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September 30, 2005

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United States Environmental Protection Agency
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Attention: TSCA 8(e) Coordinator

RE: Tetrahydrofuran – *In vitro* Percutaneous Absorption Study Using Human Cadaver Skin

Dear Sir or Madam:

Lyondell Chemical Company (Lyondell) hereby submits this letter pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA) and EPA's 1991 Section 8(e) Reporting Guide because it includes findings that EPA may consider reportable. In an *in vitro* percutaneous absorption study a 10 % solution of tetrahydrofuran (CAS RN 100-99-9) in water was found to be permeable through human cadaver skin. The calculated mean absorption rate of the tetrahydrofuran solution in this test system was 1.006 ± 0.143 $\mu g/cm^2/hr$ and the penetration coefficient (Kp) was calculated to be 0.011 ± 0.002 cm/hr. Lyondell has not made a determination as to whether a significant risk of injury to health or the environment is actually presented by these findings.

This study was conducted by PRACS Institute, Ltd. for the Tetrahydrofuran Task Force in accordance to the U.S. Environmental Protection Agency's *In vitro Dermal Absorption Rate Testing of Certain Chemicals of Interest to the Occupational Safety and Health Administration* (40 CFR Parts 9 and 799 as published in the Federal Register/Vol. 69/No. 80/Monday, April 26, 2004/Rules and Regulations).

A copy of the study draft report is enclosed for your review and a final report will be forwarded upon its availability.

Should you have any questions or require additional details, please do not hesitate to call me at 713-309-7884. I may also be reached by facsimile at 713-951-1574 or by e-mail at timothy.yagley@lyondell.com.

Sincerely,

8EHQ-05-16253

Timothy Yagley
Senior Product Safety Specialist – Regulatory
Corporate TSCA Coordinator
Lyondell Chemical Company

Enclosure

88060000025

289485

Study Title

Determination of the Percutaneous Absorption of THF, *in vitro*, using the Human Cadaver Skin Model

PRACS Study Number: R04-1387

DRAFT

Study Director and Author of Report:	Paul A. Lehman, M.Sc.
Study Conduct Dates:	May 4, 2005 – July 28, 2005
Performing Laboratory:	PRACS Institute, Ltd. Pre-Clinical Dermatology Research Division 4666 Amber Valley Parkway Fargo, North Dakota 58104 (note: see Deviation #1 for change in study laboratory name)
Location of Archived Records:	PRACS Institute, Ltd. 4801 Amber Valley Parkway Fargo, North Dakota 58104
Study Identification Number:	R04-1387
Submitter/Sponsor:	Tetrahydrofuran Task Force 1850 M Street, NW Suite 700 Washington, DC 20036

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GOOD LABORATORY PRACTICE STATEMENT

This study was conducted in accordance with U.S. EPA TSCA (40 CFR part 792) Good Laboratory Practice Standards, which are consistent with the OECD Principles of Good Laboratory Practice (as revised in 1997) published in ENV/MC/CHEM(98)17.

DRAFT

Paul A. Lehman, M.Sc. — Date
Study Director

Jessica Ross — Date
Submitter/Sponsor

QUALITY ASSURANCE STATEMENT

The PRACS Institute, Ltd., Quality Assurance Division has reviewed the final report for this study to assess adherence to PRACS Institute, Ltd., Standard Operating Procedures and study protocol, and to the TSCA GLP guidelines. The report was found to be an accurate representation of the work conducted in this study. The summary below lists the Quality Assurance audits conducted for this study.

{The dates in this table will be added by QA following final review edits}

QA Activity	Dates Conducted	Date Reported to Management	Date Reported to Study Director
In-Process Audit			
Reagent Inspection			
Records Inspection			
Pipette Audit			
Data Audit			
Final Report Audit			

Kevin Boschert
Quality Assurance Associate

Date

DRAFT

STUDY PERSONNEL

The following individuals were responsible for the conduct of the study:

Management:	James D. Carlson, Pharm.D. President, PRACS Institute, Ltd.
Study Director:	Paul A. Lehman, M.Sc. Director, Pre-Clinical Dermatology Research Division
Primary Technician:	Pi-Hsia Su, M.Sc. Scientist I Pre-Clinical Dermatology Research Division
Administrative Associate:	Heather M. Linstaedt, B.A. Administration Associate Scientific Affairs Division

CERTIFICATION

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

Reviewed by: _____ _____
Date

Date

Authored and Issued by
Study Director: _____ _____
Date

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STUDY COMPOUND INFORMATION

9th Collective Nomenclature:	Furan, tetrahydro
Synonyms/Codes[2]:	Tetrahydrofuran (THF) 1,4-epoxybutane Butylene oxide
CAS Registry Number[1,2,3]:	109-99-9
Lot No[1]:	G41764BBA
Purity[1]:	Non-radiolabeled THF: 99.99% Radiolabeled THF: 99%
Known Impurities[1]:	80 PPM Water 0.5 PPM Peroxide 305 PPM BHT
Physical Characteristics[1,2,3]:	Colorless liquid with ether-like odor Density: 0.886 Boiling Point: 66°C
Storage:	In the dark and the containers purged of air using nitrogen.
Molecular Weight[3]:	72.1066
Molecular Formula[1,2,3]:	C_4H_8O
Stability[2]:	Stable
Source of THF:	BASF Corporation, Mount Olive NJ
Date Received:	February 14, 2005

Source of information (on file):
1. Certificate of Analysis, BASF
2. MSA, BASF
3. www.ChemFinder.com

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SUMMARY

PRACS Institute, Ltd. in Fargo, North Dakota, conducted this study for Tetrahydrofuran Task Force, Washington, D.C. The study was designed to characterize the percutaneous absorption toxicokinetics of Tetrahydrofuran (THF) to determine its permeability constant (Kp), and to assess its short term absorption rate through human skin.

This study was conducted in accordance to the Environmental Protection Agency's *In Vitro Dermal Absorption Rate Testing of Certain Chemicals of Interest to the Occupational Safety and Health Administration* (40 CFR Parts 9 and 799; as published in the Federal Register/Vol. 69/No. 80/Monday, April 26, 2004/Rules and Regulations).

Three concentrations of THF were each evaluated on three cadaveric skin donors in triplicate/donor. Total absorption (penetration through the skin) for each THF solution, for each dose duration, is listed in Summary Table 1.

Summary Table 1: Total Absorption of THF
Mean ± SE as micrograms; n= 3 donors, with triplicate determinations/donor/formulation
(10% and 30% solutions in water)

Dose Duration	10%-THF	30%-THF	100%-THF[1]
10 minutes	0.05 ± 0.02	0.81 ± 0.23	0.24 ± 0.09
60 minutes	1.42 ± 0.36	16.03 ± 2.78	4.61 ± 2.01
14 hours	15.64 ± 1.39	na	na

The penetration coefficient (Kp) for THF, from a 10% solution in water, was calculated to be 0.011 ± 0.002 cm/hr (mean ± sd) from a mean absorption rate of 1.006 ± 0.143 $\mu g/cm^2/hr$.

INTRODUCTION

The *in vitro* human cadaver skin model has proven to be a valuable tool for the study of percutaneous absorption and the determination of the pharmacokinetics of topically applied drugs. The model uses human cadaver skin mounted in specially designed diffusion chambers which allow the skin to be maintained at a temperature and humidity that match typical *in vivo* conditions.[2] A controlled amount of test article is

[1] Throughout the text, "100% THF" refers to the undiluted neat THF obtained from BASF labeled as 99.99% pure.
[2] Franz, TJ: Percutaneous absorption: on the relevance of *in vitro* data. J Invest Derm 1975, 64: 190-195.

applied to the outer surface of the skin and test article absorption is measured by monitoring its rate of appearance in the receptor solution bathing the inner surface of the skin. Data defining total absorption, rate of absorption, as well as skin content can be accurately determined in this model. This method has historic precedent for accurately predicting *in vivo* percutaneous absorption kinetics.[3]

This study was conducted in accordance to the Environmental Protection Agency's *In Vitro Dermal Absorption Rate Testing of Certain Chemicals of Interest to the Occupational Safety and Health Administration* (40 CFR Parts 9 and 799; as published in the Federal Register/Vol. 69/No. 80/Monday, April 26, 2004/Rules and Regulations). The test standard describes procedures for determining a permeability constant (Kp) and two short-term dermal absorption rates for test substances in liquid form. The test substance of interest in this study was Tetrahydrofuran, which was evaluated on human cadaver skin, *in vitro*, using static Franz Diffusion Cells.

The Protocol and Protocol Amendment are provided in Appendix 1.

This study was conducted in three parts: two Pilot studies and the final Pivotal study.

Pilot Study #1 was conducted as the first look to understand the rate and extent of THF absorption through human cadaver skin. Specifically, the pilot study was designed to evaluate the volume to dose, sufficiency of dose specific activity, control of dose evaporation, selection of receptor solution, mass balance of applied dose, and the potential for barrier damage following dose application. The design and results for Pilot Study #1 are presented in Appendix 2.

Pilot study #2 was conducted to refine the observations made from Pilot study #1. Specifically, this pilot study was designed to evaluate an improvement in chamber seal (to prevent dose evaporation), an increased dose amount, a modified sampling schedule, a revised radiolabel specific activity, and further evaluation for barrier damage following dose application. Barrier damage and absorption was assessed versus different concentrations of THF in water ranging from 10%- to 100%-THF. The design and results for Pilot study #2 are presented in Appendix 3.

In collaboration with the study Sponsor, based on the two Pilot studies, the Pivotal study was designed with the following primary parameters:

- Dose Amount of 800 µL per skin section,
- Testing of 3 concentrations of THF in water for the short dose duration evaluations (10%-, 30%- and 100%-THF),
- Testing of 10%-THF in water for the long dose duration evaluation,
- Assessment of steady-state rate of penetration over a 14-hour dose duration,

[3] Franz TJ: The finite dose technique as a valid *in vitro* model for the study of percutaneous absorption in man. In: Skin: Drug Application and Evaluation of Environmental Hazards, Current Problems in Dermatology, vol. 7, G. Simon, Z. Paster, M. Klingberg, M. Kaye (Eds), Basel, Switzerland, S. Karger, 1978, pp 58-68.

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- Use of phosphate buffered saline (PBS) as the reservoir solution.
- Assessment of barrier function damage, post dose, using $^{3}H_{2}0$, 30 minutes following dose removal, and at 8 hours following dose removal.

The reasoning behind the use of diluted THF, was based on the Pilot study results suggesting that barrier function damage occurs at concentrations greater than 25%-THF. Rather than using just one diluted concentration of THF, the study Sponsor believed that the additional information obtained from 3 different dilutions in the short dose duration studies would be of value.

Each dose duration and THF concentration was conducted on triplicate sections from three different human skin donors. The text to follow describes the materials and methods used for the conduct of the final Pivotal study.

OBJECTIVE

To characterize the percutaneous absorption toxicokinetics of Tetrahydrofuran (THF) to determine its permeability constant (Kp), and to assess its absorption rates at two short-term dermal exposure durations (i.e. 10 and 60 minutes).

MATERIALS AND METHODS

A. Test Article(s)

Neat Tetrahydrofuran (THF) was obtained from BASF Corporation (Mount Olive, NJ 07828), Lot # G41764BBA. Purity was indicated as 99.99%. The Certificate of Analysis is attached in Appendix 8.

Radiolabeled ^{14}C-THF ($^{14}C_4H_8O$) was prepared by and purchased from American Radiolabeled Chemicals, Inc. (St. Louis, MO 63146), Lot # 050418. ^{14}C-THF was provided as a neat liquid, with a reported specific activity of 5 mCi/mmol at 99% radiolabeled purity. The Certificate of Analysis is attached in Appendix 8.

B. Radiolabel Test Article Preparation and Specific Activity

The ^{14}C-THF was provided as being 99% radiolabeled pure.

The received stock ^{14}C-THF was diluted with 4 mL neat THF and stored at -20°C. Prior to study conduct, the diluted stock solution was further diluted to target a final specific activity of approximately 4,000 DPM/µL (1.8 nCi/µL). The final specific activity for each test solution used in the pivotal study was found to be 10%-THF = 4311.4 DPM/µL, 30%-THF = 4034.3 DPM/µL, and 100%-THF = 4088.5 DPM/µL.

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C. Reagents

Other reagents used in the conduct of the study included:

Phosphate Buffered Saline	Fisher Biotech (Fair Lawn, NJ; Lot # BP399-20)
Dodecyl Sulfate, Sodium Salt (SDS)	Sigma-Aldrich (St. Louis, MO; Lot # 02825PB)
$^3H_20$ (tritiated water)	PerkinElmer (Boston, MA; Lot # 3538-134)
ScintiVerse Scintillation Fluid	Fisher Scientific (Fair Lawn, NJ; Lot # 026559)
Soluene-350 Tissue Solubilizer	PerkinElmer (Boston, MA; Lot # 24-041201)

D. Skin and Cell Preparation

Percutaneous absorption was measured using the *in vitro* cadaver skin Franz Diffusion Cell model. Cryopreserved human cadaver trunk skin (New York Firefighter's Skin Bank, NY, NY) without obvious signs of skin disease, obtained within 24 hours of death, was used in this study. At collection, the skin was collected by dermatome, to be approximately 0.25 - 0.90 mm thick, processed for cryopreservation, sealed in a water-impermeable plastic bag, and stored at ≤ -70°C until the day of each experiment. Prior to use it was thawed by placing the bag in ~37°C water, then rinsed in tap water to remove any adherent blood or other material from the surface. Skin thickness was determined and recorded.

Skin from a single donor was cut into multiple smaller sections large enough to fit on 0.8 cm^2 static Franz Diffusion Cells (Crown Glass Co., Somerville, NJ). The dermal chamber was filled to capacity with a receptor solution of phosphate-buffered isotonic saline (PBS), pH 7.4 ± 0.1 and the epidermal chamber was left open to ambient laboratory environment. The cells were then placed in a diffusion apparatus in which the dermal receptor solution was stirred magnetically at ~600 RPM and its temperature maintained to achieve a skin surface temperature of 32.0 ± 1.0 °C.

To assure the integrity of each skin section, its permeability to tritiated water was determined before application of the test products.[4] Following a brief (0.5-1 hour) equilibrium period, ^3H_2O (PerkinElmer, Boston, MA, sp. Act. ~ 0.5 µCi/mL) was layered across the top of the skin by dropper so that the entire exposed surface was covered (approximately 100-150 µL). After 5 minutes the ^3H_2O aqueous layer was removed. At 30 minutes after dosing the receptor solution was collected and analyzed for radioactive content by liquid scintillation counting. Skin specimens in which absorption of ^3H_2O was less than 1.75 µL-equ. were considered acceptable. In addition, the same integrity test method was used for post-study assessment of the skin following exposure to the test article (approximately 1 hour and 8-24 hours after dose removal.).

[4] Franz TJ, Lehman PA: The use of water permeability as a means of validation for skin integrity in *in vitro* percutaneous absorption studies. Abst. J Invest Dermatol 1990, 94:525.

E. THF Administration and Occlusion

Following the initial tritiated water integrity test, the Cell reservoir was replenished with fresh PBS. Subsequently, the test article was applied to triplicate sections of the same donor skin at a target dose of 800 µL using a calibrated positive displacement pipette. Following dose application (60 min, and 14 hr duration Cells only), the Cell chimney was occluded with a silicone stopper[5] over-wrapped with a nitrile membrane held in placed with an O-ring, all to prevent THF evaporation from the surface of the skin.

F. Dose Duration Study Designs

1. 10 Minute Dose Duration Study
The test formulations consisted of 10%- and 30%-THF in water, and 100%-THF, with each having been spiked with radiolabeled ^{14}C-THF. Each formulation was dosed to triplicate sections of skin from 3 donors. Ten minutes after dosing, the reservoir solution was collected, the residual dose removed, the surface of the skin blotted with tissue (Kimwipes™), and the surface wash conducted (0.1% SDS; 0.5 mL x 3). The skin section remained un-occluded following the surface wash. Fifty minutes following the surface wash the first post-exposure water integrity test was conducted. Twenty-four hours after the surface wash the second post-exposure water integrity test was conducted. Following the last integrity test the skin was removed from the Cell and split into epidermis and dermis and saved for subsequent analysis. Finally, the reservoir cell was rinsed with 25% THF in water.

2. 60 Minute Dose Duration Study
The test formulations consisted of 10%- and 30%-THF in water, and 100%-THF, with each having been spiked with radiolabeled ^{14}C-THF. The conduct of this study was identical to the 10 Minute Dose Duration Study with two exceptions: occlusion of the dose (Cell chimney) throughout the dose exposure period, and collection of the reservoir solution 60 minutes after dosing. The skin section remained un-occluded following the surface wash. Sixty minutes following the surface wash the first post-exposure water integrity test was conducted. Eight and one-half (8.5) hours after the surface wash the second post-exposure water integrity test was conducted.

3. 14 Hour Dose Duration Study
The test formulation consisted of the 10%-THF in water solution having been spiked with radiolabeled ^{14}C-THF. Skin preparation, dose and occlusion were performed as previously described. Reservoir samples were collected at 0.5, 1, 2,

[5] The silicone stopper was first perforated with an 18-gauge needle so that when the stopper was inserted into the dose half-cell, the needle would allow the compressing air to escape, and normal pressure would then be maintained in the dead-air volume between the THF and the stopper. Once the stopper was secured in place the needle was removed allowing the silicone stopper to re-seal the needle perforation.

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4, 6, 8, 10, 12, and 14 hours after dosing by the complete evacuation of the reservoir followed by replenishment with fresh PBS solution. The skin section remained un-occluded following the surface wash. Thirty minutes following the surface wash the first post-exposure water integrity test was conducted. Eight and one-half (8.5) hours after the surface wash the second post-exposure water integrity test was conducted.

G. Sample Collection and Processing

Skin Thickness was obtained from 6-7 replicate measurements at random locations across the donor skin sheet using a gap micrometer.

Reservoir Solution: A 1 mL aliquot of each reservoir solution sample was mixed with 5 mL scintillation fluid and counted.

Residual Dose Recovery: The residual dose was removed from the surface of the skin by pipette, and a 25 µL aliquot was added to 5 mL scintillation fluid, mixed and counted.

Surface Wash: The surface wash was conducted with 0.1% Sodium Dodecyl Sulfate in water solution by repetitive pipette dispensing of 0.5 mLs, repeated three times for a total of 1.5 mLs solution. The surface wash solution was added to 15 mL scintillation fluid, mixed and counted.

Surface Blotting Material: Following the wash, the surface was blotted dry with a single laboratory tissue (Kimwipes®). Each tissue wipe was added to 5 mL scintillation fluid, mixed and counted.

Skin: Following the final tritiated water integrity test, the skin was removed from the chamber, the dosed area manually split into epidermis and dermis, and each dissolved in a tissue solubilizer (0.5 mL for epidermis; 1.0 mL for dermis; Soluene-350®). The samples were then incubated at room temperature or in a water bath (50°C) until the tissue was dissolved (addition of heat only accelerates the dissolution process, ~3-6 hrs at 50°C, ~18-24 hrs at room temperature), added to 5 mL scintillation fluid, mixed and counted.

Chamber: After skin removal, the reservoir chamber was rinsed twice with a 0.5 mL of 25% THF (non-radiolabeled) in water. The two rinses were combined added to 15 mL scintillation fluid, mixed and counted.

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H. Isotope Analysis

All scintillation fluid mixed samples were counted in a PerkinElmer Liquid Scintillation Analyzer (Tri-Carb 3100TR) for duplicate 5 minute count durations. Counts per minute (CPM) were automatically converted to disintegrations per minute (DPM) using the internal standard quench correction method. The scintillation counter was programmed to separate the energy windows for tritium and carbon-14. Specific activity of the test article was determined in triplicate prior to study conduct.

I. Data Analysis

Raw DPM data were corrected for background and then collated by skin section. Flux and extent of penetration was then calculated for each skin section with appropriate corrections for chamber volume, surface area, applied dose and dose concentration (specific activity). Values less than background appear as negative values in the Cell calculation sheets, but were then assigned a value of zero for the calculation of the means within and across donors.

Individual replicate skin sections from each donor, within each set (e.g. time and concentration), were averaged to obtain the replicate within-donor average (±SD). The Donor averages were tabulated to obtain the across-donor population mean (±SE).

STUDY DEVIATIONS AND OBSERVATIONS

1. The protocol states that the study was designated for conduct at PRACS Dermatology LLC, San Diego, CA. While waiting for the synthesis of the radiolabeled material, the laboratory relocated to the PRACS main facility in Fargo, ND and renamed as the Pre-Clinical Dermatology Research Division of PRACS Institute, Ltd. The entire study conduct was performed at the Fargo facility. Both locations are owned and operated by PRACS Institute, Ltd.
2. For clarification, the Franz Diffusion Cell is often considered synonymous with the "*in vitro* cadaver skin finite dose technique". In practice, the same system can be used with both finite and infinite dose applications to the skin. Here, an infinite dose is defined as one that is of sufficient size or volume to not be significantly depleted during the course of the study and where the compound of interest is available for diffusion throughout the course of the study conduct.
3. Whereas the Protocol indicated that the dermatomed skin would be approximately 0.25 - 0.5 mm thick, it was found that the mean thickness of the cadaver skin used were approximately 0.28 - 0.79 mm thick (range = 0.18 - 0.91 mm). The first three measurements for each donor were collected after skin section removal from the cell, whereas the remaining measurements were collected prior to mounting the skin onto the cells. In the Investigator's opinion, these measurements reflect a reasonable assessment of the skin thickness.

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4. Whereas the Protocol indicated that all chambers would be occluded following dose application. Due to the shortness of the 10-min dose exposure sub-study, and the time necessary to place and secure the occlusion, the 10-min dose exposure chambers were not occluded. In the opinion of the Investigator, this Protocol deviation did not have an impact on the outcome of the study, the data, or the conclusions drawn from the data.
5. The Protocol indicated that occlusion of the chambers would be accomplished using Saran Wrap™ or Parafilm™. However, as discovered in the initial Pilot study (presented in Appendix 2), these cover materials were found to be soluble in THF. To achieve occlusion, a silicon stopper over-wrapped with a nitrile membrane was used. It was further determined that the silicon stopper did not adsorb the THF dose (Pilot study #2; Appendix #3) so was not included in the mass balance assessment portion of the Pivotal study. This study deviation was discussed with the Sponsor, and was considered an affirmative approach for continuance of the study conduct.
6. The Protocol Amendment indicates that the post-study tritiated water test would be conducted "30 minutes following dose removal (surface wash) and 8 hours following dose removal". As there is a difference between the dose removal step (pipette removal of the residual dose) and the surface wash event (which follows the dose removal), the technician based the post-study integrity tests to follow the surface wash event (as this step would have accomplished the final removal of all of the residual THF). Specifically, the first post-study integrity test was conducted 30 ± 5 minutes following skin surface wash (which was 60 ± 10 minutes following residual dose removal), and the second post-study integrity test was conducted 8 hours following the surface wash (8.5 hrs following residual dose removal). There was one real deviation in this process: due to a scheduling oversight, the second tritiated test, post-study, for Donor #1 (SS012005) was conducted at 24 hrs rather than at 8 hrs. In the opinion of the Investigator, this time deviation did not impact the interpretation of the results as the intent of the 8 hr post-study duration was to allow the skin to return to a normal hydration condition, which would still be normal at 24 hrs.
7. The Protocol indicated that a Packard LSC1900 scintillation counter was to be used in the conduct of this study. However, with the relocation of the laboratory (see comment #1 of this section), and the obsolesces of the LSC1900 model, a new PerkinElmer Liquid Scintillation Analyzer (Tri-Carb 3100TR) was purchased, installed by the manufacturer, and operationally verified by installing technician and the PRACS Metrology Division prior to study conduct. This scintillation counter was used throughout study conduct.
8. The Protocol indicated that the surface wash sample and chamber rinse sample would be mixed with 5-7 mL scintillation fluid for counting. In the conduct of the first pilot study it was found that this volume of scintillation fluid was insufficient to fully inter-mix with the sample. To ensure complete counting efficiency, the scintillation fluid volume was increased to 15 mL to allow full miscibility of these samples.
9. The Protocol indicated that a separate aliquot of the recovered dose would be saved to assess the stability and specific activity of the test article. The specific

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activity of the recovered dose from the skin section surface was retained and specific activity determined (as DPM/μL). This information is presented in the discussion of Pilot study #1 and is included in the calculated data in the Appendix. However, the amount of isotope recovered from these samples was below limits of quantification for assessment of radiolabel purity (stability) via high pressure liquid chromatography.

In the opinion of the Investigator these deviations did not affect the integrity or outcome of the study or the interpretation of the results.

RESULTS AND DISCUSSION

A. Donor Demographics

Donor ID	Age	Race	Sex	Thickness (mm)*	Pre-Study Water Integrity Test Result (μL)**
SS012005	61	Caucasian	Female	0.28 ± 0.12	0.42 ± 0.11
FD090404	56	Hispanic	Male	0.38 ± 0.11	0.81 ± 0.25
KS032805	44	African American	Male	0.79 ± 0.13	0.46 ± 0.18

* Mean ± SD from 6 or 7 replicate measurements.
**Across all section used (n=22) for that donor.

B. Barrier Function Integrity Test

The barrier function integrity was conducted using ^3H_2O water dosed for a 5-minute duration, with the reservoir solution being sampled at 30 minutes post dose application (the approach developed by this laboratory). The integrity test was repeated approximately 30 minutes, and again after eight hours following the skin surface wash, to assess for damage that may have occurred from the THF exposure

Data were calculated as percent change from pre-dose results. Statistical comparisons were made using the Student's t-test to the control (non-dosed) skin sections. The results are presented in Table 1.

Due to high residual carbon-14 content in selected samples in the 30 minute post-dose integrity test, the scintillation counter was un-able to differentiate the low level tritium from the carbon-14 using the dual-label quench curve discrimination calculations. In other words, the remaining THF that was still diffusing out of the skin when the first post-study integrity test was conducted overwhelmed the amount of tritium present from the tritiated water such that the dual-label calculation would indicate that no tritium was present. In those situations, the data in the table reflects only those chambers that provided a tritium value above background (those which could not be determined are indicated as "unavailable).

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The data indicate that the ability to assess barrier function at 30 minutes following the skin surface wash is problematic due to 1) residual ^{14}C-THF diffusion from the skin, and 2) hydration of the skin from the occlusive nature of the applied dose (and occlusion of the dosing half-cell chimney). The second barrier function test, conducted greater than eight hours after dose removal is more likely representative of barrier function as essentially any residual ^{14}C-THF had an opportunity to have been cleared from the system, and that the skin (with occlusion removed) having an opportunity to return to a more normal state of hydration when left open to ambient laboratory conditions.

As can be seen in Table 1, the data indicate that barrier function damage is likely to have occurred in only those chambers having been exposed to 100% THF ($p<0.05$).

C. 10 Minute Dose Duration Study

To three donors, each in triplicate for each THF concentration, were dosed with either 10%-, 30%- or 100%-THF spiked with ^{14}C-THF. Ten minutes following dose application, the reservoir solution was collected, the surface dose removed and the skin processed as previously described.

The results from the 10-minute dose exposure are presented in Table 2.

D. 60 Minute Dose Duration Study

To three donors, each in triplicate for each THF concentration, were dosed with either 10%-, 30%- or 100%-THF spiked with ^{14}C-THF. Sixty minutes following dose application, the reservoir solution was collected, the surface dose removed and the skin processed as previously described.

The results from the 60-minute dose exposure are presented in Table 3.

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Table 1: Percent Change in Barrier Function based on the Tritiated Water Integrity Test (Mean ± SD; 'n' of 9 total sections)

THF Concentration	THF Dose Duration	1st Post-Dose Test % Change	2nd Post-Dose Test % Change
10%	10 min	-71.4 ± 17.0 (6)	-40.4 ± 12.5 (9)
30%	10 min	Unavailable (0)	-35.8 ± 15.0 (9)
100%	10 min	112.6 ± 56.8 (9) *	72.3 ± 55.9 (9) *
10%	60 min	84.3± 197.8 (3)	-36.9 ± 22.3 (9)
30%	60 min	Unavailable (0)	-27.3 ± 6.1 (9) *
100%	60 min	565.5 ± 213.5 (9) **	460.4 ± 213.7 (9) **
Control (no Dose)	14 hr	-33.2 ± 11.5 (3)	-46.2 ± 11.2 (9)
10%	14 hr	-43.1 ± 0 (2)	-41.6 ± 10.3 (9)

* $p < 0.05$ to Control skin sections.
** $p < 0.005$ to Control skin sections.

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Table 2: Rate and Extent of ^{14}C-THF Absorption following the 10-Minute Dose Duration
(Mean ± SE; 3 Donors, 3 replicates/formulation/donor)

Source	10%-THF	30%-THF	100%-THF
Flux (µg /cm^2/hr)	0.353 ± 0.119	6.10 ± 1.74	1.78 ± 0.69
Total Absorbed (µg)	0.05 ± 0.02	0.81 ± 0.23	0.24 ± 0.09
Total Absorbed (% Dose)	0.07 ± 0.02	0.38 ± 0.11	0.03 ± 0.01
Dermal Content (% Dose)	0	0	0
Epidermal Content (% Dose)	0	0	0

Note: zero values reflect amounts below lower limit of detection (background count)

Table 3: Rate and Extent of ^{14}C-THF Absorption following the 60-Minute Dose Duration
(Mean ± SE; 3 Donors, 3 replicates/formulation/donor)

Source	10%-THF	30%-THF	100%-THF
Flux (µg /cm^2/hr)	1.77 ± 0.45	20.04 ± 3.47	5.76 ± 2.51
Total Absorbed (µg)	1.42 ± 0.36	16.03 ± 2.78	4.61 ± 2.01
Total Absorbed (% Dose)	2.00 ± 0.51	7.54 ± 1.31	0.65 ± 0.28
Dermal Content (% Dose)	0	0	0
Epidermal Content (% Dose)	0	0	0

Note: zero values reflect amounts below lower limit of detection (background count)

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E. 14 Hour Dose Duration Study

To three donors, each in triplicate, were dosed with 10%, THF spiked with ^{14}C-THF. Over the following fourteen hours reservoir solution samples were collected at 0.5, 1, 2, 4, 6, 8, 10, 12 and 14 hours. Following the last reservoir sample collection, the reservoir solution was collected, the surface dose removed and the skin processed as previously described.

The results from the 14 hour dose exposure are presented in Tables 4 and 5.

Table 4: Rate of ^{14}C-THF Absorption over the 14-Hour Dose Duration (Mean ± SE; 3 Donors, 3 replicates/formulation/donor)

Sample	Flux (ug/cm^2/hr)	Mid-Time (hr)*	Cumulative Penetration (µg)	Time (hr)*
1	1.10 ± 0.26	0.25	0.44 ± 0.10	0.5
2	1.86 ± 0.18	0.75	1.19 ± 0.17	1
3	2.01 ± 0.19	1.5	2.79 ± 0.32	2
4	1.72 ± 0.15	3	5.55 ± 0.56	4
5	1.54 ± 0.14	5	8.02 ± 0.77	6
6	1.36 ± 0.12	7	10.19 ± 0.96	8
7	1.23 ± 0.11	9	12.17 ± 1.13	10
8	1.16 ± 0.09	11	14.03 ± 1.27	12
9	1.01 ± 0.08	13	15.64 ± 1.39	14

* Note: "Mid-time" is the central point of the sample collection period and is associated to Flux data. "Time" is the cumulative time for each sample collection and is associated to the cumulative penetration data.

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Table 5: Extent of ^{14}C-THF Absorption over the 14-Hour Dose Duration (Mean ± SE; 3 Donors, 3 replicates/formulation/donor)

Source	10%-THF
Total Absorbed (µg)	15.64 ± 1.39
Total Absorbed (% Dose)	22.07 ± 1.96
Dermal Content (% Dose)	0
Epidermal Content (% Dose)	0.001 ± 0.000

Note: zero values reflect amounts below lower limit of detection (background count)

F. Determination of Kp

The determination of Kp was performed as defined in the Dermal Test Rule. Specifically, the steady-state rate of absorption is divided by the concentration of the test substance applied. As the flux profile for ^{14}C-THF demonstrated an initial peak before settling down into a more steady rate of absorption, the steady-state rate of absorption value, for each skin section, was calculated from the rate of penetration defined by the slope of the cumulative penetration data from t=4 hrs to t=14 hrs. The results are shown in Table 6. The mean cumulative penetration profile is shown in Figure 1.

Table 6: Steady-State Rate of Penetration ($T_{4\text{-}14hrs}$) and Associated Kp Value by Chamber
Concentration = 10% THF in Water (88.6 µg/cm^3)

Chamber ID	Flux Rate$_{(t=4\text{-}14\ hr)}$ (µg/cm^2/hr)	Kp (cm/hr)
20	1.085	0.0122
21	1.255	0.0142
22	1.116	0.0126
26	0.937	0.0106
27	0.992	0.0112
28	1.093	0.0123
38	0.811	0.0092
39	0.920	0.0104
40	0.849	0.0096
Mean:	**1.006**	**0.011**
SD:	**0.143**	**0.002**

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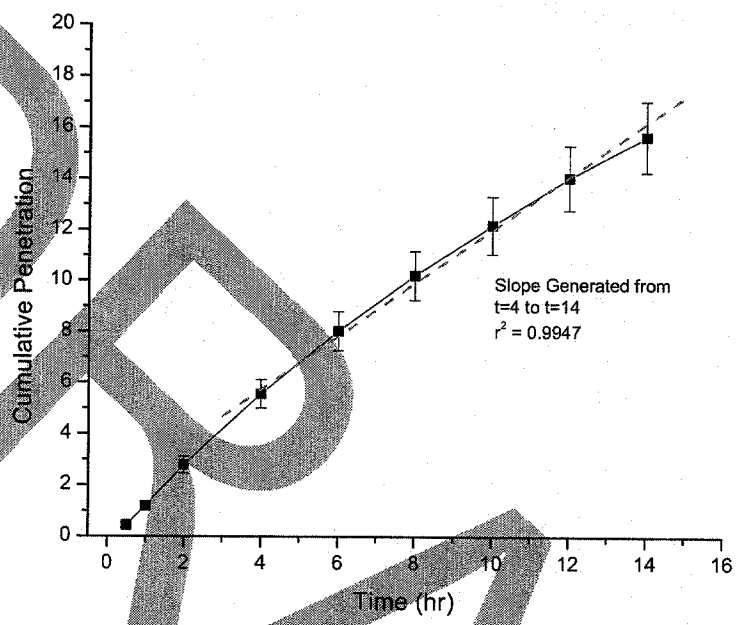
Figure 1: Cumulative Penetration of ^{14}C-THF over the 14-hr Dose Duration
(Mean ± SE, n=3 Donors, each in triplicate.)
Dash line = linear regression interpretation of data from T = 4-14 hr.



G. Supplemental Data

Supplemental data collected, to include mass balance (accountability of the applied dose), can be found in Appendix 6 for both the Pilot and Pivotal studies.

CONCLUSIONS

The data indicate that the 10%- and 30%-THF in water solutions did not significantly alter the barrier function of the skin, as assessed by the percutaneous absorption of $^{3}H_2O$ in the barrier integrity test. However, neat (100%) THF exposure to the skin did alter the skin's barrier function to $^{3}H_2O$ suggesting damage did occur to the stratum corneum of the skin. Therefore, the results from the 10%- and 30%-THF solutions may better represent human skin permeability to THF in un-damage skin from short term exposures.

All values discussed in the following conclusion statement are represented as mean ± standard error.

From the 10%-THF, 10-minute dose exposure study, ^{14}C-THF demonstrates a mean flux rate of 0.353 ± 0.119 μg/cm^2/hr, within the exposure period, with 0.05 ± 0.02 μg ^{14}C-

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THF penetrating through the skin. No measurable amounts of ^{14}C-THF were found in the dermis or epidermis following the 10 minute dose exposure duration.

From the 30%-THF, 10-minute dose exposure study, ^{14}C-THF demonstrates a mean flux rate of 6.10 ± 1.74 μg/cm^2/hr, within the exposure period, with 0.81 ± 0.23 μg ^{14}C-THF penetrating through the skin. No measurable amounts of ^{14}C-THF were found in the dermis or epidermis following the 10 minute dose exposure duration.

From the 100%-THF, 10-minute dose exposure study, ^{14}C-THF demonstrates a mean flux rate of 1.78 ± 0.69 μg/cm^2/hr, within the exposure, period with 0.24 ± 0.09 μg ^{14}C-THF penetrating through the skin. No measurable amounts of ^{14}C-THF were found in the dermis or epidermis following the 10 minute dose exposure duration.

From the 10%-THF, 60-minute dose exposure study, ^{14}C-THF demonstrates a mean flux rate of 1.77 ± 0.45 μg/cm^2/hr, within the exposure period, with 1.42 ± 0.36 μg ^{14}C-THF penetrating through the skin. No measurable amounts of ^{14}C-THF were found in the dermis or epidermis following the 60 minute dose exposure duration.

From the 30%-THF, 60-minute dose exposure study, ^{14}C-THF demonstrate a mean flux rate of 20.04 ± 3.47 μg/cm^2/hr, within the exposure period, with 16.03 ± 2.78 μg ^{14}C-THF penetrating through the skin. No measurable amounts of ^{14}C-THF were found in the dermis or epidermis following the 60 minute dose exposure duration.

From the 100%-THF, 60-minute dose exposure study, ^{14}C-THF demonstrates a mean flux rate of 5.76 ± 2.51 μg/cm^2/hr, within the exposure period, with 4.61 ± 2.01 μg ^{14}C-THF penetrating through the skin. No measurable amounts of ^{14}C-THF were found in the dermis or epidermis following the 60 minute dose exposure duration.

From the 100%-THF, 14 hour dose exposure study, ^{14}C-THF demonstrates a flux range of 1.01 – 2.01 μg/cm^2/hr) with a mean flux rate (t=4 to 14 hrs) of 1.006 ± 0.143 μg/cm^2/hr (n=9), with 15.64 ± 1.39 μg ^{14}C-THF penetrating through the skin (t=0 to 14 hrs). No measurable amounts of ^{14}C-THF were found in the dermis. The epidermal layer demonstrated a trace (0.001 μg) amount of ^{14}C-THF at the end of the 14 hour dose exposure duration.

The permeability coefficient (Kp) was calculated to be 0.011 ± 0.002 cm/hr from the mean rate of penetration derived from the time span t=4 to t=14 hrs observed during the 14 hour dose duration study.

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APPENDICES

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1. PROTOCOL AND AMENDMENTS

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2. PILOT STUDY #1

Pilot Study #1 was conducted as the first look to understand the rate and extent of THF absorption through human cadaver skin. Specifically, this pilot study was designed to assess the volume to dose, sufficiency of dose specific activity, control of dose evaporation, selection of receptor solution, mass balance of applied dose, and the potential for barrier damage following dose application.

Methods:

The methods described in the body of the text were followed but with the following exceptions:

a) 12 skin sections were mounted onto static Franz Chambers from 1 donor (DM112804).
b) 10 skin sections were dosed with 500 µL of ^{14}C-THF (neat THF) at a specific activity of 13,853 DPM/µL.
c) 3 of the 10 dosed skin sections used PBS as the reservoir solution and were sampled over a 48 hour period at 0.17, 0.5, 1, 2, 4, 8, 12, 24, 32 and 48 hrs.
d) 3 of the 10 dosed sections contained PBS with 6% polyethylene glycol 20 oleyl ether (PEG) and were sampled over a 48 hour period at 0.17, 0.5, 1, 2, 4, 8, 12, 24, 32 and 48 hrs.
e) 2 of the 10 dosed sections contained PBS as the reservoir solution and were sampled and processed 10 minutes after dosing.
f) 2 of the 10 dosed sections contained PBS as the reservoir solution and were sampled and processed 60 minutes after dosing.
g) The 2 remaining skin sections were not dosed but sampled and processed as control skin sections.
h) The post-dose tritiated water test was conducted 30 minutes after dose removal.

The initial attempts at occluding the dose half-cell (to prevent THF evaporation) became problematic as it was quickly discovered that the Saran™ and Parafilm™ occlusive covers (as suggested in the Protocol) readily dissolved upon exposure to the THF dose. A partially successful alternative was found using a double layer of nitrile glove membrane held in-place with an O-ring. Subsequent post study evaluations resolved the occlusion problem with the use of silicone stoppers of sufficient size to fit into the dose half-cell opening. The use of the silicone stoppers in the Pivotal section is as described in the text body Methods Section.

Results:

The results from Pilot Study #1 are presented in Tables A1-A3, and Figure A1.

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Table A1: Rate of Absorption of Neat ^{14}C-THF over the 48 hour Dose Period
Mean ± SD as µg/cm^2/hr from 2-3 replicates/evaluation from 1 donor.

Sample #	PBS Reservoir	PBS+6% PEG Reservoir	Mid-Time (hr)
1	0.60 ± 0.21	6.54 ± 8.01	0.083
2	4.14 ± 0.90	11.89 ± 8.65	0.333
3	5.25 ± 0.71	12.40 ± 6.62	0.75
4	7.67 ± 1.01	17.00 ± 16.90	1.50
5	23.62 ± 3.25	16.78 ± 19.59	3.0
6	26.30 ± 7.86	2.71 ± 3.92	6.0
7	2.17 ± 0.95	0.23 ± 0.26	10.0
8	0.08 ± 0.02	0.03 ± 0.02	18.0
9	0.02 ± 0.01	0.01 ± 0.01	28.0
10	0.009 ± 0.004	0.007 ± 0.003	40.0

Table A2: Extent of Absorption of Neat ^{14}C-THF over the Indicated Dose Period
Mean ± SD as µg/cm^2/hr from 2-3 replicates/evaluation from 1 donor.

Chamber System	Dose Duration	Short Term Flux Rate (µg/cm^2/hr)	Total Absorbed (µg)
PBS	10 minutes	0.09 ± 0.09	0.01 ± 0.01
PBS	60 minutes	10.42 ± 0.67	6.86 ± 1.30
PBS Reservoir	48 hours	na	139.31 ± 27.78
PBS+6% PEG Reservoir	48 hours	na	59.31 ± 59.37

Table A3: Change in Barrier Integrity Test Results
Mean as Percent Change from Pre-Dose from 2-3 replicates/evaluation from 1 donor.

Chamber System	Dose Duration	% Change
Control (no Dose)	48 hours	205.5 ± 117.3
PBS	10 minutes	Unavailable
PBS	60 minutes	311.4 ± 67.1
PBS Reservoir	48 hours	3194.7 ± 83.2
PBS+6% PEG Reservoir	48 hours	1995.3 ± 1767.9

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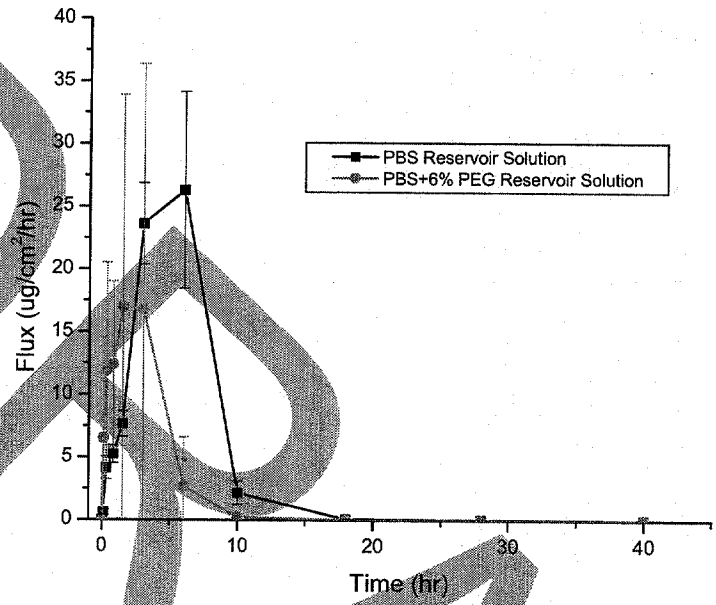
Figure A1: Rate of Absorption of Neat ^{14}C-THF over the 48 hour Dose Period
Mean ± SD as µg/cm^2/hr from 3 replicates/evaluation from 1 donor.



The change in dose specific activity is presented in Appendix 2 and 3 for each Pilot study. The data indicate that the longer the THF dose was in contact with the skin, the greater the decrease in the specific activity of the residual dose. For example when the dose was in contact with the skin, with occlusion, for 48 hrs, the specific activity decreased from 13,850 DPM/µL to 0.33 DPM/µL, where as for the 10 and 60 minute dose durations the specific activity of the dose decreased marginally as a function of duration and THF concentration. In the Investigator's opinion this change is mostly likely attributable to the dilution of the applied dose from trans-epidermal water diffusion across the skin, to the surface of the skin. Trans-epidermal water diffusion, under normal non-occluded conditions ranges from 5 – 13 gms/hr/m^2 (Nilsson, G.E.: *On the Measurement of Evaporative Water Loss, Methods and Clinical Applications*, Department of Medical Engineering, Linköping University, Linköping, Sweden, 1977). During skin occlusion (either by the THF dose or by the occlusive barrier) trans-epidermal water diffusion to the skin surface increases appreciably. Thus, the decrease in dose specific activity, when in contact with the skin is most likely due to its diffusion from water emerging from the skin surface.

Discussion:

The data indicate that steady-state absorption was not achieved primarily due to the loss of the applied dose from evaporation (insufficient dose half-cell occlusion). By 5 hours it was visually apparent that the volume of applied dose had diminished, and by 10 hours there was virtually no applied dose remaining on the surface of the skin.

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The data further indicate that there is no substantially apparent difference in which type of reservoir solution is used, and that the specific activity of the applied dose was more than sufficient to assess the percutaneous absorption of the ^{14}C-THF in the various kinds of samples collected.

The barrier function, post dose removal, as assessed using the $^{3}H_20$, indicate that there was a dramatic change in barrier function. However, this change could have been attributed to either the exposure to the THF, residual ^{14}C-THF diffusion from the skin, or to the fact that the skin was still fully hydrated following the long dose-hydration exposure period.

It was concluded from the results of Pilot Study #1 that a second pilot study was needed to assess improvements in the occlusion of the dose half-cell, to prevent THF evaporation. In addition, as there was indication of barrier damage associated to the exposure to neat THF, dilutions of THF in water were considered for evaluation, and, that the post-dose barrier function test should be extended to allow the skin to return to normal hydration.

3. PILOT STUDY #2

Pilot study #2 was conducted to refine the observations made from Pilot study #1. Specifically, this pilot study was designed to evaluate an improvement in chamber seal (to prevent dose evaporation), an increased dose amount, a modified sampling schedule, a revised radiolabel specific activity, and further evaluation for barrier damage following dose application. Barrier damage potential and THF absorption would be assessed from different concentrations of THF in water ranging from 10%- to 100%-THF.

Methods:

The methods described in the body of the text were followed but with the following exceptions:

a) 12 skin sections were mounted onto static Franz Chambers from 1 donor (SR122704).
b) 10 skin sections were dosed with 800 µL of ^{14}C-THF (neat THF) at a specific activity of 849 – 3,275 DPM/µL (varied with THF concentration).
c) 10 of 12 reservoir cells were filled with PBS + 6% PEG solution, the remaining 2 cells received PBS.
d) All reservoirs were sampled at 0.17, 1, 4, 8, 12, 24, 28, 32, 36 and 48 hours after dosing.
e) 2 skin sections were dosed with a 10%-THF in water solution.
f) 2 skin sections were dosed with a 25%-THF in water solution.
g) 2 skin sections were dosed with a 50%-THF in water solution.
h) 2 skin sections were dosed with a 100% (neat) THF (PBS + 6% PEG reservoir)

i) 2 skin sections were dosed with a 100% (neat) THF (PBS reservoir)
j) The 2 remaining skin sections were not dosed but sampled and processed as control skin sections.
k) The post-dose tritiated water test was conducted 4 hrs after dose removal.

Results:

The results from Pilot Study #2 are presented in Tables A4-A6, and Figure A2.

Table A4: Rate of Absorption of ^{14}C-THF over the 48 hour Dose Period
Mean ± SD as µg/cm^2/hr from 2 replicates/formulation from 1 donor.

Sample #	10% THF (PBS + 6% PEG)	25% THF (PBS + 6% PEG)	50% THF (PBS + 6% PEG)	100% THF (PBS + 6% PEG)	100% THF (PBS)	Mid-Time (hr)
1	0.48 ± 0.08	6.41 ± 0. 45	25.74 ± 0.71	21.23 ± 27.46	96.05 ± 133.54	0.083
2	0.59 ± 0.10	5.18 ± 0.84	21.60 ± 3.00	29.11 ± 39.07	84.38 ± 117.66	0.583
3	0.93± 0.11	6.25 ± 0.63	24.04 ± 1.35	25.09 ± 29.18	28.39 ± 30.54	2.5
4	0.81 ± 0.04	4.18 ± 0.46	17.48 ± 2.58	24.38 ± 15.44	26.16 ± 24.99	6.0
5	0.83 ± 0.05	1.85 ± 2.62	11.71 ± 1.05	34.81 ± 4.89	23.24 ± 8.86	10.0
6	0.57 ± 0.05	2.27 ± 0.45	4.79 ± 0.78	15.79 ± 7.61	16.18 ± 10.34	18.0
7	0.57 ± 0.01	1.70 ± 0.17	3.16 ± 0.78	8.77 ± 2.15	11.30 ± 5.36	26.0
8	0.46 ± 0.00	1.37 ± 0.03	2.24 ± 0.36	6.11 ± 1.89	6.21 ± 2.90	30.0
9	0.45 ± 0.01	1.23 ± 0.10	1.75 ± 0.30	4.85 ± 1.97	4.39 ± 2.36	34.0
10	0.36 ± 0.01	0.86 ± 0.05	1.26 ± 0.15	2.16 ± 0.46	0.92 ± 0.40	42.0

Table A5: Extent of Absorption of Neat ^{14}C-THF over the 48-hr Dose Period
Mean ± SD as µg/cm^2/hr from 2 replicates/formulation from 1 donor.

Applied Dose	Reservoir Solution	Total Absorbed (µg)
10%-THF	PBS + 6% PEG	21.57 ± 1.25
25%-THF	PBS + 6% PEG	82.39 ± 1.02
50%-THF	PBS + 6% PEG	249.91 ± 3.45
100%-THF	PBS + 6% PEG	507.37 ± 36.78
100%-THF	PBS	529.49 ± 140.80

Table A6: Change in Barrier Integrity Test Results
Mean Percent Change from Pre-Dose from 2 replicates/formulation from 1 donor

Applied Dose	Reservoir Solution	% Change
Control (no Dose)	PBS + 6% PEG	139.1 ± 177.1
10%-THF	PBS + 6% PEG	31.4 ± 33.9
25%-THF	PBS + 6% PEG	2792.5 ± 328.8
50%-THF	PBS + 6% PEG	430.8 ± 104.1
100%-THF	PBS + 6% PEG	18711.8 ± 7337.3
100%-THF	PBS	8860.4 ± 5712.8

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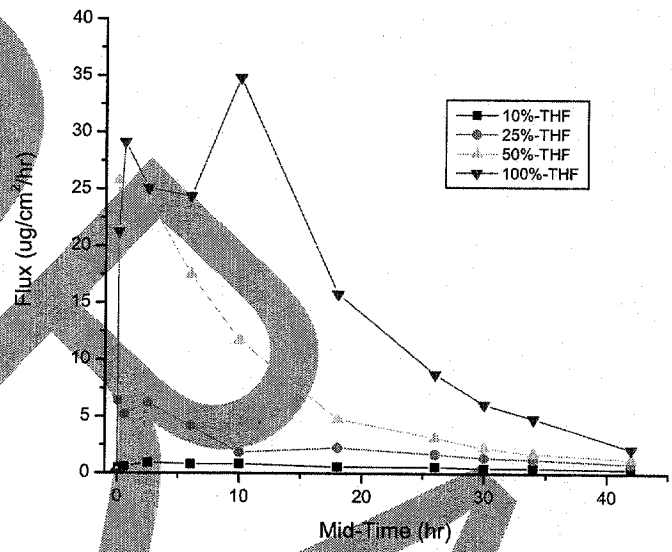
Figure A2: Rate of Absorption of ^{14}C-THF from various Concentrations over the 48 hour Dose Period

Mean ± SD as µg/cm^2/hr from 3 replicates from 1 donor.



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Discussion:

It was observed that the use of the silicone stopper in the dosing half-cell significantly limited the evaporation of the THF dose.

The barrier function test, as assessed with $^3H_20$ suggests that a 48 hr exposure to 25%-THF or greater may cause barrier function damage. The issue of residual ^{14}C-THF cross contaminating the tritium channel was resolved by extending out the post-dose barrier test and by replacing the reservoir solution with fresh prior to performing the test. However, as the control sample barrier test results are still elevated, possibly still attributable to skin hydration, it was recommended that an the post dose removal barrier test be conducted at least eight hours after THF dose removal to allow for the skin to return to more normal hydration conditions (un-occluded).

The rate and extent of THF absorption observed in this Pilot suggests a concentration correlation between 10%- and 25%-THF, but insufficient data is available to extend the correlation beyond 25%-THF as the 50%- and 100%-THF results demonstrate similar peak flux rates and very high variability between their duplicate skin sections.

The 10%-THF flux results indicate a near steady-state like rate of THF absorption over the dose duration period, in particular within the 2 – 15 hour range (following which a slow decline in THF absorption occurs, which could be attributable to the decline in THF

dose concentration, either from its own absorption or the trans-epidermal water diffusion from the reservoir through the skin into the applied dose).

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4. DATA INTERPRETATION AID

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Flow Chart for Interpreting the Study Calculations

To trace the source of data and calculations, follow the numbers on the spreadsheets as outlined below:

"ACROSS DONOR SUMMARY"

This sheet has on it the final summary of results.
There may be multiple "ACROSS DONOR SUMMARY" sheets depending on the number of products te
The numbers are the means of the replicates obtained from each donor.
The calculated numbers for each donor came from each "WITHIN DONOR SUMMARY" sheet.
Consider these results as the study "population" mean.

"WITHIN DONOR SUMMARY"

This sheet has on it the replicate skin section's (individual chamber) results.
Typically there will be from 3 to 4 skin replicates tested for each donor skin.
There will be multiple "WITHIN DONOR SUMMARY" sheets, one for each donor studied.
The calculated numbers came from each "INDIVIDUAL CHAMBER SHEET"
Consider these results as the individual "donor" mean.

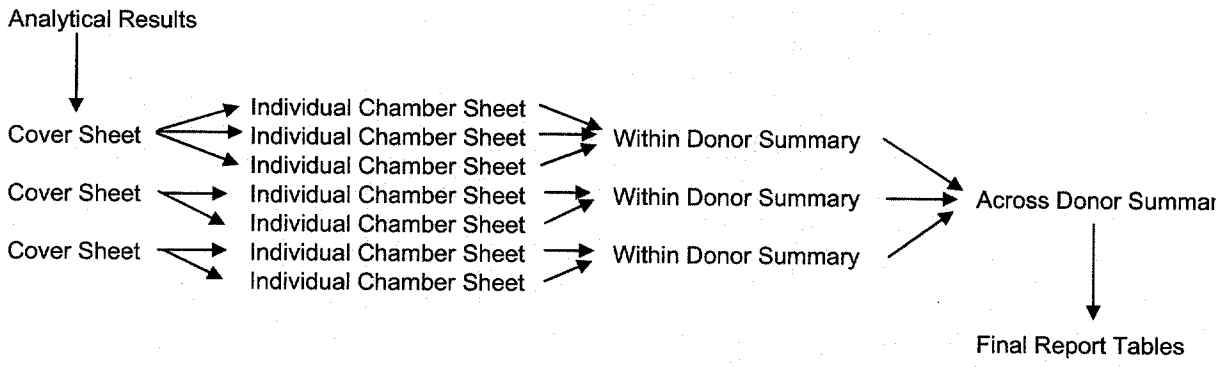
"INDIVIDUAL CHAMBER SHEET"

This sheet has on it the source calculations for each individual skin section (chamber).
Two skin sections (chambers) are typically presented on each sheet.
The information and numbers came from the "COVER SHEET"
There will be multiple sets of this sheet representing all the chambers for that donor.

"COVER SHEET"

This sheet is the starting document that contains all the experimental information for that individual donor, for that study.
There will be multiple "COVER SHEETS", one for each donor studied.
Each "COVER SHEET" lists the source information for what product was applied to which skin sections at what dose, when samples were collected, and the analytical results for each sample.

Example Data Flow:



This table shows the final summary results across the subjects tested.

ACROSS DONOR SUMMARY: FLUX AND MASS BALANCE

The units for the data

Project: Sponsor Name
Date: 03/02/2000

All Flux values are ug/cm2/hr.
All "%" are percent of applied dose.

First Product Evaluated

Product "B"

These are the means of the replicates for each donor tested. In this case 3 donors were studied.

These are the receptor solution results as rates of penetration. In this case 4 samples were collected over 48 hours after dosing.

Sample	AB040190	TJ092297	JW081597	Mean	SE	Mid-t (hr)
1	0.014	0.000	0.000	0.005	0.005	3
2	0.011	0.011	0.009	0.010	0.001	9
3	0.004	0.005	0.006	0.005	0.000	18
4	0.002	0.003	0.003	0.003	0.000	36

Since these results (upper section) are a "rate" value, the data is matched to the mid time point within the sample interval collected.

Total Absorption into the receptor solution (all the way through the skin).

Total Abs (ug):	0.206	0.149	0.147	0.167	0.019

The mass balance results: total recovery of drug in the receptor solution, dermis, epidermis and surface wash as percent of applied dose at 48 hours.

% Abs:	0.176	0.121	0.137	0.145	0.016
% Derm:	0.084	0.029	0.101	0.071	0.022
% Epi:	8.849	6.728	6.521	7.366	0.744
% Surface was	19.424	5.815	8.125	11.121	4.205
% Total Rec:	28.533	12.693	14.883	18.703	4.956

This column shows the variability across the donors as standard error of the population mean.

Total drug recovered as percent of applied dose.

This column shows the final population mean across the donors tested.

Product "E"

This starts the next section for the next product tested.

Sample	AB040190	TJ092297	JW081597	Mean	SE	Mid-t (hr)
1	0.006	0.000	0.000	0.002	0.002	3
2	0.006	0.007	0.016	0.010	0.003	9
3	0.003	0.003	0.004	0.003	0.000	18
4	0.002	0.003	0.003	0.002	0.000	36

Total Abs (ug):	0.116	0.119	0.167	0.134	0.017
% Abs:	0.066	0.060	0.101	0.076	0.013
% Derm:	0.181	0.096	0.145	0.140	0.025
% Epi:	11.497	4.737	7.324	7.852	1.969
% Surface was	16.380	7.831	9.302	11.171	2.639
% Total Rec:	28.124	12.723	16.872	19.240	4.601

These are the individual chamber identifications. Each chamber has a skin section. Each skin section is a replicate from the same donor. This example shows 4 replicates

This table shows the results from the replicate skin sections tested within one donor.

All results on this page came from this donor.

WITHIN DONOR SUMMARY

Project: Sponsor Name

Date: 03/02/2000

Donor ID: JW081597

This column shows the variability of the replicates as the Standard Deviation of the mean.

Product "B"

Sample	U	V	X	W	Mean	SD	mid-t
1	0.000	0.000	0.000	0.000	0.000	0.000	3
2	0.012	0.011	0.011	0.000	0.009	0.006	9
3	0.006	0.005	0.005	0.006	0.006	0.001	18
4	0.003	0.003	0.003	0.003	0.003	0.000	36
Total Abs:	0.165	0.151	0.153	0.117	0.147	0.021	
% Abs:	0.162	0.150	0.129	0.106	0.137	0.025	
Derm:	0.085	0.111	0.145	0.061	0.101	0.036	
Epi:	2.373	7.256	6.705	9.750	6.521	3.066	
Surface:	10.108	7.849	7.926	6.616	8.125	1.452	
Total Rec:	12.728	15.366	14.905	16.533	14.883	1.592	

Results for the first product tested.

This column is the mean result across the replicates for this donor. The numbers in this column are transferred to the "Across Donor Summary" Table.

The description of the numbers here are the same as presented in the "Across Donor Summary" Table.

Product "E"

Sample	M	N	O	Mean	SD	mid-t
1	0.000	0.000	0.000	0.000	0.000	3
2	0.011	0.012	0.026	0.016	0.008	9
3	0.005	0.000	0.006	0.004	0.003	18
4	0.003	0.003	0.003	0.003	0.000	36
Total Abs:	0.149	0.115	0.237	0.167	0.063	
% Abs:	0.078	0.075	0.150	0.101	0.042	
Derm:	0.107	0.305	0.022	0.145	0.145	
Epi:	10.174	6.516	5.281	7.324	2.545	
Surface:	5.044	10.373	12.490	9.302	3.837	
Total Rec:	15.403	17.269	17.943	16.872	1.316	

Results for the second product tested.

Cover Data

Determination of the Percutaneous Absorption of THF, in vitro, Using the Human Cadaver Skin Model

Each row in this section is for each skin section (chamber) used. Multiple entries represent the replicates performed on each product. This example shows 4 skin sections for Product B, 2 for Product E and 3 for Product G. When extra skin is available a non-dosed skin section (Blank) is also set up to evaluated for endogenous compounds that may interfer with the analytical process.

This form represents one of the actual studies performed on one donor.

Surface area of the skin section tested.

Volume of that chamber.

Dose is the amount of product applied to the skin section.

The concentration of drug in the Product.

Used to calculate the specific activity of the drug if radiolabeled, otherwise it's the same as the concentration of the drug in the Product.

The units envolved for each column of information.

This section relates to sample processing such as sample concentration, dilution and collection

Duration between receptor solution samples. This example shows 4 samples collected over the 48 hour dose duration.

These are the actual results from each receptor solution sample. Presented as either a concentration (e.g. ug/mL) or as DPM (radioactive drug).

These are the results from the dermis, epidermis and surface wash samples.

Results for the tritiated water integrity test are entered in this row if performed.

Study Name:	Sponsor and Study

Skin ID #	Exper. Date:	Assay Date:	Todays Date:
JW081597	01/12/2000	01/25/2000	01/26/2000

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
Product B	Drug Name	U	0.8	4.0	5.1	20.0	20.0
Product B	Drug Name	V	0.8	5.2	6.7	20.0	20.0
Product B	Drug Name	W	0.8	5.4	5.2	20.0	20.0
Product B	Drug Name	X	0.8	5.4	7.3	30.0	30.0
Product E	Drug Name	M	0.8	4.0	6.3	30.0	30.0
Product E	Drug Name	N	0.8	5.2	4.6	30.0	30.0
Product G	Drug Name	A	0.8	5.2	5.7	20.0	20.0
Product G	Drug Name	B	0.8	5.0	5.2	20.0	20.0
Product G	Drug Name	C	0.8	5.4	5.6	20.0	20.0
Blank	Drug Name	D	0.8	5.2	6.0	20.0	20.0
Water Standard:	1500	Units:	cm²	ml	mg	ug/mg	ug/mg Veh

Sample Time	Hours
1	6
2	6
3	12
4	24
5	
6	
7	

Sample Volume Collected:	4.00
Final Sample Volume:	0.20

Drug Background	0.00
Water Background	0.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0

Sample Results	U	V	W	X	M	N
1	0.118	0.496	0.197	0.122	0.122	0.123
2	0.226	0.285	0.157	0.121	0.123	0.095
3	0.128	0.230	0.145	0.117	0.124	0.119
4	0.111	0.247	0.142	0.123	0.126	0.120
5						
6						
7						
Dermis	0.082	0.043	0.143	0.023	0.056	0.687
Epidermis	10.974	13.437	5.834	22.644	33.882	8.554
Surface Wash	26.090	15.340	21.780	23.670	25.290	34.150
Water Test						

Sample Results	A	B	C	D		
1	0.116	0.113	0.135	0.119		
2	0.122	0.116	0.125	0.125		
3	0.118	0.126	0.130	0.134		
4	0.128	0.133	0.140	0.123		
5						
6						
7						
Dermis	0.137	0.029	0.031	0.007		
Epidermis	5.550	5.522	3.872	0.586		
Surface Wash	27.410	16.610	12.440	0.000		
Water Test						

HPCL_enc V2: Last Revised 1/18/98

This sheet shows the calculations for two of the individual chambers (skin sections) studied for this donor.

Donor Identification.

All of this information comes from that experiment's Cover Sheet.

IN VITRO STUDY

Skin ID: **JW081597**

Drug: Drug Name
Drug Conc: 20 ug/mg
Chamber Area: 0.8 cm²
Sample Vol: 4.0 ml

Date of Exp: ########
Vehicle: Product B
Standard: 20 ug/mg Veh
Spec. Act. 1.000
Bkg: 0.0

This is the chamber identification.

Chamber: **U**

Chamber Vol: 4.0 ml

Veh Dose: 5.1 mg
Drug Dose: 101 µg

This section is for the rate of penetration in the receptor solution calculations

Sample	Conc	Conc-b	Total Mass	Delta T	Flux (mass)	CumPen(mass)	Mid-T
1	0.118	0.006	0.024	6.0	0.005	0.024	3.0
2	0.226	0.011	0.045	6.0	0.009	0.069	9.0
3	0.128	0.006	0.026	12.0	0.003	0.095	18.0
4	0.111	0.006	0.022	24.0	0.001	0.117	36.0

This section shows the calculations of the receptor solutions. From sample concentration, to total mass absorbed in that sample, ending in the rate (flux) and cumulative penetration of drug.

This section is for the Mass Balance Calculations.

	Conc	Conc-b	Vol.	Total Mass	Mass	% Dose
Total Absorbed:	From	Above	NA	0.117	0.117	0.116
Dermis:	0.082	0.082	1	0.082	0.082	0.081
Epidermis:	10.974	10.974	1	10.974	10.974	10.865
Surface Wash:	26.090	26.090	1	26.090	26.090	25.832
Total Recovery:						36.894 %

This section shows the calculations of the Dermis, Epidermis and Surface wash. From Sample concentration, to total mass present to % of applied dose.

This starts the section for the next chamber.

Chamber: **V**

Chamber Vol: 5.2 ml
Drug Conc: 20.00 ug/mg

Vehicle: Product B
Veh Dose: 6.7 mg
Drug Dose: 133.4 µg

Sample	Conc	Conc-b	Total Mass	Delta T	Flux (mass)	CumPen(mass)	Mid-T
1	0.496	0.025	0.129	6.0	0.027	0.129	3.0
2	0.285	0.014	0.074	6.0	0.015	0.203	9.0
3	0.230	0.011	0.060	12.0	0.006	0.263	18.0
4	0.247	0.012	0.064	24.0	0.003	0.327	36.0

	Conc	Conc-b	Vol:	Total Mass	Mass	% Dose
Total Absorbed:	From	Above	NA	0.327	0.327	0.245
Dermis:	0.043	0.043	1	0.043	0.043	0.032
Epidermis:	13.437	13.437	1	13.437	13.437	10.073
Surface Wash:	15.340	15.340	1	15.340	15.340	11.499
Total Recovery:						21.849 %

5. CELL CALCULATIONS

DRAFT

Across Donor Summaries

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Determination of the Percutaneous Absorption of THF, in vitro, Using the Human Cadaver Skin Model

Summary R04-1387 THF 090905

Socma **R04-1387** **Across Donor Summary**

THF

Formulation 10% THF (10 min)

Sample	SS012005	FD090404	KS032805	Average	SE
1	0.507	0.433	0.119	0.353	0.119
Tot Pen (ug)	0.068	0.058	0.016	0.047	0.016
Tot Pen (%)	0.095	0.081	0.022	0.066	0.022
Dermis (%)	0.000	0.000	0.000	0.000	0.000
Epi (%)	0.000	0.000	0.000	0.000	0.000
S. Wash (%)	0.011	0.153	0.160	0.108	0.049
Total Rec (%)	0.106	0.235	0.182	0.174	0.037

Formulation 30% THF (10 min)

Sample	SS012005	FD090404	KS032805	Average	SE
1	8.589	6.797	2.904	6.097	1.735
Tot Pen (ug)	1.159	0.906	0.374	0.813	0.231
Tot Pen (%)	0.545	0.426	0.176	0.382	0.108
Dermis (%)	0.000	0.000	0.000	0.000	0.000
Epi (%)	0.000	0.001	0.000	0.000	0.000
S. Wash (%)	0.032	0.179	0.417	0.209	0.112
Total Rec (%)	0.577	0.606	0.593	0.592	0.008

Formulation 100% THF (10 min)

Sample	SS012005	FD090404	KS032805	Average	SE
1	2.991	1.726	0.613	1.777	0.687
Tot Pen (ug)	0.399	0.230	0.082	0.237	0.092
Tot Pen (%)	0.056	0.032	0.012	0.033	0.013
Dermis (%)	0.000	0.000	0.000	0.000	0.000
Epi (%)	0.000	0.000	0.000	0.000	0.000
S. Wash (%)	0.008	0.233	0.385	0.209	0.109
Total Rec (%)	0.064	0.265	0.396	0.242	0.096

Formulation 10% THF (60 min)

Sample	SS012005	FD090404	KS032805	Average	SE
1	1.856	2.509	0.953	1.773	0.451
Tot Pen (ug)	1.485	2.008	0.763	1.418	0.361
Tot Pen (%)	2.095	2.832	1.076	2.001	0.509
Dermis (%)	0.000	0.000	0.000	0.000	0.000
Epi (%)	0.000	0.000	0.000	0.000	0.000
S. Wash (%)	0.026	0.278	0.349	0.218	0.098
Total Rec (%)	2.121	3.110	1.425	2.219	0.489

Formulation 30% THF (60 min)

Sample	SS012005	FD090404	KS032805	Average	SE
1	21.253	25.356	13.510	20.039	3.473
Tot Pen (ug)	17.002	20.285	10.808	16.032	2.778
Tot Pen (%)	7.996	9.539	5.083	7.539	1.307
Dermis (%)	0.000	0.000	0.000	0.000	0.000
Epi (%)	0.001	0.000	0.000	0.000	0.000
S. Wash (%)	0.029	0.254	0.408	0.230	0.110
Total Rec (%)	8.025	9.793	5.491	7.770	1.248

Formulation 100% THF (60 min)

Sample	SS012005	FD090404	KS032805	Average	SE
1	3.613	10.755	2.904	5.757	2.507
Tot Pen (ug)	2.890	8.604	2.324	4.606	2.006
Tot Pen (%)	0.408	1.214	0.328	0.650	0.283
Dermis (%)	0.000	0.000	0.000	0.000	0.000
Epi (%)	0.000	0.000	0.000	0.000	0.000
S. Wash (%)	0.010	0.363	0.449	0.274	0.134
Total Rec (%)	0.418	1.577	0.777	0.924	0.342

Formulation 10% THF (14 hours)

Sample	SS012005	FD090404	KS032805	Average	SE	Mid - T
1	1.356	1.362	0.591	1.103	0.256	0.25
2	2.084	1.986	1.515	1.862	0.176	0.75
3	2.254	2.134	1.636	2.008	0.189	1.5
4	1.959	1.768	1.446	1.724	0.150	3
5	1.772	1.555	1.304	1.544	0.135	5
6	1.576	1.342	1.157	1.358	0.121	7
7	1.397	1.267	1.033	1.233	0.106	9
8	1.325	1.151	1.018	1.164	0.089	11
9	1.150	0.990	0.882	1.007	0.078	13
Tot Pen (ug)	17.864	15.962	13.095	15.640	1.386	
Tot Pen (%)	25.204	22.520	18.475	22.066	1.956	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.002	0.001	0.001	0.001	0.000	
S. Wash (%)	0.118	0.324	0.239	0.227	0.060	
Total Rec (%)	25.323	22.845	18.715	22.294	1.927	

Formulation Blank (14 hours)

Sample	SS012005	FD090404	KS032805	Average	SE
1	0.000	0.000	0.000	0.000	0.000
2	0.000	0.000	0.000	0.000	0.000
3	0.000	0.000	0.000	0.000	0.000
4	0.000	0.000	0.000	0.000	0.000
5	0.000	0.000	0.000	0.000	0.000
6	0.000	0.000	0.000	0.000	0.000
7	0.000	0.000	0.000	0.000	0.000
8	0.000	0.000	0.000	0.000	0.000
9	0.000	0.000	0.000	0.000	0.000
Tot Pen (ug)	0.000	0.000	0.000	0.000	0.000
Tot Pen (%)	0.000	0.000	0.000	0.000	0.000
Dermis (%)	0.000	0.000	0.000	0.000	0.000
Epi (%)	0.000	0.000	0.000	0.000	0.000
S. Wash (%)	0.005	0.001	0.001	0.003	0.001
Total Rec (%)	0.004	0.001	0.000	0.002	0.001

Formulation 10% THF (14 hours) - CumPen

Sample	SS012005	FD090404	KS032805	Average	SE	Time
1	0.542	0.545	0.236	0.441	0.102	0.5
2	1.376	1.339	0.842	1.186	0.172	1
3	3.179	3.047	2.151	2.792	0.323	2
4	6.314	5.875	4.464	5.551	0.558	4
5	9.149	8.363	6.550	8.021	0.769	6
6	11.670	10.510	8.402	10.194	0.957	8
7	13.906	12.538	10.055	12.166	1.127	10
8	16.025	14.379	11.684	14.029	1.265	12
9	17.864	15.962	13.095	15.640	1.386	14

Slope	Slope	Slope	(samples 4hr - 14 hr) Mean	SE
1.152	1.007	0.860	1.006	0.084
0.9943	0.9944	0.9955	0.9947	0.0004

Socma **R04-1387** **Across Donor Summary**

THF

Formulation 10% THF (10 min)

Sample	SS012005	FD090404	KS032805	Average	SE
Risidual Dose (%)	82.320	86.893	81.754	83.656	1.627
S. Wash (%)	0.011	0.153	0.160	0.108	0.049
Kimwipe (%)	0.000	0.000	0.000	0.000	0.000
Chamber rinse (%)	0.000	0.000	0.000	0.000	0.000
Total Abs (%)	0.095	0.081	0.022	0.066	0.022
Total Rec (%)	82.426	87.127	81.936	83.830	1.655

Formulation 30% THF (10 min)

Sample	SS012005	FD090404	KS032805	Average	SE
Risidual Dose (%)	89.176	89.924	84.775	87.958	1.606
S. Wash (%)	0.032	0.179	0.417	0.209	0.112
Kimwipe (%)	0.000	0.000	0.000	0.000	0.000
Chamber rinse (%)	0.000	0.000	0.000	0.000	0.000
Total Abs (%)	0.545	0.426	0.176	0.382	0.109
Total Rec (%)	89.753	90.529	85.368	88.550	1.607

Formulation 100% THF (10 min)

Sample	SS012005	FD090404	KS032805	Average	SE
Risidual Dose (%)	99.995	107.099	103.458	103.517	2.051
S. Wash (%)	0.008	0.233	0.385	0.209	0.109
Kimwipe (%)	0.000	0.000	0.000	0.000	0.000
Chamber rinse (%)	0.000	0.000	0.000	0.000	0.000
Total Abs (%)	0.056	0.032	0.012	0.033	0.013
Total Rec (%)	100.059	107.364	103.854	103.759	2.109

Formulation 10% THF (14 hours)

Sample	SS012005	FD090404	KS032805	Average	SE
Risidual Dose (%)	35.692	36.827	36.016	36.178	0.337
S. Wash (%)	0.118	0.324	0.239	0.227	0.060
Kimwipe (%)	0.000	0.000	0.001	0.000	0.000
Chamber rinse (%)	0.000	0.000	0.000	0.000	0.000
Total Abs (%)	25.204	22.520	18.475	22.066	1.956
Total Rec (%)	61.015	59.671	54.730	58.472	1.911

Formulation 10% THF (60 min)

Sample	SS012005	FD090404	KS032805	Average	SE
Risidual Dose (%)	72.599	72.538	75.378	73.505	0.937
S. Wash (%)	0.026	0.278	0.349	0.218	0.098
Kimwipe (%)	0.002	0.000	0.000	0.000	0.001
Chamber rinse (%)	0.000	0.000	0.000	0.000	0.000
Total Abs (%)	2.095	2.832	1.076	2.001	0.509
Total Rec (%)	74.722	75.649	76.803	75.725	0.602

Formulation 30% THF (60 min)

Sample	SS012005	FD090404	KS032805	Average	SE
Risidual Dose (%)	73.378	72.816	77.706	74.633	1.545
S. Wash (%)	0.029	0.254	0.408	0.230	0.110
Kimwipe (%)	0.000	0.000	0.000	0.000	0.000
Chamber rinse (%)	0.000	0.000	0.000	0.000	0.000
Total Abs (%)	7.996	9.539	5.083	7.539	1.307
Total Rec (%)	81.402	82.610	83.197	82.403	0.528

Formulation 100% THF (60 min)

Sample	SS012005	FD090404	KS032805	Average	SE
Risidual Dose (%)	101.733	104.052	104.369	103.384	0.831
S. Wash (%)	0.010	0.363	0.449	0.274	0.134
Kimwipe (%)	0.000	0.000	0.000	0.000	0.000
Chamber rinse (%)	0.000	0.000	0.000	0.000	0.000
Total Abs (%)	0.408	1.214	0.328	0.650	0.283
Total Rec (%)	102.151	105.628	105.145	104.308	1.088

DRAFT

Donor 1

(SS012005)

DRAFT

Socma R04-1387 **Within Donor Summary** Donor: SS012005

Drug: THF

Formulation 10% THF (10 min)

Sample	19	20	21	Average	SD	Mid - T
1	0.768	0.310	0.442	0.507	0.236	0.1
Tot Pen (ug)	0.102	0.041	0.059	0.068	0.031	
Tot Pen (%)	0.144	0.058	0.083	0.095	0.044	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.010	0.014	0.009	0.011	0.003	
Total Rec (%)	0.154	0.072	0.091	0.106	0.043	

Formulation 30% THF (10 min)

Sample	22	23	24	Average	SD	Mid - T
1	3.919	9.695	12.452	8.689	4.355	0.1
Tot Pen (ug)	0.523	1.293	1.660	1.159	0.581	
Tot Pen (%)	0.246	0.608	0.781	0.545	0.273	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.016	0.033	0.048	0.032	0.016	
Total Rec (%)	0.261	0.641	0.828	0.577	0.289	

Formulation 100% THF (10 min)

Sample	25	26	27	Average	SD	Mid - T
1	2.074	3.773	3.127	2.991	0.857	0.1
Tot Pen (ug)	0.277	0.503	0.417	0.398	0.114	
Tot Pen (%)	0.039	0.071	0.059	0.056	0.016	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.003	0.018	0.003	0.008	0.009	
Total Rec (%)	0.042	0.089	0.062	0.064	0.024	

Formulation 10% THF (14 hours)

Sample	20	21	22	Average	SD	Mid - T
1	1.074	1.431	1.564	1.356	0.253	0.25
2	1.939	2.263	2.049	2.084	0.164	0.75
3	1.560	3.061	2.140	2.254	0.757	1.5
4	1.844	2.203	1.831	1.959	0.211	3
5	1.570	2.077	1.669	1.772	0.269	5
6	1.497	1.682	1.548	1.576	0.095	7
7	1.362	1.433	1.397	1.397	0.036	9
8	1.228	1.501	1.245	1.325	0.153	11
9	1.110	1.231	1.108	1.150	0.071	13
Tot Pen (ug)	16.229	20.128	17.236	17.864	2.024	
Tot Pen (%)	22.897	28.397	24.317	25.204	2.855	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.002	0.002	0.001	0.002	0.000	
S. Wash (%)	0.154	0.139	0.062	0.118	0.049	
Total Rec (%)	23.052	28.538	24.380	25.323	2.862	

Formulation 10% THF (14 hours) - CumPen

Sample	20	21	22	Average	SD	Time
1	0.430	0.572	0.626	0.542	0.101	0.5
2	1.205	1.477	1.445	1.376	0.149	1
3	2.453	3.926	3.157	3.179	0.737	2
4	5.404	7.451	6.087	6.314	1.042	4
5	7.916	10.774	8.757	9.149	1.469	6
6	10.311	13.465	11.235	11.670	1.621	8
7	12.489	15.757	13.471	13.906	1.677	10
8	14.454	18.159	15.463	16.025	1.915	12
9	16.229	20.128	17.236	17.864	2.024	14

Slope	Slope	Slope	Average	
1.085	1.255	1.116	1.152	(samples 4hr - 14 hr)
0.9958	0.9927	0.9644	0.9943	

Formulation 10% THF (60 min)

Sample	40	41	42	Average	SD	Mid - T
1	1.736	2.365	1.467	1.856	0.461	0.5
Tot Pen (ug)	1.389	1.882	1.174	1.485	0.369	
Tot Pen (%)	1.960	2.670	1.656	2.095	0.520	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.006	0.027	0.045	0.026	0.019	
Total Rec (%)	1.966	2.697	1.701	2.121	0.516	

Formulation 30% THF (60 min)

Sample	43	44	45	Average	SD	Mid - T
1	18.891	22.884	21.983	21.253	2.094	0.5
Tot Pen (ug)	15.113	18.307	17.587	17.002	1.675	
Tot Pen (%)	7.107	8.609	8.271	7.996	0.788	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.001	0.001	0.001	0.001	0.000	
S. Wash (%)	0.026	0.038	0.022	0.029	0.009	
Total Rec (%)	7.134	8.649	8.293	8.025	0.792	

Formulation 100% THF (60 min)

Sample	46	47	48	Average	SD	Mid - T
1	2.925	5.258	2.656	3.613	1.431	0.5
Tot Pen (ug)	2.340	4.206	2.125	2.890	1.145	
Tot Pen (%)	0.330	0.593	0.300	0.408	0.162	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.004	0.011	0.016	0.010	0.006	
Total Rec (%)	0.334	0.604	0.316	0.418	0.162	

Formulation Blank (14 hours)

Sample	19	Average	Mid - T
1	0.000	0.000	0.25
2	0.000	0.000	0.75
3	0.000	0.000	1.5
4	0.000	0.000	3
5	0.000	0.000	5
6	0.000	0.000	7
7	0.000	0.000	9
8	0.000	0.000	11
9	0.000	0.000	13
Tot Pen (ug)	0.000	0.000	
Tot Pen (%)	0.000	0.000	
Dermis (%)	0.000	0.000	
Epi (%)	0.000	0.000	
S. Wash (%)	0.005	0.005	
Total Rec (%)	0.004	0.004	

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Donor 1

Chamber Results (10 Minutes)

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Study Name:	Socma, donor 1, 10 min	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
SS012005	07/14/2005	07/17/2005	07/17/2005	07/19/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	19	0.8	5.3	800	0.0886	4311.4
10% THF	THF	20	0.8	4.6	800	0.0886	4311.4
10% THF	THF	21	0.8	5.2	800	0.0886	4311.4
30% THF	THF	22	0.8	5.2	800	0.2658	4034.3
30% THF	THF	23	0.8	5.2	800	0.2658	4034.3
30% THF	THF	24	0.8	4.6	800	0.2658	4034.3
100% THF	THF	25	0.8	5.0	800	0.8860	4088.5
100% THF	THF	26	0.8	5.0	800	0.8860	4088.5
100% THF	THF	27	0.8	5.4	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.17
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1543.65
Receptor Solution:	1x PBS

Sample Results	19	20	21	22	23	24
1	959.000	456.000	570.000	1544.000	3792.000	5497.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	14.000	14.000	11.000	9.000	11.000	10.000
Epidermis	17.000	16.000	16.000	21.000	20.000	22.000
Surface Wash	351.000	508.000	313.000	533.000	1096.000	1563.000
Other						
Water Test	145.00	152.00	129.00	101.00	102.00	150.00

Sample Results	25	26	27			
1	274.000	483.000	375.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	14.000	12.000	13.000			
Epidermis	15.000	15.000	19.000			
Surface Wash	124.000	619.000	131.000			
Other						
Water Test	144.00	146.00	160.00			

Skin CalculationsV7

Study Name:	Socma, donor 1, 10 min (2nd cover sheet)	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
SS012005	07/14/2005	07/17/2005	07/17/2005	07/19/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	19	0.8	5.3	800	0.0886	4311.4
10% THF	THF	20	0.8	4.6	800	0.0886	4311.4
10% THF	THF	21	0.8	5.2	800	0.0886	4311.4
30% THF	THF	22	0.8	5.2	800	0.2658	4034.3
30% THF	THF	23	0.8	5.2	800	0.2658	4034.3
30% THF	THF	24	0.8	4.6	800	0.2658	4034.3
100% THF	THF	25	0.8	5.0	800	0.8860	4088.5
100% THF	THF	26	0.8	5.0	800	0.8860	4088.5
100% THF	THF	27	0.8	5.4	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.17
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1543.65
Receptor Solution:	1x PBS

Sample Results	19	20	21	22	23	24
1	959.000	456.000	570.000	1544.000	3792.000	5497.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	87337.000	87136.000	91767.000	92691.000	87632.000	89558.000
Top residual activity (DPM/µL)	3493.5	3485.4	3670.7	3707.6	3505.3	3582.3
Kimwipe	12.000	12.000	13.000	15.000	16.000	13.000
Chamber wash	20.000	29.000	27.000	28.000	23.000	26.000
Water Test	145.00	152.00	129.00	101.00	102.00	150.00

Sample Results, (ug/uL)	25	26	27			
1	274.000	483.000	375.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	93687.000	104390.000	108597.000			
Top residual activity (DPM/µL)	3747.5	4175.6	4343.9			
Kimwipe	15.000	14.000	13.000			
Chamber wash	26.000	24.000	27.000			
Water Test	144.00	146.00	160.00			

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 10 min**

Date Dosed: 07/14/05

Chamber: **19** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	959.000	940.250	4983.325	0.2	0.768	0.102	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.102	0.102	0.144
Dermis:	14.000	-4.750	1	-4.750	0.000	0.000
Epidermis:	17.000	-1.750	1	-1.750	0.000	0.000
Surface Wash:	351.000	332.250	1	332.250	0.007	0.010
Other						
Total Recovery:						0.154 %

Chamber: **20** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	456.000	437.250	2011.350	0.2	0.310	0.041	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.041	0.041	0.058
Dermis:	14.000	-4.750	1	-4.750	0.000	0.000
Epidermis:	16.000	-2.750	1	-2.750	0.000	0.000
Surface Wash:	508.000	489.250	1	489.250	0.010	0.014
Other						
Total Recovery:						0.072 %

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R04-1387 INDIVIDUAL CHAMBER RESULTS

Skin ID: SS012005 **Sponsor:** Socma, donor 1, 10 min

Date Dosed: 07/14/05

Chamber: 21 **Vehicle:** 10% THF
Drug: THF

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	570.000	551.250	2866.500	0.2	0.442	0.059	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.059	0.059	0.083
Dermis:	11.000	-7.750	1	-7.750	0.000	0.000
Epidermis:	16.000	-2.750	1	-2.750	0.000	0.000
Surface Wash:	313.000	294.250	1	294.250	0.006	0.009
Other						
Total Recovery:						0.091 %

Chamber: 22 **Vehicle:** 30% THF
Drug: THF

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	1544.000	1525.250	7931.300	0.2	3.919	0.523	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.523	0.523	0.246
Dermis:	9.000	-9.750	1	-9.750	-0.001	0.000
Epidermis:	21.000	2.250	1	2.250	0.000	0.000
Surface Wash:	533.000	514.250	1	514.250	0.034	0.016
Other						
Total Recovery:						0.261 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 10 min**

Date Dosed: 07/14/05

Chamber: **23** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	3792.000	3773.250	19620.900	0.2	9.695	1.293	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.293	1.293	0.608
Dermis:	11.000	-7.750	1	-7.750	-0.001	0.000
Epidermis:	20.000	1.250	1	1.250	0.000	0.000
Surface Wash:	1096.000	1077.250	1	1077.250	0.071	0.033
Other						
Total Recovery:						0.641 %

Chamber: **24** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	5497.000	5478.250	25199.950	0.2	12.452	1.660	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.660	1.660	0.781
Dermis:	10.000	-8.750	1	-8.750	-0.001	0.000
Epidermis:	22.000	3.250	1	3.250	0.000	0.000
Surface Wash:	1563.000	1544.250	1	1544.250	0.102	0.048
Other						
Total Recovery:						0.828 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 10 min**

Date Dosed: 07/14/05

Chamber: **25** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	274.000	255.250	1276.250	0.2	2.074	0.277	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.277	0.277	0.039
Dermis:	14.000	-4.750	1	-4.750	-0.001	0.000
Epidermis:	15.000	-3.750	1	-3.750	-0.001	0.000
Surface Wash:	124.000	105.250	1	105.250	0.023	0.003
Other						
Total Recovery:						0.042 %

Chamber: **26** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	483.000	464.250	2321.250	0.2	3.773	0.503	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.503	0.503	0.071
Dermis:	12.000	-6.750	1	-6.750	-0.001	0.000
Epidermis:	15.000	-3.750	1	-3.750	-0.001	0.000
Surface Wash:	619.000	600.250	1	600.250	0.130	0.018
Other						
Total Recovery:						0.089 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 10 min**

Date Dosed: 07/14/05

Chamber: **27** **Vehicle:** **100% THF**

Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	375.000	356.250	1923.750	0.2	3.127	0.417	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.417	0.417	0.059
Dermis:	13.000	-5.750	1	-5.750	-0.001	0.000
Epidermis:	19.000	0.250	1	0.250	0.000	0.000
Surface Wash:	131.000	112.250	1	112.250	0.024	0.003
Other						
Total Recovery:						0.062 %

Chamber: **0** **Vehicle:**

Drug:

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1							

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.000	0.000	0.000
Dermis:						
Epidermis:						
Surface Wash:						
Other						
Total Recovery:						0.000 %

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R04-1387
Water Integrity Test and Product Dose Summary by Product

Donor: SS012005 Date: 07/14/2005

Dose units: uL

Product: 10% THF

Replicate	Chamber	uL	Product Dose
1	19	0.44	800.00
2	20	0.40	800.00
3	21	0.37	800.00
4			
5			
6			
7			
8			
Mean:		**0.40**	**800.00**
SD:		0.03	0.00
CV:		7.75	0.00

Product: 30% THF

Replicate	Chamber	uL	Product Dose
1	22	0.28	800.00
2	23	0.28	800.00
3	24	0.39	800.00
4			
5			
6			
7			
8			
Mean:		**0.32**	**800.00**
SD:		0.06	0.00
CV:		20.31	0.00

Product: 100% THF

Replicate	Chamber	uL	Product Dose
1	25	0.41	800.00
2	26	0.41	800.00
3	27	0.50	800.00
4			
5			
6			
7			
8			
Mean:		**0.44**	**800.00**
SD:		0.05	0.00
CV:		11.23	0.00

Across Donor Mean

Replicate	Chamber	Pre-test uL	Post (H2) DPM	Post (H2) µL	Post (H3) DPM	Post (H3) µL
1	19	0.44	46	0.10	124	0.36
2	20	0.40	11	0.00	111	0.28
3	21	0.37	6	0.00	88	0.24
4	22	0.28	0	0.00	97	0.27
5	23	0.28	0	0.00	97	0.27
6	24	0.39	0	0.00	78	0.18
7	25	0.41	293	0.89	249	0.75
8	26	0.41	515	1.61	428	1.33
19	27	0.50	306	1.01	281	0.92
10						
11						
12						
13						
14						
15						
16						
17						
18						
Mean:		**0.39**		**0.40**		**0.51**
SD:		0.07		0.61		0.40
CV:		17.89		152.04		78.33

Product: 0

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: 0

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: 0

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Study Name:	Socma, donor 1, 10 min	Study #:	R04-1387

Top residual (25 µL)

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Orig. Vol. (µL)***	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	87337	18.75	25	800	87318.25	4311.4	0.0886	57.42			81%		
10% THF	20	87136	18.75	25	800	87117.25	4311.4	0.0886	57.29			81%		
10% THF	21	91767	18.75	25	800	91748.25	4311.4	0.0886	60.33	58.35	1.72	85%	82.320	0.024
30% THF	22	92691	18.75	25	800	92672.25	4034.3	0.2658	195.38			92%		
30% THF	23	87632	18.75	25	800	87613.25	4034.3	0.2658	184.71			87%		
30% THF	24	89558	18.75	25	800	89539.25	4034.3	0.2658	188.78	189.62	5.38	89%	89.176	0.025
100% THF	25	93657	18.75	25	800	93668.25	4088.5	0.8860	649.56			92%		
100% THF	26	104390	18.75	25	800	104371.25	4088.5	0.8860	723.78			102%		
100% THF	27	108597	18.75	25	800	108578.25	4088.5	0.8860	752.95	708.76	53.31	106%	99.995	0.075

Surface Wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	351	18.75	1500	1500	332.25	4311.4	0.0886	0.01			0%		
10% THF	20	508	18.75	1500	1500	489.25	4311.4	0.0886	0.01			0%		
10% THF	21	313	18.75	1500	1500	294.25	4311.4	0.0886	0.01	0.01	0.00	0%	0.011	0.000
30% THF	22	533	18.75	1500	1500	514.25	4034.3	0.2658	0.03			0%		
30% THF	23	1096	18.75	1500	1500	1077.25	4034.3	0.2658	0.07			0%		
30% THF	24	1563	18.75	1500	1500	1544.25	4034.3	0.2658	0.10	0.07	0.03	0%	0.032	0.000
100% THF	25	124	18.75	1500	1500	105.25	4088.5	0.8860	0.02			0%		
100% THF	26	619	18.75	1500	1500	600.25	4088.5	0.8860	0.13			0%		
100% THF	27	131	18.75	1500	1500	112.25	4088.5	0.8860	0.02	0.06	0.06	0%	0.008	0.000

Kimwipe

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	12	18.75	NA	NA	-6.75	4311.4	0.0886	0.00			0%		
10% THF	20	12	18.75	NA	NA	-6.75	4311.4	0.0886	0.00			0%		
10% THF	21	13	18.75	NA	NA	-5.75	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	22	15	18.75	NA	NA	-3.75	4034.3	0.2658	0.00			0%		
30% THF	23	16	18.75	NA	NA	-2.75	4034.3	0.2658	0.00			0%		
30% THF	24	13	18.75	NA	NA	-5.75	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	25	15	18.75	NA	NA	-3.75	4088.5	0.8860	0.00			0%		
100% THF	26	14	18.75	NA	NA	-4.75	4088.5	0.8860	0.00			0%		
100% THF	27	13	18.75	NA	NA	-5.75	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

Chamber wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	20	18.75	1000	1000	1.25	4311.4	0.0886	0.00			0%		
10% THF	20	29	18.75	1000	1000	10.25	4311.4	0.0886	0.00			0%		
10% THF	21	27	18.75	1000	1000	8.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	22	28	18.75	1000	1000	9.25	4034.3	0.2658	0.00			0%		
30% THF	23	23	18.75	1000	1000	4.25	4034.3	0.2658	0.00			0%		
30% THF	24	26	18.75	1000	1000	7.25	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	25	26	18.75	1000	1000	7.25	4088.5	0.8860	0.00			0%		
100% THF	26	24	18.75	1000	1000	5.25	4088.5	0.8860	0.00			0%		
100% THF	27	27	18.75	1000	1000	8.25	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

* µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM / Sample Vol.) / (Spec. Act.) * (Drug Conc.) * Orig. Vol.
** µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM) / (Spec. Act.) * (Drug Conc.)
*** Assumed the residual volume is the same as the dosed volume.
**** % recovered = µg / (Drug Conc. * 800 µL)

Donor 1

Chamber Results (60 Minutes)

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Cover Data

Study Name:	Socma, donor 1, 60 min	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
SS012005	07/14/2005	07/17/2005	07/17/2005	07/19/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	40	0.8	5.4	800	0.0886	4311.4
10% THF	THF	41	0.8	4.9	800	0.0886	4311.4
10% THF	THF	42	0.8	4.6	800	0.0886	4311.4
30% THF	THF	43	0.8	4.6	800	0.2658	4034.3
30% THF	THF	44	0.8	4.4	800	0.2658	4034.3
30% THF	THF	45	0.8	5.2	800	0.2658	4034.3
100% THF	THF	46	0.8	5.2	800	0.8860	4088.5
100% THF	THF	47	0.8	4.5	800	0.8860	4088.5
100% THF	THF	48	0.8	4.6	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	1.00
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	7543.65
Receptor Solution:	1x PBS

Sample Results	40	41	42	43	44	45
1	12537.000	18810.000	12434.000	49886.000	63170.000	51352.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	16.000	17.000	19.000	17.000	15.000	14.000
Epidermis	30.000	31.000	27.000	47.000	53.000	42.000
Surface Wash	230.000	949.000	1558.000	857.000	1256.000	722.000
Other						
Water Test	100.00	150.00	106.00	160.00	162.00	176.00

Sample Results	46	47	48			
1	2095.000	4332.000	2150.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	15.000	15.000	13.000			
Epidermis	19.000	20.000	25.000			
Surface Wash	162.000	381.000	537.000			
Other						
Water Test	161.00	138.00	123.00			

Skin CalculationsV7.

DRAFT

Study Name:	Socma, donor 1, 60 min (2nd cover sheet)	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
SS012005	07/14/2005	07/17/2005	07/17/2005	07/19/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	40	0.8	5.4	800	0.0886	4311.4
10% THF	THF	41	0.8	4.9	800	0.0886	4311.4
10% THF	THF	42	0.8	4.6	800	0.0886	4311.4
30% THF	THF	43	0.8	4.6	800	0.2658	4034.3
30% THF	THF	44	0.8	4.4	800	0.2658	4034.3
30% THF	THF	45	0.8	5.2	800	0.2658	4034.3
100% THF	THF	46	0.8	5.2	800	0.8860	4088.5
100% THF	THF	47	0.8	4.5	800	0.8860	4088.5
100% THF	THF	48	0.8	4.6	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	1.00
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1543.65
Receptor Solution:	1x PBS

Sample Results	40	41	42	43	44	45
1	12537.000	18810.000	12434.000	49886.000	63170.000	51352.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	77914.000	77856.000	79038.000	74198.000	74095.000	73791.000
Top residual activity (DPM/µL)	3116.6	3114.2	3161.5	2967.7	2963.8	2951.6
Kimwipe	11.000	152.000	52.000	19.000	14.000	18.000
Chamber wash	24.000	24.000	24.000	28.000	26.000	23.000
Water Test	100.00	150.00	106.00	160.00	162.00	176.00

Sample Results	46	47	48			
1	2095.000	4332.000	2150.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	104022.000	105244.000	102738.000			
Top residual activity (DPM/µL)	4160.9	4209.8	4109.5			
Kimwipe	18.000	12.000	11.000			
Chamber wash	22.000	27.000	24.000			
Water Test	161.00	138.00	123.00			

Skin CalculationsV7.

DRAFT

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 60 min**

Date Dosed: 07/14/05

Chamber: **40** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	12537.000	12518.250	67598.550	1.0	1.736	1.389	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.389	1.389	1.960
Dermis:	16.000	-2.750	1	-2.750	0.000	0.000
Epidermis:	30.000	11.250	1	11.250	0.000	0.000
Surface Wash:	230.000	211.250	1	211.250	0.004	0.006
Other						
Total Recovery:						1.966 %

Chamber: **41** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	18810.000	18791.250	92077.125	1.0	2.365	1.892	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.892	1.892	2.670
Dermis:	17.000	-1.750	1	-1.750	0.000	0.000
Epidermis:	31.000	12.250	1	12.250	0.000	0.000
Surface Wash:	949.000	930.250	1	930.250	0.019	0.027
Other						
Total Recovery:						2.697 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 60 min**

Date Dosed: 07/14/05

Chamber: **42** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	12434.000	12415.250	57110.150	1.0	1.467	1.174	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.174	1.174	1.656
Dermis:	19.000	0.250	1	0.250	0.000	0.000
Epidermis:	27.000	8.250	1	8.250	0.000	0.000
Surface Wash:	1558.000	1539.250	1	1539.250	0.032	0.045
Other						
Total Recovery:						1.701 %

Chamber: **43** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	49886.000	49867.250	229389.350	1.0	18.891	15.113	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	15.113	15.113	7.107
Dermis:	17.000	-1.750	1	-1.750	0.000	0.000
Epidermis:	47.000	28.250	1	28.250	0.002	0.001
Surface Wash:	857.000	838.250	1	838.250	0.055	0.026
Other						
Total Recovery:						7.134 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 60 min**

Date Dosed: 07/14/05

Chamber: **44** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	63170.000	63151.250	277865.500	1.0	22.884	18.307	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	18.307	18.307	8.609
Dermis:	15.000	-3.750	1	-3.750	0.000	0.000
Epidermis:	53.000	34.250	1	34.250	0.002	0.001
Surface Wash:	1256.000	1237.250	1	1237.250	0.082	0.038
Other						
Total Recovery:						8.649 %

Chamber: **45** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	51352.000	51333.250	266932.900	1.0	21.983	17.587	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	17.587	17.587	8.271
Dermis:	14.000	-4.750	1	-4.750	0.000	0.000
Epidermis:	42.000	23.250	1	23.250	0.002	0.001
Surface Wash:	722.000	703.250	1	703.250	0.046	0.022
Other						
Total Recovery:						8.293 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 60 min**

Date Dosed: 07/14/05

Chamber: **46** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	2095.000	2076.250	10796.500	1.0	2.925	2.340	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	2.340	2.340	0.330
Dermis:	15.000	3.750	1	-3.750	-0.001	0.000
Epidermis:	19.000	0.250	1	0.250	0.000	0.000
Surface Wash:	162.000	143.250	1	143.250	0.031	0.004
Other						
Total Recovery:						0.334 %

Chamber: **47** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	4332.000	4313.250	19409.625	1.0	5.258	4.206	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	4.206	4.206	0.593
Dermis:	15.000	-3.750	1	-3.750	-0.001	0.000
Epidermis:	20.000	1.250	1	1.250	0.000	0.000
Surface Wash:	381.000	362.250	1	362.250	0.079	0.011
Other						
Total Recovery:						0.604 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 60 min**

Date Dosed: 07/14/05

Chamber: **48** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	2150.000	2131.250	9803.750	1.0	2.656	2.125	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	2.125	2.125	0.300
Dermis:	13.000	5.750	1	-5.750	-0.001	0.000
Epidermis:	25.000	6.250	1	6.250	0.001	0.000
Surface Wash:	537.000	518.250	1	518.250	0.112	0.016
Other						
Total Recovery:						0.316 %

Chamber: **0** **Vehicle:**
Drug:

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1							

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.000	0.000	0.000
Dermis:						
Epidermis:						
Surface Wash:						
Other						
Total Recovery:						0.000 %

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Determination of the Percutaneous Absorption of THF, in vitro, Using the Human Cadaver Skin Model

Water Test Results

R04-1387

Water Integrity Test and Product Dose Summary by Product

Donor: **SS012005** Date: **07/14/2005** **Dose units:** uL

Product: **10% THF**

Replicate	Chamber	uL	Product Dose
1	40	0.29	800.00
2	41	0.42	800.00
3	42	0.26	800.00
4			
5			
6			
7			
8			
Mean:		**0.32**	**800.00**
SD:		0.08	0.00
CV:		26.13	0.00

Product: **30% THF**

Replicate	Chamber	uL	Product Dose
1	43	0.42	800.00
2	44	0.41	800.00
3	45	0.53	800.00
4			
5			
6			
7			
8			
Mean:		**0.46**	**800.00**
SD:		0.07	0.00
CV:		14.71	0.00

Product: **100% THF**

Replicate	Chamber	uL	Product Dose
1	46	0.48	800.00
2	47	0.35	800.00
3	48	0.31	800.00
4			
5			
6			
7			
8			
Mean:		**0.38**	**800.00**
SD:		0.09	0.00
CV:		23.27	0.00

Across Donor Mean

Replicate	Chamber	Pre-test µL	Post (H2) DPM	Post (H2) µL	Post (H3) DPM	Post (H3) µL
1	40	0.29	288	0.94	88	0.24
2	41	0.42	0	0.00	97	0.25
3	42	0.26	10	0.00	90	0.21
4	43	0.42	0	0.00	118	0.30
5	44	0.41	0	0.00	118	0.29
6	45	0.53	0	0.00	142	0.42
7	46	0.48	1144	3.79	984	3.25
8	47	0.35	1406	4.05	1123	3.22
19	49	0.31	800	2.33	875	2.55
10						
11						
12						
13						
14						
15						
16						
17						
18						
Mean:		**0.39**		**1.23**		**1.19**
SD:		0.09		1.71		1.38
CV:		23.40		138.37		115.45

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

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Study Name:	Socma, donor 1, 60 min	Study #:	R04-1387

Top residual (25 µL)

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Orig. Vol. (µL)***	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	40	77914	18.75	25	800	77895.25	4311.4	0.0886	51.22			72%		
10% THF	41	77856	18.75	25	800	77837.25	4311.4	0.0886	51.19			72%		
10% THF	42	79036	18.75	25	800	79019.25	4311.4	0.0886	51.96	51.46	0.44	73%	72.599	0.006
30% THF	43	74193	18.75	25	800	74174.25	4034.3	0.2658	156.38			74%		
30% THF	44	74095	18.75	25	800	74076.25	4034.3	0.2658	156.17			73%		
30% THF	45	73791	18.75	25	800	73772.25	4034.3	0.2658	155.53	156.03	0.44	73%	73.378	0.002
100% THF	46	104022	18.75	25	800	104003.25	4088.5	0.8860	721.23			102%		
100% THF	47	105244	18.75	25	800	105225.25	4088.5	0.8860	729.70			103%		
100% THF	48	102738	18.75	25	800	102719.25	4088.5	0.8860	712.32	721.08	8.69	100%	101.733	0.012

Surface Wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	40	230	18.75	1500	1500	211.25	4311.4	0.0886	0.00			0%		
10% THF	41	949	18.75	1500	1500	930.25	4311.4	0.0886	0.02			0%		
10% THF	42	1558	18.75	1500	1500	1539.25	4311.4	0.0886	0.03	0.02	0.01	0%	0.026	0.000
30% THF	43	857	18.75	1500	1500	838.25	4034.3	0.2658	0.06			0%		
30% THF	44	1256	18.75	1500	1500	1237.25	4034.3	0.2658	0.08			0%		
30% THF	45	722	18.75	1500	1500	703.25	4034.3	0.2658	0.05	0.06	0.02	0%	0.029	0.000
100% THF	46	162	18.75	1500	1500	143.25	4088.5	0.8860	0.03			0%		
100% THF	47	381	18.75	1500	1500	362.25	4088.5	0.8860	0.08			0%		
100% THF	48	537	18.75	1500	1500	518.25	4088.5	0.8860	0.11	0.07	0.04	0%	0.010	0.000

Kimwipe

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	40	11	18.75	NA	NA	-7.75	4311.4	0.0886	0.00			0%		
10% THF	41	152	18.75	NA	NA	133.25	4311.4	0.0886	0.00			0%		
10% THF	42	52	18.75	NA	NA	33.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.002	0.000
30% THF	43	19	18.75	NA	NA	0.25	4034.3	0.2658	0.00			0%		
30% THF	44	14	18.75	NA	NA	-4.75	4034.3	0.2658	0.00			0%		
30% THF	45	18	18.75	NA	NA	-0.75	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	46	18	18.75	NA	NA	-0.75	4088.5	0.8860	0.00			0%		
100% THF	47	12	18.75	NA	NA	-6.75	4088.5	0.8860	0.00			0%		
100% THF	48	11	18.75	NA	NA	-7.75	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

Chamber wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	40	24	18.75	1000	1000	5.25	4311.4	0.0886	0.00			0%		
10% THF	41	24	18.75	1000	1000	5.25	4311.4	0.0886	0.00			0%		
10% THF	42	24	18.75	1000	1000	5.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	43	28	18.75	1000	1000	9.25	4034.3	0.2658	0.00			0%		
30% THF	44	26	18.75	1000	1000	7.25	4034.3	0.2658	0.00			0%		
30% THF	45	23	18.75	1000	1000	4.25	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	46	22	18.75	1000	1000	3.25	4088.5	0.8860	0.00			0%		
100% THF	47	27	18.75	1000	1000	8.25	4088.5	0.8860	0.00			0%		
100% THF	48	24	18.75	1000	1000	5.25	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

* µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM / Sample Vol.) / (Spec. Act.) * (Drug Conc.) * Orig. Vol.

** µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM) / (Spec. Act.) * (Drug Conc.)

*** Assumed the residual volume is the same as the dosed volume.

**** % recovered = µg / (Drug Conc. * 800 µL)

Donor 1

Chamber Results (14 Hours)

DRAFT

Cover Data

Study Name:	Socma, donor 1, 14 hours	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
SS012005	07/27/2005	07/29/2005	07/29/2005	08/01/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
Blank	No dose	19	0.8	5.0	800	0.0886	4311.4
10% THF	THF	20	0.8	5.6	800	0.0886	4311.4
10% THF	THF	21	0.8	5.1	800	0.0886	4311.4
10% THF	THF	22	0.8	5.3	800	0.0886	4311.4
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.50
2	0.50
3	1
4	2
5	2
6	2
7	2
8	2
9	2
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	19	20	21	22		
1	14.000	3752.000	5479.000	5762.000		
2	12.000	6760.000	8654.000	7544.000		
3	16.000	10862.000	23383.000	15736.000		
4	17.000	25655.000	33653.000	26922.000		
5	11.000	21848.000	31723.000	24534.000		
6	16.000	20829.000	25692.000	22765.000		
7	17.000	18950.000	21894.000	20547.000		
8	19.000	17092.000	22920.000	18308.000		
9	16.000	15445.000	18811.000	16298.000		
10						
11						
12						
Dermis	6.000	6.000	6.000	13.000		
Epidermis	6.000	71.000	83.000	62.000		
Surface Wash	190.000	5320.000	4827.000	2149.000		
Other						
Water Test	146.00	181.00	170.00	175.00		

Sample Results						
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis						
Epidermis						
Surface Wash						
Other						
Water Test						

Skin CalculationsV7.

DRAFT

Study Name:	Socma, donor 1, 14 hours (2nd cover sheet)	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
SS012005	07/27/2005	07/29/2005	07/29/2005	08/01/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
Blank	No dose	19	0.8	5.0	800	0.0886	4311.4
10% THF	THF	20	0.8	5.6	800	0.0886	4311.4
10% THF	THF	21	0.8	5.1	800	0.0886	4311.4
10% THF	THF	22	0.8	5.3	800	0.0886	4311.4
		Units:	cm^2	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.50
2	0.50
3	1
4	2
5	2
6	2
7	2
8	2
9	2
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	19	20	21	22		
1	14.000	3752.000	5479.000	5762.000		
2	12.000	6760.000	8654.000	7544.000		
3	16.000	10862.000	23383.000	15736.000		
4	17.000	25655.000	33653.000	26922.000		
5	11.000	21848.000	31723.000	24534.000		
6	16.000	20829.000	25692.000	22765.000		
7	17.000	18950.000	21894.000	20547.000		
8	19.000	17092.000	22929.000	18308.000		
9	16.000	15445.000	18811.000	16298.000		
10						
11						
12						
Top residual (25 µL)	13.000	39858.000	36466.000	39144.000		
Top residual activity (DPM/µL)	0.5	1594.3	1458.6	1565.8		
Kimwipe	13.000	22.000	46.000	18.000		
Chamber wash	22.000	26.000	27.000	21.000		
Water Test	146.00	181.00	170.00	175.00		

Sample Results						
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)						
Top residual activity (DPM/µL)						
Kimwipe						
Chamber wash						
Water Test						

Skin CalculationsV7.

DRAFT

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 14 hours**

Date Dosed: 07/27/05

Chamber: **19** **Vehicle:** **Blank**
Drug: **No dose**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	14.000	-4.750	-23.750	0.5	-0.001	0.000	0.3
2	12.000	-6.750	-33.750	0.5	-0.002	-0.001	0.8
3	16.000	-2.750	-13.750	1.0	0.000	-0.001	1.5
4	17.000	-1.750	-8.750	2.0	0.000	-0.002	3.0
5	11.000	-7.750	-38.750	2.0	0.000	-0.002	5.0
6	16.000	-2.750	-13.750	2.0	0.000	-0.003	7.0
7	17.000	-1.750	-8.750	2.0	0.000	-0.003	9.0
8	19.000	0.250	1.250	2.0	0.000	-0.003	11.0
9	16.000	-2.750	-13.750	2.0	0.000	-0.003	13.0

	Conc From	Conc-b Above	Vol.	Total	Mass	% Dose
Total Absorbed:			NA	0.000	0.000	-0.001
Dermis:	6.000	-12.750	1	-12.750	0.000	0.000
Epidermis:	6.000	-12.750	1	-12.750	0.000	0.000
Surface Wash:	190.000	171.250	1	171.250	0.004	0.005
Other						
Total Recovery:						0.004 %

Chamber: **20** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	3752.000	3733.250	20906.200	0.5	1.074	0.430	0.3
2	6760.000	6741.250	37751.000	0.5	1.939	1.205	0.8
3	10862.000	10843.250	60722.200	1.0	1.560	2.453	1.5
4	25655.000	25636.250	143563.000	2.0	1.844	5.404	3.0
5	21848.000	21829.250	122243.800	2.0	1.570	7.916	5.0
6	20829.000	20810.250	116537.400	2.0	1.497	10.311	7.0
7	18950.000	18931.250	106015.000	2.0	1.362	12.489	9.0
8	17092.000	17073.250	95610.200	2.0	1.228	14.454	11.0
9	15445.000	15426.250	86387.000	2.0	1.110	16.229	13.0

	Conc From	Conc-b Above	Vol.	Total	Mass	% Dose
Total Absorbed:			NA	16.229	16.229	22.897
Dermis:	6.000	-12.750	1	-12.750	0.000	0.000
Epidermis:	71.000	52.250	1	52.250	0.001	0.002
Surface Wash:	5320.000	5301.250	1	5301.250	0.109	0.154
Other						
Total Recovery:						23.052 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **SS012005** **Sponsor:** **Socma, donor 1, 14 hours**

Date Dosed: 07/27/05

Chamber: **21** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	5479.000	5460.250	27847.275	0.5	1.431	0.572	0.3
2	8654.000	8635.250	44039.775	0.5	2.263	1.477	0.8
3	23383.000	23364.250	119157.675	1.0	3.061	3.926	1.5
4	33653.000	33634.250	171534.675	2.0	2.203	7.451	3.0
5	31723.000	31704.250	161691.675	2.0	2.077	10.774	5.0
6	25692.000	25673.250	130933.575	2.0	1.682	13.465	7.0
7	21894.000	21875.250	111563.775	2.0	1.433	15.757	9.0
8	22929.000	22910.250	116842.275	2.0	1.501	18.159	11.0
9	18811.000	18792.250	95840.475	2.0	1.231	20.128	13.0

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	20.128	20.128	28.397
Dermis:	6.000	-12.750	1	-12.750	0.000	0.000
Epidermis:	83.000	64.250	1	64.250	0.001	0.002
Surface Wash:	4827.000	4808.250	1	4808.250	0.099	0.139
Other						
Total Recovery:						28.538 %

Chamber: **22** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	5762.000	5743.250	30439.225	0.5	1.564	0.626	0.3
2	7544.000	7525.250	39883.825	0.5	2.049	1.445	0.8
3	15736.000	15717.250	83301.425	1.0	2.140	3.157	1.5
4	26922.000	26903.250	142587.225	2.0	1.831	6.087	3.0
5	24534.000	24515.250	129930.825	2.0	1.669	8.757	5.0
6	22765.000	22746.250	120555.125	2.0	1.548	11.235	7.0
7	20547.000	20528.250	108799.725	2.0	1.397	13.471	9.0
8	18308.000	18289.250	96933.025	2.0	1.245	15.463	11.0
9	16298.000	16279.250	86280.025	2.0	1.108	17.236	13.0

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	17.236	17.236	24.317
Dermis:	13.000	-5.750	1	-5.750	0.000	0.000
Epidermis:	62.000	43.250	1	43.250	0.001	0.001
Surface Wash:	2149.000	2130.250	1	2130.250	0.044	0.062
Other						
Total Recovery:						24.380 %

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Determination of the Percutaneous Absorption of THF, in vitro, Using the Human Cadaver Skin Model

Water Test Results

R04-1387
Water Integrity Test and Product Dose Summary by Product

Donor: **SS012005** Date: **07/27/2005**

Dose units: uL

Product: **Blank**

Replicate	Chamber	uL	Product Dose
1	19	0.47	800.00
2			
3			
4			
5			
6			
7			
8			
Mean:		**0.47**	**800.00**
SD:		#DIV/0!	#DIV/0!
CV:		#DIV/0!	#DIV/0!

Product: **10% THF**

Replicate	Chamber	uL	Product Dose
1	20	0.67	800.00
2	21	0.57	800.00
3	22	0.61	800.00
4			
5			
6			
7			
8			
Mean:		**0.62**	**800.00**
SD:		0.05	0.00
CV:		8.23	0.00

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Across Donor Mean

Replicate	Chamber	Pre-test µL	Post (H2) DPM	Post (H2) µL	Post (H3) DPM	Post (H3) µL
1	19	0.47	91	0.27	97	0.29
2	20	0.67	0	0.00	73	0.23
3	21	0.57	0	0.00	127	0.41
4	22	0.61	0	0.00	72	0.21
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
Mean:		**0.58**		**0.07**		**0.28**
SD:		0.08		0.13		0.09
CV:		14.54		200.00		31.70

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Study Name:	Socma, donor 1, 14 hours	Study #:	R04-1387

Terminal (25 µL)

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Orig. Vol. (µL)***	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	20	39858	18.75	25	800	39839.25	4311.4	0.0886	26.20			37%		
10% THF	21	36466	18.75	25	800	36447.25	4311.4	0.0886	23.97			34%		
10% THF	22	39144	18.75	25	800	39125.25	4311.4	0.0886	25.73	25.30	1.18	36%	35.692	0.017

Surface Wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	20	5320	18.75	1500	1500	5301.25	4311.4	0.0886	0.11			0%		
10% THF	21	4827	18.75	1500	1500	4808.25	4311.4	0.0886	0.10			0%		
10% THF	22	2149	18.75	1500	1500	2130.25	4311.4	0.0886	0.04	0.08	0.04	0%	0.118	0.000

Kimwipe

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	20	22	18.75	NA	NA	3.25	4311.4	0.0886	0.00			0%		
10% THF	21	46	18.75	NA	NA	27.25	4311.4	0.0886	0.00			0%		
10% THF	22	18	18.75	NA	NA	-0.75	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000

Chamber wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	20	26	18.75	1000	1000	7.25	4311.4	0.0886	0.00			0%		
10% THF	21	27	18.75	1000	1000	8.25	4311.4	0.0886	0.00			0%		
10% THF	22	21	18.75	1000	1000	2.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000

* µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM / Sample Vol.) / (Spec. Act. * Drug Conc.) * Orig. Vol.
** µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM) / (Spec. Act. * Drug Conc.)
*** Assumed the residual volume is the same as the dosed volume.
**** % recovered = µg / (Drug Conc. * 800 µL)

Donor 2

(FD090404)

DRAFT

Within Donor Summary Donor: FD090404

Drug: THF

Formulation 10% THF (10 min)

Sample	19	20	21	Average	SD	Mid - T
1	0.663	0.393	0.241	0.433	0.213	0.1
Tot Pen (ug)	0.088	0.052	0.032	0.058	0.028	
Tot Pen (%)	0.125	0.074	0.045	0.081	0.040	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.001	0.001	0.000	0.000	
S. Wash (%)	0.072	0.138	0.249	0.153	0.089	
Total Rec (%)	0.197	0.212	0.295	0.235	0.053	

Formulation 30% THF (10 min)

Sample	22	23	24	Average	SD	Mid - T
1	5.513	7.880	3.999	6.797	2.444	0.1
Tot Pen (ug)	1.135	1.051	0.633	0.906	0.326	
Tot Pen (%)	0.534	0.494	0.251	0.426	0.153	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.001	0.001	0.001	0.001	0.000	
S. Wash (%)	0.145	0.265	0.126	0.179	0.076	
Total Rec (%)	0.679	0.760	0.377	0.606	0.202	

Formulation 100% THF (10 min)

Sample	25	26	27	Average	SD	Mid - T
1	1.810	1.709	1.660	1.726	0.077	0.1
Tot Pen (ug)	0.241	0.228	0.221	0.230	0.010	
Tot Pen (%)	0.034	0.032	0.031	0.032	0.001	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.221	0.206	0.272	0.233	0.034	
Total Rec (%)	0.255	0.238	0.303	0.265	0.034	

Formulation 10% THF (14 hours)

Sample	26	27	28	Average	SD	Mid - T
1	1.198	1.038	1.849	1.362	0.428	0.25
2	1.721	1.994	2.244	1.986	0.261	0.75
3	1.883	2.006	2.513	2.134	0.334	1.5
4	1.614	1.659	2.030	1.768	0.228	3
5	1.445	1.562	1.659	1.555	0.107	5
6	1.243	1.355	1.428	1.342	0.093	7
7	1.163	1.223	1.416	1.267	0.132	9
8	1.083	1.115	1.253	1.151	0.090	11
9	0.937	0.964	1.067	0.990	0.068	13
Tot Pen (ug)	14.650	15.425	17.811	15.962	1.648	
Tot Pen (%)	20.668	21.762	25.129	22.520	2.325	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.001	0.002	0.002	0.001	0.000	
S. Wash (%)	0.215	0.271	0.486	0.324	0.143	
Total Rec (%)	20.884	22.035	25.616	22.845	2.465	

Formulation 10% THF (14 hours) - CumPen

Sample	26	27	28	Average	SD	Time
1	0.479	0.415	0.739	0.545	0.172	0.5
2	1.168	1.213	1.637	1.339	0.259	1
3	2.674	2.819	3.647	3.047	0.525	2
4	5.256	5.474	6.894	5.875	0.890	4
5	7.568	7.973	9.549	8.363	1.047	6
6	9.556	10.141	11.834	10.510	1.183	8
7	11.417	12.097	14.099	12.538	1.394	10
8	13.150	13.882	16.104	14.379	1.538	12
9	14.650	15.425	17.811	15.962	1.648	14

Formulation 10% THF (60 min)

Sample	37	38	39	Average	SD	Mid - T
1	2.834	2.648	2.046	2.509	0.412	0.5
Tot Pen (ug)	2.267	2.118	1.637	2.008	0.329	
Tot Pen (%)	3.199	2.989	2.310	2.832	0.465	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.189	0.338	0.308	0.278	0.079	
Total Rec (%)	3.387	3.327	2.617	3.110	0.428	

Formulation 30% THF (60 min)

Sample	40	41	42	Average	SD	Mid - T
1	27.353	20.807	27.907	25.356	3.949	0.5
Tot Pen (ug)	21.882	16.646	22.325	20.285	3.159	
Tot Pen (%)	10.291	7.828	10.499	9.539	1.486	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.118	0.300	0.344	0.254	0.120	
Total Rec (%)	10.409	8.128	10.843	9.793	1.458	

Formulation 100% THF (60 min)

Sample	43	44	45	Average	SD	Mid - T
1	4.838	13.001	14.425	10.755	5.173	0.5
Tot Pen (ug)	3.871	10.401	11.540	8.604	4.138	
Tot Pen (%)	0.546	1.467	1.628	1.214	0.584	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.332	0.499	0.259	0.363	0.123	
Total Rec (%)	0.877	1.966	1.886	1.577	0.607	

Formulation Blank (14 hours)

Sample	25	Average	Mid - T
1	0.000	0.000	0.25
2	0.000	0.000	0.75
3	0.000	0.000	1.5
4	0.000	0.000	3
5	0.000	0.000	5
6	0.000	0.000	7
7	0.000	0.000	9
8	0.000	0.000	11
9	0.000	0.000	13
Tot Pen (ug)	0.000	0.000	
Tot Pen (%)	0.000	0.000	
Dermis (%)	0.000	0.000	
Epi (%)	0.000	0.000	
S. Wash (%)	0.001	0.001	
Total Rec (%)	0.001	0.001	

Slope	Slope	Slope	Average	
0.937	0.992	1.093	1.007	(samples 4hr - 14 hr)
0.9950	0.9931	0.9958	0.9944	

DRAFT

Donor 2

Chamber Results (10 Minutes)

DRAFT

Cover Data

Study Name:	Socma, donor 2, 10 min	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
FD090404	07/19/2005	07/20/2005	07/20/2005	07/20/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	19	0.8	5.4	800	0.0886	4311.4
10% THF	THF	20	0.8	4.0	800	0.0886	4311.4
10% THF	THF	21	0.8	5.2	800	0.0886	4311.4
30% THF	THF	22	0.8	5.1	800	0.2658	4034.3
30% THF	THF	23	0.8	4.4	800	0.2658	4034.3
30% THF	THF	24	0.8	4.4	800	0.2658	4034.3
100% THF	THF	25	0.8	5.4	800	0.8860	4088.5
100% THF	THF	26	0.8	5.2	800	0.8860	4088.5
100% THF	THF	27	0.8	5.0	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.17
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00

Drug Background	18.75
Water Background	16.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	

Water Standard:	1360.447

Receptor Solution:	1x PBS

Sample Results	19	20	21	22	23	24
1	815.000	657.000	320.000	3397.000	3643.000	1858.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	0.000	0.000	0.000	0.000	0.000	0.000
Epidermis	33.000	36.000	38.000	52.000	59.000	66.000
Surface Wash	2505.000	4769.000	8602.000	4686.000	8583.000	4078.000
Other						
Water Test	157.00	190.00	155.00	196.00	202.00	261.00

Sample Results	25	26	27			
1	225.000	221.000	223.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	0.000	4.000	0.000			
Epidermis	20.000	28.000	28.000			
Surface Wash	7236.000	6758.000	8905.000			
Other						
Water Test	164.00	153.00	353.00			

Skin CalculationsV7

DRAFT

Study Name:	Socma, donor 2, 10 min (2nd cover sheet)	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
FD090404	07/19/2005	07/20/2005	07/20/2005	07/20/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	19	0.8	5.4	800	0.0886	4311.4
10% THF	THF	20	0.8	4.0	800	0.0886	4311.4
10% THF	THF	21	0.8	5.2	800	0.0886	4311.4
30% THF	THF	22	0.8	5.1	800	0.2658	4034.3
30% THF	THF	23	0.8	4.4	800	0.2658	4034.3
30% THF	THF	24	0.8	4.4	800	0.2658	4034.3
100% THF	THF	25	0.8	5.4	800	0.8860	4088.5
100% THF	THF	26	0.8	5.2	800	0.8860	4088.5
100% THF	THF	27	0.8	5.0	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.17
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	16.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	19	20	21	22	23	24
1	815.000	657.000	320.000	3397.000	3643.000	1858.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	93224.000	93701.000	94102.000	92028.000	92551.000	87566.000
Top residual activity (DPM/µL)	3729.0	3748.0	3764.1	3681.1	3702.0	3502.6
Kimwipe	14.000	19.000	16.000	25.000	15.000	18.000
Chamber wash	25.000	23.000	23.000	25.000	24.000	28.000
Water Test	157.00	190.00	155.00	196.00	202.00	261.00

Sample Results	25	26	27			
1	225.000	221.000	223.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	109579.000	110144.000	108734.000			
Top residual activity (DPM/µL)	4383.2	4405.8	4349.4			
Kimwipe	13.000	15.000	14.000			
Chamber wash	23.000	23.000	26.000			
Water Test	164.00	153.00	353.00			

Skin CalculationsV7

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 10 min**

Date Dosed: 07/19/05

Chamber: **19** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	815.000	796.250	4299.750	0.2	0.663	0.088	0.1

	Conc From	Conc-b Above	Vol.	Total	Mass	% Dose
Total Absorbed:			NA	0.088	0.088	0.125
Dermis:	0.000	-18.750	1	-18.750	0.000	-0.001
Epidermis:	33.000	14.250	1	14.250	0.000	0.000
Surface Wash:	2505.000	2486.250	1	2486.250	0.051	0.072
Other						
Total Recovery:						0.197 %

Chamber: **20** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	657.000	638.250	2553.000	0.2	0.393	0.052	0.1

	Conc From	Conc-b Above	Vol.	Total	Mass	% Dose
Total Absorbed:			NA	0.052	0.052	0.074
Dermis:	0.000	-18.750	1	-18.750	0.000	-0.001
Epidermis:	36.000	17.250	1	17.250	0.000	0.001
Surface Wash:	4769.000	4750.250	1	4750.250	0.098	0.138
Other						
Total Recovery:						0.212 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 10 min**

Date Dosed: 07/19/05

Chamber: **21** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	320.000	301.250	1566.500	0.2	0.241	0.032	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.032	0.032	0.045
Dermis:	0.000	-18.750	1	-18.750	0.000	-0.001
Epidermis:	38.000	19.250	1	19.250	0.000	0.001
Surface Wash:	8602.000	8583.250	1	8583.250	0.176	0.249
Other						
Total Recovery:						0.294 %

Chamber: **22** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	3397.000	3378.250	17229.075	0.2	8.513	1.135	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.135	1.135	0.534
Dermis:	0.000	-18.750	1	-18.750	-0.001	-0.001
Epidermis:	52.000	33.250	1	33.250	0.002	0.001
Surface Wash:	4686.000	4667.250	1	4667.250	0.307	0.145
Other						
Total Recovery:						0.679 %

DRAFT

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 10 min**

Date Dosed: 07/19/05

Chamber: **23** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	3643.000	3624.250	15946.700	0.2	7.880	1.051	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.051	1.051	0.494
Dermis:	0.000	-18.750	1	-18.750	-0.001	-0.001
Epidermis:	59.000	40.250	1	40.250	0.003	0.001
Surface Wash:	8583.000	8564.250	1	8564.250	0.564	0.265
Other						
Total Recovery:						0.760 %

Chamber: **24** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	1858.000	1839.250	8092.700	0.2	3.999	0.533	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.533	0.533	0.251
Dermis:	0.000	-18.750	1	-18.750	-0.001	-0.001
Epidermis:	66.000	47.250	1	47.250	0.003	0.001
Surface Wash:	4078.000	4059.250	1	4059.250	0.267	0.126
Other						
Total Recovery:						0.377 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 10 min**

Date Dosed: 07/19/05

Chamber: **25** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	225.000	206.250	1113.750	0.2	1.810	0.241	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.241	0.241	0.034
Dermis:	0.000	-18.750	1	-18.750	-0.004	-0.001
Epidermis:	20.000	1.250	1	1.250	0.000	0.000
Surface Wash:	7236.000	7217.250	1	7217.250	1.564	0.221
Other						
Total Recovery:						0.254 %

Chamber: **26** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	221.000	202.250	1051.700	0.2	1.709	0.228	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.228	0.228	0.032
Dermis:	4.000	-14.750	1	-14.750	-0.003	0.000
Epidermis:	28.000	9.250	1	9.250	0.002	0.000
Surface Wash:	6758.000	6739.250	1	6739.250	1.460	0.206
Other						
Total Recovery:						0.238 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 10 min**

Date Dosed: 07/19/05

Chamber: **27** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	223.000	204.250	1021.250	0.2	1.660	0.221	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.221	0.221	0.031
Dermis:	0.000	-18.750	1	-18.750	-0.004	-0.001
Epidermis:	28.000	9.250	1	9.250	0.002	0.000
Surface Wash:	8905.000	8886.250	1	8886.250	1.926	0.272
Other						
Total Recovery:						0.303 %

Chamber: **0** **Vehicle:**
Drug:

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1							

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.000	0.000	0.000
Dermis:						
Epidermis:						
Surface Wash:						
Other						
Total Recovery:						0.000 %

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R04-1387
Water Integrity Test and Product Dose Summary by Product

Donor: **FD090404** Date: **07/19/2005**

Dose units: uL

Product: **10% THF**

Replicate	Chamber	uL	Product Dose
1	19	0.56	800.00
2	20	0.51	800.00
3	21	0.53	800.00
4			
5			
6			
7			
8			
Mean:		**0.53**	**800.00**
SD:		0.02	0.00
CV:		4.52	0.00

Product: **30% THF**

Replicate	Chamber	uL	Product Dose
1	22	0.67	800.00
2	23	0.60	800.00
3	24	0.79	800.00
4			
5			
6			
7			
8			
Mean:		**0.69**	**800.00**
SD:		0.10	0.00
CV:		13.96	0.00

Product: **100% THF**

Replicate	Chamber	uL	Product Dose
1	25	0.59	800.00
2	26	0.52	800.00
3	27	1.24	800.00
4			
5			
6			
7			
8			
Mean:		**0.78**	**800.00**
SD:		0.40	0.00
CV:		50.51	0.00

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Across Donor Mean

Replicate	Chamber	Pre-test µL	Post (H2) DPM	Post (H2) µL	Post (H3) DPM	Post (H3) µL
1	19	0.56	61	0.18	93	0.31
2	20	0.51	184	0.49	125	0.32
3	21	0.53	37	0.08	99	0.32
4	22	0.67	0	0.00	166	0.56
5	23	0.60	0	0.00	111	0.31
6	24	0.79	10	0.00	148	0.43
7	25	0.59	349	1.32	332	1.25
8	26	0.52	323	1.17	267	0.96
19	27	1.24	627	2.25	372	1.31
10						
11						
12						
13						
14						
15						
16						
17						
18						
Mean:		**0.67**		**0.61**		**0.64**
SD:		0.23		0.80		0.42
CV:		34.56		130.75		65.49

Study Name:	Socma, donor 2, 10 min	Study #:	R04-1387

Tape residual (25 µL)

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Orig. Vol. (µL)***	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	93224	18.75	25	800	93205.25	4311.4	0.0886	61.29			86%		
10% THF	20	93701	18.75	25	800	93682.25	4311.4	0.0886	61.61			87%		
10% THF	21	94102	18.75	25	800	94083.25	4311.4	0.0886	61.87	61.59	0.29	87%	86.893	0.004
30% THF	22	92028	18.75	25	800	92009.25	4034.3	0.2658	193.98			91%		
30% THF	23	92551	18.75	25	800	92532.25	4034.3	0.2658	195.09			92%		
30% THF	24	87566	18.75	25	800	87547.25	4034.3	0.2658	184.58	191.21	5.78	87%	89.924	0.027
100% THF	25	109579	18.75	25	800	109560.25	4088.5	0.8860	759.76			107%		
100% THF	26	110144	18.75	25	800	110125.25	4088.5	0.8860	763.68			108%		
100% THF	27	108734	18.75	25	800	108715.25	4088.5	0.8860	753.90	759.11	4.92	106%	107.099	0.007

Surface Wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	2505	18.75	1500	1500	2486.25	4311.4	0.0886	0.05			0%		
10% THF	20	4769	18.75	1500	1500	4750.25	4311.4	0.0886	0.10			0%		
10% THF	21	8602	18.75	1500	1500	8583.25	4311.4	0.0886	0.18	0.11	0.06	0%	0.153	0.001
30% THF	22	4686	18.75	1500	1500	4667.25	4034.3	0.2658	0.31			0%		
30% THF	23	8583	18.75	1500	1500	8564.25	4034.3	0.2658	0.56			0%		
30% THF	24	4078	18.75	1500	1500	4059.25	4034.3	0.2658	0.27	0.38	0.16	0%	0.179	0.001
100% THF	25	7236	18.75	1500	1500	7217.25	4088.5	0.8860	1.56			0%		
100% THF	26	6758	18.75	1500	1500	6739.25	4088.5	0.8860	1.46			0%		
100% THF	27	8905	18.75	1500	1500	8886.25	4088.5	0.8860	1.93	1.65	0.24	0%	0.233	0.000

Kimwipe

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	14	18.75	NA	NA	-4.75	4311.4	0.0886	0.00			0%		
10% THF	20	19	18.75	NA	NA	0.25	4311.4	0.0886	0.00			0%		
10% THF	21	16	18.75	NA	NA	-2.75	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	22	25	18.75	NA	NA	6.25	4034.3	0.2658	0.00			0%		
30% THF	23	15	18.75	NA	NA	-3.75	4034.3	0.2658	0.00			0%		
30% THF	24	18	18.75	NA	NA	-0.75	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	25	13	18.75	NA	NA	-5.75	4088.5	0.8860	0.00			0%		
100% THF	26	15	18.75	NA	NA	-3.75	4088.5	0.8860	0.00			0%		
100% THF	27	14	18.75	NA	NA	-4.75	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

Chamber wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	25	18.75	1000	1000	6.25	4311.4	0.0886	0.00			0%		
10% THF	20	23	18.75	1000	1000	4.25	4311.4	0.0886	0.00			0%		
10% THF	21	23	18.75	1000	1000	4.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	22	25	18.75	1000	1000	6.25	4034.3	0.2658	0.00			0%		
30% THF	23	24	18.75	1000	1000	5.25	4034.3	0.2658	0.00			0%		
30% THF	24	28	18.75	1000	1000	9.25	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	25	23	18.75	1000	1000	4.25	4088.5	0.8860	0.00			0%		
100% THF	26	23	18.75	1000	1000	4.25	4088.5	0.8860	0.00			0%		
100% THF	27	26	18.75	1000	1000	7.25	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

* µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM / Sample Vol.) / (Spec. Act.) * (Drug Conc.) * Orig. Vol.
** µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM) / (Spec. Act.) * (Drug Conc.)
*** Assumed the residual volume is the same as the dosed volume.
**** % recovered = µg / (Drug Conc. * 800 µL)

Donor 2

Chamber Results (60 minutes)

DRAFT

Study Name:	Socma, donor 2, 60 min	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
FD090404	07/19/2005	07/20/2005	07/20/2005	07/20/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	37	0.8	5.9	800	0.0886	4311.4
10% THF	THF	38	0.8	5.3	800	0.0886	4311.4
10% THF	THF	39	0.8	4.6	800	0.0886	4311.4
30% THF	THF	40	0.8	4.8	800	0.2658	4034.3
30% THF	THF	41	0.8	5.2	800	0.2658	4034.3
30% THF	THF	42	0.8	5.2	800	0.2658	4034.3
100% THF	THF	43	0.8	5.0	800	0.8860	4088.5
100% THF	THF	44	0.8	5.0	800	0.8860	4088.5
100% THF	THF	45	0.8	4.6	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	1.00
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	16.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	37	38	39	40	41	42
1	18717.000	19469.000	17336.000	89213.000	48606.000	65184.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	5.000	5.000	6.000	2.000	5.000	8.000
Epidermis	17.000	21.000	17.000	23.000	24.000	19.000
Surface Wash	6521.000	11693.000	10640.000	3835.000	9704.000	11121.000
Other						
Water Test	159.00	237.00	147.00	364.00	308.00	264.00

Sample Results	43	44	45			
1	3591.000	9618.000	11595.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	6.000	7.000	6.000			
Epidermis	16.000	19.000	16.000			
Surface Wash	10867.000	16344.000	8474.000			
Other						
Water Test	234.00	331.00	277.00			

Skin CalculationsV7.

Study Name:	Socma, donor 2, 60 min (2nd cover sheet)	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
FD090404	07/19/2005	07/20/2005	07/20/2005	07/20/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	37	0.8	5.9	800	0.0886	4311.4
10% THF	THF	38	0.8	5.3	800	0.0886	4311.4
10% THF	THF	39	0.8	4.6	800	0.0886	4311.4
30% THF	THF	40	0.8	4.8	800	0.2658	4034.3
30% THF	THF	41	0.8	5.2	800	0.2658	4034.3
30% THF	THF	42	0.8	5.2	800	0.2658	4034.3
100% THF	THF	43	0.8	5.0	800	0.8860	4088.5
100% THF	THF	44	0.8	5.0	800	0.8860	4088.5
100% THF	THF	45	0.8	4.6	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	1.00
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	16.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	37	38	39	40	41	42
1	18717.000	19469.000	17336.000	69213.000	48606.000	65184.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	78479.000	78022.000	78109.000	78528.000	74252.000	72601.000
Top residual activity (DPM/µL)	3139.2	3120.9	3124.4	2941.1	2970.1	2904.0
Kimwipe	15.000	16.000	16.000	16.000	21.000	16.000
Chamber wash	23.000	26.000	23.000	19.000	28.000	25.000
Water Test	159.00	237.00	147.00	364.00	308.00	264.00

Sample Results	43	44	45			
1	3591.000	9618.000	11595.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	105032.000	103597.000	110485.000			
Top residual activity (DPM/µL)	4201.3	4143.9	4419.4			
Kimwipe	12.000	17.000	20.000			
Chamber wash	19.000	23.000	22.000			
Water Test	234.00	331.00	277.00			

Skin CalculationsV7.

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 60 min**

Date Dosed: 07/19/05

Chamber: **37** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	18717.000	18698.250	110319.675	1.0	2.834	2.267	0.5

	Conc From	Conc-b Above	Vol.	Total	Mass	% Dose
Total Absorbed:			NA	2.267	2.267	3.199
Dermis:	5.000	-13.750	1	-13.750	0.000	0.000
Epidermis:	17.000	-1.750	1	-1.750	0.000	0.000
Surface Wash:	6521.000	6502.250	1	6502.250	0.134	0.189
Other						
Total Recovery:						3.387 %

Chamber: **38** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	19469.000	19450.250	103086.325	1.0	2.648	2.118	0.5

	Conc From	Conc-b Above	Vol.	Total	Mass	% Dose
Total Absorbed:			NA	2.118	2.118	2.989
Dermis:	5.000	-13.750	1	-13.750	0.000	0.000
Epidermis:	21.000	2.250	1	2.250	0.000	0.000
Surface Wash:	11693.000	11674.250	1	11674.250	0.240	0.338
Other						
Total Recovery:						3.327 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 60 min**

Date Dosed: 07/19/05

Chamber: **39** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	17336.000	17317.250	79659.350	1.0	2.046	1.637	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.637	1.637	2.310
Dermis:	6.000	-12.750	1	-12.750	0.000	0.000
Epidermis:	17.000	-1.750	1	-1.750	0.000	0.000
Surface Wash:	10640.000	10621.250	1	10621.250	0.218	0.308
Other						
Total Recovery:						2.617 %

Chamber: **40** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	69213.000	69194.250	332132.400	1.0	27.353	21.882	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	21.882	21.882	10.291
Dermis:	2.000	-16.750	1	-16.750	-0.001	-0.001
Epidermis:	23.000	4.250	1	4.250	0.000	0.000
Surface Wash:	3835.000	3816.250	1	3816.250	0.251	0.118
Other						
Total Recovery:						10.409 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 60 min**

Date Dosed: 07/19/05

Chamber: **41** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	48606.000	48587.250	252653.700	1.0	20.807	16.646	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	16.646	16.646	7.828
Dermis:	5.000	-13.750	1	-13.750	-0.001	0.000
Epidermis:	24.000	5.250	1	5.250	0.000	0.000
Surface Wash:	9704.000	9685.250	1	9685.250	0.638	0.300
Other						
Total Recovery:						8.128 %

Chamber: **42** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	65184.000	65165.250	338859.300	1.0	27.907	22.325	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	22.325	22.325	10.499
Dermis:	8.000	-10.750	1	-10.750	-0.001	0.000
Epidermis:	19.000	0.250	1	0.250	0.000	0.000
Surface Wash:	11121.000	11102.250	1	11102.250	0.731	0.344
Other						
Total Recovery:						10.843 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 60 min**

Date Dosed: 07/19/05

Chamber: **43** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	3591.000	3572.250	17861.250	1.0	4.838	3.871	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	3.871	3.871	0.546
Dermis:	6.000	-12.750	1	-12.750	-0.003	0.000
Epidermis:	16.000	-2.750	1	-2.750	-0.001	0.000
Surface Wash:	10867.000	10848.250	1	10848.250	2.351	0.332
Other						
Total Recovery:						0.877 %

Chamber: **44** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	9618.000	9599.250	47996.250	1.0	13.001	10.401	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	10.401	10.401	1.467
Dermis:	7.000	-11.750	1	-11.750	-0.003	0.000
Epidermis:	19.000	0.250	1	0.250	0.000	0.000
Surface Wash:	16344.000	16325.250	1	16325.250	3.538	0.499
Other						
Total Recovery:						1.966 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 60 min**

Date Dosed: 07/19/05

Chamber: **45** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	11595.000	11576.250	53250.750	1.0	14.425	11.540	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	11.540	11.540	1.628
Dermis:	6.000	-12.750	1	-12.750	-0.003	0.000
Epidermis:	16.000	-2.750	1	-2.750	-0.001	0.000
Surface Wash:	8474.000	8455.250	1	8455.250	1.832	0.259
Other						
Total Recovery:						1.886 %

Chamber: **0** **Vehicle:**
Drug:

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1							

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.000	0.000	0.000
Dermis:						
Epidermis:						
Surface Wash:						
Other						
Total Recovery:						0.000 %

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Determination of the Percutaneous Absorption of THF, in vitro, Using the Human Cadaver Skin Model

Water Test Results

R04-1387
Water Integrity Test and Product Dose Summary by Product

Donor: **FD090404** Date: **07/19/2005**

Dose units: uL

Product: **10% THF**

Replicate	Chamber	uL	Product Dose
1	37	0.62	800.00
2	38	0.86	800.00
3	39	0.44	800.00
4			
5			
6			
7			
8			
Mean:		**0.64**	**800.00**
SD:		0.21	0.00
CV:		32.71	0.00

Product: **30% THF**

Replicate	Chamber	uL	Product Dose
1	40	1.23	800.00
2	41	1.12	800.00
3	42	0.95	800.00
4			
5			
6			
7			
8			
Mean:		**1.10**	**800.00**
SD:		0.14	0.00
CV:		12.84	0.00

Product: **100% THF**

Replicate	Chamber	uL	Product Dose
1	43	0.80	800.00
2	44	1.16	800.00
3	45	0.88	800.00
4			
5			
6			
7			
8			
Mean:		**0.95**	**800.00**
SD:		0.19	0.00
CV:		19.73	0.00

Across Donor Mean

Replicate	Chamber	Pre-test uL	Post (H2) DPM	Post (H2) µL	Post (H3) DPM	Post (H3) µL
1	37	0.62	78	0.27	136	0.52
2	38	0.86	115	0.39	139	0.48
3	39	0.44	5	0.00	138	0.41
4	40	1.23	0	0.00	325	1.09
5	41	1.12	0	0.00	246	0.88
6	42	0.95	0	0.00	184	0.64
7	43	0.80	765	2.75	963	3.48
8	44	1.16	1495	5.44	1384	5.03
9	45	0.88	1649	5.52	1281	4.28
10						
11						
12						
13						
14						
15						
16						
17						
18						
Mean:		**0.90**		**1.60**		**1.87**
SD:		0.26		2.37		1.85
CV:		28.52		148.44		98.98

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

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Study Name:	Socma, donor 2, 60 min	Study #:	R04-1387

Top residual (25 µL)

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Orig. Vol. (µL)***	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	37	78479	18.75	25	800	78460.25	4311.4	0.0886	51.60			73%		
10% THF	38	78022	18.75	25	800	78003.25	4311.4	0.0886	51.30			72%		
10% THF	39	78109	18.75	25	800	78090.25	4311.4	0.0886	51.35	51.42	0.16	72%	72.538	0.002
30% THF	40	73528	18.75	25	800	73509.25	4034.3	0.2658	154.98			73%		
30% THF	41	74252	18.75	25	800	74233.25	4034.3	0.2658	156.51			74%		
30% THF	42	72601	18.75	25	800	72582.25	4034.3	0.2658	153.02	154.84	1.74	72%	72.816	0.008
100% THF	43	105032	18.75	25	800	105013.25	4088.5	0.8860	728.23			103%		
100% THF	44	103597	18.75	25	800	103578.25	4088.5	0.8860	718.28			101%		
100% THF	45	110485	18.75	25	800	110466.25	4088.5	0.8860	766.04	737.52	25.20	108%	104.052	0.036

Surface Wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	37	6521	18.75	1500	1500	6502.25	4311.4	0.0886	0.13			0%		
10% THF	38	11693	18.75	1500	1500	11674.25	4311.4	0.0886	0.24			0%		
10% THF	39	10640	18.75	1500	1500	10621.25	4311.4	0.0886	0.22	0.20	0.06	0%	0.278	0.001
30% THF	40	3835	18.75	1500	1500	3816.25	4034.3	0.2658	0.25			0%		
30% THF	41	9704	18.75	1500	1500	9685.25	4034.3	0.2658	0.64			0%		
30% THF	42	11121	18.75	1500	1500	11102.25	4034.3	0.2658	0.73	0.54	0.25	0%	0.254	0.001
100% THF	43	10867	18.75	1500	1500	10848.25	4088.5	0.8860	2.35			0%		
100% THF	44	16344	18.75	1500	1500	16325.25	4088.5	0.8860	3.54			0%		
100% THF	45	8474	18.75	1500	1500	8455.25	4088.5	0.8860	1.83	2.57	0.87	0%	0.363	0.001

Kimwipe

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	37	15	18.75	NA	NA	-3.75	4311.4	0.0886	0.00			0%		
10% THF	38	16	18.75	NA	NA	-2.75	4311.4	0.0886	0.00			0%		
10% THF	39	16	18.75	NA	NA	-2.75	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	40	16	18.75	NA	NA	-2.75	4034.3	0.2658	0.00			0%		
30% THF	41	21	18.75	NA	NA	2.25	4034.3	0.2658	0.00			0%		
30% THF	42	16	18.75	NA	NA	-2.75	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	43	12	18.75	NA	NA	-6.75	4088.5	0.8860	0.00			0%		
100% THF	44	17	18.75	NA	NA	-1.75	4088.5	0.8860	0.00			0%		
100% THF	45	20	18.75	NA	NA	1.25	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

Chamber wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	37	23	18.75	1000	1000	4.25	4311.4	0.0886	0.00			0%		
10% THF	38	26	18.75	1000	1000	7.25	4311.4	0.0886	0.00			0%		
10% THF	39	23	18.75	1000	1000	4.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	40	19	18.75	1000	1000	0.25	4034.3	0.2658	0.00			0%		
30% THF	41	28	18.75	1000	1000	9.25	4034.3	0.2658	0.00			0%		
30% THF	42	25	18.75	1000	1000	6.25	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	43	19	18.75	1000	1000	0.25	4088.5	0.8860	0.00			0%		
100% THF	44	23	18.75	1000	1000	4.25	4088.5	0.8860	0.00			0%		
100% THF	45	22	18.75	1000	1000	3.25	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

* µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM / Sample Vol.) / (Spec. Act.) * (Drug Conc.) * Orig. Vol.
** µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM) / (Spec. Act.) * (Drug Conc.)
*** Assumed the residual volume is the same as the dosed volume.
**** % recovered = µg / (Drug Conc. * 800 µL)

Donor 2

Chamber Results (14 Hours)

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Cover Data

Study Name:	Socma, donor 2, 14 hours	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
FD090404	07/27/2005	07/29/2005	07/29/2005	08/01/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
Blank	No dose	25	0.8	5.3	800	0.0886	4311.4
10% THF	THF	26	0.8	5.4	800	0.0886	4311.4
10% THF	THF	27	0.8	4.3	800	0.0886	4311.4
10% THF	THF	28	0.8	5.2	800	0.0886	4311.4
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.50
2	0.50
3	1
4	2
5	2
6	2
7	2
8	2
9	2
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	25	26	27	28		
1	17.000	4338.000	4748.000	6938.000		
2	15.000	6223.000	9045.000	8417.000		
3	14.000	13591.000	18196.000	18830.000		
4	16.000	23289.000	30066.000	30407.000		
5	17.000	20850.000	28295.000	24859.000		
6	17.000	17935.000	24553.000	21400.000		
7	15.000	16786.000	22157.000	21213.000		
8	13.000	15637.000	20214.000	18784.000		
9	18.000	13533.000	17481.000	15996.000		
10						
11						
12						
Dermis	3.000	5.000	12.000	6.000		
Epidermis	16.000	62.000	72.000	71.000		
Surface Wash	70.000	7435.000	9380.000	16791.000		
Other						
Water Test	298.00	240.00	255.00	289.00		

Sample Results						
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis						
Epidermis						
Surface Wash						
Other						
Water Test						

Skin CalculationsV7.

Study Name:	Socma, donor 2, 14 hours (2nd cover sheet)	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
FD090404	07/27/2005	07/29/2005	07/29/2005	08/01/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
Blank	No dose	25	0.8	5.3	800	0.0886	4311.4
10% THF	THF	26	0.8	5.4	800	0.0886	4311.4
10% THF	THF	27	0.8	4.3	800	0.0886	4311.4
10% THF	THF	28	0.8	5.2	800	0.0886	4311.4
		Units:	cm^2	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.50
2	0.50
3	1
4	2
5	2
6	2
7	2
8	2
9	2
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	25	26	27	28		
1	17.000	4338.000	4718.000	6938.000		
2	15.000	6223.000	9045.000	8417.000		
3	14.000	13591.000	18196.000	18830.000		
4	16.000	23289.000	30066.000	30407.000		
5	17.000	20850.000	28295.000	24859.000		
6	17.000	17935.000	24553.000	21400.000		
7	15.000	16786.000	22157.000	21213.000		
8	13.000	15637.000	20214.000	18784.000		
9	18.000	13533.000	17481.000	15996.000		
10						
11						
12						
Top residual (25 µL)	12.000	39438.000	40584.000	39114.000		
Top residual activity (DPM/µL)	0.5	1577.5	1623.4	1564.6		
Kimwipe	13.000	36.000	24.000	25.000		
Chamber wash	22.000	24.000	35.000	24.000		
Water Test	298.00	240.00	255.00	289.00		

Sample Results						
1						
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)						
Top residual activity (DPM/µL)						
Kimwipe						
Chamber wash						
Water Test						

Skin CalculationsV7

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 14 hours**

Date Dosed: 07/27/05

Chamber: **25** **Vehicle:** **Blank**
Drug: **No dose**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	17.000	-1.750	-9.275	0.5	0.000	0.000	0.3
2	15.000	-3.750	-19.875	0.5	-0.001	-0.001	0.8
3	14.000	-4.750	-25.175	1.0	-0.001	-0.001	1.5
4	16.000	-2.750	-14.575	2.0	0.000	-0.001	3.0
5	17.000	-1.750	-9.275	2.0	0.000	-0.002	5.0
6	17.000	-1.750	-9.275	2.0	0.000	-0.002	7.0
7	15.000	-3.750	-19.875	2.0	0.000	-0.002	9.0
8	13.000	-5.750	-30.475	2.0	0.000	-0.003	11.0
9	18.000	-0.750	-3.975	2.0	0.000	-0.003	13.0

	Conc From	Conc-b Above	Vol. NA	Total 0.000	Mass 0.000	% Dose 0.000
Total Absorbed:						
Dermis:	3.000	-15.750	1	-15.750	0.000	0.000
Epidermis:	16.000	-2.750	1	-2.750	0.000	0.000
Surface Wash:	70.000	51.250	1	51.250	0.001	0.001
Other						
Total Recovery:						0.001 %

Chamber: **26** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	4338.000	4319.250	23323.950	0.5	1.198	0.479	0.3
2	6223.000	6204.250	33502.950	0.5	1.721	1.168	0.8
3	13591.000	13572.250	73290.150	1.0	1.883	2.674	1.5
4	23289.000	23270.250	125659.350	2.0	1.614	5.256	3.0
5	20850.000	20831.250	112488.750	2.0	1.445	7.568	5.0
6	17935.000	17916.250	96747.750	2.0	1.243	9.556	7.0
7	16786.000	16767.250	90543.150	2.0	1.163	11.417	9.0
8	15637.000	15618.250	84338.550	2.0	1.083	13.150	11.0
9	13533.000	13514.250	72976.950	2.0	0.937	14.650	13.0

	Conc From	Conc-b Above	Vol. NA	Total 14.650	Mass 14.650	% Dose 20.668
Total Absorbed:						
Dermis:	5.000	-13.750	1	-13.750	0.000	0.000
Epidermis:	62.000	43.250	1	43.250	0.001	0.001
Surface Wash:	7435.000	7416.250	1	7416.250	0.152	0.215
Other						
Total Recovery:						20.884 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **FD090404** **Sponsor:** **Socma, donor 2, 14 hours**

Date Dosed: 07/27/05

Chamber: **27** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	4718.000	4699.250	20206.775	0.5	1.038	0.415	0.3
2	9045.000	9026.250	38812.875	0.5	1.994	1.213	0.8
3	18196.000	18177.250	78162.175	1.0	2.008	2.819	1.5
4	30066.000	30047.250	129203.175	2.0	1.659	5.474	3.0
5	28295.000	28276.250	121587.875	2.0	1.562	7.973	5.0
6	24553.000	24534.250	105497.275	2.0	1.355	10.141	7.0
7	22157.000	22138.250	95194.475	2.0	1.223	12.097	9.0
8	20214.000	20195.250	86839.575	2.0	1.115	13.882	11.0
9	17481.000	17462.250	75087.675	2.0	0.964	15.425	13.0

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	15.425	15.425	21.762
Dermis:	12.000	-6.750	1	-6.750	0.000	0.000
Epidermis:	72.000	53.250	1	53.250	0.001	0.002
Surface Wash:	9380.000	9361.250	1	9361.250	0.192	0.271
Other						
Total Recovery:						22.035 %

Chamber: **28** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	6938.000	6919.250	35980.100	0.5	1.849	0.739	0.3
2	8417.000	8398.250	43670.900	0.5	2.244	1.637	0.8
3	18830.000	18811.250	97818.500	1.0	2.513	3.647	1.5
4	30407.000	30388.250	158018.900	2.0	2.030	6.894	3.0
5	24859.000	24840.250	129169.300	2.0	1.659	9.549	5.0
6	21400.000	21381.250	111182.500	2.0	1.428	11.834	7.0
7	21213.000	21194.250	110210.100	2.0	1.416	14.099	9.0
8	18784.000	18765.250	97579.300	2.0	1.253	16.104	11.0
9	15996.000	15977.250	83081.700	2.0	1.067	17.811	13.0

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	17.811	17.811	25.129
Dermis:	6.000	-12.750	1	-12.750	0.000	0.000
Epidermis:	71.000	52.250	1	52.250	0.001	0.002
Surface Wash:	16791.000	16772.250	1	16772.250	0.345	0.486
Other						
Total Recovery:						25.616 %

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Determination of the Percutaneous Absorption of THF, in vitro, Using the Human Cadaver Skin Model

Water Test Results

R04-1387
Water Integrity Test and Product Dose Summary by Product

Donor: **FD090404** Date: **07/27/2005**

Dose units: uL

Product: **Blank**

Replicate	Chamber	uL	Product Dose
1	25	1.09	800.00
2			
3			
4			
5			
6			
7			
8			
Mean:		**1.09**	**800.00**
SD:		#DIV/0!	#DIV/0!
CV:		#DIV/0!	#DIV/0!

Product: **10% THF**

Replicate	Chamber	uL	Product Dose
1	26	0.88	800.00
2	27	0.75	800.00
3	28	1.04	800.00
4			
5			
6			
7			
8			
Mean:		**0.89**	**800.00**
SD:		0.14	0.00
CV:		16.15	0.00

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Across Donor Mean

Replicate	Chamber	Pre-test uL	Post (H2) DPM	Post (H2) µL	Post (H3) DPM	Post (H3) µL
1	25	1.09	194	0.69	181	0.64
2	26	0.88	161	0.57	237	0.87
3	27	0.75	17	0.00	126	0.34
4	28	1.04	151	0.51	171	0.58
5						
6						
7						
8						
9						
10						
11						
12						
13						
14						
15						
16						
17						
18						
Mean:		**0.94**		**0.44**		**0.61**
SD:		0.15		0.30		0.22
CV:		16.48		68.73		35.63

Study Name:	Socma, donor 2, 14 hours	Study #:	R04-1387

Top residual (25 µL)

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Orig. Vol. (µL)***	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	26	39438	18.75	25	800	39419.25	4311.4	0.0886	25.92			37%		
10% THF	27	40584	18.75	25	800	40565.25	4311.4	0.0886	26.68			38%		
10% THF	28	39114	18.75	25	800	39095.25	4311.4	0.0886	25.71	26.10	0.51	36%	36.827	0.007

Surface Wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	26	7435	18.75	1500	1500	7416.25	4311.4	0.0886	0.15			0%		
10% THF	27	9380	18.75	1500	1500	9361.25	4311.4	0.0886	0.19			0%		
10% THF	28	16791	18.75	1500	1500	16772.25	4311.4	0.0886	0.34	0.23	0.10	0%	0.324	0.001

Kimwipe

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	26	36	18.75	NA	NA	17.25	4311.4	0.0886	0.00			0%		
10% THF	27	24	18.75	NA	NA	5.25	4311.4	0.0886	0.00			0%		
10% THF	28	25	18.75	NA	NA	6.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000

Chamber wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	26	24	18.75	1000	1000	5.25	4311.4	0.0886	0.00			0%		
10% THF	27	35	18.75	1000	1000	16.25	4311.4	0.0886	0.00			0%		
10% THF	28	24	18.75	1000	1000	5.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000

* µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM / Sample Vol.) / (Spec. Act.) * (Drug Conc.) * Orig. Vol.
** µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM) / (Spec. Act.) * (Drug Conc.)
*** Assumed the residual volume is the same as the dosed volume.
**** % recovered = µg / (Drug Conc. * 800 µL)

Donor 3

(KS032805))

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Within Donor Summary

Donor: KS032805

Drug: THF

Formulation 10% THF (10 min)

Sample	19	20	21	Average	SD	Mid - T
1	0.227	0.043	0.087	0.119	0.096	0.1
Tot Pen (ug)	0.030	0.006	0.012	0.016	0.013	
Tot Pen (%)	0.043	0.008	0.016	0.022	0.018	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.095	0.162	0.223	0.160	0.064	
Total Rec (%)	0.137	0.170	0.239	0.182	0.052	

Formulation 10% THF (60 min)

Sample	37	38	39	Average	SD	Mid - T
1	0.829	0.832	1.198	0.953	0.212	0.5
Tot Pen (ug)	0.663	0.666	0.959	0.763	0.170	
Tot Pen (%)	0.936	0.940	1.352	1.076	0.239	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.308	0.609	0.129	0.349	0.243	
Total Rec (%)	1.244	1.549	1.481	1.425	0.160	

Formulation 30% THF (10 min)

Sample	22	23	24	Average	SD	Mid - T
1	4.080	1.463	2.868	2.804	1.310	0.1
Tot Pen (ug)	0.544	0.195	0.382	0.374	0.175	
Tot Pen (%)	0.256	0.092	0.180	0.176	0.082	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.278	0.499	0.474	0.417	0.121	
Total Rec (%)	0.534	0.591	0.653	0.593	0.060	

Formulation 30% THF (60 min)

Sample	40	41	42	Average	SD	Mid - T
1	9.519	19.652	11.358	13.510	5.398	0.5
Tot Pen (ug)	7.615	15.722	9.087	10.808	4.319	
Tot Pen (%)	3.581	7.394	4.273	5.083	2.031	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.231	0.427	0.567	0.408	0.169	
Total Rec (%)	3.813	7.820	4.841	5.491	2.081	

Formulation 100% THF (10 min)

Sample	25	26	27	Average	SD	Mid - T
1	0.319	0.991	0.520	0.610	0.344	0.1
Tot Pen (ug)	0.043	0.132	0.070	0.082	0.046	
Tot Pen (%)	0.006	0.019	0.010	0.012	0.006	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.658	0.261	0.235	0.385	0.237	
Total Rec (%)	0.663	0.279	0.245	0.396	0.232	

Formulation 100% THF (60 min)

Sample	43	44	45	Average	SD	Mid - T
1	3.289	1.882	3.542	2.904	0.894	0.5
Tot Pen (ug)	2.631	1.506	2.834	2.324	0.715	
Tot Pen (%)	0.371	0.212	0.400	0.328	0.101	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.000	0.000	0.000	0.000	0.000	
S. Wash (%)	0.783	0.258	0.306	0.449	0.290	
Total Rec (%)	1.154	0.470	0.706	0.777	0.347	

Formulation 10% THF (14 hours)

Sample	38	39	40	Average	SD	Mid - T
1	0.640	0.709	0.423	0.591	0.149	0.25
2	1.473	1.568	1.206	1.515	0.333	0.75
3	1.562	1.875	1.470	1.636	0.212	1.5
4	1.368	1.572	1.397	1.446	0.111	3
5	1.247	1.410	1.255	1.304	0.092	5
6	1.138	1.247	1.087	1.157	0.082	7
7	0.956	1.075	1.069	1.033	0.067	9
8	0.955	1.112	0.986	1.018	0.083	11
9	0.777	0.933	0.936	0.882	0.091	13
Tot Pen (ug)	12.402	14.289	12.594	13.095	1.039	
Tot Pen (%)	17.497	20.160	17.768	18.475	1.465	
Dermis (%)	0.000	0.000	0.000	0.000	0.000	
Epi (%)	0.001	0.001	0.001	0.001	0.000	
S. Wash (%)	0.243	0.272	0.202	0.239	0.035	
Total Rec (%)	17.741	20.432	17.971	18.715	1.492	

Formulation Blank (14 hours)

Sample	37	Average	Mid - T
1	0.000	0.000	0.25
2	0.000	0.000	0.75
3	0.000	0.000	1.5
4	0.000	0.000	3
5	0.000	0.000	5
6	0.000	0.000	7
7	0.000	0.000	9
8	0.000	0.000	11
9	0.000	0.000	13
Tot Pen (ug)	0.000	0.000	
Tot Pen (%)	0.000	0.000	
Dermis (%)	0.000	0.000	
Epi (%)	0.000	0.000	
S. Wash (%)	0.001	0.001	
Total Rec (%)	0.000	0.000	

Formulation 10% THF (14 hours) - CumPen

Sample	38	39	40	Average	SD	Time
1	0.256	0.284	0.169	0.236	0.060	0.5
2	0.845	1.030	0.651	0.842	0.189	1
3	2.095	2.530	1.827	2.151	0.355	2
4	4.283	5.046	4.062	4.464	0.516	4
5	6.278	7.303	6.070	6.550	0.660	6
6	8.099	9.297	7.809	8.402	0.789	8
7	9.629	11.017	9.520	10.055	0.835	10
8	11.158	12.797	11.097	11.684	0.964	12
9	12.402	14.289	12.594	13.095	1.039	14

Slope	Slope	Slope	Average	
0.811	0.920	0.849	0.860	(samples 4hr - 14 hr)
0.9937	0.9954	0.9975	0.9956	

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Donor 3

Chamber Results (10 Minutes)

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Study Name:	Socma, donor 3, 10 min	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
KS032805	07/21/2005	07/22/2005	07/22/2005	07/25/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	19	0.8	5.2	800	0.0886	4311.4
10% THF	THF	20	0.8	5.4	800	0.0886	4311.4
10% THF	THF	21	0.8	5.0	800	0.0886	4311.4
30% THF	THF	22	0.8	5.0	800	0.2658	4034.3
30% THF	THF	23	0.8	5.2	800	0.2658	4034.3
30% THF	THF	24	0.8	4.4	800	0.2658	4034.3
100% THF	THF	25	0.8	5.0	800	0.8860	4088.5
100% THF	THF	26	0.8	5.2	800	0.8860	4088.5
100% THF	THF	27	0.8	4.0	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0:17
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	19	20	21	22	23	24
1	302.000	70.000	131.000	1670.000	588.000	1338.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	1.000	9.000	5.000	6.000	15.000	15.000
Epidermis	19.000	16.000	17.000	22.000	21.000	19.000
Surface Wash	3283.000	5604.000	7710.000	9004.000	16129.000	15306.000
Other						
Water Test	158.00	110.00	114.00	175.00	162.00	123.00

Sample Results	25	26	27			
1	58.000	136.000	100.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	14.000	11.000	17.000			
Epidermis	18.000	18.000	13.000			
Surface Wash	21528.000	8556.000	7716.000			
Other						
Water Test	119.00	119.00	124.00			

Skin CalculationsV7

DRAFT

Study Name:	Socma, donor 3, 10 min (2nd cover sheet)	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
KS032805	07/21/2005	07/22/2005	07/22/2005	07/25/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	19	0.8	5.2	800	0.0886	4311.4
10% THF	THF	20	0.8	5.4	800	0.0886	4311.4
10% THF	THF	21	0.8	5.0	800	0.0886	4311.4
30% THF	THF	22	0.8	5.0	800	0.2658	4034.3
30% THF	THF	23	0.8	5.2	800	0.2658	4034.3
30% THF	THF	24	0.8	4.4	800	0.2658	4034.3
100% THF	THF	25	0.8	5.0	800	0.8860	4088.5
100% THF	THF	26	0.8	5.2	800	0.8860	4088.5
100% THF	THF	27	0.8	4.0	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	0.17
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	19	20	21	22	23	24
1	302.000	70.000	131.000	1670.000	588.000	1338.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	90075.000	90322.000	84012.000	87883.000	83239.000	85444.000
Top residual activity (DPM/µL)	3603.0	3612.9	3360.5	3515.3	3329.6	3417.8
Kimwipe	20.000	16.000	14.000	18.000	16.000	15.000
Chamber wash	26.000	23.000	24.000	21.000	38.000	24.000
Water Test	158.00	110.00	114.00	175.00	162.00	123.00

Sample Results	25	26	27			
1	58.000	136.000	100.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	105946.000	100504.000	110843.000			
Top residual activity (DPM/µL)	4237.8	4020.2	4433.7			
Kimwipe	13.000	13.000	12.000			
Chamber wash	26.000	26.000	22.000			
Water Test	119.00	119.00	124.00			

Skin CalculationsV7

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 10 min**

Date Dosed: 07/21/05

Chamber: **19** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	302.000	283.250	1472.900	0.2	0.227	0.030	0.1

	Conc From	Conc-b Above	Vol. NA	Total 0.030	Mass 0.030	% Dose 0.043
Total Absorbed:						
Dermis:	1.000	-17.750	1	-17.750	0.000	-0.001
Epidermis:	19.000	0.250	1	0.250	0.000	0.000
Surface Wash:	3283.000	3264.250	1	3264.250	0.067	0.095
Other						
Total Recovery:						0.137 %

Chamber: **20** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	70.000	51.250	276.750	0.2	0.043	0.006	0.1

	Conc From	Conc-b Above	Vol. NA	Total 0.006	Mass 0.006	% Dose 0.008
Total Absorbed:						
Dermis:	9.000	-9.750	1	-9.750	0.000	0.000
Epidermis:	16.000	-2.750	1	-2.750	0.000	0.000
Surface Wash:	5604.000	5585.250	1	5585.250	0.115	0.162
Other						
Total Recovery:						0.170 %

DRAFT

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 10 min**

Date Dosed: 07/21/05

Chamber: **21** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	131.000	112.250	561.250	0.2	0.087	0.012	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.012	0.012	0.016
Dermis:	5.000	-13.750	1	-13.750	0.000	0.000
Epidermis:	17.000	-1.750	1	-1.750	0.000	0.000
Surface Wash:	7710.000	7691.250	1	7691.250	0.158	0.223
Other						
Total Recovery:						0.239 %

Chamber: **22** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	1670.000	1651.250	8256.250	0.2	4.080	0.544	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.544	0.544	0.256
Dermis:	6.000	-12.750	1	-12.750	-0.001	0.000
Epidermis:	22.000	3.250	1	3.250	0.000	0.000
Surface Wash:	9004.000	8985.250	1	8985.250	0.592	0.278
Other						
Total Recovery:						0.534 %

DRAFT

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 10 min**

Date Dosed: 07/21/05

Chamber: **23** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	588.000	569.250	2960.100	0.2	1.463	0.195	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.195	0.195	0.092
Dermis:	15.000	-3.750	1	-3.750	0.000	0.000
Epidermis:	21.000	2.250	1	2.250	0.000	0.000
Surface Wash:	16129.000	16110.250	1	16110.250	1.061	0.499
Other						
Total Recovery:						0.591 %

Chamber: **24** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	1338.000	1319.250	5804.700	0.2	2.868	0.382	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.382	0.382	0.180
Dermis:	15.000	-3.750	1	-3.750	0.000	0.000
Epidermis:	19.000	0.250	1	0.250	0.000	0.000
Surface Wash:	15306.000	15287.250	1	15287.250	1.007	0.474
Other						
Total Recovery:						0.653 %

DRAFT

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 10 min**

Date Dosed: 07/21/05

Chamber: **25** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	58.000	39.250	196.250	0.2	0.319	0.043	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.043	0.043	0.006
Dermis:	14.000	-4.750	1	-4.750	-0.001	0.000
Epidermis:	18.000	-0.750	1	-0.750	0.000	0.000
Surface Wash:	21528.000	21509.250	1	21509.250	4.661	0.658
Other						
Total Recovery:						0.663 %

Chamber: **26** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	136.000	117.250	609.700	0.2	0.991	0.132	0.1

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.132	0.132	0.019
Dermis:	11.000	-7.750	1	-7.750	-0.002	0.000
Epidermis:	18.000	-0.750	1	-0.750	0.000	0.000
Surface Wash:	8556.000	8537.250	1	8537.250	1.850	0.261
Other						
Total Recovery:						0.279 %

DRAFT

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 10 min**

Date Dosed: 07/21/05

Chamber: **27** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	100.000	81.250	325.000	0.2	0.528	0.070	0.1

	Conc From	Conc-b Above	Vol. NA	Total 0.070	Mass 0.070	% Dose 0.010
Total Absorbed:						
Dermis:	17.000	-1.750	1	-1.750	0.000	0.000
Epidermis:	13.000	-5.750	1	-5.750	-0.001	0.000
Surface Wash:	7716.000	7697.250	1	7697.250	1.668	0.235
Other						
Total Recovery:						0.245 %

Chamber: **0** **Vehicle:**
Drug:

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1							

	Conc From	Conc-b Above	Vol. NA	Total 0.000	Mass 0.000	% Dose 0.000
Total Absorbed:						
Dermis:						
Epidermis:						
Surface Wash:						
Other						
Total Recovery:						0.000 %

DRAFT

Determination of the Percutaneous Absorption of THF, in vitro, Using the Human Cadaver Skin Model

Water Test Results

R04-1387
Water Integrity Test and Product Dose Summary by Product

Donor: **KS032805** Date: **07/21/2005**

Dose units: uL

Product: **10% THF**

Replicate	Chamber	uL	Product Dose
1	19	0.54	800.00
2	20	0.37	800.00
3	21	0.35	800.00
4			
5			
6			
7			
8			
Mean:		**0.42**	**800.00**
SD:		0.10	0.00
CV:		24.39	0.00

Product: **30% THF**

Replicate	Chamber	uL	Product Dose
1	22	0.58	800.00
2	23	0.55	800.00
3	24	0.34	800.00
4			
5			
6			
7			
8			
Mean:		**0.49**	**800.00**
SD:		0.13	0.00
CV:		26.60	0.00

Product: **100% THF**

Replicate	Chamber	uL	Product Dose
1	25	0.37	800.00
2	26	0.39	800.00
3	27	0.31	800.00
4			
5			
6			
7			
8			
Mean:		**0.36**	**800.00**
SD:		0.04	0.00
CV:		11.05	0.00

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Across Donor Mean

Replicate	Chamber	Pre-test uL	Post (H2) DPM	Post (H2) µL	Post (H3) DPM	Post (H3) µL
1	19	0.54	18	0.00	72	0.21
2	20	0.37	33	0.06	65	0.19
3	21	0.35	32	0.05	66	0.18
4	22	0.58	0	0.00	120	0.37
5	23	0.55	0	0.00	65	0.18
6	24	0.34	0	0.00	74	0.18
7	25	0.37	105	0.32	152	0.49
8	26	0.39	192	0.67	111	0.36
9	27	0.31	244	0.66	157	0.41
10						
11						
12						
13						
14						
15						
16						
17						
18						
Mean:		**0.42**		**0.20**		**0.28**
SD:		0.10		0.28		0.12
CV:		24.36		145.51		43.20

Study Name:	Socma, donor 3, 10 min	Study #:	R04-1387

Top residual (25 µL)

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Orig. Vol. (µL)***	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	90075	18.75	25	800	90056.25	4311.4	0.0886	59.22			84%		
10% THF	20	90322	18.75	25	800	90303.25	4311.4	0.0886	59.38			84%		
10% THF	21	84012	18.75	25	800	83993.25	4311.4	0.0886	55.23	57.95	2.35	78%	81.754	0.033
30% THF	22	87883	18.75	25	800	87864.25	4034.3	0.2658	185.24			87%		
30% THF	23	83239	18.75	25	800	83220.25	4034.3	0.2658	175.45			83%		
30% THF	24	85444	18.75	25	800	85425.25	4034.3	0.2658	180.10	180.27	4.90	85%	84.775	0.023
100% THF	25	105946	18.75	25	800	105927.25	4088.5	0.8860	734.57			104%		
100% THF	26	100504	18.75	25	800	100485.25	4088.5	0.8860	696.83			98%		
100% THF	27	110843	18.75	25	800	110824.25	4088.5	0.8860	768.53	733.31	35.87	108%	103.458	0.051

Surface Wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	3283	18.75	1500	1500	3264.25	4311.4	0.0886	0.07			0%		
10% THF	20	5604	18.75	1500	1500	5585.25	4311.4	0.0886	0.11			0%		
10% THF	21	7710	18.75	1500	1500	7691.25	4311.4	0.0886	0.16	0.11	0.05	0%	0.160	0.001
30% THF	22	9004	18.75	1500	1500	8985.25	4034.3	0.2658	0.59			0%		
30% THF	23	16129	18.75	1500	1500	16110.25	4034.3	0.2658	1.06			0%		
30% THF	24	15306	18.75	1500	1500	15287.25	4034.3	0.2658	1.01	0.89	0.26	0%	0.417	0.001
100% THF	25	21528	18.75	1500	1500	21509.25	4088.5	0.8860	4.66			1%		
100% THF	26	8556	18.75	1500	1500	8537.25	4088.5	0.8860	1.85			0%		
100% THF	27	7716	18.75	1500	1500	7697.25	4088.5	0.8860	1.67	2.73	1.68	0%	0.385	0.002

Kimwipe

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	20	18.75	NA	NA	1.25	4311.4	0.0886	0.00			0%		
10% THF	20	16	18.75	NA	NA	-2.75	4311.4	0.0886	0.00			0%		
10% THF	21	14	18.75	NA	NA	-4.75	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	22	18	18.75	NA	NA	-0.75	4034.3	0.2658	0.00			0%		
30% THF	23	16	18.75	NA	NA	-2.75	4034.3	0.2658	0.00			0%		
30% THF	24	15	18.75	NA	NA	-3.75	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	25	13	18.75	NA	NA	-5.75	4088.5	0.8860	0.00			0%		
100% THF	26	13	18.75	NA	NA	-5.75	4088.5	0.8860	0.00			0%		
100% THF	27	12	18.75	NA	NA	-6.75	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

Chamber wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	19	26	18.75	1000	1000	7.25	4311.4	0.0886	0.00			0%		
10% THF	20	23	18.75	1000	1000	4.25	4311.4	0.0886	0.00			0%		
10% THF	21	24	18.75	1000	1000	5.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	22	21	18.75	1000	1000	2.25	4034.3	0.2658	0.00			0%		
30% THF	23	38	18.75	1000	1000	19.25	4034.3	0.2658	0.00			0%		
30% THF	24	24	18.75	1000	1000	5.25	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	25	26	18.75	1000	1000	7.25	4088.5	0.8860	0.00			0%		
100% THF	26	26	18.75	1000	1000	7.25	4088.5	0.8860	0.00			0%		
100% THF	27	22	18.75	1000	1000	3.25	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

* µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM / Sample Vol.) / (Spec. Act.) * (Drug Conc.) * Orig. Vol.
** µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM) / (Spec. Act.) * (Drug Conc.)
*** Assumed the residual volume is the same as the dosed volume.
**** % recovered = µg / (Drug Conc. * 800 µL)

Donor 3

Chamber Results (60 Minutes)

DRAFT

Study Name:	Socma, donor 3, 60 min	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
KS032805	07/21/2005	07/22/2005	07/22/2005	07/25/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	37	0.8	5.1	800	0.0886	4311.4
10% THF	THF	38	0.8	5.2	800	0.0886	4311.4
10% THF	THF	39	0.8	5.4	800	0.0886	4311.4
30% THF	THF	40	0.8	4.6	800	0.2658	4034.3
30% THF	THF	41	0.8	5.3	800	0.2658	4034.3
30% THF	THF	42	0.8	4.8	800	0.2658	4034.3
100% THF	THF	43	0.8	5.0	800	0.8860	4088.5
100% THF	THF	44	0.8	4.4	800	0.8860	4088.5
100% THF	THF	45	0.8	5.0	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	1.00
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1860.447
Receptor Solution:	1x PBS

Sample Results	37	38	39	40	41	42
1	6348.000	6251.000	8657.000	25146.000	45043.000	28752.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	18.000	13.000	14.000	31.000	10.000	14.000
Epidermis	23.000	27.000	23.000	39.000	34.000	46.000
Surface Wash	10647.000	21031.000	4463.000	7476.000	13791.000	18318.000
Other						
Water Test	114.00	113.00	100.00	191.00	138.00	116.00

Sample Results	43	44	45			
1	2447.000	1598.000	2634.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Dermis	13.000	17.000	20.000			
Epidermis	18.000	16.000	20.000			
Surface Wash	25636.000	8451.000	10031.000			
Other						
Water Test	136.00	136.00	182.00			

Skin CalculationsV7.

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Study Name:	Socma, donor 3, 60 min (2nd cover sheet)	Study #:	R04-1387

Skin ID #	Date Dosed	Assay Start	Assay Finish	Entry Date
KS032805	07/21/2005	07/22/2005	07/22/2005	07/25/2005

Vehicle	Tracer	Chambers	Area	Volume	Dose	Drug Conc.	Standard
10% THF	THF	37	0.8	5.1	800	0.0886	4311.4
10% THF	THF	38	0.8	5.2	800	0.0886	4311.4
10% THF	THF	39	0.8	5.4	800	0.0886	4311.4
30% THF	THF	40	0.8	4.6	800	0.2658	4034.3
30% THF	THF	41	0.8	5.3	800	0.2658	4034.3
30% THF	THF	42	0.8	4.8	800	0.2658	4034.3
100% THF	THF	43	0.8	5.0	800	0.8860	4088.5
100% THF	THF	44	0.8	4.4	800	0.8860	4088.5
100% THF	THF	45	0.8	5.0	800	0.8860	4088.5
		Units:	cm²	ml	uL	ug/uL	DPM/uL

Sample Time	Hours
1	1.00
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	

Sample Volume Collected:	1.00
Final Sample Volume:	1.00
Drug Background	18.75
Water Background	18.00
Dermal Dilution:	1.0
Epidermal Dilution:	1.0
Surface Wash Dilution:	1.0
Other Samples	
Water Standard:	1360.447
Receptor Solution:	1x PBS

Sample Results	37	38	39	40	41	42
1	6348.000	6251.000	8657.000	25146.000	45043.000	28752.000
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	82630.000	81976.000	79188.000	79042.000	77804.000	78330.000
Top residual activity (DPM/µL)	3305.2	3279.0	3167.5	3161.7	3112.2	3133.2
Kimwipe	16.000	13.000	14.000	19.000	20.000	27.000
Chamber wash	24.000	25.000	26.000	33.000	26.000	22.000
Water Test	114.00	113.00	100.00	191.00	138.00	116.00

Sample Results	43	44	45			
1	2447.000	1598.000	2634.000			
2						
3						
4						
5						
6						
7						
8						
9						
10						
11						
12						
Top residual (25 µL)	105540.000	106327.000	108219.000			
Top residual activity (DPM/µL)	4221.6	4253.1	4328.8			
Kimwipe	13.000	15.000	13.000			
Chamber wash	27.000	25.000	28.000			
Water Test	136.00	136.00	182.00			

Skin CalculationsV7.

R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 60 min**

Date Dosed: 07/21/05

Chamber: **37** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	6348.000	6329.250	32279.175	1.0	0.829	0.663	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.663	0.663	0.936
Dermis:	18.000	-0.750	1	-0.750	0.000	0.000
Epidermis:	23.000	4.250	1	4.250	0.000	0.000
Surface Wash:	10647.000	10628.250	1	10628.250	0.218	0.308
Other						
Total Recovery:						1.244 %

Chamber: **38** **Vehicle:** **10% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	6251.000	6232.250	32407.700	1.0	0.832	0.666	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.666	0.666	0.940
Dermis:	13.000	-5.750	1	-5.750	0.000	0.000
Epidermis:	27.000	8.250	1	8.250	0.000	0.000
Surface Wash:	21031.000	21012.250	1	21012.250	0.432	0.609
Other						
Total Recovery:						1.549 %

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R04-1387 INDIVIDUAL CHAMBER RESULTS

Skin ID: KS032805 **Sponsor:** Socma, donor 3, 60 min

Date Dosed: 07/21/05

Chamber: 39 **Vehicle:** 10% THF
Drug: THF

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	8657.000	8638.250	46646.550	1.0	1.198	0.959	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.959	0.959	1.352
Dermis:	14.000	-4.750	1	-4.750	0.000	0.000
Epidermis:	23.000	4.250	1	4.250	0.000	0.000
Surface Wash:	4463.000	4444.250	1	4444.250	0.091	0.129
Other						
Total Recovery:						1.481 %

Chamber: 40 **Vehicle:** 30% THF
Drug: THF

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	25146.000	25127.250	115585.350	1.0	9.519	7.615	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	7.615	7.615	3.581
Dermis:	31.000	12.250	1	12.250	0.001	0.000
Epidermis:	39.000	20.250	1	20.250	0.001	0.001
Surface Wash:	7476.000	7457.250	1	7457.250	0.491	0.231
Other						
Total Recovery:						3.813 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 60 min**

Date Dosed: 07/21/05

Chamber: **41** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	45043.000	45024.250	238628.525	1.0	19.652	15.722	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	15.722	15.722	7.394
Dermis:	10.000	-8.750	1	-8.750	-0.001	0.000
Epidermis:	34.000	15.250	1	15.250	0.001	0.000
Surface Wash:	13791.000	13772.250	1	13772.250	0.907	0.427
Other						
Total Recovery:						7.821 %

Chamber: **42** **Vehicle:** **30% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	28752.000	28733.250	137919.600	1.0	11.358	9.087	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	9.087	9.087	4.273
Dermis:	14.000	-4.750	1	-4.750	0.000	0.000
Epidermis:	46.000	27.250	1	27.250	0.002	0.001
Surface Wash:	18318.000	18299.250	1	18299.250	1.206	0.567
Other						
Total Recovery:						4.841 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 60 min**

Date Dosed: 07/21/05

Chamber: **43** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	2447.000	2428.250	12141.250	1.0	3.289	2.631	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	2.631	2.631	0.371
Dermis:	13.000	5.750	1	-5.750	-0.001	0.000
Epidermis:	18.000	-0.750	1	-0.750	0.000	0.000
Surface Wash:	25636.000	25617.250	1	25617.250	5.551	0.783
Other						
Total Recovery:						1.154 %

Chamber: **44** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	1598.000	1579.250	6948.700	1.0	1.882	1.506	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	1.506	1.506	0.212
Dermis:	17.000	-1.750	1	-1.750	0.000	0.000
Epidermis:	16.000	-2.750	1	-2.750	-0.001	0.000
Surface Wash:	8451.000	8432.250	1	8432.250	1.827	0.258
Other						
Total Recovery:						0.470 %

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R04-1387 **INDIVIDUAL CHAMBER RESULTS**

Skin ID: **KS032805** **Sponsor:** **Socma, donor 3, 60 min**

Date Dosed: 07/21/05

Chamber: **45** **Vehicle:** **100% THF**
Drug: **THF**

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1	2634.000	2615.250	13076.250	1.0	3.542	2.834	0.5

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	2.834	2.834	0.400
Dermis:	20.000	1.250	1	1.250	0.000	0.000
Epidermis:	20.000	1.250	1	1.250	0.000	0.000
Surface Wash:	10031.000	10012.250	1	10012.250	2.170	0.306
Other						
Total Recovery:						0.706 %

Chamber: **0** **Vehicle:**
Drug:

Sample	Conc	C-b	Total Mass	Delta T	Flux	CumPen	Mid-T
1							

	Conc	Conc-b	Vol.	Total	Mass	% Dose
Total Absorbed:	From	Above	NA	0.000	0.000	0.000
Dermis:						
Epidermis:						
Surface Wash:						
Other						
Total Recovery:						0.000 %

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Determination of the Percutaneous Absorption of THF, in vitro, Using the Human Cadaver Skin Model

Water Test Results

R04-1387
Water Integrity Test and Product Dose Summary by Product

Donor: **KS032805** Date: **07/21/2005**

Dose units: uL

Product: **10% THF**

Replicate	Chamber	uL	Product Dose
1	37	0.36	800.00
2	38	0.36	800.00
3	39	0.33	800.00
4			
5			
6			
7			
8			
Mean:		**0.35**	**800.00**
SD:		0.02	0.00
CV:		5.97	0.00

Product: **30% THF**

Replicate	Chamber	uL	Product Dose
1	40	0.58	800.00
2	41	0.47	800.00
3	42	0.35	800.00
4			
5			
6			
7			
8			
Mean:		**0.47**	**800.00**
SD:		0.12	0.00
CV:		25.66	0.00

Product: **100% THF**

Replicate	Chamber	uL	Product Dose
1	43	0.43	800.00
2	44	0.38	800.00
3	45	0.60	800.00
4			
5			
6			
7			
8			
Mean:		**0.47**	**800.00**
SD:		0.12	0.00
CV:		24.46	0.00

Across Donor Mean

Replicate	Chamber	Pre-test uL	Post (H2) DPM	Post (H2) µL	Post (H3) DPM	Post (H3) µL
1	37	0.36	0	0.00	47	0.11
2	38	0.36	0	0.00	49	0.12
3	39	0.33	0	0.00	59	0.16
4	40	0.58	0	0.00	148	0.44
5	41	0.47	0	0.00	89	0.28
6	42	0.35	0	0.00	79	0.22
7	43	0.43	1044	3.77	460	1.62
8	44	0.38	656	2.06	554	1.73
9	45	0.60	739	2.65	731	2.62
10						
11						
12						
13						
14						
15						
16						
17						
18						
Mean:		**0.43**		**0.94**		**0.81**
SD:		0.10		1.48		0.93
CV:		24.01		156.90		114.99

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

Product: **0**

Replicate	Chamber	uL	Product Dose
1			
2			
3			
4			
5			
6			
7			
8			
Mean:			
SD:			
CV:			

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Study Name:	Socma, donor 3, 60 min	Study #:	R04-1387

Top residual (25 µL)

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Orig. Vol. (µL)***	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	37	82630	18.75	25	800	82611.25	4311.4	0.0886	54.33			77%		
10% THF	38	81976	18.75	25	800	81957.25	4311.4	0.0886	53.90			76%		
10% THF	39	79188	18.75	25	800	79169.25	4311.4	0.0886	52.06	53.43	1.20	73%	75.378	0.017
30% THF	40	79042	18.75	25	800	79023.25	4034.3	0.2658	166.60			78%		
30% THF	41	77804	18.75	25	800	77785.25	4034.3	0.2658	163.99			77%		
30% THF	42	78330	18.75	25	800	78311.25	4034.3	0.2658	165.10	165.23	1.31	78%	77.706	0.006
100% THF	43	105540	18.75	25	800	105521.25	4088.5	0.8860	731.75			103%		
100% THF	44	106327	18.75	25	800	106308.25	4088.5	0.8860	737.21			104%		
100% THF	45	108219	18.75	25	800	108200.25	4088.5	0.8860	750.33	739.76	9.55	106%	104.369	0.013

Surface Wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg *	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	37	10647	18.75	1500	1500	10628.25	4311.4	0.0886	0.22			0%		
10% THF	38	21031	18.75	1500	1500	21012.25	4311.4	0.0886	0.43			1%		
10% THF	39	4463	18.75	1500	1500	4444.25	4311.4	0.0886	0.09	0.25	0.17	0%	0.349	0.002
30% THF	40	7476	18.75	1500	1500	7457.25	4034.3	0.2658	0.49			0%		
30% THF	41	13791	18.75	1500	1500	13772.25	4034.3	0.2658	0.91			0%		
30% THF	42	18318	18.75	1500	1500	18299.25	4034.3	0.2658	1.21	0.87	0.36	1%	0.408	0.002
100% THF	43	25636	18.75	1500	1500	25617.25	4088.5	0.8860	5.55			1%		
100% THF	44	8451	18.75	1500	1500	8432.25	4088.5	0.8860	1.83			0%		
100% THF	45	10031	18.75	1500	1500	10012.25	4088.5	0.8860	2.17	3.18	2.06	0%	0.449	0.003

Kimwipe

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	37	16	18.75	NA	NA	-2.75	4311.4	0.0886	0.00			0%		
10% THF	38	13	18.75	NA	NA	-5.75	4311.4	0.0886	0.00			0%		
10% THF	39	14	18.75	NA	NA	-4.75	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	40	19	18.75	NA	NA	0.25	4034.3	0.2658	0.00			0%		
30% THF	41	20	18.75	NA	NA	1.25	4034.3	0.2658	0.00			0%		
30% THF	42	27	18.75	NA	NA	8.25	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	43	13	18.75	NA	NA	-5.75	4088.5	0.8860	0.00			0%		
100% THF	44	15	18.75	NA	NA	-3.75	4088.5	0.8860	0.00			0%		
100% THF	45	13	18.75	NA	NA	-5.75	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

Chamber wash

Vehicle	Chamber #	Raw Data (DPM)	Background (DPM)	Sample Vol. (µL)	Vol. Counted (µL)	Corrected DPM	Spec. Act. (DPM/µL)	Drug Conc. (µg/µL)	µg **	Average (µg)	SD (µg)	% Dose	Average (% Dose)	SD (% Dose)
10% THF	37	24	18.75	1000	1000	5.25	4311.4	0.0886	0.00			0%		
10% THF	38	25	18.75	1000	1000	6.25	4311.4	0.0886	0.00			0%		
10% THF	39	26	18.75	1000	1000	7.25	4311.4	0.0886	0.00	0.00	0.00	0%	0.000	0.000
30% THF	40	33	18.75	1000	1000	14.25	4034.3	0.2658	0.00			0%		
30% THF	41	26	18.75	1000	1000	7.25	4034.3	0.2658	0.00			0%		
30% THF	42	22	18.75	1000	1000	3.25	4034.3	0.2658	0.00	0.00	0.00	0%	0.000	0.000
100% THF	43	27	18.75	1000	1000	8.25	4088.5	0.8860	0.00			0%		
100% THF	44	25	18.75	1000	1000	6.25	4088.5	0.8860	0.00			0%		
100% THF	45	28	18.75	1000	1000	9.25	4088.5	0.8860	0.00	0.00	0.00	0%	0.000	0.000

* µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM / Sample Vol.) / (Spec. Act.) * (Drug Conc.) * Orig. Vol.
** µg = (DPM/µL Sample) / (DPM/µL THF) * Conc. * Vol. = (Corrected DPM) / (Spec. Act.) * (Drug Conc.)
*** Assumed the residual volume is the same as the dosed volume.
**** % recovered = µg / (Drug Conc. * 800 µL)