

TRADE SECRET

Study Title

8-2 Telomer B Alcohol: Developmental Toxicity Study in Rats

Laboratory Project ID: DuPont-10157

TEST GUIDELINES: United States (U.S.) Environmental Protection Agency (EPA),
Office of Prevention, Pesticides, and Toxic Substances (OPPTS)
Health Effects Test Guidelines. OPPTS 870.3700
Prenatal Developmental Toxicity Study. (August 1998).

Organisation for Economic Cooperation and Development
(OECD/OCDE). Guidelines for Testing of Chemicals, 414.
(22nd January 2001).

AUTHOR: Susan M. Munley, M.A.

STUDY COMPLETED ON: January 30, 2004

PERFORMING LABORATORY: E.I. du Pont de Nemours and Company
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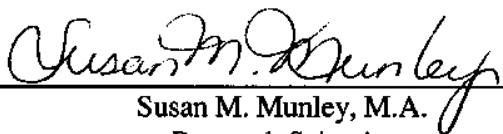
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GOOD LABORATORY PRACTICE COMPLIANCE STATEMENT

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

Test substance characterization was performed at Regional Analytical Services (RAS), Deepwater, N.J. None of the aforementioned analyses were performed under Good Laboratory Practice Standards; however, the analyses were conducted in compliance with ISO9002 regulations. All of the analyses are considered valid and sufficient for the purposes of this study.

Study Director:  30-JAN-2004
Susan M. Munley, M.A. Date
Research Scientist

QUALITY ASSURANCE STATEMENT

Haskell Sample Number(s):

24691

Dates of Inspections:

Protocol: January 30, 2003; February 3, 2003

Conduct: February 20,21, 2003

Records, Reports: May 7, 2003; June 3-6,23, 2003; July 29-30, 2003

Dates Findings Reported to:

Study Director: January 30, 2003; February 20,26, 2003; May 9, 2003;
June 7, 2003, July 30, 2003

Management: February 20,26, 2003; May 9, 2003; August 6, 2003;
January 22, 2004

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Matthew Jentel for KBB
Kimberly B. Brebner
Staff Quality Assurance Auditor

30-Jan-2004
Date

CERTIFICATION

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

Analytical Evaluations by: Janet C. Maslanka Jan-30-2004
Janet C. Maslanka, B.S. Date
Senior Staff Chemist

Approved by: Eve Mylchreest Jan-30-2004
Eve Mylchreest, Ph.D. Date
Manager

Issued by Study Director: Susan M. Munley 30-JAN-2004
Susan M. Munley, M.A. Date
Research Scientist

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STUDY INFORMATION

9th Collective Nomenclature: 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-Heptadecafluoro-1-decanol

Synonyms/Codes: (Perfluorooctyl)ethanol
β.-(Heptadecafluorooctyl)ethanol
1,1,2,2-Tetrahydroheptadecafluorodecanol
1,1,2,2-Tetrahydroperfluorodecan-1-ol
1,1,2,2-Tetrahydroperfluorodecanol
1,1,2,2-Tetrahydroperfluorodecyl alcohol
1H,1H,2H,2H-Perfluorodecan-1-ol
1H,1H,2H,2H-Perfluorodecanol
2-(Heptadecafluorooctyl)ethanol
2-(Perfluorooctyl)ethanol
2-(Perfluorooctyl)ethyl alcohol
C-8 Telomer B Alcohol
2-Perfluorooctyl ethanol
8-2 Telomer B Alcohol
P.00/001 (Lot No.)

Haskell Number: 24691

CAS Registry Number: 678-39-7

Composition: C-8 Telomer B Alcohol

Purity: 99.2 Wt. %

Known Impurities: C7F15CF=CHCH2OH (0.8 Wt. %)

Physical Characteristics: White to yellow wax

Stability: The test substance appeared to be stable under the conditions of the study; no evidence of instability was observed.

Sponsor: Telomer Research Program
1200 South Hayes Street
Arlington, Virginia 22202-5050
U.S.A.

Study Initiated/Completed: January 30, 2003 / (see report cover page)

In-Life Initiated/Completed: February 3, 2003 / February 24, 2003

STUDY PERSONNEL

Study Director: Susan M. Munley, M.A.

Management: Eve Mylchreest, Ph.D.

Supervisor: Deborah L. Tyler

Primary Technician: Sandra E. Karr, A.A.S.

Analytical Chemist: Janet C. Maslanka, B.S.

Management: S. Mark Kennedy, Ph.D.

Toxicology Report Preparation: Mary K. LaRoe

Management: Nancy S. Selzer, M.S.

Laboratory Veterinarian: Thomas W. Mayer, D.V.M., A.C.L.A.M.

SUMMARY

The objective of this study was to evaluate the potential maternal and developmental toxicity of 8-2 Telomer B Alcohol when administered by oral gavage to pregnant rats daily from around the time of implantation to the end of gestation, days 6-20 of gestation (days 6-20G).

Groups of 22 time-mated Crl:CD[®](SD)IGS BR rats were administered formulations of the test substance in 0.5% aqueous methylcellulose over days 6 through 20 of gestation (G) at daily dose levels of 0, 50, 200, or 500 mg/kg. During the in-life portion of the study, body weight, food consumption, and clinical observation data were collected. On day 21G, all surviving dams were euthanized and dissected; the abdominal and thoracic viscera were examined grossly. The uterus of each pregnant rat was removed and dissected to permit examination of the uterine contents. The fetuses were removed, individually identified, weighed, sexed, and examined for external, visceral, head, and skeletal alterations.

Under the conditions of this study, adverse maternal toxicity was produced at 500 mg/kg/day and consisted of maternal mortality, decreased body weights and body weight gains, and increased clinical observations of toxicity. One litter at 500 mg/kg/day consisted of one early resorption; persistent reductions in food consumption and body-weight gain and increased clinical observations indicative of toxicity were reported during the study for this female. Therefore, this litter consisting of a single early resorption is believed to be secondary to overt maternal toxicity in this dam. Developmental toxicity at 500 mg/kg/day consisted of increased skeletal variations (delayed pelvic bone ossification and wavy ribs). At 200 and 500 mg/kg/day, there were non-adverse, test substance-related, transient reductions in maternal food consumption. In addition, there were slight increases in the incidence of delayed skull bone ossification at 200 and 500 mg/kg/day that were not considered adverse. Thus, the no-observed-effect level (NOEL)^a for both maternal and developmental toxicity was considered 200 mg/kg/day.

a The NOEL for this study is defined as the highest dose at which adverse effects attributable to the test substance were not detected. Thus, for this study, the NOEL is equivalent to the NOEL as defined by the U.S. EPA⁽¹³⁾ and to the no-observed-adverse-effect level (NOAEL) as defined by the European Union.⁽¹⁴⁾

OBJECTIVE

The objective of this study was to evaluate the potential maternal and developmental toxicity of 8-2 Telomer B Alcohol when administered by oral gavage to pregnant rats daily from around the time of implantation to the end of gestation, days 6-20 of gestation (days 6-20G). The test substance, 8-2 Telomer B Alcohol, is an organofluorine compound. The 50, 200, and 500 mg/kg/day dose levels were selected for the current study based on findings from two previously conducted studies. The first study was an 84-day range-finding study⁽¹⁾ with 8-2 Telomer B Alcohol in which dose levels of 5, 25, and 125 mg/kg/day were tested. Evaluation of in-life data from the first few weeks of this study indicated that no compound-related toxicity was observed at doses $\leq$ 125 mg/kg/day. The evaluation of data from the 84-day study was limited to that which was collected during the first few weeks of dosing because in a developmental toxicity study, time-mated rats are only dosed for 15 consecutive days. The second study dataset that was considered was from a rat developmental toxicity study with a similar fluorotelomer-based alcohol in which dose levels of 50, 200, and 500 mg/kg/day were evaluated.⁽²⁾ Maternal and developmental toxicity were produced at 500 mg/kg/day and were limited to reductions in maternal body weight gain and food consumption, increased clinical signs, and increased fetal skeletal variations. No toxicologically significant or adverse compound-related effects were seen in dams or fetuses at 50 or 200 mg/kg/day. Thus, for the current study, a high dose level of 500 mg/kg/day was expected to produce maternal and developmental toxicity; the intermediate level of 200 mg/kg/day was expected to produce minimal to no toxicity, and the low dose of 50 mg/kg/day was expected to be the no-observed-adverse-effect level (NOAEL).

SPONSOR AND TEST FACILITY

The study was sponsored by the Telomer Research Program, 1200 South Hayes Street, Arlington, Virginia, 22202-5050. The Sponsor's approval of the protocol was considered effective the date the Sponsor authorized the Work Authorization Form. The study will be conducted at DuPont Haskell Laboratory for Health and Environmental Sciences, E. I. du Pont de Nemours and Company, Newark, Delaware.

REGULATORY COMPLIANCE

The study design complies with the following test guidelines:

- United States (U.S.) Environmental Protection Agency (EPA), Office of Prevention, Pesticides, and Toxic Substances (OPPTS) Health Effects Test Guidelines. OPPTS 870.3700 Prenatal Developmental Toxicity Study. (August 1998).
- Organisation for Economic Cooperation and Development (OECD/OCDE). Guidelines for Testing of Chemicals, 414. (22nd January 2001).

STUDY DESIGN

A. Experimental Design

The study design is as follows:

Group	Dose ^a (mg/kg/day)	Concentration (mg/mL) ^b	Time-Mated Females
I	0 ^c	0.0	22
II	50	10.0	22
III	200	40.0	22
IV	500	100.0	22

a Formulations of test substance in 0.5% aqueous methylcellulose were administered once daily by oral gavage on days 6-20G at a dosing volume of 5 mL/kg.

b To achieve these concentrations of active ingredient, the formulations were adjusted for sample purity.

c The control group animals received vehicle (0.5% aqueous methylcellulose) only at a dosing volume of 5 mL/kg.

MATERIALS AND METHODS

A. Test Substance

The test substance, a waxy solid with known purity (99.2%) and composition, was supplied by the Sponsor. The test substance was assigned the Haskell Laboratory Number H-24691. The Sponsor was responsible for characterization and analysis of identity, stability, and purity of the bulk test substance. Available information on the purity, composition, contaminants, synonyms, CAS registry number, basic physical properties, hazards, and hazardous material classification(s) was provided by the Sponsor and is available on the Haskell Laboratory Sample Evaluation Form. The Sponsor also provided a Certificate of Analysis to the Study Director. The original Sample Evaluation Form and the Certificate of Analysis are retained in the official Work Request file for the study. A reserve sample of the test substance was collected and retained by the Testing Facility.

B. Vehicle

The vehicle was 0.5% aqueous methylcellulose. Lot number(s) and expiration date(s) were recorded in the study records.

C. Preparation, Administration, and Analyses of Dosing Formulations

Formulations of the test substance in the vehicle were prepared daily. The method of mixing the test substance with the vehicle was documented in the study records.

The test substance was administered by oral gavage because this route is recommended by regulatory agencies for this type of study. The volume administered (5 mL/kg) was based on the most recent body weight.

Samples of each test formulation were taken 3 times during the study. Analyses addressed concentration, uniformity of mixing, and stability. Samples were submitted shortly after preparation to the Analytical Chemistry Group at Haskell Laboratory.

1. Analytical Methods

a. Recovery Sample Analysis

Concurrent with dosing formulation analysis, recovery of the test substance from spiked 0.5% methylcellulose was tested at the low level (10 mg/mL), at the mid level (40 mg/mL) and at the high level (100 mg/mL) to confirm the analytical method. The test substance was weighed (approximately 30 mg, 120 mg, and 330 mg on test days 1 and 11 and approximately 20 mg, 90 mg, and 260 mg on test day 20, respectively) and diluted with 3 mL (2 mL for test days 11 and 20) of 0.5% methylcellulose. All recovery samples were then mixed to disperse the test substance in the methylcellulose. The samples were then processed and analyzed in the same manner as the samples at similar concentrations.

b. Dosing Formulation Treatment

Each dosing sample (3 mL for test day 1; 2 mL for test days 11 and 20) was diluted to 100 mL with methanol and mixed to dissolve the test substance in the formulation. The dosing samples were analyzed without further dilution or were further diluted with the 0 mg/mL sample (initial dilution) to an expected concentration of approximately 0.06 mg/mL (a.i.) prior to analysis. Before all final dilutions, the internal standard diluted solution (refer to Calibration and Quantitation Section) was added to each test sample to give a final concentration of approximately 0.09 mg/mL. Each sample (final dilution) was adjusted to have an equivalent amount of matrix (final dilution of the 0.0 mg/mL control) when analyzed.

Samples submitted for analysis were analyzed the day the formulations were received by the testing group.

c. Chromatographic Conditions

Instrument:	Hewlett-Packard Model 6890 GC
Column:	J & W, DB-1701, 30 m, 0.32 mm ID, 1 um film thickness
Injector:	Split, 250°C
Detector:	FID; 250°C
Carrier Gas:	Helium (2.1 mL/min)

Split vent:	22.3 mL/min
Injection Volume:	2 microliter
Oven Program:	Gradient
Initial Temperature:	100°C
Initial Time:	1.00 min.
Level 1 Rate:	20.0°C/min.
Level 1 Temperature:	260°C
Level 1 Time:	0.00 min.
Total run time:	9.00 min.

d. Calibration and Quantitation

A separate sample of the test substance was obtained to use as the analytical reference standard. A stock solution was prepared in methanol. This stock solution was sonicated to assure that all material was in solution. Before analysis, appropriate aliquots of the stock were diluted with the 0 mg/mL sample (initial dilution) to make calibration standards, which bracketed the target concentration of the diluted dosing samples. A stock solution of internal standard (1H, 1H, 2H, 2H-perfluoro-9-methyldecan-1-ol, 98% pure) was prepared in methanol and added to each calibration standard and test sample to give a final concentration of approximately 0.09 mg/mL. The ratio of the internal standard and the test substance 1 peak heights from replicate GC analysis of these solutions were used to construct a calibration curve by least squares regression (see Appendix A, Figure 1 for a representative curve). Measured concentrations for the dosing samples were determined by applying the peak height ratios from replicate injections of each sample to the calibration curve.

Test substance homogeneity and uniformity in the vehicle was evaluated by calculating the coefficient of variation ($C.V. = \text{standard deviation}/\text{mean} \times 100$) of the measured concentrations in the top, middle, and bottom samples (homogeneity) or duplicate samples (concentration verification) for each dosing level. A coefficient of variation of less than or equal to 10% is considered indicative of acceptable distribution of the test substance throughout the solution. However, if the test substance has been shown to be difficult to disperse in the vehicle or the analysis has shown variability, a coefficient of variation greater than 10 may be acceptable.

The mean result of the homogeneity samples or concentration verification duplicate samples for each dosing level was used to determine the concentration of the test substance for the respective dosing levels. Stability was evaluated by using the mean result of the homogeneity samples as the baseline for comparing the corresponding stability results.

Spiked recoveries samples at each level were prepared and monitored to show the effect on the quantitation of the study due to sampling into 100 mL volumetric flasks. Based on the spiked recovery for each level on the day of the analysis, a correction was applied to all results in the study.

D. Test Species

The CrI:CD[®](SD)IGS BR rat was selected for this study because it is a preferred species for developmental toxicity testing as recommended by the applicable regulatory guidelines. The strain was selected because background data are available from the literature, the supplier, and previous studies at Haskell Laboratory.

Eighty-eight nulliparous, time-mated females were received on January 31, 2003 (66 females) and February 3, 2003 (22 females) from Charles River Laboratories, Inc., Raleigh, North Carolina. Body weights from the day the rats were mated, day 0 of gestation (day 0G), were supplied by the vendor and ranged from 230 to 270 grams. The rats for this study were requested to be approximately 63 days old and at either 1, 2, or 3 days of gestation upon receipt.

Each rat was assigned a unique number and identified with an AVID microchip implant by the supplier prior to shipping. Upon receipt, each rat was assigned a unique Haskell animal number. Both the Haskell animal number and the number provided by the supplier were recorded on each cage card. A master list of unique Haskell animal numbers and corresponding unique supplier-provided animal numbers was maintained with the study records.

E. Animal Husbandry

1. Housing

Animal rooms were maintained at an acceptable temperature of 18-26°C (targeted at 22°-24°C) and maintained at an acceptable relative humidity of 30%-70% (targeted at 40 %- 60%). Occasional excursions outside the accepted ranges were minor and did not affect the study. Animal rooms were artificially illuminated (fluorescent light) on a 12-hour light/dark cycle (approximately 0600-1800 hours). Animals were housed individually in suspended, wire-mesh, stainless steel cages. Nesting material was not provided because the dams were euthanized prior to parturition.

2. Feed and Water

PMI Nutrition International, Inc. Certified Rodent LabDiet[®] 5002 (formerly known as Purina[®] Certified Rodent[®] Chow) was available *ad libitum*. Water from United Water Delaware was available *ad libitum*.

3. Health Monitoring Program

As specified in the Haskell Laboratory animal health and environmental monitoring program, the following procedures are performed periodically to ensure that contaminant levels are below those that would be expected to impact the scientific integrity of the study:

- Water samples are analyzed for total bacterial counts, and the presence of coliforms, lead, and other contaminants.

- Feed samples are analyzed for total bacterial, spore and fungal counts.
- Samples from freshly washed cages and cage racks are analyzed to ensure adequate sanitation by the cagewashers.

Certified animal feed is used, guaranteed by the manufacturer to meet specified nutritional requirements and not to exceed stated maximum concentrations of key contaminants, including specified heavy metals, aflatoxin, chlorinated hydrocarbons, and organophosphates. The presence of these contaminants below the maximum concentration stated by the manufacturer would not be expected to impact the integrity of the study.

The animal health and environmental monitoring program is administered by the attending laboratory animal veterinarian. Evaluation of these data did not indicate any conditions that affected the validity of the study.

F. Quarantine and Pretest Period

Rats were quarantined according to procedures outlined in Haskell Laboratory SOP LA003-P, and then released for the study upon approval of the Laboratory Animal Veterinarian designee.

G. Randomization

Dams were assigned to lots according to their gestation day. Then, they were ranked within their respective lots on the basis of day 0G body weights and assigned to control and experimental groups by random sampling from the ranked list. The distribution resulted in mean body weights for all groups that were not statistically different ($p > 0.05$).

H. Parameters Studied

1. In-life Observations of Females

a. Clinical Observations

Clinical observations were recorded on the day after arrival and daily until the end of the study; clinical observations were recorded twice daily on days 6-20G.

b. Body Weight

Body weights were recorded on the day after arrival and daily until the end of the study.

c. Food Consumption

Food consumption was measured on days 4, 6, 8, 10, 12, 14, 16, 18, 20, and 21G.

2. Postmortem Observations of Females Surviving to Scheduled Euthanasia

The abdominal and thoracic viscera were examined grossly immediately after euthanasia on day 21G. The intact and the empty uterus of each dam having at least one viable fetus was weighed to permit calculation of maternal body weight adjusted to exclude the products of conception. The corpora lutea count for each ovary of females with viable fetuses was recorded.

For each female with visible implantation sites, the types of implants (live and dead fetuses, and resorptions) and their relative positions were recorded. The uterus of each apparently "nonpregnant" female was stained with ammonium sulfide⁽³⁾ to detect very early resorptions.

3. Fetuses of Females Surviving to Scheduled Euthanasia

For each fetus, the following parameters were recorded: identification number, intrauterine location, sex, and body weight. The external alterations detected for each live fetus were also recorded.

For each litter, the first live fetus and every other live fetus thereafter (approximately 50% of the fetuses) were examined for visceral alterations.⁽⁴⁾ Retarded renal development was classified using the scheme of Woo and Hoar.⁽⁵⁾ In addition, all live fetuses with malformations visible at external examination were examined for soft tissue alterations; decapitation of these fetuses was at the discretion of the study director or a designee.

After fixation in Bouin's fixative, the heads of decapitated fetuses (fetuses that were decapitated prior to visceral examination; approximately 50% of the fetuses) were examined and alterations were recorded. Examinations were based on the method of Barrow and Taylor.⁽⁶⁾ After alcohol fixation, the alizarin-stained skeletons were examined and skeletal alterations were recorded for all live fetuses, excluding the fetal heads fixed in Bouin's fixative.

I. Animal Euthanasia

Females were euthanized by carbon dioxide asphyxiation. Fetuses were decapitated before proceeding with visceral examinations; those to be visceraally examined without decapitation were injected with sodium pentobarbital. All other fetuses also were injected with sodium pentobarbital before fixation.

J. Control of Bias

In addition to random assignment to groups, all females were coded before scheduled euthanasia and remained coded during the collection of postmortem and fetal data.

K. Statistical Analyses

Descriptive statistics were performed for all quantitative endpoints listed below. Sequential two-tailed trend testing⁽⁷⁾ was applied to the data for each parameter as tabulated below. If a significant dose-response was detected, data from the top dose group was excluded and the test repeated until no significant trend was detected. For litter parameters, the proportion of affected fetuses per litter or the litter mean was used as the experimental unit for statistical evaluation.⁽⁸⁾ The level of significance selected was $p < 0.05$.

Where the data were tied and the standard large sample version of Jonckheere's test was not applicable, exact p values were calculated using permutation methodology.⁽⁹⁾

<u>Parameter</u>	<u>Trend Test</u>
Maternal weight Maternal weight changes Maternal food consumption	Linear contrast of means ⁽¹⁰⁾
Live fetuses Dead fetuses Resorptions (total, early, late) Implantations Incidence of fetal alterations	Jonckheere's test ⁽¹¹⁾
Incidence of pregnancy Clinical observations Maternal mortality Females with total resorptions Early deliveries	Cochran-Armitage test ⁽¹⁰⁾
Fetal weight (Covariates: litter size, sex ratio) Sex ratio (Covariate: litter size)	Linear contrast of least square means ⁽¹²⁾

RESULTS AND DISCUSSION

ANALYTICAL EVALUATIONS

A. Chromatography (Appendix A)

The test substance eluted from the GC column as resolved peak with a retention time of approximately 3.7 minutes. The internal standard eluted from the GC column as a resolved peak with a retention time of approximately 4.1 minutes. Representative GC chromatograms are shown in Figures 2(a - d). Test substance was not detected in the 0 mg/mL control.

B. Recovery Samples (Appendix A)

Detailed analytical results of recovery samples are summarized in Appendix A, Table I. The variability of the analytical method was demonstrated by the coefficients of variation of the recovery results at each targeted dosing concentration (approximately 10, 40, 100 mg/mL) over the course of the study. The range of the measured concentrations of the test substance for the 10 mg/mL level was 84.5% to 92.6% of nominal (mean percent recovery = $88.9\% \pm 3.3$, C.V. = 4%). The range of the measured concentrations of the test substance for the 40 mg/mL level was 81.9%, to 93.5% of nominal (mean percent recovery = $85.5\% \pm 4.7$, C.V. = 5%). The range of the measured concentrations of the test substance for the 100 mg/mL level was 76.4% to 90.2% of nominal (mean percent recovery = $83.0\% \pm 5.1$, C.V. = 6%). Based on this data, a correction was applied to all sample results using the spiked recovery for each level on the day of analysis.

C. Homogeneity and Stability Samples (Table 1, Appendix A)

Analytical results from dosing formulations collected on test day 1 (February 3, 2003) and analyzed for homogeneity, concentration verification, and stability are shown in Summary Table 1 and Appendix A, Table II.

The following table summarizes the results for all homogeneity and/or concentration verification and stability analyses.

Test Day Sample Type	Nominal mg/mL	Measured T,M,B ^{a,b} mg/mL	Mean (T,M,B) % Nominal	C.V. (%)	Stability ^c % Nominal
Test Day 1 Homogeneity	0	ND ^d	---	---	---
	10	8.92 ^e , 8.73 ^e , 10.0	92.2	7	95.6
	40	40.5, 40.0, 39.8	100.3	1	102.8
	100	96.5, 98.3 ^e , 94.8	96.5	2	104.0

- a Mean results for the analysis of the top (T), middle (M), and bottom (B) samples.
b All results corrected for spiked recovery based on the level and day of analysis (Refer to Table I).
c Samples held 5 hours at room temperature.
d Denotes none detected.
e Mean result of the original analysis and duplicate reanalysis of the original sample.

The data for samples collected on Test Day 1 indicates that the test substance was homogeneously mixed in the vehicle at all levels (C.V.'s = 7, 1, and 2, respectively). The test substance was at the targeted concentration in the samples ($\pm 7.8\%$ of nominal) and was stable in the vehicle when held for 5 hours at room temperature.

D. Concentration Verification Samples (Table 1, Appendix A)

Analytical results from dosing formulations collected test day 11 (February 12, 2003) and test day 20 (February 21, 2003) and analyzed for concentration verification are shown in Summary Table 1 and Appendix A, Table III.

The following table summarizes the results for concentration verification analyses of the the test substance samples for test days 11 and 20.

Preparation Day	Nominal mg/mL	Measured ^{a, b} mg/mL	Average % Nominal	CV %
Test Day 11	10	7.28 ^c , 7.23 ^c , 8.71 ^d	77.4	11
	40	39.9 ^c , 39.7 ^c , 41.1 ^d	100.5	2
	100	100 ^c , 101 ^c , 98.2 ^d	99.7	1
Test Day 20	10	9.45, 9.57	95.1	1
	40	35.0, 37.8	91.0	5
	100	94.6, 91.9	93.2	2

- a Duplicate samples per level were submitted and analyzed. C.V. calculated to verify uniformity of mixture.
b All results corrected for spiked recovery based on the level and day of analysis (Refer to Table I).
c Mean result of the original analysis and duplicate reanalysis of the original sample.
d Results of the analysis of a 3rd sample collected from the dosing preparations.

Results from analysis of the samples that were collected on Test Day 11 for concentration verification indicated that test substance was homogeneously mixed (CV = 2, 1) and at the targeted concentration ($\pm 0.5\%$ of nominal) for all samples except for the 10 mg/mL level

(CV = 11, $\pm$ 22.6% of nominal). The 3rd sample collected from the 10 mg/mL level (87.1% of nominal) indicated that the original samplings had been collected before the preparation was adequately mixed and consequently the CV greater than 10 for the replicates and a recovery of less than $\pm$ 20% of nominal for the level.

Results from analysis of the samples that were collected on Test Day 20 for concentration verification indicated that test substance was homogeneously mixed (CV = 1, 5, 2) and at the targeted concentration ($\pm$ 9.0% of nominal) for all samples.

E. Analytical Conclusions

Results from the analysis of the test substance dosing formulations at the start of the study indicated that the test substance was homogeneously mixed, at the targeted concentrations and stable in the vehicle under the conditions of the study. Results from the analysis of the test substance dosing formulations for the concentration verification indicated that the test substance was at the targeted concentration during the study except for the 10 mg/mL level on the first sampling for the concentration verification analysis on test day 11. Subsequent sampling of this formulation indicated that the original samples had been collected before the formulation was adequately mixed.

DEVELOPMENTAL TOXICOLOGY

A. Mortality, Post Mortem Findings, and Clinical Observations (Table 2, Appendices B and G)

Test substance-related mortality was produced at 500 mg/kg/day. Four dams were sacrificed *in extremis* on either day 10, 11, 12, or 13G and one dam was found dead on day 16G. Clinical observations preceding death in these animals included hunched-over posture, weakness, diarrhea, and wet and/or stained fur. Two of these five dams appeared normal at the gross necropsy whereas three dams had pale kidneys and/or discolored liver or lungs. There was no mortality at either 50 or 200 mg/kg/day.

Test substance-related clinical observations were produced at 500 mg/kg/day and included increased occurrences of alopecia, diarrhea, hunched-over posture, weakness, and fur-staining. There were no test substance-related clinical observations at either 50 or 200 mg/kg/day. All other clinical observations recorded were considered incidental and unrelated to the test substance.

B. Body Weights and Body Weight Changes (Tables 3 and 4, Appendices C and D)

Test substance-related reductions in maternal body weight and weight gain were evident at 500 mg/kg/day. Reductions in maternal weight gain occurred at the onset of the dosing period and persisting for the duration of the study. Mean weight gain over the course of the study (days 6-21G) was 25% lower than for the control group; when the final body weights were adjusted for the weight of the uterine contents, the mean weight gain over the same time period was 57% lower than for the control group. These reductions in maternal body weight gain resulted in lower or significantly lower mean maternal body weights beginning as early as day 7G and persisting for the duration of the study; mean final body weights were 9% lower than the control group. There were no test substance-related effects on maternal body weight or weight gain at either 50 or 200 mg/kg/day; data from these two groups were generally comparable to control group data.

C. Food Consumption (Table 5, Appendix E)

There were slight and occasionally statistically significant test substance-related reductions in mean maternal food consumption at 200 and 500 mg/kg/day. These reductions were most pronounced over the first few days of dosing but generally were subtle enough such that there was no appreciable impact on food consumption at these levels when data were averaged over the course of the dosing period. Therefore, these slight test substance-related, transient reductions were not considered indicative of adverse toxicity.

D. Postmortem Findings (Table 6, Appendix F)

With the exception of those gross postmortem findings described previously for animals that were either sacrificed *in extremis* or found dead, there were no remarkable test substance-related necropsy observations. One dam from the 500 mg/kg/day group had pale kidneys; all other surviving dams at 500 mg/kg/day appeared normal. There were no remarkable, test substance-related necropsy observations at 50 or 200 mg/kg/day.

E. Reproductive Outcome and Litter Data (Table 6, Appendices G and H)

There were no test substance-related effects evident in the reproductive outcome and litter data for animals that survived until scheduled euthanasia and had live litters. Litter mean data for corpora lutea and implantation counts, litter sizes, incidences of resorptions, fetal weight, and sex ratio were comparable across all groups on study.

There was one dam at 500 mg/kg/day whose litter consisted of one early resorption. Although this dam survived until scheduled euthanasia, this animal was in relatively poor condition by the end of the study. During the course of the study, this animal exhibited persistent reductions in food consumption, body-weight loss, and clinical signs of toxicity. Based on these data, the resorption of one fetus was considered likely to be secondary to overt maternal toxicity.

F. Fetal Alterations (Tables 7 and 8, Appendix H)

1. Malformations (Table 7, Appendix H)

There were no malformed fetuses in the current study.

2. Variations (Table 8, Appendix H)

There were test substance-related and statistically significant increases in fetal skeletal variations at 200 and 500 mg/kg/day. At 500 mg/kg/day, there were increased occurrences of delayed pelvic bone ossification and wavy ribs. At 200 and 500 mg/kg/day, there were increased incidences of delayed skull bone ossification. These findings were all considered to be test substance-related and are consistent with skeletal variations produced by a similar fluorotelomer-based alcohol.⁽²⁾ However, the effects on skull bone ossification, in particular, the increase observed at 200 mg/kg, were not considered adverse for several reasons. Retarded skull bone ossification is a relatively common observation in general and is therefore, not typically considered a tremendously reliable indicator of developmental toxicity, especially in the absence of clear test substance-related effects on fetal body weight. Relevant historical control data are provided in the table below and the incidences for all groups in the current study fall within the range of historical control data.

Historical Control Incidence for Retarded Skull Bone Ossification

Year Study Conducted	Reference	No. Affected Fetuses	No. Affected Litters
1997	1998-01367	19	10
1998	1998-01382	24	11
1998	DuPont-1165	11	8
1998	DuPont-1559	37	13
1999	1998-01500	18	8
1999	DuPont-2287	19	12
1999	DuPont-1454	21	10
1999	DuPont-3378	36	14
2000	DuPont-4177	47	14
2000	DuPont-4341	6	6
2000	DuPont-4902	35	7
2001	DuPont-5676	58	19
2001	DuPont-5991	7	7
2001	DuPont-6515	25	10
2002	DuPont-10309	54	16
2002	DuPont-11347	16	7
2002	DuPont-11358	15	11

CONCLUSIONS

Under the conditions of this study, adverse maternal toxicity was produced at 500 mg/kg/day and consisted of maternal mortality, decreased body weights and body weight gains, and increased clinical observations of toxicity. One litter at 500 mg/kg/day consisted of one early resorption; persistent reductions in food consumption and body-weight gain and increased clinical observations indicative of toxicity were reported during the study for this female. Therefore, this litter consisting of a single early resorption is believed to be secondary to overt maternal toxicity in this dam. Developmental toxicity at 500 mg/kg/day consisted of increased skeletal variations (delayed pelvic bone ossification and wavy ribs). At 200 and 500 mg/kg/day, there were non-adverse, test substance-related, transient reductions in maternal food consumption. In addition, there were slight increases in the incidence of delayed skull bone ossification at 200 and 500 mg/kg/day that were not considered adverse. Thus, the no-observed-effect level (NOEL)^a for both maternal and developmental toxicity was considered 200 mg/kg/day.

RECORDS AND SAMPLE STORAGE

Laboratory-specific or site-specific raw data, such as personnel files and equipment records will be retained by the facility where the work was done.

A sample of the test substance was collected for archive purposes and retained at Haskell Laboratory. Specimens, raw data, test substance characterization data, and the final report will be retained at Haskell Laboratory, Newark, Delaware, or at Iron Mountain Records Management, Wilmington, Delaware.

a The NOEL for this study is defined as the highest dose at which adverse effects attributable to the test substance were not detected. Thus, for this study, the NOEL is equivalent to the NOEL as defined by the U.S. EPA⁽¹³⁾ and to the no-observed-adverse-effect level (NOAEL) as defined by the European Union.⁽¹⁴⁾

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TABLES

Tables

Explanatory Notes

Notes

Day C21 = Corrected final maternal body weight = final maternal body weight minus the gravid uterine weight plus the empty uterine weight.

Abbreviations

--- = No Data
S.D. = Standard Deviation
S.E. = Standard Error
N = Number in Group

TABLE 1
SUMMARY OF DOSING ANALYSES

Nominal: Homogeneity Samples Test Day 1	Dosing Concentration of 8-2 Telomer B Alcohol (mg/mL)		
	<u>10</u>	<u>40</u>	<u>100</u>
Top	8.92 ^a (89.2) ^b	40.5 (101.3)	96.5 (96.5)
Middle	8.73 ^a (87.3)	40.0 (100.0)	98.3 ^a (98.3)
Bottom	10.0 (100.0)	39.8 (99.5)	94.8 (94.8)
Average Measured Conc. ^c	9.22	40.1	96.5
Average Percent Nominal	(92.2)	(100.3)	(96.5)
Standard Deviation ^c	± 0.69	± 0.37	± 1.8
Coefficient of Variation ^c	7%	1%	2%
Stability Samples			
5 Hour Room Temperature	9.56 (95.6)	41.1 (102.8)	104 (104.0)
Concentration Verification Test Day 11			
#1	7.28 ^a (72.8)	39.9 ^a (99.8)	100 ^a (100.0)
#2	7.23 ^a (72.3)	39.7 ^a (99.3)	101 ^a (101.0)
#3	8.71 ^d (87.1)	41.1 ^d (102.6)	98.2 ^d (98.2)
Average Measured Conc. ^e	7.74	40.2	99.7
Average Percent Nominal ^e	(77.4)	(100.5)	(99.7)
Standard Deviation ^e	± 0.84	± 0.76	± 1.4
Coefficient of Variation ^e	11%	2%	1%
Test Day 20			
#1	9.45 (94.5)	35.0 (87.5)	94.6 (94.6)
#2	9.57 (95.7)	37.8 (94.5)	91.9 (91.9)
Average Measured Conc. ^f	9.51	36.4	93.2
Average Percent Nominal ^f	(95.1)	(91.0)	(93.2)
Standard Deviation ^f	± 0.09	± 2.0	± 1.9
Coefficient of Variation ^f	1%	5%	2%

a Mean result of the original analysis and duplicate reanalysis of original sample.

b Numbers in parentheses are the respective percent of nominal values.

c Statistics based on the average measured concentration of the top, middle and bottom of each dosing level.

d Result of the analysis for the third sample collected from the dosing preparations.

e Statistics based on the average measured concentration of triplicate samples for the dosing level.

f Statistics based on the average measured concentration of duplicate samples for the dosing level.

TABLE 2
CLINICAL OBSERVATIONS

DAY OF GESTATION	OBSERVATION:	GROUP : DOSE RATE (MG/KG/DAY) : NO. EXAMINED :	I 0 22	II 50 22	III 200 22	IV 500 22
6-21	NO. SACRIFICED IN EXTREMIS		0	0	0	4*
	NO. FOUND DEAD		0	0	0	1
	ALOPECIA		5	2	6	10*
	DIARRHEA		0	0	0	6*
	HUNCHED OVER		0	0	0	6*
	PALLOR		0	0	0	1
	SORE		0	0	0	1
	STAIN CAGEBOARD		0	0	1	1
	STAIN FACE		0	0	0	1
	STAIN PERINEUM		0	0	0	3*
	WEAK		0	0	0	5*
	WET PERINEUM		0	0	0	1

* Statistically significant trend (Cochran-Armitage test); $p < 0.05$.

TABLE 3
MEAN MATERNAL BODY WEIGHTS (grams)^a

	DAY 0	DAY 4	DAYS OF GESTATION		DAY 7	DAY 8	DAY 9
			DAY 5	DAY 6			
GROUP I: 0 MG/KG/DAY							
GROUP MEAN	249.4	265.7	270.2	277.5	284.5	289.9	293.9
S.D.	10.26	11.68	11.37	12.33	11.77	11.88	11.65
S.E.	2.19	2.49	2.42	2.63	2.51	2.53	2.48
N	22	22	22	22	22	22	22
GROUP II: 50 MG/KG/DAY							
GROUP MEAN	249.6	264.6	271.0	276.3	281.5	287.9	291.6
S.D.	11.52	11.61	12.86	12.99	12.38	11.15	10.33
S.E.	2.51	2.53	2.81	2.84	2.70	2.43	2.26
N	21	21	21	21	21	21	21
GROUP III: 200 MG/KG/DAY							
GROUP MEAN	249.8	259.1	269.2	274.6	278.2	284.8	287.7
S.D.	11.38	16.20	13.81	13.09	12.21	13.59	11.90
S.E.	2.43	3.45	2.94	2.79	2.60	2.90	2.54
N	22	22	22	22	22	22	22
GROUP IV: 500 MG/KG/DAY							
GROUP MEAN	249.7	263.5	269.8	277.8	271.9*	278.3*	284.2*
S.D.	12.02	16.57	16.81	16.17	19.90	20.79	22.40
S.E.	3.00	4.14	4.20	4.04	4.97	5.20	5.60
N	16	16	16	16	16	16	16

TABLE 3 (Continued)

MEAN MATERNAL BODY WEIGHTS (grams)

	DAYS OF GESTATION						
	DAY 10	DAY 11	DAY 12	DAY 13	DAY 14	DAY 15	DAY 16
GROUP I: 0 MG/KG/DAY							
GROUP MEAN	299.6	306.8	314.3	322.4	326.0	332.8	344.3
S.D.	12.50	14.74	14.58	13.49	15.44	15.39	16.87
S.E.	2.67	3.14	3.11	2.88	3.29	3.28	3.60
N	22	22	22	22	22	22	22
GROUP II: 50 MG/KG/DAY							
GROUP MEAN	297.1	304.3	311.8	318.5	324.1	329.5	340.1
S.D.	11.84	11.02	11.99	10.86	12.77	10.78	11.37
S.E.	2.58	2.40	2.62	2.37	2.79	2.35	2.48
N	21	21	21	21	21	21	21
GROUP III: 200 MG/KG/DAY							
GROUP MEAN	292.5	299.3	308.1	316.7	320.7	330.2	341.5
S.D.	11.55	12.41	14.38	15.51	16.25	18.81	19.07
S.E.	2.46	2.65	3.07	3.31	3.46	4.01	4.07
N	22	22	22	22	22	22	22
GROUP IV: 500 MG/KG/DAY							
GROUP MEAN	287.8*	286.8*	296.0*	303.7*	313.2*	319.8*	331.2*
S.D.	17.89	21.52	25.14	23.68	20.46	23.03	23.55
S.E.	4.47	5.38	6.29	5.92	5.12	5.76	5.89
N	16	16	16	16	16	16	16

TABLE 3 (Continued)

MEAN MATERNAL BODY WEIGHTS (grams)

	DAY 17	DAY 18	DAYS OF GESTATION		DAY 21	DAY C21
			DAY 19	DAY 20		
GROUP I: 0 MG/KG/DAY						
GROUP MEAN	358.2	374.5	391.1	409.0	433.8	330.3
S.D.	17.52	18.14	20.22	21.87	25.95	20.07
S.E.	3.74	3.87	4.31	4.66	5.53	4.28
N	22	22	22	22	22	22
GROUP II: 50 MG/KG/DAY						
GROUP MEAN	354.1	369.5	385.2	401.6	427.1	332.4
S.D.	12.58	13.83	14.86	15.38	18.14	14.87
S.E.	2.74	3.02	3.24	3.36	3.96	3.24
N	21	21	21	21	21	21
GROUP III: 200 MG/KG/DAY						
GROUP MEAN	356.8	373.2	389.2	405.3	426.5	325.7
S.D.	21.47	23.80	26.02	29.39	32.75	23.20
S.E.	4.58	5.07	5.55	6.27	6.98	4.95
N	22	22	22	22	22	22
GROUP IV: 500 MG/KG/DAY						
GROUP MEAN	346.1	360.5	374.1*	386.2*	395.1*	300.4*
S.D.	25.61	27.43	28.59	28.17	34.57	29.09
S.E.	6.40	6.86	7.15	7.04	8.64	7.27
N	16	16	16	16	16	16

a Data were excluded from females that were not pregnant, found dead, sacrificed *in extremis*, or had litters consisting entirely of resorptions.

* Statistically significant trend (linear contrast of means); $p < 0.05$.

TABLE 4
MEAN MATERNAL BODY WEIGHT CHANGES (grams)^a

	DAYS OF GESTATION						
	0-6	4-6	6-8	8-10	10-12	12-14	14-16
GROUP I: 0 MG/KG/DAY							
GROUP MEAN	28.1	11.8	12.4	9.7	14.7	11.8	18.2
S.D.	8.30	3.75	4.74	4.60	5.79	4.38	4.48
S.E.	1.77	0.80	1.01	0.98	1.23	0.93	0.96
N	22	22	22	22	22	22	22
GROUP II: 50 MG/KG/DAY							
GROUP MEAN	26.7	11.7	11.5	9.2	14.8	12.3	16.0
S.D.	6.12	3.67	5.27	4.23	6.61	5.72	7.95
S.E.	1.33	0.80	1.15	0.92	1.44	1.25	1.74
N	21	21	21	21	21	21	21
GROUP III: 200 MG/KG/DAY							
GROUP MEAN	24.8	15.4	10.2	7.7	15.6	12.6	20.8
S.D.	5.77	7.95	6.47	5.14	5.52	6.31	5.71
S.E.	1.23	1.70	1.38	1.10	1.18	1.35	1.22
N	22	22	22	22	22	22	22
GROUP IV: 500 MG/KG/DAY							
GROUP MEAN	28.1	14.2	0.5*	9.5	8.2*	17.2*	18.0
S.D.	7.99	5.09	9.68	9.26	14.95	10.08	8.65
S.E.	2.00	1.27	2.42	2.31	3.74	2.52	2.16
N	16	16	16	16	16	16	16

TABLE 4 (Continued)

MEAN MATERNAL BODY WEIGHT CHANGES (grams)

	DAYS OF GESTATION			
	16-18	18-21	6-21	6-C21
GROUP I: 0 MG/KG/DAY				
GROUP MEAN	30.3	59.3	156.4	52.9
S.D.	4.18	9.91	21.46	16.15
S.E.	0.89	2.11	4.58	3.44
N	22	22	22	22

GROUP II: 50 MG/KG/DAY				
GROUP MEAN	29.4	57.6	150.8	56.1
S.D.	6.63	7.96	19.57	13.63
S.E.	1.45	1.74	4.27	2.97
N	21	21	21	21

GROUP III: 200 MG/KG/DAY				
GROUP MEAN	31.8	53.3*	151.9	51.1
S.D.	7.02	11.41	28.17	19.49
S.E.	1.50	2.43	6.01	4.16
N	22	22	22	22

GROUP IV: 500 MG/KG/DAY				
GROUP MEAN	29.3	34.6*	117.4*	22.6*
S.D.	7.50	24.96	34.43	30.68
S.E.	1.88	6.24	8.61	7.67
N	16	16	16	16

a Data were excluded from females that were not pregnant, found dead, sacrificed *in extremis*, or had litters consisting entirely of resorptions.

* Statistically significant trend (linear contrast of means); $p < 0.05$.

TABLE 5
MEAN MATERNAL FOOD CONSUMPTION (grams/day)^a

	DAYS OF GESTATION						
	4-6	6-8	8-10	10-12	12-14	14-16	16-18
GROUP I: 0 MG/KG/DAY							
GROUP MEAN	22.8	23.3	24.1	25.5	26.1	27.2	29.3
S.D.	2.78	3.47	2.35	2.94	2.68	2.65	3.83
S.E.	0.59	0.74	0.50	0.63	0.57	0.56	0.82
N	22	22	22	22	22	22	22
GROUP II: 50 MG/KG/DAY							
GROUP MEAN	23.8	21.9	23.4	25.7	26.4	26.8	30.2
S.D.	2.56	2.42	2.49	2.71	2.29	3.68	3.42
S.E.	0.56	0.53	0.54	0.59	0.50	0.80	0.75
N	21	21	21	21	21	21	21
GROUP III: 200 MG/KG/DAY							
GROUP MEAN	23.5	21.3*	22.1*	24.6	26.1	28.4	31.9*
S.D.	2.39	2.40	2.22	3.65	3.57	3.28	2.96
S.E.	0.51	0.51	0.47	0.78	0.76	0.70	0.63
N	22	22	22	22	22	22	22
GROUP IV: 500 MG/KG/DAY							
GROUP MEAN	23.7	19.9*	21.4*	20.6*	25.8	27.9	31.8*
S.D.	3.03	5.91	3.25	6.76	4.28	4.44	5.31
S.E.	0.76	1.48	0.81	1.69	1.07	1.11	1.33
N	16	16	16	16	16	16	16

TABLE 5 (Continued)

MEAN MATERNAL FOOD CONSUMPTION (grams/day)

	DAYS OF GESTATION	
	18-21	6-21
GROUP I: 0 MG/KG/DAY		
GROUP MEAN	28.1	26.4
S.D.	3.84	2.64
S.E.	0.82	0.56
N	22	22

GROUP II: 50 MG/KG/DAY		
GROUP MEAN	28.2	26.2
S.D.	2.47	2.00
S.E.	0.54	0.44
N	21	21

GROUP III: 200 MG/KG/DAY		
GROUP MEAN	28.4	26.3
S.D.	3.88	2.46
S.E.	0.83	0.52
N	22	22

GROUP IV: 500 MG/KG/DAY		
GROUP MEAN	25.4	24.7
S.D.	5.55	2.88
S.E.	1.39	0.72
N	16	16

a Data were excluded from females that were not pregnant, found dead, sacrificed *in extremis*, or had litters consisting entirely of resorptions.

* Statistically significant trend (linear contrast of means); $p < 0.05$.

TABLE 6

REPRODUCTIVE OUTCOME

Group:		I	II	III	IV
Dose (mg/kg/day):		0	50	200	500
No. Mated		22	22	22	22
No. Pregnant		22	21	22	22
No. Delivered Early		0	0	0	0
No. Deaths		0	0	0	5*
No. With Total Resorptions		0	0	0	1
No. Litters		22	21	22	16
Mean Corpora Lutea ^a		15.7 (1.61) ^b	16.0 (3.04)	16.0 (3.40)	16.1 (2.51)
Implantations (Nidations)		14.7 (1.62)	13.9 (1.56)	13.9 (1.64)	13.4 (3.87)
Resorptions:	Total	0.0 (0.21)	0.7 (1.06)	0.4 (0.79)	0.4 (0.81)
	Early	0.0 (0.21)	0.7 (1.06)	0.4 (0.79)	0.4 (0.81)
	Late	0.0	0.0	0.0	0.1 (0.25)
Dead Fetuses		0.0	0.0	0.0	0.0
Live Fetuses ^c :	Total	14.6 (1.56)	13.2 (1.81)	13.5 (1.77)	13.8 (1.95)
	Males	7.2 (1.79)	6.0 (1.58)	6.7 (2.16)	7.1 (1.84)
	Females	7.5 (1.74)	7.2 (1.69)	6.8 (1.97)	6.7 (1.89)
Mean Fetal Weight:	Total	5.55 (0.31)	5.66 (0.29)	5.77 (0.39)	5.40 (0.44)
	Males	5.68 (0.33)	5.83 (0.34)	5.94 (0.40)	5.57 (0.47)
	Females	5.43 (0.32)	5.51 (0.26)	5.59 (0.42)	5.20 (0.39)
Sex Ratio ^d		0.49 (0.11)	0.45 (0.11)	0.50 (0.14)	0.51 (0.12)

a Statistical analyses are not conducted on mean corpora lutea data; these data are presented for information only.

b Standard deviation is reported in parentheses.

c Statistical analyses are only conducted on the mean total number of live fetuses per litter and total mean fetal weight. The means for males and females are presented for information only.

d Number male fetuses/total number fetuses per litter.

Note: The pregnancy rate data, adult mortality data, and the total resorption data were statistically analyzed using the Cochran-Armitage test. All litter mean data (except for fetal weight and sex ratio) were analyzed using Jonckheere's test. Fetal weight and sex ratio were analyzed using a linear contrast of least square means.

* Statistically significant trend; $p < 0.05$.

TABLE 7
INCIDENCE OF FETAL MALFORMATIONS

	Group:	I	II	III	IV
	Dose (mg/kg/day):	0	50	200	500
<u>EXTERNAL</u>					
No. Examined ^a		322 [22]	277 [21]	297 [22]	220 [16]
No. Affected		0 [0]	0 [0]	0 [0]	0 [0]
<u>VISCERAL</u>					
No. Examined		167 [22]	142 [21]	156 [22]	113 [16]
No. Affected		0 [0]	0 [0]	0 [0]	0 [0]
<u>HEAD</u>					
No. Examined		167 [22]	142 [21]	156 [22]	113 [16]
No. Affected		0 [0]	0 [0]	0 [0]	0 [0]
<u>SKELETAL</u>					
No. Examined		322 [22]	277 [21]	297 [22]	220 [16]
No. Affected		0 [0]	0 [0]	0 [0]	0 [0]
<u>TOTAL NUMBER AFFECTED</u>					
		0 (0)	0 (0)	0 (0)	0 (0)

- a Number examined and affected, including the number affected with the listed malformations are expressed as Fetuses[Litters] or Fetuses (Litters).
 b For ease of reading, zeros have been replaced with dashes for the listed malformations.

No significant trends were detected (Jonckheere-Terpstra Trend test); $p < 0.05$.

Note: Statistical analyses are only conducted on the individual endpoints. The overall total and totals by exam type are presented for information only.

TABLE 8
INCIDENCE OF FETAL VARIATIONS

	Group:	I	II	III	IV
Dose (mg/kg/day):		0	50	200	500
DEVELOPMENTAL VARIATIONS					
<u>EXTERNAL</u>					
No. Examined ^a		322 [22]	277 [21]	297 [22]	220 [16]
No. Affected		0 [0]	0 [0]	0 [0]	0 [0]
<u>VISCERAL</u>					
No. Examined		167 [22]	142 [21]	156 [22]	113 [16]
No. Affected		0 [0]	0 [0]	0 [0]	0 [0]
<u>HEAD</u>					
No. Examined		167 [22]	142 [21]	156 [22]	113 [16]
No. Affected		0 [0]	0 [0]	0 [0]	0 [0]
<u>SKELETAL</u>					
No. Examined		322 [22]	277 [21]	297 [22]	220 [16]
Rib					
- Rudimentary Cervical		---	---	2 (1)	1 (1)
- Supernumerary		25 (11)	20 (13)	32 (15)	34 (10)
Skull - Fused		---	---	---	1 (1)
No. Affected		25 (11)	20 (13)	34 (16)	35 (11)
TOTAL WITH DEVELOPMENTAL VARIATIONS		25 (11)	20 (13)	34 (16)	35 (11)
VARIATIONS DUE TO RETARDED DEVELOPMENT					
<u>EXTERNAL</u>					
No. Examined ^a		322 [22]	277 [21]	297 [22]	220 [16]
No. Affected		0 [0]	0 [0]	0 [0]	0 [0]
<u>VISCERAL</u>					
No. Examined		167 [22]	142 [21]	156 [22]	113 [16]
Kidney ^b					
Small Papilla - Size 1		2 (2)	---	1 (1)	2 (2)
Small Papilla - Size 2		4 (3)	2 (2)	1 (1)	1 (1)
Papilla - Size 3		6 (6)	5 (5)	3 (3)	2 (1)
No. Affected		12 [9]	7 [7]	5 [5]	5 [3]

TABLE 8 (Continued)

INCIDENCE OF FETAL VARIATIONS

VARIATIONS DUE TO RETARDED DEVELOPMENT (Continued)HEAD

No. Examined	167[22]	142[21]	156[22]	113[16]
No. Affected	0[0]	0[0]	0[0]	0[0]

SKELETAL

No. Examined	322[22]	277[21]	297[22]	220[16]
Pelvis - Retarded Ossification	1(1)	---	---	9(5)*
Rib - Wavy	---	---	---	5(2)*
Skull - Retarded Ossification	22(8)	31(12)	45(16)*	55(12)*
Sternebra - Retarded Ossification	5(3)	2(2)	3(2)	8(5)
Vertebra - Retarded Ossification	37(12)	30(8)	34(13)	12(6)
No. Affected	56([15]	56[13]	72[19]	73[14]

TOTAL WITH VARIATIONS

DUE TO RETARDED DEVELOPMENT	66(17)	63(15)	76(19)	78(15)
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TOTAL NUMBER FETUSES WITH VARIATIONS	89(21)	80(19)	99(20)	106(15)
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- a Number examined and affected, including the number affected with the listed variations, are expressed as Fetuses[Litters] or Fetuses (Litters).
- b Statistical analyses are conducted on the combined incidences of small renal papillae; the details for each size are presented for information only.

* Significant trend (Jonckheere's test); $p < 0.05$.

Note: Statistical analyses are only conducted on the individual endpoints. The overall total and totals by exam are presented for information only.

APPENDICES

APPENDIX A

Analytical Chemistry Report

Table I. Recovery of 8-2 Telomer B Alcohol Added to Dosing Vehicle

Sample Type	mg/ml 8-2 Telomer B Alcohol		Percent Nominal
	Nominal	Measured	
RECOVERY ^(A)	10.5	9.37	89.2
RECOVERY ^(B)	10.5	9.55	91.0
RECOVERY ^(C)	14.8	13.7	92.6
RECOVERY ^(D)	14.8	12.5	84.5
RECOVERY ^(E)	14.8	12.6	85.1
RECOVERY ^(F)	11.8	10.7	<u>90.7</u>
		Mean:	88.9 ± 3.3, C.V. 4%
RECOVERY ^(A)	40.3	33.0	81.9
RECOVERY ^(C)	58.8	48.2	82.0
RECOVERY ^(D)	58.8	50.0	85.0
RECOVERY ^(E)	58.8	50.0	85.0
RECOVERY ^(F)	44.9	42.0	<u>93.5</u>
		Mean:	85.5 ± 4.7, C.V. 5%
RECOVERY ^(A)	109	93.7	86.0
RECOVERY ^(B)	109	93.0	85.3
RECOVERY ^(C)	144	110	76.4
RECOVERY ^(D)	144	115	79.9
RECOVERY ^(E)	144	115	79.9
RECOVERY ^(F)	132	119	<u>90.2</u>
		Mean:	83.0 ± 5.1, C.V. 6%

(A) Processed with homogeneity and concentration verification samples collected on test day 1 (February 3, 2003).

(B) Processed with homogeneity and concentration verification re-analysis samples collected on test day 1 (February 3, 2003).

(C) Processed with concentration verification samples collected on test day 11 (February 12, 2003).

(D) Processed with concentration verification duplicate re-analysis of the original samples collected test day 11 (February 12, 2003).

(E) Processed with concentration verification analysis for re-sampling of the original formulations prepared test day 11 (February 12, 2003).

(F) Processed with concentration verification samples collected on test day 20 (February 21, 2003).

Table II. Homogeneity and Stability of 8-2 Telomer B Alcohol in Dosing Formulations

Sample Type	mg/mL 8-2 Telomer B Alcohol(A)		Percent
	Nominal	Measured	Nominal
Test Day 1 (3-Feb-2003)			
<u>Homogeneity</u>			
CONTROL	0.00	ND(B)	----
TOP	10-O	8.48	84.8
	10-1	9.13	91.3
	10-2	<u>9.15</u>	91.5
	<i>Mean(C):</i>	8.92	(89.2%)
MIDDLE	10-O	8.79	87.9
	10-1	8.62	86.2
	10-2	<u>8.77</u>	87.7
	<i>Mean(C):</i>	8.73	(87.3%)
BOTTOM	10	<u>10.0</u>	100.0
	<i>Mean(D):</i>	9.22 ± 0.69	(92.2%)
		C.V. 7%	
TOP	40	40.5	101.3
MIDDLE	40	40.0	100.0
BOTTOM	40	<u>39.8</u>	99.5
	<i>Mean(D):</i>	40.1 ± 0.37	(100.3%)
		C.V. 1%	
TOP	100	96.5	96.5
MIDDLE	100-O	92.0	92.0
	100-1	102	102.0
	100-2	<u>101</u>	101.0
	<i>Mean(C):</i>	98.3	(98.3%)
BOTTOM	100	<u>94.8</u>	94.8
	<i>Mean(D):</i>	96.5 ± 1.8	(96.5%)
		C.V. 2%	
<u>Stability</u>			
5 HOUR(E)	10	9.56	95.6
	40	41.1	102.8
	100	104	104.0

(A) All results corrected for spiked recovery based on the level and day of analysis (Refer to Table I).

(B) Denotes not detected.

(C) Mean result of the original analysis (-O) and duplicate reanalysis of original sample (-1, -2).

(D) The average measured concentration, average percent of nominal (in parentheses), standard deviation, and coefficient of variation of top, middle, and bottom.

(E) Stability samples held 5 hours a room temperature.

Table III. Concentration Verification of 8-2 Telomer B Alcohol in Dosing Solutions

Preparation Day	mg/mL 8-2 Telomer B Alcohol ^(A)		Percent
Sample Type	Nominal	Measured	Nominal
Test Day 11 (12-Feb-2003)			
<u>Concentration Verification^(B)</u>			
Control	0.0	ND ^(C)	----
	10-1	6.52	65.2
	10-1A	7.63	76.3
	10-1B	<u>7.70</u>	77.0
	Mean^(D):	7.28	72.8
	10-2	6.32	63.2
	10-2A	7.88	78.8
	10-2B	<u>7.48</u>	74.8
	Mean^(D):	7.23	72.3
	10-3	<u>8.71</u>	87.1
	Mean^(E):	7.74 ± 0.84	(77.4)
		C.V. 11%	
	40-1	38.9	97.3
	40-1A	40.8	102.0
	40-1B	<u>39.9</u>	99.8
	Mean^(D):	39.9	99.8
	40-2	38.0	95.0
	40-2A	40.8	102.0
	40-2B	<u>40.2</u>	100.5
	Mean^(D):	39.7	99.3
	40-3	<u>41.1</u>	102.6
	Mean^(E):	40.2 ± 0.76	(100.5)
		C.V. 2%	
	100-1	102	102.0
	100-1A	98.7	98.7
	100-1B	<u>99.2</u>	99.2
	Mean^(D):	100	100.0
	100-2	97.1	97.1
	100-2A	102	102.0
	100-2B	<u>105</u>	105.0
	Mean^(D):	101	101.0
	100-3	<u>98.2</u>	98.2
	Mean^(E):	99.7 ± 1.4	(99.7)
		C.V. 1%	

(A) All results corrected for spiked recovery based on the level and day of analysis (Refer to Table I).

(B) Duplicate samples (-1, -2) per level were analyzed. Mean, S.D. and C.V. calculated to verify uniformity of mixture.

(C) Denotes not detected.

(D) The average measured concentration, average percent of nominal for duplicate samples (-1, and -2), and duplicate reanalysis analysis of the original sample (-1A, -1B and -2A, -2B).

(E) The average measured concentration, average percent of nominal (in parentheses), standard deviation, and coefficient of variation for duplicate samples based on footnote (D) and the analysis of the 3rd sample from the original dosing preparation (-3).

Table III. Concentration Verification of 8-2 Telomer B Alcohol in Dosing Solutions (continued)

Preparation Day	mg/mL 8-2 Telomer B Alcohol(A)		Percent
Sample Type	Nominal	Measured	Nominal
Test Day 20 (21-Feb-2003)			
<u>Concentration Verification(B)</u>			
Control	0.0	ND(C)	----
	10-1	9.45	94.5
	10-2	<u>9.57</u>	95.7
	Mean(F):	9.51 ± 0.09	(95.1)
		C.V. 1%	
	40-1	35.0	87.5
	40-2	<u>37.8</u>	94.5
	Mean(F):	36.4 ± 2.0	(91.0)
		C.V. 5%	
	100-1	94.6	94.6
	100-2	<u>91.9</u>	91.9
	Mean(F):	93.2 ± 1.9	(93.2)
		C.V. 2%	

(A) All results corrected for spiked recovery based on the level and day of analysis (Refer to Table I).

(B) Duplicate samples (-1, -2) per level were analyzed. Mean, S.D. and C.V. calculated to verify uniformity of mixture.

(C) Denotes not detected.

(F) The average measured concentration, average percent of nominal (in parentheses), standard deviation, and coefficient of variation for duplicate samples

Figure 1
Representative Analytical Calibration Curve

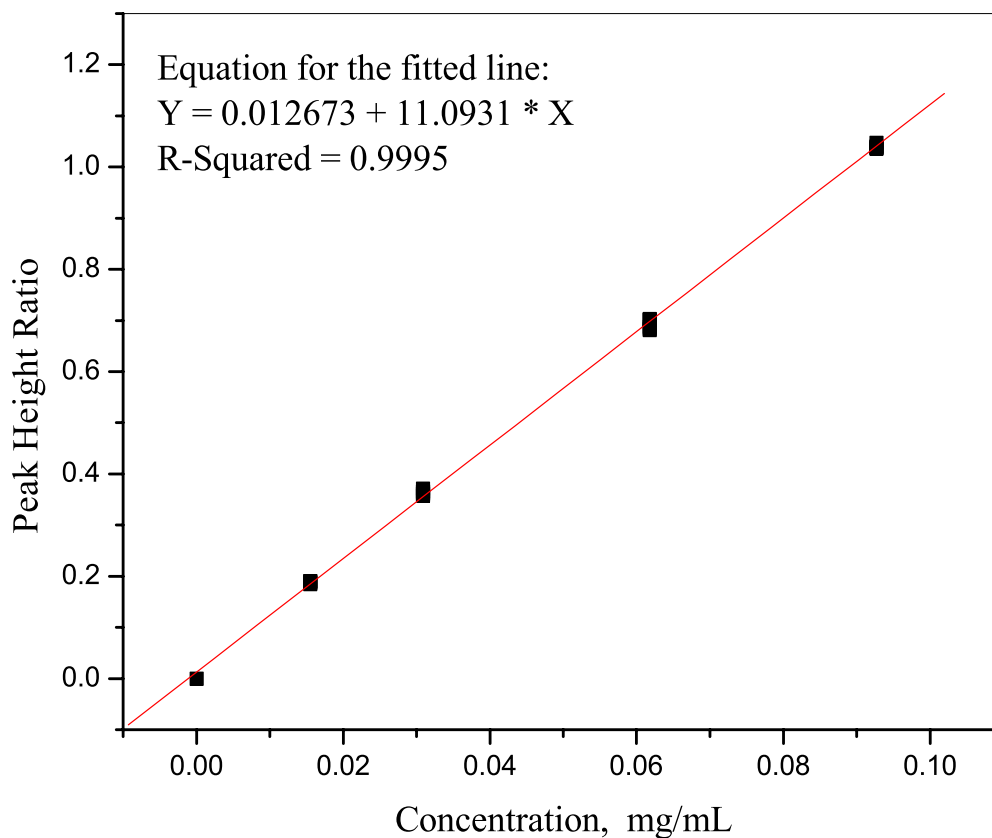


Figure 1: Calibration curve showing linear fit (line) to replicate peak height ratio measurements (squares) for calibration solutions of 8-2 Telomer B Alcohol diluted over a concentration range of 0.0155 to 0.0927 mg/mL with the 0 mg/mL control diluted sample was used as the zero.

Figure 2
Representative High Performance Liquid Chromatography Chromatograms

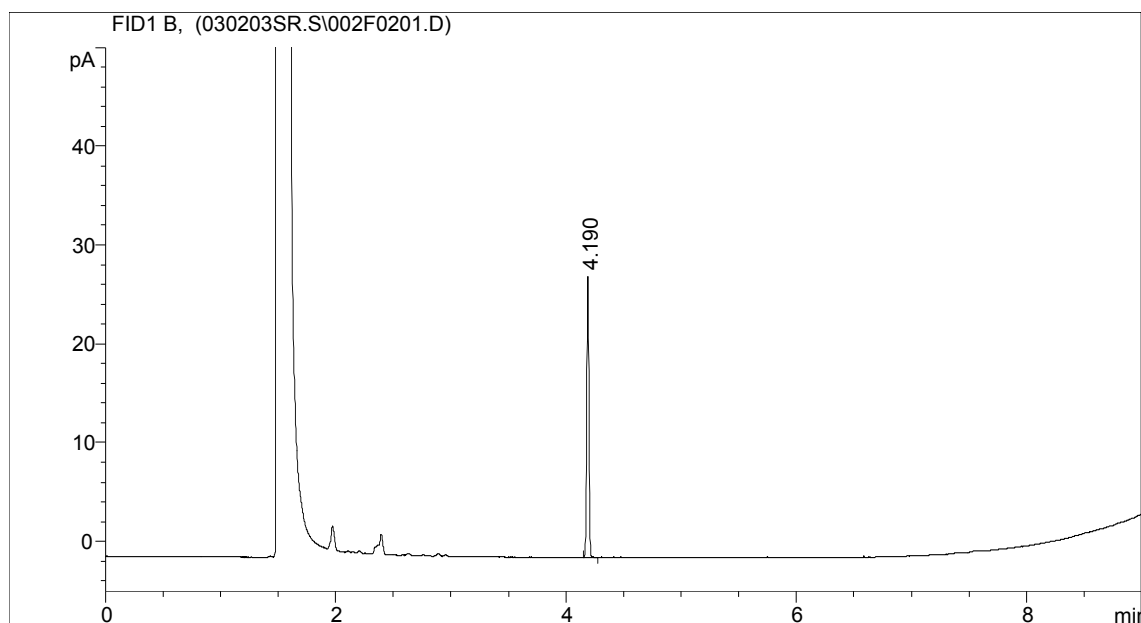


Figure 2a: Representative HPLC chromatogram of 0 mg/mL (control) sample with internal standard (1H,1H,2H,2H-perfluoro-9-methyldecan-1-ol) added. Retention time for 8-2 Telomer B Alcohol is approximately 3.7 minutes. Retention time for internal standard is approximately 4.1 minutes.

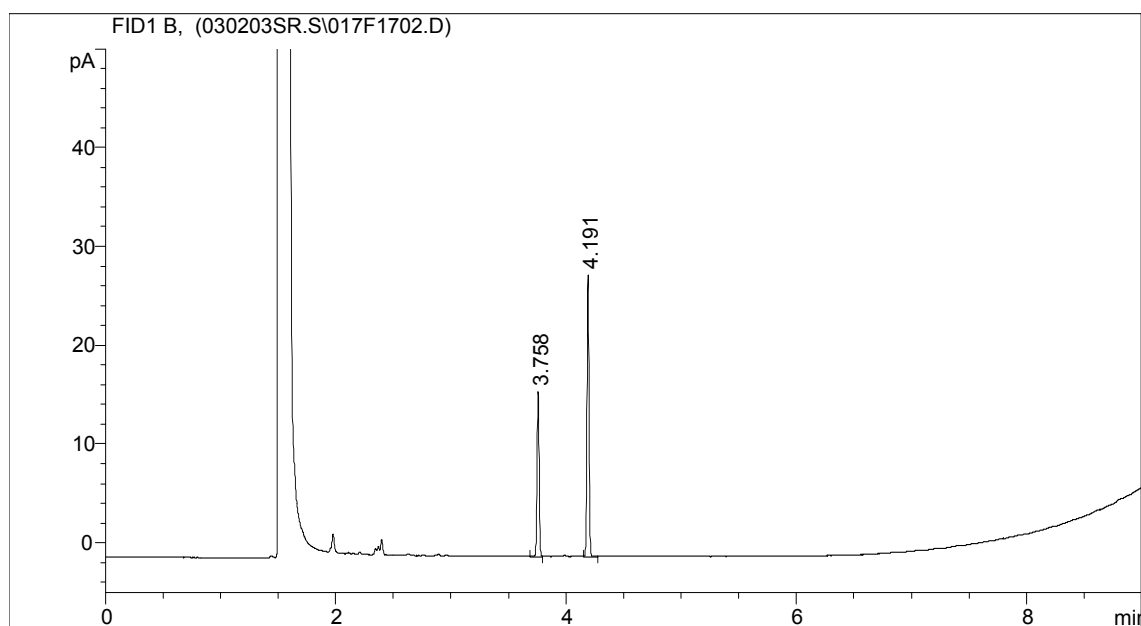


Figure 2b: Representative HPLC chromatogram of 40.0 mg/mL 8-2 Telomer B Alcohol dosing solution diluted to a nominal concentration of 0.06 mg/mL. The measured concentration of the representative solution is 41.1 mg/mL

Figure 2 (continued)
Representative High Performance Liquid Chromatography Chromatograms

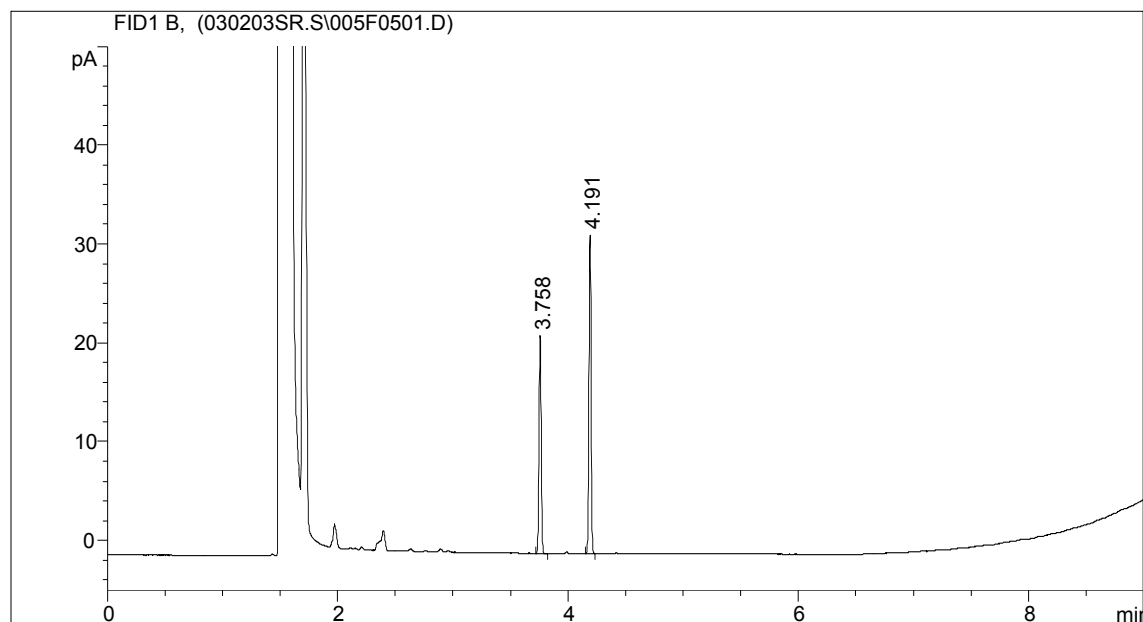


Figure 2c: Representative HPLC chromatogram of 0.0618 mg/mL 8-2 Telomer B Alcohol analytical reference solution.

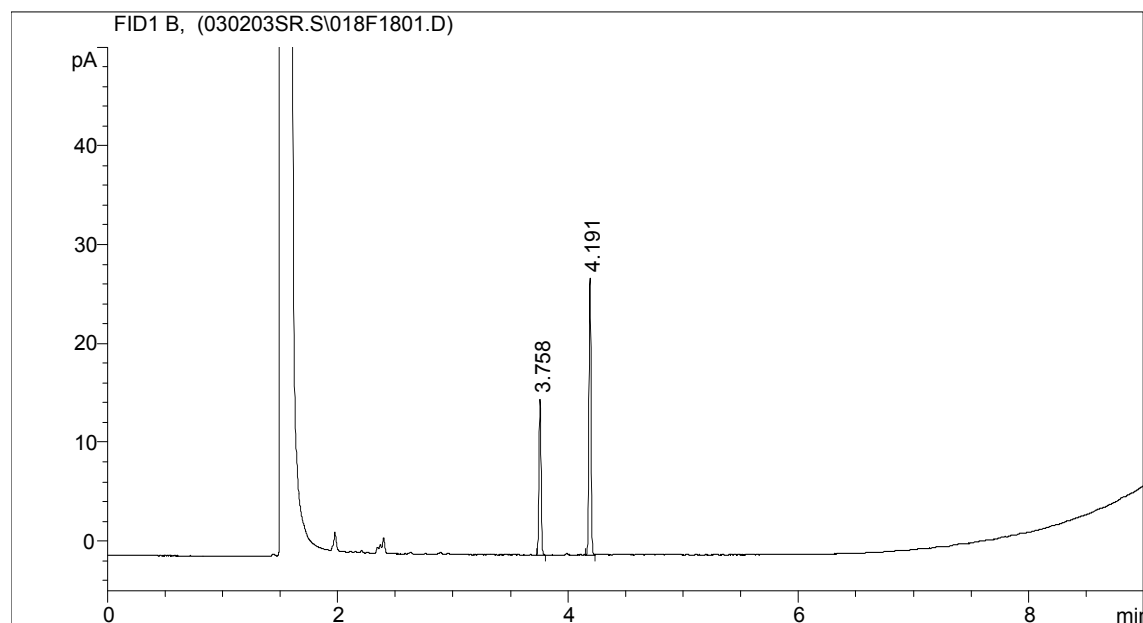


Figure 2d: Representative HPLC chromatogram of 40.3 mg/mL 8-2 Telomer B Alcohol spiked recovery solution diluted to a nominal concentration of 0.06 mg/mL. The measured concentration of the representative solution is 33.0 mg/mL.

APPENDIX B

Individual Clinical Observations

Individual Clinical Observations

Explanatory Notes

Note

The first observation recorded each day is indicated by “a”; the second by “b”. Observations were made twice daily on days 6-20G. If no abnormal signs were observed during the study examinations, the “b” entries are omitted from the report.

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER:	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
670974	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670981	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670985	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20, 21
		b: , , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20,
	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670986	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670987	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670989	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670994	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
670998	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
		b: , , , , , , , , 11, 12, 13, 14, 15, 16, 17, 18, 19, 20,
	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
670999	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
671002	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , , , , , , , 18, 19, 20, 21
		b: , , , , , , , , , , , , , , 18, 19, 20,
	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
671007	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER:	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
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671015	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , , 21
671017	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , , 21
671031	ALOPECIA RIGHT FRONT LEG	a: , , , , , , , , , , , , , 16, 17, 18, 19, 20,
		b: , , , , , , , , , , , , , 16, 17, 18, 19, ,
	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , , 21
671033	ALOPECIA BOTH FRONT LEG	a: , , , , , , , , , , , , , , 19, 20, 21
		b: , , , , , , , , , , , , , , 19, 20,
	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , , 21
671035	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , , 21
671039	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , , 21
671042	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , , 21
671044	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , , 21
671045	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , , 21
671054	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , , 21
671055	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , , 21

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER:	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
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670975	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670976	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670978	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670980	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670984	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670990	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , , 21
670993	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
671000	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
671003	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
671008	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
671012	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , , 21
671016	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , , 21

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER:	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
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671019	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , , 13, , , , , , , , ,
		b: , , , , , , , , , 13, , , , , , , , ,
	ALOPECIA RIGHT FRONT PAW	a: , , , , , , , , , 14, 15, 16, 17, 18, 19, 20, 21
		b: , , , , , , , , , 14, 15, 16, 17, 18, 19, 20, ,
	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , 21
671020	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , 21
671025	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , 21
671026	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , 21
671034	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , , , 14, 15, 16, 17, 18, 19, 20, 21
		b: , , , , , , , , , , 14, 15, 16, 17, 18, 19, 20, ,
	ALOPECIA LEFT FRONT LEG	a: , , , , , , , , , , 14, 15, , , , , , , ,
		b: , , , , , , , , , , 14, 15, , , , , , , ,
	ALOPECIA BOTH FRONT LEG	a: , , , , , , , , , , , 16, 17, 18, 19, 20, 21
		b: , , , , , , , , , , , 16, 17, 18, 19, 20, ,
	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , , , 21
671043	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , 21
671048	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , 21
671050	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , 21
671052	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , 21
671056	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , , , 21

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER:	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
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670970	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20, 21
		b: , , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20,
	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , 21
670972	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , 21
670979	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , 21
670983	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , 21
670988	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , 21
670992	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , 21
670995	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , 21
670996	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , , , 14, 15, 16, 17, 18, 19, 20, 21
		b: , , , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20,
	ALOPECIA BOTH FRONT LEG	a: , , , , , , , , , , , 15, 16, 17, 18, 19, 20, 21
		b: , , , , , , , , , , , 15, 16, 17, 18, 19, 20,
	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , 21
670997	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , 21
671009	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , 21
671010	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , 21

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER:	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
671024	ALOPECIA BOTH REAR LEG	a: , , , , , , , 11, 12, 13, 14, 15, 16, 17, , , , b: , , , , , , , 11, 12, 13, 14, 15, 16, 17, , , ,
	ALOPECIA LEFT HIND QUARTERS	a: , , , , , , , , , , , , , 17, 18, 19, 20, 21 b: , , , , , , , , , , , , , 17, 18, 19, 20,
	ALOPECIA RIGHT REAR LEG	a: , , , , , , , , , , , , , 18, 19, 20, 21 b: , , , , , , , , , , , , , 18, 19, 20,
	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , 21
671027	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , 21
671028	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , 21
671029	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , 21
671030	ALOPECIA BOTH FRONT LEG	a: , , , , , , , 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21 b: , , , , , , 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20,
	ALOPECIA CHEST	a: , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20, 21 b: , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20,
	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , , 21
671032	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , ^a , , , , , , , , , , 21
671036	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , 21
671037	STAIN CAGEBOARD RED	a: , , , , , , , , 13, , , , , , , , b: , , , , , , , , 13, , , , , , , ,
	ALOPECIA RIGHT FRONT LEG	a: , , , , , , , , , , , , , , 19, 20, 21 b: , , , , , , , , , , , , , , 19, 20,
	SACRIFICED BY DESIGN 02/24/03	a: , , , , , , , , , , , , , , , , 21

a Clinical observations for this rat were inadvertently not recorded on gestation day 10. Rat had "No Abnormalities Detected" for the morning of gestation day 10 and the morning of gestation day 11.

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP III: 200 MG/KG/DAY

ANIMAL	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED:
NUMBER:		4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21

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671038
  SACRIFICED BY DESIGN 02/24/03    a:  , , , , , , , , , , , , , , , , , , , 21

671040
  ALOPECIA ABDOMINAL                a:  , , , , , , 10,11,12,13,14,15,16,17,18,19,20,21
                                     b:  , , , , , , 10,11,12,13,14,15,16,17,18,19,20,
  ALOPECIA LEFT SIDE                a:  , , , , , , 10,11,12,13, , , , , , , , ,
                                     b:  , , , , , , 10,11,12,13, , , , , , , , ,
  ALOPECIA RIGHT HIND QUARTERS      a:  , , , , , , , 12, , , , , , , , ,
                                     b:  , , , , , , , 12, , , , , , , , ,
  ALOPECIA BOTH HIND QUARTERS       a:  , , , , , , , , 13,14,15,16,17,18,19,20,21
                                     b:  , , , , , , , , 13,14,15,16,17,18,19,20,
  ALOPECIA BOTH SIDE                a:  , , , , , , , , 14,15,16,17,18,19,20,21
                                     b:  , , , , , , , , 14,15,16,17,18,19,20,
  ALOPECIA PERINEUM                 a:  , , , , , , , , , , , , , , , 20,21
                                     b:  , , , , , , , , , , , , , , , 20,
  SACRIFICED BY DESIGN 02/24/03    a:  , , , , , , , , , , , , , , , , , , , 21

671049
  SACRIFICED BY DESIGN 02/24/03    a:  , , , , , , , , , , , , , , , , , , , 21

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INDIVIDUAL CLINICAL OBSERVATIONS

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER:	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
670971	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , 21
670973	HUNCHED OVER	a: , , , , , , , , 12, 13, , , , , , , , ,
	DIARRHEA	b: , , , , , , , 11, 12, , , , , , , , ,
	STAIN PERINEUM BROWN	a: , , , , , , , , 13, , , , , , , , ,
	WEAK	a: , , , , , , , , 13, , , , , , , , ,
	SACRIFICED IN EXTREMIS 02/10/03	a: , , , , , , , , 13, , , , , , , , ,
670977	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , 21
670982	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , , , 15, 16, 17, 18, 19, 20, 21
	SACRIFICED BY DESIGN 2/18/03	b: , , , , , , , , , , 15, 16, 17, 18, 19, 20, ,
		a: , , , , , , , , , , , , , , , , , , 21
670991	SACRIFICED BY DESIGN 2/18/03	a: , , , , , , , , , , , , , , , , , , 21
671001	ALOPECIA BOTH FRONT LEG	a: , , , , , , , , , , , 16, 17, 18, 19, 20, 21
	ALOPECIA BOTH FRONT PAW	b: , , , , , , , , , , , 16, 17, 18, 19, 20, ,
	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , 18, 19, 20, 21
		b: , , , , , , , , , , , , , 18, 19, 20, ,
		a: , , , , , , , , , , , , , , , , , , 21
671004	ALOPECIA LEFT FRONT LEG	a: , , , , , , , , , , , 15, 16, 17, , , , ,
	ALOPECIA BOTH FRONT LEG	b: , , , , , , , , , , , 15, 16, 17, , , , ,
	ALOPECIA ABDOMINAL	a: , , , , , , , , , , , , , 18, 19, 20, 21
	PALLOR	b: , , , , , , , , , , , , , 18, 19, 20, ,
	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , , , , 21
		a: , , , , , , , , , , , , , , , , , , 21

GROUP IV: 500 MG/KG/DAY

671005		
	ALOPECIA ABDOMINAL	a: , , , , , 9,10,11,12, , , , , , , , ,
		b: , , , , , 9,10,11, , , , , , , , ,
	HUNCHED OVER	a: , , , , , , 11,12, , , , , , , ,
		b: , , , , , , 10,11, , , , , , , ,
	DIARRHEA	a: , , , , , , , 12, , , , , , , ,
		b: , , , , , , , 11, , , , , , , ,
	WEAK	a: , , , , , , , 12, , , , , , , ,
	SACRIFICED IN EXTREMIS 02/10/03	a: , , , , , , , 12, , , , , , , ,
671006		
	ALOPECIA LEFT FRONT PAW	a: , , , , , , , , , 14, , , , , , ,
		b: , , , , , , , , , 14, , , , , , ,
	ALOPECIA BOTH FRONT PAW	a: , , , , , , , , , , 15,16,17,18,19,20,21
		b: , , , , , , , , , , 15,16,17,18,19,20,
	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , 21
671011		
	ALOPECIA LEFT HIND QUARTERS	a: , , , , , , , , , , , , , , 19,20,21
		b: , , , , , , , , , , , , , , 19,20,
	ALOPECIA ABDOMINAL	a: , , , , , , , , , , , , , , 19,20,21
		b: , , , , , , , , , , , , , , 19,20,
	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , 21
671013		
	SACRIFICED BY DESIGN 02/19/03	a: , , , , , , , , , , , , , , , 21
671014		
	ALOPECIA LEFT HIND QUARTERS	a: , , , , , , 10,11,12, , , , , , , , ,
		b: , , , , , , 10,11,12, , , , , , , , ,
	ALOPECIA BOTH HIND QUARTERS	a: , , , , , , , , , 13,14,15,16,17,18,19,20,21
		b: , , , , , , , , , 13,14,15,16,17,18,19,20,
	ALOPECIA RIGHT SIDE	a: , , , , , , , , , 13,14, , , , , ,
		b: , , , , , , , , , 13,14, , , , , ,
	ALOPECIA BOTH SIDE	a: , , , , , , , , , , 15,16,17,18,19,20,21
		b: , , , , , , , , , , 15,16,17,18,19,20,
	ALOPECIA BACK	a: , , , , , , , , , , 15,16,17,18,19,20,21
		b: , , , , , , , , , , 15,16,17,18,19,20,
	SACRIFICED BY DESIGN 02/20/03	a: , , , , , , , , , , , , , , , 21

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP IV: 500 MG/KG/DAY

ANIMAL	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED:
NUMBER:		4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21

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671018
  ALOPECIA BOTH FRONT LEG      a:  , , , 7,8,9,10,11,12,13,14,15,16,17,18,19,20,21
                                b:  , , 6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,
  ALOPECIA ABDOMINAL           a:  , , , 8,9,10, , , , , , , , , , ,
                                b:  , , , 8,9, , , , , , , , , , , ,
  ALOPECIA BOTH FRONT PAW      a:  , , , , 9,10,11,12,13,14,15,16,17,18,19,20,21
                                b:  , , , , 9,10,11,12,13,14,15,16,17,18,19,20,
  ALOPECIA UNDERBODY          a:  , , , , , 11,12,13,14,15,16,17,18,19,20,21
                                b:  , , , , , 10,11,12,13,14,15,16,17,18,19,20,
  ALOPECIA BOTH REAR LEG       a:  , , , , , , 12,13,14,15,16,17, , , ,
                                b:  , , , , , , 12,13,14,15,16,17, , , ,
  ALOPECIA LEFT HIND QUARTERS  a:  , , , , , , 12,13,14,15,16, , , ,
                                b:  , , , , , , 12,13,14,15,16, , , ,
  ALOPECIA CHEST               a:  , , , , , , , 13,14,15,16,17, , 19,20,21
                                b:  , , , , , , , 13,14,15,16,17, , 19,20,
  ALOPECIA BOTH HIND QUARTERS  a:  , , , , , , , , 17,18,19,20,21
                                b:  , , , , , , , , 17,18,19,20,
  SACRIFICED BY DESIGN 02/20/03 a:  , , , , , , , , , , , , , , , 21

671021
  HUNCHED OVER                 a:  , , , , , , 11, , , , , , , , ,
  DIARRHEA                     a:  , , , , , , 11, , , , , , , , ,
  STAIN FACE BROWN             a:  , , , , , , 11, , , , , , , , ,
  WEAK                         a:  , , , , , , 11, , , , , , , , ,
  STAIN PERINEUM BROWN         a:  , , , , , , 11, , , , , , , , ,
  WET PERINEUM                 a:  , , , , , , 11, , , , , , , , ,
  SACRIFICED IN EXTREMIS 02/10/03 a:  , , , , , , 11, , , , , , , , ,

671022
  SACRIFICED BY DESIGN 02/20/03 a:  , , , , , , , , , , , , , , , 21

671023
  SACRIFICED BY DESIGN 02/20/03 a:  , , , , , , , , , , , , , , , 21

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INDIVIDUAL CLINICAL OBSERVATIONS

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER:	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED: 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
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671041	WEAK	a: / / / / 9,10, / / / / / / / / / / b: / / / / 9,10, / / / / / / / / / /
	HUNCHED OVER	a: / / / / 9,10, / / / / / / / / / / b: / / / / 9,10, / / / / / / / / / /
	DIARRHEA	a: / / / / 10, / / / / / / / / / / b: / / / / 9,10, / / / / / / / / / /
	STAIN PERINEUM BROWN	a: / / / / 10, / / / / / / / / / / b: / / / / 10, / / / / / / / / / /
	SACRIFICED IN EXTREMIS 02/13/03	a: / / / / / / / / / / / / / / / / b: / / / / / 10, / / / / / / / / / /
671046	ALOPECIA LEFT HIND QUARTERS	a: / / / / 8,9,10, / / / / / / / / / / b: / / / / 8,9,10, / / / / / / / / / /
	ALOPECIA LEFT REAR LEG	a: / / / / 9,10,11,12, / / / / / / / / / / b: / / / / 9,10,11,12, / / / / / / / / / /
	ALOPECIA PERINEUM	a: / / / / 9,10,11,12,13,14,15,16,17,18, / / / b: / / / / 9,10,11,12,13,14,15,16,17,18, / / /
	ALOPECIA BOTH HIND QUARTERS	a: / / / / / / 11,12,13,14,15,16,17,18,19,20,21 b: / / / / / / 11,12,13,14,15,16,17,18,19,20,
	ALOPECIA BOTH REAR LEG	a: / / / / / / / 13,14,15,16,17,18,19,20,21 b: / / / / / / / 13,14,15,16,17,18,19,20,
	ALOPECIA ABDOMINAL	a: / / / / / / / / / / / 18, / / / b: / / / / / / / / / / / 18, / / /
	ALOPECIA UNDERBODY	a: / / / / / / / / / / / / 19,20,21 b: / / / / / / / / / / / 19,20,
	SACRIFICED BY DESIGN 02/24/03	a: / / / / / / / / / / / / / / / 21
671047	SACRIFICED BY DESIGN 02/24/03	a: / / / / / / / / / / / / / / / 21

INDIVIDUAL CLINICAL OBSERVATIONS

GROUP IV: 500 MG/KG/DAY

ANIMAL	OBSERVATION	DAYS OF GESTATION ON WHICH SIGN WAS OBSERVED:
NUMBER:		4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21

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671051
  ALOPECIA ABDOMINAL      a:  , , , , 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
                           b:  , , , 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20,
  ALOPECIA BOTH FRONT PAW a:  , , , , 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
                           b:  , , , , 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20,
  ALOPECIA RIGHT HIND QUA a:  , , , , , , , , 12, 13, 14, 15, 16, 17, 18, 19, 20, 21
                           b:  , , , , , , , , 12, 13, 14, 15, 16, 17, 18, 19, 20,
  ALOPECIA BOTH FRONT LEG a:  , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20, 21
                           b:  , , , , , , , , 13, 14, 15, 16, 17, 18, 19, 20,
  DIARRHEA                a:  , , , , , , , , 13, 14, , , , , , , ,
                           b:  , , , , , , , , 13, , , , , , , , ,
  STAIN CAGEBOARD RED     a:  , , , , , , , , , , , , , , , , ,
                           b:  , , , , , , , , , , , , , , 18, , , ,
  SORE RIGHT FRONT LEG    a:  , , , , , , , , , , , , , , , , ,
                           b:  , , , , , , , , , , , , , , 18, , , ,
  HUNCHED OVER           a:  , , , , , , , , , , , , , , , 19, 20, 21
                           b:  , , , , , , , , , , , , , , , 19, 20,
  SACRIFICED BY DESIGN 02/24/03 a:  , , , , , , , , , , , , , , , , 21

671053
  NO FECES/FEED ON CB     a:  , , , , , , , , , 13, , , , , , , ,
                           b:  , , , , , , , , , 13, , , , , , , ,
  HUNCHED OVER           a:  , , , , , , , , , , 14, 15, , , , , , ,
                           b:  , , , , , , , , , , 13, 14, 15, , , , , , ,
  NO FEED ON CB          a:  , , , , , , , , , , 14, , , , , , , ,
  DIARRHEA               a:  , , , , , , , , , , 14, , , , , , , ,
  WEAK                   a:  , , , , , , , , , , , 15, , , , , , ,
                           b:  , , , , , , , , , , , 15, , , , , , ,
  FOUND DEAD 02/19/03    a:  , , , , , , , , , , , , 16, , , , ,

671057
  SACRIFICED BY DESIGN 02/24/03 a:  , , , , , , , , , , , , , , , , 21

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APPENDIX C

Individual Body Weights

Individual Body Weights

Explanatory Notes

Notes

Day C21 = Corrected final maternal body weight = final maternal body weight minus the gravid uterine weight plus the empty uterine weight.

Reporting of body weight data that were collected prior to study start (day 6G) are limited to day 0, 4G, and 5G because weight data are available for all animals on these days. Any additional body weight data collected for the separate breeding lots of animals on days prior to day 6G are available in the raw data.

Abbreviations

--- = No Data
S.D. = Standard Deviation
S.E. = Standard Error
N = Number in Group
NP = Not Pregnant
FD = Found Dead
SE = Sacrificed *in extremis*
R = Litter totally resorbed

INDIVIDUAL ADULT BODY WEIGHTS

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	DAY 0	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 9
670974	256.0	276.7	277.0	285.1	293.3	300.7	308.8
670981	248.0	267.3	266.0	274.7	281.3	283.5	291.2
670985	248.0	263.3	269.8	277.1	277.3	283.7	285.0
670986	247.0	267.8	274.9	280.6	283.9	293.9	298.6
670987	246.0	256.2	266.0	263.6	268.7	277.5	286.1
670989	243.0	255.3	262.4	266.9	272.7	283.8	292.8
670994	230.0	248.6	257.6	264.9	277.4	277.3	283.0
670998	246.0	268.4	269.4	281.8	292.5	297.7	300.2
670999	245.0	251.5	255.7	266.4	270.9	276.2	282.5
671002	255.0	272.0	280.6	291.6	297.8	307.5	311.1
671007	244.0	257.4	270.6	273.7	283.4	290.0	297.4
671015	270.0	284.6	290.0	295.8	298.4	299.8	305.0
671017	241.0	274.1	281.9	290.1	299.9	306.0	313.1
671031	248.0	277.7	283.9	292.7	296.9	305.9	303.3
671033	259.0	274.2	282.7	285.0	292.2	293.7	293.6
671035	263.0	278.0	277.3	292.2	289.9	290.9	298.6
671039	246.0	252.8	258.2	263.7	275.0	277.3	278.2
671042	242.0	257.5	257.6	263.1	273.3	281.2	282.7
671044	249.0	260.1	263.9	270.1	280.8	281.5	283.0
671045	231.0	243.3	244.0	251.5	258.5	265.3	268.3
671054	265.0	281.2	274.5	287.6	297.4	301.5	299.2
671055	264.0	276.7	280.2	285.9	297.0	303.0	303.2
GROUP MEAN	249.4	265.7	270.2	277.5	284.5	289.9	293.9
S.D.	10.26	11.68	11.37	12.33	11.77	11.88	11.65
S.E.	2.19	2.49	2.42	2.63	2.51	2.53	2.48
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	DAY 10	DAY 11	DAY 12	DAY 13	DAY 14	DAY 15	DAY 16
670974	312.3	320.3	324.5	337.9	341.0	346.7	362.9
670981	298.9	299.0	300.4	315.0	317.1	323.9	339.0
670985	292.4	291.1	301.7	310.7	310.2	315.4	328.7
670986	307.3	312.8	324.2	334.5	337.9	351.2	359.8
670987	294.2	297.3	308.4	316.0	318.8	328.7	336.2
670989	300.1	296.4	304.3	319.5	324.9	326.4	345.2
670994	290.6	295.3	306.9	315.3	316.3	328.6	341.0
670998	301.1	309.0	316.0	328.2	333.5	337.0	357.7
670999	287.2	296.4	306.1	311.0	315.4	322.3	336.1
671002	314.5	323.5	339.2	342.8	347.9	359.7	373.0
671007	294.3	300.1	311.0	321.3	320.4	325.7	335.1
671015	307.9	315.7	323.9	325.0	327.8	335.3	340.5
671017	324.0	341.8	348.3	352.6	366.2	364.4	380.5
671031	313.2	330.8	333.1	335.8	343.7	345.9	357.2
671033	299.0	310.6	318.8	321.5	328.3	336.5	343.4
671035	303.1	312.1	312.6	320.6	317.5	327.9	329.5
671039	286.2	296.4	305.5	312.5	321.3	330.6	340.8
671042	287.5	296.8	297.2	308.9	310.7	317.0	326.0
671044	283.4	289.4	299.7	306.4	306.8	305.1	315.5
671045	271.6	281.3	288.1	294.7	299.3	307.7	316.5
671054	313.1	316.9	322.7	332.4	336.4	345.9	356.9
671055	308.3	316.0	321.6	330.1	331.4	339.4	352.6
GROUP MEAN	299.6	306.8	314.3	322.4	326.0	332.8	344.3
S.D.	12.50	14.74	14.58	13.49	15.44	15.39	16.87
S.E.	2.67	3.14	3.11	2.88	3.29	3.28	3.60
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION					
	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21	DAY C21
670974	380.6	391.4	412.3	429.0	465.1	355.8
670981	355.5	365.3	389.0	404.9	435.1	321.2
670985	341.0	352.9	370.0	389.2	406.2	314.5
670986	374.7	387.0	407.4	437.9	457.0	338.5
670987	353.9	363.9	381.2	392.9	410.2	315.1
670989	360.2	368.4	385.2	407.3	428.2	321.6
670994	345.2	367.2	381.5	402.6	427.4	319.4
670998	370.5	390.4	411.6	430.9	440.6	322.1
670999	350.8	370.4	385.1	398.4	431.0	325.3
671002	385.8	402.8	428.8	442.8	482.4	366.9
671007	347.7	372.5	391.2	412.6	433.9	322.8
671015	354.6	369.1	384.5	399.0	422.6	316.5
671017	393.0	414.6	428.9	454.4	489.5	381.2
671031	371.4	387.1	402.2	417.2	448.0	353.5
671033	355.3	374.8	383.8	393.3	419.4	334.1
671035	352.8	365.6	382.2	396.0	419.3	326.2
671039	352.6	372.3	385.7	406.4	432.2	336.1
671042	341.6	358.6	367.1	387.6	409.2	324.6
671044	323.6	339.3	349.3	364.0	382.5	296.1
671045	329.0	346.8	364.6	384.1	402.3	301.9
671054	373.1	393.9	412.4	432.3	459.5	339.8
671055	367.5	385.7	400.0	416.1	442.4	334.1
GROUP MEAN	358.2	374.5	391.1	409.0	433.8	330.3
S.D.	17.52	18.14	20.22	21.87	25.95	20.07
S.E.	3.74	3.87	4.31	4.66	5.53	4.28
N	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	DAY 0	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 9
670975	239.0	250.6	259.4	263.6	269.4	277.1	282.4
670976	261.0	267.9	278.1	282.4	288.5	296.3	299.5
670978	246.0	260.3	267.5	276.1	276.7	289.0	296.0
670980	256.0	264.6	273.6	273.8	279.1	287.6	295.3
670984	248.0	260.2	269.2	268.0	274.8	284.3	291.3
670990	242.0	260.8	266.0	265.8	269.1	281.0	290.6
670993	250.0	268.1	280.4	283.9	293.0	298.9	297.4
671000	232.0	247.5	251.6	255.3	261.0	268.3	272.7
671003	237.0	256.4	254.6	270.5	271.3	279.8	291.0
671008 (NP)	254.0	280.6	287.6	291.6	302.2	307.2	312.4
671012	253.0	261.5	270.6	276.1	280.4	286.0	295.5
671016	270.0	289.0	294.8	299.5	301.1	309.6	307.2
671019	268.0	283.7	285.1	301.5	305.7	308.3	313.2
671020	234.0	257.5	266.4	272.5	279.1	285.4	285.5
671025	257.0	279.3	283.8	291.5	295.5	294.9	296.1
671026	258.0	269.1	273.6	281.7	284.6	284.9	285.5
671034	249.0	267.2	280.3	280.6	275.1	279.3	283.9
671043	242.0	251.8	252.8	258.1	270.4	273.2	278.8
671048	237.0	253.7	254.0	264.7	271.2	278.8	277.5
671050	251.0	265.9	266.0	270.8	285.2	292.7	292.8
671052	242.0	256.4	267.1	269.1	277.4	284.4	284.0
671056	270.0	285.8	296.2	297.4	303.9	305.3	307.8
GROUP MEAN	249.8	265.4	271.8	277.0	282.5	288.7	292.6
S.D.	11.28	11.83	13.03	13.09	12.86	11.63	11.02
S.E.	2.40	2.52	2.78	2.79	2.74	2.48	2.35
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	DAY 10	DAY 11	DAY 12	DAY 13	DAY 14	DAY 15	DAY 16
670975	287.5	291.4	299.4	309.6	313.1	319.4	331.9
670976	308.0	313.5	320.1	336.2	343.5	326.4	334.5
670978	306.4	307.3	313.9	325.2	332.4	338.0	357.0
670980	300.1	305.2	308.5	321.0	331.3	333.1	343.4
670984	297.1	303.6	306.7	320.0	326.9	333.6	343.0
670990	296.1	297.2	297.7	315.9	319.2	321.6	335.4
670993	306.0	308.8	319.2	325.3	330.1	342.9	354.3
671000	275.0	285.9	300.9	307.5	312.1	326.4	338.5
671003	293.5	297.8	312.6	315.3	319.9	322.7	334.7
671008 (NP)	313.1	316.5	322.2	316.6	305.7	309.9	315.6
671012	296.4	299.6	304.7	314.8	313.6	328.4	335.7
671016	315.7	322.3	326.1	328.5	335.3	336.2	347.3
671019	317.5	330.4	342.7	341.9	351.9	353.7	357.6
671020	291.3	303.9	312.5	314.3	323.3	328.4	339.4
671025	302.4	311.2	318.4	319.2	324.9	329.4	338.2
671026	288.9	300.5	303.0	306.2	310.3	316.1	323.6
671034	293.5	301.0	304.3	304.4	306.9	316.8	324.6
671043	280.7	294.9	302.1	307.1	310.7	315.8	325.8
671048	279.6	288.1	292.9	300.7	304.2	312.8	322.6
671050	300.1	304.8	319.1	322.4	331.3	333.9	343.7
671052	287.4	302.5	313.4	319.6	323.9	338.7	352.8
671056	315.3	320.4	330.3	333.9	341.1	345.9	358.8
GROUP MEAN	297.8	304.9	312.3	318.4	323.3	328.6	339.0
S.D.	12.05	11.06	11.91	10.61	13.06	11.32	12.27
S.E.	2.57	2.36	2.54	2.26	2.78	2.41	2.62
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION					
	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21	DAY C21
670975	345.8	359.7	375.9	395.5	421.9	315.1
670976	357.8	380.3	395.5	415.6	442.4	347.0
670978	369.9	384.0	404.9	421.8	454.3	345.2
670980	363.0	378.4	387.7	402.7	423.8	331.4
670984	351.3	370.8	389.4	404.0	428.9	336.2
670990	337.6	351.3	375.1	393.5	407.2	308.5
670993	365.2	384.5	399.5	411.1	443.0	345.2
671000	351.4	373.6	391.0	404.7	433.5	325.9
671003	347.7	362.8	378.0	386.7	412.0	325.3
671008 (NP)	317.2	312.7	318.6	317.9	324.6	---
671012	353.7	367.1	382.9	396.0	421.7	329.1
671016	364.3	380.0	397.8	416.6	442.6	336.1
671019	372.2	382.5	392.1	406.1	421.2	363.0
671020	348.0	361.0	376.6	395.3	417.1	326.7
671025	355.4	365.8	385.7	396.0	432.1	337.4
671026	340.2	354.7	369.2	384.2	408.3	316.8
671034	335.7	348.2	359.3	373.9	397.5	309.2
671043	336.3	355.0	363.7	382.2	410.5	321.5
671048	336.6	344.5	359.1	381.3	400.2	316.7
671050	361.6	378.5	391.7	413.1	440.4	347.7
671052	375.9	392.7	412.1	434.3	466.1	349.9
671056	366.1	383.8	402.5	418.5	444.1	346.4
GROUP MEAN	352.4	366.9	382.2	397.8	422.4	332.4
S.D.	14.58	18.13	20.30	23.31	28.12	14.87
S.E.	3.11	3.87	4.33	4.97	5.99	3.24
N	22	22	22	22	22	21

INDIVIDUAL ADULT BODY WEIGHTS

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	DAY 0	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 9
670970	245.0	232.7	254.6	261.9	268.8	279.7	285.1
670972	254.0	264.0	272.8	276.1	280.8	292.0	301.1
670979	244.0	256.6	268.9	268.7	275.7	284.5	288.1
670983	254.0	267.1	278.1	278.0	283.0	295.4	297.5
670988	242.0	242.9	265.3	267.6	272.7	288.2	293.6
670992	239.0	258.9	262.3	267.7	273.9	276.7	283.2
670995	235.0	253.7	252.3	270.6	277.9	281.6	281.2
670996	250.0	270.6	279.9	284.4	290.0	299.0	305.3
670997	249.0	226.0	253.8	260.8	265.3	273.6	277.4
671009	263.0	256.3	283.5	286.1	293.4	298.4	301.1
671010	237.0	253.4	262.7	266.1	274.7	280.7	285.1
671024	268.0	283.5	294.8	299.7	294.4	301.3	299.9
671027	265.0	279.1	287.3	294.5	292.4	304.1	300.0
671028	270.0	284.8	292.1	296.9	300.4	305.3	302.4
671029	242.0	254.1	258.5	264.7	264.3	266.6	273.8
671030	237.0	249.3	253.5	262.1	260.4	261.5	266.9
671032	255.0	256.6	267.8	275.9	271.9	271.9	276.2
671036	240.0	250.8	261.4	262.7	268.9	272.3	270.8
671037	270.0	291.0	289.8	296.1	298.6	304.1	302.2
671038	251.0	263.9	268.6	277.9	275.7	283.5	282.2
671040	237.0	243.1	249.9	257.9	258.4	264.3	275.3
671049	249.0	262.6	264.3	264.1	279.3	280.7	281.7
GROUP MEAN	249.8	259.1	269.2	274.6	278.2	284.8	287.7
S.D.	11.38	16.20	13.81	13.09	12.21	13.59	11.90
S.E.	2.43	3.45	2.94	2.79	2.60	2.90	2.54
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						DAY 16
	DAY 10	DAY 11	DAY 12	DAY 13	DAY 14	DAY 15	
670970	291.3	288.5	303.9	316.7	325.2	331.0	346.3
670972	306.0	308.6	313.6	329.8	331.4	334.3	346.9
670979	292.0	295.8	299.2	318.8	313.5	316.7	335.3
670983	301.4	307.2	317.9	328.3	336.2	344.0	356.9
670988	296.0	302.1	309.3	336.4	336.2	344.2	352.6
670992	287.3	297.9	308.4	314.6	317.7	328.2	329.6
670995	285.8	294.5	305.3	314.1	316.6	326.8	339.6
670996	308.4	320.6	331.1	337.0	345.3	364.2	372.2
670997	286.7	290.1	301.1	305.5	305.0	328.0	328.9
671009	309.9	322.1	339.8	344.9	352.1	370.0	383.0
671010	279.4	285.4	298.7	303.9	298.7	306.2	322.2
671024	301.7	306.9	321.9	327.4	326.5	338.3	353.2
671027	306.0	313.0	321.1	327.1	332.2	342.0	351.2
671028	310.1	319.6	327.1	327.7	336.7	344.4	356.7
671029	277.7	285.5	283.6	286.4	289.0	298.6	310.3
671030	272.8	285.0	284.1	287.2	294.1	298.6	305.2
671032	283.2	290.7	301.5	308.6	312.3	310.4	321.3
671036	286.3	283.9	301.4	302.8	313.1	318.6	334.9
671037	301.2	303.9	316.3	328.3	329.0	349.6	360.3
671038	285.0	306.2	299.7	312.5	321.9	329.8	345.0
671040	276.9	288.0	292.5	303.4	308.5	317.7	326.9
671049	289.4	288.6	299.6	305.5	313.7	323.6	333.5
GROUP MEAN	292.5	299.3	308.1	316.7	320.7	330.2	341.5
S.D.	11.55	12.41	14.38	15.51	16.25	18.81	19.07
S.E.	2.46	2.65	3.07	3.31	3.46	4.01	4.07
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION					
	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21	DAY C21
670970	364.9	382.3	403.4	416.0	444.9	332.9
670972	357.5	381.9	400.3	420.2	451.1	332.0
670979	346.1	359.2	376.3	388.8	405.6	311.4
670983	367.6	383.8	397.3	411.8	439.8	343.3
670988	370.5	391.0	403.7	421.3	441.3	336.0
670992	349.1	363.9	379.8	396.1	413.6	340.4
670995	364.3	382.1	391.2	414.0	434.2	310.0
670996	401.7	419.6	434.7	455.8	473.0	359.5
670997	344.5	360.5	374.4	391.2	414.5	330.7
671009	405.6	427.3	453.5	479.3	507.4	373.2
671010	336.5	346.3	355.3	370.1	376.9	285.2
671024	365.8	380.5	400.9	415.9	440.3	337.9
671027	368.6	383.2	401.3	416.0	437.1	345.4
671028	367.4	380.8	397.9	413.9	432.0	330.8
671029	326.1	336.4	345.1	355.6	367.3	284.1
671030	317.7	327.0	339.4	351.0	363.3	286.7
671032	338.0	350.2	367.7	384.4	402.3	299.2
671036	344.2	359.6	378.8	399.3	427.6	317.6
671037	374.6	393.2	408.4	432.4	449.9	343.1
671038	355.9	373.2	386.8	406.6	429.3	330.6
671040	337.8	362.1	383.7	381.5	413.4	321.5
671049	345.6	366.7	383.6	394.8	418.3	314.2
GROUP MEAN	356.8	373.2	389.2	405.3	426.5	325.7
S.D.	21.47	23.80	26.02	29.39	32.75	23.20
S.E.	4.58	5.07	5.55	6.27	6.98	4.95
N	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	DAY 0	DAY 4	DAY 5	DAY 6	DAY 7	DAY 8	DAY 9
670971	244.0	235.0	246.2	258.8	261.7	247.2	271.2
670973 (SE)	250.0	273.1	274.5	277.2	255.8	262.4	246.0
670977	238.0	246.0	257.4	263.1	241.0	254.1	226.2
670982	263.0	282.6	287.8	299.8	289.9	304.2	308.0
670991	249.0	260.1	272.3	275.7	264.7	281.1	290.5
671001	242.0	260.5	265.1	274.4	269.6	272.0	279.2
671004	254.0	272.7	285.8	293.7	294.3	293.0	301.4
671005 (SE)	230.0	238.3	251.4	254.9	255.2	237.4	224.3
671006	256.0	269.7	278.9	285.8	289.6	297.3	304.6
671011	251.0	272.4	273.2	278.9	285.9	290.3	297.8
671013	236.0	258.9	265.9	275.4	271.1	288.3	290.8
671014	243.0	246.7	254.9	265.7	247.9	245.1	265.8
671018	269.0	284.0	285.8	292.9	289.8	283.7	292.3
671021 (SE)	250.0	266.8	279.8	280.0	268.2	263.5	242.8
671022	253.0	277.2	287.5	292.0	290.2	293.8	300.6
671023	262.0	281.9	284.6	292.6	278.0	290.6	295.4
671041 (SE)	264.0	275.8	271.2	286.1	279.2	256.0	243.1
671046	232.0	240.3	238.0	246.7	249.5	255.3	257.6
671047	234.0	246.7	247.0	255.3	235.4	252.7	261.2
671051 (R)	247.0	256.4	267.3	279.5	266.8	285.7	286.8
671053 (FD)	251.0	264.7	266.8	273.5	263.3	276.5	277.2
671057	269.0	282.0	286.2	293.7	291.5	304.4	303.9
GROUP MEAN	249.4	263.3	269.4	277.1	269.9	274.3	275.8
S.D.	11.48	15.52	14.98	14.69	17.67	20.50	26.25
S.E.	2.45	3.31	3.19	3.13	3.77	4.37	5.60
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHTS

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	DAY 10	DAY 11	DAY 12	DAY 13	DAY 14	DAY 15	DAY 16
670971	281.8	264.6	261.3	290.2	291.9	304.7	325.5
670973 (SE)	231.5	220.2	209.8	194.4	---	---	---
670977	260.3	265.6	277.3	293.2	304.6	311.5	331.5
670982	298.5	317.9	327.3	336.5	340.3	345.1	360.2
670991	297.1	300.1	304.3	318.6	324.9	328.0	344.7
671001	278.8	280.5	295.4	300.7	309.0	320.0	327.4
671004	308.5	312.1	334.1	335.0	345.3	354.6	364.6
671005 (SE)	209.9	196.4	183.0	---	---	---	---
671006	305.3	312.5	327.3	316.2	328.1	338.8	347.4
671011	302.3	301.8	315.0	316.2	322.2	337.2	339.6
671013	294.6	305.5	313.3	316.6	316.8	331.1	338.9
671014	254.8	276.9	261.7	247.3	277.6	276.7	287.8
671018	292.4	282.7	290.6	310.9	323.8	332.4	344.3
671021 (SE)	222.7	214.0	---	---	---	---	---
671022	302.9	280.5	288.2	306.7	318.7	324.5	340.3
671023	297.7	290.6	299.0	296.1	307.7	297.5	301.3
671041 (SE)	226.4	---	---	---	---	---	---
671046	258.4	261.6	272.8	276.3	286.6	289.2	294.8
671047	271.3	241.3	255.0	274.3	281.4	286.3	299.6
671051 (R)	267.0	249.7	229.8	215.3	231.5	247.9	247.4
671053 (FD)	282.0	258.8	246.8	233.9	220.7	207.7	---
671057	300.5	295.2	313.1	324.6	332.1	338.6	350.8
GROUP MEAN	274.8	272.8	280.3	289.6	303.5	309.5	326.2
S.D.	29.90	33.83	40.73	40.33	34.15	37.41	30.54
S.E.	6.37	7.38	9.11	9.25	8.05	8.82	7.41
N	22	21	20	19	18	18	17

INDIVIDUAL ADULT BODY WEIGHTS

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION					
	DAY 17	DAY 18	DAY 19	DAY 20	DAY 21	DAY C21
670971	337.8	353.0	373.4	393.7	411.7	307.7
670973 (SE)	---	---	---	---	---	---
670977	339.6	355.2	379.0	390.5	412.3	310.0
670982	379.0	396.6	414.1	429.9	448.5	353.3
670991	346.0	368.2	384.2	399.7	429.3	337.4
671001	348.1	360.3	375.8	390.8	401.0	289.0
671004	378.8	392.6	400.4	407.8	368.5	280.5
671005 (SE)	---	---	---	---	---	---
671006	373.4	384.0	402.1	417.6	423.0	314.2
671011	360.3	373.6	383.0	400.4	402.7	296.0
671013	347.5	356.5	372.5	383.6	410.3	333.7
671014	301.7	318.2	326.4	340.7	338.5	258.8
671018	363.7	387.9	396.1	395.5	412.2	296.1
671021 (SE)	---	---	---	---	---	---
671022	358.2	368.9	378.7	384.6	378.1	282.5
671023	330.2	333.0	352.0	363.2	324.7	245.5
671041 (SE)	---	---	---	---	---	---
671046	298.8	310.3	315.5	330.5	364.5	277.3
671047	309.3	322.3	333.5	343.7	368.3	294.6
671051 (R)	254.2	236.1	221.3	229.6	241.5	241.4
671053 (FD)	---	---	---	---	---	---
671057	364.8	387.4	399.1	407.5	428.7	330.1
GROUP MEAN	340.7	353.2	365.1	377.0	386.1	296.9
S.D.	33.34	40.20	46.26	46.76	50.09	31.60
S.E.	8.09	9.75	11.22	11.34	12.15	7.66
N	17	17	17	17	17	17

APPENDIX D

Individual Body Weight Changes

Individual Body Weight Changes

Explanatory Notes

Notes

6-C21 = Corrected final maternal body weight = final maternal body weight minus the gravid uterine weight plus the empty uterine weight.

Abbreviations

--- = No Data
S.D. = Standard Deviation
S.E. = Standard Error
N = Number in Group
NP = Not Pregnant
FD = Found Dead
SE = Sacrificed *in extremis*
R = Litter Totally Resorbed

INDIVIDUAL ADULT BODY WEIGHT CHANGES

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	0-6	4-6	6-8	8-10	10-12	12-14	14-16
670974	29.1	8.4	15.6	11.6	12.2	16.5	21.9
670981	26.7	7.4	8.8	15.4	1.5	16.7	21.9
670985	29.1	13.8	6.6	8.7	9.3	8.5	18.5
670986	33.6	12.8	13.3	13.4	16.9	13.7	21.9
670987	17.6	7.4	13.9	16.7	14.2	10.4	17.4
670989	23.9	11.6	16.9	16.3	4.2	20.6	20.3
670994	34.9	16.3	12.4	13.3	16.3	9.4	24.7
670998	35.8	13.4	15.9	3.4	14.9	17.5	24.2
670999	21.4	14.9	9.8	11.0	18.9	9.3	20.7
671002	36.6	19.6	15.9	7.0	24.7	8.7	25.1
671007	29.7	16.3	16.3	4.3	16.7	9.4	14.7
671015	25.8	11.2	4.0	8.1	16.0	3.9	12.7
671017	49.1	16.0	15.9	18.0	24.3	17.9	14.3
671031	44.7	15.0	13.2	7.3	19.9	10.6	13.5
671033	26.0	10.8	8.7	5.3	19.8	9.5	15.1
671035	29.2	14.2	-1.3	12.2	9.5	4.9	12.0
671039	17.7	10.9	13.6	8.9	19.3	15.8	19.5
671042	21.1	5.6	18.1	6.3	9.7	13.5	15.3
671044	21.1	10.0	11.4	1.9	16.3	7.1	8.7
671045	20.5	8.2	13.8	6.3	16.5	11.2	17.2
671054	22.6	6.4	13.9	11.6	9.6	13.7	20.5
671055	21.9	9.2	17.1	5.3	13.3	9.8	21.2
GROUP MEAN	28.1	11.8	12.4	9.7	14.7	11.8	18.2
S.D.	8.30	3.75	4.74	4.60	5.79	4.38	4.48
S.E.	1.77	0.80	1.01	0.98	1.23	0.93	0.96
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHT CHANGES

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER	16-18	18-21	DAYS OF GESTATION	
			6-21	6-C21

670974	28.5	73.7	180.0	70.7
670981	26.3	69.8	160.4	46.5
670985	24.2	53.3	129.1	37.4
670986	27.2	70.0	176.4	57.9
670987	27.7	46.3	146.6	51.5
670989	23.2	59.8	161.3	54.7
670994	26.2	60.2	162.5	54.5
670998	32.7	50.2	158.8	40.3
670999	34.3	60.6	164.6	58.9
671002	29.8	79.6	190.8	75.3
671007	37.4	61.4	160.2	49.1
671015	28.6	53.5	126.8	20.7
671017	34.1	74.9	199.4	91.1
671031	29.9	60.9	155.3	60.8
671033	31.4	44.6	134.4	49.1
671035	36.1	53.7	127.1	34.0
671039	31.5	59.9	168.5	72.4
671042	32.6	50.6	146.1	61.5
671044	23.8	43.2	112.4	26.0
671045	30.3	55.5	150.8	50.4
671054	37.0	65.6	171.9	52.2
671055	33.1	56.7	156.5	48.2

GROUP MEAN	30.3	59.3	156.4	52.9
S.D.	4.18	9.91	21.46	16.15
S.E.	0.89	2.11	4.58	3.44
N	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHT CHANGES

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	0-6	4-6	6-8	8-10	10-12	12-14	14-16
670975	24.6	13.0	13.5	10.4	11.9	13.7	18.8
670976	21.4	14.5	13.9	11.7	12.1	23.4	-9.0
670978	30.1	15.8	12.9	17.4	7.5	18.5	24.6
670980	17.8	9.2	13.8	12.5	8.4	22.8	12.1
670984	20.0	7.8	16.3	12.8	9.6	20.2	16.1
670990	23.8	5.0	15.2	15.1	1.6	21.5	16.2
670993	33.9	15.8	15.0	7.1	13.2	10.9	24.2
671000	23.3	7.8	13.0	6.7	25.9	11.2	26.4
671003	33.5	14.1	9.3	13.7	19.1	7.3	14.8
671008 (NP)	37.6	11.0	15.6	5.9	9.1	-16.5	9.9
671012	23.1	14.6	9.9	10.4	8.3	8.9	22.1
671016	29.5	10.5	10.1	6.1	10.4	9.2	12.0
671019	33.5	17.8	6.8	9.2	25.2	9.2	5.7
671020	38.5	15.0	12.9	5.9	21.2	10.8	16.1
671025	34.5	12.2	3.4	7.5	16.0	6.5	13.3
671026	23.7	12.6	3.2	4.0	14.1	7.3	13.3
671034	31.6	13.4	-1.3	14.2	10.8	2.6	17.7
671043	16.1	6.3	15.1	7.5	21.4	8.6	15.1
671048	27.7	11.0	14.1	0.8	13.3	11.3	18.4
671050	19.8	4.9	21.9	7.4	19.0	12.2	12.4
671052	27.1	12.7	15.3	3.0	26.0	10.5	28.9
671056	27.4	11.6	7.9	10.0	15.0	10.8	17.7
GROUP MEAN	27.2	11.7	11.7	9.1	14.5	11.0	15.8
S.D.	6.40	3.58	5.21	4.18	6.56	8.29	7.87
S.E.	1.37	0.76	1.11	0.89	1.40	1.77	1.68
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHT CHANGES

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER	16-18	18-21	DAYS OF GESTATION	
			6-21	6-C21

670975	27.8	62.2	158.3	51.5
670976	45.8	62.1	160.0	64.6
670978	27.0	70.3	178.2	69.1
670980	35.0	45.4	150.0	57.6
670984	27.8	58.1	160.9	68.2
670990	15.9	55.9	141.4	42.8
670993	30.2	58.5	159.1	61.3
671000	35.1	59.9	178.2	70.6
671003	28.1	49.2	141.5	54.8
671008 (NP)	-2.9	11.9	33.0	---
671012	31.4	54.6	145.6	53.0
671016	32.7	62.6	143.1	36.6
671019	24.9	38.7	119.7	61.5
671020	21.6	56.1	144.6	54.2
671025	27.6	66.3	140.6	45.9
671026	31.1	53.6	126.6	35.1
671034	23.6	49.3	116.9	28.6
671043	29.2	55.5	152.4	63.4
671048	21.9	55.7	135.5	52.0
671050	34.8	61.9	169.6	76.9
671052	39.9	73.4	197.0	80.8
671056	25.0	60.3	146.7	49.0

GROUP MEAN	27.9	55.5	145.4	56.1
S.D.	9.44	12.46	31.55	13.63
S.E.	2.01	2.66	6.73	2.97
N	22	22	22	21

INDIVIDUAL ADULT BODY WEIGHT CHANGES

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	0-6	4-6	6-8	8-10	10-12	12-14	14-16
670970	16.9	29.2	17.8	11.6	12.6	21.3	21.1
670972	22.1	12.1	15.9	14.0	7.6	17.8	15.5
670979	24.7	12.1	15.8	7.5	7.2	14.3	21.8
670983	24.0	10.9	17.4	6.0	16.5	18.3	20.7
670988	25.6	24.7	20.6	7.8	13.3	26.9	16.4
670992	28.7	8.8	9.0	10.6	21.1	9.3	11.9
670995	35.6	16.9	11.0	4.2	19.5	11.3	23.0
670996	34.4	13.8	14.6	9.4	22.7	14.2	26.9
670997	11.8	34.8	12.8	13.1	14.4	3.9	23.9
671009	23.1	29.8	12.3	11.5	29.9	12.3	30.9
671010	29.1	12.7	14.6	-1.3	19.3	0.0	23.5
671024	31.7	16.2	1.6	0.4	20.2	4.6	26.7
671027	29.5	15.4	9.6	1.9	15.1	11.1	19.0
671028	26.9	12.1	8.4	4.8	17.0	9.6	20.0
671029	22.7	10.6	1.9	11.1	5.9	5.4	21.3
671030	25.1	12.8	-0.6	11.3	11.3	10.0	11.1
671032	20.9	19.3	-4.0	11.3	18.3	10.8	9.0
671036	22.7	11.9	9.6	14.0	15.1	11.7	21.8
671037	26.1	5.1	8.0	-2.9	15.1	12.7	31.3
671038	26.9	14.0	5.6	1.5	14.7	22.2	23.1
671040	20.9	14.8	6.4	12.6	15.6	16.0	18.4
671049	15.1	1.5	16.6	8.7	10.2	14.1	19.8
GROUP MEAN	24.8	15.4	10.2	7.7	15.6	12.6	20.8
S.D.	5.77	7.95	6.47	5.14	5.52	6.31	5.71
S.E.	1.23	1.70	1.38	1.10	1.18	1.35	1.22
N	22	22	22	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHT CHANGES

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION			
	16-18	18-21	6-21	6-C21

670970	36.0	62.6	183.0	71.0
670972	35.0	69.2	175.0	55.9
670979	23.9	46.4	136.9	42.6
670983	26.9	56.0	161.8	65.3
670988	38.4	50.3	173.7	68.4
670992	34.3	49.7	145.9	72.7
670995	42.5	52.1	163.6	39.4
670996	47.4	53.4	188.6	75.1
670997	31.6	54.0	153.7	69.9
671009	44.3	80.1	221.3	87.1
671010	24.1	30.6	110.8	19.1
671024	27.3	59.8	140.6	38.2
671027	32.0	53.9	142.6	50.9
671028	24.1	51.2	135.1	33.9
671029	26.1	30.9	102.6	19.4
671030	21.8	36.3	101.2	24.6
671032	28.9	52.1	126.4	23.3
671036	24.7	68.0	164.9	54.9
671037	32.9	56.7	153.8	47.0
671038	28.2	56.1	151.4	52.8
671040	35.2	51.3	155.5	63.6
671049	33.2	51.6	154.2	50.1

GROUP MEAN	31.8	53.3	151.9	51.1
S.D.	7.02	11.41	28.17	19.49
S.E.	1.50	2.43	6.01	4.16
N	22	22	22	22

INDIVIDUAL ADULT BODY WEIGHT CHANGES

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	0-6	4-6	6-8	8-10	10-12	12-14	14-16
670971	14.8	23.8	-11.6	34.6	-20.5	30.6	33.6
670973 (SE)	27.2	4.1	-14.8	-30.9	-21.7	---	---
670977	25.1	17.1	-9.0	6.2	17.0	27.3	26.9
670982	36.8	17.2	4.4	-5.7	28.8	13.0	19.9
670991	26.7	15.6	5.4	16.0	7.2	20.6	19.8
671001	32.4	13.9	-2.4	6.8	16.6	13.6	18.4
671004	39.7	21.0	-0.7	15.5	25.6	11.2	19.3
671005 (SE)	24.9	16.6	-17.5	-27.5	-26.9	---	---
671006	29.8	16.1	11.5	8.0	22.0	0.8	19.3
671011	27.9	6.5	11.4	12.0	12.7	7.2	17.4
671013	39.4	16.5	12.9	6.3	18.7	3.5	22.1
671014	22.7	19.0	-20.6	9.7	6.9	15.9	10.2
671018	23.9	8.9	-9.2	8.7	-1.8	33.2	20.5
671021 (SE)	30.0	13.2	-16.5	-40.8	---	---	---
671022	39.0	14.8	1.8	9.1	-14.7	30.5	21.6
671023	30.6	10.7	-2.0	7.1	1.3	8.7	-6.4
671041 (SE)	22.1	10.3	-30.1	-29.6	---	---	---
671046	14.7	6.4	8.6	3.1	14.4	13.8	8.2
671047	21.3	8.6	-2.6	18.6	-16.3	26.4	18.2
671051 (R)	32.5	23.1	6.2	-18.7	-37.2	1.7	15.9
671053 (FD)	22.5	8.8	3.0	5.5	-35.2	-26.1	---
671057	24.7	11.7	10.7	-3.9	12.6	19.0	18.7
GROUP MEAN	27.7	13.8	-2.8	0.5	0.5	13.9	17.9
S.D.	7.08	5.42	11.94	18.72	20.81	14.24	8.39
S.E.	1.51	1.16	2.54	3.99	4.65	3.36	2.03
N	22	22	22	22	20	18	17

INDIVIDUAL ADULT BODY WEIGHT CHANGES

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER	16-18	18-21	DAYS OF GESTATION	
			6-21	6-C21

670971	27.5	58.7	152.9	48.9
670973 (SE)	---	---	---	---
670977	23.7	57.1	149.2	46.9
670982	36.4	51.9	148.7	53.5
670991	23.5	61.1	153.6	61.7
671001	32.9	40.7	126.6	14.6
671004	28.0	-24.1	74.8	-13.2
671005 (SE)	---	---	---	---
671006	36.6	39.0	137.2	28.4
671011	34.0	29.1	123.8	17.1
671013	17.6	53.8	134.9	58.3
671014	30.4	20.3	72.8	-6.9
671018	43.6	24.3	119.3	3.2
671021 (SE)	---	---	---	---
671022	28.6	9.2	86.1	-9.5
671023	31.7	-8.3	32.1	-47.1
671041 (SE)	---	---	---	---
671046	15.5	54.2	117.8	30.6
671047	22.7	46.0	113.0	39.3
671051 (R)	-11.3	5.4	-38.0	-38.1
671053 (FD)	---	---	---	---
671057	36.6	41.3	135.0	36.4

GROUP MEAN	26.9	32.9	108.2	19.1
S.D.	12.24	25.19	50.31	33.16
S.E.	2.97	6.11	12.20	8.04
N	17	17	17	17

APPENDIX E

Individual Food Consumption

Individual Food Consumption

Explanatory Notes

Abbreviations

---	=	No Data
S.D.	=	Standard Deviation
S.E.	=	Standard Error
N	=	Number in Group
NP	=	Not Pregnant
FD	=	Found Dead
SE	=	Sacrificed <i>in extremis</i>
R	=	Litter totally resorbed

INDIVIDUAL MEAN DAILY FEED CONSUMPTION

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	4-6	6-8	8-10	10-12	12-14	14-16	
670974	25.2	27.3	27.2	30.9	28.4	31.4	34.8
670981	21.0	21.1	22.8	21.8	25.0	25.4	28.3
670985	22.4	21.8	20.4	24.8	21.8	23.9	21.5
670986	24.3	24.6	25.8	29.4	27.3	31.4	26.4
670987	20.3	20.8	24.1	24.8	21.8	24.8	27.2
670989	19.2	24.3	26.2	24.4	26.4	26.8	31.1
670994	16.2	22.2	22.6	22.7	24.4	26.0	26.8
670998	21.9	24.1	22.6	25.1	28.3	29.9	33.5
670999	21.4	23.6	24.6	25.4	26.3	24.5	31.4
671002	26.4	25.7	25.9	29.2	30.0	29.8	32.3
671007	20.0	23.4	24.9	24.7	26.4	26.5	30.4
671015	22.9	16.9	26.4	24.5	24.3	24.1	27.0
671017	29.4	31.1	30.7	32.9	33.5	33.4	39.4
671031	25.3	26.9	24.1	27.4	27.0	29.1	32.7
671033	24.0	22.8	23.0	22.6	23.7	27.3	28.6
671035	22.6	31.1	24.4	21.4	24.4	25.7	29.4
671039	22.5	20.1	22.9	27.4	28.6	28.4	28.3
671042	21.3	20.9	21.1	24.2	25.1	25.8	26.5
671044	25.5	20.4	22.5	24.2	25.6	25.0	24.6
671045	22.4	21.1	23.1	26.0	26.8	26.2	28.2
671054	24.6	21.4	23.4	23.4	25.8	27.6	29.1
671055	23.1	21.1	20.9	23.9	23.4	24.9	26.1
GROUP MEAN	22.8	23.3	24.1	25.5	26.1	27.2	29.3
S.D.	2.78	3.47	2.35	2.94	2.68	2.65	3.83
S.E.	0.59	0.74	0.50	0.63	0.57	0.56	0.82
N	22	22	22	22	22	22	22

INDIVIDUAL MEAN DAILY FEED CONSUMPTION

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER	18-21	6-21
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DAYS OF GESTATION

670974	31.9	30.4
670981	28.9	25.0
670985	24.7	22.8
670986	39.8	29.9
670987	25.7	24.3
670989	28.4	26.9
670994	25.7	24.4
670998	29.2	27.6
670999	25.1	25.8
671002	31.1	29.3
671007	30.5	26.9
671015	23.2	23.8
671017	33.8	33.6
671031	29.4	28.2
671033	26.0	25.0
671035	25.4	25.9
671039	29.6	26.7
671042	26.5	24.4
671044	23.1	23.6
671045	26.5	25.5
671054	29.1	25.9
671055	25.5	23.8

GROUP MEAN	28.1	26.4
S.D.	3.84	2.64
S.E.	0.82	0.56
N	22	22

INDIVIDUAL MEAN DAILY FEED CONSUMPTION

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	4-6	6-8	8-10	10-12	12-14	14-16	
670975	23.8	23.3	23.4	25.7	24.2	27.3	31.3
670976	22.0	22.8	23.8	26.4	26.9	14.5	29.4
670978	26.0	22.8	29.8	29.4	31.0	30.3	37.1
670980	20.4	19.5	26.1	26.3	27.5	24.6	34.6
670984	19.3	19.9	21.8	29.5	24.7	28.9	31.1
670990	20.9	21.0	22.4	23.3	26.2	23.8	29.1
670993	24.8	25.6	25.1	23.9	28.2	29.9	31.5
671000	23.1	21.4	22.6	27.1	26.2	29.5	33.2
671003	22.8	21.7	23.4	27.1	26.4	26.9	31.3
671008 (NP)	24.4	24.5	22.4	24.7	20.6	18.1	22.8
671012	24.1	24.4	25.3	22.4	26.7	26.8	30.3
671016	23.9	24.8	23.8	23.7	24.7	24.6	28.3
671019	27.4	26.3	25.4	29.8	27.9	30.1	33.3
671020	26.3	24.9	27.1	27.2	29.5	32.4	32.8
671025	22.8	22.3	21.9	22.3	23.9	26.6	30.1
671026	21.6	20.2	21.5	20.9	23.6	25.3	28.1
671034	23.6	17.9	22.2	22.1	22.4	26.0	26.3
671043	22.4	19.3	20.5	28.0	25.4	27.6	26.6
671048	22.3	19.7	18.5	22.4	24.6	24.6	23.1
671050	26.9	22.1	23.3	26.6	31.0	25.8	28.7
671052	25.8	22.5	21.5	27.9	27.1	30.6	33.4
671056	29.9	18.0	21.5	27.1	26.6	26.0	24.2
GROUP MEAN	23.8	22.0	23.3	25.6	26.1	26.4	29.8
S.D.	2.50	2.43	2.44	2.66	2.55	4.04	3.69
S.E.	0.53	0.52	0.52	0.57	0.54	0.86	0.79
N	22	22	22	22	22	22	22

INDIVIDUAL MEAN DAILY FEED CONSUMPTION

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER	18-21	6-21	DAYS OF GESTATION
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670975	26.3	25.9
670976	31.6	25.5
670978	31.1	30.3
670980	28.3	26.8
670984	29.2	26.7
670990	27.9	25.0
670993	29.1	27.7
671000	29.5	27.2
671003	27.2	26.3
671008 (NP)	19.1	21.6
671012	26.3	26.0
671016	28.8	25.7
671019	30.6	29.1
671020	30.5	29.3
671025	28.7	25.4
671026	24.8	23.6
671034	22.7	22.8
671043	26.3	24.9
671048	27.1	23.1
671050	30.5	27.1
671052	31.4	28.0
671056	24.2	24.0

GROUP MEAN	27.8	26.0
S.D.	3.09	2.19
S.E.	0.66	0.47
N	22	22

INDIVIDUAL MEAN DAILY FEED CONSUMPTION

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	4-6	6-8	8-10	10-12	12-14	14-16	
670970	20.8	21.9	20.1	25.1	26.9	26.3	33.1
670972	25.6	23.5	26.4	28.8	25.9	25.4	31.1
670979	19.6	18.9	19.1	20.9	21.3	24.3	30.3
670983	22.6	21.9	21.3	24.8	25.6	27.3	31.2
670988	25.4	26.9	25.9	32.1	33.9	35.0	38.6
670992	22.6	20.6	22.8	26.9	26.4	25.9	33.8
670995	18.4	21.6	19.9	23.0	25.2	26.0	33.3
670996	22.8	23.9	24.6	27.1	27.8	31.8	38.1
670997	22.8	26.1	24.5	22.5	24.0	30.3	30.7
671009	24.4	21.9	23.8	29.8	28.2	32.3	37.3
671010	21.3	19.1	17.7	21.7	19.6	21.4	33.2
671024	26.7	21.8	19.5	18.4	23.3	32.9	31.0
671027	25.3	21.1	22.3	23.4	25.9	31.4	31.1
671028	24.1	23.6	22.6	23.0	23.9	28.4	29.1
671029	23.3	20.5	23.3	18.0	20.1	26.1	28.5
671030	21.1	17.7	20.6	25.3	22.8	26.0	28.3
671032	25.1	19.9	22.7	23.8	25.6	25.6	30.7
671036	24.3	20.3	21.8	25.1	27.6	29.5	27.7
671037	27.6	20.6	20.4	20.9	31.4	30.3	30.6
671038	27.3	19.8	21.6	30.2	31.2	30.5	32.1
671040	22.7	17.1	23.8	27.0	29.2	28.3	31.9
671049	23.9	20.9	22.0	24.2	27.8	29.8	30.0
GROUP MEAN	23.5	21.3	22.1	24.6	26.1	28.4	31.9
S.D.	2.39	2.40	2.22	3.65	3.57	3.28	2.96
S.E.	0.51	0.51	0.47	0.78	0.76	0.70	0.63
N	22	22	22	22	22	22	22

INDIVIDUAL MEAN DAILY FEED CONSUMPTION

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER	18-21	6-21
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DAYS OF GESTATION

670970	30.3	26.5
670972	31.2	27.7
670979	26.9	23.3
670983	28.9	26.1
670988	31.8	32.0
670992	30.3	26.9
670995	24.9	24.8
670996	34.1	29.9
670997	30.4	27.2
671009	37.7	30.6
671010	21.9	22.1
671024	28.7	25.3
671027	27.6	26.2
671028	26.5	25.4
671029	21.7	22.5
671030	23.2	23.4
671032	26.9	25.2
671036	29.3	26.1
671037	29.3	26.4
671038	30.9	28.2
671040	29.6	26.9
671049	23.7	25.3

GROUP MEAN	28.4	26.3
S.D.	3.88	2.46
S.E.	0.83	0.52
N	22	22

INDIVIDUAL MEAN DAILY FEED CONSUMPTION

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER	DAYS OF GESTATION						
	4-6	6-8	8-10	10-12	12-14	14-16	
670971	17.0	15.8	28.1	10.9	28.4	30.8	38.8
670973 (SE)	20.2	14.9	1.1	7.1	---	---	---
670977	24.4	12.8	14.4	28.3	30.7	30.7	37.1
670982	24.5	20.1	17.2	28.3	25.2	28.8	37.4
670991	24.1	20.6	25.1	27.6	29.6	31.6	31.1
671001	23.2	17.3	20.8	21.8	25.0	24.3	29.4
671004	27.9	20.8	22.4	26.1	29.3	29.0	35.1
671005 (SE)	21.6	14.3	2.0	0.5	---	---	---
671006	27.3	24.8	21.6	28.3	22.8	30.3	38.5
671011	25.9	24.5	24.5	22.8	23.9	26.1	32.6
671013	25.3	23.1	20.9	25.5	22.7	24.1	31.7
671014	22.9	9.7	22.6	17.7	17.0	23.9	28.4
671018	26.8	31.4	20.1	11.9	27.6	34.4	34.9
671021 (SE)	26.2	33.4	4.5	---	---	---	---
671022	25.0	29.6	22.6	10.3	26.2	33.0	31.4
671023	19.8	17.7	21.1	13.7	17.3	18.2	28.3
671041 (SE)	22.0	16.0	0.0	---	---	---	---
671046	20.0	17.8	18.3	23.6	27.4	23.8	18.4
671047	20.5	12.6	23.5	13.2	29.5	24.8	25.9
671051 (R)	29.4	15.8	17.8	0.9	8.3	22.1	17.1
671053 (FD)	28.3	22.7	22.8	5.2	0.2	0.1	---
671057	25.1	19.1	19.7	19.4	30.8	32.7	29.7
GROUP MEAN	24.0	19.8	17.8	17.2	23.4	26.0	30.9
S.D.	3.20	6.18	8.21	9.34	8.18	7.82	6.26
S.E.	0.68	1.32	1.75	2.09	1.93	1.84	1.52
N	22	22	22	20	18	18	17

INDIVIDUAL MEAN DAILY FEED CONSUMPTION

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER	18-21	6-21
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DAYS OF GESTATION

670971	33.0	27.0
670973 (SE)	---	---
670977	30.8	26.7
670982	33.3	27.6
670991	33.4	28.7
671001	23.1	23.1
671004	18.6	25.4
671005 (SE)	---	---
671006	29.2	28.0
671011	26.1	25.8
671013	28.6	25.4
671014	19.2	19.8
671018	23.8	26.1
671021 (SE)	---	---
671022	18.8	24.2
671023	16.6	18.8
671041 (SE)	---	---
671046	22.6	21.8
671047	25.7	22.4
671051 (R)	10.8	13.1
671053 (FD)	---	---
671057	23.9	25.0

GROUP MEAN	24.6	24.1
S.D.	6.44	3.97
S.E.	1.56	0.96
N	17	17

APPENDIX F

Individual Reproductive Data

Individual Reproductive Data

Explanatory Notes

Note

Nidations = Implantations

Abbreviations

--- = No Data
S.E. = Standard Error
N = Number in Group
NP = Not Pregnant
FD = Found Dead
SE = Sacrificed *in extremis*
R = Litter totally resorbed

INDIVIDUAL REPRODUCTIVE DATA

GROUP I: 0 MG/KG/DAY

ANIMAL NUMBER	CORPORA LUTEA	NIDA- TIONS	RESORPTIONS			DEAD FETUSES	LIVE FETUSES			MEAN FETAL WEIGHT (G)
			TOTAL	EARLY	LATE		TOTAL	FEMALE	MALE	
670974	18	17	0	0	0	0	17	9	8	5.21
670981	16	15	0	0	0	0	15	9	6	6.02
670985	13	13	0	0	0	0	13	6	7	5.31
670986	17	16	0	0	0	0	16	5	11	5.86
670987	13	13	0	0	0	0	13	5	8	5.69
670989	15	15	0	0	0	0	15	7	8	5.66
670994	16	15	0	0	0	0	15	8	7	5.71
670998	19	17	1	1	0	0	16	10	6	5.78
670999	15	15	0	0	0	0	15	8	7	5.30
671002	16	15	0	0	0	0	15	9	6	5.94
671007	16	16	0	0	0	0	16	7	9	5.28
671015	16	16	0	0	0	0	16	9	7	4.94
671017	16	14	0	0	0	0	14	10	4	6.05
671031	14	13	0	0	0	0	13	6	7	5.64
671033	15	12	0	0	0	0	12	6	6	5.65
671035	17	14	0	0	0	0	14	8	6	5.22
671039	15	14	0	0	0	0	14	10	4	5.57
671042	16	13	0	0	0	0	13	7	6	5.14
671044	13	12	0	0	0	0	12	4	8	5.73
671045	15	14	0	0	0	0	14	7	7	5.72
671054	18	17	0	0	0	0	17	8	9	5.61
671055	17	17	0	0	0	0	17	6	11	5.14
MEAN	15.7	14.7	0.0	0.0	0.0	0.0	14.6	7.5	7.2	5.55
S.E.	0.34	0.34	0.05	0.05	0.00	0.00	0.33	0.37	0.38	0.07
N	22	22	22	22	22	22	22	22	22	22

INDIVIDUAL REPRODUCTIVE DATA

GROUP II: 50 MG/KG/DAY

ANIMAL NUMBER	CORPORA LUTEA	NIDA- TIONS	RESORPTIONS			DEAD FETUSES	LIVE FETUSES			MEAN FETAL WEIGHT (G)
			TOTAL	EARLY	LATE		TOTAL	FEMALE	MALE	
670975	15	15	0	0	0	0	15	8	7	5.63
670976	14	14	0	0	0	0	14	8	6	5.33
670978	16	16	0	0	0	0	16	10	6	5.33
670980	16	15	2	2	0	0	13	8	5	5.71
670984	16	15	2	2	0	0	13	6	7	5.83
670990	13	12	0	0	0	0	12	6	6	6.28
670993	21	14	0	0	0	0	14	7	7	5.59
671000	20	17	1	1	0	0	16	7	9	5.17
671003	17	15	3	3	0	0	12	7	5	5.60
671008 (NP)	...	...	...	...	...	...	...	...	...	...
671012	12	12	0	0	0	0	12	7	5	5.90
671016	16	14	0	0	0	0	14	9	5	5.99
671019	11	11	3	3	0	0	8	5	3	5.63
671020	16	13	0	0	0	0	13	5	8	5.47
671025	15	13	0	0	0	0	13	6	7	5.68
671026	13	13	0	0	0	0	13	10	3	5.67
671034	20	12	0	0	0	0	12	5	7	5.90
671043	14	12	0	0	0	0	12	4	8	5.68
671048	23	14	1	1	0	0	13	7	6	5.19
671050	14	14	2	2	0	0	12	8	4	6.07
671052	18	16	0	0	0	0	16	9	7	5.79
671056	15	14	0	0	0	0	14	9	5	5.38
MEAN	16.0	13.9	0.7	0.7	0.0	0.0	13.2	7.2	6.0	5.66
S.E.	0.66	0.34	0.23	0.23	0.00	0.00	0.39	0.37	0.35	0.06
N	21	21	21	21	21	21	21	21	21	21

INDIVIDUAL REPRODUCTIVE DATA

GROUP III: 200 MG/KG/DAY

ANIMAL NUMBER	CORPORA LUTEA	NIDA- TIONS	RESORPTIONS			DEAD FETUSES	LIVE FETUSES			MEAN FETAL WEIGHT (G)
			TOTAL	EARLY	LATE		TOTAL	FEMALE	MALE	
670970	16	16	1	1	0	0	15	8	7	5.91
670972	16	15	0	0	0	0	15	10	5	6.17
670979	13	13	0	0	0	0	13	9	4	5.77
670983	18	14	1	1	0	0	13	9	4	5.86
670988	17	13	0	0	0	0	13	7	6	6.21
670992	28	14	3	3	0	0	11	7	4	4.98
670995	18	16	0	0	0	0	16	6	10	6.05
670996	14	14	0	0	0	0	14	4	10	6.40
670997	16	13	2	2	0	0	11	4	7	5.83
671009	19	17	0	0	0	0	17	8	9	6.07
671010	10	10	0	0	0	0	10	5	5	6.29
671024	17	15	0	0	0	0	15	4	11	5.45
671027	16	13	0	0	0	0	13	7	6	5.25
671028	18	15	0	0	0	0	15	9	6	5.29
671029	14	12	0	0	0	0	12	9	3	5.58
671030	14	11	0	0	0	0	11	4	7	5.48
671032	17	15	0	0	0	0	15	9	6	5.18
671036	14	14	0	0	0	0	14	5	9	6.16
671037	15	15	1	1	0	0	14	8	6	5.82
671038	13	13	0	0	0	0	13	5	8	6.08
671040	14	13	0	0	0	0	13	6	7	5.54
671049	16	14	0	0	0	0	14	6	8	5.64
MEAN	16.0	13.9	0.4	0.4	0.0	0.0	13.5	6.8	6.7	5.77
S.E.	0.73	0.35	0.17	0.17	0.00	0.00	0.38	0.42	0.46	0.08
N	22	22	22	22	22	22	22	22	22	22

INDIVIDUAL REPRODUCTIVE DATA

GROUP IV: 500 MG/KG/DAY

ANIMAL NUMBER	CORPORA LUTEA	NIDA- TIONS	RESORPTIONS			DEAD FETUSES	LIVE FETUSES			MEAN FETAL WEIGHT (G)
			TOTAL	EARLY	LATE		TOTAL	FEMALE	MALE	
670971	15	15	0	0	0	0	15	9	6	5.40
670973 (SE)	...	...	...	...	...	...	...	...	...	...
670977	15	14	0	0	0	0	14	7	7	5.68
670982	17	14	0	0	0	0	14	8	6	5.70
670991	15	14	1	1	0	0	13	9	4	5.49
671001	19	16	0	0	0	0	16	6	10	5.54
671004	15	14	1	1	0	0	13	7	6	4.95
671005 (SE)	...	...	...	...	...	...	...	...	...	...
671006	22	17	3	3	0	0	14	4	10	5.92
671011	19	17	1	1	0	0	16	8	8	5.25
671013	12	10	0	0	0	0	10	5	5	5.87
671014	14	12	0	0	0	0	12	6	6	5.16
671018	19	18	1	0	1	0	17	7	10	5.00
671021 (SE)	...	...	...	...	...	...	...	...	...	...
671022	17	15	0	0	0	0	15	10	5	4.98
671023	14	14	0	0	0	0	14	7	7	4.29
671041 (SE)	...	...	...	...	...	...	...	...	...	...
671046	14	13	0	0	0	0	13	5	8	5.49
671047	14	10	0	0	0	0	10	3	7	5.94
671051 (R)	16	1	1	1	0	0	0	0	0	...
671053 (FD)	...	...	...	...	...	...	...	...	...	...
671057	16	14	0	0	0	0	14	6	8	5.71
MEAN	16.1	14.2	0.4	0.4	0.1	0.0	13.8	6.7	7.1	5.40
S.E.	0.65	0.56	0.20	0.20	0.06	0.00	0.49	0.47	0.46	0.11
N	16	16	16	16	16	16	16	16	16	16

APPENDIX G

Gross Postmortem Findings

Gross Postmortem Findings

Explanatory Notes

Abbreviations

--- = No Data
NAD = No Abnormalities Detected
NP = Not Pregnant
FD = Found Dead
SE = Sacrificed *in extremis*
R = Litter totally resorbed

GROSS POSTMORTEM FINDINGS

Group I: 0 mg/kg/day

<u>Animal Number</u>	<u>Structure(s)</u>	<u>Finding(s)</u>
670974	---	NAD
670981	---	NAD
670985	---	NAD
670986	---	NAD
670987	---	NAD
670989	---	NAD
670994	---	NAD
670998	---	NAD
670999	---	NAD
671002	---	NAD
671007	---	NAD
671015	---	NAD
671017	---	NAD
671031	---	NAD
671033	---	NAD
671035	---	NAD
671039	---	NAD
671042	---	NAD
671044	---	NAD
671045	---	NAD
671054	---	NAD
671055	---	NAD

GROSS POSTMORTEM FINDINGS

Group II: 50 mg/kg/day

<u>Animal Number</u>	<u>Structure(s)</u>	<u>Finding(s)</u>
670975	---	NAD
670976	---	NAD
670978	---	NAD
670980	---	NAD
670984	---	NAD
670990	---	NAD
670993	---	NAD
671000	---	NAD
671003	---	NAD
671008 (NP)	---	NAD
671012	---	NAD
671016	---	NAD
671019	---	NAD
671020	---	NAD
671025	---	NAD
671026	---	NAD
671034	---	NAD
671043	---	NAD
671048	---	NAD
671050	---	NAD
671052	---	NAD
671056	---	NAD

GROSS POSTMORTEM FINDINGS

Group III: 200 mg/kg/day

<u>Animal Number</u>	<u>Structure(s)</u>	<u>Finding(s)</u>
670970	---	NAD
670972	---	NAD
670979	---	NAD
670983	---	NAD
670988	---	NAD
670992	---	NAD
670995	---	NAD
670996	---	NAD
670997	---	NAD
671009	---	NAD
671010	---	NAD
671024	---	NAD
671027	---	NAD
671028	---	NAD
671029	---	NAD
671030	---	NAD
671032	---	NAD
671036	---	NAD
671037	---	NAD
671038	---	NAD
671040	---	NAD
671049	---	NAD

GROSS POSTMORTEM FINDINGS

Group IV: 500 mg/kg/day

<u>Animal Number</u>	<u>Structure(s)</u>	<u>Finding(s)</u>
670971	---	NAD
670973 (SE)	Lungs	Discoloration – several areas Black, raised, 1-5 mm diameter
670977	---	NAD
670982	---	NAD
670991	---	NAD
671001	---	NAD
671004	Kidney	Pale, bilateral
671005 (SE)	Liver	Discoloration dark
	Lungs	Discoloration dark, diffuse
	Kidney	Pale, bilateral
671006	---	NAD
671011	---	NAD
671013	---	NAD
671014	---	NAD
671018	---	NAD
671021 (SE)	---	NAD
671022	---	NAD
671023	---	NAD
671041 (SE)	Kidney	Pale, bilateral
671046	---	NAD
671047	---	NAD
671051 (R)	---	NAD
671053 (FD)	---	NAD
671057	---	NAD

APPENDIX H

Individual Fetal Weights and Alterations

Individual Fetal Weights and Alterations

Explanatory Notes

For ease of recording, many of the findings have been abbreviated or coded, as listed below:

ar	=	arch(es)
bil	=	bilateral
cen	=	centrum or centra
lt	=	left
lu	=	lumbar
NAD	=	No Abnormalities Detected
rt	=	right
th	=	thoracic
---	=	No Data

* Subcutaneous hemorrhage that was not present *in utero*.

Renal papillary sizes refer to papillary development using the scheme of Woo and Hoar.^a

Alterations are classed as:

N	=	Notes
DV	=	Developmental Variations
VR	=	Variation due to Retarded Development
M	=	Malformations

Numbers are used to:

- Indicate renal papillary size
- Identify specific sternebra
- Refer to skeletal position for ribs or vertebra
- Specify skull bones according to the following key:

1. Interparietal	8. Squamosal
2. Parietal	9. Tympanic annulus
3. Frontal	10. Basioccipital
4. Nasal	11. Exoccipital
5. Premaxilla	12. Supraoccipital
6. Maxilla	13. Hyoid
7. Zygoma	

^a Woo, D.C. and Hoar, R.M. (1972). Apparent Hydronephrosis as a Normal Aspect of Renal Development in Late Gestation of Rats: The Effect of Methyl Salicylate. *Teratology*, 6:191-196.

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
670974				
1	5.11	Rib	Supernumerary (site 14 bil)	DV
2	5.43	Rib	Supernumerary (site 14 bil)	DV
3	5.18		NAD	
4	5.73		NAD	
5	4.97		NAD	
6	5.72		NAD	
7	5.11		NAD	
8	4.74		NAD	
9	4.29	Rib	Supernumerary (site 14 rt)	DV
10	5.40	Rib	Supernumerary (site 14 bil)	DV
11	5.03		NAD	
12	5.32		NAD	
13	5.42		NAD	
14	5.44		NAD	
15	4.97		NAD	
16	5.39		NAD	
17	5.38		NAD	
670981				
1	5.91	Vertebra	Retarded Ossification (cen th11)	VR
2	6.02		NAD	
3	5.83	Vertebra	Retarded Ossification (cen th12)	VR
4	5.73		NAD	
5	6.20		NAD	
6	6.52		NAD	
7	6.59		NAD	
8	6.53		NAD	
9	5.74		NAD	
10	6.54		NAD	
11	6.27	Vertebra	Retarded Ossification (cen th11)	VR
12	5.45		NAD	
13	5.90		NAD	
14	5.22		NAD	
15	5.80		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
670985				
1	5.29		NAD	
2	5.42		NAD	
3	5.76		NAD	
4	5.17		NAD	
5	5.25		NAD	
6	5.29	Skull	Retarded Ossification (6,7,8 bil)	VR
7	5.33		NAD	
8	5.05		NAD	
9	5.46		NAD	
10	5.22	Skull	Retarded Ossification (6,7 bil)	VR
11	5.11		NAD	
12	5.21		NAD	
13	5.48		NAD	
670986				
1	5.37		NAD	
2	5.82	Vertebra	Retarded Ossification (cen th10)	VR
3	5.83	Vertebra	Retarded Ossification (cen th 9,12)	VR
4	5.88	Vertebra	Retarded Ossification (cen th11)	VR
5	5.79	Vertebra	Retarded Ossification (cen th12)	VR
6	6.11		NAD	
7	6.07		NAD	
8	5.75		NAD	
9	5.48		NAD	
10	6.25		NAD	
11	5.87		NAD	
12	5.64	Pelvis	Retarded Ossification (pubis lt)	VR
		Skull	Retarded Ossification (6,7,8 bil)	VR
13	6.14		NAD	
14	6.04		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670986 (Cont.)				
15	6.07		NAD	
16	5.69	Skull	Retarded Ossification (6,7,8 bil)	VR
670987				
1	5.70		NAD	
2	5.67	Skull	Retarded Ossification (12;2 bil)	VR
3	5.88		NAD	
4	5.60		NAD	
5	5.70		NAD	
6	6.53	Skull	Retarded Ossification (6 bil)	VR
7	5.57	Rib	Supernumerary (site 14 lt)	DV
8	5.67		NAD	
9	5.53		NAD	
10	5.52		NAD	
11	5.22	Vertebra	Retarded Ossification (cen th10,12)	VR
12	5.78	Skull	Retarded Ossification (6 rt)	VR
13	5.60		NAD	
670989				
1	5.97		NAD	
2	6.08		NAD	
3	5.46	Vertebra	Retarded Ossification (cen th12)	VR
4	5.97		NAD	
5	6.09		NAD	
6	5.68	Sternebra Vertebra	Retarded Ossification (6) Retarded Ossification (cen th13)	VR VR
7	5.43	Sternebra Vertebra	Retarded Ossification (6) Retarded Ossification (cen th12)	ST VR
8	5.69		NAD	
9	5.97	Rib	Supernumerary (site 14 lt)	DV
10	5.22		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670989 (Cont.)				
11	5.53	Kidney	Papilla - Size 3 (bil)	VR
12	5.87		NAD	
13	4.85	Sternebra	Retarded Ossification (6)	VR
14	5.86		NAD	
15	5.26		NAD	
670994				
1	6.09	Kidney	Small Papilla - Size 2 (bil)	VR
2	6.09	Skull	Retarded Ossification (2 bil)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
3	5.74	Vertebra	Retarded Ossification (cen th11-12)	VR
4	5.57	Skull	Retarded Ossification (1,12;2 bil)	VR
5	5.81	Vertebra	Retarded Ossification (cen th10-12)	VR
6	6.13	Vertebra	Retarded Ossification (cen th11)	VR
7	5.43	Kidney	Papilla - Size 3 (lt)	VR
		Vertebra	Retarded Ossification (cen th11-12)	VR
8	5.52	Skull	Retarded Ossification (2 bil)	VR
9	5.49	Vertebra	Retarded Ossification (cen th10-12)	VR
10	5.77	Skull	Retarded Ossification (2 bil)	VR
11	5.63		NAD	
12	5.65	Skull	Retarded Ossification (12;2 bil)	VR
13	5.83	Kidney	Small Papilla - Size 2 (bil)	VR
14	5.44	Skull	Retarded Ossification (2 bil)	VR
		Vertebra	Retarded Ossification (cen th11-12)	VR
15	5.52		NAD	
670998				
1	5.80		NAD	
2	5.51		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670998 (Cont.)				
3	6.22		NAD	
4	6.26		NAD	
5	6.18		NAD	
6	5.54		NAD	
7	5.67		NAD	
8	5.85	Skull	Retarded Ossification (2 lt)	VR
9	5.55		NAD	
10	5.83		NAD	
11	5.91		NAD	
12	5.63	Rib	Supernumerary (site 14 lt)	DV
13	5.53	Kidney	Small Papilla - Size 1 (lt)	VR
14	5.46		NAD	
15	5.72	Rib	Supernumerary (site 14 lt)	DV
16	5.88		NAD	
670999				
1	4.88	Vertebra	Retarded Ossification (cen th12)	VR
2	5.61		NAD	
3	5.43		NAD	
4	4.89		NAD	
5	5.26		NAD	
6	5.72	Skull	Retarded Ossification (6 bil, 8 rt)	VR
7	5.51	Kidney	Papilla - Size 3 (rt)	VR
8	5.15		NAD	
9	5.40	Vertebra	Retarded Ossification (cen th12)	VR
10	5.40		NAD	
11	5.13		NAD	
12	5.14		NAD	
13	4.98		NAD	
14	5.61		NAD	
15	5.34		NAD	
671002				
1	6.15		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671002 (Cont.)				
2	6.67	Skull	Retarded Ossification (2 bil)	VR
3	6.29	Vertebra	Retarded Ossification (cen th 11,13)	VR
4	5.81	Skull	Retarded Ossification (2 bil)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
5	5.52		NAD	
6	6.18	Skull	Retarded Ossification (1,12;2,6 bil)	VR
7	5.98	Kidney	Small Papilla - Size 2 (rt)	VR
8	5.90	Skull	Retarded Ossification (1;2 bil)	VR
9	5.76		NAD	
10	6.40	Skull	Retarded Ossification (1;2 bil)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
11	5.24	Kidney	Small Papilla - Size 1 (bil)	VR
		Rib	Supernumerary (short 14 rt)	DV
		Vertebra	Retarded Ossification (cen th9-13)	VR
12	5.95		NAD	
13	5.37		NAD	
14	6.18	Skull	Retarded Ossification (2 bil)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
15	5.65	Vertebra	Retarded Ossification (cen th11-13)	VR
671007				
1	5.74		NAD	
2	5.53		NAD	
3	5.56	Kidney	Papilla - Size 3 (rt)	VR
4	5.70		NAD	
5	5.52	Vertebra	Retarded Ossification (cen th12)	VR
6	5.68		NAD	
7	5.53		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671007 (Cont.)				
8	4.10	Sternebra Vertebra	Retarded Ossification (6) Retarded Ossification (cen th12)	VR VR
9	3.50	Sternebra	Retarded Ossification (6)	VR
10	5.29		NAD	
11	5.45		NAD	
12	4.80		NAD	
13	5.21		NAD	
14	5.61		NAD	
15	5.65		NAD	
16	5.62		NAD	
671015				
1	4.79		NAD	
2	4.84		NAD	
3	4.78	Vertebra	Retarded Ossification (cen th12)	VR
4	5.38		NAD	
5	4.98		NAD	
6	5.09		NAD	
7	4.84		NAD	
8	4.66		NAD	
9	5.30		NAD	
10	4.14		NAD	
11	5.32		NAD	
12	4.46		NAD	
13	5.01		NAD	
14	5.61		NAD	
15	4.97		NAD	
16	4.89		NAD	
671017				
1	5.35	Kidney	Papilla - Size 3 (rt)	VR
2	5.87		NAD	
3	5.79		NAD	
4	6.45		NAD	
5	6.15		NAD	
6	5.89		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671017 (Cont.)				
7	6.17		NAD	
8	5.97		NAD	
9	6.11		NAD	
10	6.57		NAD	
11	6.18		NAD	
12	5.89		NAD	
13	5.92		NAD	
14	6.33		NAD	
671031				
1	5.64		NAD	
2	5.19		NAD	
3	5.79		NAD	
4	6.08		NAD	
5	5.86		NAD	
6	5.78		NAD	
7	4.94		NAD	
8	5.53		NAD	
9	5.85		NAD	
10	5.18		NAD	
11	5.79		NAD	
12	5.98		NAD	
13	5.66		NAD	
671033				
1	5.62		NAD	
2	5.15	Rib	Supernumerary (site 14 bil)	DV
3	5.37		NAD	
4	5.45		NAD	
5	5.78		NAD	
6	6.16		NAD	
7	5.78		NAD	
8	5.84		NAD	
9	5.80		NAD	
10	5.71		NAD	
11	5.62	Kidney	Papilla - Size 3 (bil)	VR
12	5.48	Rib	Supernumerary (site 14 lt)	DV

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671035				
1	4.95	Rib	Supernumerary (site 14 rt)	DV
2	5.64		NAD	
3	5.31		NAD	
4	5.21		NAD	
5	4.94		NAD	
6	5.13		NAD	
7	5.44		NAD	
8	4.72	Sternebra	Retarded Ossification (6)	VR
9	5.44		NAD	
10	5.26		NAD	
11	5.36		NAD	
12	5.53	Rib	Supernumerary (site 14 rt)	DV
13	5.15		NAD	
14	5.01		NAD	
671039				
1	5.33		NAD	
2	5.93		NAD	
3	5.67		NAD	
4	5.57		NAD	
5	5.42		NAD	
6	5.51		NAD	
7	5.54		NAD	
8	5.72		NAD	
9	5.60		NAD	
10	5.59		NAD	
11	5.66		NAD	
12	5.27		NAD	
13	5.74		NAD	
14	5.37	Rib	Supernumerary (site 14 bil)	DV
671042				
1	5.14	Vertebra	Retarded Ossification (cen th12)	VR
2	5.49		NAD	
3	5.13	Vertebra	Retarded Ossification (cen th10,11)	VR
4	5.31		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671042 (Cont.)				
5	5.60	Lung	Colored (rt lobe, tan, 1mm dia)	N
6	5.20		NAD	
7	5.25		NAD	
8	4.79		NAD	
9	5.03		NAD	
10	5.23	Vertebra	Retarded Ossification (cen th11)	VR
11	4.96		NAD	
12	4.26		NAD	
13	5.38		NAD	
671044				
1	5.72		NAD	
2	5.94		NAD	
3	5.58		NAD	
4	5.94	Rib	Supernumerary (short 14 bil)	DV
5	5.75	Rib	Supernumerary (site 14 bil)	DV
6	5.83	Rib	Supernumerary (site 14 bil)	DV
7	5.40		NAD	
8	5.61		NAD	
9	6.24		NAD	
10	5.50	Rib	Supernumerary (site 14 bil)	DV
11	5.41		NAD	
12	5.88		NAD	
671045				
1	5.26		NAD	
2	5.67	Rib	Supernumerary (site 14 lt)	DV
3	5.95		NAD	
4	5.84	Rib	Supernumerary (site 14 bil)	DV
5	5.86	Rib	Supernumerary (site 14 lt)	DV
6	6.10		NAD	
7	5.32		NAD	
8	5.84		NAD	
9	6.10		NAD	
10	5.59		NAD	
11	5.86		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671045 (Cont.)				
12	5.49		NAD	
13	5.26		NAD	
14	5.94		NAD	
671054				
1	5.69		NAD	
2	5.66	Vertebra	Retarded Ossification (cen th10)	VR
3	5.48		NAD	
4	5.73	Vertebra	Retarded Ossification (cen th13)	VR
5	5.54		NAD	
6	5.94		NAD	
7	5.75		NAD	
8	5.75		NAD	
9	5.34	Rib	Supernumerary (site 14 lt)	DV
10	5.31		NAD	
11	5.28	Rib	Supernumerary (site 14 rt)	DV
12	5.79		NAD	
13	5.31		NAD	
14	5.46	Vertebra	Retarded Ossification (cen th9,11)	VR
15	5.68	Rib	Supernumerary (site 14 lt)	DV
		Vertebra	Retarded Ossification (cen th13)	VR
16	5.94	Rib	Supernumerary (site 14 lt)	DV
17	5.71	Kidney	Small Papilla - Size 2 (rt)	VR
671055				
1	4.98		NAD	
2	5.23		NAD	
3	5.03		NAD	
4	4.90		NAD	
5	5.24		NAD	
6	4.94	Skull	Retarded Ossification (2 lt)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
7	5.21		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP I: 0 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671055 (Cont.)				
8	5.28		NAD	
9	5.20		NAD	
10	5.42		NAD	
11	5.03		NAD	
12	5.14		NAD	
13	5.61		NAD	
14	5.54		NAD	
15	5.11		NAD	
16	5.20		NAD	
17	4.40		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
670975				
1	5.30		NAD	
2	5.64	Sternebra	Retarded Ossification (6)	VR
3	5.79		NAD	
4	5.46	Vertebra	Retarded Ossification (cen th11,12)	VR
5	5.95	Vertebra	Retarded Ossification (cen th12)	VR
6	5.32		NAD	
7	5.64		NAD	
8	5.70	Skull	Retarded Ossification (6 bil)	VR
9	5.15		NAD	
10	5.35		NAD	
11	5.47	Vertebra	Retarded Ossification (cen th11)	VR
12	5.86		NAD	
13	6.10		NAD	
14	5.45		NAD	
15	6.29	Vertebra	Retarded Ossification (cen th10)	VR
670976				
1	6.05		NAD	
2	5.07		NAD	
3	5.77		NAD	
4	5.47	Vertebra	Retarded Ossification (cen th12)	VR
5	5.32		NAD	
6	5.80	Vertebra	Retarded Ossification (cen th11)	VR
7	6.09		NAD	
8	4.04	Skull	Retarded Ossification (2 bil)	VR
9	5.14		NAD	
10	4.61	Skull	Retarded Ossification (2 bil)	VR
11	5.29		NAD	
12	5.53		NAD	
13	4.98	Kidney	Papilla - Size 3 (rt)	VR
14	5.41		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
670978				
1	5.67		NAD	
2	5.72		NAD	
3	5.21		NAD	
4	5.82		NAD	
5	5.41		NAD	
6	5.64		NAD	
7	5.39		NAD	
8	5.28		NAD	
9	4.87		NAD	
10	5.27		NAD	
11	5.14		NAD	
12	4.37		NAD	
13	5.27		NAD	
14	5.07		NAD	
15	5.86		NAD	
16	5.29		NAD	
670980				
1	5.83		NAD	
2	5.87		NAD	
3	5.59	Rib	Supernumerary (site 14 bil)	DV
4	6.10		NAD	
5	6.12	Rib	Supernumerary (site 14 bil)	DV
6	5.27	Skull	Retarded Ossification (6 rt)	VR
7	5.50		NAD	
8	5.36		NAD	
9	5.89		NAD	
10	5.89		NAD	
11	5.68		NAD	
12	5.43		NAD	
13	5.65		NAD	
670984				
1	5.38		NAD	
2	5.87		NAD	
3	5.88		NAD	
4	5.36		NAD	
5	5.66		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670984 (Cont.)				
6	6.11		NAD	
7	5.92		NAD	
8	5.83	Rib	Supernumerary (site 14 rt)	DV
9	6.05	Vertebra	Retarded Ossification (cen th11)	VR
10	5.72		NAD	
11	5.76		NAD	
12	6.20		NAD	
13	6.11		NAD	
670990				
1	5.99		NAD	
2	6.49		NAD	
3	6.67	Kidney	Papilla - Size 3 (bil)	VR
4	5.96		NAD	
5	6.12		NAD	
6	5.77	Skull	Retarded Ossification (1;2,6 bil)	VR
7	6.43		NAD	
8	6.57		NAD	
9	6.53		NAD	
10	5.99	Skull	Retarded Ossification (2,6 bil)	VR
11	6.50		NAD	
12	6.38	Rib	Supernumerary (short 14 bil)	DV
670993				
1	5.47		NAD	
2	5.41		NAD	
3	6.11	Vertebra	Retarded Ossification (cen th12)	VR
4	5.52		NAD	
5	5.57		NAD	
6	5.60		NAD	
7	5.74	Kidney	Papilla - Size 3 (rt)	VR
8	4.48	Skull	Retarded Ossification (2 bil;1)	VR
9	5.79		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670993 (Cont.)				
10	5.94		NAD	
11	5.96		NAD	
12	6.16	Skull	Retarded Ossification (2 bil;1)	VR
13	5.21	Rib	Supernumerary (site 14 bil)	DV
14	5.27	Skull	Retarded Ossification (2,6,7,8 bil;1)	VR
671000				
1	5.65		NAD	
2	5.25		NAD	
3	5.24		NAD	
4	4.90		NAD	
5	4.97		NAD	
6	4.64	Sternebra	Retarded Ossification (6)	VR
7	5.02		NAD	
8	4.90		NAD	
9	5.05		NAD	
10	5.19		NAD	
11	5.32		NAD	
12	5.08	Skull	Retarded Ossification (6 lt)	VR
13	5.53		NAD	
14	5.14		NAD	
15	5.65		NAD	
16	5.21		NAD	
671003				
1	5.97		NAD	
2	5.64		NAD	
3	5.57		NAD	
4	5.24		NAD	
5	5.63		NAD	
6	5.68		NAD	
7	4.91		NAD	
8	6.27		NAD	
9	5.57		NAD	
10	5.91		NAD	
11	5.47		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671003 (Cont.)				
12	5.34		NAD	
671012				
1	6.16		NAD	
2	6.62		NAD	
3	5.64		NAD	
4	6.28		NAD	
5	5.53		NAD	
6	5.66		NAD	
7	5.58		NAD	
8	5.87		NAD	
9	5.98	Rib	Supernumerary (site 14 bil)	DV
10	6.01		NAD	
11	5.64	Kidney	Papilla - Size 3 (bil)	VR
12	5.87		NAD	
671016				
1	5.92		NAD	
2	6.64		NAD	
3	6.07		NAD	
4	5.96		NAD	
5	6.13		NAD	
6	5.75		NAD	
7	5.56	Rib	Supernumerary (site 14 lt)	DV
8	5.61		NAD	
9	5.80		NAD	
10	6.08		NAD	
11	6.08		NAD	
12	6.17	Skull	Retarded Ossification (2 bil;1)	VR
13	6.13		NAD	
14	5.96		NAD	
671019				
1	5.65		NAD	
2	5.74	Skull	Retarded Ossification (2 bil)	VR

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671019 (Cont.)				
		Vertebra	Retarded Ossification (cen th10-12)	VR
3	5.50	Vertebra	Retarded Ossification (cen th10-12)	VR
4	6.31	Vertebra	Retarded Ossification (cen th11)	VR
5	5.10	Vertebra	Retarded Ossification (cen th10-13)	VR
6	5.61		NAD	
7	5.52	Vertebra	Retarded Ossification (cen th10-13)	VR
8	5.60	Vertebra	Retarded Ossification (cen th10,12)	VR
671020				
1	5.03		NAD	
2	5.98		NAD	
3	5.57		NAD	
4	5.71		NAD	
5	5.60		NAD	
6	5.74	Rib	Supernumerary (site 14 rt)	DV
7	5.48		NAD	
8	5.05		NAD	
9	5.24		NAD	
10	5.38		NAD	
11	4.84		NAD	
12	5.50		NAD	
13	6.03		NAD	
671025				
1	5.62		NAD	
2	5.83	Skull	Retarded Ossification (6 bil)	VR
3	6.07		NAD	
4	5.72		NAD	
5	5.55	Kidney	Small Papilla - Size 2 (bil)	VR
6	5.85		NAD	
7	5.56		NAD	
8	4.66		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671025 (Cont.)				
9	5.76		NAD	
10	5.59		NAD	
11	5.30		NAD	
12	6.55		NAD	
13	5.75		NAD	
671026				
1	5.66	Vertebra	Retarded Ossification (cen th11-12)	VR
2	5.49	Skull	Retarded Ossification (1;2 bil)	VR
		Vertebra	Retarded Ossification (cen th8,11-12)	VR
3	6.03		NAD	
4	6.38	Skull	Retarded Ossification (1,12;2 bil)	VR
5	5.51		NAD	
6	5.14	Skull	Retarded Ossification (1,12;2 bil)	VR
		Vertebra	Retarded Ossification (cen th10-13)	VR
7	5.84	Vertebra	Retarded Ossification (cen th10)	VR
8	5.42	Skull	Retarded Ossification (1,12;2 bil)	VR
9	5.39	Vertebra	Retarded Ossification (cen th13)	VR
10	5.71	Rib	Supernumerary (site 14 lt)	DV
		Skull	Retarded Ossification (2 bil,8 lt,12)	VR
11	5.87	Vertebra	Retarded Ossification (cen th11-12)	VR
12	5.49	Skull	Retarded Ossification (1;2 bil)	VR
		Vertebra	Retarded Ossification (cen th10-13)	VR

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671026 (Cont.)				
13	5.75	Vertebra	Retarded Ossification (cen th11-12)	VR
671034				
1	6.16		NAD	
2	6.21		NAD	
3	5.66		NAD	
4	6.24		NAD	
5	5.62		NAD	
6	5.73	Subcutis	Hemorrhage (back*)	N
7	5.74		NAD	
8	6.20		NAD	
9	6.08	Rib	Supernumerary (site 14 bil)	DV
10	5.45	Rib	Supernumerary (site 14 lt)	DV
11	5.97		NAD	
12	5.75	Rib	Supernumerary (site 14 bil)	DV
671043				
1	5.78	Vertebra	Retarded Ossification (cen th12)	VR
2	5.28	Skull	Retarded Ossification (2 bil)	VR
3	6.07		NAD	
4	5.47	Skull	Retarded Ossification (1,12;2 bil)	VR
5	5.98	Vertebra	Retarded Ossification (cen th12)	VR
6	5.47	Vertebra	Retarded Ossification (cen th10)	VR
7	5.80		NAD	
8	5.83	Skull	Retarded Ossification (1;2 bil)	VR
9	5.67	Kidney	Small Papilla - Size 2 (rt)	VR
10	5.75	Skull	Retarded Ossification (1,12)	VR
11	5.31		NAD	
12	5.81	Skull	Retarded Ossification (1;2 bil)	VR

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671048				
1	5.46	Rib	Supernumerary (site 14 lt)	DV
2	4.93		NAD	
3	5.13		NAD	
4	5.51		NAD	
5	4.90		NAD	
6	4.77		NAD	
7	5.16		NAD	
8	4.98		NAD	
9	5.49		NAD	
10	5.47		NAD	
11	5.24		NAD	
12	5.51		NAD	
13	4.93		NAD	
671050				
1	6.35		NAD	
2	6.23		NAD	
3	6.01		NAD	
4	5.97		NAD	
5	6.19		NAD	
6	5.39		NAD	
7	5.91		NAD	
8	6.09	Rib	Supernumerary (site 14 lt)	DV
9	5.74		NAD	
10	6.51		NAD	
11	6.40	Kidney	Papilla - Size 3 (bil)	VR
12	6.00		NAD	
671052				
1	5.75	Rib	Supernumerary (site 14 lt)	DV
2	6.21		NAD	
3	5.49		NAD	
4	5.66		NAD	
5	6.01	Rib	Supernumerary (site 14 lt)	DV
6	5.80		NAD	
7	5.82		NAD	
8	5.86	Rib	Supernumerary (site 14 lt)	DV
9	6.14		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671052 (Cont.)				
10	6.15	Rib	Supernumerary (site 14 lt)	DV
11	5.79		NAD	
12	5.45		NAD	
13	5.71		NAD	
14	5.34		NAD	
15	5.40	Subcutis	Hemorrhage (chin*)	N
16	6.11		NAD	
671056				
1	5.04		NAD	
2	5.70	Skull	Retarded Ossification (1,12;2,3 bil,6 lt)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
3	5.63	Vertebra	Retarded Ossification (cen th12)	VR
4	5.63	Skull	Retarded Ossification (1,12;2,3,6,7,8 bil)	VR
		Vertebra	Retarded Ossification (cen th12)	VR
5	5.20		NAD	
6	4.82	Rib	Supernumerary (site 14 lt)	DV
		Skull	Retarded Ossification (1,12;2,3,6,7,8 bil)	VR
		Vertebra	Retarded Ossification (cen th12)	VR
7	5.60		NAD	
8	5.44	Skull	Retarded Ossification (1,12,2 bil)	VR
9	5.24		NAD	
10	5.49	Skull	Retarded Ossification (1,12;2 bil)	VR
11	5.36	Vertebra	Retarded Ossification (cen th12)	VR
12	4.78	Skull	Retarded Ossification (1,12;2,3 bil)	VR
13	5.61		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP II: 50 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671056 (Cont.) 14	5.73	Rib Skull	Supernumerary (site14 lt) Retarded Ossification (2 bil)	DV VR

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670970				
1	5.99	Vertebra	Retarded Ossification (cen th11)	VR
2	4.97	Skull	Retarded Ossification (2,6,7,8 bil;1)	VR
		Sternebra	Retarded Ossification (6)	VR
		Vertebra	Retarded Ossification (cen th12)	VR
3	6.14		NAD	
4	5.43		NAD	
5	5.97		NAD	
6	5.62	Skull	Retarded Ossification (6 bil)	VR
7	6.00		NAD	
8	5.99	Rib	Supernumerary (short 13 rt)	DV
		Skull	Retarded Ossification (2,bil;7 rt;12)	VR
9	5.98	Vertebra	Retarded Ossification (cen th11)	VR
10	5.68	Skull	Retarded Ossification (6 bil,1)	VR
11	6.12		NAD	
12	6.45	Skull	Retarded Ossification (6 bil)	VR
13	6.10		NAD	
14	6.06	Skull	Retarded Ossification (6 lt)	VR
15	6.10	Vertebra	Retarded Ossification (cen th10)	VR
670972				
1	6.35		NAD	
2	6.01		NAD	
3	6.32		NAD	
4	6.42		NAD	
5	5.69		NAD	
6	6.39		NAD	
7	6.86		NAD	
8	6.40		NAD	
9	6.29		NAD	
10	6.12		NAD	
11	5.63		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670972 (Cont.)				
12	6.14	Rib	Supernumerary (site 14 lt)	DV
13	6.11		NAD	
14	5.58	Skull	Retarded Ossification (2 bil)	VR
15	6.31		NAD	
670979				
1	5.70		NAD	
2	5.95		NAD	
3	5.99		NAD	
4	6.18		NAD	
5	5.77		NAD	
6	5.56		NAD	
7	5.58	Rib	Supernumerary (site 14 bil)	DV
8	5.52		NAD	
9	5.60		NAD	
10	5.47	Skull	Retarded Ossification (8 rt)	VR
11	5.58	Vertebra	Retarded Ossification (cen th11)	VR
12	5.69		NAD	
13	6.39		NAD	
670983				
1	5.47		NAD	
2	5.73		NAD	
3	5.74		NAD	
4	5.54		NAD	
5	5.72		NAD	
6	5.20	Skull	Retarded Ossification (2 bil)	VR
7	6.25		NAD	
8	5.67	Rib	Supernumerary (site 14 lt)	DV
9	6.11		NAD	
10	6.26		NAD	
11	6.04		NAD	
12	6.29		NAD	
13	6.22		NAD	
670988				
1	6.05		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670988 (Cont.)				
2	6.13	Skull	Retarded Ossification (6 bil)	VR
3	6.66		NAD	
4	6.33	Skull	Retarded Ossification (2,6,7,8 bil;1,12)	VR
		Vertebra	Retarded Ossification (cen th10)	VR
5	5.71		NAD	
6	6.23	Skull	Retarded Ossification (2,6,7,8 bil)	VR
7	6.41		NAD	
8	6.06	Skull	Retarded Ossification (2,6 bil)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
9	6.30	Vertebra	Retarded Ossification (cen th10,12)	VR
10	6.58	Vertebra	Retarded Ossification (cen th10,13)	VR
11	6.40		NAD	
12	5.65	Skull	Retarded Ossification (2,6,7,8 bil)	VR
13	6.24	Vertebra	Retarded Ossification (cen th11)	VR
670992				
1	5.37		NAD	
2	5.13		NAD	
3	4.52	Rib	Rudimentary Cervical (7 rt)	DV
4	5.20	Skull	Retarded Ossification (6,7 lt)	VR
5	5.15		NAD	
6	5.01	Skull	Retarded Ossification (6,7 bil)	VR
7	5.08		NAD	
8	4.39		NAD	
9	5.25	Rib	Rudimentary Cervical (7 rt)	DV
		Vertebra	Retarded Ossification (cen th11)	VR

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
670992 (Cont.)				
10	4.71	Subcutis	Hemorrhage (chin*)	N
11	4.96		NAD	
670995				
1	5.69	Vertebra	Retarded Ossification (cen th10,12)	VR
2	5.99	Skull	Retarded Ossification (1,12;2 bil;7 lt)	VR
3	5.90	Vertebra	Retarded Ossification (cen th12)	VR
4	5.98	Skull	Retarded Ossification (1;2 bil)	VR
5	5.90		NAD	
6	6.23	Skull	Retarded Ossification (2,6 bil)	VR
7	6.51	Kidney Vertebra	Papilla - Size 3 (rt) Retarded Ossification (cen th11)	VR VR
8	6.51	Skull	Retarded Ossification (1)	VR
9	6.05	Vertebra	Retarded Ossification (cen th9-11)	VR
10	6.11		NAD	
11	5.44		NAD	
12	6.77	Skull	Retarded Ossification (1;2 bil)	VR
		Vertebra	Retarded Ossification (cen th10,12)	VR
13	5.19	Vertebra	Retarded Ossification (cen th11)	VR
14	5.90	Skull	Retarded Ossification (1;2 bil)	VR
15	6.06		NAD	
16	6.63	Skull	Retarded Ossification (6 rt)	VR
670996				
1	5.90		NAD	
2	6.76		NAD	
3	6.64		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670996 (Cont.)				
4	6.33		NAD	
5	6.37		NAD	
6	6.84	Rib	Supernumerary (site 14 rt)	DV
7	6.04		NAD	
8	6.27		NAD	
9	6.73		NAD	
10	6.40		NAD	
11	6.68		NAD	
12	6.24	Skull	Retarded Ossification (6 bil)	VR
13	6.20		NAD	
14	6.17		NAD	
670997				
1	5.93		NAD	
2	6.68	Rib	Supernumerary (site 14 bil)	DV
3	5.82		NAD	
4	5.58		NAD	
5	5.32		NAD	
6	5.23		NAD	
7	5.85		NAD	
8	5.81	Skull	Retarded Ossification (2 bil)	VR
9	6.54		NAD	
10	5.92		NAD	
11	5.47		NAD	
671009				
1	6.21		NAD	
2	5.87	Skull	Retarded Ossification (6 bil)	VR
3	5.73		NAD	
4	6.31	Skull	Retarded Ossification (1)	VR
5	5.63		NAD	
6	5.77		NAD	
7	6.17		NAD	
8	6.20		NAD	
9	6.15		NAD	
10	6.27	Rib	Supernumerary (site 14 rt)	DV
11	6.50		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671009 (Cont.)				
12	6.29	Rib	Supernumerary (site 14 bil)	DV
		Skull	Retarded Ossification (1)	VR
13	6.28		NAD	
14	5.77	Skull	Retarded Ossification (2,7 bil;1)	VR
15	5.46		NAD	
16	6.30	Rib	Supernumerary (site 14 lt)	DV
17	6.24		NAD	
671010				
1	6.05		NAD	
2	5.89		NAD	
3	6.40		NAD	
4	6.25		NAD	
5	6.21		NAD	
6	6.71	Vertebra	Retarded Ossification (cen th11)	VR
7	6.43		NAD	
8	6.27		NAD	
9	6.44		NAD	
10	6.28		NAD	
671024				
1	5.31		NAD	
2	4.85	Subcutis	Hemorrhage (back*)	N
		Skull	Retarded Ossification (6,7 lt;1,12)	VR
3	5.21		NAD	
4	5.47		NAD	
5	5.89		NAD	
6	5.66		NAD	
7	5.28	Rib	Supernumerary (short 13 bil)	DV
8	5.68		NAD	
9	5.27		NAD	
10	5.31		NAD	
11	5.04		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671024 (Cont.)				
12	5.74	Skull	Retarded Ossification (2,6 bil;1,12)	VR
13	5.33	Kidney	Small Papilla - Size 2 (rt)	VR
14	5.48	Skull	Retarded Ossification (6 bil)	VR
15	6.17		NAD	
671027				
1	5.48		NAD	
2	5.43		NAD	
3	5.59		NAD	
4	4.99		NAD	
5	5.37	Rib	Supernumerary (site 14 bil)	DV
6	4.75		NAD	
7	5.21		NAD	
8	5.31		NAD	
9	5.08		NAD	
10	5.39	Rib	Supernumerary (site 14 bil)	DV
11	5.25		NAD	
12	5.32	Rib	Supernumerary (site 14 bil)	DV
13	5.11		NAD	
671028				
1	5.47	Subcutis	Hemorrhage (right shoulder*)	N
2	5.42		NAD	
3	5.16		NAD	
4	5.38		NAD	
5	5.66		NAD	
6	5.08		NAD	
7	5.81		NAD	
8	5.75		NAD	
9	5.29		NAD	
10	5.05		NAD	
11	5.27		NAD	
12	4.67		NAD	
13	4.63		NAD	
14	5.29		NAD	
15	5.39		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671029				
1	5.81		NAD	
2	5.78		NAD	
3	6.15		NAD	
4	5.51	Rib	Supernumerary (short 14 bil)	DV
5	5.61	Kidney	Small Papilla - Size 1 (rt)	VR
		Rib	Supernumerary (short 14 bil)	DV
6	5.45		NAD	
7	5.65		NAD	
8	5.67	Rib	Supernumerary (short 14 bil)	DV
9	5.95		NAD	
10	5.87		NAD	
11	4.31		NAD	
12	5.22	Vertebra	Retarded Ossification (cen th12)	VR
671030				
1	5.57		NAD	
2	5.49		NAD	
3	5.71		NAD	
4	5.97		NAD	
5	5.14		NAD	
6	5.23		NAD	
7	6.06		NAD	
8	5.28	Skull	Retarded Ossification (6 bil)	VR
9	5.17		NAD	
10	5.06	Rib	Supernumerary (site 14 rt)	DV
		Skull	Retarded Ossification (6 bil)	VR
		Vertebra	Retarded Ossification (cen th12)	VR
11	5.59		NAD	
671032				
1	5.04	Vertebra	Retarded Ossification (cen th9)	VR
2	5.37		NAD	
3	4.71		NAD	
4	5.00		NAD	
5	5.58		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671032 (Cont.)				
6	5.07		NAD	
7	5.72	Kidney	Papilla - Size 3 (bil)	VR
8	5.28		NAD	
9	4.81		NAD	
10	5.37	Skull	Retarded Ossification (6 bil)	VR
11	4.99		NAD	
12	5.06		NAD	
13	4.88		NAD	
14	5.32		NAD	
15	5.44		NAD	
671036				
1	5.94	Kidney	Papilla - Size 3 (bil)	VR
2	6.49	Rib Vertebra	Supernumerary (site 14 lt) Retarded Ossification (cen th12)	DV VR
3	6.35		NAD	
4	6.30		NAD	
5	6.06		NAD	
6	6.07	Rib	Supernumerary (site 14 rt)	DV
7	6.53	Rib	Supernumerary (site 14 bil)	DV
8	5.80		NAD	
9	6.39		NAD	
10	5.94	Rib Skull	Supernumerary (site 14 bil) Retarded Ossification (6 lt)	DV VR
11	6.00		NAD	
12	6.14	Rib Skull	Supernumerary (site 14 lt) Retarded Ossification (6,7 bil;1)	DV VR
13	5.72		NAD	
14	6.57		NAD	
671037				
1	6.12		NAD	
2	6.14		NAD	
3	5.97		NAD	
4	5.93		NAD	
5	5.96		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671037 (Cont.)				
6	5.98		NAD	
7	6.13		NAD	
8	5.32		NAD	
9	6.01		NAD	
10	5.74		NAD	
11	5.64		NAD	
12	5.44		NAD	
13	5.40		NAD	
14	5.69		NAD	
671038				
1	5.86	Sternebra Vertebra	Retarded Ossification (6) Retarded Ossification (cen th9-11)	VR VR
2	6.07		NAD	
3	6.28		NAD	
4	6.51	Vertebra	Retarded Ossification (cen th11)	VR
5	5.64	Rib Vertebra	Supernumerary (site 14 lt) Retarded Ossification (cen th11)	DV VR
6	6.38	Vertebra	Retarded Ossification (cen th13)	VR
7	6.08	Rib	Supernumerary (site 14 lt)	DV
8	6.19	Vertebra	Retarded Ossification (cen th10)	VR
9	5.67	Vertebra	Retarded Ossification (cen th8,10,11,13 lul)	VR
10	6.34	Rib	Supernumerary (site 14 lt)	DV
11	5.66		NAD	
12	5.92	Sternebra Vertebra	Retarded Ossification (6) Retarded Ossification (cen th13)	VR VR
13	6.49		NAD	
671040				
1	6.06		NAD	
2	6.05		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671040 (Cont.)				
3	6.04	Rib	Supernumerary (site 14 lt)	DV
4	4.15		NAD	
5	5.87		NAD	
6	5.18	Skull	Retarded Ossification (6 bil)	VR
7	5.41		NAD	
8	5.16		NAD	
9	6.04	Rib	Supernumerary (site 14 bil)	DV
		Vertebra	Retarded Ossification (cen th13)	VR
10	5.03	Rib	Supernumerary (site 14 lt)	DV
11	5.82	Rib	Supernumerary (site 14 bil)	DV
12	5.92		NAD	
13	5.33		NAD	
671049				
1	6.01	Rib	Supernumerary (site14 bil)	DV
2	5.04	Skull	Retarded Ossification (1,12;2,3,6,7,8 bil)	VR
3	5.70		NAD	
4	6.13	Skull	Retarded Ossification (2 bil)	VR
5	5.72		NAD	
6	5.43	Skull	Retarded Ossification (1,12;2,3 bil;6 rt)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
7	5.50		NAD	
8	5.84	Skull	Retarded Ossification (1,12;2,3,6,7,8 bil)	VR
9	6.00	Vertebra	Retarded Ossification (cen th10)	VR
10	5.51	Skull	Retarded Ossification (1,12;2,3,bil;6 rt)	VR
11	5.59	Vertebra	Retarded Ossification (cen th12)	VR
12	5.98	Skull	Retarded Ossification (1,12;2,3,6 bil)	VR
13	4.97	Rib	Supernumerary (site14 lt)	DV

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP III: 200 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671049 (Cont.) 14	5.55	Rib	Supernumerary (site14 rt)	DV
		Skull	Retarded Ossification (1,12;2,3,6,7,8 bil)	VR
		Vertebra	Retarded Ossification (cen th10)	VR

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
670971				
1	5.48		NAD	
2	5.40	Skull	Retarded Ossification (6 lt)	VR
3	5.65		NAD	
4	5.32		NAD	
5	5.43		NAD	
6	5.49	Skull	Retarded Ossification (6 bil)	VR
7	5.36		NAD	
8	5.27	Skull	Retarded Ossification (6 bil)	VR
9	5.68		NAD	
10	5.28	Skull	Retarded Ossification (6 rt)	VR
11	5.17		NAD	
12	5.26	Skull	Retarded Ossification (6 rt)	VR
13	5.43		NAD	
14	5.16	Skull	Retarded Ossification (6 lt)	VR
15	5.56		NAD	
670977				
1	5.84		NAD	
2	5.92	Skull	Fused (1 to 12)	DV
3	5.55		NAD	
4	5.63	Skull	Retarded Ossification (6, bil;7,8 lt)	VR
5	5.88		NAD	
6	5.73	Skull	Retarded Ossification (2 bil)	VR
7	5.69		NAD	
8	5.73		NAD	
9	5.44		NAD	
10	5.34		NAD	
11	5.52		NAD	
12	5.54		NAD	
13	5.70		NAD	
14	6.04		NAD	
670982				
1	5.65		NAD	
2	5.44	Skull	Retarded Ossification (2 bil)	VR
3	5.42	Rib	Rudimentary Cervical (7 lt)	DV

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670982 (Cont.)				
		Rib	Supernumerary (site 14 bil)	DV
4	5.10	Skull	Retarded Ossification (2 bil)	VR
5	6.26	Rib	Supernumerary (site 14 lt)	DV
6	5.30	Skull	Retarded Ossification (2 bil)	VR
7	6.33	Rib	Supernumerary (short 14 bil)	DV
8	5.23	Skull	Retarded Ossification (2 bil)	VR
9	5.83		NAD	
10	6.13	Skull	Retarded Ossification (2 bil)	VR
11	5.90		NAD	
12	5.66		NAD	
13	5.71	Rib	Supernumerary (site 14 lt)	DV
14	5.79		NAD	
670991				
1	5.32		NAD	
2	5.32	Skull	Retarded Ossification (2,6,7 bil;1,12)	VR
		Vertebra	Retarded Ossification (cen th11)	VR
3	5.80		NAD	
4	4.99	Skull	Retarded Ossification (2,6,7,8 bil;12)	VR
		Vertebra	Retarded Ossification (cen th10,11,12)	VR
5	5.49		NAD	
6	5.75	Skull	Retarded Ossification (6,7,8 bil)	VR
7	6.07	Rib	Supernumerary (site 14 bil)	DV
		Vertebra	Retarded Ossification (cen th11,12)	VR
8	6.01	Rib	Supernumerary (site 14 rt)	DV
		Skull	Retarded Ossification (6 bil)	VR
9	5.47	Pelvis	Retarded Ossification (pubis bil)	VR
10	5.74	Skull	Retarded Ossification (2,6,7,8 bil;12)	VR
11	5.04		NAD	
12	4.81		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
670991 (Cont.)				
13	5.51	Vertebra	Retarded Ossification (cen th11,12)	VR
671001				
1	5.94		NAD	
2	6.01	Skull	Retarded Ossification (2 bil,7 rt)	VR
3	5.74		NAD	
4	5.40	Skull	Retarded Ossification (2 bil)	VR
5	5.31		NAD	
6	5.14	Skull	Retarded Ossification (2 bil)	VR
		Vertebra	Retarded Ossification (cen th11-12)	VR
7	4.96	Vertebra	Retarded Ossification (cen th9-11)	VR
8	5.73	Skull	Retarded Ossification (2,6,7 bil)	VR
9	5.74		NAD	
10	5.69	Subcutis	Hemorrhage (neck*)	N
		Vertebra	Retarded Ossification (cen th11)	VR
11	5.35		NAD	
12	5.66	Skull	Retarded Ossification (2 bil)	VR
13	5.90	Rib	Supernumerary (site 14 bil)	DV
14	5.71	Skull	Retarded Ossification (1;2 bil)	VR
15	5.18	Rib	Supernumerary (site 14 bil)	DV
16	5.14	Skull	Retarded Ossification (1,12;2 bil)	VR
		Skull	Retarded Ossification (6,7,8 bil)	VR
671004				
1	4.90		NAD	
2	5.01	Skull	Retarded Ossification (2,6,7,8 bil;1,12)	VR

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671004 (Cont.)				
3	4.74	Pelvis	Retarded Ossification (pubis,ischium bil)	VR
		Sternebra	Retarded Ossification (6)	VR
4	4.94	Skull	Retarded Ossification (2,6,7,8 bil;1,12)	VR
5	4.60		NAD	
6	5.15	Rib	Wavy (7-10 rt,11 bil)	VR
		Skull	Retarded Ossification (2,3,6,7,8 bil;1)	VR
7	5.21		NAD	
8	4.88	Pelvis	Retarded Ossification (pubis,ischium bil)	VR
		Skull	Retarded Ossification (2,3,6,7,8 bil;1,12)	VR
9	5.16		NAD	
10	5.16	Pelvis	Retarded Ossification (pubis,ischium bil)	VR
		Skull	Retarded Ossification (2,3,7,8 bil;1)	VR
11	4.82	Pelvis	Retarded Ossification (ischium bil)	VR
12	4.63	Skull	Retarded Ossification (2,3,6,7,8 bil;1,12)	VR
13	5.21	Pelvis	Retarded Ossification (pubis,ischium bil)	VR
671006				
1	6.24		NAD	
2	5.84		NAD	
3	6.01	Kidney	Small Papilla - Size 2 (bil)	VR
4	5.44		NAD	
5	6.38		NAD	
6	6.20	Rib	Supernumerary (site 14 rt)	DV
7	5.24		NAD	
8	6.49		NAD	
9	5.71		NAD	
10	5.53		NAD	
11	5.38		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671006 (Cont.)				
12	5.75		NAD	
13	6.29		NAD	
14	6.34		NAD	
671011				
1	5.01		NAD	
2	5.28	Skull	Retarded Ossification (6 bil)	VR
3	5.65	Rib	Supernumerary (site 14 rt)	DV
4	5.46		NAD	
5	5.61		NAD	
6	5.17	Skull	Retarded Ossification (6 bil)	VR
7	5.58		NAD	
8	4.59		NAD	
9	5.38	Kidney	Papilla - Size 3 (bil)	VR
10	5.28		NAD	
11	5.29	Kidney	Papilla - Size 3 (bil)	VR
12	5.10	Skull	Retarded Ossification (6,7,8 bil)	VR
13	5.13		NAD	
14	5.23	Skull	Retarded Ossification (2,6,7,8 bil)	VR
15	5.21	Kidney	Small Papilla - Size 1 (lt)	VR
16	5.05		NAD	
671013				
1	6.45		NAD	
2	5.84		NAD	
3	6.53	Vertebra	Retarded Ossification (cen th10)	VR
4	5.63		NAD	
5	5.35		NAD	
6	5.61		NAD	
7	5.79		NAD	
8	6.39		NAD	
9	5.80		NAD	
10	5.35		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671014				
1	5.62		NAD	
2	5.65	Rib	Supernumerary (site 14 lt)	DV
		Skull	Retarded Ossification (6 bil)	VR
3	5.11		NAD	
4	5.53	Rib	Supernumerary (site 14 bil)	DV
5	4.92	Rib	Supernumerary (site 14 rt)	DV
6	5.23	Skull	Retarded Ossification (6 bil)	VR
		Sternebra	Retarded Ossification (6)	VR
7	4.37	Kidney	Small Papilla - Size 1 (rt, size3 lt)	VR
8	4.78	Subcutis	Hemorrhage (back*)	N
9	5.51		NAD	
10	5.11	Rib	Supernumerary (site 14 rt)	DV
11	4.85	Rib	Supernumerary (site 14 lt)	DV
12	5.24	Rib	Supernumerary (short 14 bil)	DV
671018				
1	5.17		NAD	
2	4.83	Vertebra	Retarded Ossification (cen th11)	VR
3	4.99		NAD	
4	5.66		NAD	
5	5.22		NAD	
6	4.80		NAD	
7	4.13	Rib	Supernumerary (short 14 lt)	DV
		Pelvis	Retarded Ossification (pubis lt)	VR
8	4.66	Rib	Supernumerary (site 14 lt)	DV
9	5.12	Rib	Supernumerary (short 14 lt)	DV
10	5.12	Skull	Retarded Ossification (6 lt)	VR
11	5.30		NAD	
12	5.08		NAD	
13	5.07	Vertebra	Retarded Ossification (cen th12)	VR
14	5.06		NAD	
15	4.83	Rib	Supernumerary (site 14 bil)	DV
16	5.12	Skull	Retarded Ossification (6 rt)	VR
17	4.85		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671022				
1	5.16	Sternebra	Retarded Ossification (6)	VR
2	5.19	Skull	Retarded Ossification (2,6 bil)	VR
3	5.06		NAD	
4	4.82	Skull	Retarded Ossification (2,6,7,8 bil;12,)	VR
		Sternebra	Retarded Ossification (6)	VR
5	5.00		NAD	
6	4.99	Pelvis	Retarded Ossification (pubis bil)	VR
		Skull	Retarded Ossification (2 bil;1,12)	VR
		Sternebra	Retarded Ossification (6)	VR
7	4.87		NAD	
8	4.93	Skull	Retarded Ossification (6 bil)	VR
9	5.06		NAD	
10	5.03	Skull	Retarded Ossification (2,6 bil)	VR
11	4.52		NAD	
12	5.34	Rib	Supernumerary (site 14 rt)	DV
		Skull	Retarded Ossification (6 bil)	VR
13	4.74		NAD	
14	4.69	Skull	Retarded Ossification (2,6,7,8 bil;1,12)	VR
15	5.35	Subcutis	Hemorrhage (back*)	N
671023				
1	4.62	Pelvis	Retarded Ossification (pubis lt)	VR
2	4.35	Rib	Supernumerary (site 14 bil)	DV
3	4.86	Rib	Supernumerary (site 14 rt)	DV
		Sternebra	Retarded Ossification (6)	VR
4	4.13	Skull	Retarded Ossification (6 lt)	VR
5	3.94	Sternebra	Retarded Ossification (6)	VR
6	4.09		NAD	
7	4.16		NAD	
8	4.01	Skull	Retarded Ossification (6 bil)	VR
9	4.11		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING(S)	CLASSIF- ICATION
671023 (Cont.)				
10	4.17		NAD	
11	4.74		NAD	
12	4.34	Skull	Retarded Ossification (6 bil)	VR
13	4.36	Rib	Supernumerary (site 14 lt)	DV
14	4.14	Skull	Retarded Ossification (6,8 bil)	VR
671046				
1	6.23		NAD	
2	5.00	Rib	Wavy (6-10 rt)	VR
		Skull	Retarded Ossification (2,6,7,8 bil;1,12)	VR
3	5.60		NAD	
4	5.82	Vertebra	Retarded Ossification (cen th10)	VR
5	5.23	Rib	Wavy (6-11 rt,10,11 lt)	VR
6	4.72	Rib	Wavy (4-13 bil)	VR
		Skull	Retarded Ossification (2,6,7,8 bil;1,12)	VR
		Sternebra	Retarded Ossification (6)	VR
7	5.98		NAD	
8	4.93	Rib	Wavy (5-13 bil)	VR
		Skull	Retarded Ossification (6 rt;1)	VR
9	5.72		NAD	
10	5.39		NAD	
11	5.46		NAD	
12	5.80	Skull	Retarded Ossification (2,6,7,8 bil)	VR
13	5.50		NAD	
671047				
1	5.64		NAD	
2	6.46		NAD	
3	6.01		NAD	
4	5.89		NAD	
5	5.30		NAD	
6	5.85		NAD	
7	6.38		NAD	

ALTERATIONS IN INDIVIDUAL FETUSES

GROUP IV: 500 MG/KG/DAY

DAM #/ FETUS #	FETUS WT.	STRUCTURE	FINDING (S)	CLASSIF- ICATION
671047 (Cont.)				
8	6.00		NAD	
9	5.92		NAD	
10	5.94		NAD	
671057				
1	5.26	Rib	Supernumerary (site 14 bil)	DV
2	5.64	Rib	Supernumerary (site 14 bil)	DV
3	5.88	Rib	Supernumerary (site 14 bil)	DV
4	6.15	Rib	Supernumerary (site 14 lt)	DV
5	5.70	Rib	Supernumerary (site 14 lt)	DV
6	5.60		NAD	
7	6.15		NAD	
8	5.51	Rib	Supernumerary (site 14 rt)	DV
9	5.70	Rib	Supernumerary (site 14 lt)	DV
10	5.66	Rib	Supernumerary (site 14 bil)	DV
11	6.13		NAD	
12	5.57	Rib	Supernumerary (short 14 bil)	DV
13	5.17	Rib	Supernumerary (site 14 rt)	DV
		Vertebra	Retarded Ossification (cen th11,13)	VR
14	5.85		NAD	