of the receptor fluid (Hank's Balanced Salt Solution with HEPES and Bovine Serum Albumin) were collected for an additional 60 minutes after the dose was removed. Radioactivity content in the receptor fluid was determined by liquid scintillation analysis. After the barrier integrity test was completed, the skin was dried and dosed with neat test article.

Test Article Administration

An aliquot of the neat dosing solution was drawn into a syringe and the syringe was weighed. The test material was administered and the syringe was re-weighed for gravimetric determination of the dose. Actual doses of ^{14}C-D_6 ranged from 2.34 – 6.72 mg/cm^2 of skin and applied radioactivity ranged from 1.94 – 5.55 μCi per piece of skin (Table 1).

E. Sample Collection

Immediately after dose application, a charcoal basket was placed in a specially designed holder to collect any test article that might volatilize (Figure 1). The receptor fluid was collected directly into scintillation cocktail at one-hour intervals through six hours. Between 6 and 24 hours, the receptor fluid was collected at three-hour intervals in pre-weighed empty vials because of vial volume limitations (see study deviations on page 16). At the termination of the 24-hour exposure period, charcoal baskets were removed and extracted in toluene and hexane, respectively. Each piece of skin was wiped with a dry cotton-tipped applicator, followed by moistened cotton-tipped applicators (1% soap solution) as quickly as possible. The 1% soap solution wash was repeated three times followed by a dry cotton-tipped applicator to remove any moisture. The skin was then washed in the same manner (3X) using cotton-tipped applicators, moistened with 70% ethanol, followed by a dry cotton-tipped applicator, removed from the flow cell, placed on Saran® wrap and tape stripped (5X) with D-Squame® adhesive tape to peel off the *stratum corneum*. Skin was then solubilized for radioactivity content analysis. Diffusion cells and holders used to hold charcoal baskets over the skin were removed and separately extracted.

F. Sample Processing and Analysis

Radioactivity (^{14}C) concentrations were measured by liquid scintillation analysis in the receptor fluid, in extracts of cotton-tipped applicators and D-Squame® tape, Saran® wrap, charcoal baskets, basket holders and diffusion cells, and in the solubilized skin samples. Each sample was counted for 5 minutes or a 2 sigma percent value of two, whichever came first. All counts were converted to absolute radioactivity (DPM) by automatic quench correction. Results were corrected for background radioactivity with the level of detection set at one times the background values. The receptor fluid collections at one-hour intervals were made directly into liquid scintillation cocktail while receptor fluid collections at three-hour intervals were made into empty vials. Receptor fluid collected over 3 hours was split into two aliquots that were then analyzed by LSC after addition of scintillation cocktail. In addition, the original vial that was used for receptor fluid collection was rinsed with THF to remove any ^{14}C-D_6 possibly bound to glass. The cotton-tipped applicators, Saran® wrap and D-Squame® tape were extracted in toluene (tape strips and all cotton-tipped applicators that were used to wash skin were extracted together; Saran® wrap was extracted separately). Charcoal baskets were extracted twice in toluene and once in hexane. After completion of extractions, charcoal used in the cells that passed barrier integrity test (cells 3, 4, 5, 9, 10, and 11) was oxidized (Biological Oxidizer OX500, RJ. Harvey

Instrument Corporation) and analyzed for radioactivity content by liquid scintillation counter (LSC) in order to recover all of a volatilized ^{14}C-D_6 trapped in the charcoal. Diffusion cells were extracted in absolute ethanol. The holders used to hold the charcoal baskets over the skin were extracted in absolute ethanol followed by hexane extraction. Skin was digested in 35% aqueous solution of tetraethylammonium hydroxide (TEAH), neutralized with 6N HCl and analyzed for radioactivity content by LSC.

G. Sample Identification and Storage

Samples collected were identified and stored under the following conditions:

Receptor fluid	4 ± 4 °C
Receptor fluid in cocktail	Room Temperature
Solubilized Skin	Room Temperature
Extracts	4 ± 4 °C

H. Method Development

Method development experiments was conducted separately to evaluate efficiency of washing and tape stripping procedures that were used to remove ^{14}C-D_6 from the skin surface, and to observe if ^{14}C-D_6 has a tendency to spread beyond the application site. Additional method development experiments were conducted to examine the fate of ^{14}C-D_6 that appeared in the skin after skin was washed at T=24 hr (Appendix C).

DATA ANALYSIS

A. Parameters Evaluated

Barrier integrity based on penetration of ^{3}H-H_2O

Barrier integrity was determined in the 20-minute quick test by calculating ^{3}H-H_2O penetration through the skin into receptor fluid. Skin pieces that were considered to have acceptable integrity had to pass the criteria that were established in DC Study No. 8820 (TIS Report No. 1998-I0000-45140): 1) the coefficient of variation for replicate skin samples must have been less than 60%, and 2) the percent dose absorbed must have been $\leq$ 0.21% or it was not used in the data analysis.

Percutaneous penetration of ^{14}C-D_6 throughout 24 hr:

$$\% \text{ Dose appearing in receptor fluid} = \frac{\text{Cumulative DPM in receptor fluid} \times 100}{\text{DPM Applied}}$$

^{14}C-D_6 remaining in the skin after 24 hr:

$$\% \text{ Dose appearing in the skin} = \frac{\text{Total DPM in skin}^* + \text{DPM in Saran Wrap}^{**} \times 100}{\text{DPM Applied}}$$

* after washing and stripping the application site

** Skin was placed on Saran wrap during tape stripping

Permeability Coefficient (cm/hr):

$$Kp = \frac{\text{Steady State Flux (}\mu\text{g } D_6 \text{ in receptor fluid/cm}^2 \text{ of exposed skin/hr of exposure)}}{\text{Concentration (}\mu\text{g of } D_6 \text{ /cm}^3\text{of Dosing Solution)}}$$

Steady State Flux (μg/cm²/hr):

The rate of penetration of ^{14}C-D_6 (μg/cm²/hr) through human skin into the receptor fluid was estimated by calculating the slope of regression line for the response of penetration *versus* time when article was present at an infinite concentration (Appendix B).

B. Statistical Method

Numerical data obtained during the conduct of the study were subjected to calculation of group mean values and standard error of the mean, where appropriate. The radioactivity content in the receptor fluid, skin, cotton-tipped applicators with D-Squame® adhesive tape, Saran wrap, charcoal baskets, holders for charcoal baskets and diffusion cells were reported in terms of percent of total radioactivity recovered relative to the amount of applied radioactivity. Cumulative penetration into receptor fluid was reported in μg D_6 per cm² of the skin application site (Appendix A). The statistical analysis of the data from this study was carried out using Microsoft Excel™ 2000.

DEVIATIONS

Protocol deviations are cited and discussed below. The deviations cited below and occasional minor SOP deviations documented in the study records were not considered to have an impact on the study conduct or outcome.

1. A deviation occurred in protocol with regard to section IX.E. Sample collection. Receptor fluid collected at 1-hour intervals (1-6 hr) was collected in pre-weighed vials containing approximately 10 ml of scintillation cocktail. The exact amount of cocktail was not determined because this is not significant for sample analysis. This was considered to have no impact on the study outcome.
2. A deviation occurred in protocol with regard to section IX.E. Sample collection. Receptor fluid collected at 3-hour intervals (6-24hr) was not collected directly in the cocktail but in the pre-weighed empty vials because of technical limitations (vial volume, solubility of buffer-based receptor fluid in the scintillation cocktail). Considering that the test article is not volatile this was considered to have no impact on the study outcome.
3. A deviation occurred in the protocol with regard to section IX.E. Sample collection. Additional extractions were performed: a) Charcoal baskets were extracted twice in toluene and once in hexane in order to extract most of ^{14}C-D_6; b) Holders for charcoal baskets were extracted in hexane in addition to ethanol extraction. This was considered to have no impact on the study outcome.
4. Protocol, Section IX.F Sample processing and Analysis stated that study samples would be counted for 10 minutes. Study samples were counted for 5 minutes as this is commonly considered as a sufficient time for radioactivity analysis by LSC. This was considered to have no impact on the study outcome.

RESULTS AND DISCUSSION

In this experiment, skin samples from donors No. 4704, 4869 and 5315 did not pass the barrier integrity test. These skin samples were eliminated because the mean percent of tritiated water absorbed during the barrier integrity test was greater than the cut-off level of 0.21%, the level established when the method was validated for this laboratory (DC Study No. 8820). All of the requirements for barrier integrity were met for other three donors as shown in Table 2. Skin samples from all six donors were dosed in duplicate with neat ^{14}C- D_6 before the skin integrity data were available. The average dose applied to the skin samples that passed skin integrity test (N=3) was 5.7 mg/cm^2 of skin and 7.4μCi/cm^2 of skin.

Very little ^{14}C-D_6 penetrated through the skin into receptor fluid (0.003% of applied dose ± 0.000) over 24hr of exposure. The average cumulative penetration into the receptor fluid over the 24 hr diffusion period for neat ^{14}C-D_6 was only 0.160 ± 0.014 μg/cm^2 of skin (Appendix A). Penetration of ^{14}C-D_6 per cm^2 of skin over time was plotted and analyzed to determine the linear portion of the flux curve (Figure 2 and Appendix B) in order to calculate the permeability coefficient, Kp (cm/hr). Visual inspection of the penetration curve suggested that linear portion starts about 12 hr after dosing. From 12 to 24hr radioactivity content in receptor fluid became steady from one hour to the next with a substantial amount of dose still present on the skin surface. The slope of the regression line for the response of penetration *versus* time (12-24 hr) was 0.007 μg D_6 /cm^2/hr (R^2=0.999) and represents steady state flux. The permeability coefficient, Kp, as a measure of a chemical's ability to cross the skin was determined to be $7.24*10^{-9}$ cm/hr by dividing the steady state flux by the concentration of the test article in the dosing solution (0.966 g/cm^3).

The percent of applied neat ^{14}C-D_6 recovered from all analyzed samples was 89.542 ± 4.154% (Table 3). The majority of the applied dose was found on the skin surface and within the donor compartment (46.407% of applied dose) or volatilized from the dosing site and collected in the charcoal baskets (40.057% of applied dose) after 24 hr of exposure. Individual data are included in Appendix A. The statistical analysis of the data indicated that 3.075% of the applied neat ^{14}C-D_6 was retained in the skin at the end of the assay (standard error of the mean = 0.852% of applied dose). However, it should be taken into consideration that the skin piece that is placed into the diffusion cells, is larger than the actual application site. A specially designed holder was used to secure skin and confine the application site (Figure 1). The standard procedure in this assay is to wash and tape strip only the application site (0.64 cm^2) at the time of sample collection, but to solubilize the entire skin piece for radioactivity analysis. Therefore, follow-up method development experiment was conducted to try to observe if D_6 had spread beyond the application site due to its physical properties (e.g. low surface tension) and perhaps due to applied washing procedure. In the method development experiment the outer edge of the skin was excised from the application site and analyzed separately 24 hr post-dosing. Data from this method development experiment showed that actually only 20% of the dose recovered in skin after 24 hr exposure was found in the application site after washing and tape stripping (0.55% of applied dose), while 80% was recovered from the outer edge of the skin (2.22% of applied dose) (Appendix C). These data suggest that D_6 present on the skin surface has a tendency to spread beyond the application site, possibly upon removal of the holder that confines the application area and donor compartment (holders are

removed just prior to washing). Recoveries from the outer edge of the skin piece, which has not been washed or tape stripped, may contribute to the elevated dose recoveries in the skin samples. Spreading of D_6 beyond the application site was also visualized on x-ray film when skin dosed with ^{14}C-D_6 and washed at T = 0hr, was placed on film with epidermal side down (method development). In addition, method development indicated that applied washing and tape stripping procedure was not completely efficient in removing D_6 from the skin surface (Appendix C). A final method development experiment was conducted to examine the fate of residual ^{14}C-D_6 after washing at T = 24 hr (Appendix C: Experiment No. 2). Application sites were washed with soapy water 24 hr post-dose without removing the holders, and charcoal baskets were replaced with new ones. After an additional 24 hr (at T = 48hr) skin was washed again and analyzed for radioactivity content. The data showed that the portion of applied D_6 that appeared in the skin at T=24 hr did not penetrate into receptor fluid over the next 24 hr (T = 48 hr). Also, at T = 48 hr (24 hr post-wash) there was virtually no D_6 found in the solubilized skin samples (0.001% dose in application site, 0.003% dose from the outer edge of the skin) or on the skin surface. Dose recoveries in the charcoal baskets (9.108% of applied dose) that were used to collect volatiles after skin was washed indicated that D_6 continues to evaporate from the skin surface and donor compartment.

CONCLUSIONS

This study demonstrated that after 24 hours of exposure the majority of the applied ^{14}C- D_6 has remained on the skin surface and within a donor compartment (46.41% of applied dose) or has volatilized from the dosing site and trapped in the charcoal baskets (40.06% of applied dose). Very little ^{14}C- D_6 penetrated through the skin into receptor fluid (0.003% of applied dose ± 0.000). The amount of ^{14}C- D_6 found in the skin samples (3.075 % of applied dose ± 0.852) is not considered to be part of absorbed dose. It appears that D_6 has tendency to spread beyond application site onto the outer edge of the skin piece contributing to elevated recoveries in the skin sample. Also, method development experiments demonstrated that applied washing and tape stripping procedure might not be sufficient in removing D_6 from the skin surface. Data indicated that ^{14}C- D_6 that was found in the skin after 24 hours of exposure does not penetrate through the skin to be absorbed into the receptor fluid but continues to evaporate. Therefore, under conditions of this assay no percutaneous absorption of D_6 was demonstrated.

ARCHIVE

All raw data including study protocol, protocol amendments, deviations, correspondence, study authorization form, and the final report were archived at Dow Corning Corporation, Health and Environmental Sciences, 2200west Salzburg Road, Auburn, MI 48611.

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Table 1: Individual Dosing Data

1	**Neat**	**4704[2]**	**3.6**	**5.63**	**4.64**
2	**Neat**	**4869[2]**	**3.8**	**5.94**	**4.90**
3	Neat	5067	4.2	6.56	5.42
4	Neat	5128	3.1	4.84	4.00
5	Neat	5156	4.0	6.25	5.16
6	**Neat**	**5315[2]**	**4.1**	**6.41**	**5.29**

[1] Dose D_6/cm^2 = Dose mg $D_6/0.64\ cm^2$ (the area of skin available for dosing)

[2] Eliminated due to failure to meet criteria of the barrier integrity test (in bold letters)

Average Neat Dose (N=3 donors) = 5.7 mg D_6/cm^2, 7.4 $\mu Ci/cm^2$

Table 2: Percent of ^{3}H-H_2O Absorption

Donor	Cell No.	%Dose	Skin thickness (µm)	Average %Dose	Std dev.	C.V
4704[1]	**1**	**0.376**	**310**	**0.305**	**0.103**	**33.61**
4704[1]	**7**	**0.233**	**350**			
4869[1]	**2**	**0.218**	**380**	**0.236**	**0.032**	**13.6**
4869[1]	**8**	**0.259**	**330**			
5067	3	0.110	300	0.096	0.019	19.7
5067	9	0.083	370			
5128	4	0.117	360	0.127	0.015	11.5
5128	10	0.137	220			
5156	5	0.119	360	0.129	0.013	10.1
5156	11	0.138	280			
5316[1]	**6**	**0.220**	**340**	**0.369**	**0.211**	**57.2**
5315[1]	**12**	**0.518**	**320**			

[1] Eliminated due to failure to meet criteria of the barrier integrity test (in bold letters)

Table 3: *In Vitro* Disposition of Radioactivity Following Application of ^{14}C-D_6 to Human Skin

Percent of Applied Dose ± Standard Error of the Mean

Dosing Solution	[1] Volatilized Dose	[2] Skin Surface	[3] Skin	[4] Penetrated	% Recovery
Neat ^{14}C-D_6					
(N=3)[5]	40.057 ± 0.150	46.403 ± 3.965	3.075 ± 0.862	0.003 ± 0.000	89.540 ± 4.154

Percent of Recovered Dose ± Standard Error of the Mean

Dosing Solution	[1] Volatilized Dose	[2] Skin Surface	[3] Skin	[4] Penetrated
Neat ^{14}C-D_6				
(N=3)[5]	44.775 ± 2.267	51.736 ± 2.062	3.486 ± 0.960	0.003 ± 0.000

[1] Based on radioactivity recovered in charcoal baskets.

[2] Based on the total radioactivity found in swabs, adhesive tape (tape strips), cells and holders.

[3] Based on radioactivity associated with the skin and in Saran® wrap the skin was placed on prior to tape stripping.

[4] Based on radioactivity in the receptor fluid collected over 24 hours.

[5] Skin samples from the donors No. 5067, 5128 and 5156 met criteria for the barrier integrity.

Figure 1. Schematic Presentation of Bronaugh Flow-Through Diffusion Cell

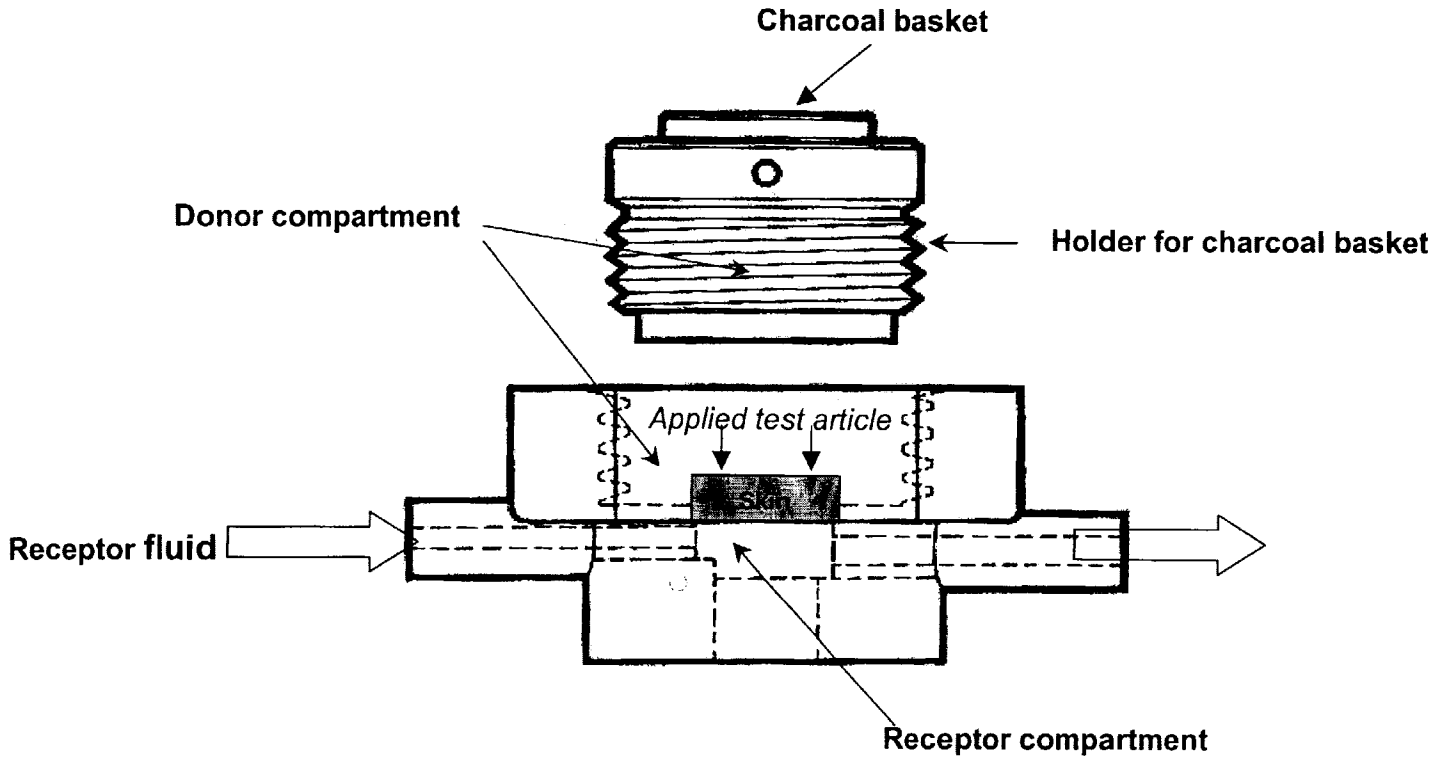
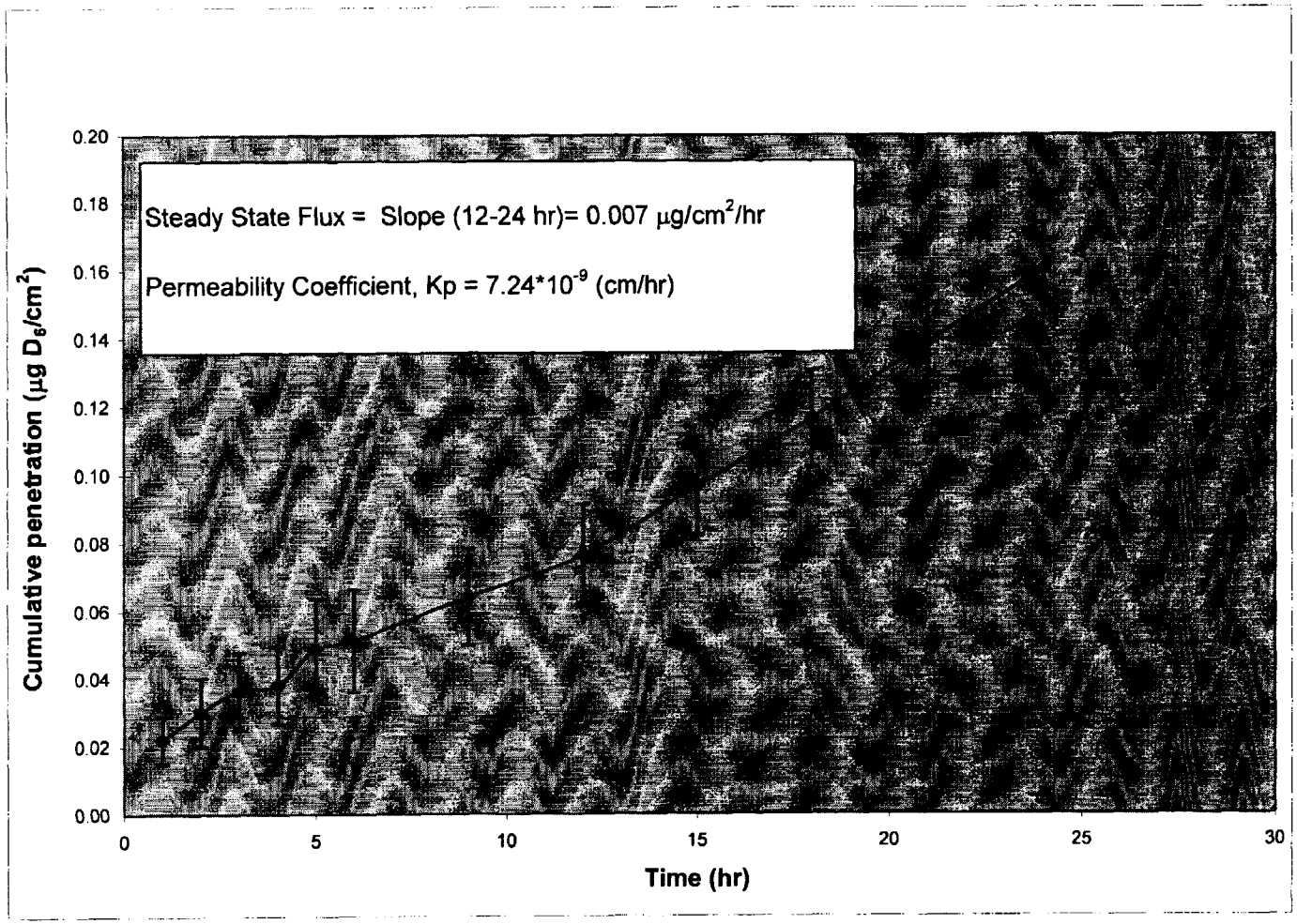


Figure 2: *In Vitro* Penetration of Neat ^{14}C-D_6 Through Human Skin



APPENDIX A

Radioactivity Spreadsheets

Calculations and Abbreviations for Excel Spreadsheets

1. **Radioactivity**
   1 μCi = 2.22 x 10^6 DPM

2. **Specific Activity (S.A.) of neat dosing solution (^{14}C-D_6):**
   Radioactivity in μCi / Weight (mg) of neat dosing solution = μCi/mg
   S.A. of ^{14}C- D_6 (μCi/mg) x 2.22 x 10^6 (DPM/ μCi) = DPM/mg
   S.A. of ^{14}C- D_6 (DPM/mg)/1000(μg/mg) = DPM/μg

3. **Dose (DPM)**
   S.A. of dosing solution (DPM/mg) x dose (mg)

4. **Dose (μCi)**
   S.A. of dosing solution (μCi/mg) x dose (mg)

5. **μg D_6 penetrated into receptor fluid per cm^2 of skin**
   Radioactivity (DPM) collected over time in a Receptor fluid / S.A. of test article (DPM/ μg D_6) / 0.64cm^2 (area of skin dosed).

6. **Cumulative penetration of D_6 (μg) / cm^2 of skin**
   Amount of D_6 per cm^2 added to the amount of the previous timepoint to get the total D_6 /cm^2 for each cell over 24 hours.

7. **Average Cumulative Penetration**
   The average cumulative penetration of D_6 for a group of cells over 24 hours.

8. **Percent Dose**
   % Dose = Total DPM in sample *100/ Applied dose (DPM)

9. **Average Percent Dose**
   Percent dose for group of test systems or average for 2 or more replicates of the same sample.

10. **Steady State Flux (μg/cm^2/hr):**
    Determined by plotting penetration of test article (μg D_6/cm^2) over time and determining the slope of the line (Figure 1).

11. **Permeability Coefficient (cm/hr):** $\frac{\text{Steady State Flux (μg/cm}^2\text{/hr)}}{\text{μg of D}_6\text{ /cm}^3\text{ of Dosing Solution}}$

    D_6 neat dosing solution: 966,000μg/cm^3 of dosing solution at room temperature.
    This concentration is based on the density of D_6 (0.966 g/cm^3 at 20°C)

12. **Reanalysis Criteria (%RR)**
    The %RR is derived by calculating the difference between two values and expressing this difference as a percentage of the mean for the two values. Samples which fail to meet the following criteria shall be re-analyzed in duplicate:

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

    An exception to the above criteria is when the % dose recovered in the sample is less than or equal to 0.1%, than no re-analysis of a sample is required, failure to meet criteria 1-3 not withstanding.

Abbreviations:

DPM = Disintegrations per minute

S.A.= Specific Activity

Rep. = Replicate

Wt. = Weight

LSC = Liquid Scintillation Counter

TEAH = Tetraethylammonium hydroxide

SD = St. Dev. = Standard Deviation

SEM = St. Error = Standard error of the mean

Eq./Equiv. = Equivalent

ID = Identification

D6/D_6 = Dodecamethylcyclohexasiloxane

No. = Number

N.D. = not determined

C.V. = Coefficient of variation

Avg. = Average

hr = Hour

mg = milligrams

μg = micrograms

%RR= Percent Relative Range

T = time

DC = Dow Corning Corporation

HES = Health and Environmental Sciences

F = flag in the study spreadsheets indicating non-uniformity of the sampling

Data in bold letters were not used in summarizing the data.

^{3}H-H_2O 1998 (DPM/mg)

Sample = Receptor Fluid

Donor	Cell No.	Vial+ Sample (g)	Vial (g)	Receptor Fluid (g)	Rep.1 (g)	Rep.2 (g)	DPM1	DPM2	DPM1/ sample	DPM2/ sample	Avg.DPM/ sample	Dose (mg)	Dose (DPM)	%Dose	skin thickness µm	Avg. %Dose	St. dev.	C.V.	
4704	**1**	**19.4632**	**16.3473**	**3.1159**	**0.1980**	**0.2017**	**100**	**95**	**1574**	**1468**	**1521**	**201.2**	**401998**	**0.378**	**310**				
4704	**7**	**19.6973**	**16.6086**	**3.0887**	**0.1963**	**0.2019**	**66**	**59**	**1038**	**903**	**971**	**208.4**	**416383**	**0.233**	**350**	**0.306**	**0.103**	**33.6**	**eliminated**
4869	**2**	**19.5850**	**16.5127**	**3.0723**	**0.1996**	**0.1990**	**55**	**64**	**847**	**988**	**917**	**215.4**	**430369**	**0.213**	**380**				
4869	**8**	**19.8358**	**16.4278**	**3.4080**	**0.1992**	**0.2016**	**60**	**60**	**1027**	**1014**	**1020**	**197.5**	**394605**	**0.259**	**330**	**0.236**	**0.032**	**13.6**	**eliminated**
5067	3	20.0136	16.4020	3.6116	0.2003	0.2000	26	25	469	451	460	209.9	419380	0.110	300				
5067	9	20.1988	16.5401	3.6587	0.2002	0.1998	21	18	384	330	357	215.4	430369	0.083	370	0.096	0.019	19.7	
5128	4	19.8266	16.4176	3.4090	0.2007	0.2008	31	28	527	475	501	214.8	429170	0.117	360				
5128	10	19.7736	16.4507	3.3229	0.1936	0.2000	30	38	515	631	573	208.9	417382	0.137	220	0.127	0.015	11.5	
5156	5	19.4401	16.4117	3.0284	0.2012	0.2014	33	35	497	526	511	214.5	428571	0.119	360				
5156	11	20.0904	16.5627	3.5277	0.1993	0.1997	30	33	531	583	557	202.4	404395	0.138	280	0.129	0.013	10.1	
5315	**6**	**19.5118**	**16.5460**	**2.9658**	**0.1997**	**0.2018**	**64**	**61**	**950**	**897**	**923**	**210.5**	**420579**	**0.220**	**340**				
5315	**12**	**19.6555**	**16.4273**	**3.2282**	**0.1994**	**0.1985**	**131**	**132**	**2121**	**2147**	**2134**	**206.2**	**411988**	**0.518**	**320**	**0.369**	**0.211**	**57.2**	**eliminated**

Data in bold letters = excluded for not meeting barrier integrity criteria

Dosing solution: **Neat ^{14}C-D6= 1.29** µCi/mg 2863800 DPM/mg

Sample = Receptor Fluid

1 HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**27.9165**	**25.7837**	**2.1328**	**76**	**0.0007**	**3.6**	**10309680**	**0.0007**	**0.0415**	**0.0415**		
4704	**7**	**27.8703**	**25.7871**	**2.0832**	**93**	**0.0009**	**3.8**	**10882440**	**0.0009**	**0.0507**	**0.0507**		
4869	**2**	**27.9301**	**25.8349**	**2.0952**	**66**	**0.0006**	**3.8**	**10882440**	**0.0006**	**0.0360**	**0.0360**		
4869	**8**	**27.7469**	**25.4652**	**2.2817**	**52**	**0.0005**	**3.6**	**10309680**	**0.0005**	**0.0284**	**0.0284**		
5067	3	27.4568	25.9243	1.5325	38	0.0003	4.2	12027960	0.0003	0.0207	0.0207		
5067	9	28.4240	26.0412	2.3828	83	0.0009	3.2	9164160	0.0009	0.0453	0.0453		
5128	4	28.2018	25.9035	2.2983	35	0.0004	3.1	8877780	0.0004	0.0191	0.0191		
5128	10	28.1073	25.8957	2.2116	19	0.0002	4.3	12314340	0.0002	0.0104	0.0104		
5156	5	27.8984	25.8952	2.0032	29	0.0003	4.0	11455200	0.0003	0.0158	0.0158		
5156	11	28.1189	25.7946	2.3243	38	0.0004	3.1	8877780	0.0004	0.0207	0.0207		
5315	**6**	**27.8051**	**25.8713**	**1.9338**	**93**	**0.0008**	**4.1**	**11741580**	**0.0008**	**0.0507**	**0.0507**		
5315	**12**	**28.6391**	**26.1994**	**2.4397**	**149**	**0.0035**	**1.5**	**4295700**	**0.0035**	**0.0813**	**0.0813**	0.0220	0.0070

2HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**27.7611**	**25.7023**	**2.0588**	**27**	**0.0003**	**3.6**	**10309680**	**0.0010**	**0.0147**	**0.0562**		
4704	**7**	**28.0339**	**26.0207**	**2.0132**	**46**	**0.0004**	**3.8**	**10882440**	**0.0013**	**0.0251**	**0.0758**		
4869	**2**	**27.9612**	**25.9255**	**2.0357**	**28**	**0.0003**	**3.8**	**10882440**	**0.0009**	**0.0153**	**0.0513**		
4869	**8**	**28.0288**	**25.8124**	**2.2164**	**21**	**0.0002**	**3.6**	**10309680**	**0.0007**	**0.0115**	**0.0398**		
5067	3	28.9981	26.6040	2.3941	12	0.0001	4.2	12027960	0.0004	0.0065	0.0273		
5067	9	28.2437	25.8969	2.3468	35	0.0004	3.2	9164160	0.0013	0.0191	0.0644		
5128	4	27.9280	25.6572	2.2708	11	0.0001	3.1	8877780	0.0005	0.0060	0.0251		
5128	10	28.0894	25.9401	2.1493	6	0.0000	4.3	12314340	0.0002	0.0033	0.0136		
5156	5	27.8377	25.7937	2.0440	12	0.0001	4.0	11455200	0.0004	0.0065	0.0224		
5156	11	28.2394	25.9389	2.3005	14	0.0002	3.1	8877780	0.0006	0.0076	0.0284		
5315	**6**	**26.9516**	**24.9955**	**1.9561**	**44**	**0.0004**	**4.1**	**11741580**	**0.0012**	**0.0240**	**0.0747**		
5315	**12**	**28.2074**	**25.8595**	**2.3479**	**43**	**0.0010**	**1.5**	**4295700**	**0.0045**	**0.0235**	**0.1048**	0.0302	0.0101

Data in bold letters = excluded for not meeting barrier integrity criteria

3HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**27.9374**	**25.8207**	**2.1167**	**18**	**0.0002**	**3.6**	**10309680**	**0.0012**	**0.0098**	**0.0660**		
4704	**7**	**27.4609**	**25.6500**	**1.8109**	**26**	**0.0002**	**3.8**	**10882440**	**0.0015**	**0.0142**	**0.0900**		
4869	**2**	**27.9048**	**25.8505**	**2.0543**	**22**	**0.0002**	**3.8**	**10882440**	**0.0011**	**0.0120**	**0.0633**		
4869	**8**	**27.8436**	**25.8682**	**1.9754**	**15**	**0.0001**	**3.6**	**10309680**	**0.0009**	**0.0082**	**0.0480**		
5067	3	28.1764	25.6772	2.4992	15	0.0001	4.2	12027960	0.0005	0.0082	0.0355		
5067	9	28.5253	26.3981	2.1272	19	0.0002	3.2	9164160	0.0015	0.0104	0.0747		
5128	4	28.2473	25.9635	2.2838	13	0.0001	3.1	8877780	0.0007	0.0071	0.0322		
5128	10	27.7288	25.7754	1.9534	7	0.0001	4.3	12314340	0.0003	0.0038	0.0175		
5156	5	27.7833	25.7489	2.0344	7	0.0001	4.0	11455200	0.0004	0.0038	0.0262		
5156	11	27.3933	25.3699	2.0234	7	0.0001	3.1	8877780	0.0007	0.0038	0.0322		
5315	**6**	**27.8877**	**25.9368**	**1.9509**	**31**	**0.0003**	**4.1**	**11741580**	**0.0014**	**0.0169**	**0.0917**		
5315	**12**	**27.8378**	**25.6965**	**2.1413**	**17**	**0.0004**	**1.5**	**4295700**	**0.0049**	**0.0093**	**0.1140**	0.0364	0.0115

4HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**27.6111**	**25.5615**	**2.0496**	**8**	**0.0001**	**3.6**	**10309680**	**0.0013**	**0.0044**	**0.0704**		
4704	**7**	**27.3494**	**25.7050**	**1.6444**	**10**	**0.0001**	**3.8**	**10882440**	**0.0016**	**0.0055**	**0.0955**		
4869	**2**	**27.6527**	**25.5740**	**2.0787**	**12**	**0.0001**	**3.8**	**10882440**	**0.0012**	**0.0065**	**0.0698**		
4869	**8**	**27.5272**	**25.7176**	**1.8096**	**7**	**0.0001**	**3.6**	**10309680**	**0.0009**	**0.0038**	**0.0518**		
5067	3	28.3987	25.9403	2.4584	4	0.0000	4.2	12027960	0.0006	0.0022	0.0376		
5067	9	28.0477	26.1769	1.8708	3	0.0000	3.2	9164160	0.0015	0.0016	0.0764		
5128	4	28.2068	25.9350	2.2718	0	0.0000	3.1	8877780	0.0007	0.0000	0.0322		
5128	10	27.4737	25.7565	1.7172	1	0.0000	4.3	12314340	0.0003	0.0005	0.0180		
5156	5	27.8393	25.7999	2.0394	7	0.0001	4.0	11455200	0.0005	0.0038	0.0300		
5156	11	27.7037	25.8679	1.8358	5	0.0001	3.1	8877780	0.0007	0.0027	0.0349		
5315	**6**	**27.7279**	**25.7410**	**1.9869**	**16**	**0.0001**	**4.1**	**11741580**	**0.0016**	**0.0087**	**0.1004**		
5315	**12**	**28.8233**	**26.9101**	**1.9132**	**8**	**0.0002**	**1.5**	**4295700**	**0.0051**	**0.0044**	**0.1184**	0.0382	0.0115

Data in bold letters = excluded for not meeting barrier integrity criteria

Receptor Fluid

5HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm²	Cumulative ug Eq.D6/cm²	Average Cumulative ug Eq.D6/cm²	SEM
4704	**1**	**28.3663**	**26.2679**	**2.0984**	**7**	**0.0001**	**3.6**	**10309680**	**0.0013**	**0.0038**	**0.0742**		
4704	**7**	**27.3861**	**25.7816**	**1.6045**	**8**	**0.0001**	**3.8**	**10882440**	**0.0017**	**0.0044**	**0.0998**		
4869	**2**	**28.2301**	**26.1868**	**2.0433**	**6**	**0.0001**	**3.8**	**10882440**	**0.0012**	**0.0033**	**0.0731**		
4869	**8**	**27.6015**	**25.8644**	**1.7371**	**8**	**0.0001**	**3.6**	**10309680**	**0.0010**	**0.0044**	**0.0562**		
5067	3	28.4764	25.9887	2.4877	10	0.0001	4.2	12027960	0.0007	0.0055	0.0818		
5067	9	27.5826	25.7101	1.8725	8	0.0001	3.2	9164160	0.0016	0.0044	0.0807		
5128	4	28.0138	25.7262	2.2876	10	0.0001	3.1	8877780	0.0008	0.0055	0.0376		
5128	10	27.6053	25.9002	1.7051	6	0.0000	4.3	12314340	0.0003	0.0033	0.0213		
5156	5	28.0160	25.9574	2.0586	4	0.0000	4.0	11455200	0.0005	0.0022	0.0322		
5156	11	27.5934	25.7996	1.7938	8	0.0001	3.1	8877780	0.0008	0.0044	0.0393		
5315	**6**	**27.8041**	**25.8338**	**1.9703**	**9**	**0.0001**	**4.1**	**11741580**	**0.0016**	**0.0049**	**0.1053**		
5315	**12**	**27.7409**	**25.8682**	**1.8727**	**12**	**0.0003**	**1.5**	**4295700**	**0.0053**	**0.0065**	**0.1249**	0.0488	0.0150

6HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm²	Cumulative ug Eq.D6/cm²	Average Cumulative ug Eq.D6/cm²	SEM
4704	**1**	**27.7854**	**25.6791**	**2.1063**	**8**	**0.0001**	**3.6**	**10309680**	**0.0014**	**0.0044**	**0.0786**		
4704	**7**	**27.4650**	**25.8572**	**1.6078**	**9**	**0.0001**	**3.8**	**10882440**	**0.0018**	**0.0049**	**0.1048**		
4869	**2**	**28.1036**	**26.0186**	**2.0850**	**7**	**0.0001**	**3.8**	**10882440**	**0.0013**	**0.0038**	**0.0769**		
4869	**8**	**29.5550**	**27.7859**	**1.7691**	**5**	**0.0000**	**3.6**	**10309680**	**0.0010**	**0.0027**	**0.0589**		
5067	3	28.5223	26.0247	2.4976	7	0.0001	4.2	12027960	0.0007	0.0038	0.0857		
5067	9	27.7922	25.9221	1.8701	3	0.0000	3.2	9164160	0.0016	0.0016	0.0824		
5128	4	29.2596	26.9791	2.2805	3	0.0000	3.1	8877780	0.0008	0.0016	0.0393		
5128	10	27.5709	25.8561	1.7148	3	0.0000	4.3	12314340	0.0003	0.0016	0.0229		
5156	5	28.0155	25.9445	2.0710	10	0.0001	4.0	11455200	0.0006	0.0055	0.0376		
5156	11	27.7415	25.9361	1.8054	0	0.0000	3.1	8877780	0.0008	0.0000	0.0393		
5315	**6**	**27.7432**	**25.7406**	**2.0026**	**6**	**0.0001**	**4.1**	**11741580**	**0.0017**	**0.0033**	**0.1086**		
5315	**12**	**27.7752**	**25.9028**	**1.8724**	**7**	**0.0002**	**1.5**	**4295700**	**0.0055**	**0.0038**	**0.1288**	0.0512	0.0151

Data in bold letters = excluded for not meeting barrier integrity criteria

Rounding errors may occur due to electronic handling of numb

9HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**22.5934**	**16.4537**	**6.1397**	**36+23+3**	**62**	**0.0006**	**3.6**	**10309680**	**0.0020**	**0.0338**	**0.1124**		
4704	**7**	**21.1838**	**16.5003**	**4.6835**	**15+3+5**	**23**	**0.0002**	**3.8**	**10882440**	**0.0020**	**0.0125**	**0.1173**		
4869	**2**	**22.5583**	**16.5125**	**6.0458**	**13+0+3**	**16**	**0.0001**	**3.8**	**10882440**	**0.0014**	**0.0087**	**0.0857**		
4869	**8**	**21.6250**	**16.5199**	**5.1051**	**17+7+1**	**25**	**0.0002**	**3.6**	**10309680**	**0.0013**	**0.0136**	**0.0726**		
5067	3	23.6992	16.4941	7.2051	19+0+0	19	0.0002	4.2	12027960	0.0009	0.0104	0.0960		
5067	9	21.8749	16.4471	5.4278	18+2+4	24	0.0003	3.2	9164160	0.0019	0.0131	0.0955		
5128	4	23.5980	16.8647	6.7333	14+0+0	14	0.0002	3.1	8877780	0.0010	0.0076	0.0469		
5128	10	21.5375	16.5811	4.9564	17+2+19	38	0.0003	4.3	12314340	0.0006	0.0207	0.0436		
5156	5	22.8218	16.8108	6.0110	15+5+4	24	0.0002	4.0	11455200	0.0008	0.0131	0.0507		
5156	11	21.4601	16.5564	4.9037	16+7+1	24	0.0003	3.1	8877780	0.0011	0.0131	0.0524		
5315	**6**	**22.3037**	**16.5322**	**5.7715**	**15+1+2**	**18**	**0.0002**	**4.1**	**11741580**	**0.0018**	**0.0098**	**0.1184**		
5315	**12**	**21.4475**	**16.4246**	**5.0229**	**18+5+1**	**24**	**0.0006**	**1.5**	**4295700**	**0.0061**	**0.0131**	**0.1419**	0.0642	0.0142

12HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**22.7142**	**16.4113**	**6.3029**	**23+0+0**	**23**	**0.0002**	**3.6**	**10309680**	**0.0022**	**0.0125**	**0.1249**		
4704	**7**	**21.3624**	**16.5443**	**4.8181**	**16+0+0**	**16**	**0.0001**	**3.8**	**10882440**	**0.0021**	**0.0087**	**0.1260**		
4869	**2**	**22.6428**	**16.4529**	**6.1899**	**9+0+5**	**14**	**0.0001**	**3.8**	**10882440**	**0.0016**	**0.0076**	**0.0933**		
4869	**8**	**21.7243**	**16.5109**	**5.2134**	**18+5+0**	**23**	**0.0002**	**3.6**	**10309680**	**0.0015**	**0.0125**	**0.0851**		
5067	3	24.0372	16.5959	7.4413	16+1+1	18	0.0001	4.2	12027960	0.0010	0.0098	0.1058		
5067	9	22.1453	16.5942	5.5511	27+1+0	28	0.0003	3.2	9164160	0.0022	0.0153	0.1108		
5128	4	23.3250	16.3921	6.9329	14+0+0	14	0.0002	3.1	8877780	0.0011	0.0076	0.0546		
5128	10	21.5012	16.4628	5.0384	17+2+0	19	0.0002	4.3	12314340	0.0008	0.0104	0.0540		
5156	5	22.8193	16.5389	6.2804	15+0+0	15	0.0001	4.0	11455200	0.0009	0.0082	0.0589		
5156	11	21.8767	16.4888	5.3879	37+3+0	40	0.0005	3.1	8877780	0.0015	0.0218	0.0742		
5315	**6**	**22.4601**	**16.4983**	**5.9618**	**14+2+0**	**16**	**0.0001**	**4.1**	**11741580**	**0.0020**	**0.0087**	**0.1271**		
5315	**12**	**22.0267**	**16.4826**	**5.5441**	**34+1+2**	**37**	**0.0009**	**1.5**	**4295700**	**0.0069**	**0.0202**	**0.1620**	0.0764	0.0149

Data in bold letters = excluded for not meeting barrier integrity criteria

15HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**22.7681**	**16.4388**	**6.3293**	**33+2+0**	**35**	**0.0003**	**3.6**	**10309680**	**0.0026**	**0.0191**	**0.1440**		
4704	**7**	**21.5599**	**16.4760**	**5.0839**	**35+1+0**	**36**	**0.0003**	**3.8**	**10882440**	**0.0025**	**0.0196**	**0.1457**		
4869	**2**	**22.6764**	**16.4412**	**6.2352**	**36+0+0**	**36**	**0.0003**	**3.8**	**10882440**	**0.0019**	**0.0196**	**0.1129**		
4869	**8**	**21.9583**	**16.4610**	**5.4973**	**31+5+0**	**36**	**0.0003**	**3.6**	**10309680**	**0.0019**	**0.0196**	**0.1048**		
5067	3	23.8732	16.4534	7.4198	30+2+3	35	0.0003	4.2	12027960	0.0013	0.0191	0.1249		
5067	9	22.3426	16.4824	5.8602	36+0+0	36	0.0004	3.2	9164160	0.0026	0.0196	0.1304		
5128	4	23.5768	16.6033	6.9735	38+0+1	39	0.0004	3.1	8877780	0.0016	0.0213	0.0758		
5128	10	21.7028	16.3826	5.3202	35+1+2	38	0.0003	4.3	12314340	0.0011	0.0207	0.0747		
5156	5	22.8725	16.6016	6.2709	34+3+4	41	0.0004	4.0	11455200	0.0013	0.0224	0.0813		
5156	11	22.0555	16.4219	5.6336	28+2+4	34	0.0004	3.1	8877780	0.0019	0.0186	0.0928		
5315	**6**	**22.4823**	**16.4900**	**5.9923**	**34+0+10**	**44**	**0.0004**	**4.1**	**11741580**	**0.0024**	**0.0240**	**0.1511**		
5315	**12**	**22.3892**	**16.5393**	**5.8499**	**39+0+0**	**39**	**0.0009**	**1.5**	**4295700**	**0.0078**	**0.0213**	**0.1833**	0.0967	0.0144

18 HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**22.8593**	**16.5431**	**6.3162**	**34+0+0**	**34**	**0.0003**	**3.6**	**10309680**	**0.0029**	**0.0186**	**0.1626**		
4704	**7**	**22.3593**	**16.3542**	**6.0051**	**37+0+1**	**38**	**0.0003**	**3.8**	**10882440**	**0.0028**	**0.0207**	**0.1664**		
4869	**2**	**22.8085**	**16.5613**	**6.2472**	**36+0+1**	**37**	**0.0003**	**3.8**	**10882440**	**0.0022**	**0.0202**	**0.1331**		
4869	**8**	**23.0765**	**16.6029**	**6.4736**	**36+0+5**	**41**	**0.0004**	**3.6**	**10309680**	**0.0023**	**0.0224**	**0.1271**		
5067	3	23.9803	16.5143	7.4660	31+2+0	33	0.0003	4.2	12027960	0.0016	0.0180	0.1429		
5067	9	23.3502	16.4659	6.8843	39+0+0	39	0.0004	3.2	9164160	0.0030	0.0213	0.1517		
5128	4	23.3419	16.4272	6.9147	34+0+0	34	0.0004	3.1	8877780	0.0019	0.0186	0.0944		
5128	10	22.7104	16.4341	6.2763	36+3+0	39	0.0003	4.3	12314340	0.0014	0.0213	0.0960		
5156	5	22.8979	16.5950	6.3029	39+4+0	43	0.0004	4.0	11455200	0.0017	0.0235	0.1048		
5156	11	23.2507	16.5451	6.7056	28+0+1	29	0.0003	3.1	8877780	0.0022	0.0158	0.1086		
5315	**6**	**22.5724**	**16.5689**	**6.0035**	**36+1+0**	**37**	**0.0003**	**4.1**	**11741580**	**0.0027**	**0.0202**	**0.1713**		
5315	**12**	**23.2774**	**16.4111**	**6.8663**	**26+0+1**	**27**	**0.0006**	**1.5**	**4295700**	**0.0085**	**0.0147**	**0.1981**	0.1164	0.0142

Data in bold letters = excluded for not meeting barrier integrity criteria

21HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**22.7410**	**16.4332**	**6.3078**	**44+1+6**	**51**	**0.0005**	**3.6**	**10309680**	**0.0034**	**0.0278**	**0.1904**		
4704	**7**	**22.6681**	**16.6459**	**6.0222**	**37+0+0**	**37**	**0.0003**	**3.8**	**10882440**	**0.0031**	**0.0202**	**0.1866**		
4869	**2**	**22.6776**	**16.4595**	**6.2181**	**37+0+4**	**41**	**0.0004**	**3.8**	**10882440**	**0.0026**	**0.0224**	**0.1555**		
4869	**8**	**23.0565**	**16.5187**	**6.5378**	**35+0+5**	**40**	**0.0004**	**3.6**	**10309680**	**0.0026**	**0.0218**	**0.1489**		
5067	3	23.7668	16.3779	7.3889	39+0+2	41	0.0003	4.2	12027960	0.0019	0.0224	0.1653		
5067	9	23.4731	16.5526	6.9205	40+0+0	40	0.0004	3.2	9164160	0.0035	0.0218	0.1735		
5128	4	23.4155	16.4769	6.9386	42+0+0	42	0.0005	3.1	8877780	0.0024	0.0229	0.1173		
5128	10	22.6734	16.3448	6.3286	33+0+0	33	0.0003	4.3	12314340	0.0017	0.0180	0.1140		
5156	5	22.7688	16.4592	6.3096	43+2+0	45	0.0004	4.0	11455200	0.0021	0.0246	0.1293		
5156	11	23.2049	16.5295	6.6754	42+0+3	45	0.0005	3.1	8877780	0.0027	0.0246	0.1331		
5315	**6**	**22.3219**	**16.3626**	**5.9593**	**41+4+0**	**45**	**0.0004**	**4.1**	**11741580**	**0.0031**	**0.0246**	**0.1959**		
5315	**12**	**23.3986**	**16.4643**	**6.9343**	**38+3+3**	**44**	**0.0010**	**1.5**	**4295700**	**0.0095**	**0.0240**	**0.2221**	0.1388	0.0144

24HR

Donor ID	Cell No.	Vial + Sample (g)	Vial (g)	Receptor Fluid (g)	DPM / Sample	DPM / Sample	%Dose	Dose (mg)	Dose (DPM)	Cumulative % Dose	µg Equ. D6 per cm^2	Cumulative ug Eq.D6/cm^2	Average Cumulative ug Eq.D6/cm^2	SEM
4704	**1**	**22.8934**	**16.5670**	**6.3264**	**57+6+6**	**69**	**0.0007**	**3.6**	**10309680**	**0.0041**	**0.0376**	**0.2281**		
4704	**7**	**22.5485**	**16.4473**	**6.1012**	**42+3+2**	**47**	**0.0004**	**3.8**	**10882440**	**0.0036**	**0.0256**	**0.2122**		
4869	**2**	**22.7276**	**16.4908**	**6.2368**	**32+1+0**	**33**	**0.0003**	**3.8**	**10882440**	**0.0029**	**0.0180**	**0.1735**		
4869	**8**	**23.1219**	**16.5550**	**6.5669**	**41+4+4**	**49**	**0.0005**	**3.6**	**10309680**	**0.0031**	**0.0267**	**0.1757**		
5067	3	23.9895	16.5897	7.3998	27+2+0	29	0.0002	4.2	12027960	0.0022	0.0158	0.1811		
5067	9	23.5816	16.6170	6.9646	39+2+2	43	0.0005	3.2	9164160	0.0039	0.0235	0.1970		
5128	4	23.3453	16.4002	6.9451	41+0+0	41	0.0005	3.1	8877780	0.0029	0.0224	0.1397		
5128	10	22.8206	16.4507	6.3699	39+5+7	51	0.0004	4.3	12314340	0.0021	0.0278	0.1419		
5156	5	22.9640	16.6331	6.3309	27+0+0	27	0.0002	4.0	11455200	0.0023	0.0147	0.1440		
5156	11	23.2798	16.4754	6.8044	36+8+1	45	0.0005	3.1	8877780	0.0033	0.0246	0.1577		
5315	**6**	**22.5536**	**16.5424**	**6.0112**	**39+0+6**	**45**	**0.0004**	**4.1**	**11741580**	**0.0034**	**0.0246**	**0.2204**		
5315	**12**	**23.4686**	**16.5387**	**6.9299**	**31+5+7**	**43**	**0.0010**	**1.5**	**4295700**	**0.0105**	**0.0235**	**0.2455**	0.1602	0.0137

Data in bold letters = excluded for not meeting barrier integrity criteria

Dosing solution: **Neat ^{14}C-D6= 1.29 µCi/mg 2863800 DPM/mg**

Sample = TEAH + skin sample

Donor ID	Cell No.	Vial+TEAH + skin(g)	Vial (g)	Sample Wt.(g)	Rep. I (g)	Rep.II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Avg. DPM/g	Total DPM I	Total DPM II	Avg. DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**19.2533**	**17.4285**	**1.8248**	**0.2258**	**0.2162**	**31506**	**29927**	**139531**	**138423**	**138977**	**254615**	**252594**	**253605**	**3.6**	**10309680**	**2.4599**	**2.4460**	**0.80**
4704	**7**	**19.1865**	**17.3730**	**1.8135**	**0.2244**	**0.2327**	**32748**	**33962**	**145936**	**145948**	**145942**	**264655**	**264676**	**264665**	**3.8**	**10882440**	**2.4320**		**0.01**
4869	**2**	**19.0919**	**17.2861**	**1.8058**	**0.2430**	**0.2486**	**16679**	**17382**	**68638**	**69920**	**69279**	**123946**	**126261**	**125103**	**3.8**	**10882440**	**1.1496**	**2.8343**	**1.85**
4869	**8**	**19.0576**	**17.3180**	**1.7396**	**0.2256**	**0.2447**	**59190**	**66870**	**262367**	**273273**	**267820**	**456414**	**475386**	**465900**	**3.6**	**10309680**	**4.5191**		**4.07**
5067	3	19.2554	17.4489	1.8065	0.2302	0.2439	58057	64784	252202	265617	258910	455604	479837	467720	4.2	12027960	3.8886	3.0361	5.18
5067	9	19.2552	17.4417	1.8135	0.2143	0.2186	24096	23662	112441	108243	110342	203911	196299	200105	3.2	9164160	2.1836		3.80
5128	4	19.2259	17.4426	1.7833	0.2171	0.2373	25164	28715	115910	121007	118458	206702	215792	211247	3.1	8877780	2.3795	4.4112	4.30
5128	10	19.5389	17.3512	2.1877	0.2221	0.2347	82360	83201	370824	354499	362662	811252	775538	793395	4.3	12314340	6.4429		4.50
5156	5	19.1339	17.3836	1.7503	0.2230	0.2275	16705	17308	74910	76079	75495	131116	133161	132138	4.0	11455200	1.1535	1.6005	1.55
5156	11	18.8575	17.0730	1.7845	0.2265	0.2345	22808	24161	100698	103032	101865	179695	183861	181778	3.1	8877780	2.0476		2.29
5315	**6**	**19.1586**	**17.3859**	**1.7727**	**0.2216**	**0.2262**	**32631**	**32420**	**147252**	**143324**	**145288**	**261033**	**254071**	**257552**	**4.1**	**11741580**	**2.1935**	**1.1461**	**2.70**
5315	**12**	**19.1372**	**17.3323**	**1.8049**	**0.2245**	**0.2410**	**524**	**570**	**2334**	**2365**	**2350**	**4213**	**4269**	**4241**	**1.5**	**4295700**	**0.0987**		**1.32**

Data in bold letters = excluded for not meeting barrier integrity criteria

Dosing solution: **Neat ^{14}C-D6= 1.29 µCi/mg 2863800 DPM/mg**

Sample = toluene used for extraction

Donor ID	Cell No.	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep.II(g)	DPM I	DPM II	DPMI/g	DPMII/g	Average DPM/g	Total DPM I	Total DPM II	Avg. DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**25.1346**	**16.5665**	**8.5681**	**0.2509**	**0.2493**	**8**	**0**	**32**	**0**	**16**	**273**	**0**	**137**	**3.6**	**10309680**	**0.0013**	**0.0049**	**200.0**
4704	**7**	**25.0266**	**16.5239**	**8.5027**	**0.2458**	**0.2465**	**29**	**25**	**118**	**101**	**110**	**1003**	**862**	**933**	**3.8**	**10882440**	**0.0086**		**15.1**
4869	**2**	**24.9855**	**16.3897**	**8.5958**	**0.2521**	**0.2469**	**12**	**9**	**48**	**36**	**42**	**409**	**313**	**361**	**3.8**	**10882440**	**0.0033**	**0.0499**	**26.5**
4869	**8**	**25.1812**	**16.5598**	**8.6214**	**0.2487**	**0.2514**	**290**	**287**	**1166**	**1142**	**1154**	**10053**	**9842**	**9948**	**3.6**	**10309680**	**0.096**		**2.1**
5067	3	25.0294	16.4815	8.5479	0.2550	0.2477	22	20	86	81	84	737	690	714	4.2	12027960	0.006	0.0134	6.6
5067	9	25.0879	16.5294	8.5585	0.2448	0.2477	50	60	204	242	223	1748	2073	1911	3.2	9164160	0.021		17.0
5128	4	24.9276	16.3199	8.6077	0.2442	0.2354	21	20	86	85	85	740	731	736	3.1	8877780	0.008	0.1514	1.2
5128	10	25.0745	16.5558	8.5187	0.2633	0.2541	1129	1074	4288	4227	4257	36527	36006	36267	4.3	12314340	0.295		1.4
5156	5	25.0046	16.4818	8.5228	0.2427	0.2474	16	20	66	81	73	562	689	625	4.0	11455200	0.005	0.0126	20.3
5156	11	25.1595	16.5566	8.6029	0.2544	0.2517	57	46	224	183	203	1928	1572	1750	3.1	8877780	0.020		20.3
5315	**6**	**25.9689**	**16.6010**	**9.3679**	**0.2467**	**0.2467**	**1777**	**1791**	**7203**	**7260**	**7231**	**67478**	**68009**	**67744**	**4.1**	**11741580**	**0.577**	**0.2885**	**0.8**
5315	**12**	**25.1906**	**16.5467**	**8.6439**	**0.2504**	**0.2523**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**1.5**	**4295700**	**0.000**		**#DIV/0!**

Data in bold letters = excluded for not meeting barrier integrity criteria

Dosing solution: **Neat ^{14}C-D6= 1.29 µCi/mg 2863800 DPM/mg**

Sample = toluene used for extraction

Donor ID	Cell No.	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Avg. DPM/g	Total DPM I	Total DPM II	Avg. DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**25.0892**	**16.5629**	**8.5263**	**0.2501**	**0.2479**	**122615**	**121264**	**490263.9**	**489165**	**489714**	**4180137**	**4170767**	**4175452**	**3.6**	**10309680**	**40.5003**	**37.9878**	**0.22**
4704	**7**	**24.8208**	**16.5082**	**8.3126**	**0.2460**	**0.2497**	**114406**	**115807**	**465065**	**463785**	**464425**	**3865900**	**3855255**	**3860578**	**3.8**	**10882440**	**35.4753**		**0.28**
4869	**2**	**25.1009**	**16.5297**	**8.5712**	**0.2406**	**0.2332**	**86228**	**83807**	**358387.4**	**359378**	**358883**	**3071810**	**3080303**	**3076056**	**3.8**	**10882440**	**28.2662**	**33.7353**	**0.28**
4869	**8**	**24.8089**	**16.5450**	**8.2639**	**0.2556**	**0.2409**	**124928**	**117904**	**488763.7**	**489431**	**489097**	**4039094**	**4044611**	**4041853**	**3.6**	**10309680**	**39.2044**		**0.14**
5067	3	24.9851	16.4373	8.5478	0.2504	0.2474	149401	144967	596649.4	585962	591306	5100039	5008686	5054363	4.2	**12027960**	42.0218	46.0887	1.81
5067	9	25.0678	16.5055	8.5623	0.2401	0.2448	128568	131738	535476.9	538145	536811	4584914	4607763	4596338	3.2	**9164160**	50.1556		0.50
5128	4	24.9478	16.4135	8.5343	0.2584	0.2493	102909	99054	398254.6	397329	397792	3398825	3390921	3394873	3.1	**8877780**	38.2401	33.1610	0.23
5128	10	25.0508	16.4621	8.5887	0.2562	0.2571	103180	103492	402732.2	402536	402634	3458946	3457261	3458104	4.3	**12314340**	28.0819		0.05
5156	5	25.0570	16.5052	8.5518	0.2478	0.2466	122579	122255	494669.1	495762	495216	4230311	4239661	4234986	4.0	**11455200**	36.9700	32.5102	0.22
5156	11	24.9219	16.5981	8.3238	0.2452	0.2473	73397	73945	299335.2	299009	299172	2491607	2488894	2490250	3.1	**8877780**	28.0504		0.11
5315	**6**	**24.9512**	**16.5088**	**8.4424**	**0.2509**	**0.2484**	**146925**	**145796**	**585591.9**	**586940**	**586266**	**4943801**	**4955186**	**4949493**	**4.1**	**11741580**	**42.1536**	**21.1252**	**0.23**
5315	**12**	**25.0228**	**16.4488**	**8.5740**	**0.2468**	**0.2499**	**114**	**127**	**461.9125**	**508**	**485**	**3960**	**4357**	**4159**	**1.5**	**4295700**	**0.0968**		**9.54**

Data in bold letters = excluded for not meeting barrier integrity criteria

Dosing solution: **Neat ^{14}C-D6= 1.29 µCi/mg 2863800 DPM/mg**

Sample = ethanol used for extraction

Donor ID	Cell No.	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep.II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Avg. DPM/g	Total DPM I	Total DPM II	Avg. DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**112.63**	**97.50**	**15.13**	**0.2203**	**0.2109**	**91**	**82**	**413**	**389**	**401**	**6250**	**5883**	**6066**	**3.6**	**10309680**	**0.0588**	**0.0352**	**6.05**
4704	**7**	**114.56**	**98.82**	**15.74**	**0.2212**	**0.2078**	**16**	**18**	**72**	**87**	**79**	**1139**	**1363**	**1251**	**3.8**	**10882440**	**0.0115**		**17.98**
4869	**2**	**113.53**	**97.78**	**15.75**	**0.1984**	**0.2121**	**20**	**20**	**101**	**94**	**98**	**1588**	**1485**	**1536**	**3.8**	**10882440**	**0.0141**	**0.3817**	**6.67**
4869	**8**	**114.52**	**98.93**	**15.59**	**0.2285**	**0.2202**	**1149**	**1075**	**5028**	**4882**	**4955**	**78393**	**76109**	**77251**	**3.6**	**10309680**	**0.7493**		**2.96**
5067	3	114.07	98.30	15.77	0.2251	0.2220	24	27	107	122	114	1681	1918	1800	4.2	12027960	0.0150	0.0953	13.15
5067	9	114.14	98.56	15.58	0.2156	0.2230	220	233	1020	1045	1033	15898	16279	16088	3.2	9164160	0.1756		2.37
5128	4	114.07	98.54	15.53	0.2133	0.2137	127	123	595	576	585	9247	8939	9093	3.1	8877780	0.1024	0.6027	3.39
5128	10	114.58	98.17	16.41	0.2308	0.2185	1908	1811	8267	8288	8278	135660	136011	135836	4.3	12314340	1.1031		0.26
5156	5	113.57	98.02	15.55	0.1965	0.2183	9	4	46	18	32	712	285	499	4.0	11455200	0.0044	0.0250	85.70
5156	11	114.49	98.76	15.73	0.2087	0.2188	55	55	264	251	257	4145	3954	4050	3.1	8877780	0.0456		4.73
5315	**6**	**114.83**	**98.53**	**16.30**	**0.2241**	**0.2170**	**16**	**13**	**71**	**60**	**66**	**1164**	**976**	**1070**	**4.1**	**11741580**	**0.0091**	**0.0065**	**17.50**
5315	**12**	**113.61**	**98.27**	**15.34**	**0.2013**	**0.2265**	**0**	**5**	**0**	**22**	**11**	**0**	**339**	**169**	**1.5**	**4295700**	**0.0039**		**200.00**

Data in bold letters = excluded for not meeting barrier integrity criteria

Charcoal Extracts
Extracts of the charcoal basket holders

Dosing solution: Neat ^{14}C-D6= 1.29 µCi/mg 2863800 DPM/mg

Sample = toluene, hexane or ethanol used for extraction

CHARCOAL BASKETS +TEFLON TAPE, 1st EXTRACTION

Donor ID	Cell No.	Vial +sample (g)	Vial (g)	Sample Wt.(g)	Replica I(g)	Replica II(g)	DPM I	DPM II	DPMI/g	DPMII/g	Average DPM/g	Total DPM I	Total DPM II	Average DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**114.06**	**96.88**	**17.18**	**0.2431**	**0.2474**	**51542**	**51852**	**212020**	**209588**	**210804**	**3642499**	**3600717**	**3621608**	**3.6**	**10309680**	**35.128**	**34.647**	**1.15**
4704	**7**	**114.85**	**98.17**	**16.68**	**0.2479**	**0.2483**	**55280**	**55327**	**222993**	**222823**	**222908**	**3719526**	**3716691**	**3718108**	**3.8**	**10882440**	**34.166**		**0.08**
4869	**2**	**113.61**	**97.10**	**16.51**	**0.2488**	**0.2478**	**58432**	**58027**	**234855**	**234169**	**234512**	**3877461**	**3866125**	**3871793**	**3.8**	**10882440**	**35.578**	**36.248**	**0.29**
4869	**8**	**114.84**	**98.52**	**16.32**	**0.2446**	**0.2518**	**57168**	**58596**	**233720**	**232708**	**233214**	**3814316**	**3797803**	**3806059**	**3.6**	**10309680**	**36.917**		**0.43**
5067	3	115.57	98.42	17.15	0.2504	0.248	53432	52867	213387	213173	213280	3659580	3655924	3657752	4.2	12027960	30.410	35.905	0.10
5067	9	114.02	97.23	16.79	0.2483	0.2483	56245	55967	226520	225401	225961	3803276	3784478	3793877	3.2	9164160	41.399		0.50
5128	4	114.74	97.91	16.83	0.2491	0.2444	52790	51688	211923	211489	211706	3566663	3559366	3563014	3.1	8877780	40.134	36.278	0.20
5128	10	117.40	98.44	18.96	0.2478	0.2493	52204	52473	210670	210481	210576	3994301	3990726	3992514	4.3	12314340	32.422		0.09
5156	5	114.39	97.41	16.98	0.2507	0.2481	55198	54690	220176	220435	220305	3738580	3742992	3740786	4.0	11455200	32.656	37.143	0.12
5156	11	114.55	97.04	17.51	0.2479	0.2464	52397	51936	211363	210779	211071	3700974	3690744	3695859	3.1	8877780	41.630		0.28
5315	**6**	**114.79**	**97.58**	**17.21**	**0.2499**	**0.2490**	**57940**	**57480**	**231853**	**230843**	**231348**	**3990186**	**3972814**	**3981500**	**4.1**	**11741580**	**33.909**	**57.137**	**0.44**
5315	**12**	**113.52**	**96.58**	**16.94**	**0.2491**	**0.2477**	**50707**	**50537**	**203561**	**204025**	**203793**	**3448320**	**3456184**	**3452252**	**1.5**	**4295700**	**80.365**		**0.23**

CHARCOAL BASKETS +TEFLON TAPE 2nd EXTRACTION

Donor ID	Cell No.	Vial +sample (g)	Vial (g)	Sample Wt.(g)	Replica I(g)	Replica II(g)	DPM I	DPM II	DPMI/g	DPMII/g	Average DPM/g	Total DPM I	Total DPM II	Average DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**114.9594**	**98.1004**	**16.8590**	**0.2524**	**0.2531**	**7480**	**7446**	**29635**	**29419**	**29527**	**499625**	**495978**	**497802**	**3.6**	**10309680**	**4.828**	**3.288**	**0.73**
4704	**7**	**115.1659**	**98.2611**	**16.9048**	**0.2534**	**0.2450**	**2854**	**2751**	**11263**	**11229**	**11246**	**190396**	**189817**	**190106**	**3.8**	**10882440**	**1.747**		**0.30**
4869	**2**	**115.2821**	**98.3451**	**16.9370**	**0.2493**	**0.2461**	**2820**	**2784**	**11312**	**11312**	**11312**	**191586**	**191599**	**191593**	**3.8**	**10882440**	**1.761**	**1.979**	**0.01**
4869	**8**	**114.9695**	**98.1512**	**16.8183**	**0.2477**	**0.2425**	**3336**	**3268**	**13468**	**13476**	**13472**	**226507**	**226648**	**226578**	**3.6**	**10309680**	**2.198**		**0.06**
5067	3	114.9235	97.8189	17.1046	0.2477	0.2159	3141	2741	12681	12696	12688	216898	217155	217026	4.2	12027960	1.804	2.713	0.12
5067	9	118.4479	96.8183	21.6296	0.2506	0.2485	3858	3801	15395	15296	15345	332989	330841	331915	3.2	9164160	3.622		0.65
5128	4	113.9139	97.2148	16.6991	0.2517	0.2497	3618	3616	14374	14481	14428	240037	241826	240932	3.1	8877780	2.714	2.183	0.74
5128	10	112.6820	97.6456	15.0364	0.2349	0.2472	3164	3357	13470	13580	13525	202534	204196	203365	4.3	12314340	1.651		0.82
5156	5	116.6225	98.0461	18.5764	0.2641	0.2451	2804	2640	10617	10771	10694	197229	200089	198659	4.0	11455200	1.734	1.806	1.44
5156	11	113.9394	98.7873	15.1521	0.2463	0.2474	2712	2718	11011	10986	10999	166839	166465	166652	3.1	8877780	1.877		0.22
5315	**6**	**113.3038**	**96.4785**	**16.8253**	**0.2543**	**0.2495**	**3575**	**3488**	**14058**	**13980**	**14019**	**236533**	**235217**	**235875**	**4.1**	**11741580**	**2.009**	**4.386**	**0.56**
5315	**12**	**120.7337**	**97.8703**	**22.8634**	**0.2507**	**0.2516**	**3161**	**3221**	**12609**	**12802**	**12705**	**288278**	**292699**	**290488**	**1.5**	**4295700**	**6.762**		**1.52**

Data in bold letters = excluded for not meeting barrier integrity criteria

Rounding errors may occur due to electronic handling of numbers

CHARCOAL BASKETS +TEFLON TAPE 3rd EXTRACTION IN HEXANE

Donor ID	Cell No.	Vial +sample (g)	Vial (g)	Sample Wt.(g)	Replica I(g)	Replica II(g)	DPM I	DPM II	DPMI/g	DPMII/g	Average DPM/g	Total DPM I	Total DPM II	Average Total DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**116.5562**	**99.8673**	**16.6889**	**0.1733**	**0.1747**	**639**	**663**	**3687**	**3795**	**3741**	**61536**	**63336**	**62436**	**3.6**	**10309680**	**0.606**	**0.450**	**2.88**
4704	**7**	**118.4437**	**101.8584**	**16.5853**	**0.1614**	**0.1618**	**318**	**306**	**1970**	**1891**	**1931**	**32677**	**31367**	**32022**	**3.8**	**10882440**	**0.294**		**4.09**
4869	**2**	**117.0692**	**100.7669**	**16.3023**	**0.1676**	**0.1585**	**337**	**321**	**2011**	**2025**	**2018**	**32780**	**33016**	**32898**	**3.8**	**10882440**	**0.302**	**0.312**	**0.72**
4869	**8**	**118.9877**	**102.2923**	**16.6954**	**0.1424**	**0.1598**	**288**	**311**	**2022**	**1946**	**1984**	**33766**	**32492**	**33129**	**3.6**	**10309680**	**0.321**		**3.84**
5067	3	118.7989	102.1945	16.6044	0.1523	0.1614	400	425	2626	2633	2630	43610	43723	43666	4.2	12027960	0.363	0.410	0.26
5067	9	117.8388	101.0282	16.8106	0.1544	0.1597	379	404	2455	2530	2492	41264	42527	41895	3.2	9164160	0.457		3.01
5128	4	117.9570	101.5407	16.4163	0.1621	0.1635	356	378	2196	2312	2254	36053	37953	37003	3.1	8877780	0.417	0.357	5.14
5128	10	118.7016	102.1683	16.5333	0.1255	0.1612	278	356	2215	2208	2212	36624	36513	36568	4.3	12314340	0.297		0.30
5156	5	117.6201	100.9340	16.6861	0.1592	0.1599	326	331	2048	2070	2059	34169	34541	34355	4.0	11455200	0.300	0.351	1.08
5156	11	116.9913	100.9940	15.9973	0.1261	0.1576	292	339	2316	2151	2233	37044	34410	35727	3.1	8877780	0.402		7.37
5315	**6**	**117.9581**	**101.2292**	**16.7289**	**0.1555**	**0.1557**	**299**	**320**	**1923**	**2055**	**1989**	**32167**	**34382**	**33274**	**4.1**	**11741580**	**0.283**	**0.482**	**6.66**
5315	**12**	**111.7847**	**100.3515**	**11.4332**	**0.1527**	**0.1495**	**393**	**379**	**2574**	**2535**	**2554**	**29425**	**28985**	**29205**	**1.5**	**4295700**	**0.680**		**1.51**

Data in bold letters = excluded for not meeting barrier integrity criteria

Cells that skin passed integrity test: Oxidized Charcoal

Donor ID	Cell No.	Charcoal Wt. (g)	Rep. I (g)	Rep. II (g)	Rep. III (g)	DPM I*	DPM II*	DPM III*	Total DPM I	Total DPM II	Total DPM III	Average total DPM	Dose (mg)	Dose (DPM)	%Dose	% RR
5067	3	0.5	0.1140	0.1254	0.1175	24852	18994	19696	109000	75734	83813	89515	4.2	12027960	0.74	37.16
5067	9	0.5	0.1192	0.0998	0.1264	21437	21061	24447	89920	105516	96705	97380	3.2	9164160	1.06	16.02
5128	4	0.5	0.1028	0.1015	0.1011	19922	21617	22782	96897	106488	112671	105352	3.1	8877780	1.19	9.10
5128	10	0.5	0.1195	0.1028	0.0923	23504	26227	23009	98343	127563	124642	116850	4.3	12314340	0.95	25.01
5156	5	0.5	0.1116	0.0945	0.0980	17272	19023	18772	77384	100651	95776	91270	4.0	11455200	0.80	25.49
5156	11	0.5	0.1109	0.1065	0.0902	24319	28609	19173	109644	134315	106280	116746	3.1	8877780	1.32	21.13

*DPM'S recorded are DPM minus the average DPM's for three blank charcoal samples (Blank =41DPM)

Holders (for charcoal baskets) 1st extraction in ethanol

Donor ID	Cell No.	Vial +sample (g)	Vial (g)	Sample Wt.(g)	Replica I(g)	Replica II(g)	DPM I	DPM II	DPMI/g	DPMII/g	Average DPM/g	Total DPM I	Total DPM II	Average Total DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**115.12**	**98.39**	**16.73**	**0.2219**	**0.2208**	**7109**	**7067**	**32037**	**32006**	**32022**	**535978**	**535466**	**535722**	**3.6**	**10309680**	**5.196**	**5.9971**	**0.10**
4704	**7**	**113.57**	**97.70**	**15.87**	**0.2199**	**0.2135**	**10154**	**10046**	**46176**	**47054**	**46615**	**732806**	**746745**	**739775**	**3.8**	**10882440**	**6.798**		**1.88**
4869	**2**	**112.27**	**97.16**	**15.11**	**0.2254**	**0.2246**	**21283**	**20868**	**94423**	**92912**	**93668**	**1426735**	**1403898**	**1415317**	**3.8**	**10882440**	**13.006**	**10.6699**	**1.61**
4869	**8**	**114.93**	**97.81**	**17.12**	**0.2199**	**0.2197**	**11025**	**11038**	**50136**	**50241**	**50189**	**858336**	**860130**	**859233**	**3.6**	**10309680**	**8.334**		**0.21**
5067	3	114.00	98.32	15.68	0.2064	0.2174	12436	13009	60252	59839	60045	944750	938276	941513	4.2	12027960	7.828	7.7100	0.69
5067	9	113.91	97.88	16.03	0.2257	0.2226	9771	9687	43292	43518	43405	693970	697586	695778	3.2	9164160	7.592		0.52
5128	4	114.26	97.58	16.68	0.2198	0.2276	8970	9314	40810	40923	40866	680708	682590	681649	3.1	8877780	7.678	10.6107	0.28
5128	10	114.55	97.72	16.83	0.2116	0.2142	21028	21166	99376	98814	99095	1672501	1663043	1667772	4.3	12314340	13.543		0.57
5156	5	113.17	97.38	15.79	0.2084	0.2244	11344	12376	54434	55152	54793	859509	870842	865176	4.0	11455200	7.553	8.0208	1.31
5156	11	113.63	98.00	15.63	0.2209	0.2200	10664	10595	48275	48159	48217	754542	752727	753634	3.1	8877780	8.489		0.24
5315	**6**	**113.24**	**97.80**	**15.44**	**0.1923**	**0.2265**	**10400**	**12293**	**54082**	**54274**	**54178**	**835029**	**837986**	**836508**	**4.1**	**11741580**	**7.124**	**5.0478**	**0.35**
5315	**12**	**112.54**	**98.14**	**14.40**	**0.2137**	**0.2243**	**1879**	**2004**	**8793**	**8934**	**8864**	**126615**	**128656**	**127636**	**1.5**	**4295700**	**2.971**		**1.60**

Holders (for charcoal baskets) 2nd extraction in hexane

Donor ID	Cell No.	Vial +sample (g)	Vial (g)	Sample Wt.(g)	Replica I(g)	Replica II(g)	DPM I	DPM II	DPMI/g	DPMII/g	Average DPM/g	Total DPM I	Total DPM II	Average Total DPM	Dose (mg)	Dose (DPM)	%Dose	Average %Dose	% RR
4704	**1**	**118.9764**	**99.5802**	**19.40**	**0.1281**	**0.1276**	**53**	**49**	**414**	**384**	**399**	**8025**	**7448**	**7737**	**3.6**	**10309680**	**0.075**	**0.0966**	**7.45**
4704	**7**	**118.4903**	**99.0074**	**19.48**	**0.2198**	**0.2182**	**140**	**149**	**637**	**683**	**660**	**12409**	**13304**	**12857**	**3.8**	**10882440**	**0.118**		**6.96**
4869	**2**	**118.0797**	**98.7001**	**19.38**	**0.2228**	**0.2222**	**288**	**291**	**1293**	**1310**	**1301**	**25051**	**25380**	**25215**	**3.8**	**10882440**	**0.232**	**0.1789**	**1.31**
4869	**8**	**118.7603**	**99.2966**	**19.46**	**0.2195**	**0.2164**	**132**	**159**	**601**	**735**	**668**	**11705**	**14301**	**13003**	**3.6**	**10309680**	**0.126**		**19.97**
5067	3	119.1945	99.6862	19.51	0.2047	0.2055	166	161	811	783	797	15820	15284	15552	4.2	12027960	0.129	0.1254	3.45
5067	9	117.8463	98.3437	19.50	0.193	0.2105	114	116	591	551	571	11520	10747	11133	3.2	9164160	0.121		6.94
5128	4	118.8865	99.5033	19.38	0.2175	0.2145	99	102	455	476	465	8823	9217	9020	3.1	8877780	0.102	0.1523	4.37
5128	10	118.0753	98.4567	19.62	0.2114	0.2142	286	256	1353	1195	1274	26542	23447	24994	4.3	12314340	0.203		12.38
5156	5	118.5042	99.1900	19.31	0.22	0.2111	147	133	668	630	649	12905	12169	12537	4.0	11455200	0.109	0.1193	5.88
5156	11	118.1956	98.5465	19.65	0.2195	0.2209	135	122	615	552	584	12085	10852	11468	3.1	8877780	0.129		10.75
5315	**6**	**118.6483**	**99.1532**	**19.50**	**0.2176**	**0.2103**	**146**	**138**	**671**	**656**	**664**	**13080**	**12793**	**12937**	**4.1**	**11741580**	**0.110**	**0.0798**	**2.22**
5315	**12**	**118.8481**	**99.3099**	**19.54**	**0.2178**	**0.2154**	**23**	**24**	**106**	**111**	**109**	**2063**	**2177**	**2120**	**1.5**	**4295700**	**0.049**		**5.36**

Data in bold letters = excluded for not meeting barrier integrity criteria

Charcoal Extracts
Extracts of the charcoal basket holders

Charcoal cumulative (percent of applied dose)

Donor ID	Cell No.	1st extraction %Dose	2nd extraction % Dose	3rd extraction % Dose	Oxidizer % Dose	Cumulative % Dose	Average % Dose
4704	**1**	**35.128**	**4.828**	**0.606**	**ND**	**40.562**	
4704	**7**	**34.166**	**1.747**	**0.294**	**ND**	**36.207**	**38.385**
4869	**2**	**35.578**	**1.761**	**0.302**	**ND**	**37.641**	
4869	**8**	**36.917**	**2.198**	**0.321**	**ND**	**39.436**	**38.539**
5067	3	30.410	1.804	0.363	0.74	33.322	
5067	9	41.399	3.622	0.457	1.06	46.541	39.931
5128	4	40.134	2.714	0.417	1.19	44.451	
5128	10	32.422	1.651	0.297	0.95	35.319	39.885
5156	5	32.656	1.734	0.300	0.80	35.487	
5156	11	41.630	1.877	0.402	1.32	45.225	40.356
5315	**6**	**33.909**	**2.009**	**0.283**	**ND**	**36.202**	
5315	**12**	**80.365**	**6.762**	**0.680**	**ND**	**87.807**	**62.005**
						Average	40.057
						SD	0.259
						SEM	0.150

ND= not determined

Data in bold letters = excluded for not meeting barrier integrity criteria

Holders cumulative (percent of applied dose)

Donor ID	Cell No.	1st extraction .%Dose	2nd extraction % Dose	Cumulative % Dose	Average % Dose
4704	**1**	**5.196**	**0.075**	**5.271**	
4704	**7**	**6.798**	**0.118**	**6.916**	**6.094**
4869	**2**	**13.006**	**0.232**	**13.237**	
4869	**8**	**8.334**	**0.126**	**8.460**	**10.849**
5067	3	7.828	0.129	7.957	
5067	9	7.592	0.121	7.714	7.835
5128	4	7.678	0.102	7.780	
5128	10	13.543	0.203	13.746	10.763
5156	5	7.553	0.109	7.662	
5156	11	8.489	0.129	8.618	8.140
5315	**6**	**7.124**	**0.110**	**7.234**	
5315	**12**	**2.971**	**0.049**	**3.021**	**5.128**
				Average	8.913
				SD	1.610
				SEM	0.929

Cumulative % dose appearing in receptor fluid

NEAT ^{14}C-D6

Donor ID	% Dose	Avg % Dose (N=3)	
4704	**0.0041**	**0.004**	
4704	**0.0036**		**eliminated**
4869	**0.0029**	**0.003**	
4869	**0.0031**		**eliminated**
5067	0.0022	0.003	
5067	0.0039		
5128	0.0029	0.002	
5128	0.0021		
5156	0.0023	0.003	
5156	0.0033		
5315	**0.0034**	**0.007**	
5315	**0.0105**		**eliminated**
	Average	0.003	
	St. Dev.	0.0003	
	St. Error	0.0002	

% Dose appearing in the skin (skin/Saran wrap)

NEAT ^{14}C-D6

Donor ID	Skin % Dose	Skin Avg % Dose (N=3)	Saran Wrap % Dose	Saran Wrap Avg % Dose (N=3)	% Dose in Skin	Avg. % Dose in Skin	
4704	**2.4599**	**2.446**	**0.0013**	**0.005**	**2.4612**	**2.451**	
4704	**2.4320**		**0.0086**		**2.4406**		**eliminated**
4869	**1.1496**	**2.834**	**0.0033**	**0.050**	**1.1529**	**2.884**	
4869	**4.5191**		**0.0965**		**4.6155**		**eliminated**
5067	3.8886	3.036	0.0059	0.013	3.8945	3.049	
5067	2.1836		0.0208		2.2044		
5128	2.3795	4.411	0.0083	0.151	2.3878	4.563	
5128	6.4429		0.2945		6.7374		
5156	1.1535	1.601	0.0055	0.013	1.1590	1.613	
5156	2.0476		0.0197		2.0673		
5315	**2.1935**	**1.146**	**0.5770**	**0.288**	**2.7705**	**1.435**	
5315	**0.0987**		**0.0000**		**0.0987**		**eliminated**
	Average	3.016	Average	0.059	Average	3.075	
	St. Dev.	1.4054	St. Dev.	0.0799	St. Dev.	1.4749	
	St. Error	0.8114	St. Error	0.0461	St. Error	0.8515	

Data in bold letters = excluded for not meeting barrier integrity criteria

SKIN SURFACE (swabs, tape, and cells, basket holders)

NEAT ^{14}C-D6

Donor ID	% Dose	Avg % Dose (N=3)	
4704	**45.8305**	**44.117**	
4704	**42.4028**		**eliminated**
4869	**41.5176**	**44.966**	
4869	**48.4141**		**eliminated**
5067	49.9937	54.019	
5067	58.0450		
5128	46.1223	44.527	
5128	42.9313		
5156	44.6365	40.675	
5156	36.7142		
5315	**49.3972**	**26.259**	
5315	**3.1214**		**eliminated**
	Average	46.407	
	St. Dev.	6.8679	
	St. Error	3.9652	

CHARCOAL (charcoal, teflon tape, baskets extracts)

NEAT ^{14}C-D6

Donor ID	% Dose	Avg % Dose (N=3)	
4704	**40.5623**	**38.385**	
4704	**36.2073**		**eliminated**
4869	**37.6412**	**38.539**	
4869	**39.4364**		**eliminated**
5067	33.3220	39.931	
5067	46.5407		
5128	44.4514	39.885	
5128	35.3190		
5156	35.4867	40.356	
5156	45.2251		
5315	**36.2017**	**62.005**	
5315	**87.8075**		**eliminated**
	Average	40.057	
	St. Dev.	0.2594	
	St. Error	0.1498	

TOTAL DOSE RECOVERY (% of applied dose)

NEAT ^{14}C-D6

Donor ID	% Recovery	Avg. % Recovery (N=3)	
4704	**88.8581**	**84.956**	
4704	**81.0543**		**eliminated**
4869	**80.3146**	**86.392**	
4869	**92.4692**		**eliminated**
5067	87.2125	97.003	
5067	106.7941		
5128	92.9644	88.977	
5128	84.9897		
5156	81.2844	82.647	
5156	84.0098		
5315	**88.3727**	**89.705**	
5315	**91.0380**		**eliminated**
	Average	89.542	
	St. Dev.	7.1948	
	St. Error	4.1539	

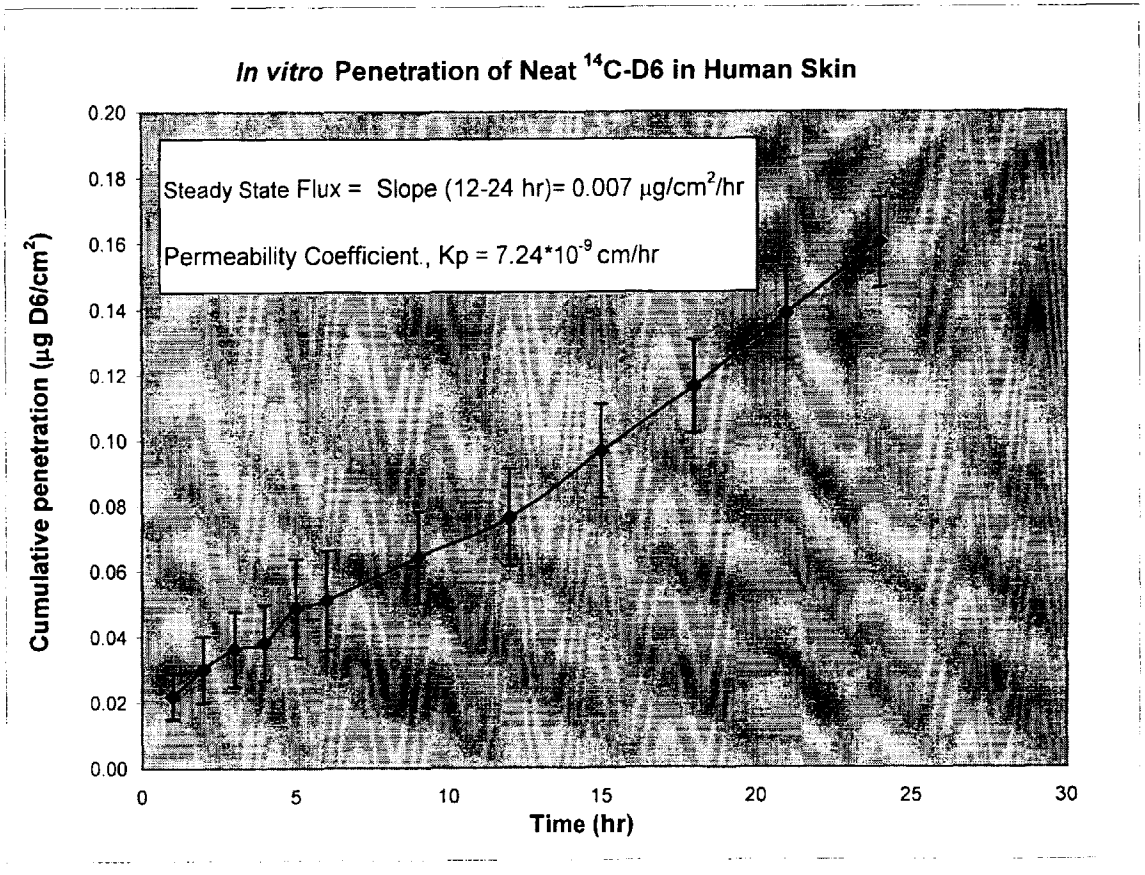
Data in bold letters = excluded for not meeting barrier integrity criteria

APPENDIX B

D_6 Penetration Rate

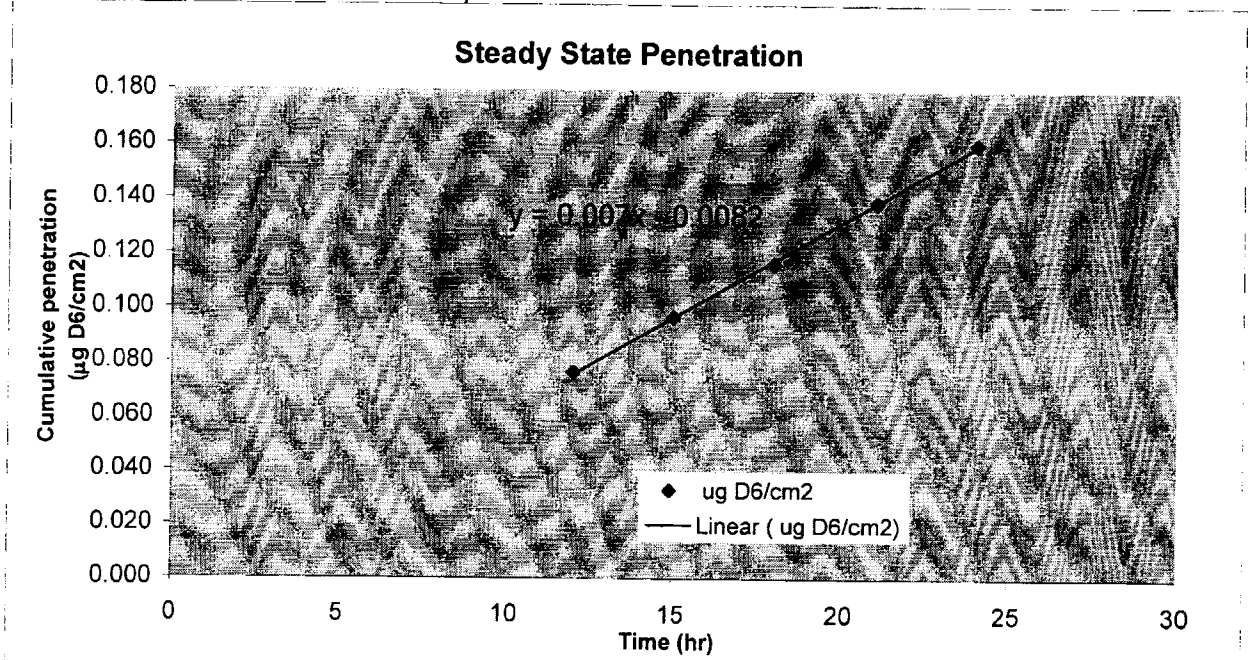
Penetration of ^{14}C-D6 into Receptor Fluid Over Time

Time (hr)	Cumulative µg D6/cm^2 of skin	SEM
1	0.0220	0.0070
2	0.0302	0.0101
3	0.0364	0.0115
4	0.0382	0.0115
5	0.0488	0.0150
6	0.0512	0.0151
9	0.0642	0.0142
12	0.0764	0.0149
15	0.0967	0.0144
18	0.1164	0.0142
21	0.1388	0.0144
24	0.1602	0.0137



Slope of the regression line fitted to a plot of penetration *vs* time at times 12 through 24 hr
(Times where slope is linear and test article present at infinite concentration)

Time (hr)	ug D6/cm^2
12	0.0764
15	0.0967
18	0.1164
21	0.1388
24	0.1602



SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.9997
R Square	0.9994
Adjusted R Square	0.9993
Standard Error	0.0009
Observations	5

ANOVA

	df	*SS*	*MS*	*F*	*ignificance F*
Regression	1	0.004401	0.004401	5395.994	5.56E-06
Residual	3	2.45E-06	8.156E-07		
Total	4	0.004403			

	Coefficients	*andard Erro*	*t Stat*	*P-value*	*Lower 95%*	*Upper 95%*	*ower 95.0%*	*pper 95.0%*
Intercept	-0.00818406	0.00176	-4.6487785	0.01877	-0.0137867	-0.002581	-0.013787	-0.002581
X Variable 1	**0.00699282**	9.52E-05	73.457432	5.56E-06	0.00668987	0.007296	0.00669	0.007296

Slope= Steady State Flux= **0.007** ugD6/cm^2/hr
D6 density @20C= **0.966** g/cm3
Kp= **7.24E-09** cm/hr
r^2 **0.999**

APPENDIX C

METHOD DEVELOPMENT

Non-Regulated Experiments No. 1 and 2: Method Development for *In Vitro* Dermal Absorption of ^{14}C-Dodecamethylcyclohexasiloxane

Experiment No. 1

The objective of Experiment 1 was to estimate efficiency of the washing procedure that was used to remove neat ^{14}C-dodecamethylcyclohexasiloxane (^{14}C-D_6) from the skin surface in DC Study No. 9613 (washing procedure: 1 dry swab followed by 3 soap swabs, 1 dry, 3 ethanol and 1 dry swab).

Data obtained in study No. 9613 showed that 46.407% of the applied ^{14}C-D_6 remained on skin surface after 24 hr of exposure. Also, data from this study showed that 3.075% of the applied dose was associated with the skin samples after completion of washing and tape stripping procedure. It is possible that some of ^{14}C-D_6 that appeared in the skin was a result of inefficient washing and tape stripping procedure, and/or that skin recoveries included some of ^{14}C-D_6 that might spread beyond application site (skin piece mounted in the cell is larger than application site). This experiment was planned to test efficiency of washing procedure immediately after dosing (T=0 hr). Also one piece of skin was placed on film, epidermal side down, immediately after the dose has been washed at T=0hr to visualize possible spreading of ^{14}C-D_6 beyond the application site. A separate set of skin samples were dosed and at T=24hr the application site was washed and tape stripped. Holders that were used to secure the skin in place and confine the application site were removed just prior to washing. After washing and tape stripping was completed, the outer edge of the skin that surrounds the application site was cut-off and analyzed separately from the application site.

Results. Data obtained in the Experiment No. 1 indicated: a) only approximately 62% of applied ^{14}C-D_6 was recovered in skin washes conducted immediately after dosing (T=0 hr); b) approximately 9% of the applied dose appeared in skin after completion of washing procedure at T=0hr; and c) some of ^{14}C-D_6 spread beyond application site at T=0 hr and T= 24 hr (at T=24hr only 0.55% of applied dose was recovered in application site while 2.22% of applied dose was recovered in the outer edge).

Experiment No. 2

In Experiment No. 2 skin was washed using cotton-tipped applicators immediately after dosing without removing the holders in an attempt to reduce possible spreading of test article beyond the application site during the washing procedure and decrease its loss at T=0 hr. Extraction efficiency of ^{14}C-D_6 spiked on cotton-tipped applicators (swabs) in toluene was determined. Also, efficiency of applied tape stripping technique in removing the *stratum corneum* was checked.

Additional cells were set-up to determine the fate of the residual D_6 found in the skin at T=24 hr. In this experiment the application site was washed with soap and water 24 hours after dosing and at that time charcoal baskets were replaced with new ones. Cells were run for an additional 24 hours collecting the receptor fluid. Twenty-four hours after washing the application site (T= 48 hr) holders were removed, skin was washed and tape stripped and charcoal baskets were collected.

Results. Data obtained in the Experiment No. 2 indicated: a) 97-99% of ^{14}C-D_6 spiked on cotton-tipped applicators was extracted in toluene; b) tape stripping may not successfully remove the *stratum corneum* as seen by microscopic examination of skin; c) ^{14}C-D_6 has a tendency to spread beyond the application site as seen on x-ray films; d) approximately 5% of the applied dose still appeared in the skin after completion of washing procedure immediately after dosing (T=0hr); e)^{14}C-D_6 that appeared in the skin after 24hr- wash does not penetrate through the skin but continues to evaporate.

Method Development, Experiment No. 1

^3H-H_2O **1998** **(DPM/mg)**

Donor ID: 4869-001-15 (Ohio Valley Tissue and Skin Center)

Cell #	Vial+ Sample (g)	Vial (g)	Receptor Fluid (g)	Rep.1 (g)	Rep.2 (g)	DPM1	DPM2	DPM1/ sample	DPM2/ sample	Avg.DPM/ sample	Dose (mg)	Dose (DPM)	%Dose	skin thickness µm	Avg. %Dose [2]	St. dev.	C.V.	Treatment after dosing with 14C-D6
1 [1]	17.7488	15.45879	2.2900	0.2380	0.2445	0	0	0	0	0	276.0	551448	0.000	330	0.154	0.029	19.1	Skin wash at T=0 hr
2	17.5429	15.3431	2.1998	0.2400	0.2400	106	106	972	972	972	266.1	531668	0.183	310				Skin wash at T=0 hr
3	18.4038	15.4677	2.9362	0.2438	0.2422	68	74	819	897	858	270.3	540059	0.159	410				Skin wash at T=0 hr
4	17.9497	15.5280	2.4217	0.23969	0.24671	70	73	707	717	712	269.2	537862	0.132	350				Skin wash at T=24 hr
5	18.1300	15.5205	2.6095	0.23775	0.2389	86	93	944	1016	980	272.5	544455	0.180	420				Skin wash at T=24 hr
6	18.0562	15.4638	2.5924	0.24338	0.24064	58	55	618	593	605	261.9	523276	0.116	470				Skin wash at T=24 hr
7	18.6897	15.5012	3.1885	0.2381	0.24677	39	50	522	646	584	279.8	559040	0.104	260	0.363	0.544	149.7	Skin wash at T=0 hr
8	18.5335	15.3765	3.1570	0.23649	0.2391	82	72	1095	951	1023	262.2	523876	0.195	360				Skin wash at T=24 hr
9	18.1958	15.4995	2.6963	0.2401	0.24275	71	58	797	644	721	254.7	508891	0.142	290				Skin wash at T=24 hr
10	18.2963	15.4283	2.8680	0.24024	0.23612	585	617	6984	7494	7239	246.3	492107	1.471	450				Skin wash at T=24 hr
11	18.3910	15.3342	3.0568	0.23738	0.24032	42	42	541	534	538	272.5	544455	0.099	750 [3]				Skin wash at T=24 hr
12	18.8144	15.4777	3.3367	0.23976	0.2451	67	62	932	844	888	262.8	525074	0.169	360				Not dosed

[1] Parafilm under the skin was not removed. However, this piece of skin was used for washing experiment at T=0 hr .

[2] Average for cells No. 2-6, and for cells No. 7-12

[3] Skin piece in cell # 11 is full thickness

Method Development, Experiment No. 2

^3H-H_2O **2886** **(DPM/mg)**

Donor ID: 5636 and 4704 from Ohio Valley Tissue and Skin Center

Donor ID	Cell #	Vial+ Sample (g)	Vial (g)	Receptor Fluid (g)	Rep.1 (g)	Rep.2 (g)	DPM1	DPM2	DPM1/ sample	DPM2/ sample	Avg.DPM/ sample	Dose (mg)	Dose (DPM)	%Dose	skin thickness µm	Avg. %Dose [1]	St. dev.	C.V.	Treatment After dosing with 14C-D6
5636	2	19.5522	17.2608	2.2914	0.3213	0.3536	1943	2153	13857	13952	13904	272.8	787301	1.766	380	1.002	0.486	48.5	Skin not washed
5636	3	19.8634	17.2460	2.6174	0.3279	0.3198	998	1001	7966	8193	8080	245	707070	1.143	200				Skin wash at T=0 hr
4704	4	19.8963	17.2144	2.6819	0.3367	0.3434	535	485	4261	3788	4025	215.9	623087	0.646	200				Skin wash at T=0 hr
5636	5	19.8761	17.2907	2.5854	0.3394	0.3444	472	430	3595	3228	3412	215.9	623087	0.548	380				Skin wash at T=0 hr
5636	6	19.4509	17.1370	2.3139	0.3151	0.3380	737	789	5412	5401	5407	205.9	594227	0.910	320				Skin wash at T=0 hr
4704	10	20.1072	17.2475	2.8597	0.3332	0.3385	192	182	1648	1538	1593	216.4	624530	0.255	340	0.349	0.083	23.6	Skin wash at T=24+48 hr
4704	11	20.0519	17.1352	2.9167	0.3371	0.3427	291	296	2518	2519	2519	213.9	617315	0.408	220				Skin wash at T=24+48 hr
4704	12	19.9918	17.0903	2.9015	0.3301	0.3333	251	256	2206	2229	2217	199.5	575757	0.385	320				Skin wash at T=24+48 hr

[1] Average for cells No. 2-6 and No. 10-12

Method Development, Experiment No. 1

Dosing solution: **Neat ^{14}C-D6= 1.38 µCi/mg 3063600 DPM/mg**

Donor ID	Cell #	Dose (mg)	Dose (uCi)	Dose (mg/cm2)	Dose (uCi/cm2)	Activity
4869	1	4.4	6.07	6.88	9.49	Cells 1-3 were used to test efficiency of washing procedure at T=O hr
	2	3.7	5.11	5.78	7.98	
	3	4.6	6.35	7.19	9.92	
	4	4.6	6.35	7.19	9.92	Cells 4-6 were used test efficiency of washing procedure at T=24 hr and
	5	5.0	6.90	7.81	10.78	if some of ^{14}C-D6 had spread beyond the application site over 24 hr of exposure
	6	5.0	6.90	7.81	10.78	
4869	7	4.8	6.62	7.50	10.35	Skin in cell# 7 was frozen and placed on film with epidermis side down immediatelly after dosing and washing (T=0 hr) to visualize if any ^{14}C-D6 had spread beyond dosing site.
	8	4.3	5.93	6.72	9.27	Skin in cells 8,9, and 11 was washed at T=24 hr, frozen and sectioned.
	9	5.1	7.04	7.97	11.00	
	10	4.5	6.21	7.03	9.70	Skin in cell # 10 was washed, epidermis removed, frozen and sectioned.
	11	5.3	7.31	8.28	11.43	
	12	0.0	0.00	0.00	0.00	Skin in cell # 12 was not dosed. After 24 hr epidermis was removed, skin sectioned, stained and examined under microscope
Average	**Cells 1-11**	**4.8**	**6.60**	**7.47**	**10.31**	
Average	Cells 1-3	4.2	5.8	6.6	9.1	
Average	Cells 4-6	4.9	6.7	7.6	10.5	

Method Development, Experiment No. 2

Dosing solution: **Neat ^{14}C-D6= 1.37 µCi/mg 3041400 DPM/mg**

Donor ID	Cell #	Dose (mg)	Dose (uCi)	Dose (mg/cm2)	Dose (uCi/cm2)	
5636	2	4.4	6.03	6.88	9.42	Skin in cell No. 2 was placed on film immediately after dosing (no washing)
5636	3	2.5	3.43	3.91	5.35	Skin in cells 3,4,5 were used to test efficiency of washing procedure at T=O hr when holder is not removed
4704	4	3.6	4.93	5.63	7.71	
5636	5	6.4	8.77	10.00	13.70	
5636	6	4.7	6.44	7.34	10.06	Skin in cell No. 6 was placed on film immediately after washing the skin with holder in place.
4704	10	4.5	6.17	7.03	9.63	Skin in cells 10,11,12 were used test efficiency of washing procedure at T=24 hr with follow up washing @ 48 hr.
4704	11	4.6	6.30	7.19	9.85	
4704	12	4.6	6.30	7.19	9.85	
Average	**Cells 2-6**	**4.2**	**5.7**	**6.5**	**8.9**	
Average	**Cells 10-12**	**4.6**	**6.3**	**7.1**	**9.8**	

Method Development, Spiking experiment

Spiking Solution : ^{14}C-D6 Specific Activity 1.37 µCi/mg 3041400

Spiking group	Vial #	Vial Wt.(g) pre-spiking	Vial Wt. (g) post-spiking	Spike wt. (mg)	Vial + spike + toluene (g)	Toluene Wt. (g)	Aliquot 1 (g)	Aliquot 2 (g)	DPM 1	DPM 2	Total DPM1	Total DPM 2	Spiked DPM	Extraction Efficiency (%)	Average Recovery (%)	
Dry swabs	*1*	*17.5669*	*17.5699*	*3.0*	*25.3200*	*7.7531*	*0.2489*	*0.241*	*251569*	*242927*	*7836238*	*7815093*	*9124200*	*85.76823*	*excluded due to loss of toluene*	
Dry swabs	2	17.5535	17.5562	2.7	24.1492	6.5957	0.221	0.2445	281589	312376	8403966	8426742	8211780	102.479		
Dry swabs	3	17.4376	17.4433	5.7	25.2761	7.8385	0.2512	0.2494	507094	503518	15823473	15825284	17335980	91.28055		
Dry swabs	4	17.6154	17.6211	5.7	25.7971	8.1817	0.2491	0.2429	508288	494494	16694741	16656244	17335980	96.19008	**96.65**	Dry swabs
Wet swabs	5	17.947	17.9495	2.5	25.3937	7.4467	0.2494	0.2481	263112	262026	7856119	7864688	7603500	103.3788		
Wet swabs	6	18.0297	18.032	2.3	25.4982	7.4685	0.2488	0.2478	224797	223471	6747976	6735243	6995220	96.37451		
Wet swabs	7	18.0651	18.0708	5.7	25.5891	7.5240	0.2565	0.2544	585509	579784	17174931	17147385	17335980	98.99157		
Wet swabs	8	17.9498	17.955	5.2	26.5679	8.6181	0.2503	0.2563	445913	457923	15353267	15397683	15815280	97.21912	**98.99**	Wet swabs

Method Development, Experiment No. 1

Dosing solution: **Neat ^{14}C-D6= 1.38 µCi/mg 3063600 DPM/mg**

DRY SWABS (First dry swab)

Time point	Cell #	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Total DPM I	Total DPM II	Total DPM	Dose (mg)	Dose (DPM)	%Dose	Avg. Average % Dose	St. Dev.
0 hr	1	24.0519	15.4352	8.6167	0.25279	0.25465	63994	64974	253151	255150	2181315	2198543	2189929	4.4	13479840	16.2460		
0hr	2	24.1144	15.5292	8.5853	0.23867	0.25258	87247	92485	365555	366161	3138381	3143586	3140983	3.7	11335320	27.7097		
0hr	3	23.9539	15.4822	8.4717	0.25259	0.25145	109181	109152	432246	434090	3661858	3677483	3669670	4.6	14092560	26.0398	23.332	6.193
24hr	4	23.8811	15.2969	8.5842	0.24793	0.25401	97067	98147	391510	386390	3360805	3316859	3338832	4.6	14092560	23.6922		
24hr	5	23.9939	15.4993	8.4946	0.24937	0.25022	70568	71243	282985	284721	2403854	2418603	2411229	5.0	15318000	15.7411		
24hr	6	24.0246	15.5126	8.5120	0.24915	0.25175	90840	91829	364600	364763	3103468	3104856	3104162	5.0	15318000	20.2648	19.899	3.988

COMBINED WET AND DRY SWABS

Time Point	Cell #	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Total DPM I	Total DPM II	Total DPM	Dose (mg)	Dose (DPM)	%Dose	Avg. Average % Dose	St. Dev.
0 hr	1	24.0078	15.4083	8.5996	0.25492	0.23409	93350	85970	366193	367252	3149101	3158205	3153653	4.4	13479840	23.3953		
0hr	2	22.7687	15.4661	7.3026	0.24492	0.25057	47186	47630	192659	190087	1406910	1388126	1397518	3.7	11335320	12.3289		
0hr	3	23.8119	15.3548	8.4571	0.25211	0.25685	31480	32214	124866	125420	1056008	1060688	1058348	4.6	14092560	7.5100	14.411	8.145
24hr	4	23.9434	15.4390	8.5044	0.24737	0.25085	75016	76277	303254	304074	2579001	2585974	2582488	4.6	14092560	18.3252		
24hr	5	23.9303	15.4619	8.4684	0.25420	0.23713	27254	25777	107215	108704	907939	920551	914245	5.0	15318000	5.9684		
24hr	6	23.9181	15.4037	8.5144	0.23684	0.25606	30609	32711	129239	127747	1100391	1087690	1094041	5.0	15318000	7.1422	10.479	6.821

TAPE STRIPS

Time Point	Cell #	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Total DPM I	Total DPM II	Total DPM	Dose (mg)	Dose (DPM)	%Dose	Avg. Average % Dose	St. Dev.
24hr	4	23.9700	15.4593	8.5107	0.19668	0.25380	2168	2814	11023	11087	93813	94362	94088	4.6	14092560	0.6676		
24hr	5	24.0214	15.4941	8.5273	0.35670	0.40135	9617	10855	26961	27046	229905	230632	230269	5.0	15318000	1.5033		
24hr	6	24.0839	15.5306	8.5533	0.39349	0.40794	13780	14303	35020	35062	299536	299892	299714	5.0	15318000	1.9566	1.376	0.654

HOLDERS

Time Point	Cell #	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Total DPM I	Total DPM II	Total DPM	Dose (mg)	Dose (DPM)	%Dose	Avg. Average % Dose	St. Dev.
0 hr	1	214.2300	169.8200	44.4100	0.21217	0.20715	16780	16773	79088	80970	3512277	3595892	3554084	4.4	13479840	26.3659		
0hr	2	205.8200	169.5700	36.2500	0.22140	0.23280	15497	16686	69995	71675	2537336	2598228	2567782	3.7	11335320	22.6529		
0hr	3	204.9900	170.2200	34.7700	0.19159	0.22432	18016	20969	94034	93478	3269567	3250232	3259900	4.6	14092560	23.1321	24.050	2.020
24hr	4	202.2400	169.9900	32.2500	0.21004	0.23017	6936	7655	33022	33258	1064969	1072571	1068770	4.6	14092560	7.5839		
24hr	5	205.9000	171.2800	34.6200	0.22154	0.22206	12676	12717	57218	57268	1980875	1982629	1981752	5.0	15318000	12.9374		
24hr	6	202.6200	171.0200	31.6000	0.23849	0.21340	21833	19218	91547	90056	2892879	2845777	2869328	5.0	15318000	18.7317	13.084	5.575

SKIN

Dosing solution: Neat ^{14}C-D6= 1.38 µCi/mg 3063600 DPM/mg

Donor ID	Cell #	Vial+TEAH + skin(g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPM/g	DPMII/g	Avg. DPM/g	Total DPM I	Total DPM II	Avg. DPM	Dose (mg)	Dose (DPM)	%Dose	Avg. %Dose	SD
whole piece	1	20.1275	17.4913	2.6363	0.20717	0.21731	152201	136552	734667	628374	681521	1936766	1656552	1796659	4.4	13479840	13.328		
T=0 Hr	2	20.2992	17.5374	2.7619	0.16397	0.19325	51219	60028	312368	310624	311496	862714	857896	860305	3.7	11335320	7.590		
	3	20.2704	17.4581	2.8123	0.19779	0.20788	74040	76109	374336	366120	370228	1052739	1029632	1041185	4.6	14092560	7.388	9.435	3.373
application																			
site	4	20.1625	17.5457	2.6168	0.21536	0.21244	1636	1518	7597	7146	7371	19879	18699	19289	4.6	14092560	0.137		
T=24 Hr	5	20.1806	17.5604	2.6203	0.21844	0.22116	5016	5299	22963	23960	23461	60169	62782	61475	5.0	15318000	0.401		
	6	20.1877	17.5061	2.6816	0.21373	0.21643	14011	13392	65555	61877	63716	175789	165926	170858	5.0	15318000	1.115	0.551	0.506
outside	4	20.1482	17.4523	2.6959	0.19385	0.20901	7534	8070	38865	38611	38738	104774	104088	104431	4.6	14092560	0.741		
of application	5	20.2401	17.51149	2.7286	0.20974	0.22227	37838	46918	180404	211086	195745	492253	575970	534112	5.0	15318000	3.487		
site	6	20.2641	17.5361	2.7280	0.22953	0.22481	29749	32396	129608	144104	136856	353565	393108	373337	5.0	15318000	2.437	2.222	1.386
T= 24 Hr																			

SUMMARY

		Percent of Applied Dose						
		Skin washed immediately after dosing						
Time Point	Cell #	Dry swab	Wet swabs	Holder	Swabs	Skin surface[1)]	Skin (whole piece)	% Dose recovery
0 hr	1	16.2460	23.3953	26.3659	39.6413	66.0072	13.3285	79.3357
0hr	2	27.7097	12.3289	22.8529	40.0386	62.6915	7.5896	70.2811
0hr	3	26.0398	7.5100	23.1321	33.5497	56.6818	7.3882	64.0700
Average		**23.3318**	**14.4114**	**24.0503**	**37.7432**	**61.7935**	**9.4354**	**71.2289**
St Dev.		**6.1931**	**8.1449**	**2.0196**	**3.6371**	**4.7271**	**3.3730**	**7.6769**

[1)] Skin surface = Swab extracts + Holder extracts

		Percent of Applied Dose							
		Skin washed 24 hr after dosing							
					Skin	Skin		Skin surface	
Time Point	Cell #	Dry swab	Wet swabs	Tape strip	Application site	Outside edge	Holder	(Swabs, Tape, Holder)	% Dose recovered on skin surface and in skin[1)]
24hr	4	23.6922	18.3252	0.6676	0.1369	0.7410	7.5839	50.2689	51.1468
24hr	5	15.7411	5.9684	1.5033	0.4013	3.4868	12.9374	36.1502	40.0384
24hr	6	20.2648	7.1422	1.9566	1.1154	2.4372	18.7317	48.0953	51.6480
Average		**19.8994**	**10.4786**	**1.3758**	**0.5512**	**2.2217**	**13.0844**	**44.8382**	**47.6111**
St Dev.		**3.9881**	**6.8206**	**0.6539**	**0.5062**	**1.3855**	**5.5754**	**7.6021**	**6.5629**

[1)] Volatilized portion not determined: Charcoal baskets not analyzed

Method Development, Experiment No. 2

Dosing solution: **Neat ^{14}C-D6= 1.37 µCi/mg 3041400 DPM/mg**

SWABS

Time point	Cell #	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Total DPM I	Total DPM II	Avg. Total DPM	Dose (mg)	Dose (DPM)	%Dose	Avg. % Dose	St. Dev.	Avg. % Dose without cell 11	St. Dev. without cell 11
0 hr*	3	25.3578	17.1997	8.1581	0.2485	0.2381	148456	154940	597408	650735	4873718	5308761	5091239	2.5	7603500	66.9592				
0hr	4	25.7386	17.2806	8.4580	0.2525	0.2502	213883	211520	847061	845404	7164445	7150424	7157435	3.6	10949040	65.3704				
0hr	5	25.7222	17.2300	8.4922	0.2514	0.2537	408801	416462	1626098	1641553	13809148	13940397	13874772	6.4	19464960	71.2808	67.8701	3.0587		
24hr*	10	25.2923	17.1851	8.1072	0.5002	0.4948	465904	460668	931435	931019	7551333	7547954	7549644	4.5	13686300	55.1620				
24hr	*11*	*25.5441*	*17.0942*	*8.4499*	*0.2134*	*0.2122*	*35031*	*34913*	*164157*	*164529*	*1387106*	*1390251*	*1388679*	*4.6*	*13990440*	*9.9259*				
24hr	12	25.6028	17.1193	8.4835	0.4986	0.5003	493718	496142	990209	991689	8400435	8412994	8406714	4.6	13990440	60.0890	41.7257	27.6493	57.6255	3.4839
48hr**	10	25.5928	17.0423	8.5505	0.2311	0.2531	11	4	48	16	407	135	271	4.5	13686300	0.0020				
48hr	*11*	*25.6815*	*17.1064*	*8.5751*	*0.2542*	*0.2551*	*76*	*85*	*299*	*333*	*2564*	*2857*	*2711*	*4.6*	*13990440*	*0.0194*				
48hr	12	25.8418	17.3156	8.5262	0.2506	0.2586	9	13	36	50	306	429	367	4.6	13990440	0.0026	0.0080	0.0099	0.0023	0.0005

*** Washes (swabs) at 0 hr and 24 hr were performed with holders in place**
****Washes (swabs) at 48 hr were performed after holders were removed**

TAPE

Time Point	Cell #	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Total DPM I	Total DPM II	Avg. Total DPM	Dose (mg)	Dose (DPM)	%Dose	Average % Dose	St. Dev.	Avg. % Dose without cell 11	St. Dev. without cell 11
48hr	10	25.5299	17.0310	8.4989	0.2484	0.2502	152	156	612	624	5201	5299	5250	4.5	13686300	0.0384				
48hr	11	*24.5948*	*17.1454*	*7.4494*	*0.2531*	*0.2603*	*492*	*499*	*1944*	*1917*	*14481*	*14281*	*14381*	*4.6*	*13990440*	*0.1028*				
48hr	12	25.7472	17.2697	8.4775	0.2532	0.2507	112	111	442	443	3750	3754	3752	4.6	13990440	0.0268	0.0560	0.0409	0.0326	0.0082

HOLDERS

Time Point	Cell #	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Total DPM I	Total DPM II	Avg. Total DPM	Dose (mg)	Dose (DPM)	%Dose	Avg. % Dose	St. Dev.	Avg. % Dose without cell 11	St. Dev. without cell 11
0 hr	3	143.5825	99.3836	44.1989	0.2209	0.2187	1717	1707	7773	7805	343547	344982	344264	2.5	7603500	4.5277				
0hr	4	144.9144	99.4495	45.4649	0.2279	0.2239	2686	2617	11786	11688	535843	531405	533624	3.6	10949040	4.8737				
0hr	5	143.1442	99.6062	43.5380	0.232	0.2262	1676	1610	7224	7118	314525	309886	312205	6.4	19464960	1.6039	3.6685	1.7963		
48hr	10	141.2746	99.2327	42.0419	0.2314	0.226	88	80	380	354	15988	14882	15435	4.5	13686300	0.1128				
48hr	*11*	*151.9750*	*99.3673*	*52.6077*	*0.2236*	*0.2254*	*89*	*25*	*398*	*111*	*20940*	*5835*	*13387*	*4.6*	*13990440*	*0.0957*				
48hr	12	146.1081	99.1154	46.9927	0.2214	0.222	57	55	257	248	12098	11642	11870	4.6	13990440	0.0848	0.0978	0.0141	0.0988	0.0198

Dosing solution: **Neat ^{14}C-D6= 1.37 µCi/mg 3041400 DPM/mg**

SKIN

Donor ID	Cell #	Vial+TEAH + skin(g)	Vial (g)	Sample Wt.(g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPMI/g	DPMII/g	Avg. DPM/g	Total DPM I	Total DPM II	Avg. DPM	Dose (mg)	Dose (DPM)	%Dose	Avg. %Dose	SD	Avg. % Dose without cell 11	St. Dev. without cell 11
whole piece T=0 Hr	3	19.5879	17.1802	2.4077	0.2196	0.2068	49161	49705	223866	240353	232110	539002	578698	558850	2.5	7603500	7.3499				
	4	19.8675	17.1835	2.6840	0.2159	0.2217	52187	57764	241718	260550	251134	648772	699317	674045	3.6	10949040	6.1562				
	5	20.1469	17.1825	2.9644	0.2151	0.2282	39348	37994	182929	166494	174712	542274	493556	517915	6.4	19464960	2.6608	5.3890	2.4369		
applicatio n site T=48 Hr	10	19.8244	17.1408	2.6836	0.1896	0.1876	25	15	132	80	106	354	215	284	4.5	13686300	0.0021				
	11	*19.8468*	*17.1464*	*2.7004*	*0.2323*	*0.2158*	*102*	*89*	*439*	*412*	*426*	*1186*	*1114*	*1150*	*4.6*	*13990440*	*0.0082*				
	12	19.8425	17.1625	2.6800	0.1907	0.1986	7	1	37	5	21	98	13	56	4.6	13990440	0.0004	0.0036	0.0041	0.0012	0.0012
outer edge T= 48 Hr	10	19.9501	17.2314	2.7187	0.2052	0.2339	43	62	210	265	237	570	721	645	4.5	13686300	0.0047				
	11	*19.8637*	*17.1659*	*2.6978*	*0.1825*	*0.2054*	*54*	*69*	*296*	*336*	*316*	*798*	*906*	*852*	*4.6*	*13990440*	*0.0061*				
	12	19.9633	17.2272	2.7361	0.2234	0.2323	13	11	58	47	53	159	130	144	4.6	13990440	0.0010	0.0039	0.0026	0.0029	0.0026

SARAN WRAP		Vial+	Vial	Sample Wt.							Total	Total	Avg. Total	Dose	Dose		Average		Avg. % Dose without	St. Dev. without
Time Point	Cell #	sample (g)	(g)	(g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPM/g	DPMII/g	DPM I	DPM II	DPM	(mg)	(DPM)	%Dose	% Dose	St. Dev.	cell 11	cell 11
48hr	10	27.3107	17.0787	10.2320	0.2614	0.2405	1	0	3.82555471	0	39	0	20	4.5	13686300	0.0001				
48hr	*11*	*25.5763*	*17.0951*	*8.4812*	*0.2492*	*0.2506*	*2*	*0*	*8.02568218*	*0*	*68*	*0*	*34*	*4.6*	*13990440*	*0.0002*				
48hr	12	25.6227	17.0482	8.5745	0.2508	0.2558	1	0	3.98724083	0	34	0	17	4.6	13990440	0.0001	0.0002	0.0001	0.0001	0.0000

RECEPTOR FLUID from 32 hr to 48 hr

Time Point	Cell #	Vial+Sample (g)	Vial (g)	Receptor Fluid (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPM/g	DPMII/g	Total DPM I	Total DPM II	Total DPM	Dose (mg)	Dose (DPM)	%Dose
32hr	10	29.6295	17.3368	12.2927	0.2889	0.2882	0	0	0	0	0	0	0	4.5	154	0.0000
32hr	11	29.8623	17.2886	12.5737	0.2880	0.2962	0	1	0	3	0	42	21	4.6	157	13.4961
32hr	12	29.3671	17.184	12.1831	0.2997	0.3346	0	0	0	0	0	0	0	4.6	157	0.0000
40hr	10	28.7813	17.2485	11.5328	0.2893	0.2865	1	1	3	3	40	40	40	4.5	154	26.0381
40hr	11	29.097	17.0982	11.9988	0.2876	0.2902	2	0	7	0	83	0	42	4.6	157	26.5283
40hr	12	29.0578	17.1743	11.8835	0.3054	0.3017	2	0	7	0	78	0	39	4.6	157	24.7421
48hr	10	31.993	17.034	14.9590	0.2978	0.2973	0	1	0	3	0	50	25	4.5	154	16.3525
48hr	11	32.7247	17.2528	15.4719	0.2942	0.2969	0	3	0	10	0	156	78	4.6	157	49.7033
48 hr	12	32.8278	17.2092	15.6186	0.2876	0.2927	0	0	0	0	0	0	0	4.6	157	0.0000

CHARCOAL used to collect volatiles from 24 to 48hr

Time Point	Cell #	Vial+ sample (g)	Vial (g)	Sample Wt. (g)	Rep. I (g)	Rep. II (g)	DPM I	DPM II	DPM/g	DPMII/g	Total DPM I	Total DPM II	Avg. Total DPM	Dose (mg)	Dose (DPM)	%Dose	Average % Dose	St. Dev.	Avg. % Dose without cell 11	St. Dev. without cell 11
48hr	10	144.8350	99.2634	45.5716	0.2453	0.2523	8492	8686	34619	34427	1577636	1568906	1573271	4.5	13686300	11.4952				
48hr	*11*	*142.8689*	*99.1722*	*43.6967*	*0.2558*	*0.23*	*8694*	*7864*	*33987*	*34191*	*1485141*	*1494047*	*1489594*	*4.6*	*13990440*	*10.6472*				
48hr	12	129.3920	99.3623	30.0297	0.2384	0.2589	7466	8103	31317	31298	940444	939863	940154	4.6	13990440	6.7200	9.6208	2.5477	9.1076	3.3766

SUMMARY

Percent of applied dose						
Skin washed immediately after dosing						
Time Point	Cell #	Swabs	Holder	(Swabs+ Holder)	(whole piece)	% Dose recovered
0 hr	3	66.959	4.528	71.487	7.350	78.837
0hr	4	65.370	4.874	70.244	6.156	76.400
0hr	5	71.281	1.604	72.885	2.661	75.545
	Average	67.870	3.668	71.539	5.389	76.928
	St Dev.	3.059	1.796	1.321	2.437	1.708

Percent of applied dose											
Skin washed 24 hr and 48 hr after dosing											
Time Point	Cell #	Swabs (24 hr)	Swabs (48 hr)	Swabs 24hr+48hr	Holder (48 hr)	Tape strip 48 hr[1]	Skin surface (Swabs, Tape, Holder)	Skin (48 hr) Application site	Skin (48 hr) Outside edge	Charcoal[2] (48 hr)	% Recovery
48hr	10	55.162	0.002	55.164	0.113	0.038	55.315	0.002	0.005	11.495	66.817
48hr	*11*	*9.926*	*0.019*	*9.945*	*0.096*	*0.103*	*10.144*	*0.008*	*0.006*	*10.647*	*20.805*
48hr	12	60.089	0.003	60.092	0.085	0.027	60.203	0.000	0.001	6.720	66.925
	Average	41.726	0.008	41.734	0.098	0.056	41.887	0.004	0.004	9.621	51.516
	St Dev.	27.649	0.010	27.640	0.014	0.041	27.695	0.004	0.003	2.548	26.596
Average	without cell 11	57.626	0.002	57.628	0.099	0.033	57.759	0.001	0.003	9.108	66.871
St. Dev.	without cell 11	3.484	0.000	3.484	0.020	0.008	3.456	0.001	0.003	3.377	0.076

[1] Only one tape strip because epidermis was removed with this 1st tape strip

[2] New charcoal basket was placed into the holder after application site was washed at 24hr. and holder after skin has been washed at T=24 hr. This charcoal basket was used to collect material that volatilized of the skin