Final
Biological Phase Report

Metabolism of N-Ethyl Perfluorooctane Sulfonamido-
(Net-Fose; [illegible] in Cynomolgus Monkeys
Administration of a Single Capsule Dose

PREPARED FOR:
3M Chemicals

COVANCE STUDY NUMBER:
6329-226

COVANCE
THE DEVELOPMENT SERVICES COMPANY

Sponsor:

3M Chemicals
St. Paul, Minnesota

Study Title:

Metabolism of N-Ethyl Perfluorooctane Sulfonamido Ethanol (Net-Fose; T-6316) in Cynomolgus Monkeys Following Administration of a Single Capsule Dose

Data Requirement:

None

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Study Completed on:

June 2, 1999

Performing Laboratory:

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Madison, Wisconsin 53704

Laboratory Project Identification:

Covance 6329-226

STATEMENT OF NO DATA CONFIDENTIALITY CLAIM

Metabolism of N-Ethyl Perfluorooctane Sulfonamido Ethanol (Net-Fose; T-6316) in Cynomolgus Monkeys Following Administration of a Single Capsule Dose

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

These data are the property of 3M Chemicals and as such are confidential for all purposes other than compliance with FIFRA Section 10. Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality that may exist under any other statute or in any other country.

Company: 3M Chemicals

Company Representative: Andrew Seacat, PhD

Title: Study Director

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Andrew M. Seacat
Signature

6/9/99
Date

COMPLIANCE STATEMENT

Metabolism of N-Ethyl Perfluorooctane Sulfonamido Ethanol (Net-Fose; T-6316) in Cynomolgus Monkeys Following Administration of a Single Capsule Dose

All aspects of this biological phase were conducted in accordance with the Environmental Protection Agency Pesticide Programs Good Laboratory Practice Standards (40 CFR 160).

Andrew Seacat, PhD Study Director 3M Chemicals	Date
Study Submitted by	Date
Sponsor	Date

QUALITY ASSURANCE STATEMENT

This report has been reviewed by the Quality Assurance Unit of Covance Laboratories Inc., in accordance with the Environmental Protection Agency (EPA) Good Laboratory Practice Standards, 40 CFR 160. The following inspections were conducted and findings reported to the study director and study director management. Written status reports of inspections and findings are issued to Covance management according to standard operating procedures.

Inspection Dates			Date Reported to Study Director and
From	To	Phase	Study Director Management
04/22/98	04/22/98	Protocol Review	05/04/98
05/13/98	05/13/98	Test Article Administration	05/13/98
06/02/98	06/02/98	Protocol Amendment Review	06/03/98
10/09/98	10/09/98	Protocol Amendment Review	10/09/98
11/06/98	11/16/98	Data Review	04/06/99
11/06/98	11/16/98	Report Review	04/06/99
11/06/98	11/16/98	Data Review	04/06/99
05/19/99	05/19/99	Report Review	06/02/99
06/01/99	06/01/99	Report Review	06/02/99

Michael J. Turner

Representative, Quality Assurance Unit

6/2/99

Date

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ABSTRACT

Tissue, plasma, serum, bile, feces, and urine specimens were provided to obtain information on the metabolism of N-ethyl perfluorooctane sulfonamido ethanol (Net-Fose; T-6316) in cynomolgus monkeys following administration of a single oral dose.

Sixteen cynomolgus male and female monkeys from Covance Research Products were dosed according to the following study design:

Group	Number and Sex of Animals	Status	Dose	Collections Postdose
1	6 Male 6 Female	Intact	50 mg/kg	Tissues from 2/sex on Days 2, 28, and 90. Urine and feces from 0-12 and 12-24 hours, then daily through 28 days, and weekly through 90 days. Blood predose, and at 1, 2, 4, 6, 12, 24, 36, and 48 hours, 7 days, and weekly through 90 days.
2	2 Male 2 Female	Bile Duct Cannulated	50 mg/kg	Tissues at 28 days. Bile from 0-12 and 12-24 hours, and daily through 28 days. Blood predose, and at 1, 2, 4, 6, 12, 24, 36 and 48 hours,7 days, and weekly through 28 days.

Separate blood samples were collected for preparation of plasma and serum. Plasma was prepared by centrifugation of the blood. Serum was prepared by allowing the blood to clot and centrifuging it to separate the cellular debris. All specimens were shipped to the Sponsor for analysis and the results of these analyses will be reported separately by the Sponsor.

TITLE

Metabolism of N-Ethyl Perfluorooctane Sulfonamido Ethanol (Net-Fose; T-6316) in Cynomolgus Monkeys Following Administration of a Single Capsule Dose

OBJECTIVE

The purpose of this study was to administer a perfluorooctane test substance to male and female cynomolgus monkeys and collect samples for determination of absorption, distribution, metabolism, and excretion.

REGULATORY COMPLIANCE

The biological phase of this study was conducted in accordance with the Environmental Protection Agency (EPA), Good Laboratory Practice Standards, 40 CFR 160 and by Covance Laboratories Inc., 3301 Kinsman Boulevard, Madison, Wisconsin, in accordance with Covance Protocol CMS 22672A1 dated April 21, 1998, and Covance Standard Operating Procedures (SOPs). The protocol, protocol amendment, and protocol deviations are in Appendix A.

All procedures in this study are in compliance with the Animal Welfare Act Regulations, 9 CFR 3, dated October 30, 1989, and as modified on March 18, 1991. In the opinion of the Sponsor and the study director, the study did not unnecessarily duplicate any previous work.

QUALITY ASSURANCE

The protocol, study conduct, data, and biological phase final report were audited by the Covance Quality Assurance Unit (QAU) in accordance with Covance SOPs. All study activities performed at 3M will be the responsibility of the 3M Quality Assurance Department.

EXPERIMENTAL DESIGN AND PROCEDURES

Study Design

Animals were assigned to two groups, one was the bile duct cannulated group and the other was intact. The group designation, number of animals, specimen collection, and target dose level were as follows:

Group	Number and Sex of Animals	Status	Dose Frequency, Route, and Level	Collections Postdose
1	6 Male 6 Female	Intact	One Capsule Oral 50 mg/kg	Tissues from 2/sex on Days 2, 28, and 90. Urine and feces from 0-12 and 12-24 hours, then daily through 28 days, and weekly through 90 days. Blood predose, and at 1, 2, 4, 6, 12, 24, 36, and 48 hours, 7 days, and weekly through 90 days.
2	2 Male 2 Female	Bile Duct Cannulated	One Capsule Oral 50 mg/kg	Tissues at 28 days. Bile from 0-12 and 12-24 hours, and daily through 28 days. Blood predose, and at 1, 2, 4, 6, 12, 24, 36 and 48 hours,7 days, and weekly through 28 days.

Justification for Dosing Route and Dose level

The oral route has been used for evaluating systemic toxicity of the compound in cynomolgus monkeys. The 50 mg/kg dose was chosen because it provides the maximum non-toxic single dose amount necessary to recover measurable concentrations of the test substance in minor tissues.

Test Substance

The test substance, T-6316, was received in the Department of Metabolic Chemistry on May 8, 1998 from the Covance Department of Toxicology. Stability and retention of a sample as specified in 40 CFR 160.105 of the test substance is the responsibility of the Sponsor. Information on synthesis methods, composition, or other characteristics that define the test substance are on file with the Sponsor.

The following information was obtained from the label on the test substance container:

Substance No.:	1084A3
Container No.:	65
Test Substance:	T-6316 (Narrow Range N-Ethyl Perfluorooctanesulfonamido Ethanol, NEtFOSE)
Lot Nos.:	30035, 30037, and 30039
Date Combined:	07-31-1997
Purity/Concentration:	98.1%
Expiration Date:	On file with the Sponsor
Storage Requirements:	Room temperature
Physical State:	Amber waxy solid, slight odor

Test Animals and Housing

The in-life portion of the study was conducted May 13, 1998, through August 11, 1998.

Eleven male and eleven female cynomolgus monkeys (nonhuman primates) from Covance Research Products were received on March 24, 1998. The animals were young adult to adult and weighed approximately 3 to 4 kg at arrival. Upon arrival, each animal was assigned a temporary identification number. Before being placed on test, each animal was randomly assigned a permanent identification number and identified with a neck tag attached to the collar.

All animals were housed in individual, suspended, stainless steel, wire-mesh cages during acclimation and housed in individual metabolism cages designed for the separation and collection of bile, urine, and feces while on test.

The primates were fed Certified Primate Diet #8726C (Harlan Teklad) *ad libitum*, except when fasted for surgery and prior to test substance administration through approximately 4 hours postdose. Diets were supplemented with appropriate fruits and cereals. Water was provided fresh daily and *ad libitum*. Environmental controls for the animal room were set to maintain 18° to 29°C, 50% ± 20% relative humidity, and a 12-hour light/12-hour dark cycle. The 12-hour dark cycle was interrupted, as necessary, to accommodate study procedures.

Animal Selection

Clinical chemistry and hematology test results and physical examination results were used to select test animals. In addition, animals were selected for the surgical procedure based on the best apparent adjustment to the jacket and tether system. Before dose administration, a laboratory animal veterinarian evaluated the health of the animals and approved their use on the study.

Justification

Studies using live animals are essential for characterizing the disposition of chemicals in animals. No acceptable non-live animal models were available. The cynomolgus monkey has been used as the non-rodent species to evaluate toxicity. This study will aid in the evaluation of test results obtained in toxicology studies conducted in monkeys and will also provide a basis for the extrapolation of safety data from animals to humans. The number of animals was the minimum number necessary to provide scientifically valid results.

Surgical Procedure

The surgical procedure was conducted in accordance with Covance Standard Operating Procedures. The animals were fasted overnight before surgery and sedated with

ketamine. An appropriate antibiotic was administered. Surgical anesthesia was maintained using oxygen and isoflurane. Lactated Ringer's solution was administered through a saphenous catheter throughout the surgical procedure or as determined by a staff veterinarian. A sterile surgical scrub was performed. The common bile duct and duodenum was cannulated and the gallbladder was removed and discarded. Analgesics were administered as recommended by the staff veterinarian. Additional antibiotics and/or fluids were administered as recommended by the staff veterinarian. The animals had at least 10 days to recover from the surgical procedure prior to dose administration.

Bile Replacement

Beginning the day after surgery through 3 days post surgery, a solution of 1% dextrose in Lactated Ringer's solution was administered via the duodenal cannula for approximately 8 hours per day at approximately 20 mL/hour to prevent dehydration. Beginning on the fourth post surgical day until sacrifice, a bile salts solution was infused via the duodenal cannula for approximately 8 hours per day at approximately 23 mL/kg/day. The bile salts solution was prepared by adding 18.0 g of cholic acid to 1 L of 0.9% sodium chloride solution. Sodium bicarbonate (1.3 g) was added to each 1 L of solution. The solution was mixed and the pH adjusted to 7.4 to 7.8 with 0.1N HCl or sodium hydroxide, as appropriate. Infusion intervals and volumes administered were recorded (See Table 3).

Dose Preparation and Analysis

The capsules (gelatin, No. 2, 0.37 mL) for the dose preparation were received from Torpac, Inc. on April 9, 1998.

The test compound was homogenized. A No. 2 capsule was tared on an analytical balance and an appropriate amount of test substance, based on animal weight and dose level, was added using a spatula. The capsules were sealed and placed in separate 20-mL scintillation vials labeled with the animal number. The capsules were stored under ambient conditions.

Dosing Procedure

The animals were fasted overnight prior to dose administration through approximately 4 hours postdose. The capsule was given to the animals by a device specific for capsule administration.

Antemortem Observations

Mortality and moribundity checks were done twice daily (a.m. and p.m.). Cageside observation for general health and appearance were done once daily. Signs of poor health or abnormal behavior were recorded as they were observed.

Physical Examinations

Physical examination were performed twice during acclimation, once pre-surgery, and once post surgery before the initiation of treatment. Animals were anesthetized with ketamine hydrochloride according to Covance Standard Operating Procedures for the examination.

Jackets were checked according to Covance Standard Operating Procedures. The animals were anesthetized as above for the examination; however, a lower dose of ketamine was administered for the limited examination.

Body Weights

Body weights were taken weekly during acclimation, within 5 days of dosing (to be used for dosing calculations), weekly after dosing, and on the day of sacrifice.

Clinical Pathology

The animals were not fasted. Blood was collected via the femoral vein before dose administration as follows: approximately 1 week before surgery from all animals and approximately 4 and 8 days post surgery from cannulated animals. When health problems developed, blood was collected for clinical pathology tests to assess health status as deemed necessary by the staff veterinarian.

Clinical Pathology Tests

The following are the tests performed by the Clinical Pathology Department:

Hematology
Red blood cell count
Hemoglobin
Hematocrit
Mean corpuscular volume
Mean corpuscular hemoglobin
Mean corpuscular hemoglobin concentration
Platelet count
White blood cell count
Differential blood cell count
Blood cell morphology
Prothrombin time
Activated partial thromboplastin time

Clinical Chemistry
Glucose
Urea nitrogen
Creatinine
Total protein
Albumin
Globulin
Total bilirubin
Serum bile acids
Cholesterol
Aspartate aminotransferase
Alanine aminotransferase
Alkaline phosphatase
Creatine kinase
Gamma glutamyltransferase
Calcium
Inorganic phosphorous
Sodium
Potassium
Chloride

Antemortem Sample Collection

No Teflon was used for this study.

Blood (Groups 1 and 2). Approximately 2 mL of blood was collected from Group 1 animals predose and approximately 2 mL was collected at 1, 2, 4, 6, 12, 24, 36, and 48 hours, 7 days, and weekly through 90 days postdose. Approximately 2 mL of blood was collected from Group 2 animals predose and approximately 2 mL was collected at 1, 2, 4, 6, 12, 24, 36, and 48 hours, and on 7, 14, 21, and 28 days postdose. The blood was collected via a femoral vein into heparinized tubes and placed immediately on wet ice. Effective June 3, 1998 (Study Day 21) and at the remaining time points, an additional 2-mL blood sample was collected into a glass tube without heparin and set aside at room temperature to clot.

Bile (Group 2). Bile was collected from the Group 2 animals via the implanted cannula into plastic containers surrounded by dry ice predose (for at least 12 hours), and at 0-12, 12-24, and continuing at 24-hour intervals through 28 days postdose.

Urine (Group 1). Urine was collected in plastic containers surrounded by dry ice at 0-12, 12-24, and continued at 24-hour intervals through 28 days, then weekly until 90 days postdose.

Feces (Group 1). Feces were collected at 0-12, 12-24, and continued for 24-hour intervals through 28 days, then weekly until 90 days postdose. Specimens were transferred into plastic containers at the time of collection.

Termination

Scheduled Sacrifice. At the time of sacrifice, animals were anesthetized with sodium pentobarbital. Cerebrospinal fluid (CSF) was collected once the animal was fully anesthetized. CSF was placed on wet ice immediately after collection and collection times were recorded. Blood was collected via cardiac puncture into glass tubes with heparin (at least 20 mL) and into glass tubes without heparin (at least 20 mL), except Animal No. I0541 that had a short sample obtained via vena cava. Following blood collection, the animals were sacrificed via exsanguination under sodium pentobarbital.

Residual urine from the bladder was added to the last urine sample. Stomach, large and small intestinal contents were collected from the two per sex Group 1 animals that were sacrificed at Day 2 only.

All tissues collected were excised, rinsed with water, blotted dry, weighed, and placed in a plastic container surrounded by wet ice. After the tissues were removed, the residual carcasses were discarded. The following tissues were collected from all animals at sacrifice, except the gallbladder that was collected from Group 1 only:

Adrenal glands
Aorta
Bone (femur)
Bone marrow (from femur)
Brain
Diaphragm
Epididymis
Esophagus
Eyes
Fat
Gallbladder
Heart
Kidneys
Large intestine
Liver
Lungs
Lymph nodes (cervical)
Lymph nodes (mesenteric)
Muscle (thigh)
Ovaries
Pancreas
Prostate
Salivary glands
Seminal vesicles
Skin (dorsal, shaved)
Small intestine
Spinal cord
Spleen
Stomach
Testes
Thymus
Thyroid/Parathyroid
Tongue
Trachea
Urinary bladder
Uterus

Sample Identification, Retention, and Disposition

Specimens were identified with the study number, sex, animal number, group, matrix, specimen number, and collection interval.

Blood, Plasma, Serum, and Cellular Fraction Preparation and Storage

Blood in glass tubes with heparin was stored at approximately 5°C prior to analysis. At the individual time points, the blood was gently inverted several times to homogenize, then approximately 700 µL was taken and placed into a labeled vial for each individual time point. At sacrifice, approximately half of the blood was homogenized and placed into a labeled vial. The subsamples were placed in a freezer at a temperature of approximately -20°C. The remaining blood was centrifuged at 2,400 rpm (1,300 x g) for approximately 10 minutes at approximately 5°C. The resulting plasma and cellular fraction was transferred to separately labeled vials and placed in freezer at a temperature of approximately -20°C until they were shipped.

The additional 2-mL blood collection in glass tubes without heparin for the collection of serum was allowed to clot at room temperature for approximately 30 to 60 minutes. The sample was then centrifuged at 2,400 rpm (1,300 x g) for approximately 10 minutes at approximately 5°C. The serum was removed and placed into a labeled vial. The cellular debris was discarded and the serum was stored in a freezer at a temperature of approximately -20°C to await shipment.

Sample Transfer

All specimens were shipped on dry ice to the Sponsor on June 12, 1998, and August 18, 1998:

Dr. Kris Hansen
Environmental Technology and Safety Services
935 Bush Avenue
Building 2-E3-09
St Paul, Minnesota 55133-3331
Phone: (612) 778-6018
Fax: (612) 788-6176

The Sponsor will be responsible for further analysis, reporting, and archiving upon completion of the study.

Disposition of Raw Data, Records, Samples, and the Final Report

The following data records to be maintained and transferred to the archives of Covance will include, but will not be limited to: protocol and amendments; study correspondence; test material receipt; final report.

The following supporting records to be retained at Covance but not archived with the study data will include, but will not be limited to: feed analysis records; water analysis records; animal room temperature and humidity records; refrigerator/freezer temperature records; instrument calibration and maintenance records; United States Department of Agriculture animal records; stock records.

The following data records to be transferred to the archives of 3M upon completion of the report will include, but will not be limited to:

In-life records:

- Animal receipt
- Acclimation
- Animal room maintenance
- Antemortem observations
- Body weights
- Physical examination records
- Clinical pathology
- Clinical pathology slides
- Dose administration
- Sample collection
- Bile salts replacement solution infusion times and amounts

All correspondence, documentation, records, protocol, and final report generated as a result of this study will be archived in the storage facilities of Covance for a period of one year following the signing of the final report. One year after signing the final report, all of the aforementioned materials will be sent to the Sponsor and a return fee will be charged. The Sponsor may elect to have the materials retained in the Covance Archives for an additional period of time and Covance will charge a storage fee. If the Sponsor chooses to have Covance dispose of the materials, a disposal fee will be charged.

RESULTS AND DISCUSSION

Quarantine and Acclimation

All animals under quarantine and acclimation beginning March 24, 1998, except Animal I05428, appeared clinically healthy and were released on April 24, 1998. Animal I05428 was observed to have diarrhea and was monitored until normal. At least one physical examination, one fecal examination, and three tuberculin tests were performed before

release from quarantine. Weekly body weights were recorded and animals were acclimated to the jacket and tether system required for bile duct cannulation.

Clinical Pathology

Results of presurgical clinical pathology tests indicated no obvious group or individual health abnormalities. Although several males in Group 1 had notably high leukocyte counts, these were attributed to excitement associated with blood collection procedures. A few females in Group 1 had mildly high values for alanine aminotransferase activity consistent with Hepatitis A infection, a subclinical condition commonly observed in cynomolgus monkeys that does not adversely effect liver function or animal health.

Results of the clinical pathology tests following surgery demonstrated no critical complications secondary to bile duct cannulation. Four days post surgery, increased activities for aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, gamma glutamyltransferase, and creatine kinase in Group 2 animals were consistent with the surgical procedure. The total bilirubin was notably increased for only one of the males (Animal No. I05436); and one of the females (Animal No. I05441) exhibited evidence of blood loss from the surgical procedure. Eight days post surgery, the high enzyme activities generally exhibited significant reductions indicative of continued recovery from the surgical procedure, and total bilirubin was no longer elevated for Animal No. I05436. Persistent, mildly to moderately elevated activities for alkaline phosphatase (males and females) and gamma glutamyltransferase (males only) at 8 days post surgery were characteristic of mildly increased biliary pressure secondary to bile duct cannulation, but normal values for total bilirubin and serum bile acids indicated hepatic function was likely not significantly compromised.

Body Weights and Doses Administered

Individual body weights and doses administered to Groups 1 and 2 are presented in Tables 1 and 2. Actual doses administered ranged from 100.2 % to 104.4% of the nominal dose of 50 mg/kg.

Antemortem Observations

The animals appeared normal during dose administration and appeared healthy and exhibited no overt signs of toxicity throughout the study. The noted observations are listed in Appendix B. None of these observations appeared to be test substance related.

On May 22, 1998, no bile flow was noted for Animals I05437 and I05441. The swivel was flushed for Animal I05437 and the bile started to flow again. The technician found that the swivel for Animal I05441was hooked up incorrectly on the previous day, so it was connected correctly and the pump restarted. Approximately 2 hours later, there was no bile flow, so the system was rechecked and bile began to flow. On May 26, 1998 and

May 29, 1998, blood was drawn from Animal I05441 for clinical chemistry analysis to monitor her health status. The results on May 29, 1998, were indicative of cholestasis, but the results were improved from the results on May 26, 1998. The Clinical Pathologist also indicated that the hepatic dysfunction appeared minimal and concluded very little hepatocellular degeneration or necrosis occurred.

On June 4, 1998, Animal I05449 did not have a screen above the pan to separate the urine from the feces. The feces was scraped from the pan and collected; however, some cross-contamination may have occurred.

Bile flow slowed and was noted on Study Day 17, 23, and 24 then stopped on Day 25 from Animal I05446. However, the animal exhibited no signs of compromised health. Upon sacrifice it was noted that a portion of the bile duct had re-grown, evidently providing an alternate path of bile flow.

CONCLUSIONS

Samples were provided to obtain information on the pharmacokinetics, excretion and tissue distribution of N-ethyl perfluorooctane sulfonamido ethanol (Net-Fose; T-6316) after a single casule dose in cynomolgus monkeys. Bile-duct cannulated as well as intact animals were used in the study. All samples were shipped to the Sponsor for analysis and results of these analyses will be reported separately by the Sponsor. No test substance effects were noted on the monkeys.

TABLES

Table 1. Individual Body Weights of Cynomolgus Monkeys Reported in Kilograms

Animal Number	Day 1	3	8	9	16	22	23	31	35
				Group 1 Male					
I05428	4.4	4.2							
I05430	3.9	3.9							
I05431	3.8	3.8	3.8		3.9	3.9			
I05432	4.2	4.2	4.2		4.2	4.2			
I05433	4.1	4.0	4.0		4.4	4.3		4.4	4.4
I05435	4.0	3.9	4.1		4.3	4.3		4.3	4.3
				Group 1 Female					
I05439	3.1	3.1							
I05440	3.1	3.1							
I05442	3.0	2.9	2.8		3.0	2.9			
I05444	3.0	2.9	2.9		2.9	2.8			
I05447	3.2	3.1		3.2	3.3	3.3		3.5	3.6
I05449	3.3	3.3		3.4	3.3	3.2		3.3	3.3
				Group 2 Male					
I05436	3.7	3.5		3.5	3.6		3.8		
I06437	3.7	3.7		3.6	3.8		3.6		
				Group 2 Female					
I05441	3.0	3.0		2.8	3.2		3.2		
I05446	4.2	4.1		3.8	4.2		4.1		

	Day 42	49	56	63	70	77	84	91
				Group 1 Male				
I05433	4.5	4.6	4.6	4.7	4.8	4.8	4.9	4.9
I05435	4.1	4.2	4.2	4.2	4.2	4.2	4.3	4.3
				Group 1 Female				
I05447	3.5	3.5	3.5	3.5	3.6	3.6	3.7	3.6
I05449	3.4	3.4	3.4	3.4	3.5	3.5	3.7	3.7

Table 2. Individual Body Weights of and Dose Weights Administered in One Capsule to Cynomolgus Monkeys (50 mg/kg)

Animal Number	Group	Animal Weight (kg)	Test Substance Administered		
			(g)	(mg/kg)	% of Nominal
I05428	1	4.4	0.2207	50.2	100.3
I05430	1	3.9	0.1978	50.7	101.4
I05431	1	3.8	0.1930	50.8	101.6
I05432	1	4.2	0.2138	50.9	101.8
I05433	1	4.1	0.2082	50.8	101.6
I05435	1	4.0	0.2033	50.8	101.7
I05436	2	3.7	0.1884	50.9	101.8
I05437	2	3.7	0.1897	51.3	102.5
I05439	1	3.1	0.1573	50.7	101.5
I05440	1	3.1	0.1556	50.2	100.4
I05441	2	3.0	0.1522	50.7	101.5
I05442	1	3.0	0.1508	50.3	100.5
I05444	1	3.0	0.1566	52.2	104.4
I05446	2	4.2	0.2108	50.2	100.4
I05447	1	3.2	0.1616	50.5	101.0
I05449	1	3.3	0.1653	50.1	100.2

Table 3. 1% Dextrose in Lactated Ringers Solution and Bile Salt Replacement Solution Infusion Times

	Animal Identification							
	I05436		I05437		I05441		I05446	
	Time							
Day [a]	AM	PM	AM	PM	AM	PM	AM	PM
Post Surgery	Start	Finish	Start	Finish	Start	Finish	Start	Finish
1	7:07	14:55	5:59	13:58	6:00	14:01	6:26	15:03
2	5:58	13:59	6:26	14:32	6:26	14:32	6:15	14:15
3	6:26	14:31	6:15	14:00	6:15	14:17	6:22	14:01
4	6:15	14:18	6:22	14:01	6:22	14:01	7:35	15:42
5	6:22	14:01	7:35	15:42	7:35	15:42	6:38	14:36
6	7:35	15:42	6:38	14:36	6:38	14:36	6:37	14:40
7	6:38	14:40	6:37	14:40	6:37	14:40	6:23	14:24
8	6:37	14:40	6:23	14:24	6:23	14:24	7:00	14:57
9	6:23	14:28	7:00	14:57	7:00	14:57	6:24	14:12
10	7:00	15:03	6:24	14:12	6:24	14:12	6:23	14:15
11	6:24	14:12	6:23	14:15	6:23	14:15	6:42	14:44
12	6:23	14:15	6:42	14:47	6:42	14:49	6:55	15:38
13	6:42	14:44	6:55	15:38	6:55	15:38	5:21	13:23
14	6:55	15:38	5:21	13:21	5:21	13:23	6:51	14:58
15	5:21	13:22	6:51	14:58	6:51	14:58	6:16	14:25
16	6:51	14:58	6:16	14:24	6:16	14:25	5:46	13:56
17	6:16	14:24	5:46	13:56	5:46	13:56	6:48	14:51
18	5:46	13:56	6:48	14:51	6:48	14:51	6:39	14:41
19	6:48	14:51	6:39	14:41	6:39	14:40	6:38	14:46
20	6:39	14:41	6:38	14:46	6:38	14:46	6:36	14:36
21	6:38	14:46	6:36	14:38	6:36	14:37	6:53	15:01
22	6:36	14:36	6:53	15:01	6:53	15:01	6:17	14:14
23	6:53	15:01	6:17	14:18	6:17	14:20	5:50	13:47
24	6:17	14:18	5:50	13:47	5:50	13:47	5:43	13:48
25	5:50	13:47	5:43	13:48	5:43	13:48	5:46	13:44
26	5:43	13:48	5:46	13:47	5:46	13:47	6:49	14:53
27	5:46	13:48	6:49	14:53	6:49	14:53	6:39	14:41
28	6:49	14:53	6:39	14:41	6:39	14:41	6:55	14:57
29	6:39	14:41	6:58	14:57	6:55	14:57	6:36	14:42
30	6:55	14:57	6:36	14:35	6:36	14:35	6:39	14:31
31	6:36	14:35	6:39	14:31	6:39	14:31	7:02	14:59
32	6:39	14:31	7:02	15:00	7:02	14:59	6:45	14:46
33	7:02	15:00	6:45	14:46	6:45	14:46	6:41	14:39
34	6:45	14:46	6:41	14:40	6:41	14:39	6:41	14:44
35	6:41	14:40	6:41	14:44	6:41	14:44	6:45	14:05
36	6:41	14:44	6:45	14:05	6:45	14:05	7:01	14:58
37	6:45	14:05	7:01	14:58	7:01	14:58	NA [b]	NA
38	7:01	14:58	5:41	13:40	5:41	13:40	NA	NA
39	5:41	13:40	6:36	14:47	6:36	14:47	NA	NA
40	6:36	14:47	6:38	14:48	6:38	14:45	NA	NA
41	6:38	14:45	6:51	14:35	6:51	14:35	NA	NA
42	6:51	14:35						

a On Days 1 through 3, the animals were infused with 1% dextrose in Lactated Ringer's solution at approximately 20 mL/kg/hour for approximately 8 hours, and on the remaining days the animals were infused with bile salts at approximately 23 mL/kg/hour for approximately 8 hours.

b Not applicable. Since no bile was recovered, no bile salts were infused.

APPENDIX A

Protocol CMS 22672A1, Protocol Amendment No. 1, and Protocol Deviations

PROTOCOL

Sponsor

3M Chemicals
St. Paul, Minnesota

Protocol CMS 22672A1

Study Title

Metabolism of N-Ethyl Perfluorooctane Sulfonamido Ethanol (Net-Fose; T-6316) in Cynomolgus Monkeys Following Administration of a Single Capsule Dose

Testing Guideline

Environmental Protection Agency, Good Laboratory Practice Standards, 40 CFR 160

Date

April 21, 1998

Performing Laboratory

Covance Laboratories Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Laboratory Project Identification

Covance 6329-226

STUDY IDENTIFICATION

Metabolism of N-Ethyl Perfluorooctane Sulfonamido Ethanol (Net-Fose; T-6316) in Cynomolgus Monkeys Following Administration of a Single Capsule Dose

Test Substance	N-Ethyl Perfluorooctane Sulfonamido Ethanol (Net-Fose; T-6316)
Sponsor	3M Chemicals 3M Center Building 220-2E-02 St. Paul, MN 55144-1000
Study Director	Andrew Seacat, PhD 3M Chemicals 3M Center Building 220-2E-02 St. Paul, MN 55144-1000 Phone: (612) 575-3161 Fax: (612) 733-1773
Principal Analytical Investigator	Kris Hansen Environmental Technology and Safety Services 935 Bush Avenue Building 2-E3-09 St. Paul, Minnesota 55133-3331 Phone: (612) 778-6018 Fax: (612) 788-6176
Biological Phase Investigator	Frederic W. Thalacker, PhD Covance Laboratories Inc. P.O. Box 7545 Madison, Wisconsin 53707 Phone: (608) 242-2712 ext. 7370 Fax: (608) 241-7412
Biological Phase Location	Covance Laboratories Inc. 3301 Kinsman Boulevard Madison, Wisconsin 53704
Proposed Study Timetable	
In-Life Experimental Start Date	May 13, 1998
In-Life End Date	August 11, 1998

OBJECTIVE

The purpose of this study is administer a Perfluorooctane test substance to male and female cynomolgus monkeys and collect samples for determination of absorption, distribution, metabolism, and excretion.

REGULATORY COMPLIANCE

Environmental Protection Agency, Good Laboratory Practice Standards, 40 CFR 160

All procedures in this protocol are in compliance with the Animal Welfare Act Regulations, 9 CFR 3, dated October 30, 1989, and as modified on March 18, 1991. In the opinion of the Sponsor and the study director, the study does not unnecessarily duplicate any previous work.

The protocol, study conduct, data, and biological phase final report will be audited by the Covance Laboratories Inc. Quality Assurance Unit in accordance with Covance Standard Operating Procedures. All study activities performed at 3M will be the responsibility of the 3M Quality Assurance Department.

TEST SUBSTANCE

Source

The test substance will be provided by the Sponsor. The Sponsor will be responsible for analysis of the test substance.

Storage Conditions

The test substance will be stored at approximately -20°C until dosing. Any test substance remaining will be stored at approximately -20°C.

Disposition

Unused test substance will be returned to the Sponsor or a recipient designated by the Sponsor, or discarded at the Sponsor's request. The Sponsor will assume responsibility for retention of a sample of the test material as specified in 40 CFR 160.195 if the study is longer than 4 weeks in duration.

Safety Precautions

Safety precautions will be taken as required by Covance Policies and Procedures, in consideration of the Sponsor's Material Safety Data Sheet, or other relevant safety information provided by the Sponsor.

EXPERIMENTAL DESIGN

Animals

Species/Strain.	Nonhuman primate/cynomolgus
Source.	Covance Research Products (Alice, Texas, or Denver, Pennsylvania). The source of the animals will be documented in the raw data.
Weight at Arrival.	3 kg or greater
Age at Arrival.	Young adult/adult
Number and Sex.	Eight males and eight females on test, six male and six female intact and two male and two female bile duct cannulated. One male and one female extra intact and two male and two female extra cannulated will be available as possible replacement animals.
Identification.	Individually numbered collar tags

Housing

For the acclimation period, the animals will be in individual, stainless steel cages. For the test period, the animals will be in individual metabolism cages designed for the separation and collection of bile, urine, and feces.

Food

Certified Primate Diet #8726C (Harlan Teklad) *ad libitum*, except when fasted for surgery. Food will also be withdrawn overnight prior to, and returned approximately 4 hours after dose administration. Diets will be supplemented with appropriate fruits and cereals.

Water

Ad libitum, provided fresh daily

Contaminants

There are no known contaminants in the food or water that would interfere with this study.

Environment

Environmental controls for the animal room will be set to maintain 18° to 29°C, 50% ± 20% relative humidity, and a 12-hour light/12-hour dark cycle. The 12-hour dark cycle may be interrupted to accommodate study procedures.

Quarantine and Acclimation

Animals will be under quarantine for at least 30 days. At least one quality control physical, one fecal examination, and three tuberculin tests will be done before release from quarantine. Weekly body weights will be taken. Animals will be acclimated to the jacket/tether system required for bile duct cannulation.

Animal Selection

Clinical chemistry and hematology test results and physical examination results will be used to select test animals. Animals will be selected for the surgical procedure based on the best apparent adjustment to the jacket and tether system. In the case that all or most animals adjust well, animals will be selected in numerical order based on the individual collar tag numbers previously assigned. Before dose administration, a laboratory animal veterinarian will evaluate the health of the animals and approve their use on the study.

Justification

Studies using live animals are essential for characterizing the disposition of chemicals in animals. No acceptable non-live animal models are available. The cynomolgus monkey has been used as the non-rodent species to evaluate toxicity. This study will aid in the evaluation of test results obtained in toxicology studies conducted in monkeys and will also provide a basis for the extrapolation of safety data from animals to humans. The number of animals is the minimum number necessary to provide scientifically valid results.

Surgical Procedure

The surgical procedure will be conducted in accordance with Covance Standard Operating Procedures. The animals will be fasted overnight before surgery and sedated with ketamine. An appropriate antibiotic will be administered. Surgical anesthesia will be maintained using oxygen and isoflurane. Lactated Ringer's solution will be administered through a saphenous catheter throughout the surgical procedure or as

determined by a staff veterinarian. A sterile surgical scrub will be performed. The common bile duct and duodenum will be cannulated and the gallbladder removed and discarded. Analgesics will be administered as recommended by the staff veterinarian. Additional antibiotics and/or fluids may be administered as recommended by the staff veterinarian. The animals will have at least 10 days to recover from the surgical procedure prior to dose administration.

Bile Replacement

Beginning the day after surgery through 3 days post surgery, a solution of 1% dextrose in Lactated Ringer's solution will be administered via the duodenal cannula for approximately 8 hours per day (approximately 20 mL/hour) to prevent dehydration. Beginning on the fourth post surgical day until sacrifice, an appropriate amount of mixed bile salts solution will be infused via the duodenal cannula for approximately 8 hours per day. The volume of bile salts solution to be administered will be approximately 23 mL/kg/day. Bile salts solution will be prepared by adding 18.0 g of cholic acid to 1 L of 0.9% sodium chloride solution. Sodium bicarbonate (1.3 g) will be added to each 1 L of solution. The solution will be mixed and the pH adjusted to 7.4 to 7.8 with 0.1N HCl or sodium hydroxide, as appropriate. Infusion intervals and volumes administered will be recorded.

Group Designations and Dose Level

Group	Number and Sex	Status	Dose Frequency, Route, and Level	Collections Postdose
1	6 Male 6 Female	Intact	One Capsule 50 mg/kg	Tissues from 2/sex on Days 2, 28, and 90. Urine and feces from 0-12 and 12-24 hours, then daily through 28 days, and weekly through 90 days. Blood predose, and at 1, 2, 4, 6, 12, 24, 36, and 48 hours, 7 days, and weekly through 90 days.
2	2 Male 2 Female	Bile Duct Cannulated	One Capsule 50 mg/kg	Tissues at 28 days. Bile from 0-12 and 12-24 hours, and daily through 28 days. Blood predose, and at 1, 2, 4, 6, 12, 24, 36 and 48 hours,7 days, and weekly through 28 days.

Justification for Dosing Route/Dose Level. The oral route has been used for evaluating systemic toxicity of the compound in cynomolgus monkeys. The 50 mg/kg dose was chosen because it provides the maximum non-toxic single dose amount necessary to recover measurable concentrations in minor tissues.

Dosing Procedure

Predose and Postdose Feeding. Animals will be fasted overnight prior to dose administration through approximately 4 hours postdose.

Dose Administration. The capsule will be administered by a device specific for capsule administration.

Observation of Animals

Antemortem Observations. Mortality and moribundity checks will be done twice daily (a.m. and p.m.). Cageside observation for general health and appearance will be done once daily. Signs of poor health or abnormal behavior will be recorded as they are observed.

Physical Examinations. Twice during acclimation, once pre-surgery, and once post surgery before the initiation of treatment. Animals will be anesthetized with ketamine hydrochloride according to Covance Standard Operating Procedures for the examination.

Jackets will be checked according to Covance Standard Operating Procedures and will be replaced as necessary. The animals will be anesthetized as above for the examination; however, a lower dose of ketamine may be administered for the limited examination.

Body Weights. Weekly during acclimation, on the day of dosing, weekly thereafter, and on the day of sacrifice. Additional body weights may be taken at the discretion of the Biological Phase Investigator or a staff veterinarian.

Clinical Pathology. The animals will not be fasted. Blood will be collected via the femoral vein before dose administration as follows: approximately 1 week before surgery from all animals and approximately 4 and 8 days post surgery from cannulated animals. If health problems develop, blood will be collected for clinical pathology tests to assess health status as deemed necessary by the staff veterinarian. Any blood samples taken after modification of the ports for collection of bile will be collected before the administration of the bile salts replacement solution for the day.

Tests

Clinical Chemistry	Hematology
Glucose	Red blood cell count
Urea nitrogen	Hemoglobin
Creatinine	Hematocrit
Total protein	Mean corpuscular volume
Albumin	Mean corpuscular hemoglobin
Globulin	Mean corpuscular hemoglobin concentration
Total bilirubin	Platelet count
Serum bile acids	White blood cell count
Cholesterol	Differential blood cell count
Aspartate aminotransferase	Blood cell morphology
Alanine aminotransferase	Prothrombin time
Alkaline phosphatase	Activated partial thromboplastin time
Creatine kinase	
Gamma glutamyltransferase	
Calcium	
Inorganic phosphorous	
Sodium	
Potassium	
Chloride	

Antemortem Sample Collection

NO TEFLON IS TO BE USED FOR THIS STUDY.

Blood (Groups 1 and 2). Approximately 2 mL of blood will be collected from Group 1 animals predose and approximately 2 mL will be collected at 1, 2, 4, 6, 12, 24, 36, and 48 hours, 7 days, and weekly through 90 days postdose. Approximately 2 mL of blood will be collected from Group 2 animals predose and approximately 2 mL will be collected at 1, 2, 4, 6, 12, 24, 36, and 48 hours, and on 7, 14, 21, and 28 days postdose. The blood will be collected via a femoral vein into heparinized tubes and placed immediately on wet ice. The animals may be re-hydrated with lactated Ringer's solution given subcutaneously or via the duodenal cannula at the discretion of the Biological Phase Investigator or Laboratory Animal Veterinarian following blood collections, if the total blood volumes collected exceed the recommendations in Covance Standard Operating Procedures.

Bile (Group 2). Bile will be collected from the Group 2 animals via the implanted cannula into plastic containers surrounded by dry ice predose (for at least 12 hours), and at 0-12, 12-24, and continuing at 24-hour intervals through 28 days postdose.

Urine (Group 1). Urine will be collected in plastic containers surrounded by dry ice at 0-12, 12-24, and continuing at 24-hour intervals through 28 days, then weekly until 90 days postdose.

Feces (Group 1). Feces will be collected at 0-12, 12-24, and continuing at 24 hour intervals through 28 days, then weekly until 90 days postdose. Samples will be transferred into plastic containers at the time of collection.

Termination

Unscheduled Sacrifices and Deaths. The carcasses will be retained and may undergo postmortem examination for any gross changes. Further examination may be performed upon Sponsor's request.

Scheduled Sacrifice. At the time of sacrifice, animals will be anesthetized with sodium pentobarbital. Cerebrospinal fluid (CSF) will be collected once the animal is fully anesthetized. CSF will be placed on wet ice immediately after collection and collection times will be recorded. Blood (at least 20 mL) will be collected via cardiac puncture into heparinized tubes. Following blood collection, the animals will be sacrificed via exsanguination under sodium pentobarbital.

Residual urine from the bladder will be added to the last urine sample. Stomach, large and small intestinal contents will be collected from the two per sex Group 1 animals that are sacrificed at Day 2 only.

All tissues collected will be excised, rinsed with water, blotted dry, weighed, and placed in a plastic container surrounded by ice. The following tissues will be collected from all animals at sacrifice, except the gallbladder will be collected from Group 1 only:

Adrenal glands (~0.5 g)	Muscle (thigh)
Aorta (~0.5 g)	Ovaries (~0.5 g)
Bone (femur)	Pancreas
Bone Marrow (from femur)	Prostate
Brain	Salivary Glands
Diaphragm	Seminal vesicles
Epididymis	Skin (dorsal, shaved)
Esophagus	Small Intestine
Eyes	Spinal Cord
Fat	Spleen
Gallbladder (~0.5 g)	Stomach
Heart	Testes
Kidneys	Thymus
Large Intestine	Thyroid/Parathyroid (~0.75 g)
Liver	Tongue
Lungs	Trachea
Lymph nodes (cervical)	Urinary Bladder
Lymph nodes (mesenteric)	Uterus

Sample Identification, Retention and Disposition

Specimens will be identified with the study number, sex, animal number, group, matrix, specimen number, and collection interval.

Sample Preparation and Storage

All specimens will be stored at approximately -20°C until shipment.

Blood samples will be stored at approximately 5°C until centrifugation. A subsample, approximately 1 mL at the individual time points and approximately half of the sacrifice blood, will be removed and placed in a separate labeled vial. The remaining blood will be centrifuged to separate plasma. The blood, cellular fraction of the blood (RBC), and plasma will be frozen immediately and stored at approximately -20°C.

Sample Transfer

All specimens will be shipped on dry ice to the Sponsor. The specimens will be shipped to the following person and address:

Dr. Kris Hansen
Environmental Technology and Safety Services
935 Bush Avenue
Building 2-E3-09
St Paul, Minnesota 55133-3331
Phone: (612) 778-6018
Fax: (612) 788-6176

The Sponsor will be responsible for further analysis, reporting, and archiving upon completion of the study.

REPORT

A biological phase draft report including, but not limited to, those items listed below will be submitted to the Sponsor for review and comment. Then, a biological phase final report will be provided.

Experimental Design and Methods

As defined by the protocol, protocol amendments, and any protocol deviations.

Data and Results

Animal receipt and acclimation
Antemortem observations
Body weights
Physical examinations
Clinical pathology
Dose administration
Sample collection
Bile salts replacement solution infusion times and amounts

Maintenance of Raw Data, Records, and Specimens

The following data records to be maintained and transferred to the archives of Covance will include, but will not be limited to:

Protocol and amendments
Study correspondence
Test material receipt
Final report

The following supporting records to be retained at Covance but not archived with the study data will include, but will not be limited to:

Feed analysis records
Water analysis records
Animal room temperature and humidity records
Refrigerator/freezer temperature records
Instrument calibration and maintenance records
United States Department of Agriculture animal records
Stock records

The following data records to be transferred to the archives of 3M will include, but will not be limited to:

In-life records:
Animal receipt
Acclimation
Animal room maintenance
Antemortem observations
Body weights
Physical examination records
Clinical pathology
Clinical pathology slides
Dose administration
Sample collection
Bile salts replacement solution infusion times and amounts

All correspondence, documentation, records, protocol, and final report generated as a result of this study will be archived in the storage facilities of Covance for a period of one year following the signing of the final report. One year after signing the final report, all of the aforementioned materials will be sent to the Sponsor and a return fee will be charged. The Sponsor may elect to have the materials retained in the Covance Archives for an additional period of time and Covance will charge a storage fee. If the Sponsor chooses to have Covance dispose of the materials, a disposal fee will be charged.

PROTOCOL APPROVAL

Andrew Seacat, PhD
Study Director
3M Chemicals

4/23/98
Date

Frederic W. Thalacker, PhD
Biological Phase Investigator
Metabolic Chemistry
Covance Laboratories Inc.

April 21, 1998
Date

Philip J. Teitelbaum, PhD
Associate Director
Metabolic Chemistry
Covance Laboratories Inc.

April 21, 1998
Date

PROTOCOL AMENDMENT NO. 1

Covance 6329-226

Metabolism of N-Ethyl Perfluorooctane Sulfonamido Ethanol (Net-Fose; T-6316) in Cynomolgus Monkeys Following Administration of a Single Capsule Dose

Sponsor

3M Chemicals
3M Center
Building 220-2E-02
St. Paul, MN 55144-1000

Contractor

Covance Laboratories Inc.
3301 Kinsman Boulevard
Madison, Wisconsin 53704

Study Director

Andrew Seacat, PhD
3M Center
Building 220-2E-02
St. Paul, MN 55144-1000

Biological Phase Investigator

Fred Thalacker, PhD
Covance Laboratories Inc.
P.O. Box 7545
Madison, Wisconsin 53707

This amendment modifies the following portions of the protocol:

Effective May 11, 1998

1. Page 7, **EXPERIMENTAL DESIGN, Observation of Animals, Body Weights.** To accurately reflect when the body weights will be taken, replace the first sentence with the following:

   Weekly during acclimation, on the day of randomization (to be used for dosing calculations), weekly after dosing, and on the day of sacrifice.

2. Page 9, **EXPERIMENTAL DESIGN, Termination, Scheduled Sacrifice.** To clarify the disposition of the animal carcass, please add a sentence following the first sentence of the third paragraph:

   After the tissues have been removed, the residual carcass will be discarded.

3. Page 10, **EXPERIMENTAL DESIGN, Sample Preparation and Storage** Since a subsample of less than 1 mL of whole blood may need to be removed, please replace the second sentence of paragraph two with the following:

   A subsample at the individual time points and approximately half of the sacrifice blood will be removed and placed in a separately labeled vial.

Effective May 13, 1998

4. Page 3, **TEST SUBSTANCE, Storage Conditions** Upon actual receipt of the test substance, it was noted that the storage was to be room temperature. Therefore, replace the first and second sentence with the following:

   The test substance and any remaining test substance will be stored at room temperature.

Effective June 2, 1998

To indicate that an additional 2 mL blood sample will be removed for serum collection for the remaining time points, the following changes to the protocol are necessary.

5. Page 8, **EXPERIMENTAL DESIGN, Antemortem Sample Collection, Blood (Groups 1 and 2).** Add the following sentence after the third line:

   Effective June 3, 1998 (Study Day 21) and at the remaining time points, an additional 2 mL blood sample will be collected into a glass tube without heparin and set aside at room temperature to allow clotting.

6. Page 10, **EXPERIMENTAL DESIGN, Sample Preparation and Storage** Add a new third paragraph as follows:

   Remove the serum and place it into a separately labeled vial. Discard the cellular debris and store the serum at approximately -20°C for shipment.

To indicate that additional blood will be removed for serum collection at sacrifice, the following changes to the protocol are necessary.

7. Page 9, **EXPERIMENTAL DESIGN, Antemortem Sample Collection, Scheduled Sacrifice.** Replace the fourth line with the following:

   Blood will be collected via cardiac puncture into glass tubes with heparin (at least 20 mL) and into glass tubes without heparin (at least 20 mL).

PROTOCOL AMENDMENT APPROVAL

Andrew Seacat, PhD
Study Director
3M Chemicals

10/25/98
Date

Fred Thalacker, PhD
Biological Phase Investigator
Metabolic Chemistry
Covance Laboratories Inc.

5/17/99
Date

Philip J. Teitelbaum, PhD
Associate Director
Metabolic Chemistry
Covance Laboratories Inc.

5/17/99
Date

PROTOCOL DEVIATIONS

Protocol	Actual
Environmental controls for the animal room will be set to maintain a relative humidity of 50% ±20%	April 25, 1998, ranged from 80.1% to 86.2% between 2:27 and 8:00 May 28, 1998, ranged from 73.4% to 73.9% between 19:08 and 20:30 June 11, 1998, ranged from 71.5% to73.6% between 7:30 and 10:00 and ranged from 75.3% to 82.6% between 17:19 and 21:00 June 20, 1998, ranged from 70.2% to 72.8% between 13:19 and 15:00 June 27, 1998, ranged from 71.3% to 78.1% between 6:38 and 9:00
At sacrifice, blood will be collected via cardiac puncture into glass tubes with heparin (at least 20 mL) and into glass tubes without heparin (at least 20 mL).	A short sample was collected via the vena cava for serum and plasma.
Body Weights. Weekly during acclimation, on the day of randomization (to be used for dosing calculations), weekly after dosing, and on the day of sacrifice.	The body weights were not taken on the day of randomization, because no randomization was needed. The animals were selected by test results and adjustment to the jacket and tether system. The weights were taken within 5 days of dosing to be used for dosing calculations.

These deviations would not be expected to have had an effect on the outcome of the study.

APPENDIX B

Summary of Antemortem Observations,
Clinical Pathology Codes and Abbreviations, and
Clinical Pathology Data Tables

Table B1. Summary of Antemortem Observations

Animal ID	Sacrifice Day and Sex	Observation Noted	Study Day
		Group 1 (Intact)	
I05428	2 Day, Male	Urine appears to contain water	1
I05430	2 Day, Male	No observations noted	
I05431	28 Day, Male	Urine discolored, brown	21
I05432	28 Day, Male	Urine appears to contain water	10
		Few feces	2
I05433	91 Day, Male	No observations noted	
I05435	91 Day, Male	Urine appears to contain water	19
		Urine appears to contain water	64
		Urine discolored, red	66
		Low food consumption	72
		Low food consumption	73
		Low food consumption	74
		Low food consumption	75
		Low food consumption	76
		Low food consumption	77
I05439	2 Day, Female	No observations noted	
I05440	2 Day, Female	Few feces	2
I05442	28 Day, Female	Urine appears to contain water	17
		Urine appears to contain water	19
		Second container used for urine	17
		Low food consumption	11
		Low food consumption	12
I05444	28 Day, Female	Urine appears to contain water	19
		Urine appears discolored, red	9
		Urine appears discolored, red	10
		Few feces	2
		Low food consumption	11
		Low food consumption	12

Table B1. Continued

Animal ID	Sacrifice Day and Sex	Observation Noted	Study Day
I05447	91 Day, Female	Urine contained feces	22
		Urine appears to contain water	10
		Urine appears to contain water	12
		Urine appears to contain water	13
		Urine appears to contain water	15
		Urine appears to contain water	16
		Urine appears to contain water	17
		Urine appears to contain water	18
		Urine appears to contain water	19
		Urine appears to contain water	23
		Urine appears to contain water	43
		Urine appears to contain water	64
		Urine appears to contain water	78
		Second container used for urine	15
		Second container used for urine	16
		Second container used for urine	17
		Second container used for urine	64
		Second container used for urine	78
		Urine appears discolored, red	10
		Discharge, appeared to be menstruating	10
		No feces	2
		Few feces	50
		Low food consumption	73
I05449	91 Day, Female	Urine appears to contain water	10
		Urine appears to contain water	43
		Urine appears to contain water	50
		Urine appears to contain water	57
		Urine appears to contain water	64
		Urine appears to contain water	71
		Urine appears to contain water	78
		Second container used for urine	57
		Second container used for urine	64
		Second container used for urine	78
		Few feces	2

Table B1. Continued

Animal ID	Sacrifice Day and Sex	Observation Noted	Study Day
		Group 2 (Bile Duct Cannulated)	
I05436	Bile collected	Discharge, vomitus containing food	8
	28 Day	Low food consumption	6
	Male		
I05437	Bile collected	Small amount of bile	10
	2 Day	Liquid feces	12
	Male	Liquid feces	13
		Non-formed feces	6
		Non-formed feces	7
		Non-formed feces	23
		Low food consumption	10
		Low food consumption	11
		Low food consumption	12
		No feces	10
I05441	Bile collected	Small amount of bile	10
	28 Day	Non-formed feces	6
	Female	Non-formed feces	22
		Non-formed feces	23
		Low food consumption	10
		Low food consumption	11
		No feces	10
I05446	Bile collected	Small amount of bile	17
	2 Day	Small amount of bile	23
	Female	Small amount of bile	24
		No bile present	25
		No bile present	26
		No bile present	27
		No bile present	28
		No bile present	29
		Non-formed feces	1
		Non-formed feces	2
		Non-formed feces	5
		Non-formed feces	7

Codes for Clinical Pathology

GENERAL CODES

NS	No sample
QS/QNS	Quantity not sufficient
NR	No repeat (sample volume not sufficient for repeat analysis)
FS	Fibrin strands
SC	Sample clotted
SH	Slightly hemolyzed
H	Hemolyzed
SL	Slightly lipemic
L	Lipemic
SI	Slightly icteric
I	Icteric
U	Unscheduled/moribund bleed
RE	Recording error (recorded incorrect data, e.g., wrong number, spelling error, incorrect date)
EE	Entry error (incorrect keyboard entry)
SE	Sampling error
PC	Platelets clumped
PD	Platelets decreased
PI	Platelets increased
PL	Platelets large
PA	Platelets appear adequate
CO	Color interferes with test
HB	Heinz bodies observed
PLASMO	Plasmodium
NO AGG	No aggregation
FR	Fractious

CODES FOR BLOOD CELL MORPHOLOGY

The following scale was used to measure the degree of anisocytosis (ANISO), poikilocytosis (POIK), polychromasia (POLY), hypochromasia (HYPO), or basophilic stippling (BASTIP) or the presence of Howell-Jolly bodies (HJBODY), toxic neutrophils (TOXNEUT), or atypical lymphocytes (ATYPLYM):

Scale	Degree	Presence
-	Normal for the species	Not present
1	Slight	Rare
2	Moderate	Few
3	Marked	Moderate
4	Not applicable	Many

Abbreviations and Units for Clinical Hematology

Test	Abbreviation (Units)
Red blood cell count	RBC (E6/UL or X$10^6/\mu$L)
Hemoglobin	HGB (G/DL)
Hematocrit	HCT (%)
Mean corpuscular volume	MCV (FL)
Mean corpuscular hemoglobin	MCH (PG)
Mean corpuscular hemoglobin concentration	MCHC (%)
Platelet count	PLT (E3/UL or X$10^3/\mu$L))
Prothrombin time	PT (SEC)
Activated partial thromboplastin time	PTT (SEC)
White blood cell count	WBC (E3/UL or X$10^3/\mu$L)
Differential blood cell count	
Nucleated red blood cell count	NRBC (/100 WBC)
Segmented neutrophil count	N-SEG (E3/UL or X$10^3/\mu$L) and %
Band neutrophil count	N-BAND (E3/UL or X$10^3/\mu$L) and %
Lymphocyte count	LYMPH (E3/UL or X$10^3/\mu$L) and %
Monocyte count	MONO (E3/UL or X$10^3/\mu$L) and %
Eosinophil count	EOSIN (E3/UL or X$10^3/\mu$L) and %
Basophil count	BASO (E3/UL or X$10^3/\mu$L) and %
Anisocytosis	ANISO (-,1,2,3)
Polychromasia	POLY (-,1,2,3)
Poikilocytosis	POIK (-,1,2,3)
Hypochromasia	HYPO (-,1,2,3)
Toxic neutrophils	TOXNEUT (-,1,2,3,4)

Abbreviations and Units for Clinical Chemistry

Test	Abbreviation (Units)
Glucose	GLU (MG/DL)
Urea nitrogen	UN (MG/DL)
Creatinine	CREAT (MG/DL)
Total protein	T PRO (G/DL)
Albumin	ALB (G/DL)
Globulin	GLOB (G/DL)
Total bilirubin	T BILI (MG/DL)
Cholesterol	CHOL (MG/DL)
Triglycerides	TRIG (MG/DL)
Aspartate aminotransferase	AST/SGOT (IU/L)
Alanine aminotransferase	ALT/SGPT (IU/L)
Alkaline phosphatase	ALK PHOS (IU/L)
Gamma glutamyltransferase	GGT (IU/L)
Creatine kinase	CK (IU/L)
Calcium	CA (MG/DL)
Inorganic phosphorus	I PHOS (MG/DL)
Sodium	NA (MMOL/L)
Potassium	K (MMOL/L)
Chloride	CL (MMOL/L)
Serum bile acids	SBA (UMOL/L or MG/DL)

Summary and Individual Clinical Chemistry Data

Males Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	GLU MG/DL	UN MG/DL	CREAT MG/DL	T PRO G/DL	ALB G/DL	GLOB G/DL	T BILI MG/DL	CHOL MG/DL	SBA umol/L
Group: 1	Dose Level: 50		Dosage Unit: mg/kg						
I05428	134	16	1.1	8.8	4.6	4.2	.2	85	13
I05430	77	17	1.0	8.0	4.4	3.6	.2	95	10
I05431	80	20	1.0	8.4	4.6	3.8	.2	150	8
I05432	124	20	1.1	9.1	4.8	4.3	.3	128	7
I05433	99	17	1.0	8.6	4.6	4.0	.4	94	10
I05435	118	13	1.1	8.8	4.7	4.1	.3	137	12
MEAN	105	17	1.0	8.6	4.6	4.0	.3	115	10
S.D.	23.7	2.6	.05	.38	.13	.26	.08	26.9	2.3
N	6	6	6	6	6	6	6	6	6
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05436	100	17	1.3	8.4	4.8	3.6	.3	138	14
I05437	106	17	1.0	8.4	4.6	3.8	.1	146	11
MEAN	103	17	1.2	8.4	4.7	3.7	.2	142	12
S.D.	4.2	.0	.21	.00	.14	.14	.14	5.7	2.1
N	2	2	2	2	2	2	2	2	2
Extra									
I05429	124	19	1.3	8.4	4.8	3.6	.2	172	11
I05434	105	16	1.2	9.3	4.7	4.6	.2	133	17
I05438	103	18	1.3	7.8	4.7	3.1	.4	113	8
MEAN	111	18	1.3	8.5	4.7	3.8	.3	139	12
S.D.	11.6	1.5	.06	.75	.06	.76	.12	30.0	4.6
N	3	3	3	3	3	3	3	3	3

Summary and Individual Clinical Chemistry Data

Males Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	AST/SGOT IU/L	ALT/SGPT IU/L	ALK PHOS IU/L	GGT IU/L	CK IU/L	CA MG/DL	I PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
Group: 1	Dose Level: 50		Dosage Unit: mg/kg							
I05428	32	58	413	76	361	9.9	6.2	155	4.3	101
I05430	62	28	421	94	571	9.5	3.6	147	4.6	100
I05431	56	33	547	111	761	9.0	6.2	146	4.9	97
I05432	56	116	604	189	316	10.2	7.9	155	5.7	107
I05433	39	78	452	43	125	9.4	5.8	154	4.2	106
I05435	35	24	566	157	367	10.6	6.5	152	4.8	99
MEAN	47	56	500	112	417	9.8	6.0	152	4.8	102
S.D.	12.8	35.8	81.8	53.5	220.5	.58	1.40	4.0	.54	4.0
N	6	6	6	6	6	6	6	6	6	6
Group: 2	Dose Level: 50		Dosage Unit: mg/kg							
I05436	39	38	370	53	340	10.9	6.8	160	5.1	105
I05437	35	25	295	82	348	10.2	4.4	152	4.3	99
MEAN	37	32	332	68	344	10.6	5.6	156	4.7	102
S.D.	2.8	9.2	53.0	20.5	5.7	.49	1.70	5.7	.57	4.2
N	2	2	2	2	2	2	2	2	2	2
Extra										
I05429	50	34	607	138	1055	9.6	6.4	151	5.2	103
I05434	48	120	297	122	1019	11.1	5.9	159	4.8	103
I05438	34	28	416	111	255	10.4	5.5	156	5.2	109
MEAN	44	61	440	124	776	10.4	5.9	155	5.1	105
S.D.	8.7	51.5	156.4	13.6	451.8	.75	.45	4.0	.23	3.5
N	3	3	3	3	3	3	3	3	3	3

Summary and Individual Clinical Chemistry Data

Females Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	GLU MG/DL	UN MG/DL	CREAT MG/DL	T PRO G/DL	ALB G/DL	GLOB G/DL	T BILI MG/DL	CHOL MG/DL	SBA umol/L
Group: 1	Dose Level: 50		Dosage Unit: mg/kg						
I05439	112	17	1.1	8.4	4.6	3.8	.2	122	26
I05440	116	18	1.2	9.7	4.7	5.0	.4	182	49
I05442	128	19	.9	8.5	4.4	4.1	.3	123	9
I05444	111	18	1.0	9.0	4.6	4.4	.3	148	9
I05447	78	22	1.0	8.8	3.6	5.2	.2	126	12
I05449	114	26	1.0	9.4	4.5	4.9	.3	141	13
MEAN	110	20	1.0	9.0	4.4	4.6	.3	140	20
S.D.	16.8	3.4	.10	.51	.40	.55	.08	23.0	15.7
N	6	6	6	6	6	6	6	6	6
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05441	98	16	1.2	9.3	4.7	4.6	.2	181	11
I05446	91	16	.8	8.3	4.1	4.2	.3	201	7
MEAN	94	16	1.0	8.8	4.4	4.4	.2	191	9
S.D.	4.9	.0	.28	.71	.42	.28	.07	14.1	2.8
N	2	2	2	2	2	2	2	2	2
Extra									
I05443	88	16	.9	7.7	4.0	3.7	.4	202	10
I05445	94	14	.9	9.2	4.3	4.9	.2	155	20
I05448	114	12	1.1	8.4	4.4	4.0	.6	136	5
MEAN	99	14	1.0	8.4	4.2	4.2	.4	164	12
S.D.	13.6	2.0	.12	.75	.21	.62	.20	34.0	7.6
N	3	3	3	3	3	3	3	3	3

Summary and Individual Clinical Chemistry Data

Females Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	AST/SGOT IU/L	ALT/SGPT IU/L	ALK PHOS IU/L	GGT IU/L	CK IU/L	CA MG/DL	I PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
Group: 1	Dose Level: 50		Dosage Unit: mg/kg							
I05439	57	134	363	98	218	10.2	6.3	155	4.8	105
I05440	95	199	233	90	160	10.7	6.2	157	4.2	104
I05442	27	25	215	44	104	9.2	4.7	153	5.1	105
I05444	38	94	192	87	256	10.1	6.0	156	4.3	105
I05447	55	233	284	52	202	9.1	4.3	149	4.0	107
I05449	42	216	407	69	239	10.0	4.6	158	4.3	107
MEAN	52	150	282	73	196	9.9	5.4	155	4.4	106
S.D.	23.7	80.8	86.2	21.9	56.1	.62	.91	3.3	.41	1.2
N	6	6	6	6	6	6	6	6	6	6
Group: 2	Dose Level: 50		Dosage Unit: mg/kg							
I05441	46	34	296	78	1061	10.5	6.2	161	5.0	107
I05446	34	37	184	92	134	9.4	3.9	151	5.1	108
MEAN	40	36	240	85	598	10.0	5.0	156	5.0	108
S.D.	8.5	2.1	79.2	9.9	655.5	.78	1.63	7.1	.07	.7
N	2	2	2	2	2	2	2	2	2	2
Extra										
I05443	31	82	160	76	147	9.1	3.1	153	3.7	106
I05445	28	95	308	64	205	11.1	4.5	159	4.5	109
I05448	44	118	195	108	652	9.5	4.2	152	4.5	106
MEAN	34	98	221	83	335	9.9	3.9	155	4.2	107
S.D.	8.5	18.2	77.3	22.7	276.3	1.06	.74	3.8	.46	1.7
N	3	3	3	3	3	3	3	3	3	3

Summary and Individual Clinical Chemistry Data

Males ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	GLU MG/DL	UN MG/DL	CREAT MG/DL	T PRO G/DL	ALB G/DL	GLOB G/DL	T BILI MG/DL	CHOL MG/DL	SBA umol/L
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05436	75	27	1.2	7.8	3.7	4.1	2.4	181	33
I05437	99	18	.9	8.1	4.2	3.9	.5	81	83
MEAN	87	22	1.0	8.0	4.0	4.0	1.4	131	58
S.D.	17.0	6.4	.21	.21	.35	.14	1.34	70.7	35.4
N	2	2	2	2	2	2	2	2	2
Extra									
I05434	84	15	1.1	8.3	3.9	4.4	2.1	148	245

Summary and Individual Clinical Chemistry Data

Males ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	AST/SGOT IU/L	ALT/SGPT IU/L	ALK PHOS IU/L	GGT IU/L	CK IU/L	CA MG/DL	I PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
Group: 2	Dose Level: 50		Dosage Unit: mg/kg							
I05436	175	316	1231	267	1652	9.6	5.5	153	4.9	109
I05437	194	131	453	228	2328	10.0	4.0	149	4.5	111
MEAN	184	224	842	248	1990	9.8	4.8	151	4.7	110
S.D.	13.4	130.8	550.1	27.6	478.0	.28	1.06	2.8	.28	1.4
N	2	2	2	2	2	2	2	2	2	2
Extra										
I05434	397	364	1278	237	3267	9.8	5.1	150	5.3	110

Summary and Individual Clinical Chemistry Data

Females ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	GLU MG/DL	UN MG/DL	CREAT MG/DL	T PRO G/DL	ALB G/DL	GLOB G/DL	T BILI MG/DL	CHOL MG/DL	SBA umol/L
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05441	91	15	1.1	6.9	3.5	3.4	.4	103	6
I05446	108	25	.9	8.5	3.8	4.7	.4	153	2
MEAN	100	20	1.0	7.7	3.6	4.0	.4	128	4
S.D.	12.0	7.1	.14	1.13	.21	.92	.00	35.4	2.8
N	2	2	2	2	2	2	2	2	2
Extra									
I05443	90	14	.8	7.3	3.6	3.7	.9	139	1

Summary and Individual Clinical Chemistry Data

Females ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	AST/SGOT IU/L	ALT/SGPT IU/L	ALK PHOS IU/L	GGT IU/L	CK IU/L	CA MG/DL	I PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
Group: 2	Dose Level: 50			Dosage Unit: mg/kg						
I05441	248	232	258	48	1802	9.6	3.9	156	4.6	112
I05446	123	123	246	67	2832	10.2	4.2	159	4.9	118
MEAN	186	178	252	58	2317	9.9	4.0	158	4.8	115
S.D.	88.4	77.1	8.5	13.4	728.3	.42	.21	2.1	.21	4.2
N	2	2	2	2	2	2	2	2	2	2
Extra										
I05443	153	150	145	63	2669	9.2	3.7	155	4.6	112

Summary and Individual Clinical Chemistry Data

Males ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	GLU MG/DL	UN MG/DL	CREAT MG/DL	T PRO G/DL	ALB G/DL	GLOB G/DL	T BILI MG/DL	CHOL MG/DL	SBA umol/L
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05436	85	24	1.2	7.8	3.9	3.9	.6	121	4
I05437	98	18	1.0	7.6	4.1	3.5	.3	76	5
MEAN	92	21	1.1	7.7	4.0	3.7	.4	98	4
S.D.	9.2	4.2	.14	.14	.14	.28	.21	31.8	.7
N	2	2	2	2	2	2	2	2	2
Extra									
I05434	110	14	1.1	8.5	3.9	4.6	3.8	240	932

Summary and Individual Clinical Chemistry Data

Males ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	AST/SGOT IU/L	ALT/SGPT IU/L	ALK PHOS IU/L	GGT IU/L	CK IU/L	CA MG/DL	I PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
Group: 2	Dose Level: 50		Dosage Unit: mg/kg							
I05436	36	141	1141	281	468	9.5	5.5	149	4.7	107
I05437	27	63	690	260	214	10.3	3.0	146	4.4	103
MEAN	32	102	916	270	341	9.9	4.2	148	4.6	105
S.D.	6.4	55.2	318.9	14.8	179.6	.57	1.77	2.1	.21	2.8
N	2	2	2	2	2	2	2	2	2	2
Extra										
I05434	345	444	4815	364	533	10.2	4.2	153	4.5	109

Summary and Individual Clinical Chemistry Data

Females ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	GLU MG/DL	UN MG/DL	CREAT MG/DL	T PRO G/DL	ALB G/DL	GLOB G/DL	T BILI MG/DL	CHOL MG/DL	SBA umol/L
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05441	114	10	1.2	7.4	3.8	3.6	.2	63	5
I05446	115	19	.8	8.2	3.8	4.4	.4	152	5
MEAN	114	14	1.0	7.8	3.8	4.0	.3	108	5
S.D.	.7	6.4	.28	.57	.00	.57	.14	62.9	.0
N	2	2	2	2	2	2	2	2	2
Extra									
I05443	74	6	.7	7.1	3.6	3.5	1.6	135	382

Summary and Individual Clinical Chemistry Data

Females ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	AST/SGOT IU/L	ALT/SGPT IU/L	ALK PHOS IU/L	GGT IU/L	CK IU/L	CA MG/DL	I PHOS MG/DL	NA MMOL/L	K MMOL/L	CL MMOL/L
Group: 2	Dose Level: 50		Dosage Unit: mg/kg							
I05441	38	101	377	52	88	10.7	3.5	156	5.8	106
I05446	35	58	229	66	1048	10.1	3.7	144	5.7	107
MEAN	36	80	303	59	568	10.4	3.6	150	5.8	106
S.D.	2.1	30.4	104.7	9.9	678.8	.42	.14	8.5	.07	.7
N	2	2	2	2	2	2	2	2	2	2
Extra										
I05443	396	374	841	262	617	9.1	3.0	148	4.1	109

Summary and Individual Clinical Hematology Data

Males Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	RBC $X10^6/\mu L$	HGB G/DL	HCT %	MCV FL	MCH PG	MCHC %	PLT $X10^3/\mu L$	PT SEC	PTT SEC
Group: 1	Dose Level: 50		Dosage Unit: mg/kg						
I05428	6.55	12.8	43.2	65.9	19.6	29.7	754	9.6	15.9
I05430	5.97	11.6	37.9	63.5	19.4	30.6	352	8.7	13.9
I05431	5.35	9.9	32.6	60.9	18.5	30.4	529	9.3	18.6
I05432	5.90	12.4	40.9	69.3	21.1	30.4	375	8.9	13.4
I05433	6.14	11.1	38.9	63.3	18.0	28.5	371	8.6	15.3
I05435	6.41	12.7	43.4	67.8	19.8	29.2	653	9.7	15.9
MEAN	6.05	11.8	39.5	65.1	19.4	29.8	506	9.1	15.5
S.D.	.426	1.12	4.03	3.13	1.08	.83	169.0	.47	1.84
N	6	6	6	6	6	6	6	6	6
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05436	6.80	12.9	44.9	66.0	19.0	28.8	547	9.3	12.9
I05437	6.21	11.5	38.5	62.1	18.5	29.8	383	9.3	14.3
MEAN	6.50	12.2	41.7	64.0	18.8	29.3	465	9.3	13.6
S.D.	.417	.99	4.53	2.76	.35	.71	116.0	.00	.99
N	2	2	2	2	2	2	2	2	2
Extra									
I05429	7.85	15.1	48.7	62.0	19.3	31.0	491	9.3	15.1
I05434	6.29	12.6	42.6	67.7	20.1	29.7	545	9.4	12.6
I05438	6.05	11.5	38.7	63.9	19.0	29.8	390	9.6	13.3
MEAN	6.73	13.1	43.3	64.5	19.5	30.2	475	9.4	13.7
S.D.	.977	1.84	5.04	2.90	.57	.72	78.7	.15	1.29
N	3	3	3	3	3	3	3	3	3

Summary and Individual Clinical Hematology Data

Males Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	WBC $X10^3/\mu L$	N-SEG $X10^3/\mu L$	LYMPH $X10^3/\mu L$	MONO $X10^3/\mu L$	EOSIN $X10^3/\mu L$	BASO $X10^3/\mu L$	N-SEG%	LYMPH%	MONO%	EOSIN%	BASO%
Group: 1	Dose Level: 50		Dosage Unit: mg/kg								
I05428	35.6	16.4	14.2	2.2	2.8	.1	46	40	6	8	0
I05430	29.9	17.2	9.9	2.0	.8	.1	57	33	7	3	0
I05431	12.7	5.5	5.6	1.2	.3	.0	43	44	10	2	0
I05432	26.8	13.0	11.6	1.8	.2	.0	49	43	7	1	0
I05433	27.0	14.6	10.2	1.8	.5	.1	54	38	7	2	0
I05435	25.3	14.3	8.9	.9	1.1	.0	57	35	4	4	0
MEAN	26.2	13.5	10.1	1.6	1.0	.0	51	39	7	3	0
S.D.	7.56	4.20	2.86	.50	.96	.05	5.9	4.4	1.9	2.5	.0
N	6	6	6	6	6	6	6	6	6	6	6
Group: 2	Dose Level: 50		Dosage Unit: mg/kg								
I05436	15.3	10.2	4.1	.9	.1	.0	67	27	6	1	0
I05437	17.6	10.0	5.6	1.6	.5	.0	57	32	9	3	0
MEAN	16.4	10.1	4.8	1.2	.3	.0	62	30	8	2	0
S.D.	1.63	.14	1.06	.49	.28	.00	7.1	3.5	2.1	1.4	.0
N	2	2	2	2	2	2	2	2	2	2	2
Extra											
I05429	19.1	10.5	6.7	1.2	.7	.0	55	35	7	3	0
I05434	16.5	7.2	8.1	.8	.4	.0	44	49	5	2	0
I05438	16.7	9.8	4.7	1.8	.5	.0	58	28	11	3	0
MEAN	17.4	9.2	6.5	1.3	.5	.0	52	37	8	3	0
S.D.	1.45	1.74	1.71	.50	.15	.00	7.4	10.7	3.1	.6	.0
N	3	3	3	3	3	3	3	3	3	3	3

Individual Clinical Hematology Data

Males Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	ANISO	POLY	POIK	HYPO	TOXNEUT
Group: 1	Dose Level: 50		Dosage Unit: mg/kg		
I05428	-	-	-	-	-
I05430 a	-	-	-	-	-
I05431	-	-	-	-	-
I05432	-	-	-	-	-
I05433	-	-	-	-	-
I05435	-	-	-	-	-
Group: 2	Dose Level: 50		Dosage Unit: mg/kg		
I05436	-	-	-	-	-
I05437	-	-	-	-	-
Extra					
I05429	-	-	-	-	-
I05434	-	-	-	-	-
I05438	-	-	-	-	-

a Plasmodium was observed.

Summary and Individual Clinical Hematology Data

Females Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	RBC $X10^6/\mu L$	HGB G/DL	HCT %	MCV FL	MCH PG	MCHC %	PLT $X10^3/\mu L$	PT SEC	PTT SEC
Group: 1	Dose Level: 50		Dosage Unit: mg/kg						
I05439	7.08	12.9	44.3	62.5	18.3	29.3	556	9.5	14.7
I05440	6.97	11.9	41.9	60.2	17.1	28.4	421	10.2	18.1
I05442	5.29	11.0	35.4	66.8	20.8	31.2	531	9.6	14.3
I05444	6.52	11.5	39.7	60.9	17.6	29.0	291	9.1	14.0
I05447	6.07	11.7	39.2	64.7	19.2	29.7	324	9.4	15.9
I05449	7.01	13.1	45.8	65.3	18.7	28.6	444	9.5	15.5
MEAN	6.49	12.0	41.1	63.4	18.6	29.4	428	9.6	15.4
S.D.	.702	.82	3.77	2.61	1.31	1.01	106.7	.36	1.50
N	6	6	6	6	6	6	6	6	6
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05441	7.64	14.1	50.8	66.6	18.5	27.8	449	10.0	17.3
I05446	5.58	10.4	33.6	60.2	18.7	31.1	446	9.6	13.2
MEAN	6.61	12.2	42.2	63.4	18.6	29.4	448	9.8	15.2
S.D.	1.457	2.62	12.16	4.53	.14	2.33	2.1	.28	2.90
N	2	2	2	2	2	2	2	2	2
Extra									
I05443	6.37	12.2	37.8	59.3	19.2	32.3	392	9.9	14.2
I05445	6.29	11.3	38.0	60.5	17.9	29.6	402	9.3	13.2
I05448	5.99	11.5	38.9	64.9	19.2	29.6	402	9.7	16.0
MEAN	6.22	11.7	38.2	61.6	18.8	30.5	399	9.6	14.5
S.D.	.200	.47	.59	2.95	.75	1.56	5.8	.31	1.42
N	3	3	3	3	3	3	3	3	3

Summary and Individual Clinical Hematology Data

Females Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	WBC $X10^3/\mu L$	N-SEG $X10^3/\mu L$	LYMPH $X10^3/\mu L$	MONO $X10^3/\mu L$	EOSIN $X10^3/\mu L$	BASO $X10^3/\mu L$	N-SEG%	LYMPH%	MONO%	EOSIN%	BASO%
Group: 1	Dose Level: 50		Dosage Unit: mg/kg								
I05439	14.7	6.4	6.4	1.5	.4	.0	43	43	10	3	0
I05440	9.7	2.4	6.5	.5	.2	.0	25	67	5	2	0
I05442	21.0	6.4	13.4	.6	.6	.0	30	64	3	3	0
I05444	12.2	5.0	5.4	1.6	.2	.0	41	44	13	2	0
I05447	10.8	4.3	5.4	.6	.5	.0	40	50	6	5	0
I05449	11.4	5.0	5.7	.6	.1	.0	44	50	5	1	0
MEAN	13.3	4.9	7.1	.9	.3	.0	37	53	7	3	0
S.D.	4.13	1.49	3.11	.51	.20	.00	7.8	10.2	3.7	1.4	.0
N	6	6	6	6	6	6	6	6	6	6	6
Group: 2	Dose Level: 50		Dosage Unit: mg/kg								
I05441	15.2	7.6	5.5	1.2	.9	.0	50	36	8	6	0
I05446	12.3	5.7	5.7	.6	.3	.0	46	46	5	2	0
MEAN	13.8	6.6	5.6	.9	.6	.0	48	41	6	4	0
S.D.	2.05	1.34	.14	.42	.42	.00	2.8	7.1	2.1	2.8	.0
N	2	2	2	2	2	2	2	2	2	2	2
Extra											
I05443	14.3	4.3	8.2	1.1	.6	.1	30	58	8	4	0
I05445	12.5	5.4	5.5	1.5	.2	.0	43	44	12	1	0
I05448	10.8	3.0	5.5	1.9	.3	.0	28	51	18	2	0
MEAN	12.5	4.2	6.4	1.5	.4	.0	34	51	13	2	0
S.D.	1.75	1.20	1.56	.40	.21	.06	8.1	7.0	5.0	1.5	.0
N	3	3	3	3	3	3	3	3	3	3	3

Individual Clinical Hematology Data

Females Presurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	ANISO	POLY	POIK	HYPO	TOXNEUT
Group: 1	Dose Level: 50		Dosage Unit: mg/kg		
I05439	-	-	-	-	-
I05440	-	-	-	-	-
I05442	-	-	-	-	-
I05444	-	-	-	-	-
I05447	-	-	-	-	-
I05449	-	-	-	-	-
Group: 2	Dose Level: 50		Dosage Unit: mg/kg		
I05441	-	-	-	-	-
I05446	-	-	-	-	-
Extra					
I05443	-	-	-	-	-
I05445	-	-	-	-	-
I05448	-	-	-	-	-

Summary and Individual Clinical Hematology Data

Males ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	RBC $X10^6/\mu L$	HGB G/DL	HCT %	MCV FL	MCH PG	MCHC %	PLT $X10^3/\mu L$	PT SEC	PTT SEC
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05436	6.46	11.9	39.7	61.4	18.4	30.0	679	9.0	15.8
I05437	6.62	11.9	39.8	60.1	17.9	29.9	519	8.9	14.1
MEAN	6.54	11.9	39.8	60.8	18.2	30.0	599	9.0	15.0
S.D.	.113	.00	.07	.92	.35	.07	113.1	.07	1.20
N	2	2	2	2	2	2	2	2	2
Extra									
I05434	5.81	11.2	37.7	64.9	19.2	29.6	498	9.7	15.3

Summary and Individual Clinical Hematology Data

Males ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	WBC $X10^3/\mu L$	N-SEG $X10^3/\mu L$	LYMPH $X10^3/\mu L$	MONO $X10^3/\mu L$	EOSIN $X10^3/\mu L$	BASO $X10^3/\mu L$	N-SEG%	LYMPH%	MONO%	EOSIN%	BASO%
Group: 2	Dose Level: 50		Dosage Unit: mg/kg								
I05436	14.7	10.2	3.6	.8	.1	.0	70	24	5	1	0
I05437	9.4	5.2	3.1	.9	.3	.0	55	32	9	3	0
MEAN	12.0	7.7	3.4	.8	.2	.0	62	28	7	2	0
S.D.	3.75	3.54	.35	.07	.14	.00	10.6	5.7	2.8	1.4	.0
N	2	2	2	2	2	2	2	2	2	2	2
Extra											
I05434	10.3	3.6	5.7	.7	.2	.1	35	55	7	2	1

Individual Clinical Hematology Data

Males ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	ANISO	POLY	POIK	HYPO	TOXNEUT
Group: 2	Dose Level: 50		Dosage Unit: mg/kg		
I05436	-	-	-	-	-
I05437	-	-	-	-	-
Extra					
I05434	-	-	-	-	-

Summary and Individual Clinical Hematology Data

Females - 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	RBC $X10^6/\mu L$	HGB G/DL	HCT %	MCV FL	MCH PG	MCHC %	PLT $X10^3/\mu L$	PT SEC	PTT SEC
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05441	3.77	7.3	25.8	68.6	19.5	28.4	458	9.3	16.2
I05446	5.76	10.7	35.6	61.7	18.5	30.0	598	8.7	12.6
MEAN	4.76	9.0	30.7	65.2	19.0	29.2	528	9.0	14.4
S.D.	1.407	2.40	6.93	4.88	.71	1.13	99.0	.42	2.55
N	2	2	2	2	2	2	2	2	2
Extra									
I05443	6.37	11.3	37.3	58.5	17.7	30.2	522	9.1	13.5

Summary and Individual Clinical Hematology Data

Females ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	WBC $X10^3/\mu L$	N-SEG $X10^3/\mu L$	LYMPH $X10^3/\mu L$	MONO $X10^3/\mu L$	EOSIN $X10^3/\mu L$	BASO $X10^3/\mu L$	N-SEG%	LYMPH%	MONO%	EOSIN%	BASO%
Group: 2	Dose Level: 50		Dosage Unit: mg/kg								
I05441	12.4	5.3	5.4	1.4	.2	.2	43	44	11	2	1
I05446	15.3	7.7	5.6	1.7	.2	.1	50	36	11	1	1
MEAN	13.8	6.5	5.5	1.6	.2	.2	46	40	11	2	1
S.D.	2.05	1.70	.14	.21	.00	.07	4.9	5.7	.0	.7	.0
N	2	2	2	2	2	2	2	2	2	2	2
Extra											
I05443	10.4	3.8	5.5	.8	.2	.0	37	53	8	2	0

Individual Clinical Hematology Data

Females ~ 4 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	ANISO	POLY	POIK	HYPO	TOXNEUT
Group: 2	Dose Level: 50		Dosage Unit: mg/kg		
I05441	1	1	-	-	-
I05446	-	-	-	-	-
Extra					
I05443	-	-	-	-	-

Summary and Individual Clinical Hematology Data

Males ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	RBC $X10^6/\mu L$	HGB G/DL	HCT %	MCV FL	MCH PG	MCHC %	PLT $X10^3/\mu L$	PT SEC	PTT SEC
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05436	6.10	11.5	38.0	62.2	18.9	30.4	651	9.1	15.2
I05437	6.28	11.5	37.5	59.7	18.3	30.6	424	8.7	14.0
MEAN	6.19	11.5	37.8	60.9	18.6	30.5	538	8.9	14.6
S.D.	.127	.00	.35	1.77	.42	.14	160.5	.28	.85
N	2	2	2	2	2	2	2	2	2
Extra									
I05434	5.91	11.5	38.4	65.0	19.5	30.0	516	9.6	14.9

Summary and Individual Clinical Hematology Data

Males ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	WBC $X10^3/\mu L$	N-SEG $X10^3/\mu L$	LYMPH $X10^3/\mu L$	MONO $X10^3/\mu L$	EOSIN $X10^3/\mu L$	BASO $X10^3/\mu L$	N-SEG%	LYMPH%	MONO%	EOSIN%	BASO%
Group: 2	Dose Level: 50		Dosage Unit: mg/kg								
I05436	13.5	7.9	4.4	1.0	.2	.1	58	33	7	1	0
I05437	11.6	5.9	4.2	.9	.6	.0	51	36	8	5	0
MEAN	12.6	6.9	4.3	1.0	.4	.0	54	34	8	3	0
S.D.	1.34	1.41	.14	.07	.28	.07	4.9	2.1	.7	2.8	.0
N	2	2	2	2	2	2	2	2	2	2	2
Extra											
I05434	7.6	2.5	4.4	.6	.1	.0	33	58	8	1	0

Individual Clinical Hematology Data

Males ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	ANISO	POLY	POIK	HYPO	TOXNEUT
Group: 2	Dose Level: 50		Dosage Unit: mg/kg		
I05436	-	-	-	-	-
I05437	-	-	-	-	-
Extra					
I05434	-	-	-	-	-

Summary and Individual Clinical Hematology Data

Females ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	RBC $X10^6/\mu L$	HGB G/DL	HCT %	MCV FL	MCH PG	MCHC %	PLT $X10^3/\mu L$	PT SEC	PTT SEC
Group: 2	Dose Level: 50		Dosage Unit: mg/kg						
I05441	4.80	9.4	33.9	70.7	19.5	27.6	773	9.0	15.3
I05446	5.91	10.8	35.8	60.5	18.3	30.2	652	8.9	13.8
MEAN	5.36	10.1	34.9	65.6	18.9	28.9	712	9.0	14.5
S.D.	.785	.99	1.34	7.21	.85	1.84	85.6	.07	1.06
N	2	2	2	2	2	2	2	2	2
Extra									
I05443	5.76	10.7	34.4	59.7	18.6	31.2	497	10.0	16.2

Summary and Individual Clinical Hematology Data

Females ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	WBC $X10^3/\mu L$	N-SEG $X10^3/\mu L$	LYMPH $X10^3/\mu L$	MONO $X10^3/\mu L$	EOSIN $X10^3/\mu L$	BASO $X10^3/\mu L$	N-SEG%	LYMPH%	MONO%	EOSIN%	BASO%
Group: 2	Dose Level: 50		Dosage Unit: mg/kg								
I05441	14.6	5.8	6.7	1.8	.2	.1	40	46	12	2	1
I05446	16.5	6.5	7.6	1.3	1.0	.1	39	46	8	6	1
MEAN	15.6	6.2	7.2	1.6	.6	.1	40	46	10	4	1
S.D.	1.34	.49	.64	.35	.57	.00	.7	.0	2.8	2.8	.0
N	2	2	2	2	2	2	2	2	2	2	2
Extra											
I05443	9.9	3.3	5.5	.9	.2	.0	33	55	9	2	0

Individual Clinical Hematology Data

Females ~ 8 Days Postsurgery

METABOLISM OF N-ETHYL PERFLUOROOCTANE SULFONAMIDO ETHANOL (NET-FOSE; T-6316) IN CYNOMOLGUS MONKEYS FOLLOWING ADMINISTRATION OF A SINGLE CAPSULE DOSE

ANIMAL NUMBER	ANISO	POLY	POIK	HYPO	TOXNEUT
Group: 2	Dose Level: 50		Dosage Unit: mg/kg		
I05441	-	-	-	-	-
I05446	-	-	-	-	-
Extra					
I05443	-	-	-	-	-

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