8a) OECD 407, Repeated dose
Range Finding Study 132-006

A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

STUDY NUMBER: 132-006

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STUDY DATES

Study Initiation: June 26, 2000
Animal Phase Initiation: June 27, 2000
Animal Phase Completion: July 7, 2000
Study Completion: October 11, 2000

QUALITY ASSURANCE STATEMENT

Study Number: 132-006

This study was not conducted under GLP guidelines; however, the following reviews were performed by the Quality Assurance Unit:

DATE OF AUDIT/INSPECTION	TYPE OF AUDIT/INSPECTION	DATES REPORTED TO STUDY DIRECTOR AND MANAGEMENT
06/26/00	Protocol	06/26/00
07/17/00	Amendment #1	07/17/00
10/11/00	Final Report	10/11/00

APPROVED BY:

Val Gartner 10/11/00

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TITLE

A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

APPROVED BY:

John Seng 10/11/00

John Seng, Ph.D. Date
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A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

STUDY ABSTRACT

The objective of this study was to identify a maximum tolerated dose of T-7485 and identify dose levels for a 28-day repeated dose study.

Healthy male and female rats were acclimated for seven days prior to Study Day 1 and were examined by the Staff Veterinarian prior to being released for use on the study. Twenty males and twenty females were randomly assigned to groups, and doses were administered via oral gavage for ten consecutive days. The study design was as follows:

Group Number	Group Designation	Dosage Level (mg/kg)	Dosage Concentration (mg/mL)	Dosage Volume (mL/kg)	Number of Animals	
					Males	Females
1	Control	0	0	25	5	5
2	Mid-dose	100	4	25	5	5
3	Mid-high dose	300	12	25	5	5
4	High-dose	1000	40	25	5	5

Observations for mortality and moribundity were recorded twice daily (a.m. and p.m.). During the ten-day repeated dose range-finding study of T-7485, there was no mortality recorded at any level of treatment for either male or female rats. Clinical observations were recorded once daily, and no adverse clinical observations were recorded at any level of treatment for either male or female rats.

Body weights were recorded on Study Days 1, 7, 10, and 11. There were no significant effects of T-7485 treatment on male or female rat body weights. On Study Day 10, mean male body weights ranged between 275.8 and 286.2 grams, while female rats ranged between 193.2 and 206.2 grams. There were no significant effects of T-7485 treatment on male or female body weight changes. Between Study Days 1 and 10, the range of mean male body weight change was 62.4 to 75.0 grams, while in females the range was 27.8 to 32.4 grams.

Feed consumption was measured on Study Days 1, 7, and 10. Relative to body weights and body weight changes, there was no adverse effect of T-7485 on absolute feed consumption for either male or female rats. On Study Days 1 through 10, the mean feed consumption ranged in males from 28.0 to 29.5 grams/day, while in female rats the mean feed consumption ranged from 20.8 to 12.9 grams/day.

All hematological measurements in test material treated groups were comparable to the vehicle control with the exception of elevated segmented neutrophils ($1.2 \pm 0.3410^3/mm^3$ vs. 0.5 ± 0.25 $10^3/mm^3$ vehicle control) in females that received 1000 mg/kg/day T-7485. At 1000 mg/kg/day of T-7485, female mean glucose levels were significantly increased when compared to the vehicle control (163 ± 23.5 vs. 107 ± 17.1 mg/dL, respectively). Both the hematological and clinical chemistry changes reported in female rats that received 1000 mg/kg/day T-7485 appear to be isolated changes that occurred in one gender and had no clear association with other reported findings (including histopathology). Therefore, it is unclear if these marginal changes are related to the test material.

Necropsy observations included: diverticulum of the small intestine, liver foci, small seminal vesicles, enlarged mandibular lymph nodes, lung foci, and kidney dilatation. Many of the gross findings correlated with microscopic findings. Three singular incidences of enlarged mandibular lymph nodes were noted in males that received vehicle and females that received 300 or 1000 mg/kg/day of T-7485. Enlarged mandibular lymph nodes correlated with either mild

lymphoid hyperplasia (vehicle control males and high dose females, respectively) or mild plasmacytosis (females that received 300 mg/kg/day T-7485). In males that received 100 mg/kg/day of T-7485, kidney dilatation and diverticulum of the small intestine were correlated microscopically with unilateral moderate hydronephrosis and diverticulum, respectively. In males that received 1000 mg/kg/day of T-7485, lung foci was correlated microscopically with moderate focal hemorrhage. Finally, in females that received 1000 mg/kg/day T-7485, lung foci were correlated microscopically with mild chronic focal inflammation accompanied with mild focal crystalline material.

Organ weights were recorded for the following organs prior to fixation: adrenal glands, brain, heart, kidneys, liver, ovaries, spleen, testes, and thymus. Paired organs were weighed together. Absolute and relative organ weights were similar to the corresponding vehicle control groups for both male and female rats with the exception of absolute and relative liver weights. Mean percent increases in absolute, % body weight, and % brain weight liver weight changes in males (female percentages are in parenthesis) that received 1000 mg/kg/day/day were 36% (22%), 34% (18%), and 40% (22%), respectively.

Histopathology was performed on the above listed tissues from the vehicle control and high-dose group animals and gross lesions from all animals. Non-neoplastic microscopic lesions included the following: necrosis of the heart; inflammation and hemorrhage of the esophagus; inflammation and edema of the stomach; ultimobronchial cyst of the thyroid; lymphoid hyperplasia and plasmacytosis of the mandibular lymph node; hemorrhage of the thymus; inflammation, hemorrhage, and crystalline material of the lung; and tubular degeneration, mineralization, and hydronephrosis of the kidneys.

None of the microscopic lesions appear to be related to administration of the test material. The most common lesion was focal/multifocal necrosis of the cardiac muscle of the heart. This necrosis occurred in both the vehicle control animals and rats that received 1000 mg/kg/day T-7485. This lesion probably represents early cardiomyopathy, which is a common spontaneous lesion in Sprague-Dawley rats.

In summary, clinical observations, body weights, body weight changes, feed consumption, gross findings, and histopathology failed to reveal any adverse effects associated with ten days of administration of ≤1000 mg/kg/day T-7485. Both the hematological and clinical chemistry changes reported in female rats that received 1000 mg/kg/day T-7485 appear to be isolated changes in one gender and had no clear association with other reported findings (including histopathology). It is therefore unclear if these marginal changes are related to the test material. Furthermore, in the absence of supportive clinical chemistry and histopathology, the marginal but significant differences in absolute and relative liver weights for both male and female rats that received 1000 mg/kg/day T-7485 were not considered biologically or toxicologically significant.

In conclusion, these data suggest ≤1000 mg/kg/day T-7485 will be well-tolerated in rats that receive repeated doses of test material for 28 days.

OBJECTIVE

The objective of this study was to identify a maximum tolerated dose of T-7485 and identify dose levels for a 28-day repeated dose study.

MATERIALS AND METHODS

TEST AND CONTROL MATERIALS: The test material and vehicle were identified as follows:

Test Material:	T-7485 (Potassium Perfluoro Butane Sulfonate)
Lot Number:	2
Date Received:	April 6, 2000
Physical Description:	White Powder
Storage:	Room temperature, protected from light
Amount Received:	500 grams
Vehicle:	Carboxymethylcellulose (medium viscosity)
Supplier:	Sigma Chemical Co.
Lot Number:	69H0028

The Sponsor assumed responsibility for characterization determinations of the test material. The test material was inventoried when received at Primedica Redfield, and a record of all test material usage was maintained. The Certificate of Analysis for the test material is in Appendix 10.

Doses were prepared by Primedica Redfield on the day of use. The vehicle was prepared once to a concentration of 1% by mixing 10 grams of powdered medium viscosity carboxymethylcellulose with deionized water using a Waring blender. Additional deionized water was added to yield 1000 mL of prepared vehicle. The vehicle was stored refrigerated when not in use. The test material was dissolved daily in the prepared vehicle to the required concentrations. The formulated test materials were stored refrigerated.

Samples of the formulated test materials were collected and frozen at approximately -20°C. These samples have not been shipped for analysis. From a single preparation, samples for stability analysis were collected immediately after the first preparation and 7, 14, 21, 28, and 32 days from the date of the first preparation and frozen at -20°C. These samples were shipped to Serquest (Birmingham, Alabama) for analysis.

TEST ANIMALS: Healthy male and female Crl: CD® (SD) IBS BR Stock out-bred albino rats were received from Charles River Laboratories, Inc., for use on the study. The animals were individually housed in screen-bottom stainless steel cages. Animal identification consisted of uniquely numbered ear tags and color-coded cage cards. On Study Day 1, the animals were approximately seven weeks old. The males weighed 196 to 223 grams, and the females weighed 156 to 183 grams.

Teklad Certified Rodent Diet #8728 and filtered tap water were provided *ad libitum*. The feed and water were routinely analyzed for contaminants. There were no known contaminants in the feed or water that would be expected to affect the results of the study. The results of these analyses are on file at Primedica Redfield.

Environmental controls were set to maintain temperatures of 18° to 26°C (64° to 79°F) with a relative humidity of 30% to 70%. These parameters were recorded at least once daily. A 12:12 hour light:dark cycle was maintained in the animal room.

GROUP DESIGNATION AND TREATMENT: The animals were acclimated for seven days prior to Study Day 1 and were examined by the Staff Veterinarian prior to being released for use on the

study. Twenty males and twenty females were randomly assigned to groups by a computer generated weight-ordered distribution such that individual body weights did not exceed ±20% of the mean weight for each sex. The study design was as follows:

Group Number	Group Designation	Dosage Level (mg/kg)	Dosage Concentration (mg/mL)	Dosage Volume (mL/kg)	Number of Animals	
					Males	Females
1	Control	0	0	25	5	5
2	Mid-dose	100	4	25	5	5
3	Mid-high dose	300	12	25	5	5
4	High-dose	1000	40	25	5	5

Doses were administered via oral gavage for ten consecutive days. The first day of dosing was designated as Study Day 1. Individual dose volumes were calculated based on the most recently collected body weight for each animal.

JUSTIFICATION FOR SPECIES SELECTION, ROUTE OF ADMINISTRATION, AND DOSE LEVEL: Rats are an animal model for acute toxicity studies of this type. In the assessment and evaluation of the toxic characteristics of a substance, determination of acute oral toxicity is the usual initial step. Dose levels were chosen by the Sponsor.

CLINICAL OBSERVATIONS: Observations for mortality and moribundity were recorded twice daily (a.m. and p.m.). Clinical observations were recorded once daily.

BODY WEIGHTS: Body weights were recorded on Study Days 1, 7, 10, and 11. The Study Day 11 body weights were only used for relative organ weight calculations.

FEED CONSUMPTION: Feed consumption was measured on Study Days 1, 7, and 10.

HEMATOLOGY: Blood samples for hematological analysis were obtained via cardiac puncture prior to necropsy. The animals were anesthetized with carbon dioxide for the collection. Feed was withheld overnight prior to collection. The blood samples were evaluated for the following parameters: total and relative differential leukocyte counts, erythrocyte counts, hemoglobin concentration, hematocrit value, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet counts, prothrombin time, and activated partial thromboplastin time. Specific methods for hematology analyses are located in Appendix 1.

CLINICAL CHEMISTRY: Blood samples were obtained via cardiac puncture prior to necropsy. The animals were anesthetized with carbon dioxide for the collection. Feed was withheld overnight prior to collection. The samples were processed and evaluated for the following parameters: total protein, albumin, globulin, albumin/globulin ratio, glucose, cholesterol, triglycerides, total bilirubin, urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyltransferase, calcium, phosphorus, sodium, potassium, and chloride. Specific methods for clinical chemistry analyses are located in Appendix 1.

NECROPSY AND ORGAN WEIGHTS: On Study Day 11, the animals were humanely euthanized via anesthesia with carbon dioxide followed by exsanguination. All animals were submitted for a complete necropsy examination. A complete necropsy was defined as examination of the external surface of the body, all orifices, and the cranial, thoracic, and abdominal cavities and their contents.

Organ weights were recorded for the following organs prior to fixation: adrenal glands, brain, heart, kidneys, liver, ovaries, spleen, testes, and thymus. Paired organs were weighed together.

The following organs and tissues were examined *in situ*, dissected free, and fixed in 10% neutral buffered formalin: adrenal glands, aorta, bone marrow (sternum), brain (brain stem, cerebellum, cerebrum), cervix, epididymides, esophagus, eyes (with optic nerve), femur (with articular surface), gross lesions, Harderian gland, heart, large intestine (cecum, colon, rectum), small intestine (duodenum, ileum, jejunum), kidneys, lacrimal gland, liver, lungs (with bronchi), lymph nodes (mandibular, mesenteric), mammary gland, ovaries, oviducts, pancreas, pituitary gland, prostate gland, salivary gland (mandibular), sciatic nerve, seminal vesicles, skeletal muscle, skin (abdominal), spinal cord (cervical, thoracic, lumbar), spleen, stomach (forestomach, glandular), testes, thymus, thyroid/parathyroid, tongue, trachea, uterus, urinary bladder, Zymbal's gland, and vagina.

HISTOPATHOLOGY: Fixed tissues were trimmed, embedded, sectioned, and stained with hematoxylin and eosin. The slides were delivered to Toxicology Pathology Associates for microscopic evaluation by Charles Frith, D.V.M., Ph.D.

Histopathology was performed on all tissues from the vehicle control and high-dose group animals and gross lesions from all animals.

STATISTICS: Means and standard deviations were calculated for all quantitative data. Treated groups of the same sex were compared to Group 1 at common time points using an ANOVA with a *post hoc* Dunnett's t Test (Dunnett, C.W., J. Amer. Statis. Assoc., 50:1096-1121, 1955). A two-sided α of 0.05 or 0.01 was used to determine if statistically significant differences existed between the vehicle control and the treated groups. If no significant differences existed at the 0.05 level, then no comparison was necessary at the 0.01 level.

ARCHIVAL STATEMENT

All original data and the original final report will be retained at Primedica Redfield's archives, located at 100 East Boone Street, Redfield, Arkansas, for a period of five years after issuance of the final report. Wet tissues, slides, and blocks (as appropriate) will be retained for at least one year. After this time, the Sponsor will be contacted for disposition instructions.

RESULTS

FORMULATED TEST MATERIAL STABILITY: From a single preparation, samples for stability analysis were collected immediately after the first preparation and 7, 14, 21, 28, and 32 days from the date of the first preparation and frozen at -20°C. Data for the stability of the formulated test material is included in Appendix 9.

With the exception of Study Day 1, stability data indicate the actual versus the theoretical concentrations for 4, 12, 40 mg/mL were within 10%. On Study Day 1, the 4 and 12 mg/mL actual values were 14% and 32% of their theoretical concentrations, respectively. It is unclear why these values are outside of 10% theoretical concentrations but these data support that at ≤40 mg/mL T-7485 does not decline but is stable for 32 days after the initial formulation.

MORTALITY: The summary of mortality is in Table 1. The individual observations are in Appendix 3.

Observations for mortality and moribundity were recorded twice daily (a.m. and p.m.). During the study, there were no mortality recorded at any level of treatment for either male or female rats.

CLINICAL OBSERVATIONS: The summary of clinical observations is in Table 1. The individual observations are in Appendix 3.

Clinical observations were recorded once daily, and no adverse clinical observations were recorded at any level of treatment for either male or female rats.

BODY WEIGHTS AND BODY WEIGHT CHANGES: The summaries of body weights and body weight changes are in Tables 2 and 3, respectively. The individual body weights are in Appendix 4.

Body weights were recorded on Study Days 1, 7, 10, and 11. There were no significant effects of T-7485 treatment on male or female body weights. On Study Day 10, mean male body weights ranged between 275.8 and 286.2 grams, while female rats ranged between 193.2 and 206.2 grams.

There were no significant effects of T-7485 treatment on male or female rat body weight changes. Between Study Days 1 and 10, the range of mean male body weight change was 62.4 to 75.0 grams, while in females the range was 27.8 to 32.4 grams.

FEED CONSUMPTION: The summary of absolute feed consumption is in Table 4. The individual data are in Appendix 5.

Feed consumption was measured on Study Days 1, 7, and 10. Relative to body weights and body weight changes, there was no adverse effect of T-7485 on absolute feed consumption for either male or female rats. On Study Days 1 through 10, the mean feed consumption ranged in males from 28.0 to 29.5 grams/day, while in female rats the mean feed consumption ranged from 20.8 to 12.9 grams/day.

HEMATOLOGY: The summary of hematology data is in Table 5. The individual hematology data are in Appendix 6. Values in parenthesis indicate mean ± one standard deviation.

Blood samples for hematological analysis were obtained via cardiac puncture prior to necropsy. The animals were anesthetized with carbon dioxide for the collection. Feed was withheld overnight prior to collection. All hematological measurements in test material-treated groups were comparable to the vehicle control with the exception of elevated segmented neutrophils ($1.2 \pm 0.3410^3/mm^3$ vs. $0.5 \pm 0.25\ 10^3/mm^3$ vehicle control) in females that received 1000 mg/kg/day T-7485. This elevation in segmented neutrophils appears to be an isolated

change that occurred only in one gender and had no clear association with other reported findings (including histopathology). It is therefore, unclear if this marginal change is related to the test material.

CLINICAL CHEMISTRY: The summary of clinical chemistry data is in Table 6. The individual clinical chemistry data are in Appendix 7. Values in parenthesis indicate mean ± one standard deviation.

- At 100 mg/kg/day/day of T-7485, male mean albumin levels were significantly decreased when compared to the vehicle control (3.9 ± 0.39 vs. 4.4 ± 0.10 g/dL, respectively).
- At 300 mg/kg/day of T-7485, male mean gamma-glutamyltransferase (GGT) was significantly elevated when compared to the vehicle control (4 ± 2.4 vs. 0 ± 0 U/L, respectively).
- At 100 and 300 mg/kg/day T-7485, male mean chloride levels were significantly elevated when compared to the vehicle control (89 ± 2.2, 90 ± 1.5, and 87 ± 1.1; respectively).
- At 300 mg/kg/day T-7485, female mean alkaline phosphatase levels were significantly decreased when compared to the vehicle control (140 ± 41.2 vs. 221 ± 26.3, respectively).
- At 1000 mg/kg/day T-7485, female mean glucose levels were significantly increased when compared to the vehicle control (163 ± 23.5 vs. 107 ± 17.1 mg/dL, respectively).

In summary, with the exception of the elevated glucose level in females that received 1000 mg/kg/day, T-7485 had no dose-dependent effect on clinical chemistry parameters. The elevated glucose level was an isolated, gender specific change and it is unclear if this is related to the test material.

NECROPSY: The individual necropsy observations are included in the pathology report in Appendix 2.

Necropsy observations included: diverticulum of the small intestine, liver foci, small seminal vesicles, enlarged mandibular lymph nodes, lung foci, and kidney dilatation. Many of the gross findings correlated with microscopic findings. Three singular incidences of enlarged mandibular lymph nodes were noted in males that received vehicle control and females that received 300 or 1000 mg/kg/day T-7485. Enlarged mandibular lymph nodes correlated with either mild lymphoid hyperplasia (vehicle control male and high dose female, respectively) or mild plasmacytosis (females that received 300 mg/kg/day T-7485). In males that received 100 mg/kg/day T-7485, kidney dilatation and diverticulum of the small intestine were correlated microscopically with unilateral moderate hydronephrosis and diverticulum, respectively. In males that received 1000 mg/kg/day T-7485, lung foci was correlated microscopically with moderate focal hemorrhage. Finally, in females that received 1000 mg/kg/day T-7485, lung foci were correlated microscopically with mild chronic focal inflammation accompanied by mild focal crystalline material.

ORGAN WEIGHTS: The summary of organ weights is in Table 7. The individual organ weights are in Appendix 8.

Organ weights were recorded for the following organs prior to fixation: adrenal glands, brain, heart, kidneys, liver, ovaries, spleen, testes, and thymus. Paired organs were weighed together. Absolute and relative organ weights were similar to the corresponding vehicle control groups for both male and female rats with the exception of absolute and relative liver weights. Mean percent increases in absolute, % body weight, and % brain weight liver weights in males (female percentages are in parenthesis) that received 1000 mg/kg/day/day were 36% (22%), 34% (18%), and 40% (22%), respectively.

HISTOPATHOLOGY: The pathology report is in Appendix 2.

Histopathology was performed on all tissues from the vehicle control and high-dose group animals and gross lesions from all animals. Non-neoplastic microscopic lesions included the following: necrosis of the heart; inflammation and hemorrhage of the esophagus; inflammation and edema of the stomach; ultimobranchial cyst of the thyroid; lymphoid hyperplasia and plasmacytosis of the mandibular lymph nodes; hemorrhage of the thymus; inflammation, hemorrhage, and crystalline material of the lung; and tubular degeneration, mineralization, and hydronephrosis of the kidneys.

None of the microscopic lesions appear to be related to administration of the test material. The most common lesion was focal/multifocal necrosis of the cardiac muscle of the heart. This necrosis occurred in both the vehicle control rats and rats that received 1000 mg/kg/day T-7485. This lesion probably represents early cardiomyopathy, which is a common spontaneous lesion in Sprague-Dawley rats.

DISCUSSION

As indicated, clinical observations, body weights, body weight changes, feed consumption, gross findings, and histopathology failed to reveal any adverse effects associated with ten days of administration of ≤1000 mg/kg/day T-7485.

Both the hematological and clinical chemistry changes reported in female rats that received 1000 mg/kg/day T-7485 appear to be isolated changes in one gender and had no clear association with other reported findings (including histopathology). Therefore, it is unclear if these marginal changes are related to the test material.

In the absence of supportive clinical chemistry and histopathology, the marginal but significant absolute and relative liver weights recorded in both male and female rats that received 1000 mg/kg/day T-7485 are not considered biologically or toxicologically significant.

CONCLUSION

In conclusion, these data suggest ≤1000 mg/kg/day T-7485 will be well-tolerated in rats that receive repeated doses of test material for 28 days.

TABLES

TABLE 1
SUMMARY OF CLINICAL OBSERVATIONS

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

TABLE 1: CLINICAL OBSERVATIONS - SUMMARY - MALE RATS

DOSE GROUP (MG/KG/DAY)	1 0 (CONTROL)	2 100	3 300	4 1000
MORTALITY	0	0	0	0
NO ADVERSE FINDINGS				

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

TABLE 1: CLINICAL OBSERVATIONS - SUMMARY - FEMALE RATS

DOSE GROUP (MG/KG/DAY)	1 0 (CONTROL)	2 100	3 300	4 1000
MORTALITY	0	0	0	0
NO ADVERSE FINDINGS				

TABLE 2
SUMMARY OF BODY WEIGHTS

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

TABLE 2: BODY WEIGHTS - SUMMARY - MALE RATS

DOSE GROUP (MG/KG/DAY)			1 0 (CONTROL)	2 100	3 300	4 1000
RATS - TESTED			5	5	5	5
BODY WEIGHT (G)						
SD	1	MEAN±S.D.	211.0 ± 10.9	213.4 ± 9.0	209.4 ± 6.7	213.0 ± 5.7
SD	7	MEAN±S.D.	258.4 ± 12.6	257.8 ± 20.6	259.0 ± 9.0	260.0 ± 6.7
SD	10	MEAN±S.D.	282.2 ± 14.7	275.8 ± 32.7	284.4 ± 10.7	286.2 ± 8.0

SD = STUDY DAY
There were no significant differences noted.

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

TABLE 2: BODY WEIGHTS - SUMMARY - FEMALE RATS

DOSE GROUP (MG/KG/DAY)			1 0 (CONTROL)	2 100	3 300	4 1000
RATS - TESTED			5	5	5	5
BODY WEIGHT (G)						
SD	1	MEAN±S.D.	168.8 ± 8.5	165.4 ± 6.8	165.8 ± 6.2	173.8 ± 5.5
SD	7	MEAN±S.D.	190.2 ± 10.7	186.4 ± 9.1	186.0 ± 8.5	195.2 ± 7.2
SD	10	MEAN±S.D.	198.6 ± 12.6	193.2 ± 10.7	194.2 ± 10.7	206.2 ± 6.8

SD = STUDY DAY
There were no significant differences noted.

TABLE 3
SUMMARY OF BODY WEIGHT CHANGES

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

TABLE 3: BODY WEIGHT CHANGES - SUMMARY - MALE RATS

DOSE GROUP (MG/KG/DAY)			1 0 (CONTROL)	2 100	3 300	4 1000
RATS - TESTED			5	5	5	5
BODY WEIGHT CHANGE (G)						
SD	1 - 7	MEAN±S.D.	+47.4 ± 5.1	+44.4 ± 13.6	+49.6 ± 3.4	+47.0 ± 5.1
SD	7 - 10	MEAN±S.D.	+23.8 ± 3.3	+18.0 ± 13.0	+25.4 ± 3.6	+26.2 ± 2.9
SD	1 - 10	MEAN±S.D.	+71.2 ± 5.0	+62.4 ± 26.3	+75.0 ± 6.4	+73.2 ± 6.3

SD = STUDY DAY
There were no significant differences noted.

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

TABLE 3: BODY WEIGHT CHANGES - SUMMARY - FEMALE RATS

DOSE GROUP (MG/KG/DAY)			1 0 (CONTROL)	2 100	3 300	4 1000
RATS - TESTED			5	5	5	5
BODY WEIGHT CHANGE (G)						
SD	1 - 7	MEAN±S.D.	+21.4 ± 5.3	+21.0 ± 4.7	+20.2 ± 5.3	+21.4 ± 5.3
SD	7 - 10	MEAN±S.D.	+8.4 ± 2.7	+6.8 ± 2.3	+8.2 ± 2.8	+11.0 ± 2.5
SD	1 - 10	MEAN±S.D.	+29.8 ± 6.9	+27.8 ± 5.9	+28.4 ± 6.9	+32.4 ± 6.9

SD = STUDY DAY
There were no significant differences noted.

TABLE 4
SUMMARY OF ABSOLUTE FEED CONSUMPTION

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

TABLE 4: ABSOLUTE FEED CONSUMPTION - SUMMARY - MALE RATS

DOSE GROUP (MG/KG/DAY)			1 0 (CONTROL)	2 100	3 300	4 1000
RATS - TESTED			5	5	5	5
FEED CONSUMPTION (G/DAY)						
SD	1 - 7	MEAN±S.D.	27.9 ± 1.4	28.5 ± 4.6	28.8 ± 1.6	27.3 ± 1.4
SD	7 - 10	MEAN±S.D.	29.9 ± 1.4	28.5 ± 7.5	30.8 ± 0.9	29.2 ± 2.0
SD	1 - 10	MEAN±S.D.	28.6 ± 1.4	28.5 ± 5.5	29.5 ± 0.8	28.0 ± 1.4

SD = STUDY DAY
There were no significant differences noted.

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

TABLE 4: ABSOLUTE FEED CONSUMPTION - SUMMARY - FEMALE RATS

DOSE GROUP (MG/KG/DAY)			1 0 (CONTROL)	2 100	3 300	4 1000
RATS - TESTED			5	5	5	5
FEED CONSUMPTION (G/DAY)						
SD	1 - 7	MEAN±S.D.	21.2 ± 2.0	21.1 ± 1.9	20.9 ± 2.1	21.9 ± 1.6
SD	7 - 10	MEAN±S.D.	21.6 ± 2.5	20.2 ± 1.4	20.9 ± 2.2	22.1 ± 1.0
SD	1 - 10	MEAN±S.D.	21.3 ± 2.2	20.8 ± 1.7	20.9 ± 2.1	21.9 ± 1.3

SD = STUDY DAY
There were no significant differences noted.

TABLE 5
SUMMARY OF HEMATOLOGY DATA

KEY TO HEMATOLOGY TABLES

ABBREVIATION	TERMINOLOGY	UNITS
WBC	White Blood Cells (Leukocytes)	10^3/cu mm
RBC	Red Blood Cells (Erythrocytes)	10^6/cu mm
HGB	Hemoglobin	g/dL
HCT	Hematocrit (Packed Cell Volume)	%
MCV	Mean Corpuscular Volume	fL or cu micron
MCH	Mean Corpuscular Hemoglobin	pg or picograms
MCHC	Mean Corpuscular Hemoglobin Concentration	%
PLT	Platelets	10^3/cu mm
NRBC	Nucleated Red Blood Cell Count	
Lymphocyte	Lymphocytes	10^3/cu mm
Segmented	Segmented Neutrophils	10^3/cu mm
	Bands	10^3/cu mm
	Monocytes	10^3/cu mm
Eosinophil	Eosinophils	10^3/cu mm
	Basophils	10^3/cu mm
Abnormal L	Abnormal Lymphocytes	10^3/cu mm
APTT	Activated Partial Thromboplastin Time	seconds
PT	Prothrombin time	seconds
Other	Other Cells	10^3/cu mm

TABLE 5

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	PT
UNITS:	THSN/CU MM	MILL/CU MM	GRAMS/DL	%	CU MICRONS	PICO GRAMS	%	THSN/CU MM	seconds
Group: 1-M									
MEAN	10.4	6.47	15.2	40.7	62.8	23.5	37.5	1211	13.3
SD	6.13	0.994	2.21	7.08	2.71	0.94	1.14	93.2	0.37
N	5	5	5	5	5	5	5	5	5
Group: 2-M									
MEAN	12.7	6.23	14.7	39.2	63.1	23.7	37.6	1097	13.8
SD	4.87	0.953	1.69	5.37	1.83	1.20	1.05	186.9	0.89
N	5	5	5	5	5	5	5	5	5
Group: 3-M									
MEAN	8.4	6.29	14.3	39.2	62.5	22.9	36.6	1025	13.5
SD	2.68	0.870	1.62	4.89	1.18	0.89	0.76	174.3	0.63
N	5	5	5	5	5	5	5	5	5
Group: 4-M									
MEAN	12.4	6.30	14.9	40.2	63.8	23.7	37.2	1265	13.2
SD	2.87	0.292	0.51	1.88	0.74	0.46	0.51	113.2	0.44
N	5	5	5	5	5	5	5	5	5

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TABLE 5
Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	APTT	NRBC	Lymphocyte	Segmented	Bands	Monocytes	Eosinophil	Basophils	Abnormal L
UNITS:	seconds	COUNT	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM
Group: 1-M									
MEAN	21.0	0	9.2	1.1	0.0	0.0	0.0	0.0	0.0
SD	2.89	0.0	5.47	0.82	0.00	0.09	0.00	0.00	0.00
N	5	5	5	5	5	5	5	5	5
Group: 2-M									
MEAN	19.8	0	10.8	1.6	0.0	0.2	0.1	0.0	0.0
SD	0.95	0.0	4.15	0.65	0.00	0.30	0.09	0.00	0.04
N	5	5	5	5	5	5	5	5	5
Group: 3-M									
MEAN	23.7	0	7.6	0.8	0.0	0.0	0.0	0.0	0.0
SD	6.07	0.0	2.64	0.29	0.00	0.05	0.00	0.00	0.00
N	5	5	5	5	5	5	5	5	5
Group: 4-M									
MEAN	23.9	0	11.4	1.0	0.0	0.0	0.0	0.0	0.0
SD	5.43	0.5	2.72	0.29	0.00	0.00	0.04	0.00	0.00
N	5	5	5	5	5	5	5	5	5

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TABLE 5

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	Other
UNITS:	THSN/CU MM
Group: 1-M	
MEAN	0.0
SD	0.00
N	5
Group: 2-M	
MEAN	0.0
SD	0.00
N	5
Group: 3-M	
MEAN	0.0
SD	0.00
N	5
Group: 4-M	
MEAN	0.0
SD	0.00
N	5

LABCAT HE4.41c 20-JUL-2000

TABLE 5

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT	PT
UNITS:	THSN/CU MM	MILL/CU MM	GRAMS/DL	%	CU MICRONS	PICO GRAMS	%	THSN/CU MM	seconds
Group: 1-F									
MEAN	8.0	6.81	15.6	42.6	62.7	22.9	36.5	1225	13.2
SD	3.34	0.485	0.32	1.14	3.22	1.23	0.38	270.7	0.62
N	5	5	5	5	5	5	5	5	5
Group: 2-F									
MEAN	7.5	6.60	15.3	41.7	63.2	23.2	36.7	1091	13.4
SD	4.20	0.324	0.70	2.07	0.91	0.47	0.24	125.2	0.26
N	5	5	5	5	5	5	5	5	5
Group: 3-F									
MEAN	9.5	6.55	15.2	41.1	62.8	23.2	36.9	1151	13.4
SD	3.37	0.258	0.73	1.94	1.98	0.59	0.44	102.7	0.16
N	5	5	5	5	5	5	5	5	5
Group: 4-F									
MEAN	9.5	6.36	15.0	40.5	63.7	23.6	37.0	1284	13.4
SD	4.27	0.640	1.30	3.86	1.93	0.78	0.45	236.1	0.32
N	5	5	5	5	5	5	5	5	5

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TABLE 5

Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	APTT	NRBC	Lymphocyte	Segmented	Bands	Monocytes	Eosinophil	Basophils	Abnormal L
UNITS:	seconds	COUNT	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM	THSN/CU MM
Group: 1-F									
MEAN	19.3	0	7.4	0.5	0.0	0.0	0.0	0.0	0.0
SD	3.82	0.4	3.24	0.25	0.00	0.04	0.05	0.00	0.04
N	5	5	5	5	5	5	5	5	5
Group: 2-F									
MEAN	20.4	0	6.8	0.6	0.0	0.0	0.0	0.0	0.0
SD	3.79	0.4	3.99	0.38	0.00	0.04	0.04	0.00	0.00
N	5	5	5	5	5	5	5	5	5
Group: 3-F									
MEAN	23.7	0	8.8	0.6	0.0	0.0	0.1	0.0	0.0
SD	3.94	0.0	3.38	0.24	0.00	0.04	0.13	0.00	0.00
N	5	5	5	5	5	5	5	5	5
Group: 4-F									
MEAN	17.3	0	8.3	1.2**	0.0	0.0	0.0	0.0	0.0
SD	2.04	0.0	4.16	0.34	0.00	0.04	0.00	0.00	0.00
N	5	5	5	5	5	5	5	5	5

**-Significant Difference from Control P < .01

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TABLE 5
Study Report for Hematology

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	Other
UNITS:	THSN/CU MM
Group: 1-F	
MEAN	0.0
SD	0.00
N	5
Group: 2-F	
MEAN	0.0
SD	0.00
N	5
Group: 3-F	
MEAN	0.0
SD	0.00
N	5
Group: 4-F	
MEAN	0.0
SD	0.00
N	5

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TABLE 6
SUMMARY OF CLINICAL CHEMISTRY DATA

KEY TO CLINICAL CHEMISTRY TABLES

ABBREVIATION	TERMINOLOGY	UNITS
ALP	Alkaline Phosphatase	U/L
AST	Aspartate Aminotransferase	U/L
ALT	Alanine Aminotransferase	U/L
CHOL	Cholesterol	mg/dL
GLU	Glucose	mg/dL
BUN	Blood Urea Nitrogen	mg/dL
CREAT	Creatinine	mg/dL
TRIG	Triglycerides	mg/dL
PHOS	Phosphorus (inorganic)	mg/dL
TP	Total Protein	g/dL
ALB	Albumin	g/dL
GLOB	Globulin	g/dL
A/G	Albumin/Globulin Ratio	
CA	Calcium	mg/dL
CL	Chloride	mEq/L or mmol/L
NA	Sodium	mEq/L or mmol/L
K	Potassium	mEq/L or mmol/L
GGT	Gamma-glutamyltransferase	U/L
T-BIL	Total Bilirubin	mg/dL

TABLE 6

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	ALT U/L	AST U/L
Group: 1-M									
MEAN	6.3	4.4	174	48	0.1	16	0.3	48	173
SD	0.28	0.10	37.3	6.0	0.05	1.1	0.05	8.0	85.9
N	5	5	5	5	5	5	5	5	5
Group: 2-M									
MEAN	5.9	3.9**	152	47	0.1	16	0.2	42	189
SD	0.42	0.39	26.0	7.5	0.04	1.9	0.04	6.6	109.2
N	5	5	5	5	5	5	5	5	5
Group: 3-M									
MEAN	6.1	4.2	198	51	0.1	15	0.2	53	187
SD	0.27	0.08	24.7	11.9	0.07	1.6	0.05	5.1	66.2
N	5	5	5	5	5	5	5	5	5
Group: 4-M									
MEAN	6.2	4.5	208	41	0.1	17	0.3	57	167
SD	0.23	0.19	55.1	10.9	0.04	4.4	0.07	7.2	80.2
N	5	5	5	5	5	5	5	5	5

**-Significant Difference from Control P < .01

LABCAT CC4.41c 20-JUL-2000

TABLE 6

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	ALP	GGT	CA	PHOS	TRIG	NA	K	CL	GLOB
UNITS:	U/L	U/L	mg/dL	mg/dL	mg/dL	mmol/L	mmol/L	mmol/L	g/dL
Group: 1-M									
MEAN	320	0	11.9	14.4	27	149	8.0	87	1.9
SD	60.1	0.0	0.88	1.68	16.7	1.5	1.26	1.1	0.19
N	5	5	5	5	5	5	5	5	5
Group: 2-M									
MEAN	291	3	12.0	15.0	22	150	7.9	89*	2.0
SD	86.7	1.1	0.74	2.80	7.4	1.5	1.55	2.2	0.34
N	5	5	5	5	5	5	5	5	5
Group: 3-M									
MEAN	291	4*	11.9	15.1	24	149	8.1	90**	1.9
SD	53.7	2.4	0.86	2.19	5.8	1.3	1.28	1.5	0.24
N	5	5	5	5	5	5	5	5	5
Group: 4-M									
MEAN	351	3	12.0	14.7	32	149	7.3	88	1.7
SD	42.7	2.6	0.64	2.36	15.6	1.8	1.01	1.3	0.12
N	5	5	5	5	5	5	5	5	5

*-Significant Difference from Control P < .05 **-Significant Difference from Control P < .01

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TABLE 6

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	A/G
UNITS:	none
Group: 1-M	
MEAN	2.3
SD	0.23
N	5
Group: 2-M	
MEAN	2.0
SD	0.40
N	5
Group: 3-M	
MEAN	2.2
SD	0.27
N	5
Group: 4-M	
MEAN	2.6
SD	0.23
N	5

LABCAT CC4.41c 20-JUL-2000

TABLE 6

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	ALT U/L	AST U/L
Group: 1-F									
MEAN	6.5	4.6	107	56	0.2	16	0.3	48	212
SD	0.30	0.35	17.7	13.4	0.05	0.8	0.04	7.0	101.0
N	5	5	5	5	5	5	5	5	5
Group: 2-F									
MEAN	6.3	4.5	112	64	0.2	16	0.3	49	270
SD	0.23	0.26	17.1	6.1	0.04	1.6	0.05	13.0	91.4
N	5	5	5	5	5	5	5	5	5
Group: 3-F									
MEAN	6.2	4.3	118	59	0.1	16	0.3	49	241
SD	0.44	0.32	18.1	8.1	0.05	2.4	0.04	8.6	113.0
N	5	5	5	5	5	5	5	5	5
Group: 4-F									
MEAN	6.2	4.5	163**	66	0.1	16	0.2	48	243
SD	0.17	0.17	23.5	15.9	0.05	1.7	0.05	10.5	157.6
N	5	5	5	5	5	5	5	5	5

**-Significant Difference from Control P < .01

LABCAT CC4.41c 20-JUL-2000

TABLE 6

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	ALP U/L	GGT U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L	CL mmol/L	GLOB g/dL
Group: 1-F									
MEAN	221	3	12.1	15.0	26	147	8.4	91	1.9
SD	26.3	1.2	0.66	1.77	14.0	0.5	0.58	2.7	0.12
N	5	5	5	5	5	5	5	5	5
Group: 2-F									
MEAN	191	2	11.8	14.1	26	149	8.5	93	1.8
SD	47.8	1.3	0.78	1.92	6.2	1.9	1.79	1.9	0.19
N	5	5	5	5	5	5	5	5	5
Group: 3-F									
MEAN	140**	2	12.9	16.6	26	148	8.8	92	1.9
SD	41.2	1.6	0.55	2.10	6.2	2.0	1.45	1.3	0.13
N	5	5	5	5	5	5	5	5	5
Group: 4-F									
MEAN	179	2	12.8	15.8	36	148	8.8	91	1.8
SD	31.6	2.0	0.69	1.66	16.2	0.9	1.22	1.5	0.26
N	5	5	5	5	5	5	5	5	5

**-Significant Difference from Control P < .01

LABCAT CC4.41c 20-JUL-2000

TABLE 6

Study Report for Clinical Chemistry

SUMMARY REPORT
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	A/G
UNITS:	none
Group: 1-F	
MEAN	2.5
SD	0.30
N	5
Group: 2-F	
MEAN	2.6
SD	0.33
N	5
Group: 3-F	
MEAN	2.3
SD	0.11
N	5
Group: 4-F	
MEAN	2.6
SD	0.44
N	5

LABCAT CC4.41c 20-JUL-2000

TABLE 7
SUMMARY OF ORGAN WEIGHTS

TABLE 7
ORGAN WEIGHT SUMMARY (ABSOLUTE)

TABLE 7

ORGAN WEIGHT SUMMARY (ABSOLUTE)

STUDY: T-7485
SEX: MALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-M	2-M	3-M	4-M
BODY WEIGHT (G)(ABSOLUTE)				
MEAN	250.000	246.200	254.800	254.200
SD	11.7898	26.2812	9.8590	8.8148
N	5	5	5	5
ADRENAL GLANDS (G)(ABSOLUTE)				
MEAN	0.070	0.084	0.077	0.076
SD	0.0043	0.0160	0.0165	0.0059
N	5	5	5	5
BRAIN (G)(ABSOLUTE)				
MEAN	1.962	1.968	1.998	1.896
SD	0.0991	0.1001	0.0981	0.0449
N	5	5	5	5
HEART (G)(ABSOLUTE)				
MEAN	1.158	1.156	1.073	1.134
SD	0.0457	0.1230	0.1114	0.0740
N	5	5	5	5
KIDNEYS (G)(ABSOLUTE)				
MEAN	2.580	2.665	2.581	2.557
SD	0.1713	0.2169	0.1544	0.1218
N	5	5	5	5
LIVER (G)(ABSOLUTE)				
MEAN	9.338	10.012	10.573	12.725**
SD	0.7433	1.0423	0.6789	1.6508
N	5	5	5	5
SPLEEN (G)(ABSOLUTE)				
MEAN	0.597	0.693	0.652	0.650
SD	0.0896	0.1664	0.0874	0.0826
N	5	5	5	5

** - Significant difference P<.01
REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7

ORGAN WEIGHT SUMMARY (ABSOLUTE)

STUDY: T-7485
SEX: MALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-M	2-M	3-M	4-M
TESTES (G)(ABSOLUTE)				
MEAN	2.818	2.838	2.671	2.917
SD	0.2088	0.1144	0.1927	0.1408
N	5	5	5	5
THYMUS (G)(ABSOLUTE)				
MEAN	0.667	0.592	0.563	0.620
SD	0.1450	0.1051	0.1421	0.0542
N	5	5	5	5

REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7

ORGAN WEIGHT SUMMARY (ABSOLUTE)

STUDY: T-7485
SEX: FEMALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-F	2-F	3-F	4-F
BODY WEIGHT (G)(ABSOLUTE)				
MEAN	179.400	173.200	176.800	186.000
SD	10.7842	8.3487	8.2280	6.4031
N	5	5	5	5
ADRENAL GLANDS (G)(ABSOLUTE)				
MEAN	0.076	0.071	0.070	0.081
SD	0.0144	0.0154	0.0051	0.0098
N	5	5	5	5
BRAIN (G)(ABSOLUTE)				
MEAN	1.832	1.803	1.870	1.842
SD	0.0937	0.0598	0.0749	0.0385
N	5	5	5	5
HEART (G)(ABSOLUTE)				
MEAN	0.810	0.810	0.809	0.901
SD	0.0770	0.0758	0.1050	0.0943
N	5	5	5	5
KIDNEYS (G)(ABSOLUTE)				
MEAN	1.809	1.745	1.797	1.982
SD	0.2449	0.1428	0.0728	0.2484
N	5	5	5	5
LIVER (G)(ABSOLUTE)				
MEAN	6.815	6.570	7.161	8.359*
SD	0.7907	0.3965	1.0154	0.8842
N	5	5	5	5
OVARIES (G)(ABSOLUTE)				
MEAN	0.089	0.077	0.087	0.097
SD	0.0204	0.0170	0.0157	0.0070
N	5	5	5	5

* - Significant difference P<.05
REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7

ORGAN WEIGHT SUMMARY (ABSOLUTE)

STUDY: T-7485
SEX: FEMALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-F	2-F	3-F	4-F
SPLEEN (G)(ABSOLUTE)				
MEAN	0.444	0.422	0.464	0.507
SD	0.0559	0.0336	0.0495	0.0694
N	5	5	5	5
THYMUS (G)(ABSOLUTE)				
MEAN	0.606	0.497	0.569	0.571
SD	0.0632	0.0945	0.0766	0.0849
N	5	5	5	5

REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7
ORGAN WEIGHT SUMMARY (% BODY WEIGHT)

TABLE 7

ORGAN WEIGHT SUMMARY (% BODY WEIGHT)

STUDY: T-7485
SEX: MALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-M	2-M	3-M	4-M
ADRENAL GLANDS (% BODY WEIGHT)				
MEAN	0.028	0.034	0.030	0.030
SD	0.0019	0.0067	0.0061	0.0029
N	5	5	5	5
BRAIN (% BODY WEIGHT)				
MEAN	0.785	0.809	0.784	0.747
SD	0.0347	0.1160	0.0188	0.0362
N	5	5	5	5
HEART (% BODY WEIGHT)				
MEAN	0.464	0.471	0.421	0.446
SD	0.0158	0.0415	0.0352	0.0255
N	5	5	5	5
KIDNEYS (% BODY WEIGHT)				
MEAN	1.032	1.089	1.013	1.007
SD	0.0295	0.1088	0.0381	0.0556
N	5	5	5	5
LIVER (% BODY WEIGHT)				
MEAN	3.731	4.072	4.156	5.006**
SD	0.1368	0.1828	0.3373	0.6324
N	5	5	5	5
SPLEEN (% BODY WEIGHT)				
MEAN	0.238	0.280	0.256	0.255
SD	0.0266	0.0496	0.0318	0.0293
N	5	5	5	5
TESTES (% BODY WEIGHT)				
MEAN	1.129	1.165	1.049	1.148
SD	0.1045	0.1542	0.0670	0.0464
N	5	5	5	5

** - Significant difference P<.01
REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7

ORGAN WEIGHT SUMMARY (% BODY WEIGHT)

STUDY: T-7485
SEX: MALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-M	2-M	3-M	4-M
THYMUS (% BODY WEIGHT)				
MEAN	0.266	0.241	0.221	0.244
SD	0.0552	0.0353	0.0509	0.0212
N	5	5	5	5

REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7

ORGAN WEIGHT SUMMARY (% BODY WEIGHT)

STUDY: T-7485
SEX: FEMALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-F	2-F	3-F	4-F
ADRENAL GLANDS (% BODY WEIGHT)				
MEAN	0.042	0.041	0.039	0.043
SD	0.0056	0.0079	0.0027	0.0048
N	5	5	5	5
BRAIN (% BODY WEIGHT)				
MEAN	1.025	1.042	1.059	0.991
SD	0.0903	0.0353	0.0639	0.0354
N	5	5	5	5
HEART (% BODY WEIGHT)				
MEAN	0.451	0.468	0.457	0.484
SD	0.0206	0.0358	0.0437	0.0357
N	5	5	5	5
KIDNEYS (% BODY WEIGHT)				
MEAN	1.006	1.008	1.017	1.063
SD	0.0864	0.0772	0.0415	0.0978
N	5	5	5	5
LIVER (% BODY WEIGHT)				
MEAN	3.789	3.793	4.041	4.487**
SD	0.2092	0.1152	0.4551	0.3388
N	5	5	5	5
OVARIES (% BODY WEIGHT)				
MEAN	0.050	0.044	0.049	0.052
SD	0.0120	0.0082	0.0087	0.0034
N	5	5	5	5
SPLEEN (% BODY WEIGHT)				
MEAN	0.247	0.245	0.262	0.272
SD	0.0259	0.0254	0.0217	0.0353
N	5	5	5	5

** - Significant difference P<.01
REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7

ORGAN WEIGHT SUMMARY (% BODY WEIGHT)

STUDY: T-7485
SEX: FEMALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-F	2-F	3-F	4-F
THYMUS (% BODY WEIGHT)				
MEAN	0.337	0.287	0.322	0.307
SD	0.0182	0.0508	0.0378	0.0437
N	5	5	5	5

REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7
ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

TABLE 7

ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

STUDY: T-7485
SEX: MALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-M	2-M	3-M	4-M
ADRENAL GLANDS (% BRAIN WEIGHT)				
MEAN	3.588	4.298	3.814	4.000
SD	0.3627	0.9244	0.6724	0.3423
N	5	5	5	5
HEART (% BRAIN WEIGHT)				
MEAN	59.138	58.926	53.668	59.798
SD	3.3619	7.9812	4.1340	3.8433
N	5	5	5	5
KIDNEYS (% BRAIN WEIGHT)				
MEAN	131.660	136.106	129.258	134.866
SD	8.7128	17.3572	6.2149	6.3555
N	5	5	5	5
LIVER (% BRAIN WEIGHT)				
MEAN	475.820	510.798	531.090	670.346**
SD	24.4282	70.5064	53.1680	76.0171
N	5	5	5	5
SPLEEN (% BRAIN WEIGHT)				
MEAN	30.402	35.396	32.630	34.336
SD	3.9486	9.4985	3.9612	4.8245
N	5	5	5	5
TESTES (% BRAIN WEIGHT)				
MEAN	143.944	144.602	133.760	153.854
SD	13.7108	10.8629	8.4162	6.8824
N	5	5	5	5
THYMUS (% BRAIN WEIGHT)				
MEAN	34.078	30.126	28.054	32.694
SD	7.6567	5.6885	6.0509	2.6521
N	5	5	5	5

** - Significant difference P<.01
REDFIELD LABORATORIES STUDY NUMBER 132-006

TABLE 7

ORGAN WEIGHT SUMMARY (% BRAIN WEIGHT)

STUDY: T-7485
SEX: FEMALE FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES
ANALYSIS OF VARIANCE USING DUNNETT'S PROCEDURE

GROUP:	1-F	2-F	3-F	4-F
ADRENAL GLANDS (% BRAIN WEIGHT)				
MEAN	4.176	3.938	3.744	4.388
SD	0.7894	0.8482	0.2554	0.5215
N	5	5	5	5
HEART (% BRAIN WEIGHT)				
MEAN	44.296	44.942	43.382	48.916
SD	4.4872	4.0631	6.6835	4.9685
N	5	5	5	5
KIDNEYS (% BRAIN WEIGHT)				
MEAN	98.830	96.756	96.280	107.616
SD	12.6826	7.1336	7.3105	13.5825
N	5	5	5	5
LIVER (% BRAIN WEIGHT)				
MEAN	373.052	364.316	383.750	453.804*
SD	49.7104	17.6486	60.2532	49.0385
N	5	5	5	5
OVARIES (% BRAIN WEIGHT)				
MEAN	4.870	4.280	4.634	5.254
SD	1.0200	0.9210	0.7124	0.3455
N	5	5	5	5
SPLEEN (% BRAIN WEIGHT)				
MEAN	24.310	23.438	24.852	27.458
SD	3.2759	2.0511	2.8453	3.2939
N	5	5	5	5
THYMUS (% BRAIN WEIGHT)				
MEAN	33.130	27.600	30.374	30.936
SD	3.8695	5.4349	3.1201	4.2188
N	5	5	5	5

* - Significant difference P<.05
REDFIELD LABORATORIES STUDY NUMBER 132-006

APPENDICES

APPENDIX 1
METHODS USED FOR CLINICAL PATHOLOGY PROCEDURES

HEMATOLOGY

The Baker System 9110 + Plus Automated Cell Counter is used for complete blood counts.

White Blood Cell (WBC), Red Blood Cell (RBC) and Platelet counts - The instrument electronically counts WBC, RBC, and platelets by employing the impedance principle. This principle of electronic counting and sizing is based on the difference in conductivity between blood cells and the diluent in which they are suspended. Pulse editing is used to discriminate between red blood cells and platelets.

Mean Corpuscular Volume (MCV) - Measurement of MCV is based on the RBC impedance pulse amplitude. RBC pulses are sized according to their voltage and an average is taken. The average is then compared to the MCV reference that is set during the Hematocrit calibration.

Hemoglobin - The hemoglobin determination is accomplished by a cyanmethemoglobin procedure. The color intensity of this reaction is measured by a photometric cell.

Hematocrit (HCT), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC) - calculated from the measured parameters using the following formulas:

$$HCT = \frac{MCV \times RBC}{10}$$

$$MCH = \frac{HGB \times 10}{RBC}$$

$$MCHC = \frac{HGB \times 100}{HCT}$$

Differentials and RBC morphology are done manually.
Stain used - VOLU-SOL Wright's stain.

COAGULATION

MCA 110 - a fully integrated microprocessor driven instrument designed to perform coagulation tests on plasma specimens.

The MCA 110 operates on the principles of optical density measurement enhanced by electronic light amplification, differentiation and signal processing. Utilizing light generated by light diodes and solid state photo-detectors.

Prothrombin Time
Bio/Data Corporation
Plastinex Thromboplastin Reagent
No. 101158

Activated Partial Thromboplastin Time
Bio/Data Corporation
Cephalinex Activated PTT Reagent (Silica Activated)
No. 101162

CLINICAL CHEMISTRY

The Boehringer Mannheim Hitachi - 717 Analyzer is a fully automated computerized chemistry analyzer. It is a multi-channel, discrete instrument capable of performing potentiometric and photometric assays of a wide range of analyses.

The Hitachi - 717 utilizes a unique reagent and sampling system which allows the analysis of 750 test/hour including Ion Selective Electrodes.

Total Protein (Biuret)
Colorimetric Determination
BMC

Albumin (Bromcresol Green)
Colorimetric Determination
BMC

Glucose (Hexokinase)
Enzymatic Determination
BMC

Cholesterol
Enzymatic Determination
BMC

Blood Urea Nitrogen (RATE)
Enzymatic Determination
BMC

Creatinine
Kinetic Determination
BMC

Total Bilirubin
Colorimetric Determination
BMC

Alanine Aminotransferase
Kinetic Determination
BMC

Aspartate Aminotransferase
Kinetic Determination
BMC

Alkaline Phosphatase
Kinetic Determination
BMC

Creatine Kinase
Kinetic Determination
BMC

Lactate Dehydrogenase
Kinetic Determination
BMC

Gamma-Glutamyltransferase
Kinetic Determination
BMC

Triglyceride (GPO-Trinder)
Enzymatic Determination
BMC

Calcium
Colorimetric Determination
BMC

Phosphorus (Inorganic)
Ultraviolet Determination
BMC

Direct Bilirubin
Colorimetric Determination
BMC

Amylase/EPS
Enzymatic Colorimetric Test
BMC

Lipase
Ultraviolet Determination
BMC

Sorbitol Dehydrogenase
Enzymatic Determination
Sigma

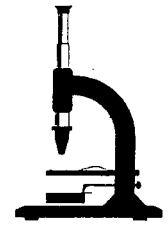
Sodium - Ion Selective Electrode, Boehringer Mannheim Procedure

Potassium - Ion Selective Electrode, Boehringer Mannheim Procedure

Chloride - Ion Selective Electrode, Boehringer Mannheim Procedure

BMC = Boehringer Mannheim Corporation Reagents

APPENDIX 2
PATHOLOGY REPORT



TOXICOLOGY PATHOLOGY ASSOCIATES

A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

STUDY NUMBER: 132-006

SPONSOR:
3M Pharmaceuticals
3M Center, Building 220-2E-02
P.O. Box 33220
St. Paul, MN 55133-3320
Tel: 651-733-1962
Fax: 651-733-1773

TESTING FACILITY:
Primedica Redfield
P.O. Box 308
100 East Boone Street
Redfield, Arkansas 72132
Tel: 501-397-2540
Fax: 501-397-2002

EVALUATION FACILITY:
Toxicology Pathology Associates
14201 Clarborne Ct.
Little Rock, Arkansas 72211-5590
Tel: 501-224-5939
Fax: 501-224-5939
E-mail: ISIS@Aristotle.net

Charles H. Frith

Charles H. Frith, D.V.M., Ph.D.

10-10-00

Date

Study 132-006

TABLE OF CONTENTS

Study 132-006

Summary

Treatment of male and female Sprague-Dawley rats with a 14-day repeated dose of T-7485 did not result in any gross or microscopic findings.

Introduction

The objective of this study was to identify a maximum tolerated dose of T-7485 and identify dose levels for a 28-day repeated dose study.

Materials and Methods

Necropsy technicians at Primedica Redfield, Redfield, Arkansas, under the supervision of a pathologist, performed necropsies. The following tissues were routinely fixed in 10% neutral buffered formalin: adrenal glands, aorta, bone marrow (sternum), brain (brain stem), brain (cerebellum), brain (cerebrum), cervix, epididymides, esophagus, eyes with optic nerve, femur with articular surface, Harderian gland, heart, intestine, large (cecum), intestine, large (colon), intestine, large (rectum), intestine, small (duodenum), intestine, small (ileum), intestine, small (jejunum), kidneys, lacrimal gland, liver, lungs with bronchi, lymph nodes (mandibular), lymph nodes (mesenteric), mammary gland, ovaries, oviducts, pancreas, pituitary gland, prostate gland, salivary gland (mandibular), sciatic nerve, seminal vesicles, skeletal muscle, skin (abdominal), spinal cord (cervical), spinal cord (lumbar), spinal cord (thoracic), spleen, stomach (forestomach), stomach (glandular), testes, thymus, thyroid, parathyroid, tongue, trachea, urinary bladder, uterus, vagina, Zymbal's gland, and gross lesions. Fixed tissues were routinely trimmed, processed, embedded, sectioned, and stained with hematoxylin and eosin (H&E). The microscopic glass slides were delivered to Toxicology Pathology Associates, Little Rock, Arkansas, for microscopic evaluation.

Tissues identified in the above paragraph from the vehicle control (Group 1) and the high dose (Group 4) animals, all gross lesions, and all animals found dead or sacrificed *in extremis* were processed for microscopic evaluation. Tissues were evaluated for the presence of non-neoplastic lesions. Non-neoplastic lesions were graded as to severity as trace (1), mild (2), moderate (3), and severe (4).

Study 132-006

The experimental design is outlined below:

Group Number	Group Designation	Dosage Level (mg/kg)	Dosage Concentration (mg/mL)	Dosage Volume (mL/kg)	Number of Animals	
					Males	Females
1	Control	0	0	25	5	5
2	Mid-dose	100	4	25	5	5
3	Mid-high dose	300	12	25	5	5
4	High-dose	1000	40	25	5	5

Results

Gross Observations

Gross observations were collected on all animals by necropsy technicians on a specially designed Individual Animal Necropsy Record (IANR) under the supervision of a pathologist. These findings were entered into the ADP[1] Computer Pathology system by the Study Pathologist for all animals. It was necessary to enter the gross data into the ADP Pathology system in order to generate Gross Summary Tables and to correlate gross and microscopic findings.

At the time of necropsy, the fate of the all animals was recorded on the IANR as scheduled sacrifice.

Only a small number of gross observations were seen in the study, and none of them appeared to be related to administration of the test article.

Histopathological Observations

Microscopic lesions were recorded on a Gateway Pentium computer utilizing the ADP automated pathology data collection system. For convenience of data collection and reporting, all data were collected utilizing the animal numbers provided by Primedica Redfield.

Non-neoplastic Microscopic Lesions

A small number of microscopic findings were seen, but none of them appeared to be related to administration of the test article.

[1]ISIS, Bellingham, Washington, markets ADP.

Study 132-006

Correlation of Gross and Microscopic Findings

The Gross and Microscopic Correlation Report correlates gross findings with microscopic findings by group.

Discussion

Gross Observations

Only a small number of gross observations were seen in the study, and none of them appeared to be related to administration of the test article.

Histopathologic Lesions

A small number of microscopic findings were seen, but none of them appeared to be related to administration of the test articles. The most common lesion was focal/multifocal necrosis of the cardiac muscle of the heart. This necrosis occurred in both the vehicle control animals (Group 1) and the high dose (Group 4) animals. This lesion probably represents early cardiomyopathy, which is a common spontaneous lesion in Sprague-Dawley rats.

Conclusion

Treatment of male and female Sprague-Dawley rats with a 14-day repeated dose of T-7485 did not result in any gross or microscopic findings.

Study 132-006

Reports

Study 132-006

Reports

The following reports are provided in the Reports Section.

1) Study Groups and Associated Animals - Lists the dose groups, dose levels, and identification numbers of respective animals in each group.
2) Gross Pathology Group Incidence Summary – This report provides the number of organs examined and the incidence of gross findings by group.
3) Histopathology Non-neoplastic Morphology Incidence Summary - This report provides the number of organs examined and the incidence of non-neoplastic findings by group.
4) Gross and Microscopic Correlation Report – This report correlates gross findings with microscopic findings by group.
5) Individual Animal Necropsy Observation (Gross Pathology) – This report was generated by Artemis Computer Pathology System and includes all gross findings for a specific animal.
6) Individual Animal Report (Histopathology) - This report includes all microscopic findings for a specific animal.

Study 132-006

Abbreviations Code Table

NR = Not remarkable

Correlate NP = Correlate Not Present

Study Groups and Associated Animals

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 1
Compound: T-7485 Date:07/25/00
Species: Rat Study Groups and The Associated Animals Time: 11:04
Pathologist: C.H. Frith ADP916 V3.0

Group: Group 1 Dose: 0 (mg/kg) Sex: Male Number in Group: 5

6391 6393 6395 6397 6399

Group: Group 1 Dose: 0 (mg/kg) Sex: Female Number in Group: 5

6392 6394 6396 6398 6400

Group: Group 2 Dose: 100 (mg/kg) Sex: Male Number in Group: 5

6401 6403 6405 6407 6409

Group: Group 2 Dose: 100 (mg/kg) Sex: Female Number in Group: 5

6402 6404 6406 6408 6410

Group: Group 3 Dose: 300 (mg/kg) Sex: Male Number in Group: 5

6411 6413 6415 6417 6419

Group: Group 3 Dose: 300 (mg/kg) Sex: Female Number in Group: 5

6412 6414 6416 6418 6420

Group: Group 4 Dose: 1000 (mg/kg) Sex: Male Number in Group: 5

6421 6423 6425 6427 6429

Group: Group 4 Dose: 1000 (mg/kg) Sex: Female Number in Group: 5

6422 6424 6426 6428 6430

Gross Pathology Group Incidence Summary

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 1
Compound: T-7485 Date:07/26/00
Species: Rat Gross Pathology Group Incidence Summary Time: 11:16
Pathologist: C.H. Frith ADP401 V3.0

Group	Group 1		Group 2		Group 3		Group 4	
Dose(mg/kg)	0		100		300		1000	
Sex	M	F	M	F	M	F	M	F
Animals On Study	5	5	5	5	5	5	5	5
Animals Logged	5	5	5	5	5	5	5	5
Cardiovascular System								
Aorta	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Heart	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Digestive System								
Esophagus	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Intestine, large (cecum)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Intestine, large (colon)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Intestine, large (rectum)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Intestine, small (duodenum)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Intestine, small (ileum)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Intestine, small (jejunum)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	4	5	5	5	5	5
Remarkable Observations	0	0	1	0	0	0	0	0
Diverticulum	0	0	1	0	0	0	0	0

The tissue incidence reflects the number of tissues that were processed:
Remarkable, Not Remarkable, Missing, Autolyzed or Notes Only.
The morphology incidence reflects the number of animals in which the morphology occurred.
Autolysis Only and Notes Only are tabulated if no diagnoses are tendered.

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 2
Compound: T-7485 Date: 07/26/00
Species: Rat Gross Pathology Group Incidence Summary Time: 11:16
Pathologist: C.H. Frith ADP401 V3.0

Group	Group 1		Group 2		Group 3		Group 4	
Dose(mg/kg)	0		100		300		1000	
Sex	M	F	M	F	M	F	M	F
Animals On Study	5	5	5	5	5	5	5	5
Animals Logged	5	5	5	5	5	5	5	5
Digestive System (Continued)								
Liver	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	4	5
Remarkable Observations	0	0	0	0	0	0	1	0
Focus	0	0	0	0	0	0	1	0
Pancreas	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Salivary Gland								
Salivary gland (mandibular)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Stomach								
Stomach (forestomach)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Stomach (glandular)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Endocrine System								
Adrenal glands	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Parathyroid	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Pituitary gland	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Thyroid	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5

The tissue incidence reflects the number of tissues that were processed:
Remarkable, Not Remarkable, Missing, Autolyzed or Notes Only.
The morphology incidence reflects the number of animals in which the morphology occurred.
Autolysis Only and Notes Only are tabulated if no diagnoses are tendered.

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 3
Compound: T-7485 Date:07/26/00
Species: Rat Gross Pathology Group Incidence Summary Time: 11:16
Pathologist: C.H. Frith ADP401 V3.0

Group	Group 1		Group 2		Group 3		Group 4	
Dose(mg/kg)	0		100		300		1000	
Sex	M	F	M	F	M	F	M	F
Animals On Study	5	5	5	5	5	5	5	5
Animals Logged	5	5	5	5	5	5	5	5
Genital System								
Cervix/Vagina	0	5	0	5	0	5	0	5
Not Remarkable	0	5	0	5	0	5	0	5
Epididymides	5	0	5	0	5	0	5	0
Not Remarkable	5	0	5	0	5	0	5	0
Mammary gland	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Ovaries	0	5	0	5	0	5	0	5
Not Remarkable	0	5	0	5	0	5	0	5
Oviducts	0	5	0	5	0	5	0	5
Not Remarkable	0	5	0	5	0	5	0	5
Prostate gland	5	0	5	0	5	0	5	0
Not Remarkable	5	0	5	0	5	0	5	0
Seminal vesicles	5	0	5	0	5	0	5	0
Not Remarkable	5	0	4	0	5	0	5	0
Remarkable Observations	0	0	1	0	0	0	0	0
Small	0	0	1	0	0	0	0	0
Testes	5	0	5	0	5	0	5	0
Not Remarkable	5	0	5	0	5	0	5	0
Uterus	0	5	0	5	0	5	0	5
Not Remarkable	0	5	0	5	0	5	0	5
Hematopoietic System								
Bone Marrow								
Bone marrow (sternum)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5

The tissue incidence reflects the number of tissues that were processed:
Remarkable, Not Remarkable, Missing, Autolyzed or Notes Only.
The morphology incidence reflects the number of animals in which the morphology occurred.
Autolysis Only and Notes Only are tabulated if no diagnoses are tendered.

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 4
Compound: T-7485 Date:07/26/00
Species: Rat Gross Pathology Group Incidence Summary Time: 11:16
Pathologist: C.H. Frith ADP401 V3.0

Group	Group 1		Group 2		Group 3		Group 4	
Dose(mg/kg)	0		100		300		1000	
Sex	M	F	M	F	M	F	M	F
Animals On Study	5	5	5	5	5	5	5	5
Animals Logged	5	5	5	5	5	5	5	5
Hematopoietic System (Continued)								
Lymph Node								
Mandibular lymph node	5	5	5	5	5	5	5	5
Not Remarkable	4	5	5	5	5	4	5	4
Remarkable Observations	1	0	0	0	0	1	0	1
Enlarged	1	0	0	0	0	1	0	1
Mesenteric lymph node	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Spleen	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Thymus	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Integumentary System								
Skin (abdominal)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Musculoskeletal System								
Bone								
Femur (including articular surface)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Skeletal muscle	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Tongue	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5

The tissue incidence reflects the number of tissues that were processed:
Remarkable, Not Remarkable, Missing, Autolyzed or Notes Only.
The morphology incidence reflects the number of animals in which the morphology occurred.
Autolysis Only and Notes Only are tabulated if no diagnoses are tendered.

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 5
Compound: T-7485 Date:07/26/00
Species: Rat Gross Pathology Group Incidence Summary Time: 11:16
Pathologist: C.H. Frith ADP401 V3.0

Group	Group 1		Group 2		Group 3		Group 4	
Dose(mg/kg)	0		100		300		1000	
Sex	M	F	M	F	M	F	M	F
Animals On Study	5	5	5	5	5	5	5	5
Animals Logged	5	5	5	5	5	5	5	5
Nervous System								
Brain								
Brain (brain stem)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Brain (cerebellum)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Brain (cerebrum)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Nerve								
Sciatic nerve	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Spinal Cord								
Spinal cord (cervical)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Spinal cord (lumbar)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Spinal cord (thoracic)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Respiratory System								
Lungs (with bronchi)	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	4	4
Remarkable Observations	0	0	0	0	0	0	1	1
Focus	0	0	0	0	0	0	1	1
Trachea	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Special Senses								
Eyes	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5

The tissue incidence reflects the number of tissues that were processed:
Remarkable, Not Remarkable, Missing, Autolyzed or Notes Only.
The morphology incidence reflects the number of animals in which the morphology occurred.
Autolysis Only and Notes Only are tabulated if no diagnoses are tendered.

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 6
Compound: T-7485 Date: 07/26/00
Species: Rat Gross Pathology Group Incidence Summary Time: 11:16
Pathologist: C.H. Frith ADP401 V3.0

Group	Group 1		Group 2		Group 3		Group 4	
Dose(mg/kg)	0		100		300		1000	
Sex	M	F	M	F	M	F	M	F
Animals On Study	5	5	5	5	5	5	5	5
Animals Logged	5	5	5	5	5	5	5	5
Special Senses (Continued)								
Harderian gland	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Lacrimal gland	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Optic nerve	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Zymbal's gland	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5
Urinary system								
Kidneys	5	5	5	5	5	5	5	5
Not Remarkable	5	5	4	5	5	5	5	5
Remarkable Observations	0	0	1	0	0	0	0	0
Dilatation	0	0	1	0	0	0	0	0
Urinary bladder	5	5	5	5	5	5	5	5
Not Remarkable	5	5	5	5	5	5	5	5

The tissue incidence reflects the number of tissues that were processed:
Remarkable, Not Remarkable, Missing, Autolyzed or Notes Only.
The morphology incidence reflects the number of animals in which the morphology occurred.
Autolysis Only and Notes Only are tabulated if no diagnoses are tendered.

Histopathology Non-neoplastic Morphology Incidence Summary

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 1
Compound: T-7485 Date:07/26/00
Species: Rat Histopathology Non-neoplastic Morphology Incidence Summary Time: 11:07
Pathologist: C.H. Frith ADP404 V3.0

Group	Group 1		Group 2		Group 3		Group 4	
Dose(mg/kg)	0		100		300		1000	
Sex	M	F	M	F	M	F	M	F
Animals On Study	5	5	5	5	5	5	5	5
Animals Logged	5	5	3	1	5	5		
Cardiovascular System								
Heart	5	5	0	0	5	5		
Non-Neoplastic Observations	4	1	0	0	4	3		
Necrosis	4	1	0	0	4	3		
Digestive System								
Esophagus	5	5	0	0	5	5		
Non-Neoplastic Observations	0	0	0	0	0	2		
Hemorrhage	0	0	0	0	0	1		
Inflammation	0	0	0	0	0	2		
Intestine, small (jejunum)	5	5	1	0	5	5		
Non-Neoplastic Observations	0	0	1	0	0	0		
Diverticulum	0	0	1	0	0	0		
Liver	5	5	0	0	5	5		
Non-Neoplastic Observations	1	0	0	0	0	0		
Mononuclear Cell Infiltrate	1	0	0	0	0	0		
Stomach								
Stomach (glandular)	5	5	0	0	5	5		
Non-Neoplastic Observations	0	0	0	0	0	2		
Edema	0	0	0	0	0	1		
Inflammation	0	0	0	0	0	1		
Endocrine System								
Thyroid	5	5	0	0	5	5		
Non-Neoplastic Observations	0	0	0	0	1	1		
Ultimobranchial cyst	0	0	0	0	1	1		

The tissue incidence reflects the number of tissues that were examined:
Remarkable, Not Remarkable, or Notes Only.
The morphology incidence reflects the number of animals in which the morphology occurred.

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 2
Compound: T-7485 Date:07/26/00
Species:. Rat Histopathology Non-neoplastic Morphology Incidence Summary Time: 11:07
Pathologist: C.H. Frith ADP404 V3.0

	Group	Group 1		Group 2		Group 3		Group 4	
	Dose(mg/kg)	0		100		300		1000	
	Sex	M	F	M	F	M	F	M	F
	Animals On Study	5	5	5	5	5	5	5	5
	Animals Logged	5	5	3	1	5	5		
Hematopoietic System									
Lymph Node									
Mandibular lymph node		4	4	0	1	4	5		
Non-Neoplastic Observations		3	0	0	1	0	5		
Lymphoid Hyperplasia		1	0	0	0	0	2		
Plasmacytosis		2	0	0	1	0	3		
Thymus		5	5	0	0	5	5		
Non-Neoplastic Observations		1	0	0	0	0	1		
Hemorrhage		1	0	0	0	0	1		
Respiratory System									
Lungs (with bronchi)		5	5	0	0	5	5		
Non-Neoplastic Observations		0	0	0	0	1	1		
Crystalline material		0	0	0	0	0	1		
Hemorrhage		0	0	0	0	1	0		
Inflammation		0	0	0	0	0	1		
Trachea		5	5	0	0	5	5		
Non-Neoplastic Observations		0	0	0	0	0	1		
Inflammation		0	0	0	0	0	1		
Urinary system									
Kidneys		5	5	1	0	5	5		
Non-Neoplastic Observations		2	2	1	0	3	2		
Hydronephrosis		2	1	1	0	3	0		
Mineralization		0	1	0	0	0	2		
Tubular Degeneration		0	0	0	0	1	0		

The tissue incidence reflects the number of tissues that were examined:
Remarkable, Not Remarkable, or Notes Only.
The morphology incidence reflects the number of animals in which the morphology occurred.

Gross and Microscopic Pathology Correlation Report

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 1
Compound: T-7485 Date:07/26/00
Species: Rat Gross and Microscopic Pathology Correlation Report Time: 11:20
Pathologist: C.H. Frith ADP110 V3.0

Group: Group 1 Dose: 0 (mg/kg) Sex: Males

Animal ID:	Gross Pathology Observations	Correlated Microscopic Pathology Observations
6397	*Mandibular lymph node:*	
	Enlarged, Bilateral.	Lymphoid Hyperplasia, Mild.

(Continued)

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 2
Compound: T-7485 Date:07/26/00
Species: Rat Gross and Microscopic Pathology Correlation Report Time: 11:20
Pathologist: C.H. Frith ADP110 V3.0

Group: Group 2 Dose: 100 (mg/kg) Sex: Males

Animal ID:	Gross Pathology Observations	Correlated Microscopic Pathology Observations
6401	*Kidneys*:	
	Dilatation, Right; Pelvis.	Hydronephrosis, Moderate, Unilateral.
6407	*Seminal vesicles*:	
	Small, Bilateral.	Correlate NP
6409	*Intestine, small (jejunum)*:	
	Diverticulum; 15 x 5 MM.	Diverticulum.

(Continued)

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 3
Compound: T-7485 Date:07/26/00
Species: Rat Gross and Microscopic Pathology Correlation Report Time: 11:20
Pathologist: C.H. Frith ADP110 V3.0

Group: Group 3 Dose: 300 (mg/kg) Sex: Females

Animal ID:	Gross Pathology Observations	Correlated Microscopic Pathology Observations
6412	*Mandibular lymph node:*	
	Enlarged, Bilateral.	Plasmacytosis, Mild.

(Continued)

Study ID: 132-006 Dose Range-Finding Toxicity Study in Sprague-Dawley Rats Page: 4
Compound: T-7485 Date:07/26/00
Species: Rat Gross and Microscopic Pathology Correlation Report Time: 11:20
Pathologist: C.H. Frith ADP110 V3.0

Group: Group 4 Dose: 1000 (mg/kg) Sex: Males

Animal ID:	Gross Pathology Observations	Correlated Microscopic Pathology Observations
6421	*Liver:*	
	Focus; 2 x 2 MM Median Lobe White.	Correlate NP
6427	*Lungs (with bronchi):*	
	Focus; 20 x 20 MM Left Lateral Lobe Dark.	Hemorrhage, Focal, Moderate.

(Continued)

Study ID: 132-006
Compound: T-7485
Species: Rat
Pathologist: C.H. Frith

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Gross and Microscopic Pathology Correlation Report

Page: 5
Date:07/26/00
Time: 11:20
ADP110 V3.0

Group: Group 4 Dose: 1000 (mg/kg) Sex: Females

Animal ID:	Gross Pathology Observations	Correlated Microscopic Pathology Observations
6422	*Lungs (with bronchi)*:	
	Focus; 4 x 3 MM Apical Lobe Dark.	Crystalline material, Focal, Mild.
		Inflammation, Focal, Chronic, Mild.
6424	*Mandibular lymph node*:	
	Enlarged, Bilateral.	Lymphoid Hyperplasia, Mild.

(End of Report)

Individual Animal Necropsy Observation (Gross Pathology)

REPORTS CODE TABLE

TGL	Trackable Gross Lesion

INDIVIDUAL NECROPSY OBSERVATIONS

132-006 -A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

GROUP: 1 DOSE: 0 SEX: MALE

ANIMAL NUMBER	MODE OF DEATH	DEATH DAY	DEATH (WEEK)	OBSERVATION(S)
6391	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6393	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6395	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6397	SCHEDULED SACRIFICE	11	(2)	LYMPH NODES-MANDIBULAR; BILATERAL; ENLARGED (TGL) ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS
6399	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS

INDIVIDUAL NECROPSY OBSERVATIONS

132-006 -A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

GROUP: 1 DOSE: 0 SEX: FEMALE

ANIMAL NUMBER	MODE OF DEATH	DEATH DAY	DEATH (WEEK)	OBSERVATION(S)
6392	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6394	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6396	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6398	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6400	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS

INDIVIDUAL NECROPSY OBSERVATIONS

132-006 -A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

GROUP: 2 DOSE: 30 SEX: MALE

ANIMAL NUMBER	MODE OF DEATH	DEATH DAY	DEATH (WEEK)	OBSERVATION(S)
6401	SCHEDULED SACRIFICE	11	(2)	KIDNEYS; RIGHT; DILATATION; PELVIS (TGL) ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS
6403	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6405	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6407	SCHEDULED SACRIFICE	11	(2)	SEMINAL VESICLES; BILATERAL; SMALL (TGL) ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS
6409	SCHEDULED SACRIFICE	11	(2)	SM. INTESTINE-JEJUNUM; DIVERTICULUM (TGL): 15 X 5 MM ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS

INDIVIDUAL NECROPSY OBSERVATIONS

132-006 -A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

GROUP: 2 DOSE: 30 SEX: FEMALE

ANIMAL NUMBER	MODE OF DEATH	DEATH DAY	DEATH (WEEK)	OBSERVATION(S)
6402	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6404	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6406	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6408	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6410	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS

INDIVIDUAL NECROPSY OBSERVATIONS

132-006 -A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

GROUP: 3 DOSE: 100 SEX: MALE

ANIMAL NUMBER	MODE OF DEATH	DEATH DAY	DEATH (WEEK)	OBSERVATION(S)
6411	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6413	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6415	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6417	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6419	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS

INDIVIDUAL NECROPSY OBSERVATIONS

132-006 -A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

GROUP: 3 DOSE: 100 SEX: FEMALE

ANIMAL NUMBER	MODE OF DEATH	DEATH DAY	DEATH (WEEK)	OBSERVATION(S)
6412	SCHEDULED SACRIFICE	11	(2)	LYMPH NODES-MANDIBULAR; BILATERAL; ENLARGED (TGL) ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS
6414	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6416	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6418	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6420	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS

INDIVIDUAL NECROPSY OBSERVATIONS

132-006 -A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

GROUP: 4 DOSE: 300 SEX: MALE

ANIMAL NUMBER	MODE OF DEATH	DEATH DAY	DEATH (WEEK)	OBSERVATION(S)
6421	SCHEDULED SACRIFICE	11	(2)	LIVER; MEDIAN LOBE; FOCUS; WHITE (TGL): 2 X 2 MM ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS
6423	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6425	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6427	SCHEDULED SACRIFICE	11	(2)	LUNGS W/BRONCHI; LEFT; FOCUS; DARK (TGL): 20 X 20 MM ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS
6429	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS

INDIVIDUAL NECROPSY OBSERVATIONS

132-006 -A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

GROUP: 4 DOSE: 300 SEX: FEMALE

ANIMAL NUMBER	MODE OF DEATH	DEATH DAY	DEATH (WEEK)	OBSERVATION(S)
6422	SCHEDULED SACRIFICE	11	(2)	LUNGS W/BRONCHI; APICAL LOBE; FOCUS; DARK (TGL): 4 X 3 MM ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS
6424	SCHEDULED SACRIFICE	11	(2)	LYMPH NODES-MANDIBULAR; BILATERAL; ENLARGED (TGL) ANY REMAINING PROTOCOL REQUIRED TISSUES, WHICH HAVE BEEN EXAMINED, HAVE NO VISIBLE LESIONS
6426	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6428	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS
6430	SCHEDULED SACRIFICE	11	(2)	NO VISIBLE LESIONS

Individual Animal Report (Histopathology)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 1
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 1	0	6391

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Mild.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 2
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 1	0	6393

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Trace.
Esophagus, Normal.
.Esophagus on Slide # 2 with lungs.
Liver.
Mononuclear Cell Infiltrate, Multifocal, Trace.
Mandibular lymph node.
Plasmacytosis, Mild.
Thymus.
Hemorrhage, Multifocal, Trace.
Kidneys.
Hydronephrosis, Trace, Unilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 3
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 1	0	6395

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Mild.
Mandibular lymph node, Missing.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 4
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 1	0	6397

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Mandibular lymph node.
Lymphoid Hyperplasia, Mild, Correlate #1.
Kidneys.
Hydronephrosis, Trace, Unilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 5
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 1	0	6399

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Trace.
Pancreas, Missing.
Mandibular lymph node.
Plasmacytosis, Trace.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 6
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 1	0	6392

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Kidneys.
Mineralization, Multifocal, Trace, Bilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 7
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 1	0	6394

Body Wt (g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

No Remarkable Observations.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 8
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 1	0	6396

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Mandibular lymph node, Missing.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 9
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 1	0	6398

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

No Remarkable Observations.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 10
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 1	0	6400

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Trace.
Kidneys.
Hydronephrosis, Trace, Unilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 11
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 2	100	6401

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Kidneys.
Hydronephrosis, Moderate, Unilateral, Correlate #1.

The following protocol tissues were not examined:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 12
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 2	100	6407

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Seminal vesicles, Normal, Correlate NP.

The following tissues were marked as NR:

Seminal vesicles.

The following protocol tissues were not examined:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 13
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 2	100	6409

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Intestine, small (jejunum).
Diverticulum, Correlate #1.

The following protocol tissues were not examined:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 14
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 3	300	6412

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Mandibular lymph node.
Plasmacytosis, Mild, Correlate #1.

The following protocol tissues were not examined:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 15
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 4	1000	6421

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Mild.
Liver, Normal, Correlate NP.
Sciatic nerve, Missing.
Kidneys.
Hydronephrosis, Trace, Unilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 16
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 4	1000	6423

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

No Remarkable Observations.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 17
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 4	1000	6425

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Mild.
Mandibular lymph node, Missing.
Kidneys.
Hydronephrosis, Trace, Unilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 18
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 4	1000	6427

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Mild.
Lungs (with bronchi).
Hemorrhage, Focal, Moderate, Correlate #1.
Kidneys.
Hydronephrosis, Trace, Unilateral.
Tubular Degeneration, Multifocal, Mild, Unilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID:	132-006		Page: 19
Species:	Rat	Individual Animal Report	Date: 07/26/00
Strain:	CD	Histopathology	Time: 11:20
Compound:	T-7485		ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Male	Group 4	1000	6429

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Trace.
Thyroid.
Ultimobranchial cyst, Focal, Trace, Unilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Epididymides, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mandibular lymph node, Mesenteric lymph node, Optic nerve, Pancreas, Parathyroid, Pituitary gland, Prostate gland, Salivary gland (mandibular), Sciatic nerve, Seminal vesicles, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Testes, Thymus, Tongue, Trachea, Urinary bladder, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 20
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 4	1000	6422

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Mild.
Mandibular lymph node.
Plasmacytosis, Mild.
Lungs (with bronchi).
Crystalline material, Focal, Mild, Correlate #1.
Inflammation, Focal, Chronic, Mild, Correlate #1.
Kidneys.
Mineralization, Multifocal, Trace, Bilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Mammary gland, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 21
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 4	1000	6424

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Stomach (glandular).
Edema, Multifocal, Mild.
Mandibular lymph node.
Lymphoid Hyperplasia, Mild, Correlate #1.
Thymus.
Hemorrhage, Multifocal, Trace.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 22
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 4	1000	6426

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Esophagus.
Inflammation, Focal, Chronic, Mild; Muscle.
Mandibular lymph node.
Plasmacytosis, Mild.
Trachea.
Inflammation, Focal, Chronic, Mild.
Kidneys.
Mineralization, Multifocal, Trace, Bilateral.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Eyes, Femur (including articular surface), Harderian gland, Heart, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Thyroid, Tongue, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 23
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 4	1000	6428

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Trace.
Esophagus.
Hemorrhage, Diffuse, Moderate.
Inflammation, Diffuse, Subacute, Moderate.
Parathyroid, Missing.
Thyroid.
Ultimobranchial cyst, Focal, Trace, Bilateral.
Mandibular lymph node.
Plasmacytosis, Trace.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Stomach (glandular), Thymus, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

Dose Range-Finding Toxicity Study in Sprague-Dawley Rats

Study ID: 132-006 Page: 24
Species: Rat Individual Animal Report Date: 07/26/00
Strain: CD Histopathology Time: 11:20
Compound: T-7485 ADP001 V3.0

ID Verified	Sex	Group	Dose (mg/kg)	Animal ID
No	Female	Group 4	1000	6430

Body Wt(g)	Pathologist	Date of Death	Removal Reason	Age in Days	Days on Test
	C.H. Frith	07/07/00	Terminal Sac		

The following histopathology observations were noted:

Heart.
Necrosis, Multifocal, Mild.
Stomach (glandular).
Inflammation, Focal, Acute, Mild.
Mandibular lymph node.
Lymphoid Hyperplasia, Mild.

The following tissues were marked as NR:

Adrenal glands, Aorta, Bone marrow (sternum), Brain (brain stem), Brain (cerebellum), Brain (cerebrum), Cervix/Vagina, Esophagus, Eyes, Femur (including articular surface), Harderian gland, Intestine, large (cecum), Intestine, large (colon), Intestine, large (rectum), Intestine, small (duodenum), Intestine, small (ileum), Intestine, small (jejunum), Kidneys, Lacrimal gland, Liver, Lungs (with bronchi), Mammary gland, Mesenteric lymph node, Optic nerve, Ovaries, Oviducts, Pancreas, Parathyroid, Pituitary gland, Salivary gland (mandibular), Sciatic nerve, Skeletal muscle, Skin (abdominal), Spinal cord (cervical), Spinal cord (lumbar), Spinal cord (thoracic), Spleen, Stomach (forestomach), Thymus, Thyroid, Tongue, Trachea, Urinary bladder, Uterus, Zymbal's gland.

(End of Report)

APPENDIX 3
INDIVIDUAL CLINICAL OBSERVATIONS

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

APPENDIX 3: CLINICAL OBSERVATIONS - INDIVIDUAL - MALE RATS

DOSE GROUP 1	0 (CONTROL) MG/KG/DAY
RAT #	DESCRIPTION
6391	NO ADVERSE FINDINGS
6393	NO ADVERSE FINDINGS
6395	NO ADVERSE FINDINGS
6397	NO ADVERSE FINDINGS
6399	NO ADVERSE FINDINGS
DOSE GROUP 2	100 MG/KG/DAY
RAT #	DESCRIPTION
6401	NO ADVERSE FINDINGS
6403	NO ADVERSE FINDINGS
6405	NO ADVERSE FINDINGS
6407	NO ADVERSE FINDINGS
6409	NO ADVERSE FINDINGS
DOSE GROUP 3	300 MG/KG/DAY
RAT #	DESCRIPTION
6411	NO ADVERSE FINDINGS
6413	NO ADVERSE FINDINGS
6415	NO ADVERSE FINDINGS
6417	NO ADVERSE FINDINGS
6419	NO ADVERSE FINDINGS
DOSE GROUP 4	1000 MG/KG/DAY
RAT #	DESCRIPTION
6421	NO ADVERSE FINDINGS
6423	NO ADVERSE FINDINGS
6425	NO ADVERSE FINDINGS
6427	NO ADVERSE FINDINGS
6429	NO ADVERSE FINDINGS

Animals with NO ADVERSE FINDINGS were normal until their scheduled sacrifice.

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

APPENDIX 3: CLINICAL OBSERVATIONS - INDIVIDUAL - FEMALE RATS

DOSE GROUP 1	0 (CONTROL) MG/KG/DAY
RAT #	DESCRIPTION
6392	NO ADVERSE FINDINGS
6394	NO ADVERSE FINDINGS
6396	NO ADVERSE FINDINGS
6398	NO ADVERSE FINDINGS
6400	NO ADVERSE FINDINGS
DOSE GROUP 2	100 MG/KG/DAY
RAT #	DESCRIPTION
6402	NO ADVERSE FINDINGS
6404	NO ADVERSE FINDINGS
6406	NO ADVERSE FINDINGS
6408	NO ADVERSE FINDINGS
6410	NO ADVERSE FINDINGS
DOSE GROUP 3	300 MG/KG/DAY
RAT #	DESCRIPTION
6412	NO ADVERSE FINDINGS
6414	NO ADVERSE FINDINGS
6416	NO ADVERSE FINDINGS
6418	NO ADVERSE FINDINGS
6420	NO ADVERSE FINDINGS
DOSE GROUP 4	1000 MG/KG/DAY
RAT #	DESCRIPTION
6422	NO ADVERSE FINDINGS
6424	NO ADVERSE FINDINGS
6426	NO ADVERSE FINDINGS
6428	NO ADVERSE FINDINGS
6430	NO ADVERSE FINDINGS

Animals with NO ADVERSE FINDINGS were normal until their scheduled sacrifice.

APPENDIX 4
INDIVIDUAL BODY WEIGHTS

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

APPENDIX 4: BODY WEIGHTS - INDIVIDUAL - MALE RATS

SD	1	7	10
RAT #	DOSE GROUP 1	0 (CONTROL) MG/KG/DAY	
6391	196.	247.	265.
6393	223.	272.	298.
6395	204.	246.	271.
6397	214.	256.	281.
6399	218.	271.	296.
SD	1	7	10
RAT #	DOSE GROUP 2	100 MG/KG/DAY	
6401	204.	246.	264.
6403	223.	275.	303.
6405	223.	282.	309.
6407	209.	232.	228.
6409	208.	254.	275.
SD	1	7	10
RAT #	DOSE GROUP 3	300 MG/KG/DAY	
6411	205.	258.	286.
6413	219.	271.	294.
6415	205.	250.	271.
6417	214.	265.	295.
6419	204.	251.	276.
SD	1	7	10
RAT #	DOSE GROUP 4	1000 MG/KG/DAY	
6421	206.	251.	273.
6423	222.	264.	289.
6425	212.	256.	285.
6427	212.	261.	290.
6429	213.	268.	294.

SD = STUDY DAY
All weights were reported in grams (G).

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

APPENDIX 4: BODY WEIGHTS - INDIVIDUAL - FEMALE RATS

SD	1	7	10
RAT #	DOSE GROUP 1	0 (CONTROL) MG/KG/DAY	
6392	160.	182.	192.
6394	182.	205.	217.
6396	163.	181.	186.
6398	169.	198.	206.
6400	170.	185.	192.
SD	1	7	10
RAT #	DOSE GROUP 2	100 MG/KG/DAY	
6402	156.	177.	181.
6404	163.	188.	196.
6406	173.	196.	202.
6408	171.	194.	204.
6410	164.	177.	183.
SD	1	7	10
RAT #	DOSE GROUP 3	300 MG/KG/DAY	
6412	156.	177.	184.
6414	173.	195.	208.
6416	166.	177.	183.
6418	168.	192.	200.
6420	166.	189.	196.
SD	1	7	10
RAT #	DOSE GROUP 4	1000 MG/KG/DAY	
6422	170.	186.	197.
6424	171.	189.	201.
6426	170.	198.	212.
6428	175.	201.	212.
6430	183.	202.	209.

SD = STUDY DAY
All weights were reported in grams (G).

APPENDIX 5
INDIVIDUAL FEED CONSUMPTION

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

APPENDIX 5: FEED CONSUMPTION - INDIVIDUAL - MALE RATS

	SD 1 - 7	7 - 10
RAT #	DOSE GROUP 1	0 (CONTROL) MG/KG/DAY
6391	164.	87.
6393	179.	94.
6395	160.	84.
6397	161.	89.
6399	174.	94.
	SD 1 - 7	7 - 10
RAT #	DOSE GROUP 2	100 MG/KG/DAY
6401	151.	76.
6403	184.	100.
6405	209.	109.
6407	138.	52.
6409	173.	91.
	SD 1 - 7	7 - 10
RAT #	DOSE GROUP 3	300 MG/KG/DAY
6411	165.	93.
6413	188.	88.
6415	175.	93.
6417	168.	95.
6419	167.	93.
	SD 1 - 7	7 - 10
RAT #	DOSE GROUP 4	1000 MG/KG/DAY
6421	153.	82.
6423	172.	88.
6425	159.	81.
6427	164.	95.
6429	172.	92.

SD = STUDY DAY
All weights were reported in grams (G).

PROTOCOL 132-006: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

APPENDIX 5: FEED CONSUMPTION - INDIVIDUAL - FEMALE RATS

SD	1 - 7	7 - 10
RAT #	DOSE GROUP 1	0 (CONTROL) MG/KG/DAY
6392	127.	60.
6394	146.	77.
6396	117.	58.
6398	130.	66.
6400	115.	63.
SD	1 - 7	7 - 10
RAT #	DOSE GROUP 2	100 MG/KG/DAY
6402	120.	56.
6404	126.	64.
6406	141.	65.
6408	134.	62.
6410	112.	56.
SD	1 - 7	7 - 10
RAT #	DOSE GROUP 3	300 MG/KG/DAY
6412	116.	57.
6414	125.	63.
6416	111.	56.
6418	141.	72.
6420	135.	66.
SD	1 - 7	7 - 10
RAT #	DOSE GROUP 4	1000 MG/KG/DAY
6422	121.	64.
6424	124.	63.
6426	130.	70.
6428	135.	66.
6430	146.	68.

SD = STUDY DAY
All weights were reported in grams (G).

APPENDIX 6
INDIVIDUAL HEMATOLOGY DATA

KEY TO HEMATOLOGY TABLES

ABBREVIATION	TERMINOLOGY	UNITS
WBC	White Blood Cells (Leukocytes)	10^3/cu mm
RBC	Red Blood Cells (Erythrocytes)	10^6/cu mm
HGB	Hemoglobin	g/dL
HCT	Hematocrit (Packed Cell Volume)	%
MCV	Mean Corpuscular Volume	fL or cu micron
MCH	Mean Corpuscular Hemoglobin	pg or picograms
MCHC	Mean Corpuscular Hemoglobin Concentration	%
PLT	Platelets	10^3/cu mm
NRBC	Nucleated Red Blood Cell Count	
Lymphocyte	Lymphocytes	10^3/cu mm
Segmented	Segmented Neutrophils	10^3/cu mm
	Bands	10^3/cu mm
	Monocytes	10^3/cu mm
Eosinophil	Eosinophils	10^3/cu mm
	Basophils	10^3/cu mm
Abnormal L	Abnormal Lymphocytes	10^3/cu mm
APTT	Activated Partial Thromboplastin Time	seconds
PT	Prothrombin time	seconds
Other	Other Cells	10^3/cu mm

APPENDIX 6

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 1-M								
6391	4.1	6.64	14.7	39.1	58.9	22.1	37.6	1075
6393	4.1	6.13	14.7	38.2	62.3	24.0	38.5	1277
6395	14.1	7.00	16.2	44.0	62.9	23.1	36.8	1313
6397	17.8	7.60	18.2	50.5	66.5	23.9	36.0	1215
6399	11.9	4.97	12.2	31.5	63.3	24.5	38.7	1173
MEAN	10.4	6.47	15.2	40.7	62.8	23.5	37.5	1211
SD	6.13	0.994	2.21	7.08	2.71	0.94	1.14	93.2
N	5	5	5	5	5	5	5	5
GROUP: 2-M								
6401	13.0	6.56	15.2	40.3	61.5	23.2	37.7	1326
6403	9.0	4.53	11.7	29.8	65.8	25.8	39.3	873
6405	17.2	6.79	16.0	43.5	64.1	23.6	36.8	1251
6407	17.7	6.61	15.2	40.8	61.8	23.0	37.3	1042
6409	6.7	6.65	15.2	41.4	62.2	22.9	36.7	995
MEAN	12.7	6.23	14.7	39.2	63.1	23.7	37.6	1097
SD	4.87	0.953	1.69	5.37	1.83	1.20	1.05	186.9
N	5	5	5	5	5	5	5	5
GROUP: 3-M								
6411	9.4	6.18	14.5	39.3	63.6	23.5	36.9	1313
6413	8.5	4.83	11.5	30.8	63.8	23.8	37.3	896
6415	5.3	7.01	15.1	42.8	61.0	21.5	35.3	1054
6417	12.3	6.75	15.4	42.0	62.2	22.8	36.7	890
6419	6.7	6.68	15.2	41.3	61.9	22.8	36.8	971
MEAN	8.4	6.29	14.3	39.2	62.5	22.9	36.6	1025
SD	2.68	0.870	1.62	4.89	1.18	0.89	0.76	174.3
N	5	5	5	5	5	5	5	5

LABCAT HE4.41c 20-JUL-2000

APPENDIX 6

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 4-M								
6421	8.9	6.24	14.7	39.6	63.5	23.6	37.1	1243
6423	14.7	6.19	14.7	39.1	63.1	23.7	37.6	1084
6425	11.9	6.44	15.0	40.8	63.3	23.3	36.8	1284
6427	10.5	5.93	14.5	38.4	64.8	24.5	37.8	1341
6429	15.8	6.71	15.8	43.2	64.4	23.5	36.6	1374
MEAN	12.4	6.30	14.9	40.2	63.8	23.7	37.2	1265
SD	2.87	0.292	0.51	1.88	0.74	0.46	0.51	113.2
N	5	5	5	5	5	5	5	5

LABCAT HE4.41c 20-JUL-2000

APPENDIX 6

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: MALE

Animal ID	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM	Eosinophil THSN/CU MM
GROUP: 1-M								
6391	13.1	17.2	0	3.6	0.5	0.0	0.0	0.0
6393	13.4	24.4	0	3.4	0.6	0.0	0.0	0.0
6395	13.9	23.2	0	12.5	1.6	0.0	0.0	0.0
6397	13.0	19.4	0	15.5	2.3	0.0	0.0	0.0
6399	13.1	20.9	0	11.2	0.5	0.0	0.2	0.0
MEAN	13.3	21.0	0	9.2	1.1	0.0	0.0	0.0
SD	0.37	2.89	0.0	5.47	0.82	0.00	0.09	0.00
N	5	5	5	5	5	5	5	5
GROUP: 2-M								
6401	12.8	20.6	0	10.8	2.0	0.0	0.1	0.0
6403	13.5	19.3	0	8.0	1.0	0.0	0.0	0.0
6405	13.9	18.5	0	15.3	1.7	0.0	0.0	0.2
6407	15.2	20.8	0	14.5	2.5	0.0	0.7	0.0
6409	13.5	19.6	0	5.6	1.0	0.0	0.0	0.1
MEAN	13.8	19.8	0	10.8	1.6	0.0	0.2	0.1
SD	0.89	0.95	0.0	4.15	0.65	0.00	0.30	0.09
N	5	5	5	5	5	5	5	5
GROUP: 3-M								
6411	13.3	20.4	0	8.8	0.6	0.0	0.0	0.0
6413	13.5	20.9	0	7.7	0.9	0.0	0.0	0.0
6415	14.6	34.0	0	4.2	1.0	0.0	0.1	0.0
6417	13.4	19.0	0	11.2	1.1	0.0	0.0	0.0
6419	12.9	24.2	0	6.2	0.4	0.0	0.1	0.0
MEAN	13.5	23.7	0	7.6	0.8	0.0	0.0	0.0
SD	0.63	6.07	0.0	2.64	0.29	0.00	0.05	0.00
N	5	5	5	5	5	5	5	5

LABCAT HE4.41c
20-JUL-2000

APPENDIX 6

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

Animal ID	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM	Eosinophil THSN/CU MM
GROUP: 4-M								
6421	13.0	23.3	0	8.0	0.8	0.0	0.0	0.1
6423	12.8	20.5	0	13.8	0.9	0.0	0.0	0.0
6425	13.9	33.3	1	10.7	1.2	0.0	0.0	0.0
6427	12.9	22.4	1	9.9	0.6	0.0	0.0	0.0
6429	13.2	20.0	0	14.5	1.3	0.0	0.0	0.0
MEAN	13.2	23.9	0	11.4	1.0	0.0	0.0	0.0
SD	0.44	5.43	0.5	2.72	0.29	0.00	0.00	0.04
N	5	5	5	5	5	5	5	5

LABCAT HE4.41c 20-JUL-2000

APPENDIX 6

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

Animal ID	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 1-M			
6391	0.0	0.0	0.0
6393	0.0	0.0	0.0
6395	0.0	0.0	0.0
6397	0.0	0.0	0.0
6399	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.00
N	5	5	5
GROUP: 2-M			
6401	0.0	0.1	0.0
6403	0.0	0.0	0.0
6405	0.0	0.0	0.0
6407	0.0	0.0	0.0
6409	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.04	0.00
N	5	5	5
GROUP: 3-M			
6411	0.0	0.0	0.0
6413	0.0	0.0	0.0
6415	0.0	0.0	0.0
6417	0.0	0.0	0.0
6419	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.00
N	5	5	5

LABCAT HE4.41c 20-JUL-2000

APPENDIX 6

Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: MALE

Animal ID	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 4-M			
6421	0.0	0.0	0.0
6423	0.0	0.0	0.0
6425	0.0	0.0	0.0
6427	0.0	0.0	0.0
6429	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.00
N	5	5	5

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Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 1-F								
6392	11.9	6.28	15.1	40.9	65.2	24.0	36.9	1682
6394	3.1	6.28	15.4	42.1	67.0	24.5	36.6	1239
6396	9.7	7.20	15.8	42.8	59.4	21.9	36.9	1136
6398	8.6	7.07	15.6	43.2	61.1	22.1	36.1	1074
6400	6.5	7.21	15.9	43.9	60.9	22.1	36.2	994
MEAN	8.0	6.81	15.6	42.6	62.7	22.9	36.5	1225
SD	3.34	0.485	0.32	1.14	3.22	1.23	0.38	270.7
N	5	5	5	5	5	5	5	5
GROUP: 2-F								
6402	4.8	6.53	14.9	40.7	62.4	22.8	36.6	1199
6404	4.2	7.11	16.4	45.1	63.5	23.1	36.4	1001
6406	5.2	6.22	14.6	39.6	63.6	23.5	36.9	1245
6408	14.2	6.50	15.5	41.9	64.4	23.8	37.0	959
6410	9.0	6.64	15.1	41.3	62.2	22.7	36.6	1049
MEAN	7.5	6.60	15.3	41.7	63.2	23.2	36.7	1091
SD	4.20	0.324	0.70	2.07	0.91	0.47	0.24	125.2
N	5	5	5	5	5	5	5	5
GROUP: 3-F								
6412	5.9	6.26	14.1	38.4	61.3	22.5	36.7	1050
6414	8.7	6.65	15.8	42.8	64.3	23.8	36.9	1317
6416	12.8	6.63	15.1	40.2	60.6	22.8	37.6	1100
6418	13.2	6.88	15.9	43.1	62.6	23.1	36.9	1172
6420	6.8	6.31	15.0	41.2	65.3	23.8	36.4	1114
MEAN	9.5	6.55	15.2	41.1	62.8	23.2	36.9	1151
SD	3.37	0.258	0.73	1.94	1.98	0.59	0.44	102.7
N	5	5	5	5	5	5	5	5

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Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: FEMALE

Animal ID	WBC THSN/CU MM	RBC MILL/CU MM	HGB GRAMS/DL	HCT %	MCV CU MICRONS	MCH PICO GRAMS	MCHC %	PLT THSN/CU MM
GROUP: 4-F								
6422	7.6	5.96	13.8	37.3	62.5	23.2	37.0	1363
6424	3.0	6.93	15.6	42.1	60.8	22.5	37.1	1197
6426	11.3	6.25	14.9	40.7	65.1	23.8	36.6	1547
6428	13.5	5.58	13.7	36.3	65.1	24.6	37.7	1389
6430	12.3	7.09	16.8	45.9	64.8	23.7	36.6	925
MEAN	9.5	6.36	15.0	40.5	63.7	23.6	37.0	1284
SD	4.27	0.640	1.30	3.86	1.93	0.78	0.45	236.1
N	5	5	5	5	5	5	5	5

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Study Report for Hematology

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

Animal ID	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM	Eosinophil THSN/CU MM
GROUP: 1-F								
6392	13.5	23.6	0	11.3	0.5	0.0	0.0	0.0
6394	12.3	18.2	0	2.7	0.3	0.0	0.1	0.0
6396	13.2	22.9	0	8.8	0.9	0.0	0.0	0.0
6398	14.0	17.2	0	8.3	0.3	0.0	0.0	0.1
6400	13.2	14.7	1	6.0	0.4	0.0	0.0	0.1
MEAN	13.2	19.3	0	7.4	0.5	0.0	0.0	0.0
SD	0.62	3.82	0.4	3.24	0.25	0.00	0.04	0.05
N	5	5	5	5	5	5	5	5
GROUP: 2-F								
6402	13.7	18.9	0	4.3	0.5	0.0	0.0	0.0
6404	13.5	25.8	0	4.0	0.2	0.0	0.0	0.0
6406	13.0	21.4	1	4.2	1.0	0.0	0.0	0.0
6408	13.3	20.5	0	13.1	1.0	0.0	0.0	0.1
6410	13.4	15.4	0	8.6	0.3	0.0	0.1	0.0
MEAN	13.4	20.4	0	6.8	0.6	0.0	0.0	0.0
SD	0.26	3.79	0.4	3.99	0.38	0.00	0.04	0.04
N	5	5	5	5	5	5	5	5
GROUP: 3-F								
6412	13.4	21.2	0	5.3	0.5	0.0	0.0	0.1
6414	13.1	20.8	0	7.9	0.8	0.0	0.0	0.0
6416	13.4	21.8	0	11.9	0.9	0.0	0.0	0.0
6418	13.5	30.3	0	12.7	0.3	0.0	0.0	0.3
6420	13.5	24.3	0	6.0	0.7	0.0	0.1	0.0
MEAN	13.4	23.7	0	8.8	0.6	0.0	0.0	0.1
SD	0.16	3.94	0.0	3.38	0.24	0.00	0.04	0.13
N	5	5	5	5	5	5	5	5

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INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

Animal ID	PT seconds	APTT seconds	NRBC COUNT	Lymphocyte THSN/CU MM	Segmented THSN/CU MM	Bands THSN/CU MM	Monocytes THSN/CU MM	Eosinophil THSN/CU MM
GROUP: 4-F								
6422	13.2	17.8	0	6.5	1.1	0.0	0.0	0.0
6424	13.8	16.6	0	2.0	1.0	0.0	0.0	0.0
6426	13.3	14.8	0	9.5	1.8	0.0	0.0	0.0
6428	13.6	17.1	0	12.3	1.1	0.0	0.1	0.0
6430	13.0	20.4	0	11.3	1.0	0.0	0.0	0.0
MEAN	13.4	17.3	0	8.3	1.2	0.0	0.0	0.0
SD	0.32	2.04	0.0	4.16	0.34	0.00	0.04	0.00
N	5	5	5	5	5	5	5	5

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INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: FEMALE

Animal ID	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 1-F			
6392	0.0	0.1	0.0
6394	0.0	0.0	0.0
6396	0.0	0.0	0.0
6398	0.0	0.0	0.0
6400	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.04	0.00
N	5	5	5
GROUP: 2-F			
6402	0.0	0.0	0.0
6404	0.0	0.0	0.0
6406	0.0	0.0	0.0
6408	0.0	0.0	0.0
6410	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.00
N	5	5	5
GROUP: 3-F			
6412	0.0	0.0	0.0
6414	0.0	0.0	0.0
6416	0.0	0.0	0.0
6418	0.0	0.0	0.0
6420	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.00
N	5	5	5

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INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: FEMALE
STUDY NO: 132-006

Animal ID	Basophils THSN/CU MM	Abnormal L THSN/CU MM	Other THSN/CU MM
GROUP: 4-F			
6422	0.0	0.0	0.0
6424	0.0	0.0	0.0
6426	0.0	0.0	0.0
6428	0.0	0.0	0.0
6430	0.0	0.0	0.0
MEAN	0.0	0.0	0.0
SD	0.00	0.00	0.00
N	5	5	5

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 1-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6391	Nucleated Red Cells	0	
	Lymphocytes	87	3.6
	Segmented Neutrophils	12	0.5
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		4.1
6393	Nucleated Red Cells	0	
	Lymphocytes	84	3.4
	Segmented Neutrophils	14	0.6
	Bands	0	0.0
	Monocytes	1	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.0
	Other	0	0.0
	WBC		4.1
6395	Nucleated Red Cells	0	
	Lymphocytes	89	12.5
	Segmented Neutrophils	11	1.6
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		14.1

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 1-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6397	Nucleated Red Cells	0	
	Lymphocytes	87	15.5
	Segmented Neutrophils	13	2.3
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		17.8
6399	Nucleated Red Cells	0	
	Lymphocytes	94	11.2
	Segmented Neutrophils	4	0.5
	Bands	0	0.0
	Monocytes	2	0.2
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		11.9

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 2-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6401	Nucleated Red Cells	0	
	Lymphocytes	83	10.8
	Segmented Neutrophils	15	2.0
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		13.0
6403	Nucleated Red Cells	0	
	Lymphocytes	89	8.0
	Segmented Neutrophils	11	1.0
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		9.0
6405	Nucleated Red Cells	0	
	Lymphocytes	89	15.3
	Segmented Neutrophils	10	1.7
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.2
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		17.2

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 2-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6407	Nucleated Red Cells	0	
	Lymphocytes	82	14.5
	Segmented Neutrophils	14	2.5
	Bands	0	0.0
	Monocytes	4	0.7
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		17.7
6409	Nucleated Red Cells	0	
	Lymphocytes	84	5.6
	Segmented Neutrophils	15	1.0
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		6.7

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 3-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6411	Nucleated Red Cells	0	
	Lymphocytes	94	8.8
	Segmented Neutrophils	6	0.6
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		9.4
6413	Nucleated Red Cells	0	
	Lymphocytes	90	7.7
	Segmented Neutrophils	10	0.9
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		8.5
6415	Nucleated Red Cells	0	
	Lymphocytes	80	4.2
	Segmented Neutrophils	18	1.0
	Bands	0	0.0
	Monocytes	2	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		5.3

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 3-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6417	Nucleated Red Cells	0	
	Lymphocytes	91	11.2
	Segmented Neutrophils	9	1.1
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.3
6419	Nucleated Red Cells	0	
	Lymphocytes	93	6.2
	Segmented Neutrophils	6	0.4
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		6.7

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 4-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6421	Nucleated Red Cells	0	
	Lymphocytes	90	8.0
	Segmented Neutrophils	9	0.8
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		8.9
6423	Nucleated Red Cells	0	
	Lymphocytes	94	13.8
	Segmented Neutrophils	6	0.9
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		14.7
6425	Nucleated Red Cells	1	
	Lymphocytes	90	10.7
	Segmented Neutrophils	10	1.2
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		11.9

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 4-M SEX: MALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6427	Nucleated Red Cells	1	
	Lymphocytes	94	9.9
	Segmented Neutrophils	6	0.6
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		10.5
6429	Nucleated Red Cells	0	
	Lymphocytes	92	14.5
	Segmented Neutrophils	8	1.3
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		15.8

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Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 1-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6392	Nucleated Red Cells	0	
	Lymphocytes	95	11.3
	Segmented Neutrophils	4	0.5
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	1	0.1
	Other	0	0.0
	WBC		11.9
6394	Nucleated Red Cells	0	
	Lymphocytes	88	2.7
	Segmented Neutrophils	9	0.3
	Bands	0	0.0
	Monocytes	2	0.1
	Eosinophils	1	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		3.1
6396	Nucleated Red Cells	0	
	Lymphocytes	91	8.8
	Segmented Neutrophils	9	0.9
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		9.7

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 1-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6398	Nucleated Red Cells	0	
	Lymphocytes	96	8.3
	Segmented Neutrophils	3	0.3
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		8.6
6400	Nucleated Red Cells	1	
	Lymphocytes	93	6.0
	Segmented Neutrophils	6	0.4
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		6.5

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 2-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6402	Nucleated Red Cells	0	
	Lymphocytes	89	4.3
	Segmented Neutrophils	10	0.5
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		4.8
6404	Nucleated Red Cells	0	
	Lymphocytes	95	4.0
	Segmented Neutrophils	4	0.2
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		4.2
6406	Nucleated Red Cells	1	
	Lymphocytes	80	4.2
	Segmented Neutrophils	20	1.0
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		5.2

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 2-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6408	Nucleated Red Cells	0	
	Lymphocytes	92	13.1
	Segmented Neutrophils	7	1.0
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		14.2
6410	Nucleated Red Cells	0	
	Lymphocytes	96	8.6
	Segmented Neutrophils	3	0.3
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		9.0

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WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 3-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6412	Nucleated Red Cells	0	
	Lymphocytes	90	5.3
	Segmented Neutrophils	9	0.5
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.1
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		5.9
6414	Nucleated Red Cells	0	
	Lymphocytes	91	7.9
	Segmented Neutrophils	9	0.8
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		8.7
6416	Nucleated Red Cells	0	
	Lymphocytes	93	11.9
	Segmented Neutrophils	7	0.9
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.8

LABCAT HE4.41c 20-JUL-2000

APPENDIX 6

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 3-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6418	Nucleated Red Cells	0	
	Lymphocytes	96	12.7
	Segmented Neutrophils	2	0.3
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	2	0.3
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		13.2
6420	Nucleated Red Cells	0	
	Lymphocytes	88	6.0
	Segmented Neutrophils	11	0.7
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		6.8

LABCAT HE4.41c 20-JUL-2000

APPENDIX 6

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 4-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6422	Nucleated Red Cells	0	
	Lymphocytes	86	6.5
	Segmented Neutrophils	14	1.1
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		7.6
6424	Nucleated Red Cells	0	
	Lymphocytes	66	2.0
	Segmented Neutrophils	33	1.0
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	1	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		3.0
6426	Nucleated Red Cells	0	
	Lymphocytes	84	9.5
	Segmented Neutrophils	16	1.8
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		11.3

LABCAT HE4.41c 20-JUL-2000

APPENDIX 6

Study Report for Hematology

WHITE DIFFERENTIAL DATA

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006 GROUP: 4-F SEX: FEMALE

Animal ID		TERMINAL CNT	TERMINAL ABS
6428	Nucleated Red Cells	0	
	Lymphocytes	91	12.3
	Segmented Neutrophils	8	1.1
	Bands	0	0.0
	Monocytes	1	0.1
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		13.5
6430	Nucleated Red Cells	0	
	Lymphocytes	92	11.3
	Segmented Neutrophils	8	1.0
	Bands	0	0.0
	Monocytes	0	0.0
	Eosinophils	0	0.0
	Basophils	0	0.0
	Abnormal Lymphocytes	0	0.0
	Other	0	0.0
	WBC		12.3

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APPENDIX 7
INDIVIDUAL CLINICAL CHEMISTRY DATA

KEY TO CLINICAL CHEMISTRY TABLES

ABBREVIATION	TERMINOLOGY	UNITS
ALP	Alkaline Phosphatase	U/L
AST	Aspartate Aminotransferase	U/L
ALT	Alanine Aminotransferase	U/L
CHOL	Cholesterol	mg/dL
GLU	Glucose	mg/dL
BUN	Blood Urea Nitrogen	mg/dL
CREAT	Creatinine	mg/dL
TRIG	Triglycerides	mg/dL
PHOS	Phosphorus (inorganic)	mg/dL
TP	Total Protein	g/dL
ALB	Albumin	g/dL
GLOB	Globulin	g/dL
A/G	Albumin/Globulin Ratio	
CA	Calcium	mg/dL
CL	Chloride	mEq/L or mmol/L
NA	Sodium	mEq/L or mmol/L
K	Potassium	mEq/L or mmol/L
GGT	Gamma-glutamyltransferase	U/L
T-BIL	Total Bilirubin	mg/dL

APPENDIX 7

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	ALT U/L
GROUP: 1-M								
6391	5.9	4.3	124	45	0.1	14	0.2	45
6393	6.2	4.3	147	52	0.1	16	0.3	36
6395	6.6	4.5	190	39	0.2	15	0.3	50
6397	6.4	4.4	199	50	0.1	16	0.3	49
6399	6.5	4.5	212	54	0.2	17	0.2	58
MEAN	6.3	4.4	174	48	0.1	16	0.3	48
SD	0.28	0.10	37.3	6.0	0.05	1.1	0.05	8.0
N	5	5	5	5	5	5	5	5
GROUP: 2-M								
6401	6.4	4.2	184	39	0.1	18	0.2	34
6403	5.3	3.7	135	42	0.1	13	0.2	39
6405	6.1	4.2	119	50	0.1	16	0.3	43
6407	5.7	3.3	154	44	0.1	17	0.2	52
6409	5.8	4.1	169	58	0.2	16	0.2	43
MEAN	5.9	3.9	152	47	0.1	16	0.2	42
SD	0.42	0.39	26.0	7.5	0.04	1.9	0.04	6.6
N	5	5	5	5	5	5	5	5
GROUP: 3-M								
6411	6.0	4.2	181	53	0.0	16	0.3	54
6413	5.7	4.1	182	31	0.2	13	0.2	47
6415	6.3	4.1	241	49	0.1	17	0.3	59
6417	6.3	4.3	192	60	0.1	14	0.2	49
6419	6.3	4.2	195	60	0.1	14	0.2	57
MEAN	6.1	4.2	198	51	0.1	15	0.2	53
SD	0.27	0.08	24.7	11.9	0.07	1.6	0.05	5.1
N	5	5	5	5	5	5	5	5

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Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT SEX: MALE
STUDY NO: 132-006

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	ALT U/L
GROUP: 4-M								
6421	6.0	4.3	152	32	0.1	14	0.3	60
6423	6.3	4.4	150	47	0.1	12	0.2	49
6425	6.0	4.4	266	31	0.2	22	0.3	63
6427	6.5	4.8	254	39	0.1	21	0.4	63
6429	6.0	4.4	220	57	0.1	16	0.3	49
MEAN	6.2	4.5	208	41	0.1	17	0.3	57
SD	0.23	0.19	55.1	10.9	0.04	4.4	0.07	7.2
N	5	5	5	5	5	5	5	5

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APPENDIX 7

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: MALE

Animal ID	AST U/L	ALP U/L	GGT U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 1-M								
6391	149	254	0	10.8	11.9	35	151	6.1
6393	80	295	0	11.4	13.7	16	147	9.0
6395	207	296	0	11.9	15.0	13	149	7.5
6397	126	412	0	12.8	14.8	19	148	8.3
6399	303	341	0	12.8	16.4	53	148	9.2
MEAN	173	320	0	11.9	14.4	27	149	8.0
SD	85.9	60.1	0.0	0.88	1.68	16.7	1.5	1.26
N	5	5	5	5	5	5	5	5
GROUP: 2-M								
6401	107	338	4	11.2	12.5	19	151	6.5
6403	85	194	2	11.2	12.3	18	150	6.1
6405	203	376	3	12.4	18.9	17	152	8.9
6407	362	200	1	12.5	14.9	21	148	9.7
6409	186	345	3	12.7	16.6	35	151	8.3
MEAN	189	291	3	12.0	15.0	22	150	7.9
SD	109.2	86.7	1.1	0.74	2.80	7.4	1.5	1.55
N	5	5	5	5	5	5	5	5
GROUP: 3-M								
6411	92	265	6	10.8	11.8	16	150	6.7
6413	209	283	6	11.3	14.2	22	147	7.8
6415	265	254	4	12.1	16.0	22	149	7.5
6417	216	385	4	12.5	17.5	28	150	8.5
6419	154	267	0	12.9	16.1	31	148	10.1
MEAN	187	291	4	11.9	15.1	24	149	8.1
SD	66.2	53.7	2.4	0.86	2.19	5.8	1.3	1.28
N	5	5	5	5	5	5	5	5

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Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: MALE

Animal ID	AST U/L	ALP U/L	GGT U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 4-M								
6421	148	324	0	11.1	12.4	17	151	6.1
6423	104	359	2	11.5	12.0	33	148	6.7
6425	285	397	3	12.3	17.2	24	147	8.8
6427	208	381	2	12.5	16.4	29	150	7.5
6429	91	292	7	12.5	15.4	58	151	7.2
MEAN	167	351	3	12.0	14.7	32	149	7.3
SD	80.2	42.7	2.6	0.64	2.36	15.6	1.8	1.01
N	5	5	5	5	5	5	5	5

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Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: MALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 1-M			
6391	86	1.6	2.7
6393	86	1.9	2.3
6395	88	2.1	2.1
6397	86	2.0	2.2
6399	88	2.0	2.2
MEAN	87	1.9	2.3
SD	1.1	0.19	0.23
N	5	5	5
GROUP: 2-M			
6401	92	2.2	1.9
6403	89	1.6	2.3
6405	90	1.9	2.2
6407	90	2.4	1.4
6409	86	1.7	2.4
MEAN	89	2.0	2.0
SD	2.2	0.34	0.40
N	5	5	5
GROUP: 3-M			
6411	90	1.8	2.3
6413	90	1.6	2.6
6415	91	2.2	1.9
6417	92	2.0	2.2
6419	88	2.1	2.0
MEAN	90	1.9	2.2
SD	1.5	0.24	0.27
N	5	5	5

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Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: MALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 4-M			
6421	87	1.7	2.5
6423	87	1.9	2.3
6425	89	1.6	2.8
6427	90	1.7	2.8
6429	88	1.6	2.8
MEAN	88	1.7	2.6
SD	1.3	0.12	0.23
N	5	5	5

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Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: FEMALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	ALT U/L
GROUP: 1-F								
6392	6.2	4.3	112	71	0.1	16	0.2	45
6394	7.0	5.2	118	63	0.1	15	0.3	46
6396	6.5	4.4	104	40	0.2	16	0.3	39
6398	6.4	4.5	78	44	0.2	15	0.3	56
6400	6.4	4.6	123	63	0.2	17	0.3	54
MEAN	6.5	4.6	107	56	0.2	16	0.3	48
SD	0.30	0.35	17.7	13.4	0.05	0.8	0.04	7.0
N	5	5	5	5	5	5	5	5
GROUP: 2-F								
6402	6.4	4.6	101	55	0.2	16	0.3	40
6404	6.5	4.8	97	70	0.2	19	0.3	49
6406	6.4	4.7	115	60	0.1	16	0.2	41
6408	5.9	4.3	140	67	0.2	15	0.3	42
6410	6.3	4.2	106	67	0.2	15	0.2	71
MEAN	6.3	4.5	112	64	0.2	16	0.3	49
SD	0.23	0.26	17.1	6.1	0.04	1.6	0.05	13.0
N	5	5	5	5	5	5	5	5
GROUP: 3-F								
6412	6.1	4.3	106	71	0.2	19	0.3	41
6414	6.5	4.6	147	63	0.1	16	0.3	44
6416	5.5	3.8	109	53	0.1	18	0.3	46
6418	6.5	4.5	123	58	0.2	13	0.3	63
6420	6.5	4.5	103	51	0.1	15	0.2	49
MEAN	6.2	4.3	118	59	0.1	16	0.3	49
SD	0.44	0.32	18.1	8.1	0.05	2.4	0.04	8.6
N	5	5	5	5	5	5	5	5

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Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: FEMALE

Animal ID	TP g/dL	ALB g/dL	GLU mg/dL	CHOL mg/dL	T-BIL mg/dL	BUN mg/dL	CREAT mg/dL	ALT U/L
GROUP: 4-F								
6422	6.5	4.4	161	65	0.1	16	0.2	38
6424	6.3	4.6	133	53	0.1	16	0.3	53
6426	6.1	4.5	195	47	0.1	18	0.2	45
6428	6.1	4.6	150	81	0.2	14	0.3	41
6430	6.2	4.2	174	82	0.2	14	0.2	64
MEAN	6.2	4.5	163	66	0.1	16	0.2	48
SD	0.17	0.17	23.5	15.9	0.05	1.7	0.05	10.5
N	5	5	5	5	5	5	5	5

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APPENDIX 7

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: FEMALE

Animal ID	AST U/L	ALP U/L	GGT U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 1-F								
6392	126	196	3	11.2	12.3	16	148	8.1
6394	115	237	3	12.5	15.0	49	148	7.7
6396	208	197	4	12.9	17.2	24	147	9.0
6398	250	257	4	11.8	15.6	14	147	8.2
6400	362	218	1	12.3	15.0	29	147	9.0
MEAN	212	221	3	12.1	15.0	26	147	8.4
SD	101.0	26.3	1.2	0.66	1.77	14.0	0.5	0.58
N	5	5	5	5	5	5	5	5
GROUP: 2-F								
6402	286	168	1	10.7	12.5	18	152	7.3
6404	384	221	1	11.9	14.3	24	148	9.1
6406	132	127	1	11.5	12.0	35	149	6.1
6408	252	188	4	12.6	14.8	25	147	9.9
6410	298	251	1	12.5	16.8	28	149	10.3
MEAN	270	191	2	11.8	14.1	26	149	8.5
SD	91.4	47.8	1.3	0.78	1.92	6.2	1.9	1.79
N	5	5	5	5	5	5	5	5
GROUP: 3-F								
6412	252	164	3	12.1	14.3	21	149	7.2
6414	105	181	4	12.7	18.8	21	150	8.7
6416	185	149	1	12.8	14.5	29	149	7.9
6418	412	74	0	13.3	17.0	35	147	9.3
6420	250	130	2	13.5	18.3	22	145	11.0
MEAN	241	140	2	12.9	16.6	26	148	8.8
SD	113.0	41.2	1.6	0.55	2.10	6.2	2.0	1.45
N	5	5	5	5	5	5	5	5

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APPENDIX 7

Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: FEMALE

Animal ID	AST U/L	ALP U/L	GGT U/L	CA mg/dL	PHOS mg/dL	TRIG mg/dL	NA mmol/L	K mmol/L
GROUP: 4-F								
6422	146	198	4	12.0	12.9	22	147	6.9
6424	298	180	4	12.2	16.2	19	149	10.2
6426	82	163	1	13.1	16.8	47	147	9.4
6428	204	135	0	13.4	16.9	33	148	8.8
6430	487	217	0	13.5	16.3	57	147	8.9
MEAN	243	179	2	12.8	15.8	36	148	8.8
SD	157.6	31.6	2.0	0.69	1.66	16.2	0.9	1.22
N	5	5	5	5	5	5	5	5

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Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006

SEX: FEMALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 1-F			
6392	93	1.9	2.3
6394	87	1.8	2.9
6396	94	2.1	2.1
6398	91	1.9	2.4
6400	92	1.8	2.6
MEAN	91	1.9	2.5
SD	2.7	0.12	0.30
N	5	5	5
GROUP: 2-F			
6402	95	1.8	2.6
6404	92	1.7	2.8
6406	90	1.7	2.8
6408	94	1.6	2.7
6410	92	2.1	2.0
MEAN	93	1.8	2.6
SD	1.9	0.19	0.33
N	5	5	5
GROUP: 3-F			
6412	91	1.8	2.4
6414	93	1.9	2.4
6416	94	1.7	2.2
6418	92	2.0	2.2
6420	91	2.0	2.2
MEAN	92	1.9	2.3
SD	1.3	0.13	0.11
N	5	5	5

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Study Report for Clinical Chemistry

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: TERMINAL

STUDY ID: REPEATED DOSE/RAT
STUDY NO: 132-006
SEX: FEMALE

Animal ID	CL mmol/L	GLOB g/dL	A/G none
GROUP: 4-F			
6422	88	2.1	2.1
6424	92	1.7	2.7
6426	91	1.6	2.8
6428	91	1.5	3.1
6430	91	2.0	2.1
MEAN	91	1.8	2.6
SD	1.5	0.26	0.44
N	5	5	5

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APPENDIX 8
INDIVIDUAL ORGAN WEIGHTS

APPENDIX 8

INDIVIDUAL ORGAN WEIGHTS

STUDY: T-7485
SEX: MALE GROUP: 1-M
FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES

ANIMAL ID:	6391	6393	6395	6397	6399
BODY WEIGHT (G)	237.000	262.000	243.000	245.000	263.000
ADRENAL GLANDS (G)	0.066	0.075	0.074	0.070	0.066
% BODY WEIGHT	0.028	0.029	0.030	0.029	0.025
% BRAIN WEIGHT	3.393	3.874	4.011	3.564	3.115
BRAIN (G)	1.945	1.936	1.845	1.964	2.119
% BODY WEIGHT	0.821	0.739	0.759	0.802	0.806
HEART (G)	1.079	1.188	1.159	1.185	1.180
% BODY WEIGHT	0.455	0.453	0.477	0.484	0.449
% BRAIN WEIGHT	55.476	61.364	62.818	60.336	55.687
KIDNEYS (G)	2.445	2.835	2.448	2.496	2.678
% BODY WEIGHT	1.032	1.082	1.007	1.019	1.018
% BRAIN WEIGHT	125.707	146.436	132.683	127.088	126.380
LIVER (G)	8.607	9.736	8.870	9.041	10.438
% BODY WEIGHT	3.632	3.716	3.650	3.690	3.969
% BRAIN WEIGHT	442.519	502.893	480.759	460.336	492.591
SPLEEN (G)	0.550	0.708	0.480	0.590	0.659
% BODY WEIGHT	0.232	0.270	0.198	0.241	0.251
% BRAIN WEIGHT	28.278	36.570	26.016	30.041	31.100
TESTES (G)	2.672	2.563	3.088	2.824	2.941
% BODY WEIGHT	1.127	0.978	1.271	1.153	1.118
% BRAIN WEIGHT	137.378	132.386	167.371	143.788	138.792
THYMUS (G)	0.458	0.781	0.643	0.826	0.627
% BODY WEIGHT	0.193	0.298	0.265	0.337	0.238
% BRAIN WEIGHT	23.548	40.341	34.851	42.057	29.589

REDFIELD LABORATORIES STUDY NUMBER 132-006

APPENDIX 8

INDIVIDUAL ORGAN WEIGHTS

STUDY: T-7485
SEX: MALE GROUP: 2-M
FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES

ANIMAL ID:	6401	6403	6405	6407	6409
BODY WEIGHT (G)	231.000	269.000	274.000	211.000	246.000
ADRENAL GLANDS (G)	0.075	0.077	0.109	0.091	0.069
% BODY WEIGHT	0.032	0.029	0.040	0.043	0.028
% BRAIN WEIGHT	3.904	4.096	5.758	4.461	3.275
BRAIN (G)	1.921	1.880	1.893	2.040	2.107
% BODY WEIGHT	0.832	0.699	0.691	0.967	0.857
HEART (G)	0.981	1.258	1.288	1.135	1.116
% BODY WEIGHT	0.425	0.468	0.470	0.538	0.454
% BRAIN WEIGHT	51.067	66.915	68.040	55.637	52.966
KIDNEYS (G)	2.739	2.956	2.710	2.541	2.381
% BODY WEIGHT	1.186	1.099	0.989	1.204	0.968
% BRAIN WEIGHT	142.582	157.234	143.159	124.559	113.004
LIVER (G)	9.011	10.622	11.484	9.140	9.802
% BODY WEIGHT	3.901	3.949	4.191	4.332	3.985
% BRAIN WEIGHT	469.079	565.000	606.656	448.039	465.211
SPLEEN (G)	0.458	0.845	0.862	0.641	0.658
% BODY WEIGHT	0.198	0.314	0.315	0.304	0.267
% BRAIN WEIGHT	23.842	44.947	45.536	31.422	31.229
TESTES (G)	2.886	2.816	2.887	2.950	2.652
% BODY WEIGHT	1.249	1.047	1.054	1.398	1.078
% BRAIN WEIGHT	150.234	149.787	152.509	144.608	125.866
THYMUS (G)	0.546	0.493	0.753	0.528	0.639
% BODY WEIGHT	0.236	0.183	0.275	0.250	0.260
% BRAIN WEIGHT	28.423	26.223	39.778	25.882	30.327

REDFIELD LABORATORIES STUDY NUMBER 132-006

APPENDIX 8

INDIVIDUAL ORGAN WEIGHTS

STUDY: T-7485
SEX: MALE GROUP: 3-M
FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES

ANIMAL ID:	6411	6413	6415	6417	6419
BODY WEIGHT (G)	263.000	263.000	241.000	259.000	248.000
ADRENAL GLANDS (G)	0.091	0.096	0.074	0.064	0.058
% BODY WEIGHT	0.035	0.037	0.031	0.025	0.023
% BRAIN WEIGHT	4.367	4.580	3.842	3.182	3.100
BRAIN (G)	2.084	2.096	1.926	2.011	1.871
% BODY WEIGHT	0.792	0.797	0.799	0.776	0.754
HEART (G)	1.012	1.234	1.010	1.142	0.967
% BODY WEIGHT	0.385	0.469	0.419	0.441	0.390
% BRAIN WEIGHT	48.560	58.874	52.440	56.788	51.684
KIDNEYS (G)	2.533	2.796	2.383	2.656	2.536
% BODY WEIGHT	0.963	1.063	0.989	1.025	1.023
% BRAIN WEIGHT	121.545	133.397	123.728	132.074	135.543
LIVER (G)	10.029	9.944	10.308	11.443	11.143
% BODY WEIGHT	3.813	3.781	4.277	4.418	4.493
% BRAIN WEIGHT	481.238	474.428	535.203	569.020	595.564
SPLEEN (G)	0.583	0.708	0.637	0.771	0.561
% BODY WEIGHT	0.222	0.269	0.264	0.298	0.226
% BRAIN WEIGHT	27.975	33.779	33.074	38.339	29.984
TESTES (G)	2.663	2.675	2.619	2.967	2.430
% BODY WEIGHT	1.013	1.017	1.087	1.146	0.980
% BRAIN WEIGHT	127.783	127.624	135.981	147.539	129.877
THYMUS (G)	0.599	0.793	0.515	0.435	0.474
% BODY WEIGHT	0.228	0.302	0.214	0.168	0.191
% BRAIN WEIGHT	28.743	37.834	26.739	21.631	25.334

REDFIELD LABORATORIES STUDY NUMBER 132-006

APPENDIX 8

INDIVIDUAL ORGAN WEIGHTS

STUDY: T-7485
SEX: MALE GROUP: 4-M
FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES

ANIMAL ID:	6421	6423	6425	6427	6429
BODY WEIGHT (G)	242.000	260.000	251.000	253.000	265.000
ADRENAL GLANDS (G)	0.084	0.072	0.070	0.073	0.080
% BODY WEIGHT	0.035	0.028	0.028	0.029	0.030
% BRAIN WEIGHT	4.428	3.863	3.714	3.702	4.296
BRAIN (G)	1.897	1.864	1.885	1.972	1.862
% BODY WEIGHT	0.784	0.717	0.751	0.779	0.703
HEART (G)	1.112	1.148	1.017	1.195	1.196
% BODY WEIGHT	0.460	0.442	0.405	0.472	0.451
% BRAIN WEIGHT	58.619	61.588	53.952	60.598	64.232
KIDNEYS (G)	2.608	2.545	2.350	2.641	2.639
% BODY WEIGHT	1.078	0.979	0.936	1.044	0.996
% BRAIN WEIGHT	137.480	136.534	124.668	133.925	141.729
LIVER (G)	10.846	11.523	13.150	15.106	13.000
% BODY WEIGHT	4.482	4.432	5.239	5.971	4.906
% BRAIN WEIGHT	571.745	618.187	697.613	766.024	698.174
SPLEEN (G)	0.678	0.664	0.548	0.596	0.764
% BODY WEIGHT	0.280	0.255	0.218	0.236	0.288
% BRAIN WEIGHT	35.741	35.622	29.072	30.223	41.031
TESTES (G)	2.767	3.021	2.782	3.083	2.931
% BODY WEIGHT	1.143	1.162	1.108	1.219	1.106
% BRAIN WEIGHT	145.862	162.071	147.586	156.339	157.411
THYMUS (G)	0.573	0.550	0.660	0.665	0.652
% BODY WEIGHT	0.237	0.212	0.263	0.263	0.246
% BRAIN WEIGHT	30.206	29.506	35.013	33.722	35.016

REDFIELD LABORATORIES STUDY NUMBER 132-006

APPENDIX 8

INDIVIDUAL ORGAN WEIGHTS

STUDY: T-7485
SEX: FEMALE GROUP: 1-F
FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES

ANIMAL ID:	6392	6394	6396	6398	6400
BODY WEIGHT (G)	173.000	195.000	169.000	186.000	174.000
ADRENAL GLANDS (G)	0.064	0.100	0.074	0.078	0.066
% BODY WEIGHT	0.037	0.051	0.044	0.042	0.038
% BRAIN WEIGHT	3.482	5.297	3.909	4.673	3.524
BRAIN (G)	1.838	1.888	1.893	1.669	1.873
% BODY WEIGHT	1.062	0.968	1.120	0.897	1.076
HEART (G)	0.786	0.944	0.758	0.802	0.761
% BODY WEIGHT	0.454	0.484	0.449	0.431	0.437
% BRAIN WEIGHT	42.764	50.000	40.042	48.053	40.630
KIDNEYS (G)	1.759	2.241	1.645	1.718	1.684
% BODY WEIGHT	1.017	1.149	0.973	0.924	0.968
% BRAIN WEIGHT	95.702	118.697	86.899	102.936	89.909
LIVER (G)	6.366	8.073	6.189	7.116	6.331
% BODY WEIGHT	3.680	4.140	3.662	3.826	3.639
% BRAIN WEIGHT	346.355	427.595	326.941	426.363	338.014
OVARIES (G)	0.076	0.103	0.118	0.081	0.069
% BODY WEIGHT	0.044	0.053	0.070	0.044	0.040
% BRAIN WEIGHT	4.135	5.456	6.233	4.853	3.684
SPLEEN (G)	0.494	0.509	0.394	0.438	0.387
% BODY WEIGHT	0.286	0.261	0.233	0.235	0.222
% BRAIN WEIGHT	26.877	26.960	20.814	26.243	20.662
THYMUS (G)	0.565	0.709	0.584	0.619	0.551
% BODY WEIGHT	0.327	0.364	0.346	0.333	0.317
% BRAIN WEIGHT	30.740	37.553	30.851	37.088	29.418

REDFIELD LABORATORIES STUDY NUMBER 132-006

APPENDIX 8

INDIVIDUAL ORGAN WEIGHTS

STUDY: T-7485
SEX: FEMALE GROUP: 2-F
FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES

ANIMAL ID:	6402	6404	6406	6408	6410
BODY WEIGHT (G)	164.000	176.000	178.000	183.000	165.000
ADRENAL GLANDS (G)	0.069	0.060	0.064	0.098	0.064
% BODY WEIGHT	0.042	0.034	0.036	0.054	0.039
% BRAIN WEIGHT	4.012	3.343	3.393	5.379	3.569
BRAIN (G)	1.720	1.795	1.886	1.822	1.793
% BODY WEIGHT	1.049	1.020	1.060	0.996	1.087
HEART (G)	0.826	0.739	0.849	0.908	0.729
% BODY WEIGHT	0.504	0.420	0.477	0.496	0.442
% BRAIN WEIGHT	48.023	41.170	45.016	49.835	40.658
KIDNEYS (G)	1.648	1.567	1.770	1.936	1.803
% BODY WEIGHT	1.005	0.890	0.994	1.058	1.093
% BRAIN WEIGHT	95.814	87.298	93.849	106.257	100.558
LIVER (G)	6.377	6.389	6.869	7.090	6.124
% BODY WEIGHT	3.888	3.630	3.859	3.874	3.712
% BRAIN WEIGHT	370.756	355.933	364.210	389.133	341.551
OVARIES (G)	0.076	0.075	0.079	0.102	0.054
% BODY WEIGHT	0.046	0.043	0.044	0.056	0.033
% BRAIN WEIGHT	4.419	4.178	4.189	5.598	3.012
SPLEEN (G)	0.398	0.413	0.390	0.437	0.473
% BODY WEIGHT	0.243	0.235	0.219	0.239	0.287
% BRAIN WEIGHT	23.140	23.008	20.679	23.985	26.380
THYMUS (G)	0.560	0.429	0.488	0.620	0.388
% BODY WEIGHT	0.341	0.244	0.274	0.339	0.235
% BRAIN WEIGHT	32.558	23.900	25.875	34.029	21.640

REDFIELD LABORATORIES STUDY NUMBER 132-006

APPENDIX 8

INDIVIDUAL ORGAN WEIGHTS

STUDY: T-7485
SEX: FEMALE GROUP: 3-F
FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES

ANIMAL ID:	6412	6414	6416	6418	6420
BODY WEIGHT (G)	168.000	187.000	169.000	182.000	178.000
ADRENAL GLANDS (G)	0.071	0.077	0.068	0.071	0.063
% BODY WEIGHT	0.042	0.041	0.040	0.039	0.035
% BRAIN WEIGHT	3.667	3.951	3.738	4.002	3.364
BRAIN (G)	1.936	1.949	1.819	1.774	1.873
% BODY WEIGHT	1.152	1.042	1.076	0.975	1.052
HEART (G)	0.700	0.837	0.709	0.950	0.848
% BODY WEIGHT	0.417	0.448	0.420	0.522	0.476
% BRAIN WEIGHT	36.157	42.945	38.977	53.551	45.275
KIDNEYS (G)	1.723	1.803	1.790	1.914	1.753
% BODY WEIGHT	1.026	0.964	1.059	1.052	0.985
% BRAIN WEIGHT	88.998	92.509	98.406	107.892	93.593
LIVER (G)	6.362	7.367	5.870	8.102	8.105
% BODY WEIGHT	3.787	3.940	3.473	4.452	4.553
% BRAIN WEIGHT	328.616	377.989	322.705	456.708	432.728
OVARIES (G)	0.087	0.102	0.081	0.064	0.101
% BODY WEIGHT	0.052	0.055	0.048	0.035	0.057
% BRAIN WEIGHT	4.494	5.233	4.453	3.608	5.392
SPLEEN (G)	0.440	0.479	0.391	0.495	0.516
% BODY WEIGHT	0.262	0.256	0.231	0.272	0.290
% BRAIN WEIGHT	22.727	24.577	21.495	27.903	27.549
THYMUS (G)	0.597	0.669	0.470	0.520	0.591
% BODY WEIGHT	0.355	0.358	0.278	0.286	0.332
% BRAIN WEIGHT	30.837	34.325	25.838	29.312	31.554

REDFIELD LABORATORIES STUDY NUMBER 132-006

APPENDIX 8

INDIVIDUAL ORGAN WEIGHTS

STUDY: T-7485
SEX: FEMALE GROUP: 4-F
FATES: SCHEDULED SACRIFICE ALL DAYS ALL BALANCES

ANIMAL ID:	6422	6424	6426	6428	6430
BODY WEIGHT (G)	178.000	181.000	191.000	193.000	187.000
ADRENAL GLANDS (G)	0.066	0.083	0.077	0.087	0.091
% BODY WEIGHT	0.037	0.046	0.040	0.045	0.049
% BRAIN WEIGHT	3.616	4.568	4.100	4.825	4.817
BRAIN (G)	1.825	1.817	1.878	1.803	1.889
% BODY WEIGHT	1.025	1.004	0.983	0.934	1.010
HEART (G)	0.759	0.854	0.961	0.989	0.944
% BODY WEIGHT	0.426	0.472	0.503	0.512	0.505
% BRAIN WEIGHT	41.589	47.001	51.171	54.853	49.974
KIDNEYS (G)	1.697	1.805	2.204	2.270	1.936
% BODY WEIGHT	0.953	0.997	1.154	1.176	1.035
% BRAIN WEIGHT	92.986	99.340	117.359	125.901	102.488
LIVER (G)	7.776	7.265	8.820	9.532	8.402
% BODY WEIGHT	4.369	4.014	4.618	4.939	4.493
% BRAIN WEIGHT	426.082	399.835	469.649	528.674	444.786
OVARIES (G)	0.099	0.085	0.104	0.098	0.098
% BODY WEIGHT	0.056	0.047	0.054	0.051	0.052
% BRAIN WEIGHT	5.425	4.678	5.538	5.435	5.188
SPLEEN (G)	0.475	0.440	0.506	0.489	0.623
% BODY WEIGHT	0.267	0.243	0.265	0.253	0.333
% BRAIN WEIGHT	26.027	24.216	26.944	27.121	32.980
THYMUS (G)	0.596	0.466	0.695	0.529	0.567
% BODY WEIGHT	0.335	0.257	0.364	0.274	0.303
% BRAIN WEIGHT	32.658	25.647	37.007	29.340	30.016

APPENDIX 9
FORMULATED TEST MATERIAL STABILITY DATA

Southern Research Institute

Project: A098.1

32 Day Stability Analysis Summary
Perfluorobutane Sulfonate (1% CMC)

	Dose Levels* (mg/mL)			
Day	0 mg/mL	4 mg/mL	12 mg/mL	40 mg/mL
1	ND	4.57	8.20	39.91
7	ND	4.12	10.80	39.79
14	ND**	4.13	11.48	40.38
21	ND	3.74	11.47	38.86
28	——***	3.80	11.54	39.63
32	——***	3.89	11.62	39.31

ND = not detected

* Results represent average of duplicate analysis

** One of the day 14 controls (0 mg/mL) was inadvertently contaminated during preparation. Result based on single analysis.

*** No sample received

TurboQuan™, version 1.0
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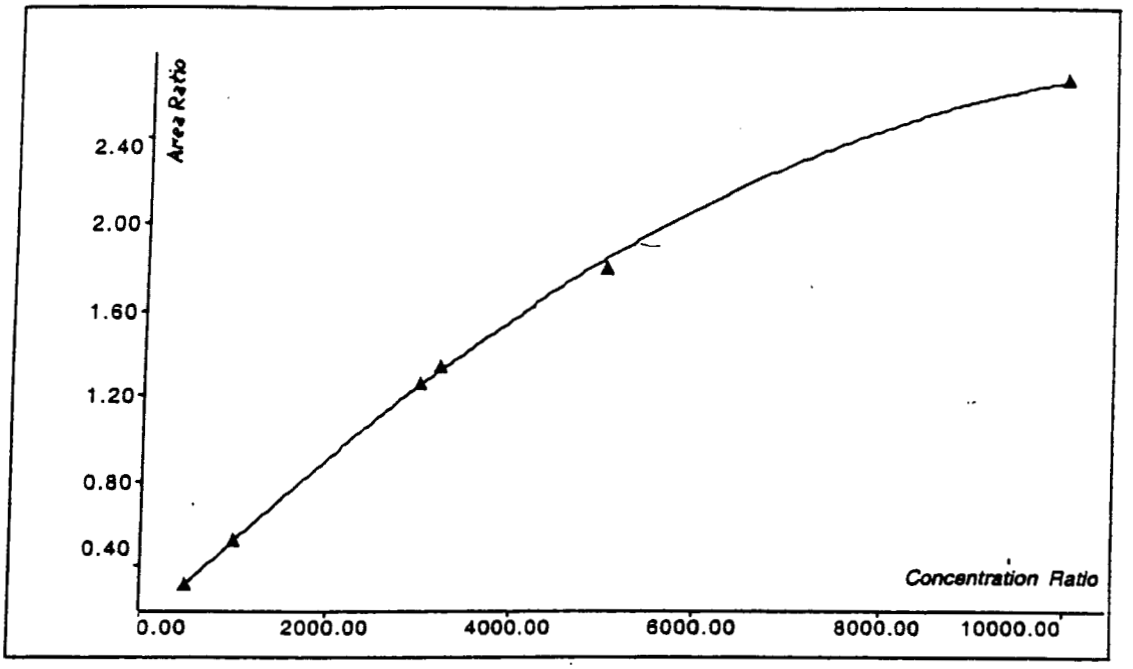
Printed by: greg gorman



Compound:	PFBS 40mg/ml dose
Internal Standard:	IS
Fit:	Quadratic
Fit Parameter:	Area Ratio
Weighting:	1÷X
Equation:	y = - 1.8300e-8 * x ² x +0.00044 * x + 0.09467
Correlation Coefficient (r):	0.999770
Chi Square:	0.00000

TurboQuan™, version 1.0
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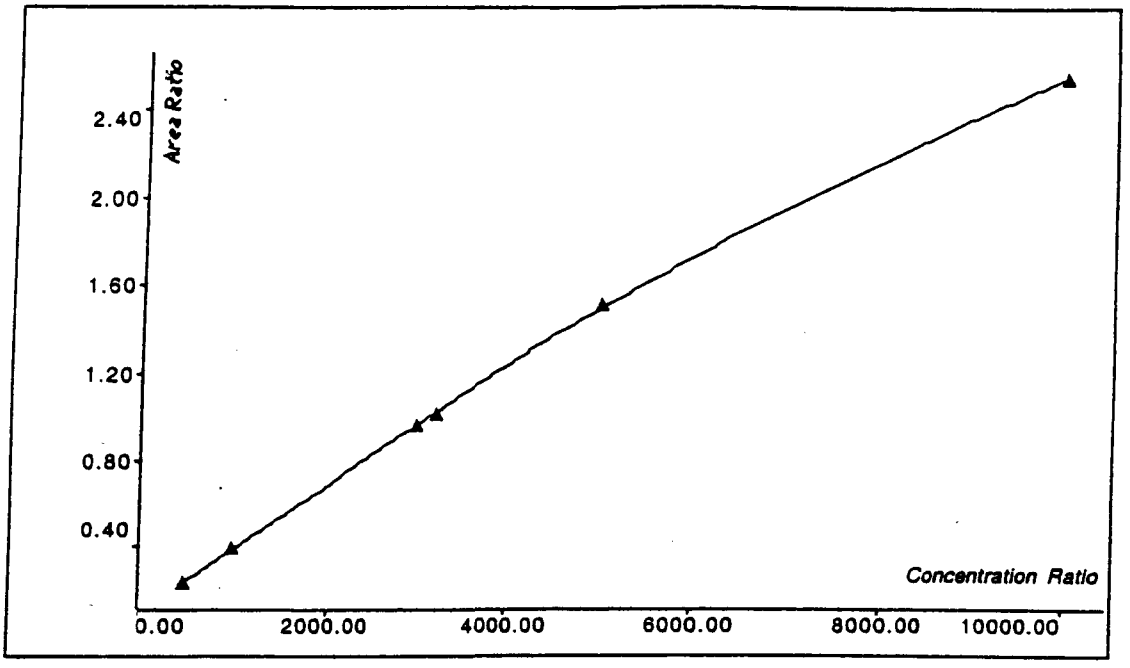
Printed by: greg gorman



Compound:	PFBS 4mg/mL Base
Internal Standard:	IS
Fit:	Quadratic
Fit Parameter:	Area Ratio
Weighting:	1÷X
Equation:	y = - 7.2158e-9 * x * x +0.00032 * x + 0.07261
Correlation Coefficient (r):	0.999933
Chi Square:	0.00000

TurboQuan™, version 1.0
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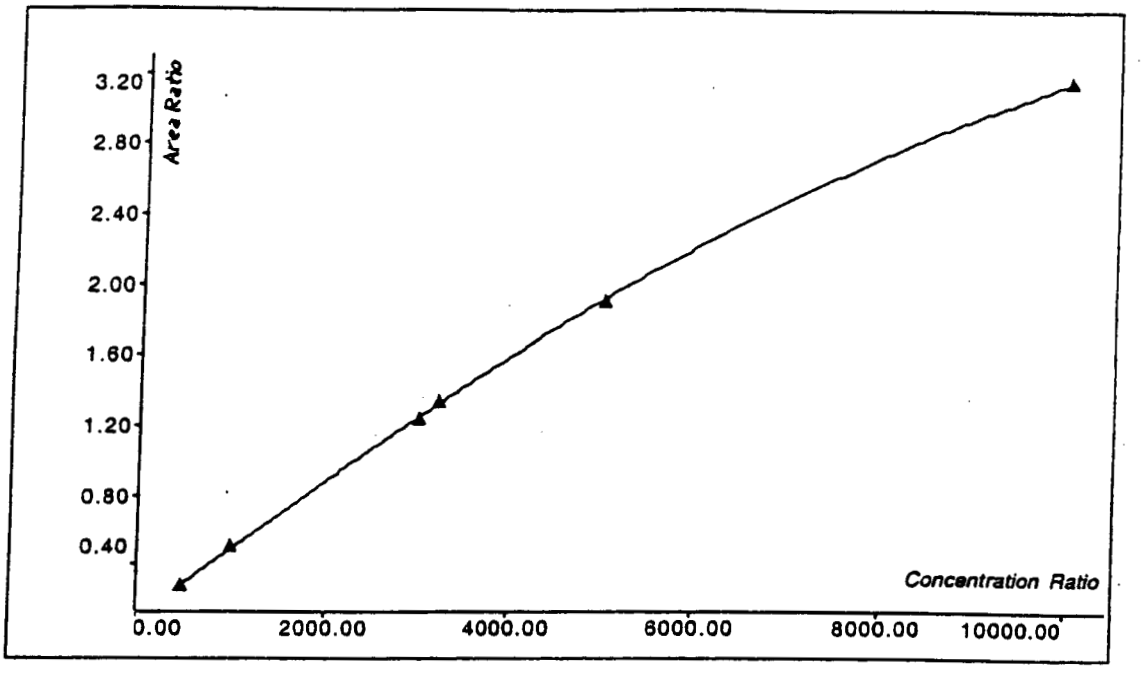

Compound:	PFBS 12mg/ml Dose
Internal Standard:	IS
Fit:	Quadratic
Fit Parameter:	Area Ratio
Weighting:	1÷X
Equation:	y = - 1.2325e-8 * x * x +0.00043 * x + 0.06769
Correlation Coefficient (r):	0.999886
Chi Square:	0.00000

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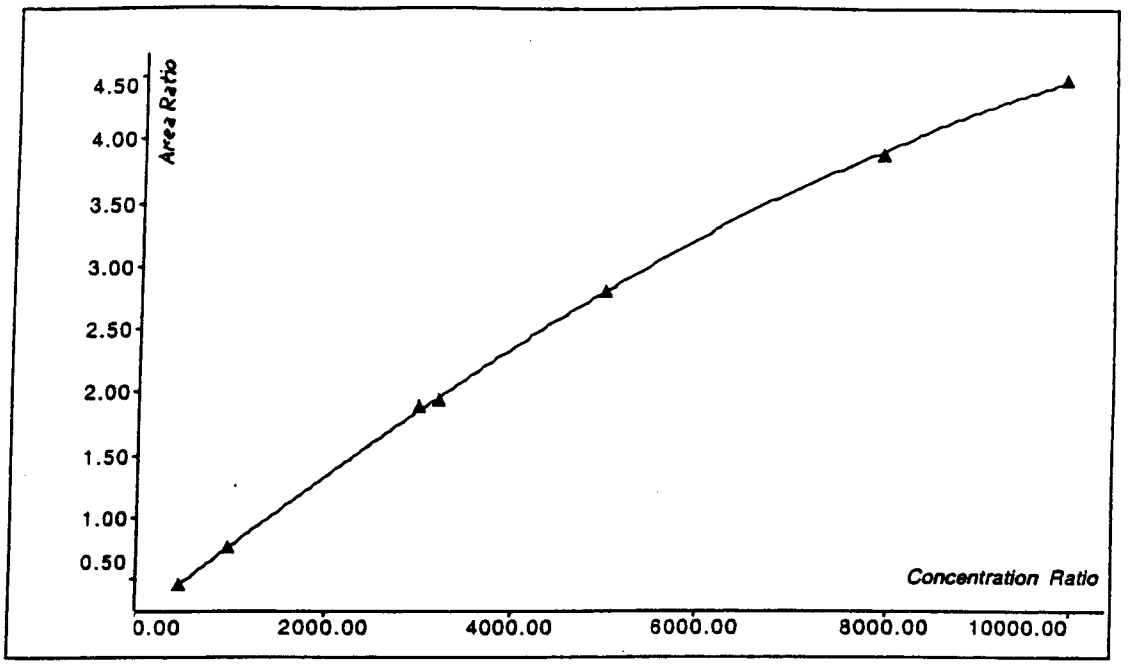
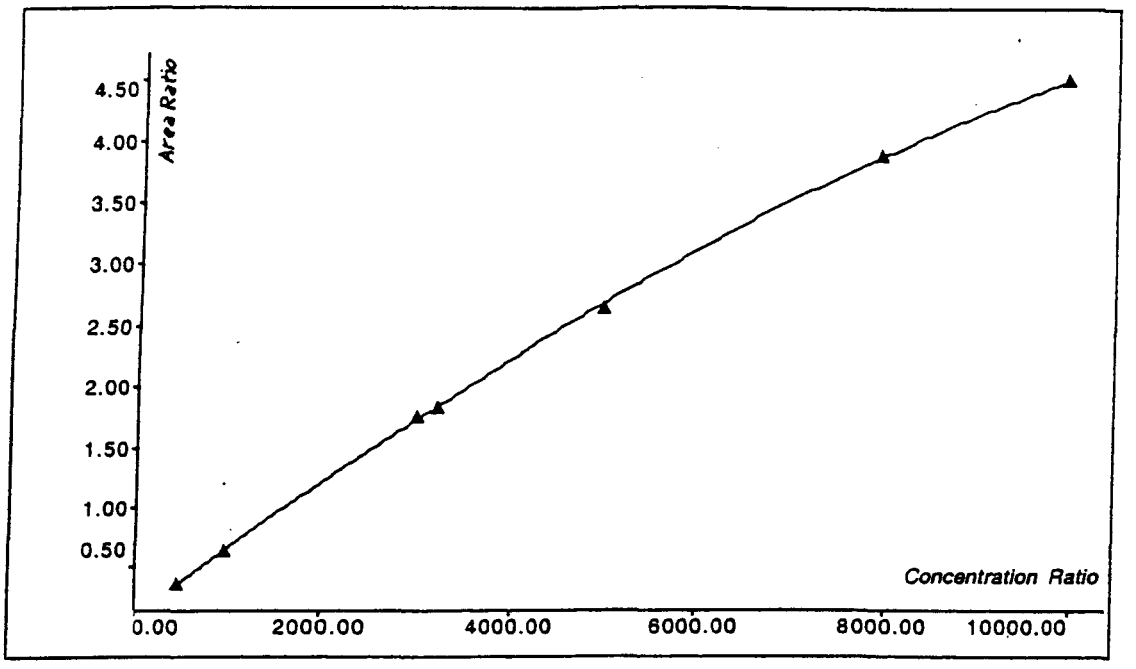


Compound:	PFBS Day 28 40mg/mL
Internal Standard:	IS
Fit:	Quadratic
Fit Parameter:	Area Ratio
Weighting:	1÷X
Equation:	y = - 2.0220e-6 * x * x +0.00064 * x + 0.13885
Correlation Coefficient (r):	0.999946
Chi Square:	0.00000

TurboQuan™, version 1.0
Printed: 07/28/00 08:32
Results Table: ...Folder:july2000:data:7/26 dose: 7/27 dose 07/28/00 08:15

Printed by: greg gorman



Compound:	PFBS
Internal Standard:	IS
Fit:	Quadratic
Fit Parameter:	Area Ratio
Weighting:	1÷X
Equation:	y = - 1.5830e-8 * x * x +0.00061 * x + 0.06038
Correlation Coefficient (r):	0.999920
Chi Square:	0.00000

Day 28 12 mg/mL

TurboQuan™, version 1.0
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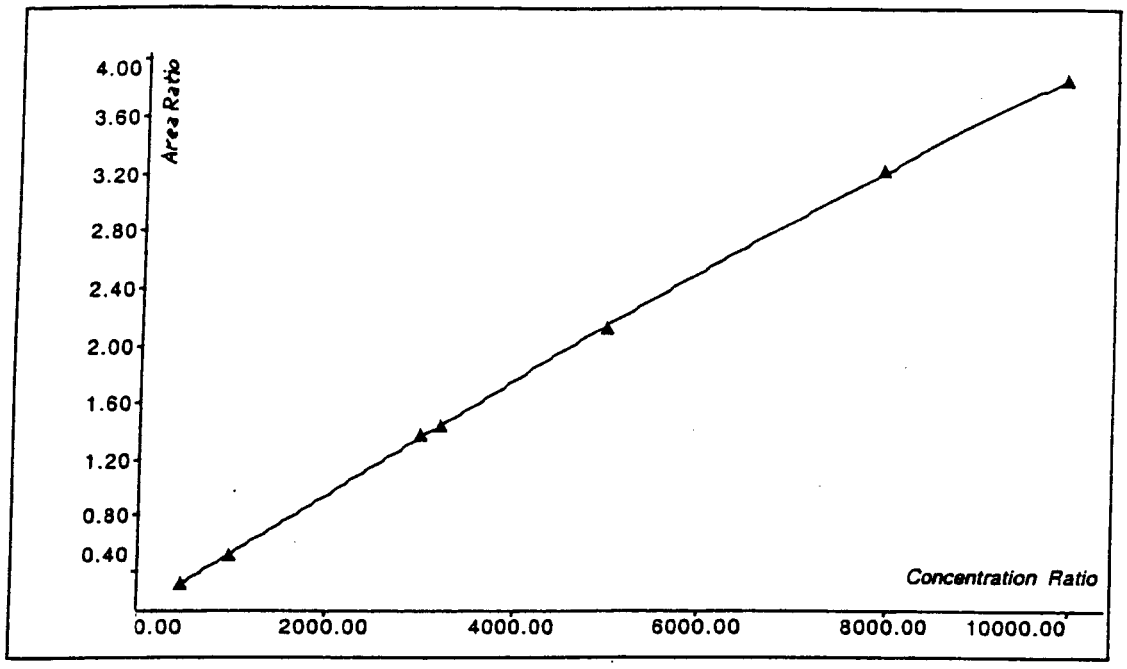

Compound:	PFBS
Internal Standard:	IS
Fit:	Quadratic
Fit Parameter:	Area Ratio
Weighting:	1÷X
Equation:	y = - 6.4338e-9 * x * x +0.00044 * x + 0.08808
Correlation Coefficient (r):	0.999985
Chi Square:	0.00000

Day 28 4mg/mL

APPENDIX 10
CERTIFICATE OF ANALYSIS

Certificate Of Analysis

$C_4F_9SO_3^-K^+$ (PFBS), Lot 2

March 10, 2000

This sample was analyzed using ! and elemental analyses techniques. The results of these tests show the sample to contain the following weight percent composition:

	0.13 %
$C_4F_9SO_3^-K^+$	99.82 %
	0.04 %

Additionally, the isomer distribution of the sample was determined using ^{19}F-NMR techniques and found to contain the following weight percent composition:

$CF_3(CF_2)_3$-$SO_3^-K^+$	97.86 %
	1.96 %

APPENDIX 11
PROTOCOL AND AMENDMENTS

Primedica Redfield Protocol

Protocol Number: 132-006

A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

PROTOCOL NO.: 132-006

OBJECTIVE: To identify a maximum tolerated dose of T-7485 and identify dose levels for a 28-day repeated dose study.

LOCATION OF STUDY AND CONDITIONS OF TESTING:

It is the intention of 3M Pharmaceuticals, through the conduct of this study, to generate animal safety data that may be submitted to regulatory authorities. Primedica Redfield, 100 East Boone Street, Redfield, Arkansas, 72132, is accredited by AAALAC and licensed by the United States Department of Agriculture to conduct research in laboratory animals. All the conditions of testing will conform to the Animal Welfare Act (CFR 9) and its amendments. Primedica Redfield will follow all requirements specified in this approved protocol as well as Primedica Redfield's Standard Operating Procedures. Changes in the protocol may be made by consultation with and approval from 3M Pharmaceuticals followed by written verification of the change. 3M Pharmaceuticals reserves the right to inspect facilities and procedures used for this study by means of announced or unannounced site visits. Primedica Redfield will notify 3M Pharmaceuticals promptly by telephone prior to release of any data for review.

SPONSOR:
3M Pharmaceuticals
3M Center, Building 220-2E-02
P.O. Box 33220
St. Paul, MN 55133-3320

SPONSOR'S REPRESENTATIVE:

TESTING FACILITY:
Primedica Redfield
Mail: P.O. Box 308
Deliveries: 100 East Boone St.
Redfield, AR 72132
Telephone: 501-397-2540
FAX: 501-397-2002

PERSONNEL:
Study Director: John Seng, Ph.D.
Principle Investigator: Karen Tranter, B.A., LATG
Veterinarian: Allan Manus, D.V.M., M.Sc., ACLAM
Clinical Pathology: Phyllis Powell, B.S., M.T., ASCP
Head Technician: Jennifer Dedman, B.S.

PROPOSED STUDY DATES:
Experimental Start Date: June 27, 2000
Experimental Termination Date: July 7, 2000
Draft Report Date: August 15, 2000

Primedica Redfield Protocol

Protocol Number: 132-006

1. REGULATORY COMPLIANCE AND QUALITY ASSURANCE

This study will not be required to be conducted under GLP guidelines, however, the protocol, amendments, and the final report will be audited by the Quality Assurance Unit.

2. INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE REVIEW

The protocol will be reviewed and approved by Primedica Redfield's Institutional Animal Care and Use Committee (IACUC) for compliance with regulations prior to study initiation.

In the opinion of the Sponsor, indicated by the signature on this protocol, the study does not unnecessarily duplicate any previous work.

3. MATERIALS

TEST MATERIAL	T-7485 (Potassium perfluorobutane sulfonate, PFBS)
IDENTIFICATION	The lot number will be listed in the raw data and final report.
PHYSICAL DESCRIPTION	White powder
VEHICLE	1% carboxymethylcellulose (aqueous, medium viscosity)
IDENTIFICATION	The lot number will be listed in the raw data and final report.
PHYSICAL DESCRIPTION	White powder

STORAGE CONDITIONS

The bulk test material will be stored in its original container and will be stored at room temperature. The formulated test and control material will be stored at 2° to 8°C.

ANALYTICAL CHEMISTRY

The Sponsor assumes responsibility for characterization (identity, purity, and stability) of the bulk test material (including under test conditions). Information on the composition and method of synthesis of the bulk test material will be held by the Sponsor. The doses, unless otherwise stated, will be calculated assuming the test material to be 100% pure.

DOSE PREPARATION AND CONCENTRATION

Doses will be prepared by Primedica Redfield. The carboxymethylcellulose will be prepared at 1% in deionized water and may be prepared prior to Study Day 1.

INVENTORY

The test material container(s) will be inventoried when received at the testing laboratory, and a record of all test material use will be maintained. The technician dosing the animals will: 1) Record the weight or volume of the test material container immediately before and after dosing; 2) Compute and record the amount used and compare it to the theoretical amount immediately after dosing; 3) Keep the formulated test material use log in the animal study books at all times; 4) Assure the dose used is within ±10% of theoretical.

ANALYTICAL SAMPLES

A sample of the formulated test material will be retained and frozen at approximately -20°C for possible analysis. If no analysis is performed, the sample will be discarded upon finalization of the study report, or as authorized by the Sponsor.

TEST MATERIAL RETENTION

Unused test material may be returned to the Sponsor or designee at the termination of the study, or retained for use on future studies. The Sponsor will be notified in advance of shipping, and a transmittal letter will accompany the shipment. The material will be packed in a suitable container to maintain the conditions specified by the Sponsor during transit plus an adequate margin of safety for any transit delays.

SAFETY PRECAUTIONS

General safety precautions as required by Primedica Redfield's policies and procedures will be followed. The Sponsor's Representative will be notified of any personnel exposures requiring a physician's examination or care.

4. *ANIMALS*

Species:	Rat
Strain/Source:	Crl:CD®(SD) BR VAF®/Plus out-bred albino rats, Charles River Laboratories, Inc.
Age at Initiation:	Six to eight weeks
Number and Sex:	20 male and 20 female (female nulliparous and non pregnant)
Identification:	Uniquely numbered ear tag and cage card

ANIMAL HUSBANDRY

HOUSING

The animals will be individually housed in stainless steel cages. The cages conform to standards set forth in the Guide for the Care and Use of Laboratory Animals, National Academy Press, Washington, D.C., 1996.

FEED

Teklad Certified Rodent Diet #8728 will be provided *ad libitum*. This diet is routinely analyzed by the manufacturer for nutritional components and environmental contaminants. Results of the manufacturer's analyses are on file at Primedica Redfield.

WATER

Filtered tap water will be provided *ad libitum*. Samples of the water are analyzed for total dissolved solids, hardness, specified microbiological content, and for environmental contaminants. Results of these analyses are on file at Primedica Redfield.

CONTAMINANTS

There are no known contaminants in the feed or water that would be expected to interfere with this study.

ENVIRONMENT

Environmental controls are set to maintain a temperature of 18° to 26°C (64° to 79°F) with a relative humidity of 30% to 70%. These parameters are recorded at least once daily. A 12:12 hour light:dark cycle is maintained.

ACCLIMATION

Animals will be acclimated for a minimum of seven days prior to the study start. An adequate number of extra animals will be purchased so that no animal in obviously poor health is placed on test. At the request of the Study Director, excess animals may be used as replacement animals. Animals will be examined by the Staff Veterinarian prior to release of that shipment of animals for use on the study.

JUSTIFICATION FOR SPECIES SELECTION AND NUMBER OF ANIMALS

Rats are an animal model for acute toxicity studies of this type. The number of animals assigned to this study represents the minimum required to meet the objective(s) of the study.

5. *EXPERIMENTAL METHODOLOGY*

STUDY DESIGN

Group Number	Group Designation	Dosage Level (mg/kg)	Dosage Concentration (mg/mL)	Dosage Volume (mL/kg)	Number of Animals	
					Males	Females
1	Control	0	0	25	5	5
2	Mid-dose	100	4	25	5	5
3	Mid-high dose	300	12	25	5	5
4	High-dose	1000	40	25	5	5

ASSIGNMENT TO GROUPS

Animals will be randomly assigned to groups by a weight-ordered distribution such that individual body weights will not exceed ±20% of mean weight for each sex.

FREQUENCY AND DURATION OF ADMINISTRATION

Doses will be administered via oral gavage for ten consecutive days. The dose volume will be 25 mL/kg. The first day of dosing on the study will be Study Day 1. Individual dose volumes will be calculated using the most recently collected body weights.

JUSTIFICATION FOR ROUTE OF ADMINISTRATION AND DOSE LEVEL

In the assessment and evaluation of the toxic characteristics of a substance, determination of acute oral toxicity is usually an initial step. Dose levels were chosen by the Sponsor.

ANTEMORTEM OBSERVATIONS

CLINICAL OBSERVATIONS

Observations will be performed and recorded twice daily (a.m. and p.m.) for moribundity and mortality.

Clinical observations will be performed, according to Primedica Redfield's SOPs, and recorded once daily and when a change is noted.

BODY WEIGHTS

Body weights will be recorded on Study Days 1, 7, 10, and 11.

FEED CONSUMPTION

Feed consumption will be measured on Study Days 1, 7, and 10, and will be reported as an average daily consumption.

HEMATOLOGY

Blood samples will be obtained prior to necropsy while under anesthesia (CO_2) via cardiac puncture. Feed will be withheld overnight prior to collection. Blood samples collected (using EDTA for hematology and sodium citrate for coagulation indices) will be evaluated for the parameters specified below:

- Total and relative differential leukocyte counts
- Erythrocyte counts
- Hemoglobin concentration
- Hematocrit value
- Mean corpuscular volume
- Mean corpuscular hemoglobin
- Mean corpuscular hemoglobin concentration
- Platelet counts
- Prothrombin time
- Activated partial thromboplastin time

CLINICAL CHEMISTRY

Blood samples will be obtained prior to necropsy while under anesthesia (CO_2) via cardiac puncture. Feed will be withheld overnight prior to collection. Blood samples collected for clinical chemistry will be processed and evaluated for the parameters specified below:

- Total Protein
- Albumin
- Glucose
- Triglycerides
- Urea Nitrogen
- Alanine Aminotransferase
- Alkaline Phosphatase
- Calcium
- Sodium
- Potassium
- Globulin
- Albumin/Globulin ratio
- Cholesterol
- Total Bilirubin
- Creatinine
- Aspartate Aminotransferase
- Gamma-glutamyltransferase
- Phosphorus
- Chloride

POSTMORTEM OBSERVATIONS

MORIBUND ANIMALS AND ANIMALS FOUND DEAD

Animals unlikely to survive until the next scheduled observation will be weighed, euthanized, and necropsied. Animals found dead will be weighed and necropsied. In either case, blood samples will not be collected and a complete necropsy will be performed as detailed below. Euthanasia of moribund animals will be authorized by the Study Director or Staff Veterinarian with the concurrence of the Study Director.

EUTHANASIA

All animals will be humanely euthanized via anesthesia with carbon dioxide to effect followed by exsanguination. Euthanasia will be performed in accordance with accepted American Veterinary Medical Association (AVMA) guidelines [J. Amer. Vet. Med. Assoc., 202:229-249, 1993].

NECROPSY

On Study Day 11, the animals will be sacrificed rotating sequentially through groups for each sex. All animals that die during the study, or are killed at study termination, will be subjected to a necropsy examination. A complete necropsy is defined as examination of the external surface of the body, all orifices, and the cranial, thoracic, and abdominal cavities (and their contents).

The following organs will be weighed prior to fixation: adrenal glands, brain, heart, kidneys, liver, ovaries, spleen, testes, and thymus. Paired organs will be weighed together.

Organ weights will not be taken from animals that die or are euthanized prior to scheduled necropsy.

Organs (or samples of organs) and tissues listed below will be examined *in situ*, dissected free, and fixed in 10% neutral buffered formalin or other suitable fixative for possible histopathological examination. Observations noted at necropsy will be recorded on the Individual Animal Necropsy Record.

- Adrenal glands
- Aorta
- Bone marrow
  - sternum
- Brain
  - brain stem
  - cerebellum
  - cerebrum
- Cervix
- Epididymides
- Esophagus
- Eyes
  - with optic nerve
- Lymph nodes
  - mandibular
  - mesenteric
- Mammary gland
- Ovaries
- Oviducts
- Pancreas
- Pituitary gland
- Prostate gland
- Salivary gland
  - mandibular
- Sciatic nerve
- Seminal vesicles

- Femur
  - with articular surface
- Gross lesions
- Harderian gland
- Heart
- Intestine, large
  - cecum
  - colon
  - rectum
- Intestine, small
  - duodenum
  - ileum
  - jejunum
- Kidneys
- Lacrimal gland
- Liver
- Lungs
  - with bronchi
- Skeletal muscle
- Skin
  - abdominal
- Spinal cord
  - cervical
  - lumbar
  - thoracic
- Spleen
- Stomach
  - forestomach
  - glandular
- Testes
- Thymus
- Thyroid/parathyroid
- Tongue
- Trachea
- Uterus
- Urinary bladder
- Zymbal's gland
- Vagina

Animal identification will be saved.

HISTOPATHOLOGY

Histopathology will be performed on all tissues from the vehicle control and high dose group animals, all gross lesions, and all animals found dead or sacrificed *in extremis*. Additional histopathology will be done at an additional cost to the Sponsor.

Tissues will be trimmed, embedded, and sectioned. Slides will be stained with hematoxylin and eosin. Special stains may be used at the direction of the Study Pathologist, at the approval of the Sponsor, and at additional cost. Slides will be read and interpreted by a qualified veterinary pathologist. Data will be summarized in tabular form and will be accompanied by a narrative prepared by the Study Pathologist.

6. ***STATISTICAL ANALYSIS***

Means and standard deviations will be calculated for all quantitative data. Treated groups of the same sex will be compared to Group 1 at common time points using an ANOVA with a *post hoc* Dunnett's t Test (Dunnett, C.W., J. Amer. Statis. Assoc., 50:1096-1121, 1955) or another appropriate test. A two-sided α of 0.05/0.01 will be used to determine if statistically significant differences exist between the vehicle control and treated groups. If no significant differences exist at the 0.05 level, then no comparison is necessary at the 0.01 level. Statistical program names and compile dates are available in the Primedica Research Laboratories Computer Operations Department. The SAS version is 6.12, from the SAS Institute, Inc., SAS Campus Drive, Cary, North Carolina, 27513.

7. REPORT

A draft report will be sent to the Sponsor. Revisions to the initial draft report will be provided to the Sponsor by mail or fax transmission as printed copies of the corrected pages only. Additional revisions or complete copies of the revised draft reports will be provided at additional expense to the Sponsor.

Three copies of the approved final report, two bound and one unbound, will be submitted to the Sponsor approximately two weeks after approval of the draft report. The final report will include all elements required/recommended by the regulations and guidelines.

The report will include, but is not limited to, those items listed below:

- Descriptive text of the study objective
- Summary
- Test material identification (Certificate of Analysis, stability data, and analytical analysis if any are performed)
- Methods
- Results and conclusions
- Body weights and body weight changes
- Feed consumption
- Necropsy report
- Histopathology report
- Organ weights
- Serum chemistry and hematology
- A copy of the protocol, all protocol amendments, and all protocol deviations that may affect the integrity of the study

8. MAINTENANCE OF RAW DATA AND RECORDS

Original data or copies thereof, will be available at Primedica Redfield to facilitate auditing the study during its progress and before acceptance of the final report. When the final report is completed, all original paper data and the original final report will be retained in the archives of the laboratory for at least five years. Wet tissues, slides, and blocks (if generated) will be retained at Primedica Redfield for one year. After one year, the storage of the wet tissues, slides, and blocks will be negotiated with the Sponsor. After five years, the storage of the paper data will be negotiated with the Sponsor. The Sponsor will be notified prior to disposal of any original study data.

9. QUALITY ASSURANCE REVIEW

This is to certify that this protocol has been reviewed by Quality Assurance.

Shevonya Noble 6/26/00

Shevonya Noble, B.A. Date
Quality Assurance Auditor
Primedica Redfield

Primedica Redfield Protocol

Protocol Number: 132-006

10. APPROVALS

June 26, 2000
Date

Senior Laboratory Manager
3M Corporate Toxicology

6/26/00
Date

John Seng, Ph.D.
Study Director/Director of Toxicology
Primedica Redfield

Primedica Redfield Protocol Amendment

Protocol Number: 132-006

STUDY NUMBER: 132-006

AMENDMENT: 1

STUDY TITLE: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

DATE ISSUED: July 17, 2000

AMENDMENT # 1

ITEM 1: **Page 2, Section 1, Regulatory Compliance and Quality Assurance**

CHANGED FROM: This study will not be required to be conducted under GLP guidelines, however, the protocol, amendments, and the final report will be audited by the Quality Assurance Unit.

CHANGED TO: This study will not be required to be conducted under GLP guidelines, however, the protocol, amendments, and the final report will be reviewed by the Quality Assurance Unit.

REASON: Typographical error, non-GLP studies are not audited but are reviewed.

ITEM 2: **Page 9, Approvals:**

CHANGED FROM: John Seng, Ph.D. Date
Study Director/Director of Toxicology
Primedica Redfield

CHANGED TO: John Seng, Ph.D. Date
Study Director
Primedica Redfield

REASON: Typographical error

APPROVALS:

7/19/00
Date

Senior Laboratory Manager
3M Corporate Toxicology

7/17/00
Date

John Seng, Ph.D.
Study Director
Primedica Redfield

Primedica Redfield Protocol Amendment

Protocol Number: 132-006

STUDY NUMBER: 132-006

AMENDMENT: 2

STUDY TITLE: A REPEATED DOSE RANGE-FINDING TOXICITY STUDY OF T-7485 IN SPRAGUE-DAWLEY RATS

DATE ISSUED: September 19, 2000

AMENDMENT # 2

ITEM 1: **Page 2, Section 3, Materials**

ADD:

STABILITY

Samples will be taken from a single formulation of each concentration immediately after preparation and 7, 14, 21, 28, and 32 days after preparation. These samples will be stored at -20°C until shipped to the following laboratory:

Greg Gorman, Ph.D.
Research Chemist III
Southern Research Institution
2000 Ninth Avenue South
Birmingham, AL 35205
Telephone: (205) 581-2725
FAX: (205) 581-2726

The samples will be labeled as standard protocol and will include the appropriate theoretical concentrations of T-7485, the day post-preparation, and the date of sampling. A sample of 1% CMC will also be shipped as a control.

REASON: Sponsor request for stability study prior to upcoming 28-day study.

APPROVALS:

9/24/00
Date

Senior Laboratory Manager
3M Corporate Toxicology

John Seng 9/19/00
John Seng, Ph.D. Date
Study Director
Primedica Redfield

APPENDIX 12
PROTOCOL DEVIATIONS

PROTOCOL DEVIATIONS

There were no protocol deviations that adversely affected the integrity of the study.

APPENDIX 13
KEY PERSONNEL

KEY PERSONNEL

Study Number: 132-006

Study Director	John Seng, Ph.D.
Principle Investigator	Karen Tranter, B.A., LATG
Head Technician	Jennifer Dedman, B.S.
Veterinarian	Allan Manus, D.V.M., M.Sc., ACLAM
Clinical Pathology	Phyllis Powell, B.S., M.T., ASCP
Quality Assurance	Val Gartner, B.A.
Report Coordination	Amy Babb, B.S.
Report Preparation	Tammy Peckham, Ad. Asst. Dana Rose, Ad. Asst.