

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Segment I of the Teratology - Reproduction Profile

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INTRODUCTION

The commercial grade finished product of SC-18862, a nutritive sweetening agent, may contain from 0-2% of a conversion product, SC-19192. This is also produced from SC-18862 spontaneously under various laboratory conditions. The human population consuming SC-18862 would also be exposed to varying concentrations of SC-19192; hence, the preclinical testing of SC-19192 for its potential effects on reproductive performance in rats. In this study SC-19192 was administered orally to mature male and female albino rats prior to mating and to the pregnant female during the entire period of gestation and lactation. Subsequent neonatal development was observed. Thus, cpd. effects on the gamete, the zygote, on implantation, fetal development and on delivery were evaluated as well as subsequent lactation and postnatal growth.

Such a study is commonly referred to as Segment I of the Teratology-Reproduction profile.

METHODS

Material evaluated.

SC-19192 is a fine white powder chemically named 5-benzyl-3, dioxo-2-piperazineacetic acid (diketopiperazine, DKP). Lot nos. 232A and 236B were employed during this study.

Animals, housing and diet.

Fifty six male and 144 female Charles River cd albino rats were employed. All rats were approximately 90 days of age at initiation of treatment; males were approximately 140 days and females 105 days old when mating was initiated.

Males were housed individually in suspended wire mesh cages during the two week laboratory acclimation period and the subsequent seven week pre-mating treatment period.

Prior to mating, females were individually housed in suspended wire mesh cages. After mating and throughout gestation, delivery and lactation, the females were caged individually in 10 x 11 x 14 inch metal bottom cages.

Each mating unit (one male + three females) was housed in a 10 x 11 x 14 inch cage during the 4 week mating period.

Animal quarters were air-conditioned with thermostats set to maintain 72° F temperature continuously; artificial fluorescent lighting was provided on a 12-hour daily photoperiod. Absorbent bedding (Ab-Sorb-Dri, Inc.) was employed.

Basal diet [Rockland Mouse/Rat Diet (complete); pelleted or granulated (Teklad, Inc., Monmouth, Ill.)] and chlorinated tap water were continuously available.

Chemical reagents.

Tissue fixative and preservative: 10% aqueous, neutral buffered formalin.

Experimental design.

Fifty-six male and 144 female rats were distributed into the following groups employing simple randomization procedures.

Treatment Group	Number M F		Daily Dosage Level (g/kg)					
			Intended	Actual				Mean
				Premating	Gestation	Lactation		
Control	14 ^t	60	--	0.0	→	0.0	→	0.00
Low	14 ^t	28	0.5	0.4	→	0.4	→	0.45
Medium	14 ^t	28	1.0	0.8	→	0.9	→	0.90
High	14 ^t	28	2.0	1.7	→	1.6	→	1.80

^t 12 males randomly chosen from each group were used for mating.

Compound was administered to the males for 49 days and to the females for 17 days immediately preceding the mating period; both sexes were continued on treatment throughout the mating period (in the case of males treatment terminated when all females within the mating unit were mated). Treatment of the females continued uninterrupted throughout the entire gestation and lactation periods.

For the purpose of mating, the rats were randomly subdivided into 48 mating units each containing one male and three females as indicated below.

No. of Mating Units	Composition of Each Such Mating Unit; No. of Rats*								Number of Pregnancies Produced									
	Male				Female				(♂ x ♀)									
	C	L	M	H	C	L	M	H	CC	LL	MM	HH	CL	CM	CH	LC	MC	HC
4	1				2	1			8				4					
4	1				2		1		8					4				
4	1				2			1	8						4			
12		1			1	2				24						12		
12			1		1		2				24						12	
12				1	1			2				24						12

* C = Control; L = Low Dose; M = Medium Dose; H = High Dose.

This mating design enables comparisons within each mating unit as well as between treatment levels and with regard to specific compound effects on fertility, and enables prompt identification of the affected parent. One-half of all pregnant animals were sacrificed on day 14 of gestation; the remaining females proceeded to natural delivery and lactation.

Primary evaluation of data generated was limited initially to those groups comprised of animals receiving identical compound treatment, i.e., control x control, low dose x low dose, medium dose x medium dose and high dose x high dose matings, and litters resulting therefrom. In the event of an obvious or suspected compound effect, secondary evaluation of all parameters from all groups of animals in the study was performed.

Mating.

Mating procedure. Rats were bred by placing the appropriate male into each mating unit from 4:00 p.m. on weekdays (except Friday) to 8:15 a.m. the following morning. The presence of a copulatory plug and/or spermatozoa in the vaginal smear was considered evidence of mating; this was recorded as gestation day 0.

Females who lacked the above evidence of mating but later showed signs of pregnancy (by palpation, continual diestrus vaginal smear, RBC's in the smear) were removed at such time and caged individually. The approximate week of mating was determined by examining the daily vaginal smear records and observing the last day that the animal was in the estrus phase of the cycle.

Fertility was based on evidence of successful implantation of fertilized ova. Females demonstrating any one of the following criteria were considered pregnant and were included in the fertility index data:

(1) uterine implantation sites in those mated females sacrificed during gestation; (2) parturition; or (3) uterine placental scars and/or intra-uterine fetal remnants.

Mated females not showing evidence of delivery at term were routinely sacrificed and autopsied 7 days following the expected day of delivery.

Mating period. The mating procedures were performed over a four week period designated as the mating period.

Compound formulation, administration and dosage calculation.

Diet for treated groups was prepared by admixing SC-19192 into the basal diet on a weight per weight basis in a Hobart Model V-1401 Mixer. Concentrations used during the premating treatment periods were adjusted weekly on the basis of group mean body weights and mean food consumption. For the males during this period compound-diet concentrations ranged from 0.5% - 0.8% in the low dose group, 1.0% - 1.5% in the medium dose group and 1.8% - 3.0% in the high dose group. For the females during the 17 day premating treatment period, the concentrations were fixed at 0.5% for the low dose group, 1.0% for the medium dose group and 2.0% for the high dose group.

During the mating period when treated and control animals were housed together, compound was administered orally by gastric intubation as a 2.5%, 5.0% and 10.0% suspension (w/v) in 1% aqueous (v/v) Tween-80 solution to the low,

medium and high dose groups, respectively. Two equally divided doses were given daily with an interval of at least 2 hours between doses. Control animals received divided doses of vehicle during this period in equal volumes (total maximum daily volume: 20 cc/kg body weight). Dosages were adjusted weekly to respective body weights.

Dietary administration was resumed for mated females during the gestation and lactation periods. Compound-diet concentrations were initially set at 0.5%, 1.0% and 2.0% for the low, medium and high dose groups, respectively. On postpartum day 4 compound-diet concentrations for the low, medium and high dose females were reduced to 0.3%, 0.5% and 1.0%, respectively, to compensate for the expected increase in food consumption during the remaining days of the lactation period.

Observations and examination procedures.

Examination of the sire. During the pre-mating treatment period males were examined externally and weighed on a weekly basis. Food consumption was recorded bi-weekly. During the mating period, observations and external examinations were performed periodically while manipulating the animal during daily administration of compound. Body weights continued to be recorded weekly; however, food consumption was not measured.

Examination of the dam. During the pre-mating and mating periods, females were handled similarly to the males. Body weights of mated females were recorded periodically throughout the gestation and lactation periods; food consumption was recorded daily.

One-half of the mated females were sacrificed with an overdose of carbon dioxide and autopsied (reproductive organs) on day 14 of gestation. Ovaries and uterus were examined in situ. The uterine horns were exposed; the number and position of viable, non-viable and resorbed fetuses were recorded. The ovaries were removed, freed of associated tissue(s); the number of corpora lutea in each ovary was recorded.

The remaining one-half of the mated females were allowed to deliver naturally.

Examination of the progeny. Each litter was examined by a laboratory technician shortly after delivery. The number of viable and non-viable pups and the nature of irregularities observed, e.g., excessive maternal bleeding, partially resorbed fetuses, etc., were recorded at this examination, referred to as the Litter examination.

Individual pups were thoroughly examined by a staff teratologist as soon after delivery as possible, usually in conjunction with the litter examination above. At this later examination, referred to as the Neonatal examination, each pup was examined externally, sexed and weighed.

"Litter" examinations were repeated on postpartum days 4 and 21 with the number of viable, non-viable, and missing pups recorded at each examination. "Neonatal" examinations were repeated twice, generally on postpartum days 4 and 21.

Intact non-viable pups recovered during the initial litter examinations were examined grossly for external anomalies and placed in a 10% aqueous formalin solution. Later these pups were eviscerated and processed for skeletal staining with Alizarin Red S.

Ophthalmological examination. Direct and indirect ophthalmological examinations (supplemented by slit lamp biomicroscope examinations where indicated) were performed (Dr. G. J. Youkilis) on weaned pups from the high dose group only at 21-30 days postpartum. If initial ophthalmological examinations of the high dose pups revealed an increase in the incidence of eye lesions for this group, such examinations would be extended to include all pups weaned from control, low and medium dose females.

Statistical procedures employed.

The means and standard errors of various measured parameters were calculated for each treatment group. The significance of difference between control and compound treated group means was tested using Student's t-test and the level of significance was chosen as $p < 0.05$. Chi-square test of significance was employed to compare conception rates, survival rates and data regarding incidence of litters with non-viable pups ($p < 0.05$). The mean number of non-viable pups per litter (non-viable litter size) at birth was analyzed by a rank sum test ($p < 0.05$).

RESULTS

Data on the sire.

Survival rates, physical and behavioral effects. Survival rates were 100% in the control, low and high dose groups and 93% in the medium dose

group as 1 of 14 males died. Male No. 39 died 5 days into the mating period; 2 of 3 females within the mating unit remained unmated at the time of death. A complete gross autopsy of this animal was performed and no lesions attributable to treatment were observed.

No physical or behavioral irregularities were observed among treated or control animals.

Body weight changes. Mean body weights during the seven week pre mating treatment period are presented in Figure 1. Data were comparable between control and treated groups throughout this period.

Food consumption data. Food consumption data for control and treated groups during the pre mating treatment period are presented in Figure 2. During the first four weeks of the pre mating treatment period food consumption for the various treated groups generally exceeded control levels. The following significant increases in mean food consumption were observed: low dose group at weeks 1 and 4; medium dose at weeks 3 and 4; high dose group at weeks 1, 2, 3 and 4. Mean food consumption for weeks 5, 6 and 7 of the pre mating treatment period was comparable between control and treated groups.

Data on the dam.

Survival rates, physical and behavioral effects. The survival rate was 100% in the control and all treated groups as no maternal mortality was observed during this study.

No physical or behavioral irregularities were observed among treated or control animals.

Figure 1

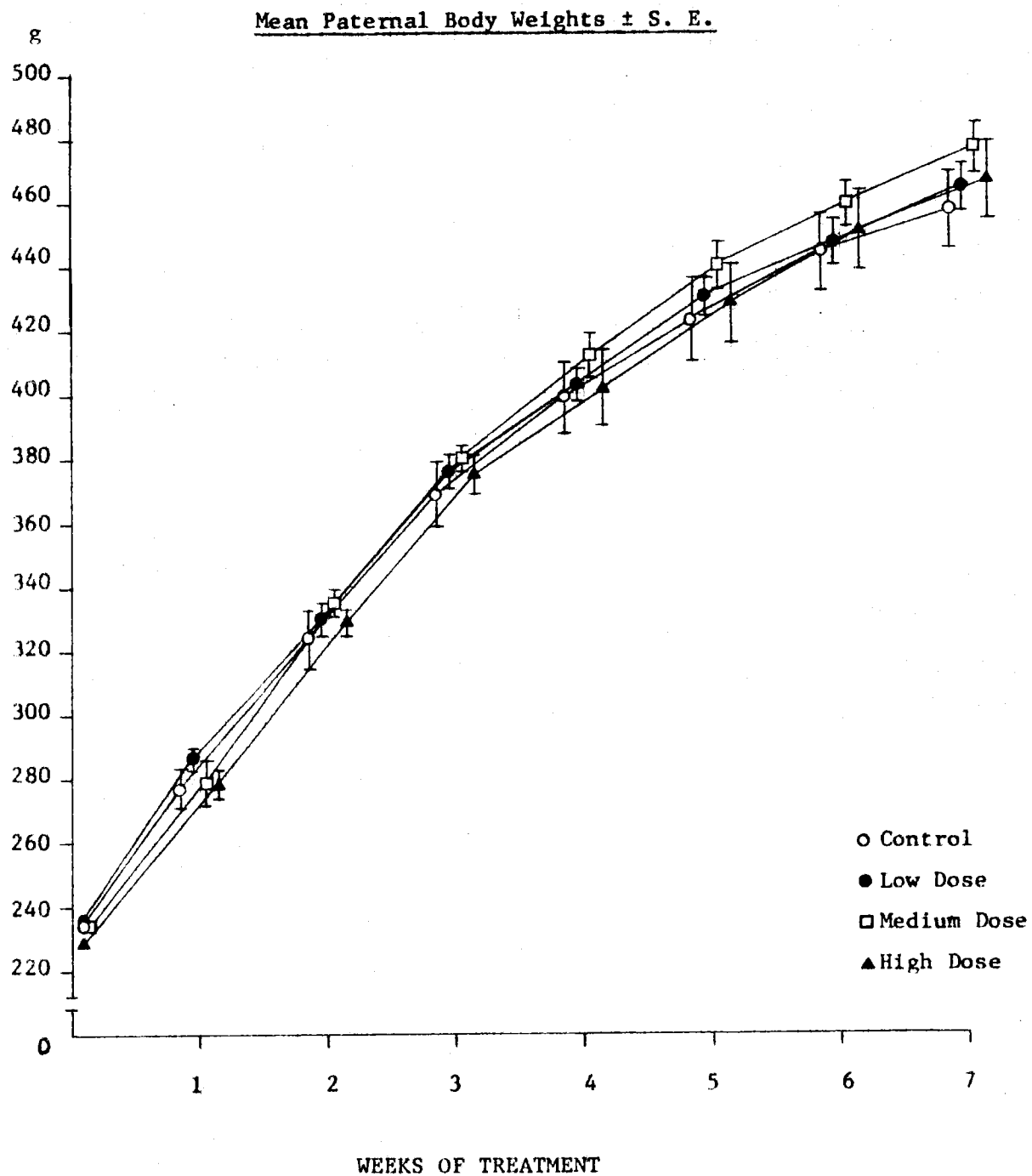
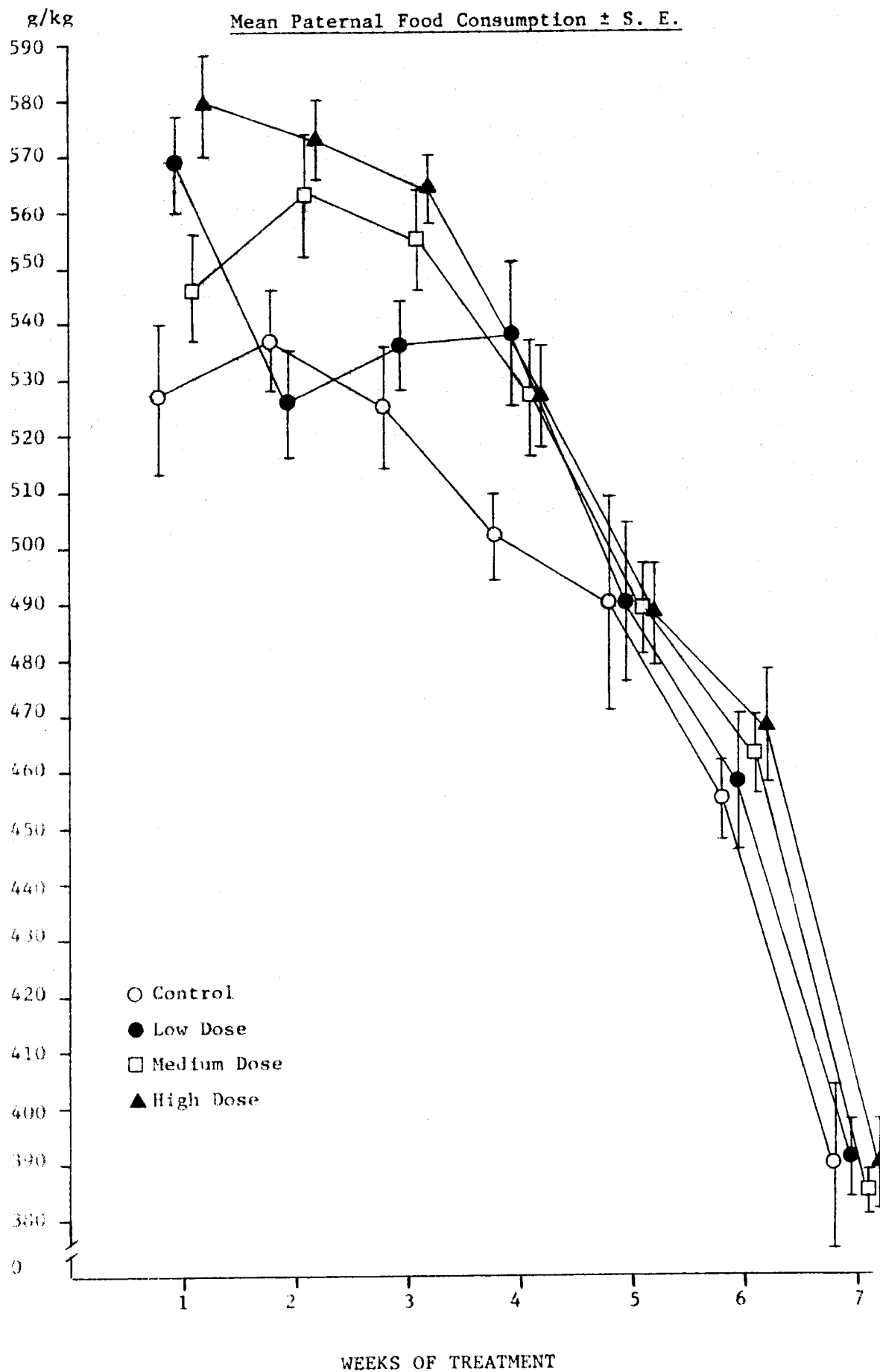
SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE
IN THE RAT

Figure 2

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE
IN THE RAT

Body weight changes. Body weight data for the pre-mating, gestation and lactation periods are presented in Table 1. Mean body weights were comparable between the control, low and medium dose groups throughout the study. In the high dose group, mean body weight was comparable during the pre-mating treatment period and through most of the gestation and lactation periods; however, on gestation day 14 and postpartum days 14 and 21, the mean body weights were significantly lower.

Food consumption data. Food consumption data for the control and treated groups during the pre-mating, gestation and lactation periods are presented in Table 2 and Figure 3. Generally, food consumption was comparable between the control and treated groups throughout the study with the following exceptions: gestation day 14, mean food consumption of the medium dose group was significantly higher; and gestation day 21 mean food consumption in the high dose group was significantly lower. Food consumption for individual females from the control and treated groups is presented in the Appendix.

Since neonatal food consumption was not measured, its influence upon maternal food consumption, especially during the last week of lactation, and compound intake data is not known. Similarly, what influence this additional exogenous source of SC-19192 has upon the results presented in the neonatal examination is indistinguishable.

SC-19192 intake.

Daily dosage levels planned for the low, medium and high dose groups (both male and female) were 0.5, 1.0 and 2.0 g/kg body weight, respectively. Mean maternal SC-19192 intake for the treated groups during the pre-mating,

Table 1

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Treatment Group	Maternal Body Weights (g)			
	Mean \pm S. E.			
	Premating Period		Gestation Period	
	(Days)		(Days)	
	1	14	7	21
Control	203.4 \pm 1.9	231.9 \pm 2.5		
Low Dose	199.0 \pm 2.8	226.4 \pm 4.4		
Medium Dose	199.5 \pm 3.2	224.2 \pm 3.8		
High Dose	200.8 \pm 2.9	225.6 \pm 3.2		
Control	244.4 \pm 4.5	274.9 \pm 4.1	321.8 \pm 7.8	420.5 \pm 14.4
Low Dose	244.5 \pm 5.8	269.8 \pm 5.7	312.8 \pm 6.4	413.7 \pm 9.3
Medium Dose	247.1 \pm 4.9	273.8 \pm 6.0	305.4 \pm 4.1	398.3 \pm 7.3
High Dose	240.8 \pm 4.5	265.6 \pm 5.0	301.5 \pm 5.3*	394.7 \pm 11.3
	Postpartum Period			
	(Days)			
	1	7	14	21
Control	318.0 \pm 11.0	344.3 \pm 11.5	346.1 \pm 7.4	332.6 \pm 7.7
Low Dose	315.7 \pm 8.7	330.0 \pm 9.0	339.6 \pm 7.7	328.4 \pm 9.1
Medium Dose	297.7 \pm 5.6	326.8 \pm 5.1	326.7 \pm 6.4	318.3 \pm 6.2
High Dose	301.3 \pm 9.6	324.0 \pm 8.7	323.4 \pm 7.3*	306.5 \pm 6.9*

* Difference statistically significant ($p < 0.05$).

Table 2

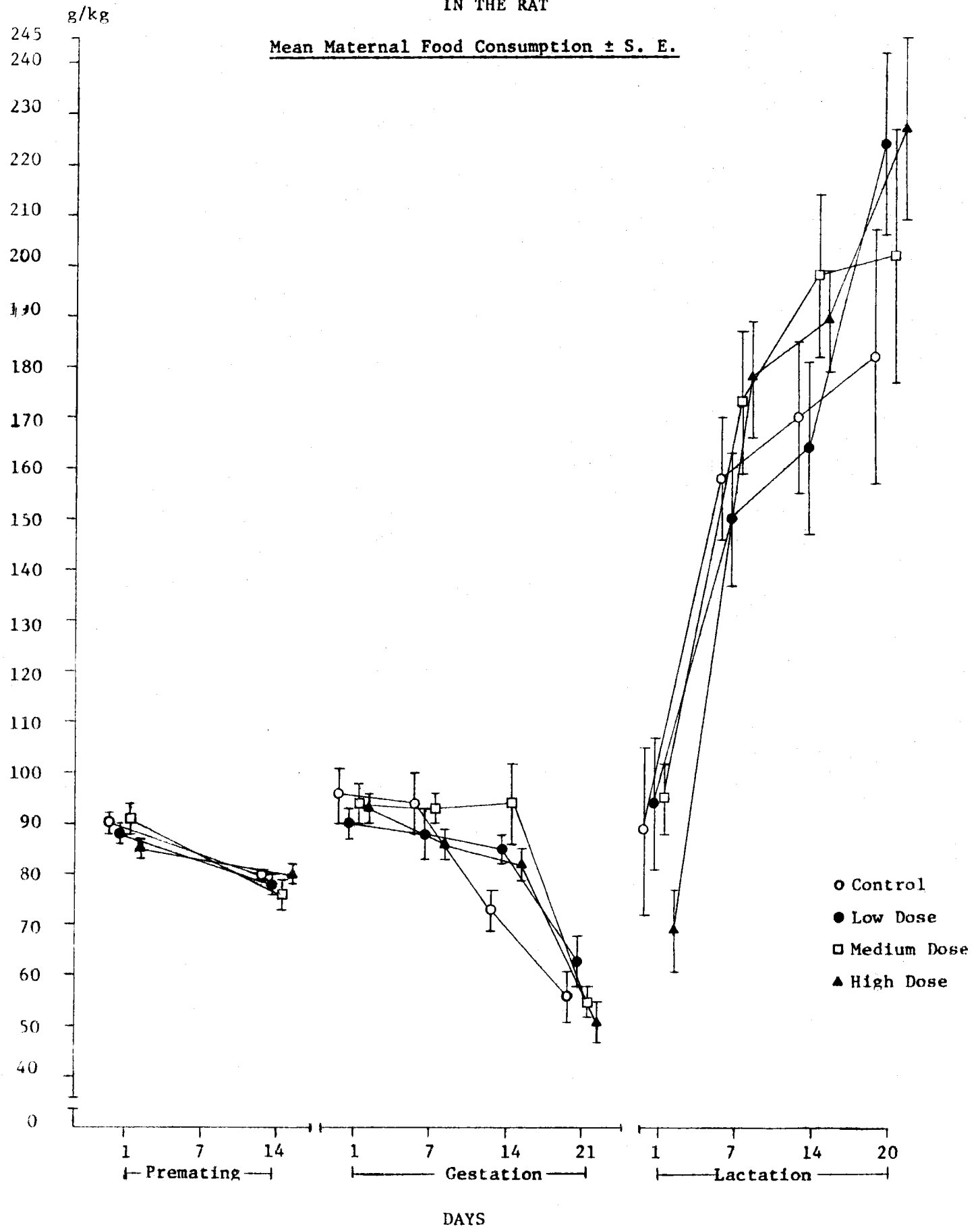
SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Maternal Food and Compound Consumption (g/kg/day)

Mean \pm S. E.

Period	Day	Control		Low Dose		Medium Dose		High Dose	
		Food Consumed	Consumed	Food Consumed	Consumed	Food Consumed	Consumed	Food Consumed	Consumed
Premating:	1	90.4(\pm 2.2)	88.3(\pm 2.0)	0.44(\pm 0.01)	0.91(\pm 0.03)	90.6(\pm 2.6)	84.8(\pm 2.4)	1.70(\pm 0.05)	
	14	79.7(\pm 0.9)	77.6(\pm 2.2)	0.38(\pm 0.01)	0.76(\pm 0.03)	76.1(\pm 2.9)	80.1(\pm 1.8)	1.60(\pm 0.04)	
Mean of Days 1 & 14		85.1	82.9	0.41	0.83	83.4	82.4	1.65	
Gestation:	1	97.7(\pm 3.9)	91.4(\pm 3.1)	0.46(\pm 0.02)	0.95(\pm 0.04)	95.0(\pm 3.9)	95.6(\pm 3.5)	1.91(\pm 0.07)	
	7	93.6(\pm 3.6)	85.2(\pm 5.1)	0.43(\pm 0.03)	0.94(\pm 0.03)	93.9(\pm 2.8)	86.9(\pm 2.8)	1.73(\pm 0.06)	
	14	78.8(\pm 2.8)	85.9(\pm 2.3)	0.43(\pm 0.01)	0.96(\pm 0.07)	95.4(\pm 6.9)*	83.0(\pm 3.3)	1.65(\pm 0.07)	
	21	66.2(\pm 3.5)	62.3(\pm 4.2)	0.31(\pm 0.02)	0.59(\pm 0.03)	59.1(\pm 3.3)	53.2(\pm 3.9)*	1.06(\pm 0.08)	
Mean of the Above		84.1	81.2	0.41	0.86	85.9	79.7	1.59	
Lactation (Postpartum):	1	85.8(\pm 7.2)	91.9(\pm 11.2)	0.46(\pm 0.06)	0.90(\pm 0.08)	90.3(\pm 7.9)	72.6(\pm 7.0)	1.45(\pm 0.14)	
	7	160.0(\pm 7.4)	152.9(\pm 11.4)	0.46(\pm 0.03)	0.92(\pm 0.06)	184.4(\pm 12.4)	185.9(\pm 11.2)	1.85(\pm 0.11)	
	14	173.6(\pm 7.1)	172.1(\pm 15.5)	0.51(\pm 0.05)	1.01(\pm 0.08)	202.1(\pm 17.3)	193.5(\pm 9.1)	1.94(\pm 0.09)	
	21	199.4(\pm 10.2)	221.9(\pm 15.0)	0.66(\pm 0.05)	1.05(\pm 0.11)	210.2(\pm 22.0)	212.2(\pm 18.6)	2.12(\pm 0.19)	
Mean of the Above		154.7	159.7	0.52	0.97	171.8	166.1	1.84	

* Mean differs significantly from control ($p < 0.05$).

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gestation and lactation periods is presented in Table 2. Group mean values (g/kg/day) for compound ingestion over the entire treatment period for females were within roughly 10% of the proposed doses of 0.5, 1 and 2 g/kg SC-19192. Males from the low, medium and high dose groups consumed as a daily mean 0.5, 0.9 and 1.7 g/kg SC-19192, respectively, over the seven week pre-mating treatment period (Table 3).

Reproductive performance and fertility.

Data on conception rates are presented in Table 4; no difference in conception rates between control and treated females is apparent.

Dystocia as evidenced by prolonged labor was not observed among the experimental animals allowed to deliver naturally. Similarly, mean gestation periods were comparable between control and treated groups; these mean values for the control, low, medium and high dose groups were 21.6, 21.5, 21.4 and 21.5 days, respectively.

Data on mating performance are presented in Table 5. No remarkable differences between control or treated groups of either sex were evident.

Fertility rates of control and treated animals are presented in Table 6. Again, no apparent differences between control and treated animals were evident.

Hysterotomy data.

No gross lesions of the ovaries or uterus were observed in any of the animals sacrificed. Results from the uterine examinations are summarized in Table 7; values for individual females are listed in the Appendix. Control

Table 3

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Paternal Compound Consumption (g/kg/day)

Mean \pm S. E.

Treat- ment Group	No. of Males	Premating Treatment Period (Weeks)							Mean Daily Dose†
		1	2	3	4	5	6	7	
Low	14	0.41 \pm 0.007	0.38 \pm 0.006	0.54 \pm 0.009	0.54 \pm 0.013	0.49 \pm 0.014	0.46 \pm 0.012	0.45 \pm 0.008	0.47
Medium	14	0.78 \pm 0.014	0.81 \pm 0.015	0.95 \pm 0.015	0.98 \pm 0.017	0.92 \pm 0.017	0.86 \pm 0.013	0.83 \pm 0.008	0.88
High	14	1.49 \pm 0.023	1.47 \pm 0.017	1.93 \pm 0.020	1.88 \pm 0.032	1.81 \pm 0.034	1.74 \pm 0.039	1.67 \pm 0.033	1.71

† Mean of the values as presented for the 7 weeks of the premating treatment period.

Table 4

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE
IN THE RAT

Conception Rates

<u>Treatment Group</u> (Male x Female)	<u>No. of Females</u>		<u>Conception Rate^b</u> (%)
	<u>Mated</u>	<u>Pregnant^a</u>	
Control x Control	24	22	91.7
Low Dose x Low Dose	24	22	91.7
Medium Dose x Medium Dose	24	20	83.3
High Dose x High Dose	24	22	91.7
Control x Low Dose	4	4	100.0
Control x Medium Dose	4	3	75.0
Control x High Dose	4	4	100.0
Low Dose x Control	12	8	66.7
Medium Dose x Control	12	11	91.7
High Dose x Control	11	11	100.0

^a Pregnant as indicated by one of the following observations: uterine implantation sites; parturition; or uterine placental scars and/or fetal remnants.

^b Conception rate: no. of females pregnant/no. of females mated x 100.

Table 6

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE
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Treatment Group: No. of Males	Fertility Rates Δ											
	Ratio				Percentage							
	Week 1 C* T**	Week 2 C T	Week 3 C T	Week 4 C T	Week 1 C T	Week 2 C T	Week 3 C T	Week 4 C T	Week 1 C T	Week 2 C T	Week 3 C T	Week 4 C T
Control	12 14/24 7/12	22/24 12/12	23/24 12/12	23/24 12/12	58	58	92	100	96	100	96	100
Low Dose	12 5/12 12/24	8/12 21/24	8/12 21/24	8/12 22/24	42	50	67	87	67	87	67	92
Medium Dose	13 4/12 6/24	10/12 14/24	11/12 20/24	11/12 20/24	33	25	83	58	92	83	92	83
High Dose	12 3/11 13/24	8/11 20/24	10/11 21/24	10/11 21/24	27	54	73	83	91	87	91	87

* C - Control (untreated) females.

** T - Treated females; low, medium, and high dose levels.

Δ - Fertility rate is expressed as the ratio of females pregnant per week (cumulative total)/total no. of females mated over the four week mating period.

Table 7

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE
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Hysterotomy Data from Animals Sacrificed on Gestation Day 14

Treatment Group (Male x Female)	Number of Females		Mean No. per Pregnant Female \pm S.E.			
	Mated	Pregnant*	Corpora Lutea	Implan- tation	Viable Fetal Swellings	Resorption Sites
Control x Control	14	14	14.2 \pm 0.5	13.8 \pm 0.4	13.0 \pm 0.5	0.8 \pm 0.3
Low Dose x Low Dose	11	9	14.6 \pm 0.7	13.8 \pm 0.4	12.4 \pm 0.9	1.3 \pm 0.6
Medium Dose x Medium Dose	13	10	15.1 \pm 0.6	14.1 \pm 0.5	12.8 \pm 0.7	1.3 \pm 0.4
High Dose x High Dose	12	11	13.6 \pm 0.7	12.3 \pm 1.1	11.3 \pm 1.0	1.0 \pm 0.3
Control x Low Dose	2	2	15.0	12.5	12.0	0.5
Control x Medium Dose	2	1	16.0	15.0	10.0	5.0
Control x High Dose	2	2	15.0	14.5	13.5	1.0
Low Dose x Control	6	3	14.3	13.7	13.3	0.3
Medium Dose x Control	4	3	16.0	15.0	14.7	0.3
High Dose x Control	5	5	15.2	14.4	12.8	1.6

* Pregnant includes all mated females showing implantation sites at sacrifice.

and treated groups were comparable in all parameters evaluated, namely, the number of corpora lutea, implantations, developing embryos, and resorption sites present.

Data on the progeny.

Litter examination. Results from the initial litter examinations are summarized in Table 8; data for individual litters are in the Appendix. Mean viable litter size (viable pups only) at birth was comparable between the control, low and medium dose groups and significantly lower in the high dose group. Data concerning mean non-viable litter size and mean total litter size (viable and non-viable pups included) at birth were comparable between the control and treated groups. Similarly, the incidence of litters containing both viable and non-viable pups at birth was comparable between control and treated groups.

A variable incidence of cannibalism immediately following delivery is known to occur and is expected in studies of this type. When the entire neonate is consumed prior to initial examination of the litter, such cannibalism remains undetected and its influence on the data is not indicated. However, following the initial litter examination when cannibalism is evident, the neonate is recorded as a dead or missing pup.

Mean viable litter size at weaning [postpartum (pp) day 21] was comparable between the control and treated groups; these mean values for the control, low, medium and high dose groups were 10.0, 9.7, 9.2 and 10.5 pups per litter, respectively.

Table 8

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Summary of the Litter Examination Data

Treatment Group & Mating (Male x Female)	No. Litters/Total Litters in Group						Mean Litter Size; Mean No. Pups		Sex Distribution		
	Viable Pups Only		Both Viable & Non-Viable		Non-Viable Pups Only		Viable (Mean±S.E.)	Non- Viable	Total (Mean±S.E.)	Viable Pups at Birth† (%)	No. of Pups M/F
	No.	%	No.	%	No.	%					
Control x Control	7/8	87	1/8	13	0	0	13.4±0.7	0.3	13.6±0.8	98.5	50/57
Low Dose x Low Dose	11/13	85	2/13	15	0	0	12.7±0.5	0.2	12.9±0.5	98.4	89/76
Medium Dose x Medium Dose	9/10	90	1/10	10	0	0	13.3±0.9	0.1	13.4±0.9	99.3	65/68
High Dose x High Dose	6/11	55	5/11	45	0	0	10.9±1.0*	0.8	11.7±0.7	93.2	54/66
Control x Low Dose	2/2	100	0	0	0	0	13.0	0.0	13.0	100.0	9/17
Control x Medium Dose	2/2	100	0	0	0	0	14.0	0.0	14.0	100.0	18/10
Control x High Dose	2/2	100	0	0	0	0	10.5	0.0	10.5	100.0	10/11
Low Dose x Control	4/5	80	1/5	20	0	0	10.4	0.6	11.0	94.5	22/30
Medium Dose x Control	6/8	75	2/8	25	0	0	14.0	0.4	14.4	97.2	55/57
High Dose x Control	6/6	100	0	0	0	0	13.0	0.0	13.0	100.0	33/45

* Difference statistically significant ($p < 0.05$).

† Viable pups at birth: Mean viable litter size/mean total litter size x 100.

Neonatal examination. The sex distribution of viable pups at birth is indicated in Table 8; this distribution remained essentially unchanged at the time of weaning. The sex distribution index was comparable between the control and treated groups.

Pup body weight data are presented in Table 9; data for individual litters are in the Appendix. The initial weighing was customarily done on the day of delivery; however, in some instances it was delayed to the following day (pp day 2). Mean pup weights were comparable (both sexes) between control and treated groups initially at birth and again on postpartum days 4 and 21.

Pup survival rates. Pup survival rates summarized from the individual litter data appended are presented in Table 10. Pup survival rates to postpartum days 4 and 21 were comparable between the control, low and medium dose groups and were significantly higher (both days 4 and 21) in the high dose group.

Gross external examination. Gross examination of all pups was initially performed shortly after birth and repeated on postpartum days 4 and 21. Gross malformations were not observed in the 349 control, 191 low, 161 medium and 141 high dose viable pups examined at birth and in pups surviving to postpartum day 4. At weaning (postpartum day 21) no gross malformations were observed in 116 medium or 124 high dose pups; however, 2 of 261 control pups (0.8%) and 1 of 118 low dose pups (0.8%) exhibited partial alopecia at weaning. This is considered incidental and unrelated to compound administration. The affected pups were observed in the litters of control female No. 48 and low dose female No. 80.

Table 9

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE
IN THE RAT

Pup Body Weights

Treatment Group (Male x Female)	Mean Body Wt. (g) \pm S. E.					
	Birth		4		Postpartum Day 21	
	Male	Female	Male	Female	Male	Female
Control x Control	6.3 \pm 0.2	6.0 \pm 0.2	7.8 \pm 0.6	7.6 \pm 0.5	32.7 \pm 2.1	31.5 \pm 2.7
Low Dose x Low Dose	6.5 \pm 0.2	6.2 \pm 0.1	8.6 \pm 0.5	7.9 \pm 0.5	36.5 \pm 2.9	32.2 \pm 3.0
Medium Dose x Medium Dose	6.4 \pm 0.1	6.1 \pm 0.2	8.6 \pm 0.3	8.3 \pm 0.3	31.4 \pm 2.1	31.7 \pm 1.5
High Dose x High Dose	6.4 \pm 0.2	6.1 \pm 0.1	8.9 \pm 0.5	8.7 \pm 0.3	34.1 \pm 2.1	32.7 \pm 1.7
Control x Low Dose	5.9	5.4	7.6	7.0	33.8	30.6
Control x Medium Dose	6.3	6.1	8.1	7.8	29.0	26.9
Control x High Dose	5.9	6.1	7.7	7.6	21.9	27.6
Low Dose x Control	7.2	7.1	10.3	9.5	39.1	39.3
Medium Dose x Control	6.4	6.1	8.9	8.5	33.5	33.2
High Dose x Control	6.4	6.1	9.3	8.9	33.9	33.3

Table 10

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE
IN THE RAT

Pup Survival Rates

Treatment Group (Male x Female)	Total No. of Pups Viable At Birth	Total No. of Pups Viable		Survival Rates (%)	
		4	21	4	21
Control x Control	107	98	70	91.6	65.3
Low Dose x Low Dose	165	157	97	95.1	58.8
Medium Dose x Medium Dose	133	125	92	94.0	69.2
High Dose x High Dose	120	120*	115*	100.0*	95.8*
Control x Low Dose	26	24	21	92.3	80.8
Control x Medium Dose	28	28	24	100.0	85.7
Control x High Dose	21	21	9	100.0	42.8
Low Dose x Control	52	52	48	100.0	92.3
Medium dose x Control	112	108	85	96.5	75.8
High Dose x Control	78	70	58	89.7	74.3

* Difference statistically significant ($p < 0.05$).

External, visceral and skeletal examination of the non-viable (intact) pups recovered during the initial litter examination revealed abnormalities in 1 of 8 control (12.5%) and 3 of 9 high dose (33.3%) pups; the 2 low and 1 medium dose pups so examined were unremarkable.

Anomalous non-viable pups were recovered from the following two litters:

Control female No. 41 delivered a litter of 13 pups: 11 viable normal appearing pups and 2 non-viable pups, one of which exhibited micrognathia. Skeletal examination of this anomalous non-viable pup revealed additional defects of the sternbrae (fusion & splitting). Similar examination of the normal appearing non-viable pup was unremarkable.

High dose female No. 128 delivered a litter of 7 pups: 4 viable normal appearing pups and 3 non-viable pups, one of which exhibited micrognathia with cleft palate. At skeletal examination all 3 non-viable pups exhibited "stubby" mandibles, defective ossification of the sternum (fused and/or split sternbrae) and defects of the thoracic vertebral centra (splitting). Unique to one of these pups was unilateral (L.) agenesis of the 5th thoracic rib and vertebral arch.

Skeletal anomalies of the nature described occurred in non-viable pups from both the control and the SC-19192 treated groups and are considered unrelated to compound administration.

Ophthalmological examination. Ocular lesions detected by direct or indirect ophthalmoscopy were observed in 4 of 122 pups weaned from high dose females (3.3%). These lesions consisted of corneal or iris alterations

consistent with resolving anterior segment inflammatory processes and were not considered treatment related. In addition, one pup was observed to have negligible pupil dilation of the left eye following mydriatic application; such effect was related to incomplete development of the anterior chamber. The type and degree of this lesion were considered consistent with a mild level of congenital microphthalmia occurring at the incidence rate historically encountered. Affected pups and descriptions of the ocular lesions follow.

Female No.	Pup No.	Sex	Age at Observation pp (Days)	Description of the Lesion
127	1	M	33	Unilateral (L. eye): incomplete dilation; improperly developed anterior chamber.
135	1	F	33	Unilateral (R. eye): incompletely developed orbital structure: anterior synechiae, corneal cloudiness. Diffuse corneal vascularization.
135	2	F	33	Unilateral (R. eye): anterior synechiae; incomplete dilation; pannus formation.
139	1	M	31	Unilateral (R. eye): severe anterior segment inflammation; total corneal opacification with vascularization.

SUMMARY AND CONCLUSIONS

SC-19192, a conversion product of the nutritive sweetening agent SC-18862, was evaluated for its potential effects on reproductive performance of male and female albino rats. The effects on mating performance and fertility of both sexes, on the entire course of gestation and subsequent lactation, on early and late stages of fetal development, and on postnatal development of the pups were studied.

Compound admixed with the granulated basal diet was presented to both male and female treated rats during a premating treatment period and to the female groups during gestation and lactation. During the mating period when treated and control animals were housed together, compound was administered by gastric intubation. A concurrent control (untreated) group was included.

One-half of the mated females in each group were sacrificed on day 14 of gestation and the following parameters were evaluated: the number and position of viable, non-viable and resorbed fetuses and the number of corpora lutea. The remaining females were permitted to deliver naturally and resulting litters were examined for viable and non-viable pups. Additionally, each pup was externally examined initially at birth and again at postpartum days 4 and 21. Weanling pups from the high dose group were examined ophthalmoscopically.

The group mean values for compound ingestion over the entire study were within roughly 10% of the proposed doses of 0.5, 1.0 and 2.0 g/kg/day in the low, medium and high dose groups, respectively.

Treatment with SC-19192 at the above mentioned dosages had no apparent effect upon the following parental parameters: survival rates, food consumption, mating performance and fertility rates and paternal body weight change.

Maternal body weights throughout the study were comparable between the control, low and medium dose groups. In the high dose group (1.8 g/kg) body weights were significantly depressed on gestation day 14 and again at postpartum days 14 and 21.

Hysterotomy performed on gestation day 14 revealed that control and treated groups were comparable in all parameters evaluated. Similarly, litter examination data were comparable between the control and treated groups with the exception of a significant decrease in viable litter size observed at the high dose group.

No compound induced alterations were observed in the 191 low, 161 medium or 141 high dose viable pups examined initially at birth or in surviving pups at postpartum days 4 and 21. Similarly, ophthalmological examination of 122 pups weaned from high dose females (pups aged 28-35 days postpartum) revealed no evidence of a treatment related effect.

External and/or skeletal abnormalities were observed in 1 of 2 non-viable pups recovered from the litter of control female No. 41 and in all 3 non-viable pups from the litter of high dose female No. 128. Similar examinations of the remaining 6 control, 2 low, 1 medium and 6 high dose non-viable pups recovered during the initial litter examinations were unremarkable. The nature of the defects observed in the control and high dose non-viable pups was similar; hence, these anomalies are considered unrelated to compound administration.

It is concluded that continuous dietary administration of SC-19192 to mature male and female rats up to 1.80 g/kg/day during the pre-mating, mating, gestation and lactation periods causes no adverse effects on sexual behavior, fertility, body weight or food consumption. Likewise, no evidence of treatment related effects on fetal anomalies or neonatal growth and development was encountered.

APPENDIX TABLES OF INDIVIDUAL VALUES

Key to Appendix Table 1

N.P. - Not Pregnant

N.M. - Not Mated

N.R. - Not Recorded

* - Denotes loss of a litter

† - Female sacrificed on gestation day 14

Appendix Table 1

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the Control Group)

Animal No.	Premating Day		Gestation Day			Delivery	Postpartum Day		
	1	14	1	7	14		7	14	21
1+	87.5	83.7	82.4	81.5	86.4				
2+	97.4	83.3	N.P.						
3+	84.6	76.0	92.9	109.1	N.R.				
4+	81.6	78.9	91.7	85.9	N.R.				
5+	125.0	75.7	84.7	119.6	69.3				
6+	70.3	84.1	86.2	102.0	72.3				
7+	91.9	86.5	137.2	111.1	79.3				
8+	103.8	83.7	94.0	92.6	94.9				
9+	104.9	78.4	81.6	80.4	93.9				
10+	90.7	89.5	N.P.						
11+	93.6	79.5	82.7	85.3	89.8				
12+	91.4	84.1	176.5	119.3	118.6				
13	119.2	85.4	N.P.						
14	103.2	76.4	69.5	72.5	65.0	58.6	142.9	161.5	196.8
15	89.9	68.2	90.3	86.7	74.1	80.7	132.3	172.0	201.7
16	77.5	71.3	86.4	81.6	82.1	85.7	158.6	184.6	175.7
17	103.1	76.0	92.6	69.9	32.2	95.8	158.2	177.7	167.7
18	95.6	72.5	87.8	81.6	59.2	31.5	174.4	213.4	206.6
19	80.2	72.5	84.3	79.7	63.7	86.7	177.5	210.8	248.4
20	92.3	65.5	N.P.						
21	90.9	90.7	88.7	84.5	76.2	30.0	157.6	111.1	87.7
22	108.3	71.6	108.0	72.5	82.2	87.1	119.8	167.6	174.7
23	88.1	77.9	91.3	86.2	79.6	150.6	185.4	195.7	211.4
24	89.5	63.3	88.2	121.2	86.5	47.8	165.6	147.4	228.8
25+	94.9	75.9	110.7	103.7	16.2				

Appendix Table 1 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the Control Group)

Animal No.	Premating Day		Gestation Day				Delivery	Postpartum Day		
	1	14	1	7	14	21		7	14	21
26	95.6	83.7	N.M.							
27†	99.0	83.7	135.0	91.6	N.R.					
28†	97.8	81.7	96.2	99.2	48.2					
29†	92.2	83.0	86.1	78.2	85.2					
30†	97.6	83.7	110.2	98.5	91.2					
31†	86.4	77.2	148.6	99.0	96.6					
32†	93.2	72.3	N.P.							
33†	103.8	79.0	160.9	103.2	72.4					
34†	54.1	91.5	78.9	98.9	69.1					
35†	86.2	82.6	109.2	210.9	N.R.					
36†	114.8	99.3	197.4	77.5	90.6					
37	100.0	74.1	76.7	67.5	63.6	58.9	53.2	148.7	186.2	173.6
38	82.5	79.9	99.2	86.8	92.5	52.5	137.7	158.2	198.1	231.5
39	90.5	71.1	N.R.	191.6	103.0	72.4	63.5	95.8	122.9	130.6
40	103.2	83.8	52.0	103.8	88.6	74.6	87.4	116.6	115.4	89.9
41	93.0	75.9	96.8	82.1	80.6	96.5	125.0	181.8	204.4	222.2
42	52.4	74.8	80.6	88.9	85.4	91.8	114.4	136.9	232.6	182.4
43	92.5	81.3	105.5	90.3	80.4	60.9	80.6	89.9	*	*
44	94.7	83.0	84.0	79.3	85.7	63.1	55.9	208.3	187.5	233.3
45	79.1	84.1	N.P.							
46	86.0	79.5	83.7	66.7	75.9	62.5	174.2	*	*	*
47	78.3	62.1	100.0	89.3	83.3	61.4	143.2	176.3	198.9	213.5
48	22.5	80.5	89.8	89.7	76.2	58.1	55.9	213.0	155.6	237.7
49†	104.7	80.6	74.7	N.R.	115.8					
50†	119.7	75.3	50.0	90.9	N.R.					

Appendix Table 1 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the Control Group)

Animal No.	Premating Day		Gestation Day				Delivery	Postpartum Day		
	1	14	1	7	14	21		7	14	21
51+	84.9	90.7	78.6	103.8	N.R.					
52+	66.5	93.5	115.2	83.9	N.R.					
53+	109.9	85.3	89.6	89.1	N.R.					
54	81.9	87.9	88.7	96.2	N.R.	125.3	57.5	169.3	123.1	200.0
55	42.9	73.8	90.1	78.7	69.1	71.6	63.6	253.4	146.7	288.7
56	88.9	81.7	88.9	76.7	67.1	39.8	52.9	108.0	119.8	142.4
57	92.1	71.6	N.P.							
58	96.4	84.0	89.1	89.0	78.9	39.1	131.6	151.2	219.8	203.7
59	88.5	82.9	83.3	85.3	80.6	60.8	85.7	216.0	211.2	298.8
60	99.5	77.5	135.3	61.2	85.4	63.5	80.6	164.7	177.0	236.0
Total	5426.1	4783.2	4982.0	4774.7	3386.9	1786.6	2317.4	4160.4	4341.0	4983.8
Mean	90.4	79.7	97.7	93.6	78.8	66.2	85.8	160.0	173.6	199.4

Appendix Table 1 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the Low Dose Group)

Animal No.	Premating Day		Gestation Day				Delivery	Postpartum Day		
	1	14	1	7	14	21		7	14	21
61+	84.5	76.0	N.P.							
62+	107.7	87.3	92.4	42.0	N.R.					
63+	81.6	83.7	105.0	90.9	79.9					
64+	94.7	87.6	N.R.	N.R.	N.R.					
65+	82.0	75.4	96.2	53.7	N.R.					
66+	90.4	87.2	123.0	93.3	96.8					
67	68.8	70.4	N.R.	N.R.	82.3	50.0	154.8	172.4	184.4	180.8
68	75.1	74.1	87.6	140.6	73.7	81.1	66.7	154.3	241.9	347.8
69	100.0	83.0	96.8	23.3	82.2	57.9	75.4	178.1	220.5	227.8
70	80.5	78.5	91.3	80.2	78.2	56.7	73.3	163.4	104.2	*
71	88.7	97.6	85.6	102.8	93.5	107.2	150.9	172.4	256.8	186.7
72	78.8	88.0	85.8	78.1	81.6	38.9	52.1	108.3	131.0	184.9
73+	80.3	68.6	84.0	50.0	N.R.					
74+	79.5	75.3	N.P.							
75+	100.5	73.4	92.9	112.0	79.6					
76+	87.8	69.5	88.9	76.3	N.R.					
77+	110.8	94.2	87.7	115.7	110.7					
78+	90.4	78.5	92.1	93.2	113.5					
79	100.0	69.6	90.9	112.8	93.5	58.7	76.9	159.5	221.5	195.0
80	100.0	72.3	90.5	80.9	82.2	59.1	73.4	246.7	209.6	219.4
81	88.9	61.8	86.5	83.9	76.0	69.1	86.5	146.7	159.8	220.0
82	79.3	88.0	141.2	88.7	76.9	50.5	64.6	110.5	81.2	*
83	89.7	36.5	86.1	90.6	86.2	56.7	69.7	176.1	227.5	241.2
84	88.8	77.2	86.1	92.6	78.7	49.4	93.1	186.7	139.4	287.6
85	86.1	80.6	61.7	74.9	76.7	60.2	52.2	50.0	124.7	213.8

Appendix Table 1 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the Low Dose Group)

Animal No.	Premating Day		Gestation Day				Delivery	Postpartum Day		
	1	14	1	7	14	21		7	14	21
86 ⁺	90.9	82.0	72.7	84.7	84.5					
87	95.7	74.2	81.8	85.9	88.0	75.7	204.9	140.8	106.3	157.9
88	70.0	77.6	87.5	98.5	88.8	63.5	83.9	127.5	*	*
Total	2471.5	2172.3	2194.3	2045.6	1803.5	934.7	1378.4	2293.4	2408.8	2662.9
Mean	88.3	77.6	91.4	85.2	85.9	62.3	91.9	152.9	172.1	221.9

Appendix Table 1 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the Medium Dose Group)

Animal No.	Premating Day		Gestation Day				Delivery	Postpartum Day		
	1	14	1	7	14	21		7	14	21
89†	92.1	93.6	90.9	94.7	93.0					
90†	79.9	77.1	84.7	91.9	79.2					
91†	78.4	77.9	107.3	90.2	94.0					
92†	106.4	81.5	97.8	100.0	91.2					
93†	80.6	76.5	89.3	85.4	87.1					
94†	86.0	116.7	113.8	86.8	88.2					
95	100.0	56.8	84.7	88.8	99.3	N.R.	122.7	139.2	128.8	94.9
96	73.8	56.4	89.3	80.4	75.6	50.0	70.4	219.3	264.0	313.7
97	84.8	68.8	77.7	84.5	64.1	49.3	117.2	114.6	204.8	202.5
98	106.4	60.5	105.9	94.6	90.9	42.5	114.0	206.2	225.1	200.0
99	94.9	77.7	N.R.	N.R.	109.0	73.1	32.1	217.6	135.3	211.1
100	82.6	75.0	N.P.							
101†	82.9	87.7	N.P.							
102†	97.2	88.0	137.5	98.5	208.3					
103†	93.5	59.9	N.P.							
104†	95.4	62.5	80.9	86.5	N.R.					
105†	101.6	101.2	N.P.							
106†	95.6	75.5	114.3	93.2	87.5					
107	105.7	73.9	N.P.							
108	81.8	60.5	84.4	82.5	83.8	55.5	76.4	206.7	231.2	223.1
109	70.7	75.3	57.4	136.7	N.R.	65.8	85.7	217.6	165.7	236.3
110	74.0	86.5	84.0	89.9	75.0	50.7	67.5	186.3	218.7	296.0
111	94.5	83.3	103.3	98.3	76.2	64.0	85.2	117.6	217.4	113.1
112	55.0	68.6	N.R.	N.R.	N.R.	78.1	111.9	243.5	327.8	331.1
113†	95.9	74.8	N.R.	109.2	108.2					

Appendix Table 1 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the Medium Dose Group)

Animal No.	Premating Day		Gestation Day				Delivery	Postpartum Day		
	1	14	1	7	14	21		7	14	21
114†	103.6	86.7	102.6	80.9	N.R.					
115	104.1	89.7	85.9	86.7	93.8	58.6	118.2	151.5	122.6	141.9
116	118.4	38.6	108.7	112.0	108.4	62.0	81.9	192.1	184.1	158.2
Total	2535.8	2131.2	1900.4	1971.7	1812.8	649.6	1083.2	2212.2	2425.5	2521.9
Mean	90.6	76.1	95.0	93.9	95.4	59.1	90.3	184.4	202.1	210.2

Appendix Table 1 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the High Dose Group)

Animal No.	Premating Day		Gestation Day				Delivery	Postpartum Day		
	1	14	1	7	14	21		7	14	21
117+	103.6	86.5	95.8	59.3	86.7					
118+	97.4	59.9	N.R.	N.R.	73.4					
119+	121.1	94.4	N.P.							
120+	89.5	79.9	87.5	80.5	89.1					
121+	83.3	86.7	89.4	98.5	92.4					
122+	84.6	70.7	95.0	89.6	89.4					
123	50.0	81.1	86.7	85.2	97.9	84.1	115.3	166.6	207.7	285.7
124	69.8	67.0	N.P.							
125	76.7	77.1	64.0	98.2	80.6	58.0	80.6	170.5	174.1	222.2
126	84.4	76.6	90.9	82.2	74.8	53.4	67.6	238.6	167.6	184.0
127	87.2	83.7	75.1	86.2	90.0	46.2	47.9	150.0	172.4	190.1
128	86.0	80.0	88.4	43.3	77.4	35.6	45.1	100.0	107.5	78.1
129+	80.8	73.9	90.1	96.6	N.R.					
130+	85.4	79.1	86.1	81.5	83.6					
131+	94.7	103.6	123.1	92.7	103.8					
132+	95.4	75.9	N.R.	N.R.	N.R.					
133+	85.2	80.1	86.2	88.0	64.5					
134+	88.1	73.6	97.1	92.4	N.R.					
135	84.8	74.0	95.9	83.8	62.1	51.8	111.7	175.1	203.3	267.0
136	75.7	88.2	130.2	103.3	82.0	53.9	56.0	200.0	198.7	253.4
137	95.7	82.2	113.4	98.0	56.1	51.2	70.1	202.6	221.4	283.6
138	88.6	83.3	95.0	87.7	79.3	52.3	66.9	222.2	218.3	215.2
139	72.9	63.1	88.8	92.4	84.6	59.4	81.5	250.0	235.8	99.2
140	74.4	74.5	82.3	77.1	85.8	46.2	62.1	161.6	191.3	273.3
141+	79.5	91.0	127.0	83.0	53.5					

Appendix Table 1 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Food Consumption Data (g/kg)
(Individual Values for the High Dose Group)

Animal No.	Premating Day		Gestation Day				Delivery	Postpartum Day		
	1	14	1	7	14	21		7	14	21
142 +	72.3	83.3	128.7	90.6	126.1					
143	82.1	93.9	85.5	108.3	90.9	71.0	102.6	212.2	205.6	165.5
144	86.3	78.3	93.2	87.3	84.5	28.6	36.0	167.7	212.2	241.4
Total	2375.5	2242.2	2295.4	2085.7	1908.5	691.7	943.4	2417.1	2515.9	2758.7
Mean	84.8	80.1	95.6	86.9	83.0	53.2	72.6	185.9	193.5	212.2

Appendix Table 2

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy DataIndividual Values: Control x Control
(Mating Group, σ^7 x ϕ)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
3	9	9	8	1
4	13	13	13	0
5	15	13	13	0
6	14	14	13	1
27	15	15	12	3
28	13	13	13	0
29	16	16	16	0
30	15	15	15	0
35	16	15	15	0
36	15	14	11	3
50	15	14	14	0
51	14	14	13	1
52	15	15	13	2
53	14	13	13	0
Totals	199	193	182	11
Means	14.2	13.8	13.0	0.8

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy DataIndividual Values: Low x Low
(Mating Group, ♂ x ♀)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
62	17	14	13	1
63	13	13	13	0
64	16	16	16	0
65	12	12	7	5
75	12	12	12	0
76	14	14	13	1
77	18	15	14	1
78	15	14	10	4
86	14	14	14	0
Totals	131	124	112	12
Means	14.6	13.8	12.4	1.3

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy Data

Individual Values: Medium x Medium
(Mating Group, ♂ x ♀)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
90	15	14	13	1
91	13	13	12	1
92	17	17	17	0
93	18	12	11	1
94	15	14	14	0
102	17	16	14	2
104	14	14	12	2
106	15	15	14	1
113	15	14	13	1
114	12	12	8	4
Totals	151	141	128	13
Means	15.1	14.1	12.8	1.3

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy DataIndividual Values: High x High
(Mating Group, ♂ x ♀)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
117	12	12	10	2
118	12	3	3	0
120	12	12	12	0
121	16	16	15	1
122	13	13	13	0
129	11	11	11	0
130	12	12	9	3
131	16	16	15	1
132	18	15	13	2
133	16	13	12	1
134	12	12	11	1
Totals	150	135	124	11
Means	13.6	12.3	11.3	1.0

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy Data

Individual Values: Control x Low
(Mating Group, ♂ x ♀)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
66	16	15	14	1
73	14	10	10	0
Totals	30	25	24	1
Means	15.0	12.5	12.0	0.5

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy Data

Individual Values: Control x Medium
(Mating Group, ♂ x ♀)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
89	16	15	10	5
Totals	16	15	10	5
Means	16.0	15.0	10.0	5.0

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy Data

Individual Values: Control x High
(Mating Group, ♂ x ♀)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
141	13	13	12	1
142	17	16	15	1
Totals	30	29	27	2
Means	15.0	14.5	13.5	1.0

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy Data

Individual Values: Low x Control
(Mating Group, σ^7 x ϕ)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
1	15	14	14	0
8	13	12	12	0
31	15	15	14	1
Totals	43	41	40	1
Means	14.3	13.7	13.3	0.3

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy Data

Individual Values: Medium x Control
(Mating Group, ♂ x ♀)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
11	16	16	15	1
34	16	13	13	0
49	16	16	16	0
Totals	48	45	44	1
Means	16.0	15.0	14.7	0.3

Appendix Table 2 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Hysterotomy Data

Individual Values: High x Control
(Mating Group, ♂ x ♀)

Animal Number	Corpora Lutea	Implantations	Embryos	Resorptions
7	15	14	12	2
9	16	16	15	1
12	15	15	13	2
25	17	16	13	3
33	13	11	11	0
Totals	76	72	64	8
Means	15.2	14.4	12.8	1.6

Appendix Table 3

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight Data

Control x Control
(Mating Group, $\sigma^7 \times q$)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
16	7	5	0	6	5	1	5	4	2	68.8	80.7	282.4
17	5	6	0	5	6	0	5	4	2	71.7	81.1	324.2
21	7	5	0	6	3	3	3	1	5	71.1	65.5	130.2
37	8	6	0	8	6	0	7	5	2	99.9	140.7	457.5
38	6	7	0	6	7	0	5	7	1	83.1	119.8	441.7
46	7	6	0	7	3	3	0	0	10	76.9	52.2	--
56	5	11	0	4	10	2	3	6	5	91.9	96.0	192.6
59	5	11	2	5	11	0	5	10	1	89.2	132.6	386.9
Totals:												
Per Group	50	57	2	47	51	9	33	37	28			
All Groups	107			98			70					
\bar{x} Litter Size	13.4			12.3			10.0					
\bar{x} D Pups	0.3			1.1			3.5					

*M = Male

+F = Female

**D = Dead or Missing

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight Data

Low x Low
(Mating Group, ♂ x ♀)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
67	7	5	0	7	4	1	7	2	2	86.4	110.3	311.9
68	6	4	2	5	4	1	5	4	0	71.5	104.8	487.5
70	5	5	0	5	5	0	0	0	10	67.9	91.1	--
71	6	7	0	6	7	0	6	5	2	88.9	111.9	347.8
72	8	6	0	8	6	0	3	3	8	80.8	89.0	193.4
80	8	6	0	8	6	0	7	5	2	89.9	121.1	367.6
81	8	6	0	8	6	0	8	6	0	79.0	111.9	412.5
82	4	8	0	4	8	0	0	0	12	70.6	82.5	--
83	2	8	0	2	8	0	2	5	3	62.5	89.7	334.2
84	11	5	0	11	5	0	9	5	2	95.0	145.0	432.2
85	9	6	1	9	5	1	7	4	3	97.3	122.8	359.6
87	6	7	0	6	6	1	3	1	8	76.3	71.1	104.8
88	9	3	0	6	2	4	0	0	8	73.5	42.2	--

Totals:

Per Group	89	76	3	85	72	8	57	40	60			
All Groups		165			157			97				
\bar{x} Litter Size		12.7			12.1			9.7				
\bar{x} D Pups			0.2			0.6			4.6			

*M = Male

+F = Female

**D = Dead or Missing

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight Data

Medium x Medium
(Mating Group, ♂ x ♀)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
95	9	3	0	9	3	0	1	2	9	69.2	82.4	70.9
96	6	8	0	6	8	0	6	8	0	79.7	114.6	405.0
97	5	8	0	5	8	0	4	4	5	87.1	107.4	291.3
98	6	3	0	6	3	0	4	3	2	58.2	95.4	296.4
108	10	10	0	7	8	5	6	8	1	113.6	126.6	426.4
109	6	6	0	6	6	0	6	6	0	84.1	114.8	360.1
110	5	9	0	5	9	0	5	9	0	79.7	113.6	391.3
111	6	6	0	5	4	3	2	3	4	79.5	70.4	147.9
112	6	7	1	6	7	0	4	6	3	85.8	109.6	347.5
115	6	8	0	6	8	0	3	2	9	84.8	114.4	168.4
Totals:												
Per Group	65	68	1	61	64	8	41	51	33			
All Groups		133			125			92				
\bar{x} Litter Size		13.3			12.5			9.2				
\bar{x} D Pups			0.1			0.8			3.3			

*M = Male

+F = Female

**D = Dead or Missing

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight Data

High x High
(Mating Group, ♂ x ♀)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
123	4	8	0	4	8	0	4	8	0	75.0	108.7	356.8
125	7	5	0	7	5	0	5	5	2	68.1	84.8	269.7
126	9	5	0	9	5	0	9	5	0	89.8	112.9	457.6
127	3	5	2	3	5	0	3	5	0	55.0	89.3	375.5
128	3	1	3	3	1	0	3	1	0	25.4	32.0	136.9
135	5	8	0	5	8	0	5	8	0	79.7	119.2	367.5
136	2	9	2	2	9	0	1	9	1	68.7	76.6	339.3
137	6	8	0	6	8	0	6	7	1	78.8	117.5	371.4
138	5	3	1	5	3	0	5	3	0	59.2	81.3	343.6
140	3	11	1	3	11	0	3	10	1	81.4	115.1	379.4
144	7	3	0	7	3	0	7	3	0	61.1	87.4	332.6
Totals:												
Per Group	54	66	9	54	66	0	51	64	5			
All Groups		120			120			115				
\bar{x} Litter Size		10.9			10.9			10.5				
\bar{x} D Pups			0.8			0			0.4			

*M = Male

+F = Female

**D = Dead or Missing

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight DataControl x Low
(Mating Group, $\sigma^7 \times q$)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
69	5	9	0	5	7	2	5	6	1	77.9	94.5	372.4
79	4	8	0	4	8	0	2	8	2	67.6	79.1	295.3
Totals:												
Per Group	9	17	0	9	15	2	7	14	3			
All Groups		26			24			21				
\bar{x} Litter Size		13.0			12.0			10.5				
\bar{x} D Pups			0			1.0			1.5			

*M = Male

+F = Female

**D = Dead or Missing

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight DataControl x Medium
(Mating Group, ♂ x ♀)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
99	11	5	0	11	5	0	11	5	0	96.1	129.4	421.0
116	7	5	0	7	5	0	5	3	4	78.1	94.9	241.7
Totals:												
Per Group	18	10	0	18	10	0	16	8	4			
All Groups		28			28			24				
\bar{x} Litter		14			14			12				
\bar{x} D Pups			0			0				2.0		

*M = Male

+F = Female

**D = Dead or Missing

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight Data

Control x High
(Mating Group, ♂ x ♀)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
139	8	5	0	8	5	0	3	1	9	80.8	108.1	88.3
143	2	6	0	2	6	0	1	4	3	41.0	56.1	146.7
Totals:												
Per Group	10	11	0	10	11	0	4	5	12			
All Groups		21			21			9				
\bar{x} Litter Size		10.5			10.5			4.5				
\bar{x} D Pups			0			0			6.0			

*M = Male
+F = Female
**D = Female

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight Data

Low x Control
(Mating Group, ♂ x ♀)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
23	5	5	0	5	5	0	5	5	0	71.9	93.7	412.7
40	0	2	0	0	2	0	0	2	0	23.1	26.1	91.3
47	6	9	0	6	9	0	6	7	2	105.4	153.2	468.3
48	5	7	3	5	7	0	5	6	1	81.1	110.3	373.3
54	6	7	0	6	7	0	6	6	1	95.0	146.6	507.6
Totals:												
Per Group	22	30	3	22	30	0	22	26	4			
All Groups		52			52			48				
\bar{x} Litter Size		10.4			10.4			9.6				
\bar{x} D Pups			0.6			0			0.8			

*M = Male

+F = Female

**D = Dead or Missing

*

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight Data

Medium x Control
(Mating Group, ♂ x ♀)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
14	10	2	0	9	2	1	9	2	0	78.5	102.5	357.9
18	12	6	0	12	5	1	12	5	0	105.6	147.1	481.0
22	5	10	0	4	10	1	3	6	5	84.3	88.6	310.0
41	5	6	2	5	6	0	5	6	0	72.4	102.8	458.6
43	8	7	0	8	7	0	0	0	15	89.1	102.8	--
44	3	13	1	3	12	1	3	11	1	87.4	135.5	462.4
55	6	6	0	6	6	0	6	6	0	80.9	99.3	400.4
58	6	7	0	6	7	0	5	6	2	91.7	139.8	320.9
Totals:												
Per Group	55	57	3	53	55	4	43	42	23			
All Groups		112			108			85				
\bar{x} Litter Size		14.0			13.5			10.6				
\bar{x} D Pups			0.4			0.5			2.9			

*M = Male

+F = Female

**D = Dead or Missing

Appendix Table 3 (cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Litter Size, Sex Distribution and Litter Weight Data

High x Control
(Mating Group, σ^7 x ϕ)

Animal Number	Litter Size									Litter Weight		
	Birth			Day 4			Day 21			Live Pups Only (g)		
	M*	F+	D**	M	F	D	M	F	D	Birth	Day 4	Day 21
15	5	8	0	5	7	1	4	6	2	90.1	112.3	358.2
19	5	9	0	5	9	0	5	9	0	86.5	132.9	477.9
24	5	5	0	5	5	0	5	5	0	65.7	104.9	374.9
39	8	10	0	7	5	6	2	1	9	102.2	76.4	61.6
42	4	7	0	4	7	0	3	7	1	59.8	85.5	330.9
60	6	6	0	6	5	1	6	5	0	71.2	123.0	441.6
Totals:												
Per Group	33	45	0	32	38	8	25	33	12			
All Groups		78			70			58				
\bar{x} Litter Size		13.0			11.7			9.7				
\bar{x} D Pups			0			1.3			2.0			

*M = Male

*F = Female

**D = Dead or Missing

Appendix Table 4

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)Control x Control
(Mating Group $\sigma^7 \times Q$)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
16	40.3	5.7	28.5	5.7	44.6	7.4	36.1	7.2	166.0	33.2	116.4	29.1
17	33.8	6.8	37.9	6.3	37.1	7.4	44.0	7.3	189.4	37.9	134.8	33.7
21	42.7	6.1	28.4	5.7	44.1	7.3	21.4	7.1	92.2	30.7	38.0	38.0
37	58.0	7.3	41.9	6.9	82.1	10.3	58.6	9.8	266.1	38.0	191.4	38.3
38	39.7	6.6	43.4	6.2	58.5	9.7	61.3	8.7	186.4	37.3	255.3	36.5
46	43.1	6.1	33.8	5.6	36.4	5.2	15.8	5.3	—	—	—	—
56	29.6	5.9	62.3	5.7	27.2	6.8	68.8	6.9	69.7	23.2	122.9	20.5
59	29.0	5.8	60.2	5.5	42.1	8.4	90.5	8.2	142.9	28.6	244.0	24.4
Total	50.3		47.6		62.5		60.5		228.9		220.5	
\bar{x}	6.3		6.0		7.8		7.6		32.7		31.5	

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)

Low x Low
(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
67	51.6	7.4	34.8	7.0	71.7	10.2	38.6	9.6	263.3	37.6	48.6	24.3
68	44.5	7.4	27.0	6.7	60.9	12.2	43.9	11.0	280.1	56.0	207.4	51.9
70	35.4	7.1	32.5	6.5	47.2	9.4	43.9	8.8	—	—	—	—
71	42.8	7.1	46.1	6.6	53.4	8.9	58.5	8.3	188.7	31.4	159.1	31.8
72	47.3	5.9	33.5	5.6	52.5	6.6	36.5	6.1	98.7	32.9	94.7	31.6
80	51.0	6.4	38.9	6.5	70.8	8.8	50.3	8.4	216.9	31.0	150.7	30.1
81	45.7	5.7	33.3	5.5	64.7	8.1	47.2	7.9	244.0	30.5	168.5	28.1
82	24.3	6.1	46.3	5.8	29.3	7.3	53.2	6.6	—	—	—	—
83	13.7	6.8	48.8	6.1	19.8	9.9	69.9	8.7	100.0	50.0	234.2	46.8
84	66.6	6.0	28.4	5.7	102.8	9.3	42.2	8.4	294.8	32.7	136.9	27.4
85	60.1	6.7	37.2	6.2	81.1	9.0	41.7	8.3	252.2	36.0	107.4	26.8
87	36.8	6.1	39.5	5.6	37.8	6.3	33.3	5.5	81.7	27.2	23.1	23.1
88	55.0	6.1	18.5	6.2	31.7	5.3	10.5	5.2	—	—	—	—
Total	84.8		80.0		111.3		102.8		365.3		321.9	
\bar{x}	6.5		6.2		8.6		7.9		36.5		32.2	

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)

Medium x Medium
(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
95	52.5	5.8	16.7	5.6	61.8	6.9	20.6	6.9	18.8	18.8	52.1	26.0
96	36.4	6.1	43.3	5.4	52.5	8.7	62.1	7.8	189.5	31.6	215.5	26.9
97	33.7	6.7	53.4	6.7	41.6	8.3	65.8	8.2	140.9	35.2	150.4	37.6
98	39.1	6.5	19.1	6.4	64.5	10.7	30.9	10.3	174.6	43.6	121.8	40.6
108	57.4	5.7	56.2	5.6	60.2	8.6	66.4	8.3	191.8	32.0	234.6	29.3
109	42.4	7.1	41.7	6.9	59.2	9.9	55.7	9.3	183.6	30.6	176.5	29.4
110	30.2	6.0	49.5	5.5	42.9	8.6	70.7	7.8	144.8	29.0	246.5	27.4
111	40.5	6.7	39.0	6.5	38.5	7.7	31.9	8.0	49.0	24.5	98.9	32.9
112	40.1	6.7	45.7	6.5	50.0	8.3	59.6	8.5	135.1	33.8	212.4	35.4
115	37.0	6.2	47.8	6.0	48.8	8.1	65.6	8.2	104.5	34.8	63.9	31.9
Total	63.5		61.1		85.8		83.3		313.9		317.4	
\bar{x}	6.4		6.1		8.6		8.3		31.4		31.7	

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight (g)

High x High
(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
123	26.4	6.1	48.6	6.1	38.0	9.5	70.7	8.8	126.0	31.5	230.8	28.8
125	41.1	5.9	27.0	5.4	49.8	7.1	35.0	7.0	134.3	26.9	135.4	27.1
126	59.4	6.6	30.4	6.1	93.9	10.4	49.0	9.8	298.5	33.2	159.1	31.8
127	21.7	7.2	33.3	6.7	36.2	12.1	53.1	10.6	152.0	50.7	223.5	44.7
128	19.0	6.3	6.4	6.4	23.9	8.0	8.1	8.1	101.8	33.9	35.1	35.1
135	30.9	6.2	48.8	6.1	44.6	8.9	74.6	9.3	145.5	29.1	222.0	27.7
136	12.7	6.3	56.0	6.2	12.6	6.3	64.0	7.1	32.8	32.8	306.5	34.0
137	34.9	5.8	43.9	5.5	50.5	8.4	67.0	8.4	176.0	29.3	195.4	27.9
138	38.4	7.7	20.8	6.9	52.7	10.5	28.6	9.5	221.6	44.3	122.0	40.7
140	18.1	6.0	63.3	5.7	25.1	8.4	90.0	8.2	88.4	29.5	291.0	29.1
144	43.6	6.2	17.5	5.8	61.0	8.7	26.4	8.8	234.8	33.5	97.8	32.6
Total	70.3		66.9		98.3		95.6		374.7		359.5	
\bar{x}	6.4		6.1		8.9		8.7		34.1		32.7	

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)Control x Low
(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
69	29.7	5.9	48.2	5.3	42.1	8.4	52.4	7.5	178.4	35.7	194.0	32.3
79	23.6	5.9	44.0	5.5	26.9	6.7	52.2	6.5	63.9	31.9	231.4	28.9
Total	11.8		10.8		15.1		14.0		67.6		61.2	
\bar{x}	5.9		5.4		7.6		7.0		33.8		30.6	

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)Control x Medium
(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
99	67.3	6.1	28.8	5.8	90.4	8.2	39.0	7.8	293.2	26.6	127.8	25.6
116	45.9	6.6	32.2	6.4	56.0	8.0	38.9	7.8	156.9	31.4	84.8	28.3
Total	12.7		12.2		16.2		15.6		58.0		53.9	
\bar{x}	6.3		6.1		8.1		7.8		29.0		26.9	

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)Control x High
(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
139	50.6	6.3	30.2	6.0	67.6	8.4	40.5	8.1	64.0	21.3	24.3	24.3
143	11.3	5.6	37.7	6.3	14.1	7.0	42.0	7.0	22.5	22.5	124.2	31.0
Total		11.9		12.3		15.4		15.1		43.8		55.3
\bar{x}		5.9		6.1		7.7		7.6		21.9		27.6

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)Low x Control
(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
23	37.2	7.4	34.7	6.9	48.8	9.8	44.9	9.0	209.6	41.9	203.1	40.6
40	---	---	15.4	7.7	---	---	17.4	8.7	---	---	91.3	45.6
47	43.6	7.3	61.8	6.9	63.2	10.5	90.0	10.0	222.3	37.0	246.0	35.1
48	34.0	6.8	47.1	6.7	46.2	9.2	64.1	9.1	169.9	34.0	203.4	33.9
54	45.1	7.5	49.9	7.1	70.0	11.7	76.6	10.9	260.2	43.4	247.4	41.2
Total	29.0		35.3		41.2		47.7		156.3		196.4	
\bar{x}	7.2		7.1		10.3		9.5		39.1		39.3	

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)

Medium x Control
(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
14	65.2	6.5	12.7	6.3	84.5	9.4	18.0	9.0	292.4	32.5	65.5	32.7
18	70.4	5.9	35.2	5.9	103.0	8.6	44.1	8.8	336.1	28.0	144.9	29.0
22	28.6	5.7	55.7	5.6	26.8	6.7	61.8	6.2	97.8	32.6	212.2	35.4
41	35.1	7.0	37.3	6.2	50.3	10.1	52.5	8.7	219.5	43.9	239.1	39.8
43	48.9	6.1	40.2	5.7	57.0	7.1	45.8	6.5	—	—	—	—
44	17.6	5.9	69.8	5.4	29.2	9.7	106.3	9.7	106.2	35.4	356.2	32.4
55	40.8	6.9	40.1	6.7	50.0	8.3	49.3	8.2	197.1	32.8	203.3	33.9
58	44.3	7.4	47.4	6.8	66.3	11.0	73.5	10.5	146.4	29.3	174.5	29.1
Total	51.3		48.6		70.9		67.6		234.5		232.3	
\bar{x}	6.4		6.1		8.9		8.5		33.5		33.2	

Appendix Table 4 (Cont.)

SC-19192: EVALUATION OF REPRODUCTIVE PERFORMANCE IN THE RAT

Male-Female Litter Weight Data (g)

High x Control

(Mating Group ♂ x ♀)

Animal Number	Birth				Day 4				Day 21			
	Male		Female		Male		Female		Male		Female	
	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}	Ttl	\bar{x}
15	35.1	7.0	55.0	6.9	46.6	9.3	65.7	9.4	139.7	34.9	218.5	36.4
19	32.0	6.4	54.5	6.1	50.0	10.0	82.9	9.2	181.7	36.3	296.2	32.9
24	34.3	6.9	31.4	6.3	54.3	10.9	50.6	10.1	192.9	38.6	182.0	36.4
39	46.2	5.8	56.0	5.6	46.8	6.7	29.6	5.9	39.5	19.7	22.1	22.1
42	24.5	6.1	35.3	5.9	31.1	7.8	54.4	7.8	98.7	32.9	232.2	33.2
60	36.7	6.1	34.5	5.7	68.2	11.4	54.8	11.0	246.4	41.1	195.2	39.0
Total	38.3		36.5		56.1		53.4		203.5		200.0	
\bar{x}	6.4		6.1		9.3		8.9		33.9		33.3	