HAZLETON
LABORATORIES AMERICA, INC.
9200 LEESBURG TURNPIKE VIENNA VIRGINIA 22180 U S A

RAT TERATOLOGY STUDY

T-3352

FINAL REPORT

Submitted to

3M Company
St. Paul, Minnesota

March 21, 1984

HAZLETON LABORATORIES AMERICA, INC
9200 LEESBURG TURNPIKE VIENNA VIRGINIA 22180

OFFICE OF QUALITY ASSURANCE

Project Title: Rat Teratology Study

Project No.: 154-161

Quality Assurance inspections of the study and review of the final report of the above referenced project were conducted according to the standard operating procedures of the Office of Quality Assurance and according to the general requirements of the Good Laboratory Practice regulations that were issued on December 22, 1978, by the Food and Drug Administration for compliance on and after June 20, 1979. Findings from the inspections and final report review were reported to management and to the study director on the following dates:

Inspections/Review	Findings Reported	Inspector/Reviewer
Protocol 6/15/83	6/15/83	E. Burroughs
Inspection 8/3-5/83	8/5/83	E. Burroughs
Report Review 2/11,12,14,15/84	2/24/84	P. Miller

Frederick C. Snyder
Director
Office of Quality Assurance

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SUBJECT: Rat Teratology Study
Project No. 154-161

We, the undersigned, hereby declare that the work was performed under our supervision, according to the procedures herein described.

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LABORATORIES AMERICA, INC.

SPONSOR: 3M Company

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MATERIAL: T-3352

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SUMMARY

T-3352, suspended in corn oil at concentrations intended to deliver 1, 10, or 30 mg/kg/day (Groups 2, 3, and 4, respectively) was administered by oral intubation to mated female Sprague-Dawley derived CD® rats on presumed gestation Days 6-15. A fourth group (Group 1) of mated females served as the control group and received the vehicle only.

During treatment with T-3352, significantly lower than control food consumption values and body weight gains were noted for Group 4 females. Loss of body weight occurred in Group 4 females during Days 6 to 12 of gestation. Mean gravid uterine weights were comparable for all groups, whereas the mean terminal body weight minus the gravid uterine weight was significantly less than control in the Group 4 animals.

Most cesarean data measured appeared unchanged following treatment with T-3352. Statistically, male and female fetuses derived from Group 4 dams weighed significantly less than control fetuses. Although not significant, there was an increase in the incidence of skeletal variants in fetuses obtained from Group 4 dams.

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The data from this study show that T-3352 is not teratogenic in rats at doses as high as 30 mg/kg of body weight, although that dose produced deleterious effects in the dams.

INTRODUCTION

This study was designed to evaluate the embryo/fetal toxicity and teratogenic potential of T-3352 when administered by oral gavage to pregnant rats during the period of fetal organogenesis. On July 18, 1983, breeding of the rats was begun, and cesarean sections were completed on August 11, 1983. The study was conducted according to a protocol designed to satisfy existing guidelines of the Food and Drug Administration as well as Good Laboratory Practice Regulations. This report presents and discusses the methods and results from the study.

CONTROL AND TEST MATERIALS

The vehicle and control material, Duke's® Corn Oil (Lot No. 80275), a slightly viscous, yellow liquid, was received from the C. F. Sauer Co., Richmond, Virginia, and was stored at room temperature.

The test material, T-3352, large chunks of off-white compound, was received from the sponsor on January 5, 1983, and was stored at room temperature. The test material was assumed to be 100% active compound. Information on the methods of synthesis, stability, as well as data on composition, or other characteristics which define the test material, are on file with the sponsor.

TEST ANIMALS

Two hundred fifty-nine (130 male and 129 female) sexually mature, cesarean-derived Sprague-Dawley Crl:CD® (SD)BR rats were received from Charles River Breeding Laboratories, Inc., Kingston, New York, on June 29, 1983. The rat was selected for use in this study because historically this species has been used in teratology studies and is required by appropriate regulatory agencies. The animals were housed individually in elevated stainless-steel cages and acclimated to laboratory conditions for approximately three weeks prior to initiation of the study. During this time, one female rat was euthanatized due to an unthrifty appearance and one female was found dead. Following an examination by a staff veterinarian for health status, 120 rats/sex were placed in breeding on July 18, 1983, and the remaining 7 rats/sex were placed in breeding one day later due to caging limitations.

The rats were housed one male and one female per cage during breeding. Following confirmation of mating, the females were uniquely identified by ear tags and individually housed in elevated stainless-steel cages. Food (Purina Rodent Laboratory Chow® 5001) and tap water (via an automatic watering system) were available ad libitum. The mean room temperature ± the standard deviation was 73.6°F ± 1.68 and the mean relative humidity ± the standard deviation was 59.4% ± 3.44 during the study. A twelve-hour light/dark cycle was maintained.

METHODS

Mating Period

During the mating period, one female was paired with one male until mating was confirmed or until two weeks had elapsed. A sufficient number of mated females, during the course of this study, were obtained after four days of cohabitation and mating was discontinued. Daily vaginal examinations of each female were performed to detect the presence and viability of sperm or the presence of a copulatory plug. The day of observation of sperm or copulatory plug was designated as "Day 0" of gestation.

Groups and Dosage Levels

Upon confirmation of mating, each female was assigned to one of the following groups by use of a table of random numbers (Cochran and Cox, 1957).

Group	Number of Females	Dose[a] mg/kg/day
1	25	0
2	25	1
3	25	10
4	25	30

[a] Based on individual animal body weights at each weighing interval during the dosing period. Animals were dosed on Days 6 through 15 of presumed gestation.

Dose levels were selected based upon information obtained in a range finding study. The results from that study were reported separately.

All males and all remaining females were sacrificed via carbon dioxide asphyxiation and discarded without necropsy once a sufficient number of matings was confirmed.[a]

Compound Preparation and Administration

Suspensions of the test material in the corn oil vehicle were prepared on a weight per volume basis. The compound was first ground in a mortar and pestle into a workable powder. The required amount of compound for each level was then weighed on an electronic Arbor 126 balance and transferred to a 7 ml tissue grinder. Approximately 3 ml of corn oil was added and the test material was ground into a fine suspension. This suspension was transferred to a precalibrated beaker[b] and any remaining compound in the tissue grinder was rinsed into the beaker. Additional corn oil was added to the suspension to produce the desired concentration and the suspension was mixed on a magnetic stirrer.

Females were given the appropriate dosing suspension or vehicle by oral intubation on a daily basis beginning on Day 6 and continuing through Day 15 of presumed gestation. The dose administered to each female was based on the most recently recorded individual body weight. The test material was administered orally because of the relative ease and accuracy of dosing.

[a] One female was euthanized following mating confirmation due to alopecia.

[b] Due to the amount of compound required to prepare Group 4 suspensions, the compound was divided into four tissue grinders and subsequently transferred to one precalibrated beaker.

Fresh suspensions of the test substance for dosing were prepared weekly. Samples of each test mixture as well as the vehicle were sent to the sponsor for analysis. A 10 gram sample of compound and a 30 ml sample of corn oil were taken on August 4, 1983, and stored at room temperature.

Maternal Observations and Records

All animals were observed twice daily for mortality and moribundity (from day of receipt through animal sacrifice). The females were also examined once daily for clinical signs of toxicity and pharmacologic effects (throughout gestation). Individual body weights were recorded at initiation and on Days 6, 8, 12, 16, and 20 of gestation. Food consumption during gestation was determined on Days 6, 8, 12, 16, and 20.

Sacrifice at Time of Cesarean Sectioning

A gross necropsy was performed on all females. Prior to terminal sacrifice and cesarean section on Day 20 of gestation, all females were assigned random numbers so that all personnel performing cesarean sections and/or external, visceral, or skeletal examinations of the fetuses were unaware of the dose level from which the animals were derived.

On Day 20 of gestation, all females were weighed and sacrificed by carbon dioxide asphyxiation. The uterus from each female was excised, weighed, and examined for the number and placement of implantation sites, number of live and dead fetuses, number of early and late resorbing

fetuses, and any abnormalities. The ovaries were examined for the number of corpora lutea. Each female was examined grossly for any abnormalities.

Each fetus was sexed, weighed, examined externally, and tagged for identification. Beginning at the ovarian end of the left uterine horn and continuing past the cervix into the right uterine horn, the first available fetus was fixed in Bouin's solution for visceral evaluation. The next two fetuses were processed for skeletal evaluation. This process was repeated until all available fetuses were selected for evaluation. Dead fetuses were discarded without examination.

Visceral Examination of Fetuses

Approximately one-third of all live fetuses from each litter were fixed in Bouin's solution and sectioned by the Wilson Technique for assessing soft tissue development (Wilson, 1965). During examination of the fetuses' viscera, particular attention was paid to examination of the eyes, palate, and brain. Stainless-steel razor blades (Gem®) were used for sectioning procedures.

Skeletal Examination of Fetuses

The remaining fetuses were eviscerated and placed in 95% ethyl alcohol. After proper fixation, dehydration, and maceration, the skeletons were stained in 1% KOH, with an alizarin red solution and cleared in glycerol (modified Staples and Schnell, 1964). This evaluation included examination of the skull, long bones, vertebral column, rib cage, extremities, and pectoral and pelvic girdles. Bone alignment and degree of ossification were assessed.

Tissue Preservation

The following are the procedures for preservation of the various tissues: (1) The uterus and ovaries of each animal were preserved in 10% neutral buffered formalin; (2) The fetuses examined by Wilson's technique were placed in tissue capsules, preserved in 95% ethyl alcohol, and sealed in plastic bags after sectioning; (3) Fetuses stained for skeletal examination were preserved in plastic bags containing a glycerol:ethyl alcohol (1:1) solution with several crystals of thymol to retard bacterial and mold growth.

Statistical Analyses

Maternal body weight changes (Days 6-8, 6-16, 16-20, and 0-20), total food consumption (Days 7-8, 7-16, 17-20, and 0-20), gravid uterine weight, and terminal body weight minus gravid uterine weight data of the control group were compared statistically against the data of the compound-treated groups of the same sex.

Analyses of the above data were performed in the following order: Levene's test for homogeneity of variance (Levene, 1960; Draper and Hunter, 1969) was performed and if the variances proved to be homogeneous, the data were analyzed by one-way classification analysis of variance (ANOVA) (Winer, 1971). If the variance proved to be heterogeneous, a series of transformations was performed until variance homogeneity was achieved. These transformations were $\log_{10}$, square (X^2), square root ($X^{1/2}$), reciprocal (1/X), angular (arcsine $X^{1/2}$), and rank, in that order. If rank transformation was ineffective in removing

variance heterogeneity, ANOVA of ranked data was completed. If ANOVA of untransformed or transformed data was significant, Dunnett's t-test (Dunnett, 1955 and 1964) was used for control vs. compound-treated group mean comparisons. If ANOVA was not significant, the analysis was complete.

Data transformations are designated throughout this report as follows:

A = Data analyzed following $\log_{10}$ transformation.

B = Data analyzed following square (X^2) transformation.

C = Data analyzed following square root ($X^{1/2}$) transformation.

D = Data analyzed following reciprocal (1/X) transformation.

E = Data analyzed following angular (arcsine $X^{1/2}$) transformation.

F = Data analyzed following rank transformation.

Mean fetal body weights per litter were statistically analyzed as follows: Bartlett's test for homogeneity of variances (Bartlett, 1937) was performed by one-way classification of covariance (ANCOVA) (Winer, 1971). If ANCOVA was significant, control vs. treatment group comparisons were analyzed using the Games and Howell Modification of the Tukey-Kramer honestly significant difference test (Games and Howell, 1976).

Tests for homogeneity of variances, ANOVA, and ANCOVA were evaluated at the 5.0% one-tailed probability level. Control vs. compound-treated group mean comparisons of the above data were evaluated at the 5.0% two-tailed probability level.

In addition to the above data, fetal viability was analyzed by nonparametric one-way ANOVA (Kruskal and Wallis, 1952, 1953; Miller, 1966). The litter was used as the experimental unit. The number of fetuses exhibiting skeletal variants of the rib cage and bone alignment and the total number of fetuses affected by skeletal variants were analyzed using the Cochran-Armitage test for linear trend in proportions (Cochran, 1954; Armitage, 1955; Fleiss, 1981) and Fisher's "exact" test (Fisher, 1950). If a significant trend was noted, the results of Fisher's "exact" test were evaluated at the one-tailed, 5% level. If a significant trend was not observed, or if there was a significant trend with severe departure from it, the results of Fisher's "exact" test were evaluated at the two-tailed, 5% level. When using these statistical tests on indices, the actual proportions prior to conversion to percentages were the data that were analyzed.

Statistical references are appended to this report, and statistically significant differences, as indicated by the aforementioned tests, are designated throughout this report by the term "significant" and/or as follows:

S+ = Significantly higher than the control value.

S- = Significantly lower than the control value.

Specimen, Raw Data, and Final Report Storage

All specimens, raw data, and the final report are stored in the archives of Hazleton Laboratories America, Inc.

RESULTS - MATERNAL DATA

Mortality and Clinical Observations

Individual clinical observations are presented in Appendix 1. A summary of clinical observations is presented in Table 1.

No animals were found dead or sacrificed *in extremis* during the study.

Clinical observations were considered incidental. These observations included hunched and/or thin appearance, languid behavior, anorexia, soft feces, alopecia, and rough haircoat.

Body Weights and Food Consumption

Individual and mean body weights and body weight changes are presented in Appendix 2 and Table 2, respectively. Individual and mean food consumption values are presented in Appendix 3 and Table 3, respectively.

Evaluation of the body weight changes revealed a significant decrease in body weight gain during treatment (Days 6-15) for the Group 4 females, resulting in a significantly lower overall body weight gain during gestation. Group 3 females also gained less weight than control females during gestation, although that finding was not statistically significant. Body weight gains during the nontreatment phases (Days 0-6 and 16-20) were comparable between the control and compound-treated groups.

A decrease in overall mean food consumption was noted in the Group 4 females after Day 9 of gestation. Mean total food consumption values for Group 4 were significantly lower than control for Days 7-16 and 17-20. Slightly lower mean food consumption values were noted for Groups 3 and 4 over Days 13-16 and 0-20 and for Group 3 over Days 7-16. All other food consumption values were comparable to control.

Uterine Weights

Individual and mean terminal body weights, gravid uterine weights, and terminal body weights minus gravid uterine weights are presented in Appendix 4 and Table 4, respectively.

Gravid uterine weights were comparable between the control and treated groups. Terminal body weights were decreased and terminal body weights minus gravid uterine weights were significantly decreased in the Group 4 females when compared to control.

Gross Pathology

A summary of maternal gross pathology findings is presented in Table 5.

Gross pathology findings noted at necropsy were considered incidental.

RESULTS - DATA OBTAINED AT CESAREAN SECTIONING

Individual and mean ovarian and uterine data are presented in Appendix 5. Individual and mean litter data are presented in Appendix 6. Individual visceral and skeletal findings in fetuses are presented in Appendices 7 and 8, respectively. Summary ovarian and uterine data are presented in Table 6. Summary litter data are presented in Table 7. Summaries of the external, visceral, and skeletal findings are presented in Tables 8 through 14.

Pregnancy Rates, Corpora Lutea, and Uterine Implantations

Pregnancy rates, number of corpora lutea, and implantation efficiencies were comparable for all groups.

Fetal Viability, Weight, and Sex

The mean incidences of early, late, and total resorptions, fetal loss, and the number of dead fetuses were comparable between the control and treated groups. The mean fetal weights of the Group 4 males and females were significantly lower than their respective controls. The percent of male fetuses was 49.54%, 51.24%, and 51.20% for Groups 2, 3, and 4, respectively, and 53.26% for the control group.

Fetal Development

The percents of external and visceral variants and anomalies in fetuses were comparable between the control and treated groups. Gross external examination of fetuses at cesarean section revealed one Group 1

fetus with an undeveloped tail, one Group 3 fetus with a short trunk and no tail, one Group 3 fetus with a cleft palate, and one Group 4 fetus with an underdeveloped tail.

Cryptorchism was noted in two Group 1 fetuses and in one Group 3 fetus examined viscerally by Wilson's sectioning. One fetus from Group 3 was noted to have fused kidneys. No other visceral anomalies were observed. Visceral variants consisted mainly of dilated renal pelves and distended ureters in Groups 1 and 2 fetuses.

No skeletal anomalies were observed. Comparing the number of fetuses with skeletal variants (treated groups versus control) showed that the number of fetuses affected by skeletal variants was not significantly different than control for any group. However, the number of bone alignment and rib cage variants in fetuses derived from Group 4 dams, animals in which toxicity was observed, was significantly higher than control fetuses.

Table 1
Summary of Maternal Clinical Observations[a]
Rat Teratology Study of T-3352

Observation	Pretreatment Days 0-5				Treatment Days 6-15				Posttreatment Days 16-20			
Group:	1	2	3	4	1	2	3	4	1	2	3	4
Dose Level (mg/kg):	0	1	10	30	0	1	10	30	0	1	10	30
Number of females examined	23(2)	24(1)	24(1)	21(4)	23(2)	24(1)	24(1)	21(4)	23(2)	24(1)	24(1)	21(4)
Number of females appearing normal	23(2)	24(1)	24(1)	21(4)	20(2)	21(1)	24(1)	17(2)	19(2)	21(1)	21(1)	16(1)
Number of females found dead or sacrificed prior to Day 20	0	0	0	0	0	0	0	0	0	0	0	0
Hunched								2(2)				1(2)
Thin								1(1)				(3)
Languid								1				
Anorexia												(1)
Soft feces						1		1				
Alopecia					3	2		3	4	3	3	5(1)
Rough haircoat												(1)

[a] Numerals indicate the number of animals with that particular finding.
() = Observations noted in nonpregnant females.

Table 2
Mean Maternal Body Weights and Body Weight Changes
Rat Teratology Study of T-3352

Body Weight	Day(s)		Group 1 0 mg/kg	Group 2 1 mg/kg	Group 3 10 mg/kg	Group 4 30 mg/kg
Mean Weight (g)	0		230.77	230.15	238.63	237.34
		N:	23	24	24	21
	6		260.93	259.94	268.94	268.60
		N:	23	24	24	21
	8		264.78	263.75	272.81	265.33
		N:	23	24	24	21
	12		282.82	283.36	287.05	267.37
		N:	23	24	24	21
	16		308.71	311.02	310.81	287.92
		N:	23	24	24	21
	20		365.16	368.01	367.30	345.03
		N:	23	24	24	21
Mean Change (g)	0-6		30.17	29.80	30.32	31.25
	6-8		3.85	3.81	3.87	-3.02^{S-}
	6-12		21.89	23.42	18.11	-1.22
	6-16^{F}		47.78	51.08	41.87	19.33^{S-}
	6-20		104.23	108.08	98.35	76.44
	16-20		56.44	57.00	56.49	57.11
	0-20		134.39	137.03	128.67	107.69^{S-}

N: Indicates the sample size on which mean calculations were based. Only pregnant females were used in mean calculations.

Table 3
Mean Maternal Food Consumption (g)
Rat Teratology Study of T-3352

Interval Days		Group 1 0 mg/kg	Group 2 1 mg/kg	Group 3 10 mg/kg	Group 4 30 mg/kg
0-6		131.76	129.11	131.05	130.34
	N:	23	24	24	20
7-8[F]		37.98	38.37	38.62	36.60
	N:	23	24	24	21
9-12		78.93	80.75	73.69	71.21
	N:	23	24	23	16
13-16		84.49	85.40	78.24	68.45
	N:	23	23	23	13
17-20		104.56	103.76	100.76	96.47[S-]
	N:	23	24	24	20
7-16[B]		201.40	202.70	188.23	173.64[S-]
	N:	23	23	22	12
0-20[F]		437.72	435.50	417.40	399.16
	N:	23	23	22	11

N: Indicates the sample size on which the mean calculations were based. Only pregnant females were used in mean calculations. Invalid food consumption values were not included in mean calculations.

Table 4
Mean Terminal Body Weights, Gravid Uterine Weights, and Terminal Body Weights
Minus Gravid Uterine Weights
Rat Teratology Study of T-3352

Group and Dose Level		Terminal Body Weight	Gravid Uterine Weight	Terminal Body Weight Minus Gravid Uterine Weight
1 0 mg/kg	N:	365.16 23	69.52 23	295.64 23
2 1 mg/kg	N:	368.01 24	73.62 23	293.56 23
3 10 mg/kg	N:	367.30 24	67.51 24	299.78 24
4 30 mg/kg	N:	345.03 21	66.47 20	280.33[S-] 20

N: Indicates the sample size on which the mean calculations were based. Only pregnant females were used in mean calculations.

Table 5
Summary of Maternal Gross Pathology Findings
Rat Teratology Study of T-3352

ORGAN AND DESCRIPTION	Group: / Dose Level (mg/kg):	1 / 0	2 / 1	3 / 10	4 / 30
Number of animals examined		23(2)	24(1)	24(1)	21(4)
Number with no gross pathology		19(2)	24(1)	20(1)	18(3)
LUNG					
Dark red focal areas				1	
LIVER					
Irregular shape				1	
Lobes adhered to one another				1	
KIDNEY(S)					
Pelvis dilated		4		1	3
OVARY(IES)					
Cystic				1	
Clear				1	
CERVIX					
Contained yellowish-green viscous material					(1)
UTERUS/UTERINE HORN					
Distended with clear fluid					(1)

( ) = Finding present in nonpregnant females.

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Key to Tables 6-14

Pregnancy rate (percent) - (number of pregnant rats/number of rats inseminated) x 100.

Survival Rate (percent) - (number of rats surviving to Day 20/number of rats placed on study at initiation) x 100.

Mean Implantation Efficiency (percent) - Group mean of ([implantations per litter/ corpora lutea per litter] x 100).

Mean Incidence of Resorptions (percent)[a] - Group mean of ([resorptions per litter/ implantations per litter] x 100).

Mean Incidence of Fetal Mortality (percent) - Group mean of ([dead and resorbing fetuses per litter/ implantations per litter] x 100).

Mean Incidence of Fetal Viability (percent) - Group mean of ([live fetuses per litter/implantations per litter] x 100).

Mean Incidence of External Variants (percent) - Group mean of ([number of fetuses per litter with external variants/ number of fetuses per litter examined externally] x 100).

Mean Incidence of External Anomalies (percent) - Group mean of ([number of fetuses per litter with external anomalies/ number of fetuses per litter examined externally] x 100).

Mean Incidence of Visceral Variants (percent) - Group mean of ([number of fetuses per litter with visceral variants/ number of fetuses per litter examined viscerally] x 100).

Mean Incidence of Visceral Anomalies (percent) - Group mean of ([number of fetuses per litter with visceral anomalies/ number of fetuses per litter examined viscerally] x 100).

Mean Incidence of Skeletal Variants (percent) - Group mean of ([number of fetuses per litter with skeletal variants/ number of fetuses per litter examined skeletally] x 100).

Mean Incidence of Skeletal Anomalies (percent) - Group mean of ([number of fetuses per litter with skeletal anomalies/ number of fetuses per litter examined skeletally] x 100).

[a] Values calculated separately for early, late, and total resorptions.

Table 6
Summary of Mean Ovarian and Uterine Data
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
Number of females	25	25	25	25
Number of pregnant females	23	24	24	21
Pregnancy rate (%)	92	96	96	84
Number of females surviving to Day 20	25	25	25	25
Survival rate (%)	100	100	100	100
Mean number of:				
Corpora lutea	16.1	16.2	15.6	16.2
Implantations	13.5	14.5	14.2	14.0
Early resorptions	0.9	1.2	1.3	1.0
Late resorptions	0.0	0.0	0.1	0.0[a]
Total resorptions	0.9	1.2	1.5	1.0
Indices calculated on a per litter basis:				
Mean implantation efficiency (%)	85.16	89.02	91.78	86.76
Mean incidence of early resorptions (%)	7.09	7.46	9.97	7.32
Mean incidence of late resorptions (%)	0.00	0.00	0.88	0.34
Mean incidence of total resorptions (%)	7.09	7.46	10.85	7.66

[a] One late resorption was noted for female No. 27228, therefore, the actual mean was 0.04.

Table 7
Summary of Mean Litter Data[a]
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
Mean number of:				
Fetuses - dead	0.0	0.0	0.0	0.0
- live	12.5	13.3	12.8	13.0
Indices calculated on a per litter basis:				
Mean incidence of fetal mortality (%)	7.39	7.46	10.85	7.66
Mean incidence of fetal viability (%)	92.61	92.55	89.15	92.35
Mean percent males (%)	53.26	49.54	51.24	51.20
Live fetuses				
Mean body weight (g)[b]				
Males - unadjusted mean	3.39	3.27	3.21	2.95
- covariance adjusted mean	3.39	3.27	3.21	2.95[S-]
Females - unadjusted mean	3.18	3.15	3.05	2.80
- covariance adjusted mean	3.18	3.15	3.05	2.80[S-]

[a] Sex, percent males, and mean body weight data include values for live fetuses only.
[b] Statistical analysis performed on covariance adjusted means.

Table 8
Summary of External Findings
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
Number of fetuses examined	289	320	306	272
Number of fetuses within normal limits	288	320	304	271
Number of fetuses with variants	0	0	1	1
Number of fetuses with anomalies	1	0	2	0
Number and type of variants	0	0	1	1
Trunk - short			1	
Tail - underdeveloped				1[a]
Number and type of anomalies	1	0	2	0
Palate - cleft			1	
Tail - undeveloped	1[a]			
- no tail			1	

[a] Finding confirmed at skeletal evaluation.

Table 9
Summary of Visceral Findings
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
Number of fetuses examined	104	116	112	98
Number of fetuses within normal limits	89	106	107	96
Number of fetuses with variants	14	10	3	2
Number of fetuses with anomalies	2	0	2	0
Number and type of variants	18	14	3	2
Brain - left ventricle dilated		1		
- dark material around brain		1		
Liver - dark areas on lobe			1	
- all lobes appeared dark			1	
- dark area in liver				1
Kidney(s) - dilated renal pelvis	8	7		
Ureter(s) - distended	8	5	1	1
Testes - small	1			
Skin - edema between skin and peritoneal wall	1			
Number and type of anomalies	2	0	2	0
Kidney(s) - fused			1	
Cryptorchism	2		1	

Table 10
Summary of Skeletal Findings
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
Number of fetuses examined	185	204	194	174
Number of fetuses within normal limits	94	115	103	76
Number of fetuses with variants	91	89	91	98
Number of fetuses with anomalies	0	0	0	0
Number and type of variants	171	153	152	195
Lagging ossification				
Skull - incomplete closure (<75%)	4	6	9	5
- interparietal ossification incomplete	36	31	49	33
- parietals ossification irregular	3	5	6	4
- supraoccipital ossification incomplete	23	15	16	20
- supraoccipital nonfused	1			
- hyoid ossification incomplete/nonossified	41	34	19	13
Rib cage - sternebrae bipartite	2	7	5	28
- sternebrae <3 ossified	1	1		2
- ribs >13 pairs ossified	1	4	2	19
- ribs <13 pairs ossified	1			
- ribs ossification irregular				1
Vertebral column - thoracic centra ossification incomplete	36	24	28	31
- thoracic centra nonfused	7	11	11	6
- lumbar ossification incomplete/nonossified	1			1
- lumbar arches fused	1			
- caudals <3 ossified	5	8	6	17
- caudal vertebrae nonossified	1			
- sacral vertebrae nonossified	1			2
Pelvic girdle - pubis ossification incomplete/nonossified	4	5		2
- ischium ossification incomplete	3			
Hindlimbs - <4 ossified		1		3
Bone alignment				
Ribs - fused				1
- forked				1
- malaligned thoracic centra and arches				1
- angulated	1	1	1	2
Sternebrae - checkered			1	2
Vertebrae malaligned - thoracic				1

Table 11
Incidence of External Findings Per Litter
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
Number of litters examined	23	24	24	21
Number of litters within normal limits	22	24	22	20
Number and percent of litters with variants	0/0.00	0/0.00	1/4.17	1/4.76
Number and percent of litters with anomalies	1/4.35	0/0.00	2/8.33	0/0.00
Number and percent with variants				
Trunk - short			1/4.17	
Tail - underdeveloped				1/4.76[a]
Number and type with anomalies				
Palate - cleft			1/4.17	
Tail - undeveloped	1/4.35[a]			
- no tail			1/4.17	

[a] Finding confirmed at skeletal evaluation.

Table 12
Incidence of Visceral Findings Per Litter
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
Number of litters examined	23	24	24	21
Number of litters within normal limits	12	18	20	19
Number and percent of litters with variants	10/43.48	6/25.00	2/8.33	2/9.52
Number and percent of litters with anomalies	2/8.70	0/0.00	2/8.33	0/0.00
Number and percent with variants				
Brain - left ventricle dilated		1/4.17		
- dark material around brain		1/4.17		
Liver - dark areas on lobe			1/4.17	
- all lobes appeared dark			1/4.17	
- dark area in liver				1/4.76
Kidney(s) - dilated renal pelvis	4/17.39	5/20.83		
Ureter(s) - distended	7/30.43	4/16.67	1/4.17	1/4.76
Testes - small	1/4.35			
Skin - edema between skin and peritoneal wall	1/4.35			
Number and percent with anomalies				
Kidney(s) - fused			1/4.17	
Cryptorchism	2/8.70		1/4.17	

Table 13
Incidence of Skeletal Findings Per Litter
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
Number of litters examined	23	24	24	21
Number of litters within normal limits	1	2	4	1
Number and percent of litters with variants	22/95.65	22/91.67	20/83.33	20/95.24
Number and percent of litters with anomalies	0/0.00	0/0.00	0/0.00	0/0.00
Number and percent with variants				
Lagging ossification				
Skull - incomplete closure (<75%)	4/17.39	3/12.50	6/25.00	4/19.05
- interparietal ossification incomplete	16/69.57	12/50.00	15/62.50	13/61.90
- parietals ossification irregular	2/8.70	3/12.50	5/20.83	2/9.52
- supraoccipital ossification incomplete	11/47.83	7/29.17	7/29.17	9/42.86
- supraoccipital nonfused	1/4.35			
- hyoid ossification incomplete/nonossified	17/73.91	14/58.33	9/37.50	8/38.10
Rib cage - sternebrae bipartite	1/4.35	2/8.33	4/16.67	8/38.10
- sternebrae <3 ossified	1/4.35	1/4.17		2/9.52
- ribs >13 pairs ossified	1/4.35	2/8.33	2/8.33	9/42.86
- ribs <13 pairs ossified	1/4.35			
- ribs ossification irregular				1/4.76
Vertebral column - thoracic centra ossification incomplete	16/69.57	13/54.17	14/58.33	13/61.90
- thoracic centra nonfused	7/30.43	7/29.17	7/29.17	6/28.57
- lumbar ossification incomplete/nonossified	1/4.35			1/4.76
- lumbar arches fused	1/4.35			
- caudals <3 ossified	5/21.74	5/20.83	4/16.67	10/47.62
- caudal vertebrae nonossified	1/4.35			
- sacral vertebrae nonossified	1/4.35			2/9.52
Pelvic girdle - pubis ossification incomplete/nonossified	3/13.04	5/20.83		2/9.52
- ischium ossification incomplete	2/8.70			
Hindlimbs - <4 ossified		1/4.17		3/14.29
Bone alignment				
Ribs - fused				1/4.76
- forked				1/4.76
- malaligned thoracic centra and arches				1/4.76
- angulated	1/4.35	1/4.17	1/4.17	1/4.17
Sternebrae - checkered			1/4.17	2/9.52
Vertebrae malaligned - thoracic				1/4.76

Table 14
Mean Incidence of External, Visceral, and Skeletal Findings Per Litter
Rat Teratology Study of T-3352

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	10	30
External				
Mean values calculated on a per litter basis:				
Number with variants	0.0	0.0	0.0	0.0
Number with anomalies	0.0	0.0	0.1	0.0
Incidence of variants (%)	0.0	0.0	0.4	0.3
Incidence of anomalies (%)	0.9	0.0	2.1	0.0
Visceral				
Mean values calculated on a per litter basis:				
Number with variants	0.6	0.4	0.1	0.1
Number with anomalies	0.1	0.0	0.1	0.0
Incidence of variants (%)	13.3	8.9	2.1	1.9
Incidence of anomalies (%)	2.0	0.0	1.9	0.0
Skeletal				
Mean values calculated on a per litter basis:				
Number with variants	4.0	3.7	3.8	4.7
Number with anomalies	0.0	0.0	0.0	0.0
Incidence of variants (%)	47.5	44.9	45.4	54.3
Incidence of anomalies (%)	0.0	0.0	0.0	0.0

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Appendix 1
Individual Clinical Signs[a]
Rat Teratology Study of T-3352

Maternal Number	Group	Observation	Body Area	Day(s)
27134	1	Alopecia	Abdomen	17-20
		Alopecia	Leg-fore-right	16-20
27136	1	Alopecia	Abdomen	9-20
		Alopecia	Legs-hind-both	13-15, 20
		Alopecia	Leg-hind-left	8-12, 16-19
27141	1	Alopecia	Legs-fore-both	15-19
		Alopecia	Leg-fore-left	12-14
27152	1	Alopecia	Legs-fore-both	9-20
		Alopecia	Paws-fore-both	6-8
27160	2	Soft feces		7
27172	2	Alopecia	Paw-fore-right	11-18
27178	2	Alopecia	Paws-fore-both	15-17
		Alopecia	Paw-fore-left	18-19
27179	2	Alopecia	Paws-fore-both	18-20
27190	3	Alopecia	Leg-hind-left	20
27201	3	Alopecia	Leg-fore-left	20
27202	3	Alopecia	Paw-fore-left	18-19
27205	4	Alopecia	Abdomen	13-20
		Alopecia	Hips-both	16-20
		Alopecia	Hip-right	13-15
		Alopecia	Leg-hind-right	18-20
27208	4	Thin		16, 18-19
27211	4	Soft feces		10
27212	4	Hunched		13-20
		Thin		16-19
		Anorexia		16
		Alopecia	Paw-fore-left	20
		Rough haircoat		16-19
27213	4	Alopecia	Abdomen	15-20
27215	4	Alopecia	Abdomen	20
27221	4	Alopecia	Abdomen	9-20
		Alopecia	Chest	14-18
		Alopecia	Hips-both	12-20
27224	4	Hunched		11-17
		Thin		12-15
		Languid		11-12
		Alopecia	Paws-fore-both	16-18
27225	4	Hunched		14-20
		Thin		14-18
27228	4	Hunched		13

[a] All animals not included in this table appeared normal throughout the study.

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Key to Appendices 2, 3, and 4

P = Pregnant

NP = Not Pregnant

C = Cesarean Section Performed (preceded by day of gestation)

() = Data excluded from mean calculation.

Explanation of Footnotes

[a] Only data from pregnant animals surviving to Day 20 cesarean section were used in mean calculations.

[b] Invalid food consumption value not included in mean calculations.

[c] Gravid uterine weight inadvertently not recorded.

Appendix 2
Individual and Mean Maternal Body Weights and Body Weight Changes[a]
Rat Teratology Study of T-3352
Group 1 - 0 mg/kg

Maternal Number	Disposition	Body Weight (g) Day of Gestation 0	6	8	12	16	20	Body Weight Change (g) Days 0-6	6-8	6-12	6-16[F]	6-20	16-20	0-20
27130	P, 20-C	228.9	246.4	248.1	269.7	283.7	340.6	17.5	1.7	23.3	37.3	94.2	56.9	111.7
27131	NP, 20-C	(246.5)	(278.6)	(278.8)	(276.3)	(271.8)	(282.1)	(32.1)	(0.2)	(-2.3)	(-6.8)	(3.5)	(10.3)	(35.6)
27132	P, 20-C	236.9	254.7	258.8	278.8	299.8	368.0	17.8	4.1	24.1	45.1	113.3	68.2	131.1
27133	P, 20-C	216.7	246.4	253.8	274.7	297.9	363.5	29.7	7.4	28.3	51.5	117.1	65.6	146.8
27134	P, 20-C	217.0	254.8	260.2	286.8	304.8	375.2	37.8	5.4	32.0	50.0	120.4	70.4	158.2
27135	NP, 20-C	(221.4)	(260.3)	(262.4)	(249.3)	(252.3)	(258.6)	(38.9)	(2.1)	(-11.0)	(-8.0)	(-1.7)	(6.3)	(37.2)
27136	P, 20-C	212.5	241.4	247.5	268.5	291.8	350.3	28.9	6.1	27.1	50.4	108.9	58.5	137.8
27137	P, 20-C	225.6	248.6	251.5	271.0	297.2	352.5	23.0	2.9	22.4	48.6	103.9	55.3	126.9
27138	P, 20-C	261.2	300.5	298.4	322.9	341.3	413.2	39.3	-2.1	22.4	40.8	112.7	71.9	152.0
27139	P, 20-C	238.2	274.6	276.0	300.6	327.5	404.5	36.4	1.4	26.0	52.9	129.9	77.0	166.3
27140	P, 20-C	226.7	263.3	265.6	275.3	290.4	351.3	36.6	2.3	12.0	27.1	88.0	60.9	124.6
27141	P, 20-C	215.3	245.4	248.1	264.8	291.9	344.5	30.1	2.7	19.4	46.5	99.1	52.6	129.2
27142	P, 20-C	228.3	248.9	248.2	271.3	302.9	357.2	20.6	-0.7	22.4	54.0	108.3	54.3	128.9
27143	P, 20-C	228.2	260.1	264.9	279.6	284.8	316.9	31.9	4.8	19.5	24.7	56.8	32.1	88.7
27144	P, 20-C	206.6	238.6	237.4	262.8	286.9	340.9	32.0	-1.2	24.2	48.3	102.3	54.0	134.3
27145	P, 20-C	250.4	289.3	296.0	318.3	349.6	407.8	38.9	6.7	29.0	60.3	118.5	58.2	157.4
27146	P, 20-C	269.3	294.4	297.9	311.2	336.4	388.7	25.1	3.5	16.8	42.0	94.3	52.3	119.4
27147	P, 20-C	220.4	247.1	255.1	278.2	303.1	344.8	26.7	8.0	31.1	56.0	97.7	41.7	124.4
27148	P, 20-C	236.4	268.5	277.0	295.9	331.6	386.1	32.1	8.5	27.4	63.1	117.6	54.5	149.7
27149	P, 20-C	223.5	254.6	257.2	278.0	313.1	380.6	31.1	2.6	23.4	58.5	126.0	67.5	157.1
27150	P, 20-C	224.6	259.3	260.0	273.9	298.8	360.3	34.7	0.7	14.6	39.5	101.0	61.5	135.7
27151	P, 20-C	242.0	284.0	291.8	297.2	336.5	379.3	42.0	7.8	13.2	52.5	95.3	42.8	137.3
27152	P, 20-C	217.0	234.6	241.0	250.1	280.3	326.0	17.6	6.4	15.5	45.7	91.4	45.7	109.0
27153	P, 20-C	257.4	287.6	293.0	297.3	342.4	389.7	30.2	5.4	9.7	54.8	102.1	47.3	132.3
27154	P, 20-C	224.5	258.3	262.4	278.0	307.7	356.7	33.8	4.1	19.7	49.4	98.4	49.0	132.2
N		23	23	23	23	23	23	23	23	23	23	23	23	23
Mean		230.77	260.93	264.78	282.82	308.71	365.16	30.17	3.85	21.89	47.78	104.23	56.44	134.39
S.D.		16.219	18.872	19.049	18.256	21.529	25.625	7.188	3.023	6.131	9.472	15.393	10.770	18.029

Appendix 2 - Continued
Individual and Mean Maternal Body Weights and Body Weight Changes[a]
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

Maternal Number	Disposition	Body Weight (g) Day of Gestation 0	6	8	12	16	20	Body Weight Change (g) Days 0-6	6-8	6-12	6-16[F]	6-20	16-20	0-20
27155	P, 20-C	228.7	254.9	258.6	280.7	305.1	360.2	26.2	3.7	25.8	50.2	105.3	55.1	131.5
27156	P, 20-C	232.6	265.8	270.6	300.3	325.9	389.3	33.2	4.8	34.5	60.1	123.5	63.4	156.7
27157	P, 20-C	235.3	262.9	269.4	288.4	304.5	352.5	27.6	6.5	25.5	41.6	89.6	48.0	117.2
27158	NP, 20-C	(205.1)	(237.8)	(245.2)	(250.6)	(250.8)	(269.0)	(32.7)	(7.4)	(12.8)	(13.0)	(31.2)	(18.2)	(63.9)
27159	P, 20-C	204.5	244.5	239.8	259.4	284.9	347.0	40.0	-4.7	14.9	40.4	102.5	62.1	142.5
27160	P, 20-C	224.7	262.9	269.8	287.0	308.6	366.4	38.2	6.9	24.1	45.7	103.5	57.8	121.7
27161	P, 20-C	226.6	252.2	258.9	277.4	301.5	365.8	25.6	6.7	25.2	49.3	113.6	64.3	139.2
27162	P, 20-C	229.4	260.4	266.5	289.4	312.7	380.4	31.0	6.1	29.0	52.3	120.0	67.7	151.0
27163	P, 20-C	238.4	270.9	271.2	283.6	327.0	387.4	32.5	0.3	12.7	56.1	116.5	60.4	149.0
27164	P, 20-C	203.0	236.2	235.3	255.5	279.8	338.6	33.2	-0.9	19.3	43.6	102.4	58.8	135.6
27165	P, 20-C	223.8	254.5	259.2	280.1	300.9	362.3	30.7	4.7	25.6	46.4	107.8	61.4	138.5
27166	P, 20-C	245.2	272.0	273.1	291.5	315.9	369.9	26.8	1.1	19.5	43.9	97.9	54.0	124.7
27167	P, 20-C	219.6	253.7	258.4	279.5	318.4	373.0	34.1	4.7	25.8	64.7	119.3	54.6	153.4
27168	P, 20-C	225.5	255.8	251.5	269.8	301.2	356.1	30.3	-4.3	14.0	45.4	100.3	54.9	130.6
27169	P, 20-C	247.2	271.2	273.6	295.4	320.9	391.7	24.0	2.3	24.2	49.7	120.5	70.8	144.5
27170	P, 20-C	262.8	293.7	291.0	312.9	338.9	387.1	31.1	-2.7	19.2	45.2	93.4	48.2	124.3
27171	P, 20-C	249.7	278.9	289.1	305.1	337.5	394.7	29.2	10.2	26.2	58.6	115.8	57.2	145.0
27172	P, 20-C	221.5	246.2	250.2	271.8	301.9	352.0	24.7	4.0	25.6	55.7	105.8	50.1	130.5
27173	P, 20-C	226.0	253.4	254.4	275.0	296.9	361.9	27.4	1.0	21.6	43.5	108.5	65.0	135.9
27174	P, 20-C	215.3	245.0	255.1	275.6	307.7	357.6	29.7	10.1	30.6	62.7	112.6	49.9	142.3
27175	P, 20-C	219.2	252.2	256.6	266.6	287.9	316.0	33.0	4.4	14.4	35.7	63.8	28.1	96.8
27176	P, 20-C	216.2	250.4	250.4	272.5	298.4	360.3	34.2	0.0	22.1	48.0	109.9	61.9	144.1
27177	P, 20-C	246.9	270.3	277.7	297.1	326.6	369.1	23.4	7.4	26.8	56.3	98.8	42.5	122.2
27178	P, 20-C	254.7	283.2	297.1	314.8	354.1	418.9	28.5	13.9	31.6	70.9	135.7	64.8	164.2
27179	P, 20-C	226.7	247.3	252.6	271.2	307.2	374.1	20.6	5.3	23.9	59.9	126.8	66.9	147.4
N		24	24	24	24	24	24	24	24	24	24	24	24	24
Mean		230.15	259.94	263.75	283.36	311.02	368.01	29.80	3.81	23.42	51.08	108.08	57.00	137.03
S.D.		15.038	13.721	15.304	15.476	17.772	21.094	4.638	4.558	5.649	8.705	14.482	9.398	14.702

Appendix 2 - Continued
Individual and Mean Maternal Body Weights and Body Weight Changes[a]
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

Maternal Number	Disposition	Body Weight (g) Day of Gestation 0	6	8	12	16	20	Body Weight Change (g) Days 0-6	6-8	6-12	6-16[F]	6-20	16-20	0-20
27180	P, 20-C	249.1	275.8	278.9	294.4	312.5	365.7	26.7	3.1	18.6	36.7	89.9	53.2	116.6
27181	P, 20-C	224.5	261.2	269.3	292.2	309.9	373.6	36.7	8.1	31.0	48.7	112.4	63.7	149.1
27182	P, 20-C	214.0	251.6	265.2	277.9	297.0	353.7	37.6	13.6	26.3	45.4	102.1	56.7	139.7
27183	P, 20-C	242.5	274.3	277.9	294.5	317.8	372.6	31.8	3.6	20.2	43.5	98.3	54.8	130.1
27184	P, 20-C	226.8	258.7	260.3	276.3	295.1	358.3	31.9	1.6	17.6	36.4	99.6	63.2	131.5
27185	P, 20-C	241.4	281.3	283.3	300.1	329.5	388.9	39.9	2.0	18.8	48.2	107.6	59.4	147.5
27186	P, 20-C	227.0	262.2	265.9	282.4	282.7	334.9	35.2	3.7	20.2	20.5	72.7	52.2	107.9
27187	P, 20-C	234.5	268.9	276.3	289.0	310.1	372.5	34.4	7.4	20.1	41.2	103.6	62.4	138.0
27188	P, 20-C	234.8	257.6	266.2	279.2	309.5	362.9	22.8	8.6	21.6	51.9	105.3	53.4	128.1
27189	P, 20-C	271.6	305.1	308.1	330.9	357.0	414.2	33.5	3.0	25.8	51.9	109.1	57.2	142.6
27190	P, 20-C	227.5	247.1	243.9	257.5	274.9	332.3	19.6	-3.2	10.4	27.8	85.2	57.4	104.8
27191	P, 20-C	241.8	265.4	265.4	281.9	300.8	355.0	23.6	0.0	16.5	35.4	89.6	54.2	113.2
27192	P, 20-C	210.4	235.8	233.3	237.1	266.6	322.8	25.4	-2.5	1.3	30.8	87.0	56.2	112.4
27193	P, 20-C	218.6	250.1	251.0	267.5	285.9	341.3	31.5	0.9	17.4	35.8	91.2	55.4	122.7
27194	NP, 20-C	(238.7)	(254.8)	(252.8)	(256.9)	(253.9)	(255.2)	(16.1)	(-2.0)	(2.1)	(-0.9)	(0.4)	(1.3)	(16.5)
27195	P, 20-C	267.7	288.2	296.4	305.3	325.7	376.5	20.5	8.2	17.1	37.5	88.3	50.8	108.8
27196	P, 20-C	260.6	298.2	307.4	328.1	344.0	405.9	37.6	9.2	29.9	45.8	107.7	61.9	145.3
27197	P, 20-C	239.7	265.7	263.6	279.5	310.0	370.1	26.0	-2.1	13.8	44.3	104.4	60.1	130.4
27198	P, 20-C	202.5	232.3	237.5	246.0	281.9	336.1	29.8	5.2	13.7	49.6	103.8	54.2	133.6
27199	P, 20-C	228.8	257.2	255.2	268.3	285.7	345.4	28.4	-2.0	11.1	28.5	88.2	59.7	116.6
27200	P, 20-C	242.1	275.4	281.6	286.5	322.5	386.6	33.3	6.2	11.1	47.1	111.2	64.1	144.5
27201	P, 20-C	263.2	290.2	295.2	313.3	338.5	398.0	27.0	5.0	23.1	48.3	107.8	59.5	134.8
27202	P, 20-C	257.0	284.4	283.4	298.7	333.9	399.6	27.4	-1.0	14.3	49.5	115.2	65.7	142.6
27203	P, 20-C	244.2	272.9	280.1	294.7	329.9	390.3	28.7	7.2	21.8	57.0	117.4	60.4	146.1
27204	P, 20-C	256.7	295.0	302.1	307.9	338.0	357.9	38.3	7.1	12.9	43.0	62.9	19.9	101.2
N		24	24	24	24	24	24	24	24	24	24	24	24	24
Mean		238.63	268.94	272.81	287.05	310.81	367.30	30.32	3.87	18.11	41.87	98.35	56.49	128.67
S.D.		18.304	18.955	20.507	22.576	23.830	24.797	5.759	4.388	6.659	8.974	13.456	8.812	15.118

Appendix 2 - Continued
Individual and Mean Maternal Body Weights and Body Weight Changes[a]
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

Maternal Number	Disposition	Body Weight (g) Day of Gestation 0	6	8	12	16	20	Body Weight Change (g) Days 0-6	6-8	6-12	6-16[F]	6-20	16-20	0-20
21205	P, 20-C	219.4	244.2	240.6	244.6	263.6	316.7	24.8	-3.6	0.4	19.4	72.5	53.1	97.3
21206	P, 20-C	239.5	269.7	264.4	246.2	254.8	330.3	30.2	-0.3	-23.5	-14.9	60.6	75.5	90.8
21207	P, 20-C	209.2	242.3	244.9	260.1	278.9	344.1	33.1	2.6	17.8	36.6	101.8	65.2	134.9
21208	NP, 20-C	(217.4)	(231.3)	(233.9)	(229.9)	(224.0)	(237.8)	(13.9)	(2.6)	(-1.4)	(-7.3)	(6.5)	(13.8)	(20.4)
21209	P, 20-C	222.8	244.4	230.5	255.8	278.3	349.4	21.6	-13.9	11.4	33.9	105.0	71.1	126.6
21210	P, 20-C	249.6	282.2	288.5	294.4	306.1	364.3	32.6	6.3	12.2	23.9	82.1	58.2	114.7
21211	P, 20-C	227.0	269.7	263.7	245.7	269.0	312.6	42.7	-6.0	-24.0	-0.7	42.9	43.6	85.6
21212	NP, 20-C	(280.9)	(312.6)	(300.3)	(272.0)	(236.8)	(272.5)	(31.7)	(-12.3)	(-40.6)	(-75.8)	(-40.1)	(35.7)	(-8.4)
21213	P, 20-C	244.3	289.3	289.8	288.0	317.4	379.3	45.0	0.5	-1.3	28.1	90.0	61.9	135.0
21214	NP, 20-C	(219.8)	(255.4)	(256.2)	(259.0)	(248.1)	(270.3)	(35.6)	(0.8)	(3.6)	(-7.3)	(14.9)	(22.2)	(50.5)
21215	P, 20-C	259.0	290.1	287.4	285.9	308.0	362.7	31.1	-2.7	-4.2	17.9	72.6	54.7	103.7
21216	P, 20-C	226.5	267.3	258.4	264.9	280.1	341.7	40.8	-8.9	-2.4	12.8	74.4	61.6	115.2
21217	P, 20-C	247.3	283.7	286.4	302.3	325.8	386.5	36.4	2.7	18.6	42.1	102.8	60.7	139.2
21218	P, 20-C	225.4	255.4	243.8	254.9	281.3	343.5	30.0	-11.6	-0.5	25.9	88.1	62.2	118.1
21219	P, 20-C	237.3	266.7	263.4	274.7	287.4	336.3	29.4	-3.3	8.0	20.7	69.6	48.9	99.0
21220	P, 20-C	243.2	269.7	272.5	291.0	312.8	364.6	26.5	2.8	21.3	43.1	94.9	51.8	121.4
21221	P, 20-C	209.3	235.6	235.4	231.3	253.0	297.6	26.3	-0.2	-4.3	17.4	62.0	44.6	88.3
21222	P, 20-C	232.5	272.1	270.0	263.6	274.4	300.2	39.6	-2.1	-8.5	2.3	28.1	25.8	67.7
21223	P, 20-C	218.8	252.0	251.2	244.4	258.8	309.8	33.2	-0.8	-7.6	6.8	57.8	51.0	91.0
21224	P, 20-C	257.8	281.6	269.4	230.7	295.9	374.0	23.8	-12.2	-50.9	14.3	92.4	78.1	116.2
21225	NP, 20-C	(229.0)	(262.2)	(242.0)	(235.2)	(197.7)	(234.2)	(33.2)	(-20.2)	(-27.0)	(-64.5)	(-28.0)	(36.5)	(5.2)
21226	P, 20-C	258.4	289.5	292.7	301.0	329.7	386.3	31.1	3.2	11.5	40.2	96.8	56.6	127.9
21227	P, 20-C	231.6	260.0	258.2	265.1	291.5	346.8	28.4	-1.8	5.1	31.5	86.8	55.3	115.2
21228	P, 20-C	250.9	274.7	265.1	266.0	262.5	326.1	23.8	-9.6	-8.7	-12.2	51.4	63.6	75.2
21229	P, 20-C	274.4	300.3	295.7	304.2	317.1	372.9	25.9	-4.6	3.9	16.8	72.6	55.8	98.5
N		21	21	21	21	21	21	21	21	21	21	21	21	21
Mean		237.34	268.60	265.33	267.37	287.92	345.03	31.25	-3.02[S-]	-1.22	19.33[S-]	76.44	57.11	107.69[S-]
S.D.		17.470	17.970	19.666	23.236	24.033	27.680	6.528	5.589	16.688	16.454	20.754	11.499	20.177

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Appendix 3
Individual and Mean Food Consumption[a]
Rat Teratology Study of T-3352
Group 1 - 0 mg/kg

Maternal Number	Food Consumption (g) Interval (Days of Gestation)						
	0-6	7-8[F]	9-12	13-16	17-20	7-16[B]	0-20[F]
27130	113.6	32.5	70.6	76.7	95.1	179.8	388.5
27131	(142.4)	(31.7)	(58.5)	(60.0)	(74.0)	(150.2)	(366.6)
27132	112.0	31.7	72.2	79.9	106.1	183.8	401.9
27133	125.7	37.1	75.0	83.4	103.5	195.5	424.7
27134	123.8	38.8	79.9	82.8	113.6	201.5	438.9
27135	(122.3)	(34.6)	(53.5)	(57.6)	(67.5)	(145.7)	(335.5)
27136	111.2	32.0	70.0	74.8	88.7	176.8	376.7
27137	131.9	31.2	65.8	74.6	94.5	171.6	398.0
27138	136.9	42.9	87.4	95.8	119.1	226.1	482.1
27139	128.4	39.5	81.9	88.5	113.7	209.9	452.0
27140	164.3	40.9	69.9	75.3	111.6	186.1	462.0
27141	120.0	34.4	77.0	87.3	106.3	198.7	425.0
27142	119.1	28.7	66.0	84.7	100.9	179.4	399.4
27143	186.4	41.8	87.1	82.8	101.8	211.7	499.9
27144	108.8	29.9	71.8	76.7	94.2	178.4	381.4
27145	151.1	47.6	99.2	94.1	99.8	240.9	491.8
27146	137.5	40.3	75.5	79.6	94.1	195.4	427.0
27147	121.8	36.3	76.0	79.5	92.9	191.8	406.5
27148	130.7	40.0	111.1	88.4	117.4	239.5	487.6
27149	135.7	41.8	92.5	100.3	117.1	234.6	487.4
27150	125.6	38.9	81.5	73.3	99.1	193.7	418.4
27151	139.0	42.8	79.8	87.4	104.8	210.0	453.8
27152	126.9	41.1	71.4	87.5	103.8	200.0	430.7
27153	142.8	41.8	72.0	101.6	121.1	215.4	479.3
27154	137.3	41.6	81.8	88.2	105.7	211.6	454.6
N	23	23	23	23	23	23	23
Mean	131.76	37.98	78.93	84.49	104.56	201.40	437.72
S.D.	17.761	4.988	10.880	8.071	9.290	20.254	38.302

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Appendix 3 - Continued
Individual and Mean Food Consumption[a]
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

Maternal Number	Food Consumption (g) Interval (Days of Gestation)						
	0-6	7-8[F]	9-12	13-16	17-20	7-16[B]	0-20[F]
27155	126.8	37.6	83.0	85.0	96.3	205.6	428.7
27156	134.4	42.9	87.0	92.7	110.5	222.6	467.5
27157	113.4	32.3	73.0	80.6	105.1	185.9	404.4
27158	(125.4)	(35.4)	(75.6)	(161.3)[b]	(91.3)	(272.3)[b]	(489.0)[b]
27159	123.5	38.6	81.5	78.3	96.4	198.4	418.3
27160	129.6	40.1	79.1	80.7	94.9	199.9	424.4
27161	123.5	34.4	72.0	79.7	97.7	186.1	407.3
27162	123.5	35.9	78.6	78.8	102.7	193.3	419.5
27163	127.3	36.0	64.1	93.9	106.5	194.0	427.8
27164	117.4	30.4	64.4	72.8	98.0	167.6	383.0
27165	131.6	40.2	82.6	84.1	101.4	206.9	439.9
27166	145.9	35.1	75.3	81.1	96.7	191.5	434.1
27167	124.9	32.6	128.3	(108.5)[b]	109.8	(269.4)[b]	(504.1)[b]
27168	126.2	36.7	67.2	88.4	109.7	192.3	428.2
27169	136.7	39.7	87.6	95.6	116.4	222.9	476.0
27170	139.4	41.6	76.8	88.7	101.9	207.1	448.4
27171	132.4	42.8	88.0	88.7	104.3	219.5	456.2
27172	131.3	42.7	81.0	89.6	97.7	213.3	442.3
27173	124.7	35.9	77.1	81.0	106.8	194.0	425.5
27174	115.4	39.8	84.2	89.5	106.7	213.5	435.6
27175	138.0	46.6	83.3	93.4	110.1	223.3	471.4
27176	125.2	37.9	73.2	76.4	103.0	187.5	415.7
27177	137.6	38.3	79.6	83.9	95.3	201.8	434.7
27178	136.5	47.0	87.1	92.5	114.9	226.6	478.0
27179	133.5	35.8	84.1	88.7	107.5	208.6	449.6
N	24	24	24	23	24	24	24
Mean	129.11	38.37	80.75	85.40	103.76	202.70	435.50
S.D.	7.957	4.222	12.279	6.301	6.289	14.943	23.804

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Appendix 3 - Continued
Individual and Mean Food Consumption[a]
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

Maternal Number	Food Consumption (g) Interval (Days of Gestation)						
	0-6	7-8[F]	9-12	13-16	17-20	7-16[B]	0-20[F]
27180	133.2	37.7	73.5	76.8	92.5	188.0	413.7
27181	137.5	38.3	79.2	78.5	106.0	196.0	439.5
27182	130.6	45.9	77.2	66.1	82.5	189.2	402.3
27183	132.7	37.9	71.8	71.0	92.3	180.7	405.7
27184	124.0	34.9	61.9	87.8	104.7	184.6	413.3
27185	144.7	42.3	76.0	88.7	103.2	207.0	454.9
27186	124.2	39.0	69.3	59.9	99.9	168.2	392.3
27187	121.1	36.7	71.8	69.4	98.5	177.9	397.5
27188	128.1	42.1	77.4	80.0	98.2	199.5	425.8
27189	134.0	39.4	82.0	88.4	108.6	209.8	452.4
27190	109.1	27.3	69.1	67.0	93.7	163.4	366.2
27191	129.6	36.5	75.4	78.1	94.0	190.0	413.6
27192	110.6	31.0	52.4	76.2	99.3	159.6	369.5
27193	119.3	29.4	73.4	71.7	97.3	174.5	391.1
27194	(114.5)	(33.5)	(103.0)[b]	(63.6)[b]	(70.2)	(200.1)[b]	(384.8)[b]
27195	131.0	39.8	76.0	(147.7)[b]	107.3	(263.5)[b]	(501.8)[b]
27096	149.4	44.7	94.9	83.8	108.2	223.4	481.0
27097	133.3	33.6	78.2	75.4	95.7	187.2	416.2
27098	115.3	33.1	67.8	74.7	93.2	175.6	384.1
27099	124.1	33.5	66.5	65.5	99.5	165.5	389.1
27100	132.2	36.2	66.5	70.1	95.7	172.8	400.7
27101	130.5	40.7	75.4	76.1	106.7	192.2	429.4
27102	170.5	55.4	(127.7)[b]	108.9	112.9	(292.0)[b]	(575.4)
27103	130.6	40.0	79.4	84.0	105.1	203.4	439.1
27104	149.6	51.4	79.7	101.5	123.2	232.6	505.4
N	24	24	23	23	24	22	22
Mean	131.05	38.62	73.69	78.24	100.76	188.23	417.40
S.D.	13.235	6.431	8.143	11.473	8.389	18.997	34.384

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Appendix 3 - Continued
Individual and Mean Food Consumption[a]
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

Maternal Number	Food Consumption (g) Interval (Days of Gestation)						
	0-6	7-8[F]	9-12	13-16	17-20	7-16[B]	0-20[F]
27205	124.9	30.9	50.6	58.7	83.0	140.2	348.1
27206	123.1	31.6	86.2	50.1	97.3	167.9	388.3
27207	120.3	34.2	76.3	76.6	95.2	187.3	402.6
27208	(106.8)	(29.0)	(65.7)	(52.2)[b]	(85.8)[b]	(146.9)[b]	(339.5)[b]
27209	92.9	18.5	60.5	(86.4)[b]	97.2	(165.4)[b]	(355.5)[b]
27210	140.9	41.0	81.8	74.7	107.0	197.5	445.4
27211	143.0	35.3	(106.6)[b]	(80.9)[b]	99.0	(222.8)[b]	(464.8)[b]
27212	(139.0)	(19.2)	(34.1)	(2.2)[b]	(66.8)	(55.5)[b]	(261.3)[b]
27213	157.3	64.7	80.5	(99.5)[b]	101.9	(244.7)[b]	(503.9)[b]
27214	(107.8)	(32.0)	(57.7)	(58.4)	(62.7)	(148.1)	(318.6)
27215	135.5	32.3	68.4	73.9	96.1	174.6	406.2
27216	128.8	27.5	60.5	56.9	91.2	144.9	364.9
27217	130.8	39.3	81.0	87.9	109.0	208.2	448.0
27218	122.9	28.5	60.8	(84.1)[b]	98.8	(173.4)[b]	(395.1)[b]
27219	122.6	29.5	65.4	68.8	84.6	163.7	370.9
27220	130.6	40.6	85.4	86.1	103.6	212.1	446.3
27221	113.9	28.1	(81.5)[b]	(72.6)[b]	77.6	(182.2)[b]	(373.7)[b]
27222	155.4	49.9	85.0	(237.1)[b]	(121.4)[b]	(372.0)[b]	(648.8)[b]
27223	130.0	37.6	(72.2)[b]	(73.7)[b]	88.4	(183.5)[b]	(401.9)[b]
27224	129.5	56.4	(220.0)[b]	(128.4)[b]	114.8	(404.8)[b]	(649.1)[b]
27225	(131.1)	(27.4)	(48.3)	(3.7)	(62.2)	(79.4)	(272.7)
27226	148.7	44.5	79.6	81.0	100.7	205.1	454.5
27227	132.3	35.6	(75.7)[b]	72.8	97.2	(184.1)[b]	(413.6)[b]
27228	123.3	23.9	44.2	32.8	91.4	100.9	315.6
27229	(-)[b]	38.7	73.1	69.5	95.4	181.3	(276.7)[b]
N	20	21	16	13	20	12	11
Mean	130.34	36.60	71.21	68.45	96.47[S-]	173.64[S-]	399.16
S.D.	14.541	10.755	13.023	15.381	8.931	32.816	46.421

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Appendix 4
Individual and Mean Terminal Body Weights, Gravid Uterine Weights, and Terminal Body Weights Minus Gravid Uterine Weights (g)[a]
Rat Teratology Study of T-3352
Group 1 - 0 mg/kg

Maternal Number	Terminal Body Weight	Gravid Uterine Weight	Terminal Body Weight Minus Gravid Uterine Weight
27130	340.6	68.8	271.8
27131	Not Pregnant		
27132	368.0	85.5	282.5
27133	363.5	79.9	283.6
27134	375.2	74.0	301.2
27135	Not Pregnant		
27136	350.3	74.4	275.9
27137	352.5	63.0	289.5
27138	413.2	79.1	334.1
27139	404.5	89.3	315.2
27140	351.3	46.9	304.4
27141	344.5	60.1	284.4
27142	357.2	67.2	290.0
27143	316.9	26.4	290.5
27144	340.9	68.5	272.4
27145	407.8	81.4	326.4
27146	388.7	70.7	318.0
27147	344.8	54.9	289.9
27148	386.1	71.5	314.6
27149	380.6	88.9	291.7
27150	360.3	80.0	280.3
27151	379.3	65.9	313.4
27152	326.0	64.3	261.7
27153	389.7	60.3	329.4
27154	356.7	77.9	278.8
N	23	23	23
Mean	365.16	69.52	295.64
S.D.	25.625	14.207	20.212

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Appendix 4 - Continued
Individual and Mean Terminal Body Weights, Gravid Uterine Weights, and Terminal Body Weights Minus Gravid Uterine Weights (g)[a]
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

Maternal Number	Terminal Body Weight	Gravid Uterine Weight	Terminal Body Weight Minus Gravid Uterine Weight
27155	360.2	67.5	292.7
27156	389.3	67.5	321.8
27157	352.5	48.6	303.9
27158	Not Pregnant		
27159	347.0	90.3	256.7
27160	366.4	75.7	290.7
27161	365.8	77.8	288.0
27162	380.4	81.0	299.4
27163	387.4	84.8	302.6
27164	338.6	72.4	266.2
27165	362.3	80.0	282.3
27166	369.9	70.6	299.3
27167	373.0	77.8	295.2
27168	356.1	65.8	290.3
27169	391.7	83.5	308.2
27170[c]	387.1	-	-
27171	394.7	91.8	302.9
27172	352.0	66.7	285.3
27173	361.9	88.8	273.1
27174	357.6	61.1	296.5
27175	316.0	17.0	299.0
27176	360.3	80.8	279.5
27177	369.1	68.9	300.2
27178	418.9	88.1	330.8
27179	374.1	86.8	287.3
N	24	23	23
Mean	368.01	73.62	293.56
S.D.	21.094	16.288	16.285

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Appendix 4 - Continued
Individual and Mean Terminal Body Weights, Gravid Uterine Weights, and Terminal Body Weights Minus Gravid Uterine Weights (g)[a]
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

Maternal Number	Terminal Body Weight	Gravid Uterine Weight	Terminal Body Weight Minus Gravid Uterine Weight
27180	365.7	64.5	301.2
27181	373.6	54.3	319.3
27182	353.7	66.5	287.2
27183	372.6	70.4	302.2
27184	358.3	69.6	288.7
27185	388.9	71.0	317.9
27186	334.9	52.4	282.5
27187	372.5	69.8	302.7
27188	362.9	66.5	296.4
27189	414.2	74.4	339.8
27190	332.3	70.5	261.8
27191	355.0	69.1	285.9
27192	322.8	55.8	267.0
27193	341.3	57.0	284.3
27194	Not Pregnant		
27195	376.5	72.8	303.7
27196	405.9	63.1	342.8
27197	370.1	77.2	292.9
27198	336.1	81.4	254.7
27199	345.4	59.0	286.4
27200	386.6	81.5	305.1
27201	398.0	83.8	314.2
27202	399.6	90.8	308.8
27203	390.3	78.5	311.8
27204	357.9	20.4	337.5
N	24	24	24
Mean	367.30	67.51	299.78
S.D.	24.797	13.989	22.724

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Appendix 4 - Continued
Individual and Mean Terminal Body Weights, Gravid Uterine Weights, and Terminal Body Weights Minus Gravid Uterine Weights (g)[a]
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

Maternal Number	Terminal Body Weight	Gravid Uterine Weight	Terminal Body Weight Minus Gravid Uterine Weight
27205	316.7	64.8	251.9
27206	330.3	59.9	270.4
27207	344.1	74.5	269.6
27208	Not Pregnant		
27209	349.4	73.1	276.3
27210	364.3	57.2	307.1
27211	312.6	30.2	282.4
27212	Not Pregnant		
27213	379.3	71.5	307.8
27214	Not Pregnant		
27215	362.7	73.0	289.7
27216	341.7	78.0	263.7
27217	386.5	79.0	307.5
27218	343.5	71.1	272.4
27219	336.3	68.4	267.9
27220	364.6	68.0	296.6
27221	297.6	59.5	238.1
27222	300.2	24.6	275.6
27223[c]	309.8	-	-
27224	374.0	81.4	292.6
27225	Not Pregnant		
27226	386.3	71.9	314.4
27227	346.8	74.9	271.9
27228	326.1	67.1	259.0
27229	372.9	81.2	291.7
N	21	20	20
Mean	345.03	66.47	280.33[S-]
S.D.	27.679	15.015	20.353

Appendix 5
Individual and Mean Ovarian and Uterine Data
Rat Teratology Study of T-3352
Group 1 - 0 mg/kg

Maternal Number	Ovarian Corpora Lutea	Uterine Implantations	Implantation Efficiency (%)	Early Resorptions	Early Resorptions (%)	Late Resorptions	Late Resorptions (%)	Total Resorptions	Total Resorptions (%)
27130	14	14	100.0	1	7.1	0	0.0	1	7.1
27131	Not Pregnant								
27132	20	16	80.0	1	6.3	0	0.0	1	6.3
27133	16	15	93.8	1	6.7	0	0.0	1	6.7
27134	15	15	100.0	1	6.7	0	0.0	1	6.7
27135	Not Pregnant								
27136	15	15	100.0	0	0.0	0	0.0	0	0.0
27137	13	13	100.0	2	15.4	0	0.0	2	15.4
27138	17	15	88.2	0	0.0	0	0.0	0	0.0
27139	17	16	94.1	0	0.0	0	0.0	0	0.0
27140	10	9	90.0	2	22.2	0	0.0	2	22.2
27141	16	13	81.3	2	15.4	0	0.0	2	15.4
27142[a]	(13)	(14)	(107.7)	(1)	(7.1)	(0)	(0.0)	(1)	(7.1)
27143	14	4	28.6	0	0.0	0	0.0	0	0.0
27144	14	13	92.9	1	7.7	0	0.0	1	7.7
27145	17	15	88.2	0	0.0	0	0.0	0	0.0
27146	16	15	93.8	1	6.7	0	0.0	1	6.7
27147	13	10	76.9	1	10.0	0	0.0	1	10.0
27148	18	14	77.8	1	7.1	0	0.0	1	7.1
27149	19	16	84.2	0	0.0	0	0.0	0	0.0
27150	21	15	71.4	0	0.0	0	0.0	0	0.0
27151	17	14	82.4	2	14.3	0	0.0	2	14.3
27152	13	13	100.0	2	15.4	0	0.0	2	15.4
27153	24	12	50.0	1	8.3	0	0.0	1	8.3
27154	15	15	100.0	1	6.7	0	0.0	1	6.7
Total	354	297		20		0		20	
N	22	22	22	22	22	22	22	22	22
Mean	16.1	13.5	85.16	0.9	7.09	0.0	0.00	0.9	7.09
S.D.	3.08	2.79	17.525	0.75	6.365	-	-	0.75	6.365

[a] Invalid data excluded from mean calculations.

Appendix 5 - Continued
Individual and Mean Ovarian and Uterine Data
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

Maternal Number	Ovarian Corpora Lutea	Uterine Implantations	Implantation Efficiency (%)	Early Resorptions	Early Resorptions (%)	Late Resorptions	Late Resorptions (%)	Total Resorptions	Total Resorptions (%)
27155	16	16	100.0	2	12.5	0	0.0	2	12.5
27156	16	14	87.5	1	7.1	0	0.0	1	7.1
27157	14	13	92.9	4	30.8	0	0.0	4	30.8
27158	Not Pregnant								
27159	18	18	100.0	1	5.6	0	0.0	1	5.6
27160	17	14	82.4	1	7.1	0	0.0	1	7.1
27161	16	14	87.5	0	0.0	0	0.0	0	0.0
27162	19	17	89.5	2	11.8	0	0.0	2	11.8
27163	17	16	94.1	0	0.0	0	0.0	0	0.0
27164	18	16	88.9	3	18.8	0	0.0	3	18.8
27165	17	14	82.4	0	0.0	0	0.0	0	0.0
27166	15	14	93.3	1	7.1	0	0.0	1	7.1
27167	16	15	93.8	1	6.7	0	0.0	1	6.7
27168	15	15	100.0	3	20.0	0	0.0	3	20.0
27169	14	14	100.0	0	0.0	0	0.0	0	0.0
27170	15	14	93.3	4	28.6	0	0.0	4	28.6
27171	21	16	76.2	0	0.0	0	0.0	0	0.0
27172	12	12	100.0	0	0.0	0	0.0	0	0.0
27173	16	15	93.8	0	0.0	0	0.0	0	0.0
27174	14	12	85.7	0	0.0	0	0.0	0	0.0
27175	11	3	27.3	0	0.0	0	0.0	0	0.0
27176	17	16	94.1	0	0.0	0	0.0	0	0.0
27177	15	14	93.3	1	7.1	0	0.0	1	7.1
27178	17	16	94.1	0	0.0	0	0.0	0	0.0
27179	22	19	86.4	3	15.8	0	0.0	3	15.8
Total	388	347		27		0		27	
N	24	24	24	24	24	24	24	24	24
Mean	16.2	14.5	89.02	1.2	7.46	0.0	0.00	1.2	7.46
S.D.	2.46	2.96	14.566	1.37	9.344	-	-	1.37	9.344

Appendix 5 - Continued
Individual and Mean Ovarian and Uterine Data
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

Maternal Number	Ovarian Corpora Lutea	Uterine Implantations	Implantation Efficiency (%)	Early Resorptions	Early Resorptions (%)	Late Resorptions	Late Resorptions (%)	Total Resorptions	Total Resorptions (%)
27180	19	15	78.9	3	20.0	0	0.0	3	20.0
27181	11	10	90.9	1	10.0	0	0.0	1	10.0
27182	19	13	68.4	0	0.0	0	0.0	0	0.0
27183	15	14	93.3	1	7.1	0	0.0	1	7.1
27184	14	14	100.0	1	7.1	0	0.0	1	7.1
27185	15	13	86.7	0	0.0	0	0.0	0	0.0
27186	14	13	92.9	3	23.1	0	0.0	3	23.1
27187	15	15	100.0	2	13.3	0	0.0	2	13.3
27188	15	14	93.3	1	7.1	0	0.0	1	7.1
27189	18	14	77.8	0	0.0	0	0.0	0	0.0
27190	14	14	100.0	0	0.0	1	7.1	1	7.1
27191	18	15	83.3	1	6.7	0	0.0	1	6.7
27192	13	12	92.3	1	8.3	0	0.0	1	8.3
27193	15	13	86.7	2	15.4	1	7.7	3	23.1
27194	Not Pregnant								
27195	15	15	100.0	1	6.7	0	0.0	1	6.7
27196	17	15	88.2	2	13.3	0	0.0	2	13.3
27197	16	16	100.0	1	6.3	1	6.3	2	12.5
27198	15	15	100.0	0	0.0	0	0.0	0	0.0
27199	14	14	100.0	2	14.3	0	0.0	2	14.3
27200	16	16	100.0	0	0.0	0	0.0	0	0.0
27201	16	16	100.0	0	0.0	0	0.0	0	0.0
27202	20	18	90.0	1	5.6	0	0.0	1	5.6
27203	15	15	100.0	0	0.0	0	0.0	0	0.0
27204	15	12	80.0	9	75.0	0	0.0	9	75.0
Total	374	341		32		3		35	
N	24	24	24	24	24	24	24	24	24
Mean	15.6	14.2	91.78	1.3	9.97	0.1	0.88	1.5	10.85
S.D.	2.06	1.64	9.014	1.88	15.392	0.34	2.385	1.89	15.429

Appendix 5 - Continued
Individual and Mean Ovarian and Uterine Data
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

Maternal Number	Ovarian Corpora Lutea	Uterine Implantations	Implantation Efficiency (%)	Early Resorptions	Early Resorptions (%)	Late Resorptions	Late Resorptions (%)	Total Resorptions	Total Resorptions (%)
27205	14	14	100.0	1	7.1	0	0.0	1	7.1
27206	17	16	94.1	2	12.5	0	0.0	2	12.5
27207	15	15	100.0	0	0.0	0	0.0	0	0.0
27208	Not Pregnant								
27209	16	16	100.0	1	6.3	0	0.0	1	6.3
27210	15	15	100.0	4	26.7	0	0.0	4	26.7
27211	14	5	35.7	1	20.0	0	0.0	1	20.0
27212	Not Pregnant								
27213	16	15	93.8	1	6.7	0	0.0	1	6.7
27214	Not Pregnant								
27215	14	14	100.0	1	7.1	0	0.0	1	7.1
27216	16	16	100.0	1	6.3	0	0.0	1	6.3
27217	17	17	100.0	2	11.8	0	0.0	2	11.8
27218	15	15	100.0	1	6.7	0	0.0	1	6.7
27219	16	14	87.5	0	0.0	0	0.0	0	0.0
27220	17	14	82.4	1	7.1	0	0.0	1	7.1
27221	15	12	80.0	0	0.0	0	0.0	0	0.0
27222	18	4	22.2	0	0.0	0	0.0	0	0.0
27223	16	13	81.3	3	23.1	0	0.0	3	23.1
27224	21	18	85.7	1	5.6	0	0.0	1	5.6
27225	Not Pregnant								
27226	18	15	83.3	1	6.7	0	0.0	1	6.7
27227	17	15	88.2	0	0.0	0	0.0	0	0.0
27228	15	14	93.3	0	0.0	1	7.1	1	7.1
27229	18	17	94.4	0	0.0	0	0.0	0	0.0
Total	340	294		21		1		22	
N	21	21	21	21	21	21	21	21	21
Mean	16.2	14.0	86.76	1.0	7.32	0.0	0.34	1.0	7.66
S.D.	1.69	3.45	20.606	1.05	7.790	0.22	1.549	1.02	7.608

Appendix 6
Individual and Mean Litter Data[a]
Rat Teratology Study of T-3352
Group 1 - 0 mg/kg

Maternal Number	Total Resorptions	Number of Fetuses				Sex		Percent Males	Mean Weight (g)[c]	
		Dead	Fetal Loss (%)[b]	Live	Live (%)	Males	Females		Males	Females
27130	1	0	7.1	13	92.9	6	7	46.2	3.5	3.0
27131	Not Pregnant									
27132	1	0	6.3	15	93.8	7	8	46.7	3.5	3.3
27133	1	0	6.7	14	93.3	5	9	35.7	3.6	3.6
27134	1	0	6.7	14	93.3	10	4	71.4	3.3	3.2
27135	Not Pregnant									
27136	0	0	0.0	15	100.0	7	8	46.7	3.0	3.1
27137	2	0	15.4	11	84.6	7	4	63.6	3.4	3.2
27138	0	0	0.0	15	100.0	8	7	53.3	3.6	3.5
27139	0	0	0.0	16	100.0	9	7	56.3	3.3	3.3
27140	2	0	22.2	7	77.8	4	3	57.1	3.8	3.5
27141	2	0	15.4	11	84.6	4	7	36.4	3.1	2.9
27142[d]	(1)	(0)	(7.1)	(13)	(92.9)	7	6	53.8	3.2	3.1
27143	0	0	0.0	4	100.0	3	1	75.0	3.6	2.3
27144	1	0	7.7	12	92.3	6	6	50.0	3.4	3.2
27145	0	0	0.0	15	100.0	9	6	60.0	3.3	3.1
27146	1	1	13.3	13	86.7	7	6	53.8	3.1	2.9
27147	1	0	10.0	9	90.0	7	2	77.8	3.3	3.1
27148	1	0	7.1	13	92.9	6	7	46.2	3.5	3.3
27149	0	0	0.0	16	100.0	8	8	50.0	3.2	2.9
27150	0	0	0.0	15	100.0	5	10	33.3	3.3	3.0
27151	2	0	14.3	12	85.7	7	5	58.3	3.8	3.6
27152	2	0	15.4	11	84.6	5	6	45.5	3.7	3.7
27153	1	0	8.3	11	91.7	4	7	36.4	3.1	3.1
27154	1	0	6.7	14	93.3	10	4	71.4	3.3	3.3
Total	20	1		276		151	138			
N	22	22	22	22	22	23	23	23	23	23
Unadjusted Mean	0.9	0.0	7.39	12.5	92.61	6.6	6.0	53.26	3.39	3.18
Unadjusted S.D.	0.75	0.21	6.500	2.99	6.501	1.93	2.20	12.576	0.226	0.301
Covariance Adjusted Mean									3.39	3.18
Covariance Adjusted S.D.									.005	.005

[a] Sex, percent males, and mean weight data include values for live fetuses only.
[b] Percent fetal loss includes resorptions as well as dead fetuses.
[c] Statistical analysis performed on covariance adjusted means.
[d] Invalid data excluded from mean calculations.

Appendix 6 - Continued
Individual and Mean Litter Data[a]
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

Maternal Number	Total Resorptions	Number of Fetuses				Sex		Percent Males	Mean Weight (g)[c]	
		Dead	Fetal Loss (%)[b]	Live	Live (%)	Males	Females		Males	Females
27155	2	0	12.5	14	87.5	6	8	42.9	2.9	3.2
27156	1	0	7.1	13	92.9	7	6	53.8	3.1	3.0
27157	4	0	30.8	9	69.2	6	3	66.7	3.5	3.1
27158	Not Pregnant									
27159	1	0	5.6	17	94.4	7	10	41.2	3.2	3.3
27160	1	0	7.1	13	92.9	7	6	53.8	3.4	3.3
27161	0	0	0.0	14	100.0	7	7	50.0	3.4	3.2
27162	2	0	11.8	15	88.2	8	7	53.3	3.3	2.9
27163	0	0	0.0	16	100.0	10	6	62.5	3.3	3.1
27164	3	0	18.8	13	81.3	6	7	46.2	3.4	3.2
27165	0	0	0.0	14	100.0	8	6	57.1	3.4	3.2
27166	1	0	7.1	13	92.9	5	8	38.5	3.4	3.1
27167	1	0	6.7	14	93.3	8	6	57.1	3.2	3.1
27168	3	0	20.0	12	80.0	6	6	50.0	3.5	3.2
27169	0	0	0.0	14	100.0	5	9	35.7	3.5	3.4
27170	4	0	28.6	10	71.4	2	8	20.0	3.0	2.9
27171	0	0	0.0	16	100.0	8	8	50.0	3.3	3.4
27172	0	0	0.0	12	100.0	9	3	75.0	3.5	3.6
27173	0	0	0.0	15	100.0	5	10	33.3	3.5	3.4
27174	0	0	0.0	12	100.0	5	7	41.7	2.9	2.9
27175	0	0	0.0	3	100.0	2	1	66.7	2.9	3.0
27176	0	0	0.0	16	100.0	9	7	56.3	3.2	2.9
27177	1	0	7.1	13	92.9	4	9	30.8	3.2	3.2
27178	0	0	0.0	16	100.0	9	7	56.3	3.5	3.3
27179	3	0	15.8	16	84.2	8	8	50.0	3.0	2.8
Total	27	0		320		157	163			
N	24	24	24	24	24	24	24	24	24	24
Unadjusted Mean	1.2	0.0	7.46	13.3	92.55	6.5	6.8	49.54	3.27	3.15
Unadjusted S.D.	1.37	-	9.344	2.94	9.338	2.08	2.13	12.596	0.210	0.198
Covariance Adjusted Mean									3.27	3.15
Covariance Adjusted S.D.									.005	.005

[a] Sex, percent males, and mean weight data include values for live fetuses only.
[b] Percent fetal loss includes resorptions as well as dead fetuses.
[c] Statistical analysis performed on covariance adjusted means.

Appendix 6 - Continued
Individual and Mean Litter Data[a]
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

Maternal Number	Total Resorptions	Number of Fetuses				Sex		Percent Males	Mean Weight (g)[c]	
		Dead	Fetal Loss (%)[b]	Live	Live (%)	Males	Females		Males	Females
27180	3	0	20.0	12	80.0	6	6	50.0	3.1	3.1
27181	1	0	10.0	9	90.0	7	2	77.8	3.2	2.9
27182	0	0	0.0	13	100.0	9	4	69.2	3.1	2.9
27183	1	0	7.1	13	92.9	6	7	46.2	3.3	3.1
27184	1	0	7.1	13	92.9	9	4	69.2	3.3	3.3
27185	0	0	0.0	13	100.0	8	5	61.5	3.3	3.0
27186	3	0	23.1	10	76.9	5	5	50.0	3.1	2.9
27187	2	0	13.3	13	86.7	6	7	46.2	3.2	3.0
27188	1	0	7.1	13	92.9	8	5	61.5	3.0	3.0
27189	0	0	0.0	14	100.0	10	4	71.4	3.0	2.9
27190	1	0	7.1	13	92.9	5	8	38.5	3.3	3.1
27191	1	0	6.7	14	93.3	5	9	35.7	2.8	2.8
27192	1	0	8.3	11	91.7	8	3	72.7	3.3	3.1
27193	3	0	23.1	10	76.9	5	5	50.0	3.0	2.9
27194	Not Pregnant									
27195	1	0	6.7	14	93.3	4	10	28.6	3.2	3.0
27196	2	0	13.3	13	86.7	4	9	30.8	3.0	2.9
27197	2	0	12.5	14	87.5	8	6	57.1	3.4	3.3
27198	0	0	0.0	15	100.0	8	7	53.3	3.1	2.9
27199	2	0	14.3	12	85.7	6	6	50.0	3.1	2.8
27200	0	0	0.0	16	100.0	5	11	31.3	3.2	3.0
27201	0	0	0.0	16	100.0	8	8	50.0	3.5	3.3
27202	1	0	5.6	17	94.4	6	11	35.3	3.5	3.2
27203	0	0	0.0	15	100.0	4	11	26.7	3.2	3.1
27204	9	0	75.0	3	25.0	2	1	66.7	3.9	3.8
Total	35	0		306		152	154			
N	24	24	24	24	24	24	24	24	24	24
Unadjusted Mean	1.5	0.0	10.85	12.8	89.15	6.3	6.4	51.24	3.21	3.05
Unadjusted S.D.	1.89	-	15.429	2.83	15.429	1.97	2.81	15.255	0.221	0.217
Covariance Adjusted Mean									3.21	3.05
Covariance Adjusted S.D.									.005	.005

[a] Sex, percent males, and mean weight data include values for live fetuses only.
[b] Percent fetal loss includes resoprtions as well as dead fetuses.
[c] Statistical analysis performed on covariance adjusted means.

Appendix 6 - Continued
Individual and Mean Litter Data[a]
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

Maternal Number	Total Resorptions	Number of Fetuses				Sex		Percent Males	Mean Weight (g)[c]	
		Dead	Fetal Loss (%)[b]	Live	Live (%)	Males	Females		Males	Females
27205	1	0	7.1	13	92.9	6	7	46.2	2.8	2.8
27206	2	0	12.5	14	87.5	7	7	50.0	2.4	2.2
27207	0	0	0.0	15	100.0	8	7	53.3	3.1	2.9
27208	Not Pregnant									
27209	1	0	6.3	15	93.8	8	7	53.3	3.0	2.9
27210	4	0	26.7	11	73.3	4	7	36.4	3.2	3.1
27211	1	0	20.0	4	80.0	3	1	75.0	3.0	2.7
27212	Not Pregnant									
27213	1	0	6.7	14	93.3	6	8	42.9	2.9	2.8
27214	Not Pregnant									
27215	1	0	7.1	13	92.9	7	6	53.8	3.3	3.2
27216	1	0	6.3	15	93.8	5	10	33.3	3.0	2.8
27217	2	0	11.8	15	88.2	8	7	53.3	3.0	2.8
27218	1	0	6.7	14	93.3	8	6	57.1	3.1	3.2
27219	0	0	0.0	14	100.0	6	8	42.9	2.7	2.7
27220	1	0	7.1	13	92.9	6	7	46.2	3.3	3.0
27221	0	0	0.0	12	100.0	7	5	58.3	2.9	2.7
27222	0	0	0.0	4	100.0	2	2	50.0	3.1	2.9
27223	3	0	23.1	10	76.9	4	6	40.0	2.7	2.5
27224	1	0	5.6	17	94.4	9	8	52.9	2.5	2.6
27225	Not Pregnant									
27226	1	0	6.7	14	93.3	10	4	71.4	3.3	3.0
27227	0	0	0.0	15	100.0	11	4	73.3	2.8	2.7
27228	1	0	7.1	13	92.9	5	8	38.5	3.0	2.7
27229	0	0	0.0	17	100.0	8	9	47.1	2.8	2.6
Total	22	0		272		138	134			
N	21	21	21	21	21	21	21	21	21	21
Unadjusted Mean	1.0	0.0	7.66	13.0	92.35	6.6	6.4	51.20	2.95	2.80
Unadjusted S.D.	1.02	-	7.608	3.41	7.610	2.25	2.18	11.412	0.246	0.235
Covariance Adjusted Mean									2.95[S-]	2.80[S-]
Covariance Adjusted S.D.									.005	.005

[a] Sex, percent males, and mean weight data include values for live fetuses only.
[b] Percent fetal loss includes resorptions as well as dead fetuses.
[c] Statistical analysis performed on covariance adjusted means.

Appendix 7
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3352
Group 1 - 0 mg/kg

Maternal Number:	27130	27131	27132	27133	27134	27135	27136	27137	27138	27139	27140	27141	27142
Number of fetuses examined	5	NP	5	5[a]	5	NP	5	4	5	6	3	4	5
Number of fetuses within normal limits	5		4	3	5		5	3	5	5	2	4	5
Number of fetuses having one or more visceral variants	0		1	2	0		0	1	0	1	1	0	0
Percent of fetuses having one or more visceral variants (%)	0.00		20.00	40.00	0.00		0.00	25.00	0.00	16.67	33.33	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - left ventrical dilated													
- dark material around brain													
Liver - dark areas on lobe													
- all lobes appeared dark													
- dark area in liver													
Kidney(s) - dilated renal pelvis				DM						P	D		
Ureter(s) - distended			H	DM						P	D		
Testes - small								H					
Skin - edema between skin and peritoneal wall													
Number of fetuses having one or more visceral anomalies	0		0	0	0		0	0	0	0	0	0	0
Percent of fetuses having one or more visceral anomalies(%)	0.00		0.00	0.00	0.00		0.00	0.00	0.00	0.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Kidney(s) - fused													
Cryptorchism													

NP = Not Pregnant.
[a] Fetus K was noted to have an undeveloped tail during external examination. This finding was confirmed at skeletal examination.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3352
Group 1 - 0 mg/kg

		2	2	2	2	2	2	2	2	2	2	2	2
		7	7	7	7	7	7	7	7	7	7	7	7
		1	1	1	1	1	1	1	1	1	1	1	1
	Maternal	4	4	4	4	4	4	4	5	5	5	5	5
	Number:	3	4	5	6	7	8	9	0	1	2	3	4
Number of fetuses examined		2	4	5	5	3	5	6	5	4	4	4	5
Number of fetuses within normal limits		2	4	5	4	3	1	6	4	3	3	3	5
Number of fetuses having one or more visceral variants		0	0	0	1	0	4	0	1	1	1	0	0
Percent of fetuses having one or more visceral variants (%)		0.00	0.00	0.00	20.00	0.00	80.00	0.00	20.00	25.00	25.00	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - left ventrical dilated													
- dark material around brain													
Liver - dark areas on lobe													
- all lobes appeared dark													
- dark area in liver													
Kidney(s) - dilated renal pelvis							ADGN						
Ureter(s) - distended					N					A	K		
Testes - small													
Skin - edema between skin and peritoneal wall									J				
Number of fetuses having one or more visceral anomalies		0	0	0	0	0	1	0	0	0	0	1	0
Percent of fetuses having one or more visceral anomalies(%)		0.00	0.00	0.00	0.00	0.00	20.00	0.00	0.00	0.00	0.00	25.00	0.00
Identification letter(s) of fetuses with:													
Kidney(s) - fused													
Cryptorchism							O					B	

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

Maternal Number:	27115	27116	27117	27118	27159	27160	27161	27162	27163	27164	27165	27166	27167
Number of fetuses examined	5	5	3	NP	6	5	5	5	6	5	5	5	5
Number of fetuses within normal limits	4	4	3		6	5	5	5	6	3	5	5	5
Number of fetuses having one or more visceral variants	1	1	0		0	0	0	0	0	2	0	0	0
Percent of fetuses having one or more visceral variants (%)	20.00	20.00	0.00		0.00	0.00	0.00	0.00	0.00	40.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - left ventrical dilated													
- dark material around brain													
Liver - dark areas on lobe													
- all lobes appeared dark													
- dark area in liver													
Kidney(s) - dilated renal pelvis	L	N								K			
Ureter(s) - distended	L	N								GK			
Testes - small													
Skin - edema between skin and peritoneal wall													
Number of fetuses having one or more visceral anomalies	0	0	0		0	0	0	0	0	0	0	0	0
Percent of fetuses having one or more visceral anomalies(%)	0.00	0.00	0.00		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Kidney(s) - fused													
Cryptorchism													

NP = Not Pregnant.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

	Maternal Number:	2 7 1 6 8	2 7 1 6 9	2 7 1 7 0	2 7 1 7 1	2 7 1 7 2	2 7 1 7 3	2 7 1 7 4	2 7 1 7 5	2 7 1 7 6	2 7 1 7 7	2 7 1 7 8	2 7 1 7 9
Number of fetuses examined		4	5	4	6	4	5	4	1	6	5	6	6
Number of fetuses within normal limits		2	5	4	6	4	5	2	1	4	5	6	6
Number of fetuses having one or more visceral variants		2	0	0	0	0	0	2	0	2	0	0	0
Percent of fetuses having one or more visceral variants (%)		50.00	0.00	0.00	0.00	0.00	0.00	50.00	0.00	33.33	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - left ventrical dilated													
- dark material around brain										A			
Liver - dark areas on lobe										J			
- all lobes appeared dark													
- dark area in liver													
Kidney(s) - dilated renal pelvis		IL						GJ					
Ureter(s) - distended		I											
Testes - small													
Skin - edema between skin and peritoneal wall													
Number of fetuses having one or more visceral anomalies		0	0	0	0	0	0	0	0	0	0	0	0
Percent of fetuses having one or more visceral anomalies(%)		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Kidney(s) - fused													
Cryptorchism													

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

Maternal Number:	27180	27181	27182	27183	27184	27185	27186	27187	27188	27189	27190	27191	27192
Number of fetuses examined	4[a]	3	5	5	5	5	4	5	5	5	5	5	4
Number of fetuses within normal limits	4	3	5	5	5	5	4	5	5	5	4	5	4
Number of fetuses having one or more visceral variants	0	0	0	0	0	0	0	0	0	0	0	0	0
Percent of fetuses having one or more visceral variants (%)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - left ventrical dilated													
- dark material around brain													
Liver - dark areas on lobe													
- all lobes appeared dark													
- dark area in liver													
Kidney(s) - dilated renal pelvis													
Ureter(s) - distended													
Testes - small													
Skin - edema between skin and peritoneal wall													
Number of fetuses having one or more visceral anomalies	0	0	0	0	0	0	0	0	0	0	1	0	0
Percent of fetuses having one or more visceral anomalies(%)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	20.00	0.00	0.00
Identification letter(s) of fetuses with:													
Kidney(s) - fused													
Cryptorchism											K		

[a] Fetus N was noted to have a cleft palate during external examination.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

	2	2	2	2	2	2	2	2	2	2	2	2	
	7	7	7	7	7	7	7	7	7	7	7	7	
	1	1	1	1	1	1	1	2	2	2	2	2	
Maternal	9	9	9	9	9	9	9	0	0	0	0	0	
Number:	3	4	5	6	7	8	9	0	1	2	3	4	
Number of fetuses examined	4	NP	5	5	5	5	4[a]	6	6	6	5	1	
Number of fetuses within normal limits	4		5	5	5	5	3	5	4	6	5	1	
Number of fetuses having one or more visceral variants	0		0	0	0	0	0	1	2	0	0	0	
Percent of fetuses having one or more visceral variants (%)	0.00		0.00	0.00	0.00	0.00	0.00	16.67	33.33	0.00	0.00	0.00	
Identification letter(s) of fetuses with:													
Brain - left ventrical dilated													
- dark material around brain													
Liver - dark areas on lobe									M				
- all lobes appeared dark									P				
- dark area in liver													
Kidney(s) - dilated renal pelvis													
Ureter(s) - distended								P					
Testes - small													
Skin - edema between skin and peritoneal wall													
Number of fetuses having one or more visceral anomalies	0		0	0	0	0	1	0	0	0	0	0	
Percent of fetuses having one or more visceral anomalies(%)	0.00		0.00	0.00	0.00	0.00	25.00	0.00	0.00	0.00	0.00	0.00	
Identification letter(s) of fetuses with:													
Kidney(s) - fused							B						
Cryptorchism													

NP = Not Pregnant.
[a] Fetus B was noted to have no tail and a short trunk during external examination.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	7	7	7	7	7	7	7	7	7	7	7	7	7	7
	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Maternal	0	0	0	0	0	1	1	1	1	1	1	1	1	1
Number:	5	6	7	8	9	0	1	2	3	4	5	6	7	
Number of fetuses examined	5	5	5	NP	5	4	2	NP	5	NP	5	5	5	
Number of fetuses within normal limits	5	5	4		5	4	2		5		5	5	5	
Number of fetuses having one or more visceral variants	0	0	1		0	0	0		0		0	0	0	
Percent of fetuses having one or more visceral variants (%)	0.00	0.00	20.00		0.00	0.00	0.00		0.00		0.00	0.00	0.00	
Identification letter(s) of fetuses with:														
Brain - left ventrical dilated														
- dark material around brain														
Liver - dark areas on lobe														
- all lobes appeared dark														
- dark area in liver			D											
Kidney(s) - dilated renal pelvis														
Ureter(s) - distended														
Testes - small														
Skin - edema between skin and peritoneal wall														
Number of fetuses having one or more visceral anomalies	0	0	0		0	0	0		0		0	0	0	
Percent of fetuses having one or more visceral anomalies(%)	0.00	0.00	0.00		0.00	0.00	0.00		0.00		0.00	0.00	0.00	
Identification letter(s) of fetuses with:														
Kidney(s) - fused														
Cryptorchism														

NP = Not Pregnant.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

Maternal Number:	21718	21719	21720	21721	21722	21723	21724	21725	21726	21727	21728	21729
Number of fetuses examined	5	5[a]	5	4	2	4	6	NP	5	5	5	6
Number of fetuses within normal limits	5	5	5	4	2	4	6		5	5	4	6
Number of fetuses having one or more visceral variants	0	0	0	0	0	0	0		0	0	1	0
Percent of fetuses having one or more visceral variants (%)	0.00	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	20.00	0.00
Identification letter(s) of fetuses with:												
Brain - left ventrical dilated										•		
- dark material around brain												
Liver - dark areas on lobe												
- all lobes appeared dark												
- dark area in liver												
Kidney(s) - dilated renal pelvis												
Ureter(s) - distended												
Testes - small											N	
Skin - edema between skin and peritoneal wall												
Number of fetuses having one or more visceral anomalies	0	0	0	0	0	0	0		0	0	0	0
Percent of fetuses having one or more visceral anomalies(%)	0.00	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:												
Kidney(s) - fused												
Cryptorchism												

NP = Not Pregnant.
[a] Fetus L was noted to have an underdeveloped tail during external examination. This finding was confirmed at skeletal examination.

Appendix B
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of I-3352
Group 1 - 0 mg/kg

Maternal Number:	2 7 1 3 0	2 7 1 3 1	2 7 1 3 2	2 7 1 3 3	2 7 1 3 4	2 7 1 3 5	2 7 1 3 6	2 7 1 3 7	2 7 1 3 8	2 7 1 3 9	2 7 1 4 0	2 7 1 4 1	2 7 1 4 2
Number of fetuses examined	8	NP	10	9	9	NP	10	7	10	10	4	7	8
Number of fetuses within normal limits	2		7	7	6		1	6	6	7	2	3	2
Number of fetuses having one or more skeletal variants	6		3	2	3		9	1	4	3	2	4	6
Percent of fetuses having one or more skeletal variants (%)	75.00		30.00	22.22	33.33		90.00	14.29	40.00	30.00	50.00	57.14	75.00
Identification letter(s) of fetuses with:													
Lagging Ossification													
Skull - incomplete closure (<75%)							I			0			
- interparietal ossification incomplete	EI		IJ	B			BEIKNO			KO	C	CEIM	CEM
- parietals ossification irregular							I						
- supraoccipital ossification incomplete	EI		I				INO			0		CEIM	CJ
- supraoccipital nonfused							E						
- hyoid ossification incomplete/nonossified	E				CF		EFHIKL NO		BN	LO		EIM	CEI
Rib cage - sternebrae bipartite													
- sternebrae <3 ossified										0			
- ribs >13 pairs ossified													
- ribs <13 pairs ossified													
- ribs ossification irregular													B
Vertebral column - thoracic centra ossification incomplete	BCGL		IJL	B	H		ILO	G	KN	0		M	EM
- thoracic centra nonfused									C		B		
- lumbar ossification incomplete/nonossified				K									
- lumbar arches fused				K									
- caudals <3 ossified				K						0			
- caudal vertebrae nonossified				K									
- sacral vertebrae nonossified				K									
Pelvic Girdle - pubis ossification incomplete/ nonossified							EI						C
- ischium ossification incomplete							EI						C
Hindlimbs - <4 ossified													
Bone Alignment													
Ribs - fused													
- forked													
- malaligned thoracic centra and arches													
- angulated													
Sternebrae - checkered													
Vertebrae malaligned - thoracic													

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetuses.

Appendix 8 - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3352
Group 1 - 0 mg/kg

Maternal Number:	27143	27144	27145	27146	27147	27148	27149	27150	27151	27152	27153	27154
Number of fetuses examined	2	8	10	8	6	8	10	10	8	7	7	9
Number of fetuses within normal limits	2	7	2	2	4	5	4	5	5	1	2	6
Number of fetuses having one or more skeletal variants	0	1	8	6	2	3	6	5	3	6	5	3
Percent of fetuses having one or more skeletal variants (%)	0.00	12.50	80.00	75.00	33.33	37.50	60.00	50.00	37.50	85.71	71.43	33.33
Identification letter(s) of fetuses with:												
Lagging Ossification												
Skull - incomplete closure (<75%)					F		I					
- interparietal ossification incomplete		M	EHLNO		F		C	CF	F	L	GIJ	
- parietals ossification irregular					BF							
- supraoccipital ossification incomplete			EHL					CINO		L	I	J
- supraoccipital nonfused												
- hyoid ossification incomplete/nonossified		M	HILO	O	BF	C	BF		H	L	CFIJ	FJM
Rib cage - sternebrae bipartite						HI						
- sternebrae <3 ossified									E			
- ribs >13 pairs ossified												
- ribs <13 pairs ossified												
- ribs ossification irregular												
Vertebral column - thoracic centra ossification incomplete			CHI	FGM			BHIN		H	FHIL		FJ
- thoracic centra nonfused			E	IL						BE		
- lumbar ossification incomplete/nonossified												
- lumbar arches fused												
- caudals <3 ossified			L				I	I				
- caudal vertebrae nonossified												
- sacral vertebrae nonossified												
Pelvic Girdle - pubis ossification incomplete/ nonossified			H									
- ischium ossification incomplete												
Hindlimbs - <4 ossified												
Bone Alignment												
Ribs - fused												
- forked												
- malaligned thoracic centra and arches												
- angulated												
Sternebrae - checkered					B							
Vertebrae malaligned - thoracic												

[a] There were no skeletal anomalies noted in any fetus.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

Maternal Number:	21715	21716	21717	21718	21719	21760	21761	21762	21763	21764	21765	21766	21767
Number of fetuses examined	9	8	6	NP	11	8	9	10	10	8	9	8	9
Number of fetuses within normal limits	0	6	1		4	6	7	5	2	8	8	7	3
Number of fetuses having one or more skeletal variants	9	2	5		7	2	2	5	8	0	1	1	6
Percent of fetuses having one or more skeletal variants (%)	100.00	25.00	83.33		63.64	25.00	22.22	50.00	80.00	0.00	11.11	12.50	66.67
Identification letter(s) of fetuses with:													
Lagging Ossification													
Skull - incomplete closure (<75%)	KM												
	BFHJKM												
- interparietal ossification incomplete	NP	B			CIKO		I	P					CG
- parietals ossification irregular	M												
- supraoccipital ossification incomplete	JKM	B							EI				
- supraoccipital nonfused													
- hyoid ossification incomplete/nonossified	DJKMP	E	K		BCFIR		CI	L	BCEIKL		L		CJ
Ribcage - sternebrae bipartite													
- sternebrae <3 ossified	K												
- ribs >13 pairs ossified													
- ribs <13 pairs ossified													
- ribs ossification irregular													
Vertebral column - thoracic centra ossification incomplete			G		R	C			HO			I	EGI
- thoracic centra nonfused	K		CDL			G		J					CO
- lumbar ossification incomplete/nonossified													
- lumbar arches fused													
- caudals <3 ossified	K							IQ					
- caudal vertebrae nonossified													
- sacral vertebrae nonossified													
Pelvic Girdle - pubis ossification incomplete/ nonossified		B							I				
- ischium ossification incomplete													
Hindlimbs - <4 ossified													
Bone Alignment													
Ribs - fused													
- forked													
- malaligned thoracic centra and arches													
- angulated	M												
Sternebrae - checkered													
Vertebrae malaligned - thoracic													

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetus.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3352
Group 2 - 1 mg/kg

Maternal Number:	26718	26719	26710	26711	26712	26713	26714	26715	26716	26717	26718	26719
Number of fetuses examined	8	9	6	10	8	10	8	2	10	8	10	10
Number of fetuses within normal limits	6	5	4	8	5	5	1	0	3	8	4	9
Number of fetuses having one or more skeletal variants	2	4	2	2	3	5	7	2	7	0	6	1
Percent of fetuses having one or more skeletal variants (%)	25.00	44.44	33.33	20.00	37.50	50.00	87.50	100.00	70.00	0.00	60.00	10.00
Identification letter(s) of fetuses with:												
Lagging Ossification												
Skull - incomplete closure (<75%)		BN					EL					
- interparietal ossification incomplete		BFN			EFI	ENO	CE		KL			F
- parietals ossification irregular		BFN					E					
- supraoccipital ossification incomplete			G				EFL	BC	FKL			
- supraoccipital nonfused												
- hyoid ossification incomplete/nonossified				EI		NO	EIL	C	KL			
Rib cage - sternebrae bipartite						CN	CEHIK					
- sternebrae <3 ossified												
- ribs >13 pairs ossified	DH								IN			
- ribs <13 pairs ossified												
- ribs ossification irregular												
Vertebral column - thoracic centra ossification incomplete		H	D			CHO	EF	BC	O		CFHIN	
- thoracic centra nonfused							CL				O	
- lumbar ossification incomplete/nonossified												
- lumbar arches fused												
- caudals <3 ossified							EL	BC	C			
- caudal vertebrae nonossified												
- sacral vertebrae nonossified												
Pelvic Girdle - pubis ossification incomplete/ nonossified							E	C	L			
- ischium ossification incomplete												
Hindlimbs - <4 ossified								C				
Bone Alignment												
Ribs - fused												
- forked												
- malaligned thoracic centra and arches												
- angulated												
Sternebrae - checkered												
Vertebrae malaligned - thoracic												

[a] There were no skeletal anomalies noted in any fetus.

Appendix 8 - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

Maternal Number:	2701 80	2701 81	2701 82	2701 83	2701 84	2701 85	2701 86	2701 87	2701 88	2701 89	2701 90	2701 91	2701 92
Number of fetuses examined	8	6	8	8	8	8	6	8	8	9	8	9	7
Number of fetuses within normal limits	2	3	5	3	7	5	0	2	3	9	3	1	7
Number of fetuses having one or more skeletal variants	6	3	3	5	1	3	6	6	5	0	5	8	0
Percent of fetuses having one or more skeletal variants (%)	75.00	50.00	37.50	62.50	12.50	37.50	100.00	75.00	62.50	0.00	62.50	88.89	0.00
Identification letter(s) of fetuses with:													
Tagging Ossification													
Skull - incomplete closure (<75%)	NO							BC					
- interparietal ossification incomplete	HO	BG	CF	L			CHIL	BCIM	BCF		CFILM	FMO	
- parietals ossification irregular								BM			C		
- supraoccipital ossification incomplete			I				C					DFGIJL	
- supraoccipital nonfused												MO	
- hyoid ossification incomplete/nonossified			CE		B				CK			FGIJMO	
Rib cage - sternebrae bipartite	B			B									
- sternebrae <3 ossified													
- ribs >13 pairs ossified		J											
- ribs <13 pairs ossified													
- ribs ossification irregular													
Vertebral column - thoracic centra ossification incomplete	JL	BGJ	C	IL		L	DIKL	FN			M		
- thoracic centra nonfused				FG		IK	C	I					
- lumbar ossification incomplete/nonossified													
- lumbar arches fused													
- caudals <3 ossified								I	EK			IJ	
- caudal vertebrae nonossified													
- sacral vertebrae nonossified													
Pelvic Girdle - pubis ossification incomplete/ nonossified													
- ischium ossification incomplete													
Hindlimbs - <4 ossified													
Bone Alignment													
Ribs - fused													
- forked													
- malaligned thoracic centra and arches													
- angulated													
Sternebrae - checkered													
Vertebrae malaligned - thoracic													

[a] There were no skeletal anomalies noted in any fetus.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3352
Group 3 - 10 mg/kg

Maternal Number:	2719 3	2719 4	2719 5	2719 6	2719 7	2719 8	2719 9	2720 0	2720 1	2720 2	2720 3	2720 4
Number of fetuses examined	6	NP	9	8	9	10	8	10	10	11	10	2
Number of fetuses within normal limits	4		4	8	7	3	4	4	7	4	6	2
Number of fetuses having one or more skeletal variants	2		5	0	2	7	4	6	3	7	4	0
Percent of fetuses having one or more skeletal variants (%)	33.33		55.56	0.00	22.22	70.00	50.00	60.00	30.00	63.64	40.00	0.00
Identification letter(s) of fetuses with:												
Lagging Ossification												
Skull - incomplete closure (<75%)			O			NO		K		C		
- interparietal ossification incomplete			CDGO			BFINO		CEK	I	CFHIKN	CFKO	
- parietals ossification irregular			O			O		K				
- supraoccipital ossification incomplete			G					CK	IN	C		
- supraoccipital nonfused												
- hyoid ossification incomplete/nonossified	F					CH		CFK		C	F	
Rib cage - sternebrae bipartite	F						CF					
- sternebrae <3 ossified												
- ribs >13 pairs ossified	E											
- ribs <13 pairs ossified												
- ribs ossification irregular												
Vertebral column - thoracic centra ossification incomplete					L		CDFM	EFIN	B	O	C	
- thoracic centra nonfused			CO		E			CK				
- lumbar ossification incomplete/nonossified												
- lumbar arches fused												
- caudals <3 ossified							D					
- caudal vertebrae nonossified												
- sacral vertebrae nonossified												
Pelvic Girdle - pubis ossification incomplete/ nonossified												
- ischium ossification incomplete												
Hindlimbs - <4 ossified												
Bone Alignment												
Ribs - fused												
- forked												
- malaligned thoracic centra and arches												
- angulated			M									
Sternebrae - checkered			O									
Vertebrae malaligned - thoracic												

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetus.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

Maternal Number:	205	206	207	208	209	210	211	212	213	214	215	216	217
Number of fetuses examined	8	9	10	NP	10	7	2	NP	9	NP	8	10	10
Number of fetuses within normal limits	2	1	4		6	3	2		7		0	2	5
Number of fetuses having one or more skeletal variants	6	8	6		4	4	0		2		8	8	5
Percent of fetuses having one or more skeletal variants (%)	75.00	88.89	60.00		40.00	57.14	0.00		22.22		100.00	80.00	50.00
Identification letter(s) of fetuses with:													
Lagging Ossification													
Skull - incomplete closure (<75%)		P				J							
- interparietal ossification incomplete	IL	GLP	LNO			IJO			J		J		
- parietals ossification irregular	FI												
- supraoccipital ossification incomplete	I	GLP				J			B				
- supraoccipital nonfused													
- hyoid ossification incomplete/nonossified	L	FP	K			JLO							
Rib cage - sternebrae bipartite	D	CGIJLN									BCFGIJ LM		EFNQ
- sternebrae <3 ossified		P											
- ribs >13 pairs ossified		GIJP			JO						F	IL	F
- ribs <13 pairs ossified													
- ribs ossification irregular	I												
Vertebral column - thoracic centra ossification incomplete	FGJ	CFILP	FL		F							CM	N
- thoracic centra nonfused	D	P	K		I							P	
- lumbar ossification incomplete/nonossified													F
- lumbar arches fused													
- caudals <3 ossified		CGLP	H			J						BF	F
- caudal vertebrae nonossified													
- sacral vertebrae nonossified		P											
Pelvic Girdle - pubis ossification incomplete/ nonossified		P											
- ischium ossification incomplete													
Hindlimbs - <4 ossified						J							
Bone Alignment													
Ribs - fused													
- forked		G											
- malaligned thoracic centra and arches		G											
- angulated	FI												
Sternebrae - checkered												H	L
Vertebrae malaligned - thoracic													

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetus.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3352
Group 4 - 30 mg/kg

Maternal Number:	2 7 2 1 8	2 7 2 1 9	2 7 2 2 0	2 7 2 2 1	2 7 2 2 2	2 7 2 2 3	2 7 2 2 4	2 7 2 2 5	2 7 2 2 6	2 7 2 2 7	2 7 2 2 8	2 7 2 2 9
Number of fetuses examined	9	9	8	8	2	6	11	NP	9	10	8	11
Number of fetuses within normal limits	8	5	4	7	1	1	0		5	7	1	5
Number of fetuses having one or more skeletal variants	1	4	4	1	1	5	11		4	3	7	6
Percent of fetuses having one or more skeletal variants (%)	11.11	44.44	50.00	12.50	50.00	83.33	100.00		44.44	30.00	87.50	54.55
Identification letter(s) of fetuses with:												
Lagging Ossification												
Skull - incomplete closure (<75%)							CK					N
- interparietal ossification incomplete		EK	E				CEIKLP		BEHI	EFK	L	HIN
- parietals ossification irregular							CK					
- supraoccipital ossification incomplete	0	K				CDFJ	BCEKL					HKN
- supraoccipital nonfused												
- hyoid ossification incomplete/nonossified		EK	L							K		CH
Rib cage - sternebrae bipartite						DI	NP		B		BCFI	
- sternebrae <3 ossified												N
- ribs >13 pairs ossified			CLM			J	EHLR					
- ribs <13 pairs ossified												
- ribs ossification irregular												
Vertebral column - thoracic centra ossification incomplete			E	H	B	J	CIKLR				BCEFHI L	N
- thoracic centra nonfused							L					
- lumbar ossification incomplete/nonossified												
- lumbar arches fused												
- caudals <3 ossified		L					EFL		B	F		NQ
- caudal vertebrae nonossified												
- sacral vertebrae nonossified												N
Pelvic Girdle - pubis ossification incomplete/ nonossified							E					
- ischium ossification incomplete												
Hindlimbs - <4 ossified							E					N
Bone Alignment												
Ribs - fused							L					
- forked												
- malaligned thoracic centra and arches												
- angulated												
Sternebrae - checkered												
Vertebrae malaligned - thoracic							L			I		

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetus.

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Appendix 9
References
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STATISTICAL METHODS/LABORATORY PROCEDURES

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Appendix 9 - Continued
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Rat Teratology Study of T-3352

STATISTICAL METHODS/LABORATORY PROCEDURES

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