HAZLETON LABORATORIES AMERICA, INC.
2300 LEESBURG TURNPIKE, VIENNA, VIRGINIA 22180, U.S.A.

RAT TERATOLOGY STUDY

T-3351

FINAL REPORT

Submitted to

3M Company

St. Paul, Minnesota

December 19, 1983

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

OFFICE OF QUALITY ASSURANCE

Project Title: Rat Teratology Study

Project No.: 154-160

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
Study	7/6,8,11,12/83	7/15/83	E. Burroughs
Final report	12/6-9/83	12/16/83	P. Runge

Frederick G. Snyder
Director
Office of Quality Assurance

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

SUBJECT: Rat Teratology Study
Project No. 154-160

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

Study Director:

LAWRENCE T. WETZEL, Ph.D.
Staff Scientist
Department of Toxicology

Laboratory Supervision:

GEORGE A. BURDOCK, Ph.D.
Rodent Toxicology I
Department of Toxicology

Teratology:

RUTH S. DURLOO, B.S.
Research Associate
Department of Toxicology

Report Preparation:

BARBARA R. COLPEAN, B.A., B.S.
Technical Writer
Scientific Resources Department

tls

TABLE OF CONTENTS

TABLE OF CONTENTS - CONTINUED

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

SPONSOR: 3M Company

DATE: December 19, 1983

MATERIAL: T-3351

SUBJECT: FINAL REPORT
Rat Teratology Study
Project No. 154-160

SUMMARY

T-3351, suspended in corn oil at concentrations intended to deliver 1, 5, or 10 mg/kg/day (Groups 2, 3, and 4, respectively), was administered by oral intubation to mated female Sprague-Dawley 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.

Two Group 4 females died. Treatment-related clinical observations noted in Groups 3 and 4 included thinness, hunched appearances, rough haircoats, alopecia, and anorexia. Food consumed by Groups 3 and 4 animals was significantly less than control both during treatment and throughout gestation. Compared to control body weight gains, significantly less body weight was gained by Groups 3 and 4 females throughout gestation. Actual loss of body weight occurred in Groups 3 and 4 animals once treatment had been initiated. Terminal body weight minus gravid uterine weight was also significantly decreased in

Groups 3 and 4. Treatment-related gross pathology in Group 4 animals included incidences of gastrointestinal tract effects.

Statistical analysis revealed a positive treatment-related trend in fetal loss, attributable primarily to an increased incidence of late resorbing fetuses and dead fetuses in litters from Group 4 dams. Mean male and female fetal body weights were significantly decreased in fetuses Groups 3 and 4 litters. Significant increases in external and visceral anomalies occurred in fetuses from Group 4 dams and included subcutaneous edema, cleft palate, and cryptorchism. Anomalies were observed primarily in fetuses from Group 4 dams exhibiting signs of severe maternal toxicity, i.e., decreased food consumption and weight loss. Fetal toxicity manifested as increased numbers of late resorbing fetuses and dead fetuses, decreased fetal body weights, and delays in skeletal system ossification occurred in litters derived from that group as well.

The specificity and frequency of these results indicate that administration of T-3351 to pregnant rats during Days 6-15 of gestation at a dose of 10 mg/kg results in maternal toxicity, fetotoxicity and an increased incidence of external and visceral anomalies and skeletal variants.

T-3351 did not appear to be teratogenic in rats at dose levels less than or equal to 5 mg/kg.

INTRODUCTION

This study was designed to evaluate the embryo/fetal toxicity and teratogenic potential of T-3351 when administered by oral gavage to pregnant rats during the period of fetal organogenesis. The rats were placed in breeding on June 27, 1983, and cesarean sections were completed on July 26, 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-3351, a white powder, 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 sixty (one hundred thirty/sex) sexually mature, cesarean-derived Sprague-Dawley Crl:CD® (SD)BR rats were received from Charles River Breeding Laboratories, Inc., Kingston, New York, on June 8, 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, two male rats were euthanized due to an unthrifty appearance. Following an examination by a staff veterinarian for health status, one hundred twenty eight rats/sex were placed in breeding.

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 72.9°F ± 1.36 and the mean relative humidity ± the standard deviation was 69.1% ± 3.16 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 nine 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	5
4	25	10

[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.

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

Compound Preparation and Administration

Suspensions of the test material in the corn oil vehicle were prepared on a weight per volume basis. The required amount of compound for each level was 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 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. Prepared suspensions were mixed with a magnetic stirrer during dosing.

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.

Fresh dosing suspensions were prepared weekly and stored under refrigeration (approximately 40^{o}F). Samples of each test mixture as well as the vehicle were sent to the sponsor for analysis.

Maternal Observations and Records

All animals were examined twice daily for mortality and moribundity (from day of receipt through animal sacrifice) and 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 presumed gestation. Food consumption during gestation was determined on Days 6, 8, 12, 16, and 20.

Cesarean Sacrifice

A gross necropsy was performed on all females found dead or terminally sacrificed. The uterus and ovaries from found dead females were removed and examined for the number of implantation sites and corpora lutea. Prior to terminal sacrifice and cesarean section on Day 20 of gestation, all surviving females were assigned random numbers so that all personnel performing cesarean sections and/or subsequent 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 surviving 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 uterine implantation sites, number of live and dead fetuses, number of early and late resorbing fetuses, and any abnormalities. The uterus was not reweighed after the contents were removed. 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 was fixed in Bouin's solution and sectioned by the Wilson Technique for assessing soft tissue development (Wilson and Warkany, 1965). During visceral examination of the fetuses, particular attention was paid to examination of the eyes, palate, and brain. Stainless-steel razor blades were used for sectioning procedures.

Skeletal Examination of Fetuses

The remaining fetuses were eviscerated and placed in 95% ethyl alcohol. After proper fixation and dehydration, the skeletons were macerated and stained in 1% KOH with an alizarin red solution, and cleared in 30% 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 presented on the following page.

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, percent fetal viability, percent fetal loss (dead and resorbing fetuses), percent early, late, and total resorptions, and the number of dead fetuses were analyzed by nonparametric one-way ANOVA (Kruskal and Wallis, 1952, 1953; Miller, 1966) and the Terpstra-Jonckheere test for trend (Terpstra, 1952; Jonckheere, 1954). The litter was used as the experimental unit. The teratology data listed on the next page 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).

Visceral Anomalies	Skeletal Variants
Subcutaneous edema	Skull
Cleft palate	Pectoral girdle
Cryptorchism	Rib cage
Number of litters affected	Vertebral column
Number of fetuses affected	Pelvic girdle
	Limbs
	Bone alignment
	Number of litters affected
	Number of fetuses affected

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.

Two Group 4 females were found dead on Day 17 prior to cesarean section on Day 20 of gestation. No other animals were found dead or sacrificed *in extremis* during the study.

Treatment-related clinical observations were noted in several of the Groups 3 and 4 animals during the treatment and posttreatment phases. These observations included hunched and thin appearances, anorexia, bloody discharge from vagina, urine stains, alopecia, rough haircoat and bloody crust.

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.

Statistical analysis revealed a significantly lower than control mean body weight gain in the Groups 3 and 4 females for Days 6-8, 6-16, and 0-20 of presumed gestation. These findings were considered to be treatment related since, compared to the treatment phase, there was a proportionally greater than control increase in mean body weight gain in the treated females during the posttreatment phase (Days 16-20).

Mean total food consumption was significantly lower in the Group 4 females during Days 17-20. Significant decreases in mean food consumption were also noted in the Groups 3 and 4 females during Days 7-16 and 0-20 of presumed gestation when compared to control, concomitant with the decrease in body weight gain during the same intervals.

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.

The mean gravid uterine weight of the Group 4 females was significantly lower than control. The mean terminal body weights minus the gravid uterine weights were lower in the treated groups when compared to the control group, with significant decreases noted in the Groups 3 and 4 females.

Gross Pathology

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

An increased incidence of stomach lesions was noted in the Group 4 animals. Remaining gross pathology findings were considered incidental.

RESULTS - CESAREAN DATA

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 incidence of early resorptions was comparable between the control and treated groups. Nonparametric analyses of the mean incidence of late resorptions, total resorptions, number of dead fetuses, and fetal loss did not indicate statistical significance. However, there was a significant linear trend towards an increased incidence in these data with respect to control. The primary trend component was contributed by the high-dose group. The mean fetal weights of the Groups 3 and 4 males and females were significantly lower than their respective controls. The percent of male fetuses was 52.29%, 54.24%, and 60.38% for Groups 2, 3, and 4, respectively, and 44.01% for the control group.

Fetal Development

Statistically significant findings in the teratology data are presented in the following chart:

Statistically Significant Teratology Data

Teratology Observation	Group: 2	3	4	Trend	Departure from Trend
Visceral anomalies					
Subcutaneous edema			S+	S	S
Cleft palate			S+	S	S
Cryptorchism			S+	S	NS
Number of litters affected			S+	S	NS
Number of fetuses affected			S+	S	S
Skeletal variants					
Skull	S+		S+	S	S
Pectoral girdle			S+	S	S
Rib cage		S+	S+	S	S
Vertebral column			S+	S	S
Pelvic girdle	S-		S+	S	S
Limbs			S+	S	S
Bone alignment			S+	S	NS
Number of litters affected				S	NS
Number of fetuses affected			S+	S	S

S = Significant
NS = Not significant

Significant treatment-related increases in the incidences of visceral anomalies and skeletal variants were noted in the Group 4 fetuses.

The number of Group 4 litters containing anomalous fetuses was also significantly increased compared to control. External and visceral anomalies observed included cleft palate, subcutaneous edema, and cryptorchism. Those anomalies occurred primarily in fetuses derived from litters whose mean male or female pup body weights were significantly below those of the corresponding control litters. Dams producing affected litters had significantly decreased food consumption throughout treatment and decreased body weight gain or actual body weight loss during gestation. Numerous clinical signs of toxicity were also present in these animals.

Table 1
Summary of Maternal Clinical Observations[a]
Rat Teratology Study of T-3351

	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
Observation — Dose Level (mg/kg):	0	1	5	10	0	1	5	10	0	1	5	10
Number of females examined	25	25	25	25	25	25	25	25	25	25	25	25
Number of females appearing normal	25	25	25	25	21	21	16	11	21	20	17	5
Number of females found dead or sacrificed prior to Day 20	0	0	0	0	0	0	0	0	0	0	0	2
Hunched							2	7			2	16
Thin						1	1	7			2	15
Anorexia								1			1	11
Ataxia												1
Sensitive to touch								1				1
Soft feces								1				
Bloody discharge from vagina												3
Urine stains								1	1		1	5
Alopecia					3	3	5	9	3	5	4	12
Rough haircoat							6	6	1		2	13
Bloody crust									1		1	6
Small eye							1				1	
Swollen neck					1							

[a]Numerals indicate the number of animals with that particular finding.

Table 2
Mean Maternal Body Weights and Body Weight Changes
Rat Teratology Study of T-3351

Body Weight	Day(s)		Group 1 0 mg/kg	Group 2 1 mg/kg	Group 3 5 mg/kg	Group 4 10 mg/kg
Mean Weight (g)	0		270.08	271.03	263.25	269.30
		N:	24	23	23	22
	6		298.47	296.05	292.80	297.72
		N:	24	23	23	22
	8		301.39	298.04	288.22	293.63
		N:	24	23	23	22
	12		318.31	308.18	290.09	276.25
		N:	24	23	23	22
	16		338.53	329.20	305.34	265.12
		N:	24	23	23	22
	20		395.41	389.69	367.11	301.91
		N:	24	23	23	22
Mean Change (g)	0-6		28.38	25.03	29.54	28.43
	6-8		2.93	1.99	-4.58[S-]	-4.05[S-]
	6-12		19.84	12.13	-2.70	-21.48
	6-16[F]		40.06	33.15	12.54[S-]	-32.60[S-]
	6-20		96.95	93.64	74.32	5.40
	16-20[F]		56.88	60.45	61.77	36.63
	0-20[F]		125.33	118.67	103.86[S-]	33.45[S-]

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

Table 3
Mean Maternal Food Consumption(g)
Rat Teratology Study of T-3351

Interval Days		Group 1 0 mg/kg	Group 2 1 mg/kg	Group 3 5 mg/kg	Group 4 10 mg/kg
0-6		132.67	128.01	134.92	133.33
	N:	24	23	23	22
7-8		37.48	35.03	31.53	37.64
	N:	24	23	22	22
9-12		74.58	68.38	59.58	36.86
	N:	24	23	20	18
13-16		78.52	68.45	57.89	22.75
	N:	24	23	20	19
17-20[F]		97.25	97.17	87.87	39.33[S-]
	N:	24	23	19	14
7-16[B]		190.58	171.85	147.91[S-]	97.63[S-]
	N:	24	23	19	17
0-20[B]		420.49	397.03	363.14[S-]	262.89[S-]
	N:	24	23	18	13

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-3351

Group and Dose Level		Terminal Body Weight	Gravid Uterine Weight[B]	Terminal Body Weight Minus Gravid Uterine Weight[F]
1		395.41	74.35	321.07
0 mg/kg	N:	24	24	24
2		389.69	75.59	314.10
1 mg/kg	N:	23	23	23
3		367.11	73.46	293.38[S-]
5 mg/kg	N:	23	22[a]	22[a]
4		301.91	60.51[S-]	241.40[S-]
10 mg/kg	N:	20	20	20

[a]The gravid uterine weight of one Group 3 female was inadvertently not recorded.
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-3351

Organ and Description	Group:	1	2	3	4
	Dose Level (mg/kg):	0	1	5	10
Number of animals examined		25	25	25	23 (2)
Number with no gross pathology		22	24	19	16 (0)
THYMUS					
Firm		1			
Enlarged		1			
LUNG					
Focal areas - dark red					1
HEART					
Right atrium enlarged					1
SPLEEN					
Enlarged		1			
Cystic					1
KIDNEY(S)					
Enlarged		1			
Irregularly shaped		1			
Pale		1		2	
Pelvis dilated			1	5	2 (1)
Constricted across midline				1	
Mottled tan and dark red				1	
Pelvis had a firm, white calculus			1		
ABDOMEN					
Tissue mass		1			

( ) = Findings in animals found dead during the study.

Table 5 - Continued
Summary of Maternal Gross Pathology Findings
Rat Teratology Study of T-3351

Organ and Description	Group:	1	2	3	4
	Dose Level (mg/kg):	0	1	5	10
STOMACH					
Glandular mucosa	- pitted areas				1
	- reddened				(1)
	- depressed area - red				(1)
Nonglandular mucosa	- raised area - dark (thin section in wall)				1
	- pinpoint, depressed areas				1
	- walls thin				(1)
	- thickened area - red				(1)
	- dark foci				1
Distended with dark red material					(1)
Contained yellow mucous					1
Walls thickened					1
Walls thin					(1)
PEYER'S PATCHES					
Enlarged/prominent		1			1
MANDIBULAR LYMPH NODES					
Reddened					1
ALL LYMPH NODES					
Enlarged		1			
URINARY BLADDER					
Walls thickened					1
Contained thick white fluid					1
OVARY(IES)					
Clear fluid-filled cyst		1			

( ) = Findings in animals found dead during the study.

Key to Tables 6-14

Pregnancy rate (percent) - (number of pregnant rats/number of rats mated) 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).

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

Key to Tables 6-14 - Continued

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).

Table 6
Summary of Mean Ovarian and Uterine Data
Rat Teratology Study of T-3351

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	5	10
Number of females with mating confirmed	25	25	25	25
Number of pregnant females	24	23	23	22
Pregnancy rate (%)	96	92	92	88
Number of females surviving to Day 20	25	25	25	23
Survival rate (%)	100	100	100	92
Mean number of:				
Corpora lutea	16.6	15.9	15.8	16.6
Implantations	14.5	14.4	14.6	14.4
Early resorptions	1.0	0.8	0.7	1.6
Late resorptions	0.0	0.0	0.0[a]	0.9
Total resorptions	1.0	0.8	0.7	2.4
Indices calculated on a per litter basis:				
Mean implantation efficiency (%)	87.90	91.14	92.70	87.72
Mean incidence of early resorptions (%)	7.00	5.53	4.70	11.32
Mean incidence of late resorptions (%)	0.00	0.00	0.29	5.10
Mean incidence of total resorptions (%)	7.00	5.53	5.00	16.42

[a]One late resorption was noted for female No. 27086, therefore, the actual mean was 0.04.

Table 7
Summary of Mean Litter Data[a]
Rat Teratology Study of T-3351

	Group:	1	2	3	4
	Dose Level (mg/kg):	0	1	5	10
Mean number of:					
Fetuses	- dead	0.0	0.0	0.0[b]	0.5
	- live	13.5	13.6	13.8	11.6
Indices calculated on a per litter basis:					
Mean incidence of fetal mortality (%)[c]		7.00	5.53	5.28	19.43
Mean incidence of fetal viability (%)		93.00	94.47	94.72	80.59
Mean percent males (%)		44.01	52.29	54.24	60.38
Live fetuses					
Mean body weight (g)[d]					
Males	- unadjusted mean	3.28	3.23	3.10	2.64
	- covariance adjusted mean	3.28	3.23	3.10[S-]	2.63[S-]
Females	- unadjusted mean	3.17	3.10	2.97	2.57
	- covariance adjusted mean	3.16	3.10	2.97[S-]	2.59[S-]

[a]Sex, percent males, and mean body weight data include values for live fetuses only.
[b]One dead fetus was noted for female No. 27101, therefore, the actual mean was 0.04.
[c]Percent mortality includes resorptions as well as dead fetuses.
[d]Statistical analysis performed on covariance adjusted means.

Table 8
Summary of External Findings
Rat Teratology Study of T-3351

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	5	10
Number of fetuses examined	325	313	317	231
Number of fetuses within normal limits	325	313	317	196
Number of fetuses with variants	0	0	0	0
Number of fetuses with anomalies	0	0	0	35
Number and type of anomalies	0	0	0	45
Skin - edematous				32
Palate - cleft				13

Table 9
Summary of Visceral Findings
Rat Teratology Study of T-3351

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	5	10
Number of fetuses examined	115	113	115	81
Number of fetuses within normal limits	111	105	108	56
Number of fetuses with variants	4	8	5	1
Number of fetuses with anomalies	0	1	2	24
Number and type of variants	4	10	5	1
Brain - cerebral hemisphere contained dark area	1			
Eye(s) - contained dark material				1
Liver - dark areas			1	
Kidney(s) - pelvis dilated		4	2	
Ureter(s) - distended	3	5	2	
- undulated		1		
Number and type of anomalies	0	1	3	44
Skin - edematous		1	1	21[a]
Palate - cleft				15[b]
Cryptorchism			2	8

[a]Twelve fetuses with edematous skin seen externally were confirmed at visceral examination.
[b]Four fetuses with cleft palate seen externally were confirmed at visceral examination.

Table 10
Summary of Skeletal Findings
Rat Teratology Study of T-3351

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	5	10
Number of fetuses examined	210	200	202	150
Number of fetuses within normal limits	134	113	135	63
Number of fetuses with variants	76	87	67	87
Number of fetuses with anomalies	0	0	0	0
Number and type of variants	150	193	147	349
Lagging ossification				
Skull - incomplete closure (<75%)	6	15	17	46
- interparietal ossification incomplete/nonossified	30	40	15	29
- parietals ossification irregular	1	14	1	
- supraoccipital ossification incomplete/nonossified	23	31	23	36
- supraoccipital nonfused	1			17
- hyoid ossification incomplete/nonossified	22	46	13	8
Pectoral girdle - scapula ossification incomplete				6
Rib cage - sternebrae bipartite		1	14	62
- sternebrae 1 and 2 fused	1			
- sternebrae <3 ossified	5	1	4	9
- ribs <13 ossified[a]		1		
- ribs >13 ossified (cervical region)			2	
- ribs 13th pair small[a]	4			
- ribs ossification irregular	1	2	1	
Vertebral column - sacral arches nonossified	2		2	13
- thoracic centra ossification incomplete/nonossified	18	20	18	15
- thoracic centra nonfused	10	12	5	6
- caudals <3 ossified	13	5	14	34
Pelvic girdle - pubis ossification incomplete/nonossified	8		4	15
--ischium nonossified	1		2	2
Forelimbs - <3 ossified	1		2	5
Hindlimbs - <4 ossified	2	1	6	36
Bone Alignment				
Ribs - angulated	1	4	4	9
Sternebrae - checkered				1

[a]Possible preparation damage at time of evisceration.

Table 11
Incidence of External Findings Per Litter
Rat Teratology Study of T-3351

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	5	10
Number of litters examined	24	23	23	18
Number of litters within normal limits	24	23	23	12
Number and percent of litters with variants	0/0.00	0/0.00	0/0.00	0/0.00
Number and percent of litters with anomalies	0/0.00	0/0.00	0/0.00	6/33.33
Number and percent of litters with anomalies				
Skin - edematous				4/22.22
Palate - cleft				6/33.33

Table 12
Incidence of Visceral Findings Per Litter
Rat Teratology Study of T-3351

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	5	10
Number of litters examined	24	23	23	18
Number of litters within normal limits	20	16	18	9
Number and percent of litters with variants	4/16.67	7/30.43	4/17.39	1/5.56
Number and percent of litters with anomalies	0/0.00	1/4.35	1/4.35	8/44.44
Number and percent with variants				
Brain - cerebral hemisphere contained dark area	1/4.17			
Eye(s) - contained dark material				1/5.56
Liver - dark areas			1/4.35	
Kidney(s) - pelvis dilated		4/17.39	2/8.70	
Ureter(s) - distended	3/12.50	5/21.74	2/8.70	
- undulated		1/4.35		
Number and percent with anomalies				
Skin - edematous		1/4.35	1/4.35	5/27.78
Palate - cleft				7/38.89
Cryptorchism			1/4.35	4/22.22

Table 13
Incidence of Skeletal Findings Per Litter
Rat Teratology Study of T-3351

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	5	10
Number of litters examined	24	23	23	18
Number of litters within normal limits	1	0	4	3
Number and percent of litters with variants	23/95.83	23/100.00	19/82.61	15/83.33
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%)	4/16.67	5/21.74	6/26.09	9/50.00
- interparietal ossification incomplete	15/62.50	11/47.83	8/34.78	9/50.00
- parietals ossification irregular	1/4.17	4/17.39	1/4.35	
- supraoccipital ossification incomplete	12/50.00	12/52.17	10/43.48	11/61.11
- supraoccipital nonfused	1/4.17			4/22.22
- hyoid ossification incomplete/nonossified	10/41.67	16/69.57	9/39.13	6/33.33
Pectoral girdle - scapula ossification incomplete				2/11.11
Rib cage - sternebrae bipartite		1/4.35	4/17.39	13/72.22
- sternebrae 1 and 2 fused	1/4.17			
- sternebrae <3 ossified	3/12.50	1/4.35	2/8.70	3/16.67
- ribs <13 ossified[a]		1/4.35		
- ribs >13 ossified (cervical region)			1/4.35	
- ribs 13th pair small[a]	1/4.17			
- ribs ossification irregular	1/4.17	1/4.35	1/4.35	
Vertebral column - sacral arches nonossified	2/8.33		1/4.35	6/33.33
- thoracic centra ossification incomplete/ nonossified	9/37.50	16/69.57	11/47.83	9/50.00
- thoracic centra nonfused	6/25.00	7/30.43	2/8.70	4/22.22
- caudals <3 ossified	6/25.00	4/17.39	5/21.74	7/38.89
Pelvic girdle - pubis ossification incomplete/nonossified	4/16.67		1/4.35	4/22.22
- ischium nonossified	1/4.17		1/4.35	1/5.56
Forelimbs - <3 ossified	1/4.17		1/4.35	3/16.67
Hindlimbs - <4 ossified	2/8.33	1/4.35	2/8.70	7/38.89
Bone alignment				
Ribs - angulated	1/4.17	2/8.70	2/8.70	4/22.22
Sternebrae - checkered				1/5.56

[a] ... ...mation damage at time of evisceration

Table 14
Mean Incidence of External, Visceral, and Skeletal Findings Per Litter
Rat Teratology Study of T-3351

Group:	1	2	3	4
Dose Level (mg/kg):	0	1	5	10
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	0.0	1.9
Incidence of variants (%)	0.0	0.0	0.0	0.0
Incidence of anomalies (%)	0.0	0.0	0.0	18.9
Visceral				
Mean values calculated on a per litter basis:				
Number with variants	0.2	0.3	0.2	0.1
Number with anomalies	0.0	0.0	0.1	1.3
Incidence of variants (%)	4.0	7.0	4.3	1.1
Incidence of anomalies (%)	0.0	0.7	1.5	31.7
Skeletal				
Mean values calculated on a per litter basis:				
Number with variants	3.2	3.8	2.9	4.8
Number with anomalies	0.0	0.0	0.0	0.0
Incidence of variants (%)	36.3	44.6	32.1	60.2
Incidence of anomalies (%)	0.0	0.0	0.0	0.0

154-160

Appendix 1
Individual Clinical Signs[a]
Rat Teratology Study of T-3351

Maternal Number	Group	Observation	Body Area	Day(s)
27032	1	Alopecia	Paw-fore-right	15-17
27034	1	Urine stains		18-20
		Bloody crust	Nose	20
		Swollen	Neck	9-20
27042	1	Alopecia	Paws-fore-both	8-20
27046	1	Alopecia	Paws-fore-both	10-11
27049	1	Alopecia	Abdomen	18-20
		Alopecia	Paw-fore-right	19-20
27057	2	Alopecia	Paw-fore-left	15
		Alopecia	Paw-fore-both	16-20
27059	2	Alopecia	Hip-right	10-14
		Alopecia	Leg-hind-right	15-20
		Alopecia	Side-right	10-20
27062	2	Thin		6
27063	2	Alopecia	Paw-fore-right	17-20
27065	2	Alopecia	Paw-fore-right	17-20
27066	2	Alopecia	Abdomen	15-20
27082	3	Alopecia	Hips-both	15-20
27083	3	Alopecia	Hip-right	14-20
27084	3	Hunched		15-19
		Thin		10, 15-19
		Alopecia	Leg-fore-right	10-14
		Alopecia	Leg-hind-right	10-12,14
		Rough haircoat		10-12
27085	3	Rough haircoat		7-12
27090	3	Rough haircoat		9-11
27091	3	Alopecia	Paws-fore-both	14-20
		Rough haircoat		8-11,13
27095	3	Hunched		8-9,11
		Rough haircoat		10-12,19-20
27099	3	Alopecia	Hips-both	13-20
		Alopecia	Legs-hind-both	16-20
27100	3	Hunched		16-17,20
		Thin		16,20
		Anorexia		16,20
		Urine stains		18-20
		Rough haircoat		16,20
		Bloody crust	Eyelids-both	20
		Bloody crust	Mouth	20
		Bloody crust	Nose	20
		Bloody crust	Paws-fore-both	20
27101	3	Rough haircoat		8-9
		Small	Eye-left	15-20

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

Appendix 1 - Continued
Individual Clinical Signs[a]
Rat Teratology Study of T-3351

Maternal Number	Group	Observation	Body Area	Day(s)
27107	4	Hunched		18-20
		Thin		13-17
		Rough haircoat		13-20
27109	4	Hunched		9-12,14-20
		Thin		10-20
		Anorexia		16,18-20
		Sensitive to touch		10-14,16-18,20
		Alopecia	Hips-both	11-20
		Alopecia	Hip-left	10
		Rough haircoat		13-20
		Bloody crust	Mouth	20
		Bloody crust	Nose	20
27111	4	Alopecia	Abdomen	10-20
		Alopecia	Hips-both	10-20
27112	4	Hunched		18-20
		Thin		15-20
		Anorexia		17-20
		Urine stains		19-20
		Rough haircoat		16-20
		Bloody crust	Mouth	20
		Bloody crust	Nose	20
27113	4	Hunched		20
		Thin		12,20
		Anorexia		12,17-18,20
		Urine stains		14-18,20
		Alopecia	Abdomen	11-19
		Alopecia	Hips-both	9-18
		Alopecia	Hip-left	8,19-20
		Alopecia	Neck	8-18
		Rough haircoat		15-20
		Bloody crust	Mouth	16-20
		Bloody crust	Nose	16-20
		Bloody crust	Paws-fore-both	16-20
		Bloody crust	Vagina	18-19
27114	4	Hunched		13-20
		Thin		12,20
		Anorexia		17-20
		Rough haircoat		18-19
27115	4	Alopecia	Sides-both	8-13
		Alopecia	Side-right	14-20
27116	4	Alopecia	Paw-fore-left	19-20
27117	4	Hunched		14-20
		Thin		17,19-20
		Anorexia		16-20

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

Appendix 1 - Continued
Individual Clinical Signs[a]
Rat Teratology Study of T-3351

Maternal Number	Group	Observation	Body Area	Day(s)
27117	4	Urine stains		16-20
		Rough haircoat		9-20
		Bloody crust	Genitals	20
		Bloody crust	Mouth	16-20
		Bloody crust	Nose	18-20
		Bloody crust	Paws-fore-both	16-20
27118	4	Hunched		16-20
		Thin		16-17,19-20
		Anorexia		19
		Rough haircoat		16-18
27119	4	Hunched		12-20
		Thin		16-20
		Anorexia		16-18,20
		Ataxia		18-20
		Soft feces		8-10
		Bloody discharge	Vagina	19-20
		Urine stains		18-20
		Alopecia	Hip-left	11
		Alopecia	Hip-right	12-20
		Alopecia	Inguinal-right	13-18
		Alopecia	Side-right	15-20
		Rough haircoat		20
27120	4	Hunched		16
		Thin		16
		Anorexia		16
		Bloody discharge	Vagina	16
		Rough haircoat		16
		Found dead		17
27121	4	Hunched		7-9,11-17
		Thin		7-16
		Rough haircoat		7-11
27122	4	Hunched		16-17
27123	4	Alopecia	Abdomen	10-20
		Alopecia	Hip-right	12-20
		Alopecia	Leg-hind-right	20
		Alopecia	Side-right	18-20
27125	4	Hunched		16-20
		Thin		16,18-20
		Anorexia		16-17,20
		Alopecia	Abdomen	15-20
		Rough haircoat		8-9
		Bloody crust	Paws-fore-both	19-20

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

Appendix 1 - Continued
Individual Clinical Signs[a]
Rat Teratology Study of T-3351

Maternal Number	Group	Observation	Body Area	Day(s)
27126	4	Hunched		18,20
		Thin		19
		Anorexia		16-17,20
		Alopecia	Hip-left	17-20
27127	4	Hunched		16
		Thin		16
		Bloody discharge	Vagina	16
		Rough haircoat		16
		Found dead		17
27128	4	Hunched		14-20
		Thin		14-20
		Anorexia		17-18,20
		Alopecia	Paw-fore-right	15-17
		Rough haircoat		18-20
27129	4	Hunched		14-20
		Thin		16-20
		Anorexia		16
		Urine stains		19
		Rough haircoat		16-20
		Bloody crust	Paws-fore-both	16

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

Key to Appendices 2, 3, and 4

P = Pregnant

NP = Not Pregnant

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

D = Death (preceded by day of gestation)

MS = Moribund Sacrifice (preceded by day of gestation)

ND = Natural Delivery (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]Gavid uterine weight inadvertently not recorded.

Appendix 2
Individual and Mean Maternal Body Weights and Body Weight Changes[a]
Rat Teratology Study of T-3351
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[F]	0-20[F]
27030	P, 20-C	277.3	303.8	306.8	340.3	358.6	422.5	26.5	3.0	36.5	54.8	118.7	63.9	145.2
27031	P, 20-C	261.9	288.8	284.4	314.1	329.2	388.2	26.9	-4.4	25.3	40.4	99.4	59.0	126.3
27032	P, 20-C	245.7	282.0	292.1	317.5	338.6	404.3	36.3	10.1	35.5	56.6	122.3	65.7	158.6
27033	P, 20-C	256.5	274.3	275.5	299.9	314.4	367.8	17.8	1.2	25.6	40.1	93.5	53.4	111.3
27034	P, 20-C	250.1	263.4	259.0	281.1	300.9	341.4	13.3	-4.4	17.7	37.5	78.0	40.5	91.3
27035	P, 20-C	312.7	351.5	351.0	362.4	353.6	446.6	38.8	-0.5	10.9	2.1	95.1	93.0	133.9
27036	P, 20-C	248.7	279.5	283.3	312.9	340.2	409.0	30.8	3.8	33.4	60.7	129.5	68.8	160.3
27037	NP, 20-C	(266.4)	(260.8)	(278.7)	(272.8)	(279.2)	(287.1)	(-5.6)	(17.9)	(12.0)	(18.4)	(26.3)	(7.9)	(20.7)
27038	P, 20-C	253.8	283.4	284.7	296.4	309.1	373.1	29.6	1.3	13.0	25.7	89.7	64.0	119.3
27039	P, 20-C	291.2	321.4	330.6	343.5	365.1	427.1	30.2	9.2	22.1	43.7	105.7	62.0	135.9
27040	P, 20-C	241.6	273.8	272.0	289.2	310.9	348.8	32.2	-1.8	15.4	37.1	75.0	37.9	107.2
27041	P, 20-C	241.1	277.3	281.2	293.5	319.9	374.1	36.2	3.9	16.2	42.6	96.8	54.2	133.0
27042	P, 20-C	259.8	286.6	294.7	307.2	333.2	381.9	26.8	8.1	20.6	46.6	95.3	48.7	122.1
27043	P, 20-C	287.1	310.9	318.1	334.8	345.6	368.2	23.8	7.2	23.9	34.7	57.3	22.6	81.1
27044	P, 20-C	278.7	297.4	297.9	302.5	336.5	390.8	18.7	0.5	5.1	39.1	93.4	54.3	112.1
27045	P, 20-C	278.0	316.0	312.9	328.4	342.8	381.8	38.0	-3.1	12.4	26.8	65.8	39.0	103.8
27046	P, 20-C	269.8	293.6	294.1	313.2	336.0	384.5	23.8	0.5	19.6	42.4	90.9	48.5	114.7
27047	P, 20-C	294.0	323.6	320.1	314.5	317.3	371.1	29.6	-3.5	-9.1	-6.3	47.5	53.8	77.1
27048	P, 20-C	298.5	327.7	330.5	352.0	378.8	438.8	29.2	2.8	24.3	51.1	111.1	60.0	140.3
27049	P, 20-C	270.1	310.1	327.1	343.1	376.1	447.0	40.0	17.0	33.0	66.0	136.9	70.9	176.9
27050	P, 20-C	260.5	285.3	293.6	316.8	334.3	392.5	24.8	8.3	31.5	49.0	107.2	58.2	132.0
27051	P, 20-C	276.0	306.6	307.2	321.4	345.4	399.4	30.6	0.6	14.8	38.8	92.8	54.0	123.4
27052	P, 20-C	275.2	299.0	306.6	327.1	356.8	422.2	23.8	7.6	28.1	57.8	123.2	65.4	147.0
27053	P, 20-C	280.8	306.0	303.6	294.2	329.6	396.2	25.2	-2.4	-11.8	23.6	90.2	66.6	115.4
27054	P, 20-C	272.9	301.2	306.4	333.4	351.8	412.6	28.3	5.2	32.2	50.6	111.4	60.8	139.7
N		24	24	24	24	24	24	24	24	24	24	24	24	24
Mean		270.8	298.47	301.39	318.31	338.53	395.41	28.38	2.93	19.84	40.06	96.95	56.88	125.33
S.D.		18.790	20.580	21.463	21.071	20.479	28.666	6.658	5.364	12.585	16.908	21.937	13.752	24.174

Appendix 2 - Continued
Individual and Mean Maternal Body Weights and Body Weight Changes[a]
Rat Teratology Study of T-3351
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[F]	0-20[F]
27055	P, 20-C	268.7	290.8	294.2	310.5	329.2	381.3	22.1	3.4	19.7	38.4	90.5	51.2	112.6
27056	P, 20-C	294.4	318.8	323.2	343.3	360.2	429.0	24.4	4.4	24.5	41.4	110.2	68.8	134.6
27057	P, 20-C	262.2	286.5	282.8	295.7	301.7	372.2	24.3	-3.7	9.2	15.2	85.7	70.5	110.0
27058	P, 20-C	282.2	312.0	300.5	327.1	344.7	401.1	29.8	-11.5	15.1	32.7	89.1	56.4	118.9
27059	P, 20-C	267.8	304.9	302.4	312.6	324.8	388.4	37.1	-2.5	7.7	19.9	83.5	63.6	120.6
27060	NP, 20-C	(253.4)	(272.7)	(272.7)	(289.5)	(269.3)	(272.1)	(19.3)	(0.0)	(16.8)	(-3.4)	(-0.6)	(2.8)	(18.7)
27061	P, 20-C	270.1	301.0	296.4	303.2	319.8	379.4	30.9	-4.6	2.2	18.8	78.4	59.6	109.3
27062	P, 20-C	267.0	228.1	271.8	290.7	307.7	356.8	-38.9	43.7	62.6	79.6	128.7	49.1	89.8
27063	P, 20-C	267.9	298.0	294.7	295.1	317.3	378.7	30.1	-3.3	-2.9	19.3	80.7	61.4	110.8
27064	P, 20-C	261.8	296.0	301.8	314.7	325.3	388.7	34.2	5.8	18.7	29.3	92.7	63.4	126.9
27065	P, 20-C	259.8	299.4	294.0	302.8	329.0	397.8	39.6	-5.4	3.4	29.6	98.4	68.8	138.0
27066	P, 20-C	279.1	296.2	304.7	304.7	323.8	362.4	17.1	8.5	8.5	27.6	66.2	38.6	83.3
27067	P, 20-C	275.5	307.7	304.5	305.8	336.6	385.5	32.2	-3.2	-1.9	28.9	77.8	48.9	110.0
27068	P, 20-C	271.8	282.0	279.8	298.2	320.1	386.8	10.2	-2.2	16.2	38.1	104.8	66.7	115.0
27069	P, 20-C	283.0	314.4	317.6	329.3	355.7	413.7	31.4	3.2	14.9	41.3	99.3	58.0	130.7
27070	P, 20-C	263.6	289.4	299.7	292.4	329.6	397.6	25.8	10.3	3.0	40.2	108.2	68.0	134.0
27071	P, 20-C	265.6	291.9	293.7	295.5	300.2	377.8	26.3	1.8	3.6	8.3	85.9	77.6	112.2
27072	P, 20-C	286.2	310.4	316.6	311.1	338.9	413.3	24.2	6.2	0.7	28.5	102.9	74.4	127.1
27073	P, 20-C	275.6	301.6	290.7	306.7	334.3	407.8	26.0	-10.9	5.1	32.7	106.2	73.5	132.2
27074	P, 20-C	278.4	324.3	324.8	350.4	380.5	436.3	45.9	0.5	26.1	56.2	112.0	55.8	157.9
27075	P, 20-C	265.7	288.3	292.0	302.4	324.4	372.3	22.6	3.7	14.1	36.1	84.0	47.9	106.6
27076	P, 20-C	259.5	290.7	285.9	294.6	316.1	370.8	31.2	-4.8	3.9	25.4	80.1	54.7	111.3
27077	P, 20-C	262.8	293.6	292.5	304.5	328.6	388.4	30.8	-1.1	10.9	35.0	94.8	59.8	125.6
27078	P, 20-C	264.9	283.2	290.6	296.8	323.2	276.8	18.3	7.4	13.6	40.0	93.6	53.6	111.9
27079	NP, 20-C	(258.5)	(281.7)	(275.7)	(275.5)	(274.5)	(273.1)	(23.2)	(-6.0)	(-6.2)	(-7.2)	(-8.6)	(-1.4)	(14.6)
N		23	23	23	23	23	23	23	23	23	23	23	23	23
Mean		271.03	296.05	298.04	308.18	329.20	389.69	25.03	1.99	12.13	33.15	93.64	60.45	118.67
S.D.		9.265	18.650	13.221	15.771	18.312	20.073	15.895	10.774	13.617	14.547	14.164	9.823	16.015

Appendix 2 - Continued
Individual and Mean Maternal Body Weights and Body Weight Changes[a]
Rat Teratology Study of T-3351
Group 3 - 5 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[F]	0-20[F]
27080	P, 20-C	277.9	309.2	305.7	310.1	343.9	425.3	31.3	-3.5	0.9	34.7	116.1	81.4	147.4
27081	P, 20-C	267.1	291.4	286.9	289.2	299.9	355.0	24.3	-4.5	-2.2	8.5	63.6	55.1	87.9
27082	P, 20-C	256.1	285.0	273.2	279.5	285.2	352.7	28.9	-11.8	-5.5	0.2	67.7	67.5	96.6
27083	P, 20-C	272.9	301.1	300.1	306.6	306.0	361.1	28.2	-1.0	5.5	4.9	60.0	55.1	88.2
27084	NP, 20-C	(258.7)	(300.9)	(276.1)	(286.3)	(246.5)	(279.4)	(42.2)	(-24.8)	(-14.6)	(-54.4)	(-21.5)	(32.9)	(20.7)
27085	P, 20-C	277.1	295.2	284.7	307.1	329.1	382.6	18.1	-10.5	11.9	33.9	87.4	53.5	105.5
27086	P, 20-C	261.3	286.3	282.7	296.2	312.2	372.1	25.0	-3.6	9.9	25.9	85.8	59.9	110.8
27087	P, 20-C	274.0	305.8	294.1	304.9	318.0	415.7	31.8	-11.7	-0.9	12.2	109.9	97.7	141.7
27088	P, 20-C	229.6	251.5	251.1	263.7	269.9	342.9	21.9	-0.4	12.2	18.4	91.4	73.0	113.3
27089	P, 20-C	261.6	293.4	285.4	298.2	317.1	374.7	31.8	-8.0	4.8	23.7	81.3	57.6	113.1
27090	P, 20-C	224.7	243.2	245.8	242.7	255.1	308.6	18.5	2.6	-0.5	11.9	65.4	53.5	83.9
27091	P, 20-C	252.6	287.0	280.5	275.3	302.8	360.9	34.4	-6.5	-11.7	15.8	73.9	58.1	108.3
27092	P, 20-C	276.0	309.1	302.2	290.6	316.9	391.3	33.1	-6.9	-18.5	7.8	82.2	74.4	115.3
27093	P, 20-C	265.5	297.3	286.9	291.6	312.3	373.2	31.8	-10.4	-5.7	15.0	75.9	60.9	107.7
27094	P, 20-C	251.7	281.2	289.4	299.6	312.2	372.0	29.5	8.2	18.4	31.0	90.8	59.8	120.3
27095	P, 20-C	276.7	305.1	297.7	300.1	336.2	410.4	28.4	-7.4	-5.0	31.1	105.3	74.2	133.7
27096	P, 20-C	270.6	301.2	298.7	278.9	278.3	358.6	30.6	-2.5	-22.3	-22.9	57.4	80.3	88.0
27097	P, 20-C	290.8	319.7	320.5	314.7	335.8	398.7	28.9	0.8	-5.0	16.1	79.0	62.9	107.9
27098	P, 20-C	273.0	299.8	292.0	293.6	313.4	371.5	26.8	-7.8	-6.2	13.6	71.7	58.1	98.5
27099	P, 20-C	259.1	290.0	273.1	287.4	302.7	366.1	30.9	-16.9	-2.6	12.7	76.1	63.4	107.0
27100	P, 20-C	282.8	320.2	310.5	295.4	269.8	254.1	37.4	-9.7	-24.8	-50.4	-66.1	-15.7	-28.7
27101	P, 20-C	276.5	294.0	293.3	280.3	305.1	357.0	17.5	-0.7	-13.7	11.1	63.0	51.9	80.5
27102	P, 20-C	260.4	280.0	281.7	289.9	308.9	369.0	19.6	1.7	9.9	28.9	89.0	60.1	108.6
27103	P, 20-C	216.8	287.6	292.8	276.5	292.0	370.1	70.8	5.2	-11.1	4.4	82.5	78.1	153.3
27104	NP, 20-C	(272.7)	(282.9)	(274.9)	(251.1)	(253.7)	(275.4)	(10.2)	(-8.0)	(-31.8)	(-29.2)	(-7.5)	(21.7)	(2.7)
N		23	23	23	23	23	23	23	23	23	23	23	23	23
Mean		263.25	292.80	288.22	290.09	305.34	367.11	29.54	-4.58[S-]	-2.70	12.54[S-]	74.32	61.77	103.86[S-]
S.D.		18.525	18.070	16.876	16.252	22.346	35.036	10.523	6.103	11.235	18.834	34.272	20.386	34.851

Appendix 2 - Continued
Individual and Mean Maternal Body Weights and Body Weight Changes[a]
Rat Teratology Study of T-3351
Group 4 - 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[F]	0-20[F]
27105	P, 20-C	279.5	303.4	293.2	286.8	281.4	364.7	23.9	-10.2	-16.6	-22.0	61.3	83.3	85.2
27106	P, 20-C	274.9	310.7	302.2	307.5	322.7	378.4	35.8	-8.5	-3.2	12.0	67.7	55.7	103.5
27107	P, 20-C	239.1	255.2	255.3	228.0	212.7	271.7	16.1	0.1	-27.2	-42.5	16.5	59.0	32.6
27108	P, 20-C	285.4	315.6	312.0	299.7	291.7	377.2	30.2	-3.6	-15.9	-23.9	61.6	85.5	91.8
27109	P, 20-C	273.2	301.8	287.7	250.3	230.3	209.3	28.6	-14.1	-51.5	-71.5	-92.5	-21.0	-63.9
27110	P, 20-C	254.7	293.1	279.3	273.3	261.4	325.9	38.4	-13.8	-19.8	-31.7	32.8	64.5	71.2
27111	P, 20-C	269.9	300.4	301.1	305.9	309.8	386.7	30.5	0.7	5.5	9.4	86.3	76.9	116.8
27112	P, 20-C	251.7	281.3	281.0	274.7	238.2	222.8	29.6	-0.3	-6.6	-43.1	-58.5	-15.4	-28.9
27113	P, 20-C	294.6	334.6	318.1	274.5	254.1	235.3	40.0	-16.5	-60.1	-80.5	-99.3	-18.8	-59.3
27114	P, 20-C	287.0	318.2	313.0	282.1	254.4	240.5	31.2	-5.2	-36.1	-63.8	-77.7	-13.9	-46.5
27115	P, 20-C	242.9	274.3	271.1	263.1	265.6	351.6	31.4	-3.2	-11.2	-8.7	77.3	86.0	108.7
27116	P, 20-C	241.8	275.6	278.7	274.7	270.3	340.0	33.8	3.1	-0.9	-5.3	64.4	69.7	98.2
27117	P, 20-C	303.0	339.4	339.1	289.8	271.4	247.2	36.4	-0.3	-49.6	-68.0	-92.2	-24.2	-55.8
27118	NP, 20-C	(272.6)	(273.3)	(275.3)	(256.5)	(224.9)	(206.6)	(0.7)	(2.0)	(-16.8)	(-48.4)	(-66.7)	(-18.3)	(-66.0)
27119	P, 20-C	255.6	286.4	279.3	244.3	221.8	180.7	30.8	-7.1	-42.1	-64.6	-105.7	-41.1	-74.9
27120	P, 17-D	295.4	326.3	329.7	292.4	271.0	-	30.9	3.4	-33.9	-55.3	-	-	-
27121	P, 20-C	264.4	281.4	269.3	268.4	265.2	349.6	17.0	-12.1	-13.0	-16.2	68.2	84.4	85.2
27122	P, 20-C	253.4	275.6	277.7	270.4	265.5	331.3	22.2	2.1	-5.2	-10.1	55.7	65.8	77.9
27123	P, 20-C	310.8	332.5	338.2	319.2	335.4	414.9	21.7	5.7	-13.3	2.9	82.4	79.5	104.1
27124	P, 20-C	264.3	283.2	292.5	278.9	296.7	366.8	18.9	9.3	-4.3	13.5	83.6	80.1	102.5
27125	P, 20-C	251.8	277.0	275.9	248.9	223.2	211.4	25.2	-1.1	-28.1	-53.8	-65.6	-11.8	-40.4
27126	P, 20-C	271.2	290.5	286.2	270.0	243.9	232.2	19.3	-4.3	-20.5	-46.6	-58.3	-11.7	-39.0
27127	P, 17-D	259.9	293.4	280.2	274.5	245.9	-	33.5	-13.2	-18.9	-47.5	-	-	-
27128	NP, 20-C	(263.6)	(286.2)	(283.9)	(270.1)	(225.1)	(189.7)	(22.6)	(-2.3)	(-16.1)	(-61.1)	(-96.5)	(-35.4)	(-73.9)
27129	NP, 20-C	(297.0)	(299.5)	(293.5)	(259.4)	(234.6)	(256.8)	(2.5)	(-6.0)	(-40.1)	(-64.9)	(-42.7)	(22.2)	(-40.2)
N		22	22	22	22	22	20	22	22	22	22	20	20	20
Mean		269.30	297.72	293.63	276.25	265.12	301.91	28.43	-4.05[S-]	-21.48	-32.60[S-]	5.40	36.63	33.45[S-]
S.D.		20.329	22.698	22.916	21.762	32.153	73.253	6.951	7.115	17.769	29.333	75.133	48.285	73.412

154-160

Appendix 3
Individual and Mean Food Consumption[a]
Rat Teratology Study of T-3351
Group 1 - 0 mg/kg

Maternal Number	Food Consumption (g) Interval (Days of Gestation)						
	0-6	7-8	9-12	13-16	17-20[F]	7-16[B]	0-20[B]
27030	140.9	42.8	92.5	87.1	101.7	222.4	465.0
27031	130.0	33.1	73.2	71.3	91.1	177.6	398.7
27032	140.6	45.5	86.1	82.2	106.4	213.8	460.8
27033	123.7	32.0	75.8	80.6	96.6	188.4	408.7
27034	80.6	18.6	48.8	51.9	67.8	119.3	267.7
27035	166.0	44.7	69.8	44.8	109.1	159.3	434.4
27036	139.2	36.2	80.9	86.8	106.4	203.9	449.5
27037	(113.8)	(30.1)	(52.2)	(55.2)	(69.7)	(137.5)	(321.0)
27038	134.9	33.4	75.9	77.9	107.0	187.2	429.1
27039	145.4	43.3	76.8	91.6	107.8	211.7	464.9
27040	122.3	31.8	69.7	71.1	84.5	172.6	379.4
27041	129.9	37.2	72.2	73.0	86.5	182.4	398.8
27042	136.1	42.9	79.5	80.1	95.8	202.5	434.4
27043	142.4	44.6	89.5	81.5	93.0	215.6	451.0
27044	141.2	34.2	60.6	78.7	99.0	173.5	413.7
27045	146.9	39.1	79.1	69.4	78.4	187.6	412.9
27046	115.9	37.6	75.8	78.1	95.4	191.5	402.8
27047	123.4	29.7	41.8	82.6	71.8	154.1	349.3
27048	144.5	42.4	91.7	93.5	113.4	227.6	485.5
27049	149.3	51.3	90.8	97.7	116.4	239.8	505.5
27050	119.5	36.5	77.6	72.1	92.5	186.2	398.2
27051	132.7	36.6	74.9	74.4	112.2	185.9	430.8
27052	127.1	39.8	81.3	85.5	106.4	206.6	440.1
27053	125.0	36.2	47.1	97.3	96.7	180.6	402.3
27054	126.5	30.1	78.4	75.2	98.1	183.7	408.3
N	24	24	24	24	24	24	24
Mean	132.67	37.48	74.58	78.52	97.25	190.58	420.49
S.D.	15.924	6.812	13.416	12.317	12.693	25.916	47.701

Appendix 3 - Continued
Individual and Mean Food Consumption[a]
Rat Teratology Study of T-3351
Group 2 - 1 mg/kg

Maternal Number	Food Consumption (g) Interval (Days of Gestation)						
	0-6	7-8	9-12	13-16	17-20[F]	7-16[B]	0-20[B]
27055	122.0	35.2	63.7	71.0	92.5	169.9	384.4
27056	136.0	42.1	74.1	69.7	108.9	185.9	430.8
27057	130.8	35.2	68.0	49.6	88.6	152.8	372.2
27058	136.5	29.1	70.2	69.0	98.0	168.3	402.8
27059	141.7	38.2	64.5	71.2	112.1	173.9	427.7
27060	(108.2)	(30.2)	(67.9)	(39.8)	(77.9)[b]	(137.9)	(324.0)[b]
27061	131.5	31.6	62.8	66.0	91.3	160.4	383.2
27062	55.7	38.6	81.8	68.6	70.3	189.0	315.0
27063	135.6	34.2	61.4	70.9	98.7	166.5	400.8
27064	143.0	39.1	73.5	55.3	99.4	167.9	410.3
27065	145.9	34.7	63.1	81.3	116.9	179.1	441.9
27066	99.3	33.6	60.3	63.0	92.1	156.9	348.3
27067	144.9	35.2	63.6	72.8	88.5	171.6	405.0
27068	111.5	22.7	64.2	59.2	97.7	146.1	355.3
27069	145.8	40.4	72.6	77.0	94.0	190.0	429.8
27070	133.0	42.8	61.4	67.6	98.5	171.8	403.3
27071	119.6	34.9	60.6	41.5	101.4	137.0	358.0
27072	145.4	41.9	62.1	68.2	109.2	172.2	426.8
27073	105.6	24.4	62.8	100.6	107.1	187.8	400.5
27074	147.3	41.9	93.2	88.8	113.6	223.9	484.8
27075	127.0	40.7	72.7	68.2	84.3	181.6	392.9
27076	131.2	27.8	87.8	59.0	79.5	174.6	385.3
27077	126.4	28.1	63.2	70.0	95.9	161.3	383.6
27078	128.5	33.2	65.1	65.8	96.4	164.1	389.0
27079	(156.8)	(23.8)	(53.4)	(56.3)	(64.9)	(133.5)	(355.2)
N	23	23	23	23	23	23	23
Mean	128.01	35.03	68.38	68.45	97.17	171.85	397.03
S.D.	20.444	5.735	8.893	12.065	11.147	17.544	35.568

Appendix 3 - Continued
Individual and Mean Food Consumption[a]
Rat Teratology Study of T-3351
Group 3 - 5 mg/kg

Maternal Number	Food Consumption (g) Interval (Days of Gestation)						
	0-6	7-8	9-12	13-16	17-20[F]	7-16[B]	0-20[B]
27080	139.2	36.9	60.3	70.0	104.7	167.2	411.1
27081	139.9	34.5	48.3	60.9	82.8	143.7	366.4
27082	138.5	26.3	46.7	38.5	83.1	111.5	333.1
27083	136.1	42.7	64.6	39.5	73.4	146.8	356.3
27084	(141.5)	(21.4)	(53.2)	(11.2)	(74.2)	(85.8)	(301.5)
27085	127.7	23.3	55.7	66.7	80.5	145.7	353.9
27086	113.8	28.3	53.5	59.6	88.0	141.4	343.2
27087	146.0	32.2	(116.4)[b]	72.5	123.9	(221.1)[b]	(491.0)[b]
27088	118.1	(156.2)[b]	(86.5)[b]	(88.1)[b]	(109.3)[b]	(330.8)[b]	(558.2)[b]
27089	134.4	35.0	61.0	61.3	87.8	157.3	379.5
27090	97.9	28.3	46.9	52.3	74.7	127.5	300.1
27091	132.3	26.8	44.6	60.5	85.4	131.9	349.6
27092	147.3	36.2	153.0	67.1	95.0	256.3	498.6
27093	130.5	24.4	51.1	79.8	100.9	155.3	386.7
27094	168.5	40.4	72.5	69.0	96.1	181.9	446.5
27095	120.0	24.9	56.5	55.2	114.6	136.6	371.2
27096	136.2	34.6	(119.9)[b]	(160.8)[b]	(100.6)[b]	(315.3)[b]	(552.1)[b]
27097	145.1	40.9	57.8	53.6	100.9	152.3	398.3
27098	147.3	32.9	75.0	89.4	(135.8)[b]	197.3	(480.4)[b]
27099	177.4	26.6	67.0	(110.3)[b]	(108.9)[b]	(203.9)[b]	(490.2)[b]
27100	141.8	28.9	34.2	1.5	0.0	64.6	206.4
27101	118.9	30.1	44.0	65.1	91.9	139.2	350.0
27102	115.4	28.4	56.5	51.9	90.5	136.8	342.7
27103	130.8	31.1	42.4	43.4	95.3	116.9	343.0
27104	(138.8)	(24.5)	(27.8)	(36.9)	(64.3)	(89.2)	(292.3)
N	23	22	20	20	19	19	18
Mean	134.92	31.53	59.58	57.89	87.87	147.91[S-]	363.14[S-]
S.D.	17.356	5.567	24.302	18.350	24.771	38.131	59.846

154-160

Appendix 3 - Continued
Individual and Mean Food Consumption[a]
Rat Teratology Study of T-3351
Group 4 - 10 mg/kg

Maternal Number	Food Consumption (g) Interval (Days of Gestation)						
	0-6	7-8	9-12	13-16	17-20[F]	7-16[B]	0-20[B]
27105	126.5	30.6	41.5	17.9	80.0	90.0	296.5
27106	148.7	40.0	58.6	67.4	99.5	166.0	414.2
27107	110.0	144.4	23.6	54.2	(200.2)[b]	222.2	(532.4)[b]
27108	138.3	37.3	40.2	23.0	91.3	100.5	330.1
27109	140.5	31.7	(145.5)[b]	0.0	2.3	(177.2)[b]	(320.0)[b]
27110	143.2	31.3	55.7	35.6	85.0	122.6	350.8
27111	136.7	36.7	48.3	75.1	100.9	160.1	397.7
27112	128.9	33.8	40.1	1.6	0.0	75.5	204.4
27113	150.0	21.2	1.4	0.0	0.0	22.6	172.6
27114	142.9	30.8	21.3	0.0	1.1	52.3	196.1
27115	123.7	29.7	39.2	26.3	90.5	95.2	309.4
27116	117.4	29.0	86.5	57.1	(110.0)[b]	172.6	(400.0)[b]
27117	164.1	44.5	10.6	0.0	0.0	55.1	219.2
27118	(115.8)	(32.5)	(57.2)	(41.1)[b]	(24.9)	(130.8)[b]	(271.5)[b]
27119	124.6	28.9	15.2	0.2	0.0	44.3	168.9
27120	150.7	42.3	31.5	0.0	-	73.8	-
27121	98.5	24.3	(48.0)[b]	(126.3)[b]	(96.8)[b]	(198.6)[b]	(393.9)[b]
27122	120.6	33.5	44.3	(164.9)[b]	(152.0)[b]	(242.7)[b]	(515.3)[b]
27123	158.2	41.4	(66.2)[b]	54.5	(119.8)[b]	(162.1)[b]	(440.1)[b]
27124	137.6	34.5	(129.3)[b]	(196.3)[b]	(117.8)[b]	(360.1)[b]	(615.5)[b]
27125	115.0	28.1	17.1	0.0	0.0	45.2	160.2
27126	123.5	26.6	39.9	7.5	0.0	74.0	197.5
27127	133.7	27.5	48.4	11.8	-	87.7	-
27128	(122.7)	(31.5)	(41.1)	(20.4)[b]	(0.4)	(93.0)[b]	(216.1)[b]
27129	(113.0)	(27.9)	(15.7)	(0.0)	(72.2)	(43.6)	(228.8)
N	22	22	18	19	14	17	13
Mean	133.33	37.64	36.86	22.75	39.33[S-]	97.63[S-]	262.89[S-]
S.D.	16.209	24.571	20.179	26.380	46.891	54.321	90.464

154-160

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-3351.
Group 1 - 0 mg/kg

Maternal Number	Terminal Body Weight	Gravid Uterine Weight[B]	Terminal Body Weight Minus Gravid Uterine Weight[F]
27030	422.5	90.4	332.1
27031	388.2	90.9	297.3
27032	404.3	88.2	316.1
27033	367.8	67.8	300.0
27034	341.4	66.6	274.8
27035	446.6	97.3	349.3
27036	409.0	86.9	322.1
27037	Not Pregnant		
27038	373.1	69.2	303.9
27039	427.1	76.2	350.9
27040	348.8	54.7	294.1
27041	374.1	82.4	291.7
27042	381.9	80.1	301.8
27043	368.2	30.8	337.4
27044	390.8	80.6	310.2
27045	381.8	52.4	329.4
27046	384.5	72.3	312.2
27047	371.1	64.5	306.6
27048	438.8	74.0	364.8
27049	447.0	84.1	362.9
27050	392.5	74.8	317.7
27051	399.4	60.3	339.1
27052	422.2	83.1	339.1
27053	396.2	74.6	321.6
27054	412.6	82.1	330.5
N	24	24	24
Mean	395.41	74.35	321.07
S.D.	28.666	14.704	23.215

154-160

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-3351
Group 2 - 1 mg/kg

Maternal Number	Terminal Body Weight	Gravid Uterine Weight[B]	Terminal Body Weight Minus Gravid Uterine Weight[F]
27055	381.3	72.5	308.8
27056	429.0	88.5	340.5
27057	372.2	73.3	298.9
27058	401.1	86.5	314.6
27059	388.4	69.1	319.3
27060	Not Pregnant		
27061	379.4	69.2	310.2
27062	356.8	64.0	292.8
27063	378.7	67.4	311.3
27064	388.7	74.6	314.1
27065	397.8	80.0	317.8
27066	362.4	37.9	324.5
27067	385.5	76.1	309.4
27068	386.8	80.4	306.4
27069	413.7	83.7	330.0
27070	397.6	90.0	307.6
27071	377.8	77.8	300.0
27072	413.3	85.3	328.0
27073	407.8	84.7	323.1
27074	436.3	84.8	351.5
27075	372.3	77.3	295.0
27076	370.8	60.7	310.1
27077	388.4	83.2	305.2
27078	376.8	71.6	305.2
27079	Not Pregnant		
N	23	23	23
Mean	389.69	75.59	314.10
S.D.	20.073	11.458	14.093

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-3351
Group 3 - 5 mg/kg

Maternal Number	Terminal Body Weight	Gravid Uterine Weight[B]	Terminal Body Weight Minus Gravid Uterine Weight[F]
27080	425.3	103.9	321.4
27081	355.0	72.2	282.8
27082	352.7	72.4	280.3
27083	361.1	68.5	292.6
27084	Not Pregnant		
27085	382.6	89.8	292.8
27086	372.1	79.4	292.7
27087	415.7	76.6	339.1
27088	342.9	73.5	269.4
27089	374.7	71.2	303.5
27090	308.6	61.6	247.0
27091	360.9	75.3	285.6
27092	391.3	88.0	303.3
27093[C]	373.2	-	-
27094	372.0	71.2	300.8
27095	410.4	87.1	323.3
27096	358.6	65.4	293.2
27097	398.7	65.2	333.5
27098	371.5	68.0	303.5
27099	366.1	61.6	304.5
27100	254.1	48.2	205.9
27101	357.0	73.9	283.1
27102	369.0	72.9	296.1
27103	370.1	70.2	299.9
27104	Not Pregnant		
N	23	22	22
Mean	367.11	73.46	293.38[S-]
S.D.	35.036	11.486	28.235

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-3351
Group 4 - 10 mg/kg

Maternal Number	Terminal Body Weight	Gravid Uterine Weight[B]	Terminal Body Weight Minus Gravid Uterine Weight[F]
27105	364.7	82.3	282.4
27106	378.4	58.9	319.5
27107	271.7	54.6	217.1
27108	377.2	79.8	297.4
27109	209.3	72.2	137.1
27110	325.9	64.4	261.5
27111	386.7	86.5	300.2
27112	222.8	40.8	182.0
27113	235.3	43.3	192.0
27114	240.5	42.3	198.2
27115	351.6	82.4	269.2
27116	340.0	55.4	284.6
27117	247.2	38.5	208.7
27118	Not Pregnant		
27119	180.7	32.4	148.3
27120	Found Dead		
27121	349.6	71.7	277.9
27122	331.3	66.0	265.3
27123	414.9	79.4	335.5
27124	366.8	76.0	290.8
27125	211.4	39.7	171.7
27126	232.2	43.6	188.6
27127	Found Dead		
27128	Not Pregnant		
27129	Not Pregnant		
N	20	20	20
Mean	301.91	60.51[S-]	241.40[S-]
S.D.	73.253	17.739	59.517

Appendix 5
Individual and Mean Ovarian and Uterine Data
Rat Teratology Study of T-3351
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 (%)
27030	15	15	100.0	0	0.0	0	0.0	0	0.0
27031	17	17	100.0	1	5.9	0	0.0	1	5.9
27032	19	15	78.9	1	6.7	0	0.0	1	6.7
27033	19	15	78.9	3	20.0	0	0.0	3	20.0
27034	16	15	93.8	1	6.7	0	0.0	1	6.7
27035	20	18	90.0	1	5.6	0	0.0	1	5.6
27036	14	14	100.0	0	0.0	0	0.0	0	0.0
27037	Not Pregnant								
27038	16	14	87.5	2	14.3	0	0.0	2	14.3
27039	19	17	89.5	4	23.5	0	0.0	4	23.5
27040	16	13	81.3	1	7.7	0	0.0	1	7.7
27041	15	15	100.0	0	0.0	0	0.0	0	0.0
27042	17	15	88.2	1	6.7	0	0.0	1	6.7
27043	14	7	50.0	2	28.6	0	0.0	2	28.6
27044	18	16	88.9	1	6.3	0	0.0	1	6.3
27045	19	10	52.6	0	0.0	0	0.0	0	0.0
27046	13	13	100.0	0	0.0	0	0.0	0	0.0
27047	12	12	100.0	1	8.3	0	0.0	1	8.3
27048	15	15	100.0	1	6.7	0	0.0	1	6.7
27049	19	18	94.7	1	5.6	0	0.0	1	5.6
27050	17	14	82.4	0	0.0	0	0.0	0	0.0
27051	16	13	81.3	2	15.4	0	0.0	2	15.4
27052	16	15	93.8	0	0.0	0	0.0	0	0.0
27053	18	15	83.3	0	0.0	0	0.0	0	0.0
27054	18	17	94.4	0	0.0	0	0.0	0	0.0
Total	398	348		23		0		23	
N	24	24	24	24	24	24	24	24	24
Mean	16.6	14.5	87.90	1.0	7.00	0.0	0.00	1.0	7.00
S.D.	2.12	2.45	13.472	1.04	8.024	-	-	1.04	8.024

Appendix 5 - Continued
Individual and Mean Ovarian and Uterine Data
Rat Teratology Study of T-3351
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 (%)
27055	15	13	86.7	1	7.7	0	0.0	1	7.7
27056	17	16	94.1	1	6.3	0	0.0	1	6.3
27057	13	13	100.0	0	0.0	0	0.0	0	0.0
27058	15	15	100.0	1	6.7	0	0.0	1	6.7
27059	14	14	100.0	2	14.3	0	0.0	2	14.3
27060	Not Pregnant								
27061	12	11	91.7	0	0.0	0	0.0	0	0.0
27062	15	13	86.7	0	0.0	0	0.0	0	0.0
27063	14	13	92.9	1	7.7	0	0.0	1	7.7
27064	15	15	100.0	1	6.7	0	0.0	1	6.7
27065	17	16	94.1	0	0.0	0	0.0	0	0.0
27066	11	7	63.6	1	14.3	0	0.0	1	14.3
27067	16	16	100.0	2	12.5	0	0.0	2	12.5
27068	19	16	84.2	1	6.3	0	0.0	1	6.3
27069	25	17	68.0	2	11.8	0	0.0	2	11.8
27070	17	16	94.1	0	0.0	0	0.0	0	0.0
27071	15	14	93.3	0	0.0	0	0.0	0	0.0
27072	18	18	100.0	1	5.6	0	0.0	1	5.6
27073	17	16	94.1	0	0.0	0	0.0	0	0.0
27074	18	16	88.9	1	6.3	0	0.0	1	6.3
27075	18	15	83.3	1	6.7	0	0.0	1	6.7
27076	15	13	86.7	1	7.7	0	0.0	1	7.7
27077	13	13	100.0	0	0.0	0	0.0	0	0.0
27078	16	15	93.8	1	6.7	0	0.0	1	6.7
27079	Not Pregnant								
Total	365	331		18		0		18	
N	23	23	23	23	23	23	23	23	23
Mean	15.9	14.4	91.14	0.8	5.53	0.0	0.00	0.8	5.53
S.D.	2.85	2.31	9.694	0.67	4.804	-	-	0.67	4.804

Appendix 5 - Continued
Individual and Mean Ovarian and Uterine Data
Rat Teratology Study of T-3351
Group 3 - 5 mg/kg

Maternal Number	Ovarian Corpora Lutea	Uterine Implantations	Implantation Efficiency (%)	Early Resorptions	Early Resorptions (%)	Late Resorptions	Late Resorptions (%)	Total Resorptions	Total Resorptions (%)
27080	16	16	100.0	0	0.0	0	0.0	0	0.0
27081	14	13	92.9	0	0.0	0	0.0	0	0.0
27082	15	14	93.3	1	7.1	0	0.0	1	7.1
27083	14	14	100.0	2	14.3	0	0.0	2	14.3
27084	Not Pregnant								
27085	20	17	85.0	0	0.0	0	0.0	0	0.0
27086	15	15	100.0	0	0.0	1	6.7	1	6.7
27087	15	15	100.0	0	0.0	0	0.0	0	0.0
27088	15	14	93.3	1	7.1	0	0.0	1	7.1
27089	13	13	100.0	1	7.7	0	0.0	1	7.7
27090	13	12	92.3	0	0.0	0	0.0	0	0.0
27091	15	15	100.0	0	0.0	0	0.0	0	0.0
27092	19	17	89.5	1	5.9	0	0.0	1	5.9
27093	15	14	93.3	1	7.1	0	0.0	1	7.1
27094	14	13	92.9	0	0.0	0	0.0	0	0.0
27095	17	17	100.0	1	5.9	0	0.0	1	5.9
27096	17	16	94.1	3	18.8	0	0.0	3	18.8
27097	16	15	93.8	2	13.3	0	0.0	2	13.3
27098	18	14	77.8	2	14.3	0	0.0	2	14.3
27099	16	12	75.0	0	0.0	0	0.0	0	0.0
27100	19	16	84.2	0	0.0	0	0.0	0	0.0
27101	16	15	93.8	1	6.7	0	0.0	1	6.7
27102	16	14	87.5	0	0.0	0	0.0	0	0.0
27103	15	14	93.3	0	0.0	0	0.0	0	0.0
27104	Not Pregnant								
Total	363	335		16		1		17	
N	23	23	23	23	23	23	23	23	23
Mean	15.8	14.6	92.70	0.7	4.70	0.0	0.29	0.7	5.00
S.D.	1.86	1.47	7.017	0.88	5.859	0.21	1.397	0.86	5.781

Appendix 5 - Continued
Individual and Mean Ovarian and Uterine Data
Rat Teratology Study of T-3351
Group 4 - 10 mg/kg

Maternal Number	Ovarian Corpora Lutea	Uterine Implantations	Implantation Efficiency (%)	Early Resorptions	Early Resorptions (%)	Late Resorptions	Late Resorptions (%)	Total Resorptions	Total Resorptions (%)
27105	17	15	88.2	0	0.0	0	0.0	0	0.0
27106	17	11	64.7	1	9.1	0	0.0	1	9.1
27107	14	13	92.9	3	23.1	0	0.0	3	23.1
27108	17	16	94.1	1	6.3	0	0.0	1	6.3
27109	18	17	94.4	1	5.9	15	88.2	16	94.1
27110	21	14	66.7	0	0.0	0	0.0	0	0.0
27111	17	16	94.1	1	6.3	0	0.0	1	6.3
27112	14	13	92.9	1	7.7	0	0.0	1	7.7
27113	15	15	100.0	2	13.3	1	6.7	3	20.0
27114	18	15	83.3	2	13.3	0	0.0	2	13.3
27115	16	15	93.8	0	0.0	0	0.0	0	0.0
27116	14	12	85.7	1	8.3	0	0.0	1	8.3
27117	22	14	63.6	0	0.0	1	7.1	1	7.1
27118	Not Pregnant								
27119	15	13	86.7	13	100.0	0	0.0	13	100.0
27120[a]	17	16	94.1						
27121	15	15	100.0	0	0.0	0	0.0	0	0.0
27122	15	15	100.0	3	20.0	0	0.0	3	20.0
27123	18	15	83.3	0	0.0	0	0.0	0	0.0
27124	16	16	100.0	1	6.3	0	0.0	1	6.3
27125	16	13	81.3	0	0.0	0	0.0	0	0.0
27126	18	15	83.3	1	6.7	0	0.0	1	6.7
27127[a]	15	13	86.7						
27128	Not Pregnant								
27129	Not Pregnant								
Total	365	317		31		17		48	
N	22	22	22	20	20	20	20	20	20
Mean	16.6	14.4	87.72	1.6	11.32	0.9	5.10	2.4	16.42
S.D.	2.09	1.50	10.955	2.86	21.929	3.34	19.674	4.28	28.471

[a]Found dead on Day 17, therefore, fetal data not available.

Appendix 6
Individual and Mean Litter Data[a]
Rat Teratology Study of T-3351
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
27030	0	0	0.0	15	100.0	7	8	46.7	3.7	3.6
27031	1	0	5.9	16	94.1	8	8	50.0	3.5	3.2
27032	1	0	6.7	14	93.3	7	7	50.0	3.9	3.4
27033	3	0	20.0	12	80.0	7	5	58.3	3.3	3.2
27034	1	0	6.7	14	93.3	5	9	35.7	2.5	2.8
27035	1	0	5.6	17	94.4	12	5	70.6	3.3	3.2
27036	0	0	0.0	14	100.0	7	7	50.0	4.1	3.9
27037	Not Pregnant									
27038	2	0	14.3	12	85.7	5	7	41.7	3.5	3.3
27039	4	0	23.5	13	76.5	6	7	46.2	3.6	3.4
27040	1	0	7.7	12	92.3	7	5	58.3	2.7	2.4
27041	0	0	0.0	15	100.0	4	11	26.7	3.4	3.3
27042	1	0	6.7	14	93.3	4	10	28.6	3.5	3.4
27043	2	0	28.6	5	71.4	1	4	20.0	2.2	3.2
27044	1	0	6.3	15	93.8	12	3	80.0	3.2	2.9
27045	0	0	0.0	10	100.0	3	7	30.0	3.2	3.2
27046	0	0	0.0	13	100.0	5	8	38.5	3.3	3.2
27047	1	0	8.3	11	91.7	5	6	45.5	3.0	2.9
27048	1	0	6.7	14	93.3	6	8	42.9	3.3	3.2
27049	1	0	5.6	17	94.4	9	8	52.9	3.2	2.9
27050	0	0	0.0	14	100.0	6	8	42.9	3.1	3.1
27051	2	0	15.4	11	84.6	5	6	45.5	3.2	3.2
27052	0	0	0.0	15	100.0	7	8	46.7	3.5	3.4
27053	0	0	0.0	15	100.0	2	13	13.3	3.3	3.0
27054	0	0	0.0	17	100.0	6	11	35.3	3.1	2.8
Total	23	0		325		146	179			
N	24	24	24	24	24	24	24	24	24	24
Unadjusted Mean	1.0	0.0	7.00	13.5	93.00	6.1	7.5	44.01	3.28	3.17
Unadjusted S.D.	1.04	-	8.024	2.64	8.024	2.59	2.30	14.828	0.408	0.301
Covariance Adjusted Mean									3.28	3.16
Covariance Adjusted S.D.									0.092	0.084

[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-3351
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
27055	1	0	7.7	12	92.3	8	4	66.7	3.4	3.4
27056	1	0	6.3	15	93.8	8	7	53.3	3.3	3.3
27057	0	0	0.0	13	100.0	9	4	69.2	3.4	3.4
27058	1	0	6.7	14	93.3	8	6	57.1	3.4	3.2
27059	2	0	14.3	12	85.7	5	7	41.7	3.3	3.0
27060	Not Pregnant									
27061	0	0	0.0	11	100.0	7	4	63.6	3.8	3.6
27062	0	0	0.0	13	100.0	8	5	61.5	2.7	2.8
27063	1	0	7.7	12	92.3	3	9	25.0	3.5	3.2
27064	1	0	6.7	14	93.3	6	8	42.9	3.3	3.0
27065	0	0	0.0	16	100.0	8	8	50.0	2.8	2.8
27066	1	0	14.3	6	85.7	2	4	33.3	3.2	3.4
27067	2	0	12.5	14	87.5	5	9	35.7	2.9	2.8
27068	1	0	6.3	15	93.8	7	8	46.7	3.0	3.2
27069	2	0	11.8	15	88.2	10	5	66.7	3.3	3.3
27070	0	0	0.0	16	100.0	15	1	93.8	3.4	3.0
27071	0	0	0.0	14	100.0	7	7	50.0	3.1	2.9
27072	1	0	5.6	17	94.4	9	8	52.9	2.8	2.7
27073	0	0	0.0	16	100.0	6	10	37.5	2.9	2.9
27074	1	0	6.3	15	93.8	5	10	33.3	3.6	3.3
27075	1	0	6.7	14	93.3	8	6	57.1	3.2	3.1
27076	1	0	7.7	12	92.3	10	2	83.3	3.1	3.0
27077	0	0	0.0	13	100.0	5	8	38.5	3.5	3.2
27078	1	0	6.7	14	93.3	6	8	42.9	3.3	2.9
27079	Not Pregnant									
Total	18	0		313		165	148			
N	23	23	23	23	23	23	23	23	23	23
Unadjusted Mean	0.8	0.0	5.53	13.6	94.48	7.2	6.4	52.29	3.23	3.10
Unadjusted S.D.	0.67	-	4.804	2.27	4.802	2.66	2.45	16.688	0.278	0.240
Covariance Adjusted Mean									3.23	3.10
Covariance Adjusted S.D.									0.092	0.083

[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-3351
Group 3 - 5 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
27080	0	0	0.0	16	100.0	8	8	50.0	3.7	3.4
27081	0	0	0.0	13	100.0	8	5	61.5	3.2	2.9
27082	1	0	7.1	13	92.9	8	5	61.5	3.2	3.1
27083	2	0	14.3	12	85.7	3	9	25.0	3.1	2.8
27084	Not Pregnant									
27085	0	0	0.0	17	100.0	5	12	29.4	3.0	2.9
27086	1	0	6.7	14	93.3	7	7	50.0	3.1	3.0
27087	0	0	0.0	15	100.0	11	4	73.3	2.8	2.8
27088	1	0	7.1	13	92.9	6	7	46.2	3.4	3.3
27089	1	0	7.7	12	92.3	9	3	75.0	3.4	3.3
27090	0	0	0.0	12	100.0	8	4	66.7	3.0	2.9
27091	0	0	0.0	15	100.0	9	6	60.0	3.1	2.9
27092	1	0	5.9	16	94.1	12	4	75.0	3.2	3.2
27093	1	0	7.1	13	92.9	9	4	69.2	3.3	2.9
27094	0	0	0.0	13	100.0	7	6	53.8	3.2	3.1
27095	1	0	5.9	16	94.1	8	8	50.0	3.2	3.1
27096	3	0	18.8	13	81.3	6	7	46.2	3.2	3.1
27097	2	0	13.3	13	86.7	7	6	53.8	3.0	3.0
27098	2	0	14.3	12	85.7	6	6	50.0	3.0	3.0
27099	0	0	0.0	12	100.0	6	6	50.0	3.1	3.1
27100	0	0	0.0	16	100.0	10	6	62.5	1.5	1.7
27101	1	1	13.3	13	86.7	5	8	38.5	3.2	3.0
27102	0	0	0.0	14	100.0	6	8	42.9	3.1	2.8
27103	0	0	0.0	14	100.0	8	6	57.1	3.3	3.1
27104	Not Pregnant									
Total	17	1		317		172	145			
N	23	23	23	23	23	23	23	23	23	23
Unadjusted Mean	0.7	0.0	5.28	13.8	94.72	7.5	6.3	54.24	3.10	2.97
Unadjusted S.D.	0.86	0.21	6.028	1.57	6.018	2.04	2.01	13.293	0.392	0.322
Covariance Adjusted Mean									3.10[S-]	2.97[S-]
Covariance Adjusted S.D.									0.092	0.083

[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-3351
Group 4 - 10 mg/kg

Maternal Number	Total Resorptions	Number of Fetuses: Dead	Fetal Loss (%)[b]	Live	Live (%)	Sex: Males	Females	Percent Males	Mean Weight (g)[c]: Males	Females
27105	0	0	0.0	15	100.0	10	5	66.7	3.1	3.0
27106	1	0	9.1	10	90.9	6	4	60.0	3.2	3.2
27107	3	0	23.1	10	76.9	4	6	40.0	3.1	3.0
27108	1	0	6.3	15	93.8	9	6	60.0	3.2	3.2
27109	16	1	100.0	0	0.0					
27110	0	0	0.0	14	100.0	8	6	57.1	2.7	2.5
27111	1	0	6.3	15	93.8	7	8	46.7	3.2	3.2
27112	1	0	7.7	12	92.3	10	2	83.3	1.7	1.7
27113	3	6	60.0	6	40.0	4	2	66.7	1.9	2.0
27114	2	0	13.3	13	86.7	6	7	46.2	1.8	1.7
27115	0	0	0.0	15	100.0	9	6	60.0	3.3	3.0
27116	1	0	8.3	11	91.7	8	3	72.7	2.8	2.6
27117	1	2	21.4	11	78.6	8	3	72.7	1.6	1.5
27118	Not Pregnant									
27119	13	0	100.0	0	0.0					
27120	Found Dead									
27121	0	0	0.0	15	100.0	9	6	60.0	3.1	3.0
27122	3	0	20.0	12	80.0	6	6	50.0	3.2	3.4
27123	0	0	0.0	15	100.0	10	5	66.7	3.2	3.0
27124	1	0	6.3	15	93.8	9	6	60.0	2.8	2.9
27125	0	0	0.0	13	100.0	7	6	53.8	1.8	1.7
27126	1	0	6.7	14	93.3	9	5	64.3	1.8	1.7
27127	Found Dead									
27128	Not Pregnant									
27129	Not Pregnant									
Total	48	9		231		139	92			
N	20	20	20	20	20	18	18	18	18	18
Unadjusted Mean	2.4	0.5	19.43	11.6	80.59	7.7	5.1	60.38	2.64	2.57
Unadjusted S.D.	4.28	1.39	30.777	4.61	30.801	1.90	1.68	10.655	0.656	0.660
Covariance Adjusted Mean									2.63^{S-}	2.59^{S-}
Covariance Adjusted S.D.									0.105	0.097

[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-3351
Group 1 - 0 mg/kg

Maternal Number:	27003 0	27003 1	27003 2	27003 3	27003 4	27003 5	27003 6	27003 7	27003 8	27003 9	27004 0	27004 1	27004 2
Number of fetuses examined	5	6	5	4	5	6	5	NP	4	5	4	5	5
Number of fetuses within normal limits	5	6	5	3	5	6	5		4	5	4	5	5
Number of fetuses with one or more visceral variants	0	0	0	1	0	0	0		0	0	0	0	0
Percent of fetuses with one or more skeletal variants (%)	0.00	0.00	0.00	25.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - cerebral hemisphere contained dark area				I									
Eye(s) - contained dark material													
Liver - dark areas													
Kidney(s) - pelvis dilated													
Ureter(s) - distended													
- undulated													
Number of fetuses with one or more visceral anomalies	0	0	0	0	0	0	0		0	0	0	0	0
Percent of fetuses with 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:													
Skin - edematous													
Palate - cleft													
Cryptorchism													

NP = Not Pregnant.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3351
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
		0	0	0	0	0	0	0	0	0	0	0	0
	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	5	4	5	4	5	6	5	4	5	5	6
Number of fetuses within normal limits		2	4	3	5	3	5	6	5	4	5	5	6
Number of fetuses with one or more visceral variants		0	1	1	0	1	0	0	0	0	0	0	0
Percent of fetuses with one or more skeletal variants (%)		0.00	20.00	25.00	0.00	25.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - cerebral hemisphere contained dark area													
Eye(s) - contained dark material													
Liver - dark areas													
Kidney(s) - pelvis dilated													
Ureter(s) - distended			A	J		K							
- undulated													
Number of fetuses with one or more visceral anomalies		0	0	0	0	0	0	0	0	0	0	0	0
Percent of fetuses with 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:													
Skin - edematous													
Palate - cleft													
Cryptorchism													

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3351
Group 2 - 1 mg/kg

	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
	0	0	0	0	0	0	0	0	0	0	0	0	0
Maternal	5	5	5	5	5	6	6	6	6	6	6	6	6
Number:	5	6	7	8	9	0	1	2	3	4	5	6	7
Number of fetuses examined	4	5	4	5	4	NP	4	8	4	5	6	2	5
Number of fetuses within normal limits	4	5	4	5	4		4	8	3	5	6	2	5
Number of fetuses with one or more visceral variants	0	0	0	0	0		0	0	1	0	0	0	0
Percent of fetuses with one or more skeletal variants (%)	0.00	0.00	0.00	0.00	0.00		0.00	0.00	25.00	0.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - cerebral hemisphere contained dark area													
Eye(s) - contained dark material													
Liver - dark areas													
Kidney(s) - pelvis dilated													
Ureter(s) - distended													
- undulated									A				
Number of fetuses with one or more visceral anomalies	0	0	0	0	0		0	0	0	0	0	0	0
Percent of fetuses with 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:													
Skin - edematous													
Palate - cleft													
Cryptorchism													

NP = Not Pregnant.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3351
Group 2 - 1 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
		0	0	0	0	0	0	0	0	0	0	0	0
	Maternal	6	6	7	7	7	7	7	7	7	7	7	7
	Number:	8	9	0	1	2	3	4	5	6	7	8	9
Number of fetuses examined		5	5	6	5	6	6	5	5	4	5	5	NP
Number of fetuses within normal limits		5	5	5	5	4	6	4	4	3	4	5	
Number of fetuses with one or more visceral variants		0	0	1	0	2	0	1	1	1	1	0	
Percent of fetuses with one or more skeletal variants (%)		0.00	0.00	16.67	0.00	33.33	0.00	20.00	20.00	25.00	20.00	0.00	
Identification letter(s) of fetuses with:													
Brain - cerebral hemisphere contained dark area													
Eye(s) - contained dark material													
Liver - dark areas													
Kidney(s) - pelvis dilated						Q		A		A	G		
Ureter(s) - distended				A		N				A	G		
- undulated									A				
Number of fetuses with one or more visceral anomalies		0	0	0	0	1	0	0	0	0	0	0	
Percent of fetuses with one or more visceral anomalies (%)		0.00	0.00	0.00	0.00	16.67	0.00	0.00	0.00	0.00	0.00	0.00	
Identification letter(s) of fetuses with:													
Skin - edematous						N							
Palate - cleft													
Cryptorchism													

NP = Not Pregnant.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3351
Group 3 - 5 mg/kg

Maternal Number:	27008 0	27008 1	27008 2	27008 3	27008 4	27008 5	27008 6	27008 7	27008 8	27008 9	27009 0	27009 1	27009 2
Number of fetuses examined	6	5	5	4	NP	6	5	5	5	4	4	5	6
Number of fetuses within normal limits	4	5	4	4		6	5	5	5	3	4	5	6
Number of fetuses with one or more visceral variants	2	0	1	0		0	0	0	0	1	0	0	0
Percent of fetuses with one or more skeletal variants (%)	33.33	0.00	20.00	0.00		0.00	0.00	0.00	0.00	25.00	0.00	0.00	0.00
Identification letter(s) of fetuses with:													
Brain - cerebral hemisphere contained dark area													
Eye(s) - contained dark material													
Liver - dark areas													
Kidney(s) - pelvis dilated										A			
Ureter(s) - distended	J A		N										
- undulated													
Number of fetuses with one or more visceral anomalies	0	0	0	0		0	0	0	0	0	0	0	0
Percent of fetuses with 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:													
Skin - edematous													
Palate - cleft													
Cryptorchism													

NP = Not Pregnant.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3351
Group 3 - 5 mg/kg

Maternal Number:	27093	27094	27095	27096	27097	27098	27099	27101	27102	27103	27104	27105
Number of fetuses examined	5	5	6	5	5	4	4	6	5	5	5	NP
Number of fetuses within normal limits	5	5	6	5	5	4	4	4	5	5	4	
Number of fetuses with one or more visceral variants	0	0	0	0	0	0	0	0	0	0	1	
Percent of fetuses with one or more skeletal variants (%)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	20.00	
Identification letter(s) of fetuses with:												
Brain - cerebral hemisphere contained dark area												
Eye(s) - contained dark material												
Liver - dark areas												
Kidney(s) - pelvis dilated												
Ureter(s) - distended											M	
- undulated												
Number of fetuses with one or more visceral anomalies	0	0	0	0	0	0	0	2	0	0	0	
Percent of fetuses with one or more visceral anomalies (%)	0.00	0.00	0.00	0.00	0.00	0.00	0.00	33.33	0.00	0.00	0.00	
Identification letter(s) of fetuses with:												
Skin - edematous								A				
Palate - cleft												
Cryptorchism								AG				

NP = Not Pregnant.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3351
Group 4 - 10 mg/kg

Maternal Number:	27105	27106	27107	27108	27109	27110	27111	27112	27113	27114	27115	27116	27117
Number of fetuses examined	5	4	4	5	0[a]	5	5	4[b]	2[c]	5[d]	5	4[e]	4[f]
Number of fetuses within normal limits	4	4	4	5		5	5	3	0	0	5	4	0
Number of fetuses with one or more visceral variants	1	0	0	0		0	0	0	0	0	0	0	0
Percent of fetuses with one or more skeletal variants (%)	20.00	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 - cerebral hemisphere contained dark area													
Eye(s) - contained dark material	H												
Liver - dark areas													
Kidney(s) - pelvis dilated													
Ureter(s) - distended													
- undulated													
Number of fetuses with one or more visceral anomalies	0	0	0	0		0	0	1	2	5	0	0	4
Percent of fetuses with one or more visceral anomalies (%)	0.00	0.00	0.00	0.00		0.00	0.00	25.00	100.00	100.00	0.00	0.00	100.00
Identification letter(s) of fetuses with:													
Skin - edematous									BE	ADGJN			AEJM
Palate - cleft								A	BE	JN			AEJ
Cryptorchism													AEM

[a] All fetuses resorbed and/or dead.

[b] Fetus E was noted to have cleft palate during external examination.

[c] All fetuses were noted to have edematous skin during external examination. Fetuses B and E were confirmed at visceral examination. Fetuses C and E were noted to have cleft palate during external examination. Fetus E was confirmed at visceral examination.

[d] Fetuses H and N were noted to have edematous skin during external examination. Fetus N was confirmed at visceral examination. Fetuses H and I were noted to have cleft palate during external examination.

[e] Fetus E was noted to have cleft palate during external examination.

[f] All fetuses were noted to have edematous skin during external examination. Fetuses A, E, J, and M were confirmed at visceral examination. Fetuses A, J, and L were noted to have cleft palate during external examination. Fetuses A and J were confirmed at visceral examination.

Appendix 7 - Continued
Individual Visceral Findings in Fetuses
Rat Teratology Study of T-3351
Group 4 - 10 mg/kg

Maternal Number:	27118	27119	27120	27121	27122	27123	27124	27125	27126	27127	27128	27129
Number of fetuses examined	NP	0[a]	FD	5	4	5	5	5[b]	5	FD	NP	NP
Number of fetuses within normal limits				4	3	5	5	0	0			
Number of fetuses with one or more visceral variants				0	0	0	0	0	0			
Percent of fetuses with one or more skeletal variants (%)				0.00	0.00	0.00	0.00	0.00	0.00			
Identification letter(s) of fetuses with:												
Brain - cerebral hemisphere contained dark area												
Eye(s) - contained dark material												
Liver - dark areas												
Kidney(s) - pelvis dilated												
Ureter(s) - distended												
- undulated												
Number of fetuses with one or more visceral anomalies				1	1	0	0	5	5			
Percent of fetuses with one or more visceral anomalies (%)				20.00	25.00	0.00	0.00	100.00	100.00			
Identification letter(s) of fetuses with:												
Skin - edematous								ADGJM	BEHKN			
Palate - cleft					E			DJM	EHN			
Cryptorchism				M				G	BHK			

NP = Not Pregnant.
FD = Found Dead.

[a] All fetuses resorbed and/or dead.

[b] All fetuses were noted to have edematous skin during external examination. Fetuses A, D, G, J, and M were confirmed at visceral examination. Fetuses B, F, J, and L were noted to have cleft palate during external examination. Fetus J was confirmed at visceral examination.

Appendix 8
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3351
Group 1 - 0 mg/kg

Maternal Number:	2703 0	2703 1	2703 2	2703 3	2703 4	2703 5	2703 6	2703 7	2703 8	2703 9	2704 0	2704 1	2704 2
Number of fetuses examined	10	10	9	8	9	11	9	NP	8	8	8	10	9
Number of fetuses within normal limits	5	6	6	7	4	8	7		5	8	0	7	6
Number of fetuses with one or more skeletal variants	5	4	3	1	5	3	2		3	0	8	3	3
Percent of fetuses with one or more skeletal variants (%)	50.00	40.00	33.33	12.50	55.56	27.27	22.22		37.50	0.00	100.00	30.00	33.33
Identification letter(s) of fetuses with:													
Lagging Ossification													
Skull - incomplete closure (<75%)													
- interparietal ossification incomplete/nonossified		DI	J		FH		L		JN		BGM H		
- parietals ossification irregular													
- supraoccipital ossification incomplete/nonossified			J	N	FK				J		BH		
- supraoccipital nonfused													
- hyoid ossification incomplete/nonossified	FN	GI	DJ		FIK	H	B		J		GLM		
Pectoral girdle - scapula ossification incomplete													
Rib cage - sternebrae bipartite													
- sternebrae 1 and 2 fused													
- sternebrae <3 ossified					EF							F	
- ribs <13 ossified[b]													
- ribs >13 ossified (cervical region)													
- ribs 13th pair small[b]	CFHI												
- ribs ossification irregular													
Vertebral column - sacral arches nonossified					E						M		
- thoracic centra ossification incomplete/ nonossified					K				B		JLM		FG
- thoracic centra nonfused			I			BF					BG	CKO	D
- caudals <3 ossified					E						BCFGIL		
Pelvic girdle - pubis ossification incomplete/ nonossified											M		
- ischium nonossified					FIK								
Forelimbs - <3 ossified					F								
Hindlimbs - <4 ossified					E						M		
Bone Alignment													
Ribs - angulated													
Sternebrae - checkered													

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetuses.
[b] Possible preparation damage at time of evisceration.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3351
Group 1 - 0 mg/kg

Maternal Number:	27043	27044	27045	27046	27047	27048	27049	27050	27051	27052	27053	27054
Number of fetuses examined	3	10	6	8	7	9	11	9	7	10	10	11
Number of fetuses within normal limits	1	8	5	7	3	5	7	8	6	9	5	1
Number of fetuses with one or more skeletal variants	2	2	1	1	4	4	4	1	1	1	5	10
Percent of fetuses with one or more skeletal variants (%)	66.67	20.00	16.67	12.50	57.14	44.44	36.36	11.11	14.29	10.00	50.00	90.91
Identification letter(s) of fetuses with:												
Lagging Ossification												
Skull - incomplete closure (<75%)	D						R					E
- interparietal ossification incomplete/nonossified	DE	H	C	L	F	IL		B			EHI	BCEHIK LNQ
- parietals ossification irregular												E
- supraoccipital ossification incomplete/nonossified	D	J			F	I	ILR				EI	BFHIKL Q
- supraoccipital nonfused												E
- hyoid ossification incomplete/nonossified											EI	BEFHN
Pectoral girdle - scapula ossification incomplete												
Rib cage - sternebrae bipartite												
- sternebrae 1 and 2 fused												
- sternebrae <3 ossified							R					HI
- ribs <13 ossified[b]												
- ribs >13 ossified (cervical region)												
- ribs 13th pair small[b]												
- ribs ossification irregular												E
Vertebral column - sacral arches nonossified												
- thoracic centra ossification incomplete/ nonossified					BCFL	FH	N		J		FIK	
- thoracic centra nonfused										F		
- caudals <3 ossified	D						R				H	HI
Pelvic girdle - pubis ossification incomplete/ nonossified		J					R					HIL
- ischium nonossified												
Forelimbs - <3 ossified												
Hindlimbs - <4 ossified							R					
Bone Alignment												
Ribs - angulated												E
Sternebrae - checkered												

[a] There were no skeletal anomalies noted in any fetuses.
[b] Possible preparation damage at time of evisceration.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3351
Group 2 - 1 mg/kg

Maternal Number:	25705	25706	25707	25708	25709	25760	25761	25762	25763	25764	25765	25766	25767
Number of fetuses examined	8	10	9	9	8	NP	7	5	8	9	10	4	9
Number of fetuses within normal limits	6	9	7	5	1		2	4	0	6	5	1	5
Number of fetuses with one or more skeletal variants	2	1	2	4	7		5	1	8	3	5	3	4
Percent of fetuses with one or more skeletal variants (%)	25.00	10.00	22.22	44.44	87.50		71.43	20.00	100.00	33.33	50.00	75.00	44.44
Identification letter(s) of fetuses with:													
Lagging Ossification													
Skull - incomplete closure (<75%)					B				E		BFNO		IP
- interparietal ossification incomplete/nonossified		P			BEGHJK				CEHLM	EFK		fl	P
- parietals ossification irregular					BEGJK				CE				I
- supraoccipital ossification incomplete/nonossified		P			BGHJ				BCEFH		B		P
- supraoccipital nonfused													
- hyoid ossification incomplete/nonossified	M	P	I		BEGHJK				BCEFHI		BF		I
					M				M				
Pectoral girdle - scapula ossification incomplete													
Rib cage - sternebrae bipartite	M												
- sternebrae 1 and 2 fused													
- sternebrae <3 ossified													
- ribs <13 ossified[b]													
- ribs >13 ossified (cervical region)													
- ribs 13th pair small[b]													
- ribs ossification irregular													
Vertebral column - sacral arches nonossified									CE				
- thoracic centra ossification incomplete/ nonossified	I		F	BFFG	K				L		H	DF	I
- thoracic centra nonfused							BCEHK		C		O	G	M
- caudals <3 ossified								D					
Pelvic girdle - pubis ossification incomplete/ nonossified													
- ischium nonossified													
Forelimbs - <3 ossified													
Hindlimbs - <4 ossified													
Bone Alignment													
Ribs - angulated					J				CEH				
Sternebrae - checkered													

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetuses.
[b] Possible preparation damage at time of evisceration.

Appendix 8 - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3351
Group 2 - 1 mg/kg

Maternal Number:	26708	26709	26710	26711	26712	26713	26714	26715	26716	26717	26718	26719
Number of fetuses examined	10	10	10	9	11	10	10	9	8	8	9	NP
Number of fetuses within normal limits	8	9	7	7	0	8	8	0	3	6	6	
Number of fetuses with one or more skeletal variants	2	1	3	2	11	2	2	9	5	2	3	
Percent of fetuses with one or more skeletal variants (%)	20.00	10.00	30.00	22.22	100.00	20.00	20.00	100.00	62.50	25.00	33.33	
Identification letter(s) of fetuses with:												
Lagging Ossification												
Skull - incomplete closure (<75%)					CEFHIKL							
- interparietal ossification incomplete/nonossified				H	BECFHKLNR			BCEFHJLMO	IL	L	CO	
- parietals ossification irregular					CEFIKL							
- supraoccipital ossification incomplete/nonossified				H	BCEFKLNR	N	F	FJHO	IL	L	C	
- supraoccipital nonfused												
- hyoid ossification incomplete/nonossified	I		BHI	H	BCEFLOR		P	CFHJLM	EIL	EL	IO	
Pectoral girdle - scapula ossification incomplete												
Rib cage - sternebrae bipartite												
- sternebrae 1 and 2 fused												
- sternebrae <3 ossified					R							
- ribs <13 ossified[b]									F			
- ribs >13 ossified (cervical region)												
- ribs 13th pair small[b]												
- ribs ossification irregular												
Vertebral column - sacral arches nonossified												
- thoracic centra ossification incomplete/nonossified	O	C		L	H		F	H	B		I	
- thoracic centra nonfused	I							EJ				
- caudals <3 ossified					HR	F		O				
Pelvic girdle - pubis ossification incomplete/nonossified												
- ischium nonossified												
Forelimbs - <3 ossified												
Hindlimbs - <4 ossified					R							
Bone Alignment												
Ribs - angulated												
Sternebrae - checkered												

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetuses.
[b] Possible preparation damage at time of evisceration.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3351
Group 3 - 5 mg/kg

Maternal Number:	270080	270081	270082	270083	270084	270085	270086	270087	270088	270089	270090	270091	270092
Number of fetuses examined	10	8	8	8	NP	11	9	10	8	8	8	10	10
Number of fetuses within normal limits	8	5	7	7		8	7	1	8	7	6	6	6
Number of fetuses with one or more skeletal variants	2	3	1	1		3	2	9	0	1	2	4	4
Percent of fetuses with one or more skeletal variants (%)	20.00	37.50	12.50	12.50		27.27	22.22	90.00	0.00	12.50	25.00	40.00	40.00
Identification letter(s) of fetuses with:													
Lagging Ossification													
Skull - incomplete closure (<75%)								BE			EL	O	O
- interparietal ossification incomplete/nonossified		B	H					B					FJOP
- parietals ossification irregular													
- supraoccipital ossification incomplete/nonossified						H	O	B					
- supraoccipital nonfused												BC	JO
- hyoid ossification incomplete/nonossified	B					H	F	I				BCK	
Pectoral girdle - scapula ossification incomplete													
Rib cage - sternebrae bipartite						E		BEFHLO					
- sternebrae 1 and 2 fused													
- sternebrae <3 ossified													
- ribs <13 ossified[b]								B					
- ribs >13 ossified (cervical region)													
- ribs 13th pair small[b]													
- ribs ossification irregular													
Vertebral column - sacral arches nonossified													
- thoracic centra ossification incomplete/ nonossified	I	CH		D		HK		INO	C				
- thoracic centra nonfused								BCF					
- caudals <3 ossified								B					O
Pelvic girdle - pubis ossification incomplete/ nonossified													
- ischium nonossified													
Forelimbs - <4 ossified													
Hindlimbs - <4 ossified								B					
Bone Alignment													
Ribs - angulated													
Sternebrae - checkered													

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetuses.
[b] Possible preparation damage at time of evisceration.

Appendix 8 - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3351
Group 3 - 5 mg/kg

Maternal Number:	27093	27094	27095	27096	27097	27098	27099	27100	27101	27102	27103	27104
Number of fetuses examined	8	8	10	8	8	8	8	10	8	9	9	NP
Number of fetuses within normal limits	3	8	7	3	5	8	4	0	8	7	6	
Number of fetuses with one or more skeletal variants	5	0	3	5	3	0	4	10	0	2	3	
Percent of fetuses with one or more skeletal variants (%)	62.50	0.00	30.00	62.50	37.50	0.00	50.00	100.00	0.00	22.22	33.33	
Identification letter(s) of fetuses with:												
Lagging Ossification												
Skull - incomplete closure (<75%)								BCEFHI KLNO	N			
- interparietal ossification incomplete/nonossified	HK		FI					O		EFN		
- parietals ossification irregular			I									
- supraoccipital ossification incomplete/nonossified	CEI						L	BCEFHI KLNO	N	F		
- supraoccipital nonfused												
- hyoid ossification incomplete/nonossified				D			HL	LN		F		
Pectoral girdle - scapula ossification incomplete												
Rib cage - sternebrae bipartite					JN			BEFIK				
- sternebrae 1 and 2 fused												
- sternebrae <3 ossified								BLN				
- ribs <13 ossified[b]												
- ribs >13 ossified (cervical region)				DG								
- ribs 13th pair small[b]												
- ribs ossification irregular	K											
Vertebral column - sacral arches nonossified								LN				
- thoracic centra ossification incomplete/ nonossified				N			EK	ILN	L	N		
- thoracic centra nonfused				FI								
- caudals <3 ossified					D			BCEFHI KLNO	N			
Pelvic girdle - pubis ossification incomplete/ nonossified								BILN				
- ischium nonossified								LN				
Forelimbs - <3 ossified								LN				
Hindlimbs - <4 ossified								BEIKL				
Bone Alignment												
Ribs - angulated	IK		EI									
Sternebrae - checkered												

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetuses.
[b] Possible preparation damage at time of evisceration.

Appendix B - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3351
Group 4 - 10 mg/kg

Maternal Number:	27105	27106	27107	27108	27109	27110	27111	27112	27113	27114	27115	27116	27117
Number of fetuses examined	10	6	6	10	0[c]	9	10	8	4	8	10	7	7
Number of fetuses within normal limits	3	6	2	10		3	7	0	0	0	6	4	0
Number of fetuses with one or more skeletal variants	7	0	4	0		6	3	8	4	8	4	3	7
Percent of fetuses with one or more skeletal variants (%)	70.00	0.00	66.67	0.00		66.67	30.00	100.00	100.00	100.00	40.00	42.86	100.00
Identification letter(s) of fetuses with:													
Lagging Ossification													
Skull - incomplete closure (<75%)						B		BCEFHI KL	CDFO	BCEFHI LM	L		BCFGKL N
- interparietal ossification incomplete/nonossified						B		CE	CDFO	EFHI			BCFGKL N
- parietals ossification irregular													
- supraoccipital ossification incomplete/nonossified						CH		BFHK	CDO	BCEFHI LM	L		N
- supraoccipital nonfused								CEIL H E	F		L		BCFGKL
- hyoid ossification incomplete/nonossified													CGKLN
Pectoral girdle - scapula ossification incomplete						BEFHK		BCFHIK	CDO	BCEFHI L	BFIN	E	BFGKL
Rib cage - sternebrae bipartite	CFHILN O		CFI										
- sternebrae 1 and 2 fused								CH					CGKN
- sternebrae <3 ossified													
- ribs <13 ossified[b]													
- ribs >13 ossified (cervical region)													
- ribs 13th pair small[b]													
- ribs ossification irregular													
Vertebral column - sacral arches nonossified								CH	FO	I			CGKN
- thoracic centra ossification incomplete/ nonossified			K			K		CH	FO	BI			
- thoracic centra nonfused							BH	K			C		
- caudals <3 ossified								BCEHIK	CDFO	CEFI			BCFGKL N
Pelvic girdle - pubis ossification incomplete/ nonossified								CH		I			CFGKLN
- ischium nonossified								C					CN
Forelimbs - <3 ossified								BCEFHK L	CDFO	CEHI			BCFGKL N
Hindlimbs - <4 ossified													
Bone Alignment													
Ribs - angulated	HN							EF	CDFO				N
Sternebrae - checkered						0							

NP = Not Pregnant.
[a] There were no skeletal anomalies noted in any fetuses.
[b] Possible preparation damage at time of evisceration.
[c] All fetuses resorbed and/or dead.

Appendix 8 - Continued
Individual Skeletal Findings in Fetuses[a]
Rat Teratology Study of T-3351
Group 4 - 10 mg/kg

Maternal Number:	27118	27119	27120	27121	27122	27123	27124	27125	27126	27127	27128	27129
Number of fetuses examined	NP	0[c]	FD	10	8	10	10	8	9	FD	NP	NP
Number of fetuses within normal limits				4	5	10	3	0	0			
Number of fetuses with one or more skeletal variants				6	3	0	7	8	9			
Percent of fetuses with one or more skeletal variants (%)				60.00	37.50	0.00	70.00	100.00	100.00			
Identification letter(s) of fetuses with:												
Lagging Ossification												
Skull - incomplete closure (<75%)							B	BCEFHI	CDFIJL KL	MO		
- interparietal ossification incomplete/nonossified					B		CJMP	BFIKL	I			
- parietals ossification irregular												
- supraoccipital ossification incomplete/nonossified				CIKO	N		BCMP	HK	CIJLMO			
- supraoccipital nonfused								BCEFIL				
- hyoid ossification incomplete/nonossified				CF				K				
Pectoral girdle - scapula ossification incomplete												
Rib cage - sternebrae bipartite				FIKO	M			BCEFHI	CDFGIJ L	LMO		
- sternebrae 1 and 2 fused												
- sternebrae <3 ossified								CKL				
- ribs <13 ossified[b]												
- ribs >13 ossified (cervical region)												
- ribs 13th pair small[b]												
- ribs ossification irregular												
Vertebral column - sacral arches nonossified							B	CKL				
- thoracic centra ossification incomplete/ nonossified				C			BMP	L	IL			
- thoracic centra nonfused				HI								
- caudals <3 ossified							BI	BCEFHI	CJL			
								KL				
Pelvic girdle - pubis ossification incomplete/ nonossified								BCHIKL				
- ischium nonossified								KL				
Forelimbs - <3 ossified								KL				
Hindlimbs - <4 ossified							B	BCEFHI	CIJLO			
								KL				
Bone Alignment												
Ribs - angulated												
Sternebrae - checkered												

NP = Not Pregnant.
FD = Found Dead.
[a] There were no skeletal anomalies noted in any fetuses.
[b] Possible preparation damage at time of evisceration.
[c] All fetuses resorbed and/or dead.

154-160

Appendix 9
References
Rat Teratology Study of T-3351

STATISTICAL METHODS/LABORATORY PROCEDURES

Armitage, P., "Tests for Linear Trends in Proportions and Frequencies." Biometrics, 11:375-385, 1955.

Bartlett, M. S., "Some Examples of Statistical Methods of Research in Agriculture and Applied Biology." J. Royal Statist. Soc. Suppl., IV:137-170, 1937.

Cochran, W. G., "Some Methods of Strengthening the Common Chi-Square Tests." Biometrics, 10:417-451, 1954.

Cochran, W. G., and Cox, G. M., Experimental Designs, 2nd Ed., John Wiley and Sons, Inc., New York, 1957.

Draper, N. R., and Hunter, W. G., "Transformations: Some Examples Revisited." Technometrics, 11:23-40, 1969.

Dunnett, C. W., "A Multiple Comparison Procedure for Comparing Several Treatments with a Control." J. Am. Stat. Assoc., 50:1096-1121, 1955.

Dunnett, C. W., "New Tables for Multiple Comparisons with a Control." Biometrics, 20:482-491, 1964.

Fisher, R. A., Statistical Methods for Research Workers, Oliver & Boyd, Edinburgh, 1950.

Fleiss, J. L., Statistical Methods for Rates and Proportions, 2nd Ed., Wiley, New York, Ch. 9, 1981.

Jonckheere, A. R., "A Distribution-free k-sample Test Against Ordered Alteratives." Biometrika 41:133-45, 1954.

Kruskal, W. H. and Wallis, W. A., "Use of Ranks in One-Criterion Variance Analysis." J. Am. Stat. Assoc., 47:583-621, 1952.

Kruskal, W. H. and Wallis, W. A., "Errata to Use of Ranks in One-Criterion Variance Analysis." J. Am. Stat. Assoc., 48:907-911, 1953.

Levene, H., "Robust Tests for Equality of Variances," in I. Olkin edited, Contributions to Probability and Statistics, Stanford University Press, Palo Alto, 1960.

Miller, R. G., Jr., Simultaneous Statistical Inference, McGraw-Hill, New York, 1966, Ch. 6.1.

Appendix 9 - Continued
References
Rat Teratology Study of T-3351

STATISTICAL METHODS/LABORATORY PROCEDURES

Staples, R. E., "Detection of Visceral Alterations in Mammalian Fetuses." Teratology, 9(3):A-37, 1974.

Staples, R. E. and Schnell, V. L., "Refinements in Rapid Clearing Technic in the KOH-Alizarin Red S Method for Fetal Bone." Stain Technology, 39:61-63, 1964.

Terpstra, T. J., "The Asymptotic Normality and Consistency of Kendall's Test Against Trend, When Ties are Present in One Ranking." Indag. Math. 14:327-333, 1952.

Wilson, J. G. and Warkany, J., editors. Teratology: Principles and Techniques, The Univ. of Chicago Press, Chicago, 1965, pp. 251-277.

Winer, B. J., Statistical Principles in Experimental Design, 2nd Ed., McGraw-Hill, N.Y., Chs. 3-9, 1971.

Winer, B. J., Statistical Principles in Experimental Design, 2nd Ed., McGraw-Hill, N.Y., Ch. 10, 1971.